

Efficacy of Screening for GERD in the Dental Setting

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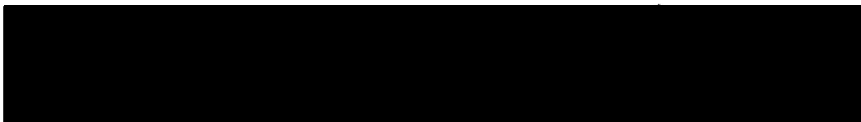
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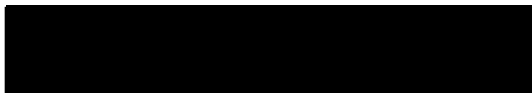


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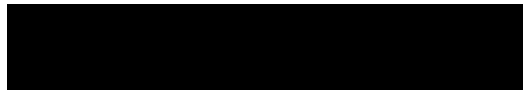


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Efficacy of Screening for GERD in the Dental Setting

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ABSTRACT

Gastroesophageal reflux disease (GERD) affects approximately 20% of the US population. Patients with dental erosion (DE) often exhibit symptoms of GERD, but are rarely referred for further treatment by the dentist. Furthermore, a subset of patients may have dental erosion and esophageal changes consistent with GERD but may not display any clinical symptoms—to include patients with a known history of GERD and empirically managed with Proton Pump Inhibitors (PPIs). **Objective:** The purpose of this study was to determine if the clinical finding of DE is a sufficient indicator to justify a medical referral for GERD. **Methods** Study patients with DE and a control group without DE completed a demographic survey and then had The Basic Erosive Wear Examination (BEWE) completed which quantified the degree of erosion. A Patient-Reported Outcome Measurement Information System (PROMIS) GERD specific survey was then completed by each participant. This NIH survey is used to measure the severity of disease. Patients with erosive patterns consistent with an endogenous source were referred to the Gastroenterology (GI) department for evaluation and endoscopy, if indicated. **Results:** Thirty-six patients with DE and 44 controls were identified. Of the 36 DE subjects, 28 followed up with GI for an evaluation and 20 underwent upper endoscopy. Ninety-six percent (27/28) of patients had a clinical diagnosis of GERD. Six of 20 (30%) subjects had a significant positive esophageal finding, including erosive esophagitis or Barrett's esophagus. BEWE and PROMIS score data for the patients with and without DE were analyzed with a Mann-Whitney U test ($\alpha=0.05$). **Conclusion:** Patients with DE had significantly greater BEWE and PROMIS scores than patients without DE ($p<0.001$). The incidence of GERD in patients with DE (96%) in this study far exceeds that of the general population (20%). Furthermore, the incidence of positive findings upon endoscopy (30%) was much greater than would be expected in the general population (7%) and in patients with established GERD currently medicated with a PPI (8-9%). These disparities indicate that medical referral for GERD should be considered by the dentist upon a finding of DE.

INTRODUCTION

Gastro-esophageal Reflux Disease (GERD) is the most prevalent gastrointestinal disease in the world and affects approximately 20% of the general population in the United States [1]. One challenge is that of the estimated 20% of the population affected, only a small portion (less than 9 million, in 2009) have been diagnosed and receive treatment [2]. Tooth erosion is both a sign and a symptom of uncontrolled GERD, and there is potential that further collaboration between dentists and gastroenterologists could prove beneficial [3]. Furthermore, a small but rapidly increasing portion of patients suffering from GERD experience dysplasia that eventually transforms to esophageal adenocarcinoma, and dentists may have an opportunity to identify early warning signs during routine examinations[4]. Early identification of systemic disease, such as GERD, would impact the military readiness of our active duty troops and their subsequent quality of life.

