Published in final edited form as:

Dis Esophagus. 2014 November ; 27(8): 703–708. doi:10.1111/dote.12141.

Administrative coding is specific, but not sensitive, for identifying eosinophilic esophagitis

David A. Rybnicek, MD^{1,2,*}, Kelly E. Hathorn, BS^{1,2,*}, Emily R. Pfaff, MS³, William J. Bulsiewicz, MD, MSC^{1,2}, Nicholas J. Shaheen, MD, MPH^{1,2}, and Evan S. Dellon, MD, MPH^{1,2}

¹Center for Esophageal Diseases and Swallowing, University of North Carolina School of Medicine, Chapel Hill, NC

²Center for Gastrointestinal Biology and Disease, Division of Gastroenterology and Hepatology, Department of Medicine, University of North Carolina School of Medicine, Chapel Hill, NC

³Carolina Data Warehouse, North Carolina Translational and Clinical Sciences Institute, University of North Carolina, Chapel Hill

Abstract

The use of administrative databases to conduct population-based studies of eosinophilic esophagitis (EoE) in the United States is limited because it is unknown whether the ICD-9 code for EoE, 530.13, accurately identifies those who truly have the disease. The aim of this retrospective study was to validate the ICD-9 code for identifying cases of EoE in administrative data. Confirmed cases of EoE as per consensus guidelines (symptoms of esophageal dysfunction and ≥ 15 eos/hpf on biopsy after 8 weeks of twice daily PPI therapy) were identified in the University of North Carolina (UNC) EoE Clinicopathologic database from 2008–2010; 2008 was the first year in which the 530.13 code was approved. Using the Carolina Data Warehouse (CDW), the administrative database for patients seen in the UNC system, all diagnostic and procedure codes were obtained for these cases. Then, with the EoE cases as the reference standard, we re-queried the CDW over the same time frame for all patients seen in the system (n=308,372) and calculated the sensitivity and specificity of the ICD-9 code 530.13 as a case definition of EoE. To attempt to refine the case definition, we added procedural codes in an iterative fashion to optimize sensitivity and specificity, and restricted our analysis to privately insured patients. We also conducted a sensitivity analysis with 2011 data to identify trends in the operating parameters of the code. We identified 226 cases of EoE at UNC to serve as the reference standard. The ICD-9 code 530.13 yielded a sensitivity of 37% (83/226; 95% CI: 31–43%) and specificity of 99% (308,111/308,146; 95% CI: 98–100%). These operating parameters were not substantially altered if the case definition required a procedure code for endoscopy or if cases were limited to those

Corresponding Author: Evan S. Dellon MD, MPH, CB#7080, Bioinformatics Building, 130 Mason Farm Rd., UNC-CH, Chapel Hill, NC 27599-7080, Phone: (919) 966-2513, Fax: (919) 843-2508, edellon@med.unc.edu.

*Co-first authors

Author contributions (all authors approved the final draft):

Rybnicek: medical record review and data extraction, data analysis/interpretation, critical revision

Hathorn: data interpretation, manuscript drafting, critical revision

Pfaff: data extraction, critical revision

Bulsiewicz: project conception, data interpretation, critical revision

Shaheen: project conception, data interpretation, critical revision, supervision

Dellon: project conception and design, data analysis/interpretation, manuscript drafting, critical revision, supervision

with commercial insurance. However, in 2011 the sensitivity of the code had increased to 61%, while the specificity remained at 99%. The ICD-9 code for EoE, 530.13, had excellent specificity for identifying cases of EoE in administrative data, though this high specificity was achieved at an academic center. Additionally, the sensitivity of the code appears to be increasing over time, and the threshold at which it will stabilize is not known. While use of this administrative code will still miss a number of cases, those identified in this manner are highly likely to have the disease.

Keywords

eosinophilic esophagitis; database; validation; ICD-9 codes; epidemiology

Introduction

Eosinophilic esophagitis (EoE) is currently defined as a chronic allergen/immune-mediated clinicopathologic disorder requiring both symptoms of esophageal dysfunction and infiltration of the esophageal mucosa by eosinophils for diagnosis.¹ In the early 1990s, several case studies described what are now viewed as the hallmark features of EoE, and since that time, there has been a significant increase in the incidence and prevalence of the disease.^{2–10} Symptoms of EoE include dysphagia, food impaction, heartburn, and in children, failure to thrive,^{3, 11–15} endoscopic abnormalities such as esophageal rings, linear furrows, or white plaques are frequently noted,^{3, 15–18} and prominent esophageal eosinophilia is demonstrated on biopsy.^{3, 19, 20} Most data regarding epidemiology of EoE are from tertiary centers,^{2–4, 6, 7, 10, 21–23} and to date there have been very few multi-center or population-based studies of EoE.

