BMJ open

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Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2012-001615
Article Type:	Research
Date Submitted by the Author:	12-Jul-2012
Complete List of Authors:	Offenbacher, Steven; Univ of NC School of Dentistry/NC Oral Health Institute/Koury Oral Health Sciences, Periodontology Beck, James; Univ of NC School of Dentistry/NC Oral Health Institute/Koury Oral Health Sciences, Dental Ecology; Univ of NC School of Dentistry/NC Oral Health Institute/Koury Oral Health Sciences, Dental Ecology Barros, Silvana; Univ of NC School of Dentistry/NC Oral Health Institute/Koury Oral Health Sciences, Periodontology Suruki, Robert; Worldwide Epidemiology, GlaxoSmithKline R&D Loewy, Zvi; Touro College of Pharmacy, Pharmaceutical and Biomedical Sciences
Primary Subject Heading:	Dentistry and oral medicine
Secondary Subject Heading:	Dentistry and oral medicine
Keywords:	Pulmonary disease, Edentulism, Chronic Obstructive disease, bronchitis

Guideline

Not applicable

Word Count: 2763

OBSTRUCTIVE LUNG DISEASE AND EDENTULISM IN THE ATHEROSCLEROSIS RISK IN COMMUNITIES (ARIC) STUDY

Running Title: COPD and Edentulism

Keywords: pulmonary disease, edentulism, chronic obstructive pulmonary disease, bronchitis

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Abstract:

Objectives: We examined the potential association between prior COPD and edentulism, and whether the association varied by COPD severity using data from the Dental ARIC Study.

Design: Case-control

Setting: Community dwelling subjects from four US communities.

Participants and Measurements: Cases were identified as edentulous (without teeth) and subjects with one or more natural teeth were identified as dentate. COPD cases were defined by spirometry measurements that showed the ratio of forced expiratory volume (one second) to vital capacity to be less than 0.7. The severity of COPD cases was also scored using a modified Global Initiative for Chronic Obstructive Lung Disease classification criteria (GOLD scoring I-IV). Multiple-logistic regression was used to examine the association between COPD and edentulism, while adjusting for age, gender, center/race, ethnicity, education level, income, diabetes, hypertension, coronary heart disease and congestive heart failure, body mass index, smoking, smokeless tobacco use and alcohol consumption.

Results: 13,465 participants were included in this analysis (2,087 edentulous; 11,378 dentate). Approximately 28.3% of edentulous participants had prior COPD compared to 19.6% among dentate participants ($p<0.0001$). After adjustment for potential confounders, we observed a 1.3(1.08-1.62) and 2.5(1.68-3.63) fold increased risk of edentulism among GOLD II and GOLD III/IV COPD, respectively, as compared to the non-COPD/dentate referent. Given the short period of time between the measurements of COPD (Visit2) and dentate status (Visit4) relative to the natural history of both diseases, neither temporality nor insight as to the directionality of the association can be ascertained.

Conclusion: We found a significant association between prior COPD and edentulism, with evidence of a positive incremental effect seen with increasing GOLD classification.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is currently the fifth leading cause of death world-wide, and is expected to rise to fourth place in 2030.[1] Although COPD has a heterogeneous clinical presentation primarily characterized by airflow limitation, generally associated with an abnormal inflammatory response of the lungs[2] , it is also often associated with a significant systemic inflammatory response[3] which has been correlated with adverse clinical effects[3,4].

Over the past decade there has been an increased interest in the link between respiratory diseases and oral infection. Higher levels of tooth-associated microorganisms (plaque) and periodontal disease have been associated with COPD [5,6,7]. Recently, in a very comprehensive oral microbiology study, high levels of diverse microbes- including several implicated in COPD and denture stomatitis- were identified on previously worn dentures[8] .Thus both the teeth and the dentures are non-desquamating oral surfaces that allow the oral biofilm to emerge eliciting periodontal disease or denture stomatitis, respectively. This raises the question as to whether denture-associated microbes may contribute to COPD in a manner analogous to that similar to periodontal organisms. Because oral infections and denture-based sources of sepsis are both treatable and preventable, the potential association of high microbial burden of oral origin to COPD may represent modifiable risk factors that may potentially improve respiratory-related morbidity. It has been suggested by Garcia and colleagues [7] that the observed association between oral health and COPD may be due to aspiration of oral pathogens, or a common underlying host susceptibility trait that places individuals at risk for both conditions such as an exaggerated inflammatory response that is triggered by oral microbes.