GERD can be characterized as “a condition which develops when the reflux of stomach contents causes troublesome symptoms and/or complications [5].” The chronic exposure of esophageal mucosa to acidic gastric fluid is associated with the transition of the squamous epithelium into columnar (intestinal) epithelium in the affected area; this condition is known as Barrett’s Esophagus (BE). GERD has been demonstrated as a primary risk factor for BE and the prevalence of BE in GERD patients is 6 to 8 times greater than that of the general population [6]. Symptoms of GERD and the presence of BE have been shown individually and collectively to heighten the risk of developing esophageal adenocarcinoma (EAC). One study found that 64% of patients that underwent surgery for EAC had preoperative GERD symptoms for more than 6 months, and, despite an endorsement from the American Gastroenterological Association, screening for the most at-risk individuals (obese white males with GERD symptoms) is not commonly performed [7]. The time lag observed between the onset of Barrett’s esophagus and the development of severe dysplasia is approximately 10 years.

Globally, esophageal cancer is the 8th most common malignancy consisting of two main subtypes: esophageal squamous cell carcinoma (ESCC) and EAC. The incidence of ESCC in the United States, and Northern Europe, has been declining over the past several decades but the overall esophageal cancer rate has been largely maintained due to a rapid increase in EAC attributed to rising rates of obesity and an aging population.

The number of EAC cases in the United States is expected to rise from 8,000 in 2005 to 15,000 in 2030 [8]. The increasing rate of malignancy developing secondarily to GERD heightens the priority of establishing an early diagnosis.

The diagnosis and classification of GERD was largely standardized by consensus of 44 experts from 18 countries and announced at the 2005 World Congress of Gastroenterology in Montreal; now often referred to as the Montreal Definition or Consensus. The Montreal Consensus stated that heartburn and reflux are the primary symptoms associated with GERD; though they also reported that chronic cough, chronic laryngitis, dysphagia, and dental erosions can be manifestations of the syndrome[5]. Refractory asthma, along with the extra-esophageal symptoms listed above, can reveal what has been termed “silent” GERD, or GERD that has gone undiagnosed due to lack of the cardinal symptoms of heartburn and reflux [9, 10]. Demographic factors that have been positively associated with individuals diagnosed with GERD include male gender, smokers, advanced age, and elevated Body Mass Index (BMI) [7]. Additional comorbidities that have been associated with GERD include hypertension, sleep disturbances, Type II diabetes, and hypercholesteremia [11, 12]. The Montreal Consensus established that an arrival to the diagnosis of GERD may be obtained on the basis of a patient’s symptoms [5]. A dissenting view is that the “gold standard” for the diagnosis of GERD be obtained by an ambulatory intranasal intubation with a pH meter for 24 hours or endoscopic evaluation which are both more definitive than reported symptoms [5, 13]. Endoscopy also offers a quantitative designation of the extent of esophageal change as described by the Los Angeles Classification system [14].

Questionnaires have been developed and evaluated to facilitate patients’ reporting symptoms with varying degrees of success. Several questionnaires have demonstrated a similar validity to a clinical exam performed by a gastroenterologist [15]. The National Institute of Health (NIH) developed and published a systematic gastrointestinal (GI) assessment utilizing the Patient-Reported Outcomes Measurement Information System (PROMIS) framework in 2015. The PROMIS approach was developed with the goals of providing standardized relevance in both clinical and research applications, though minimal corroborating research exists at this point in time due to its recent publication [16]. A questionnaire-based study in a dental setting demonstrated efficacy in identifying

GERD sufferers from survey responses, though it was not clinically correlated and lacked follow-up with medical providers [17].

The clinical correlation of dental erosion to GERD diagnosis has been well established in the literature [3-5]. Dental erosion, unlike GERD, has yet to benefit from a global Montreal-like consensus of subject matter experts to define and classify its presentation. A meta-analysis of existing tooth erosion classification systems found that a multitude of methods have been used and that their differences have made results and outcomes difficult to compare across studies. The meta-analysis referenced defines dental erosion as when, “irreversible loss of hard dental tissues is seen due to a chemical process [18].” Recognizing a need for a metric that was simple, standardized, and repeatable, Bartlett et al. established the Basic Erosive Wear Examination (BEWE). The BEWE was not designed to be exhaustive, but rather to serve as a foundation that could provide structure to a long disorganized realm of data collection [19]. The BEWE shows promise in providing convenient, accurate, clinically relevant, and academically comparable information regarding the erosive status of patients’ dentition [18] [19].