There is a need to characterize the epidemiology of EoE in the United States, but the ability to use large-scale administrative databases to conduct population-based studies is limited by the lack of a validated case definition of EoE. While there is now an International Classification of Diseases, Ninth Revision (ICD-9) code for EoE, 530.13, this was only recently approved for use in 2008. Previous research has indicated that administrative coding of upper gastrointestinal diseases, such as Barrett's esophagus, cannot be assumed to be accurate.²⁴ It remains unknown whether the ICD-9 code 530.13 can accurately identify those who carry a diagnosis of EoE.

The aim of this study was to validate the ICD-9 code for identifying cases of EoE in administrative data using patient-level claims linked to medical records and a well-characterized cohort of EoE patients as the gold standard.

Methods

Study Design and EoE patients

We conducted a retrospective cohort study of patients seen at the University of North Carolina (UNC) Hospitals. This study was approved by the UNC Institutional Review Board.

The data source for cases of EoE was the UNC EoE Clinicopathologic Database. This database contains all cases of EoE as confirmed by consensus guidelines (symptoms of esophageal dysfunction and ≥ 15 eos/hpf on biopsy after 8 weeks of twice daily PPI therapy¹) who are seen at UNC. Details of the development of this resource have been described previously.^{3, 25–27} Using this database, we identified all patients seen between January 1, 2008 and June 30, 2010, with 2008 being the earliest year of inclusion because it was the first year in which the 530.13 code was approved and used. These patients with confirmed EoE were considered our reference standard.

Data available for these patients included: demographics (age at diagnosis, gender, race); symptoms; co-existing atopic disease (allergic rhinitis and/or sinusitis, documented food allergies demonstrated by either symptomatic evidence of allergy with reintroduction of a food or by testing directed by an allergist, or asthma); endoscopic findings (rings, strictures, narrowing, linear furrows, white plaques, crepe-paper mucosa, decreased vascularity, erosive esophagitis, presence of hiatal hernia); and histologic features. The maximum eosinophil counts (in eosinophils per high-power field, eos/hpf) had previously been determined using a hpf size of 0.24mm².

Administrative Data Source

The Carolina Data Warehouse for Health (CDW) is an enterprise-wide data source containing clinical and administrative data for patients seen in the UNC system since 2004. Available data domains include patient accounting, patient demographics, diagnoses, procedures, medications, and lab results, among others. The CDW is governed by an Operations and Oversight Committee which serves to govern researchers' access to warehouse data on a case-by-case basis. After our data access was approved, we used CDW data to link administrative claims to medical records. All UNC patients with billing records with at least one claim between 2008 and 2010 were identified and comprised the denominator population for our study. For these patients, we obtained demographic data, insurance information, diagnostic, and procedure codes.

Statistical Analysis

The following iterative approach was followed to determine the validity of the 530.13 ICD-9 code. First, the confirmed cases of EoE identified in the UNC EoE Clinicopathologic Database from January 1, 2008 through June 30, 2010 served as our reference standard. Next, we queried the CDW population from the same time frame to identify all patients who had at least one 530.13 code. Then, we calculated the sensitivity and specificity of a single instance of 530.13 alone as a case definition of EoE. Our true positives were those patients with confirmed diagnosis of EoE by the database that also had a documented 530.13 ICD-9 code. Our true negatives were patients without a diagnosis of EoE who also did not have a documented 530.13 ICD-9 code. Sensitivity was calculated by dividing the number of true positives by the total number of confirmed EoE cases. Specificity was calculated by dividing the number of true negatives by the overall number of subjects without confirmed EoE.

We then repeated these calculations after performing two *a priori* sensitivity analyses. This was done to assess the accuracy of the results and refine the case definition by adding

additional administrative codes to optimize sensitivity and specificity. First, we constructed a more restrictive case definition. In addition to requiring one 530.13 code, we required the presence of at least one relevant upper endoscopy code. These were defined as the Current Procedural Terminology (CPT) codes 43239 (upper endoscopy with biopsy), 43247 (foreign body removal), 43248 (dilation over a guide wire), and 43249 (balloon dilation). Second, we repeated the analysis where the case definition only required a single instance of the ICD-9 code while limiting the study cohort to those patients who are commercially insured. This was done to obtain estimates for use in databases that might only include insured patients, such as MarketScan® or IMS LifeLink® PharMetrics. This restriction eliminated patients with Medicare, Medicaid, military insurance, and those without insurance. We also performed an additional analysis using a combination of non-530.13 ICD-9 codes related to symptoms of esophageal dysfunction (for example dysphagia, esophageal foreign body) and excluding patients with codes that might overlap with esophageal eosinophilia (for example, achalasia, Crohn's disease, and eosinophilic malignancies) in an attempt to increase the sensitivity of the administrative coding definition for EoE. Finally, in order to evaluate for possible time trends in uptake with use of the code, we repeated the primary analysis using additional data from 2011 to assess the operating characteristics of the code among incident cases of EoE.

Results

A total of 308,372 patients were identified with billing records at UNC during the study time frame, and this group comprised the overall study denominator. The mean age of patients was 38 years. 41% of these patients were male and 72% of these patients were Caucasian, consistent with the general characteristics of all adult and pediatric patients seen at UNC.

There were 226 patients with confirmed EoE enrolled in the UNC EoE Registry over that same time frame and comprised the reference standard. For the EoE cases, the mean age was 26 years, 71% were male, and 77% were Caucasian (Table 1). Common symptoms included dysphagia (54%) and food impaction (27%). Co-existing atopic disease was frequently diagnosed in a proportion of these patients as well. On endoscopy, typical findings of EoE were noted, including linear furrows (48%), esophageal rings (43%), and white plaques (27%). The maximum eosinophil count was 63 eos/hpf.

For the sensitivity and specificity calculation with a case definition of at least one 530.13 ICD-9 code, 83 of the 226 EoE cases had a documented 530.13 code (true positives), while the remaining 143 patients did not (false negatives). Therefore, the sensitivity of this case definition was 37% (95% CI; 31–43; Table 2). Of the 308,146 patients without EoE, 308,111 did not have the 530.13 ICD-9 code (true negatives). Therefore, the specificity of our analysis was 99% (95% CI; 98–100). Of the 35 false positive cases identified, 4 had eosinophilic gastroenteritis overlapping with eosinophilic esophagitis, 14 were children who had a clinical diagnosis of EoE but medical records were insufficient to confirm that these cases met consensus guidelines for diagnosis of EoE, 2 were adults with a clinical diagnosis of EoE but insufficient records to confirm this, and 1 had Crohn's disease with esophageal involvement. With this additional information considered, the sensitivity rises to 38% if the eosinophilic gastroenteritis patients are included as true positives, and to 46% if the patients

with a clinical diagnosis of EoE are included. There were few differences between the true positives (EoE cases that had the 530.13 code) and false negatives (EoE cases that did not have the code; Table 3). True positives were younger than the false negatives, had more food allergies and asthma, and had more crêpe-paper mucosa and decreased vascularity on endoscopy. However, there were no differences by sex, race, symptoms, other endoscopy findings, or eosinophil count, and after multivariable logistic regression, only younger age remained independently associated with the true positives.

We then repeated the sensitivity and specificity analysis for the more restrictive case definition requiring upper-endoscopy CPT codes. Here, the sensitivity of our analysis was found to be 33% (75/226; 95% CI; 27–40), and the specificity remained 99% (308,129/308,146; 95% CI; 98–100).

After limiting the cohort to those patients with commercial insurance, the results were similar. Our reference standard of EoE cases in this scenario decreased to 133 patients, and the overall patient population decreased to 129,343. The sensitivity for this analysis was found to be 31% (42/133; 95% CI; 24–40), and the specificity was 99% (129,201/129,210; 95% CI; 98–100). (Table 2).

Analyzing a series of non 530-13 ICD-9 codes related to esophageal dysfunction as a component of the administrative case definition resulted in an improved sensitivity for the case definition (84%). However, this was associated with a substantial decrease in sensitivity (41%).