Previous studies have identified a primary finding of severe GERD and secondarily demonstrated DE as a comorbidity, however there is limited dedicated literature investigating patients presenting with a primary finding of DE and subsequent evaluation for the possible presence of GERD. The purpose of this study was to determine if the clinical finding of DE is a sufficient indicator to justify a medical referral for GERD. The secondary aim was to evaluate the NIH PROMIS survey in the dental setting. The tertiary aim was to better understand “silent GERD” and the dentist’s potential role in identifying patients who exhibit dental erosion but lack traditional symptoms (heart burn, regurgitation, etc). The null hypothesis for this study was that there would be no difference in prevalence or severity of GERD in the DE population as compared to the general population.

METHODS

The Institutional Review Board at Wilford Hall Ambulatory Surgical Center approved protocol #FWH20180040H. A total of eighty subjects were enrolled in this study. The study population was split into two groups: DE and Control (no DE). The inclusion

criteria for the DE group consisted of adult Active Duty or DoD beneficiary patients (ages 18-85) that were examined at Dunn Dental Clinic at JBSA Lackland, TX who presented with DE on lingual and/or occlusal tooth surfaces. Patients with DE isolated on facial tooth surfaces were neither included in the DE nor Control groups as their erosion may have been due to an extrinsic rather than intrinsic (pathologic) origin [20]. Subjects were examined to determine the degree of dental erosion utilizing the BEWE wear index. The BEWE divides the dentition into sextants and assigns a score based upon the extent of the most severe tooth in a given sextant (0 for no wear, 1 for initial signs, 2 for distinct but less than 50% of tooth surface, and 3 for greater than 50% of tooth surface affected) [19]. The subjects then completed the PROMIS GERD survey and a demographic survey. The PROMIS GERD survey was developed by the National Institutes of Health (along with over 300 other physical, mental, and social health measures) in a large scale effort to provide health assessments based upon patient symptoms and standardized for clinical research. This survey consists of 13 questions regarding potential symptoms of GERD with multiple choice answers indicating a degree of severity as shown in Table 1 [16]. Patients determined to have dental erosion consistent with a likely etiology of gastric acid and not attributable to other causes (e.g., diet, habits, congenital disease) were scheduled for a second appointment at the Gastroenterology (GI) department at Wilford Hall Ambulatory Surgical Center (WHASC) or San Antonio Military Medical Center (SAMMC), JBSA Lackland, TX for examination (and upper endoscopy, if indicated by GI Standard of Care practices). Endoscopic findings of erosive esophagitis were graded based upon the Los Angeles Classification (LA) or documented in relation to observed cellular changes (e.g., Barrett's Esophagus). The LA grades are based upon the extent and affected folds in esophageal erosive lesions as shown in Table 2. Cellular changes seen in Barrett's Esophagus or dysplasia are often seen prior to the development of malignancies [14].

The inclusion criteria for the Control Group consisted of any adult Active Duty or DoD beneficiary patients (ages 18-85) that were examined at JBSA Lackland who presented with no signs of dental erosion. Patients with no dental erosion were randomly offered the opportunity to participate in this study by completing the PROMIS GERD survey and a demographic survey. Control Group patients that appeared at elevated risk

of GERD due to the results of their PROMIS survey were verbally referred to be evaluated by their Primary Care Manager (PCM).

The PROMIS GERD self-reported questionnaire to assess symptoms was administered. BEWE clinical exam was conducted and calculated. Additional demographic/ancillary questions were administered (e.g., age, sex, race, Body Mass Index (BMI), Obstructive Sleep Apnea (OSA), previous diagnosis of GERD, use of Proton Pump Inhibitors (PPIs)). A median and interquartile range of BEWE and PROMIS scores were determined for both DE and Control Groups. BEWE and PROMIS score data for the patients with and without DE were analyzed with a Mann-Whitney U test ($\alpha=0.05$).

Patients that were referred to and evaluated by GI were tracked to determine if they were positive for a clinical diagnosis of GERD. Additionally, any patients that received an endoscopic examination had findings documented in their Electronic Health Record and were communicated from GI to the study authors to be included in the anonymized data collection.

RESULTS

A total of 36 DE and 44 Control subjects were enrolled in this study. Demographic statistics can be found in Table 3. The mean subject age was 61.0 years (65.2 for DE and 57.5 for Control; range of 21-91 years) with a t-test finding no significant difference in the mean age between the DE and control groups ($p=0.067$). There were 45 males (23 DE/22 Control) and 35 females (13 DE/22 Control) with a Chi-Square test finding no statistical difference between the two genders ($p=0.21$). Age was positively correlated with BEWE ($p=0.0085$) and BMI was positively correlated with PROMIS scores ($p=0.0396$). Race, gender, and history of Obstructive Sleep Apnea were not found to be statistically correlated to either BEWE or PROMIS scores ($p<0.05$).

Analysis with the Mann-Whitney U test (see Table 4) revealed the median BEWE and PROMIS scores for the DE group were significantly higher than the Control group ($p<0.0001$). A significant correlation was found between BEWE and PROMIS scores using the Spearman Correlation ($r = .31, p < .005$). In total, 59% of patients referred to GI due to DE had elevated PROMIS scores.

The GI department evaluated 28 of the 36 DE patients referred; 20 patients underwent upper endoscopy. Several of the patients were unable to be reached by phone or were unable to schedule a visit within the timeframe of this study. Secondary to the evaluation (with/without endoscopy) by GI, 27 of 28 (96%) had a clinical diagnosis of GERD. Nine of the 28 patients referred to GI denied past history of GERD, however 8 of the 9 were diagnosed with GERD following a clinical and/or endoscopic exam. The single patient that was not diagnosed with GERD did not undergo an endoscopic exam due to advanced age (85) and lack of bothersome symptoms. Of the 8 subjects lacking a history of GERD that were diagnosed following evaluation from GI, the PROMIS risk assessments were broken down as Normal (5), Mild (2), and Moderate (1); see Table 5. The other 6 subjects that did not receive a new upper endoscopy had undergone one within the last 24 months and were being actively monitored by GI. Seventeen of the 28 (61%) evaluated by GI had a PROMIS risk category elevated above Normal.

Six of the 20 (30%) subjects that successfully underwent upper endoscopy were positive for a significant esophageal finding-- 5 with erosive esophagitis and 1 with Barrett's Esophagus. Four of the 6 had previously been diagnosed with GERD and reported taking a PPI; 1 of the 6 had a history of GERD but was not currently taking medication; and 1 of the 6 had no history of GERD and was not taking a PPI. Three of the 6 subjects positive for significant esophageal findings were in the Normal risk category according to PROMIS grading, 2 were Moderate, and 1 was Severe. All 6 were in the Medium (2) or High (4) risk (dental, not esophageal) categories according to the BEWE criteria (see Table 3). Six of 17 males and 0 of 3 females that underwent upper endoscopy had positive esophageal findings. Four of the 6 with esophageal findings were Caucasian; 2 of the 6 were identified as mixed race.