When the primary analysis was repeated using data from 2011, we identified 77 confirmed incident cases in the UNC EoE Registry. A total of 47 of these were correctly identified by the ICD-9 code, for a sensitivity of 61%, which was improved over the sensitivity from 2008–2010. Of the 24 false positives, 5 had eosinophilic gastroenteritis overlapping with EoE, 3 had PPI-responsive esophageal eosinophilia on follow-up (1 adult and 2 children), 3 were adults felt to have esophageal eosinophilia from inadequately controlled GERD, and 13 were children where there was clinical suspicion of EoE but records or follow-up were insufficient to determine case status. Specificity of the code remained excellent at 99%.

Discussion

While there has been an increase in the incidence and prevalence of EoE over the past two decades, the study of EoE in large administrative databases has not been widely pursued and is limited by the lack of a validated case definition. Due to the clinicopathologic nature of the disorder, developing such a definition is challenging as few databases that are publically available can link back to patient-level data. This study aimed to validate the ICD-9 code for EoE in administrative data using claim reports linked to medical records of a well-characterized group of EoE patients.

The results indicated that the ICD-9 code 530.13 is highly specific for EoE. However, our study also indicated that this code is not optimal for sensitivity, though the sensitivity appears to be increasing over time. The implications of this result are noteworthy. While we may fail to identify all patients with EoE using a single code, we can be relatively certain

that those cases that are identified are likely true EoE cases without substantial misclassification. An attempt to increase the sensitivity of the case definition using non-530.13 ICD-9 codes was associated with an unacceptable decline in specificity, making that strategy less appealing. A major challenge with administrative case definitions of EoE in the U.S. is that pathology findings are not available. This is not the case in countries like Denmark where registry-based definitions of EoE have recently proposed,²⁸ but it is a reason that the majority of epidemiologic studies to date are either from selected counties within a country or region, from single centers but are not population-based, or from larger databases that have limitations.

The only previously published study assessing a true population-based prevalence was the Kalixanda study²⁹. In this study, Ronkainen and colleagues studied two counties in northern Sweden and found that 4 of 1000 (0.4%) of subjects had prevalent esophageal eosinophilia and met their study's criteria for diagnosis of EoE.²⁹ However, these patients might not meet current EoE diagnostic guidelines either due to lack of appropriate associated symptoms, or due to response to PPI therapy.^{1, 22} In two additional studies, Prasad and colleagues⁷ and Hruz and colleagues^{5, 10} reported estimates on incidence and prevalence of EoE from Olmstead County, Minnesota and Olten County, Switzerland, respectively. However, the patients included in the study were not sampled in population-based frames. In a series of studies that utilized a large pathology database in the United States, the national distribution of esophageal eosinophilia and EoE was assessed, however, the data were also not population-based.^{30–32} Important data regarding the epidemiology of EoE have also been generated by retrospective single center studies, but are subject to similar limitations.^{2–4, 6, 23, 33, 34} Finally, data from the national health system in the Netherlands showed an increasing incidence of esophageal eosinophilia, but this study did not use a validated case definition of EoE.³⁵ Our validation of ICD-9 codes for identifying cases of EoE in administrative data will ultimately allow for the study of EoE, hopefully at the population level, to be conducted in large U.S. administrative databases.

The limitations and strengths of this study must also be addressed. The first limitation is that the validation cohort for this study was from a single center. Our results could be potentially biased because of local coding practices, and there might be ascertainment bias of cases at a referral center. In particular, it is not known if our observed high specificity is generalizable to other non-academic sites. The second issue is that it is possible that there could theoretically have been a misclassification of cases of EoE in the reference standard, but this is unlikely given that the included cases all met the EoE consensus diagnostic guidelines^{1, 22}. Third, because the 530.13 ICD-9 code has only been available for EoE since 2008, it is possible that its low sensitivity in our study was due to a lack of awareness by physicians. Our repeat analysis of 2011 data, showing a higher sensitivity, supports the hypothesis that the code's sensitivity is improving as use of the code increases. As can be seen by the analysis of false positive cases, some of the low sensitivity was also due to our inability to formally confirm a diagnosis of EoE in our medical records per the consensus guidelines. Future studies will shed light on the use of this code as knowledge regarding EoE continues to disseminate.