DISCUSSION

The primary purpose of this study was to determine if the clinical finding of DE is a sufficient indicator to justify a medical referral for GERD. The null hypothesis that there would be no difference in prevalence of GERD between the general population and the DE population was rejected based upon the prevalence of GERD in the patient population (with DE as the primary finding) referred to GI (96%) as compared to the incidence of

GERD in the general population (20%) [1]. Furthermore, upon undergoing upper endoscopy, 30% of the DE subjects exhibited significant esophageal changes with the potential to be pre-malignant. Figure 1 is an example of a 65 year old male subject's dentition demonstrating severe erosion (BEWE 14) paired with images of LA Grade B, D lesions found in his esophagus. Similar esophageal changes would be expected in the general population at a rate of 7% and still only at 8-9% within a population with a known history of GERD being empirically managed with PPI therapy [21]. DE appears to be a more definitive criteria of the presence of GERD than any other non-invasive technique used in common practice.

The secondary aim was to evaluate the NIH PROMIS survey in the dental setting. The proportion of DE referrals positive for GERD with elevated PROMIS scores (59%) reflected a similar, but slightly lower level of sensitivity to questionnaire-based systems amongst the general population [25]. A sensitivity (for DE alone) of 96% was higher than would be expected from questionnaires amongst the general population. Specificity was not calculated due to lack of an evaluation of Control subjects by GI; a high specificity would have indicated that subjects negative for DE would also be likely to be negative for GERD which there is no evidence to suggest. The empiric management of GERD symptoms with medication should result in lower PROMIS scores for most patients. The high incidence for GERD among referrals in this study with high PROMIS scores was likely due to the primary driver of referral (DE) rather than the incidental experience of symptoms by the subject population. While a subjective symptom-based screening questionnaire may be practical as a GERD screening tool for Primary Care medical providers, the objective finding of DE erosion apparent in routine dental exams is likely a more reliable indicator of an aggressive disease process.

The tertiary aim was to better understand "silent GERD" and the dentist's potential role in identifying patients who exhibit dental erosion but lack traditional symptoms (e.g., heart burn, regurgitation). The initial impetus for investigating silent GERD was targeted at a population that had never been diagnosed with GERD and experienced few, if any, traditional symptoms. Eight of the 9 DE patients that denied a history of GERD were determined to have GERD by GI. One of those 8 had an LA Grade B esophageal lesion discovered upon upper endoscopic exam. These patients benefited from the research

team identifying a potentially pathologic process and referral for medical specialty care. A second group of “silent” GERD subjects was identified as a cohort that was aware of a history of GERD and were being empirically managed with medication. Five of the 6 patients with significant esophageal findings were positive for a diagnosis of GERD and believed they were being adequately managed. These patients were either experiencing very few symptoms (2 of 5 Normal PROMIS risk) or continued to experience symptoms but were unaware they were of concern (2 Moderate, 1 Severe PROMIS risk). These subjects with refractory GERD, or GERD that persisted despite empiric PPI therapy, were identified on the basis of dental erosion as needing to be elevated to specialty care.

A potential criticism of DE as a metric for GERD is that it is historic in nature and tooth erosions, unlike esophageal erosions, will not resolve once the disease process has been brought under control. However, an advantage to the chronic nature of DE is that there are numerous methods to document changes non-invasively over time: dental study models, intraoral photographs, annual erosion scoring, dimensionally stable impression materials, or serial digital radiographs. Due to teeth being the most distal extent of the digestive pathway, it is likely that harmful effects of reflux may be underway long before acid routinely reaches the dentition. Figure 2 is an example of the maxillary anterior dentition of a 46 year old male found to have Barrett’s Esophagus upon undergoing upper endoscopy. DE can function as a sentinel for advanced GERD, but should not be relied upon as the disease process may often be caught at an earlier, less involved stage.

The BEWE provides a convenient and widespread scoring system for DE, but presents some challenges for assessing DE as it may pertain to pathologic processes. The BEWE scoring does not discriminate between tooth surfaces that are more likely to be exposed to external (dietary) acidic influences vs internal (gastric) processes. Thus, a BEWE score without consideration of which surfaces are involved may be of limited use for diagnostic purposes. In this particular study, BEWE scores were not calibrated for the same patient across multiple examiners and thus increased risk of bias/subjectivity is present. Additionally, the BEWE is scored in such a way that relies on a cumulative sum of erosive scores of all sextants of teeth. Individuals that are edentulous in one or more sextants or that have full coverage restorations on all teeth in a sextant will have scores that are artificially skewed. This is of particular significance when considering that caries

thrive in an acidic environment and thus it is likely that patients with a high propensity for dental erosion would have a high Decayed, Missing, Filled Teeth (DMFT) Index. Figure 3 represents the dentition of a 22 year old male with severe erosion and several visible carious lesions and Figure 4 depicts the heavily restored dentition of a 61 year old male with severe erosion that had an LA Grade B esophageal lesion—both subjects registered as “Normal” according to the PROMIS assessment. A possible improvement to the BEWE scoring would be to divide the summed score by sextants available for assessment. Further research investigating relative DMFT index scores in severe GERD patients as compared to the general population based upon anecdotal observations appreciated in this study would be of interest.

A previous study was primarily focused on primary GERD subjects, but also had a primary DE group consisting of 12 individuals. The 12 DE subjects underwent 24 hour esophageal pH monitoring and it was determined that 10/12 (83%) did, in fact, have GERD. The BEWE and PROMIS indices were not used and direct erosion/symptom comparisons could not be drawn [3]. A more recent study by Wilder-Smith et al investigated a population of 374 subjects with the primary finding of DE using both pH-impedance measurements and endoscopy. The study found that the majority of DE patients (69%) were determined to have GERD but the degree of DE did not necessarily correspond to the severity of the reflux indicators. Erosive esophagitis was found in 19% of the subjects according to the LA Classification. The median BEWE score was 13 (medium risk) and the Reflux Disease Questionnaire (RDQ) rather than the PROMIS survey was used to assess patient symptoms. The RDQ demonstrated a relatively low experience of symptoms by the DE patients (20% had symptoms greater than twice per week) suggesting an often silent oligosymptomatic reflux disease process. The Wilder-Smith study excluded any subjects with past PPI use, previous diagnosis of GERD, and was limited to include predominately Western Europeans (Swiss). Also, no control group was utilized and no distinction was drawn on the basis of affected tooth surfaces (facial/lingual/occlusal) [23].

The population observed in this study may not be representative of the general population in the United States. The average age of study participants was 61 years old, as compared to 38 years old in the general population [24]. DE was found to be positively

correlated with age (see Table 2: $r=.29$, $p=.0085$) when scored with the BEWE criteria. Race, sex, and history of OSA were not correlated to either BEWE or PROMIS scores. High BMI did correlate with increased PROMIS scores (See Table 2: $r=.23$, $p=.0396$). Additionally, DoD beneficiaries residing in South Texas may have different lifestyle factors than the general population across the country and caution should be exercised extrapolating the data without discretion. This population does not run counter to broadly observed trends that overweight, Caucasian, older males are commonly observed with esophageal lesions that may predispose them to malignancy [22].

CONCLUSIONS

DE is an objective, non-invasive finding that has long been understood to be present in cases of severe GERD. This study indicates that a clinical finding of DE is highly probable for a positive diagnosis of GERD. DE, independent of patient symptoms, indicates an increased likelihood for advanced stage manifestations of GERD as compared to other non-invasive assessments. The pathway of acid from the stomach, through the esophagus, to the mouth demonstrates an opportunity to bridge the schism that often exists between dentists and physicians. Dentists should be vigilant in their examinations for DE and have a referral system in place with GI physicians to further evaluate and treat patients at risk for GERD and its, sometimes fatal, complications.

Disclaimer: The views expressed are those of the authors and do not reflect the official views or policy of the Uniformed Services University and Department of Defense or its Components. The voluntary, fully informed consent of the subjects used in this research was obtained as required by 32 CFR 219 and DODI 3216.02_AFI 40-402. policy of the Uniformed Services University, Department of Defense, or its Components. The authors do not have any financial interest in the companies whose materials are discussed in this manuscript.

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