There are also several strengths to this study. We used a large administrative database in the form of the CDW and queried data from over 300,000 patients. We also had over 200 reference cases of confirmed EoE from the UNC EoE Clinicopathologic Database. By using cases of EoE confirmed by consensus guidelines, we are confident that these results are minimally impacted by the issue of PPI-responsive esophageal eosinophilia (PPI-REE)^{36–39} since these patients were separately identified and excluded from the EoE Database. In addition, we were able to directly link administrative data to medical records for code validation purposes. Finally, we conducted *a priori* sensitivity analyses, both with a more restrictive case definition requiring the addition of upper endoscopy CPT codes and with limiting the cohort to those with commercial insurance, to assess the robustness of the results. That the results were similar across all analyses strengthens our confidence in the sensitivity and specificity values presented here.

In conclusion, the ICD-9 code for EoE, 530.13, had relatively low sensitivity for identifying cases of EoE in administrative data, but the sensitivity appears to be increasing over time, and the threshold at which it will stabilize is not known. However, the specificity of this code was excellent. Use of this administrative code to identify EoE cases will still miss a number of cases, but those identified in this manner are highly likely to have the disease. While not every case will be captured, the 530.13 code can be a useful tool to study EoE patients in large-scale administrative databases.

Acknowledgments

Financial support: This work was funded, in part, by a UNC Junior Faculty Development Award and NIH Award K23 DK090073 (ESD). It was also supported in part by the National Center for Research Resources and the National Center for Advancing Translational Sciences, National Institutes of Health, through Grant Award Number UL1TR000083.

Potential competing interests: No conflicts of interest exist for any of the authors.

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Table 1

Characteristics of the EoE cases comprising the reference standard

	EoE (n = 226)
Age (mean years $\pm$ SD; range)	26 $\pm$ 20 (0.5–78)
Male (%)	71
White (%)	77
Symptoms (%)	
Dysphagia	54
Food impaction	27
Heartburn	33
Chest pain	10
Abdominal pain	20
Vomiting	24
Failure to thrive	14
Allergic diseases (%)	
Allergic rhinitis/sinusitis	32
Food allergies	17
Asthma	19
Endoscopy findings (%)	
Normal	16
Rings	43
Strictures	18
Narrowing	9
Linear furrows	48
White plaques	27
Crêpe-paper mucosa	7
Decreased vascularity	16
Erosive esophagitis	19
Hiatal hernia	11
Dilation performed	21
Histology	
Maximum eosinophil count (eos/hpf $\pm$ SD)	63 $\pm$ 40

Table 2

Sensitivity and specificity of 530.13 for eosinophilic esophagitis

	530.13 for all patients	530.13 + endoscopy CPT for all patients*	530.13 for all commercially insured patients
Sensitivity	37 (83/226)	33 (75/226)	31 (42/133)
95% CI	31–43	27–40	24–40
Specificity	99 (308,111/308,146)	99 (308,129/308,146)	99 (129,201/129,210)
95% CI	98–100	98–100	98–100

* CPT codes: 43239 (upper endoscopy with biopsy), 43247 (foreign body removal), 43248 (dilation over a guide wire), and 43249 (balloon dilation)

Table 3

Comparison of the EoE cases that were (true positives) and were not (false negatives) identified by the 530.13 code

	True positives [*] (n = 83)	False negatives [*] (n = 143)
Age (mean years $\pm$ SD) [†]	22 $\pm$ 22	31 $\pm$ 21
Male (%)	67	73
White (%)	78	79
Symptoms (%)		
Dysphagia	48	54
Food impaction	30	26
Heartburn	34	24
Chest pain	12	8
Allergic diseases (%)		
Allergic rhinitis/sinusitis	44	29
Food allergies [†]	28	10
Asthma [†]	33	12
Endoscopy findings (%)		
Rings	41	46
Strictures	19	23
Narrowing	13	9
Linear furrows	43	42
White plaques	27	19
Crêpe-paper mucosa [†]	14	5
Decreased vascularity [†]	24	6
Dilation performed	19	19
Histology		
Maximum eosinophil count (eos/hpf $\pm$ SD)	69 $\pm$ 45	58 $\pm$ 28

^{*} True positives are EoE cases that were correctly identified by the 530.13 code; false negatives are EoE cases that were not correctly identified by the 530.13 code.

[†] p < 0.05