Although numerous studies have examined the association between oral health and respiratory diseases in dentate individuals, the published literature are scant with respect to studies that have examined the association between edentulism and COPD status/severity. We undertook the current study to examine the potential association between COPD and edentulism using data from the Atherosclerosis Risk in

Communities (ARIC) Study. These data include not only dentate status and full-mouth periodontal examination measurements, but also includes results from direct pulmonary function tests and symptomology assessments that enabled us to classify the levels of COPD present.

METHODS

We sought to test the hypothesis that the prevalence of edentulism was greater among individuals with a reported history of lung disease, (i.e. COPD) and that the association with edentulism varied by COPD severity as determined by a modified Global Initiative for Chronic Obstructive Lung disease (GOLD) criteria. Our second hypothesis was that among dentate subjects there was a difference in the prevalence of periodontal disease according to the severity of COPD as measured by GOLD criteria.

Study Population and Study Design

The entire cohort from the ARIC study was 15,792 and the available dental cohort Dental Atherosclerosis Risk in Communities (D-ARIC) data were used to study participants with both a periodontal examination and completed spirometry data. The cohort selection process and reasons for exclusion appear in Figure 1. Descriptions of the cohort and the periodontal examination procedure have been described previously [9]. Eligible participants were all aged 45-64 at study entry (i.e., Visit 1) and had spirometry measurements at Visit 2 (3 years later) and periodontal examinations at D-ARIC Visit 4 (6 years from visit 2).

Case Definitions

Edentulism case definitions were defined as study participants without any natural teeth or implants. Participants with one or more natural teeth (comprising 11,378 subjects) were selected as the dentate subjects. The absence, presence or severity of periodontal disease among dentate subjects was determined using the joint American Association of Periodontology/Center for Disease Control (AAP/CDC) consensus definitions of Health, Early and Advanced disease.[10]

This investigation represents the first report that uses actual pulmonary function data to assess lung function as an exposure related to edentulism or periodontal disease. The measured exposure of pulmonary function was classified both as a dichotomous (e.g., COPD vs. no COPD) and ordinal categorical variable (e.g., no lung disease, restricted disease, COPD GOLD Stage I, Stage II, Stage III, and Stage IV), using the following criteria.

Lung Obstruction

Dichotomous variable (COPD/no COPD)—Prior lung obstruction (or COPD) was defined based on spirometry measurements collected during Visit 2. Participants with a ratio of forced expiratory volume in one second (FEV_1) and forced vital capacity (FVC) less than 0.7 were determined to have lung obstruction consistent with COPD.

Ordinal categorical variable (COPD GOLD Stage)—Severity of COPD was also examined in this study among COPD participants using a modification of the spirometry-based criteria for severity outlined in the GOLD guidelines.[11,12]

GOLD Stage	Spirometry Criteria
No lung disease	$FEV_1/FVC \geq 0.7$ and $FEV_1 \geq 80\%$ predicted
Restricted disease	$FEV_1/FVC \geq 0.7$ and $FVC < 80\%$ predicted
Stage 0	Presence of respiratory symptoms in the absence of any lung function abnormality; and no lung disease
Stage I	$FEV_1/FVC < 0.7$ and $FEV_1 \geq 80\%$ predicted
Stage II	$FEV_1/FVC < 0.7$ and $50\% \leq FEV_1 < 80\%$ predicted
Stage III	$FEV_1/FVC < 0.7$ and $30\% \leq FEV_1 < 50\%$ predicted
Stage IV	$FEV_1/FVC < 0.7$ and $FEV_1 < 30\%$ predicted

Variables of Interest

Smoking data (both for cigarettes and cigars) collected during Visit 4 were used to adjust for the confounding effect of smoking on the relationship between lung obstruction (COPD) and being edentulous. Smoking was treated as a five-level categorical variable, as described in detail previously [7]. Cardiovascular disease (CVD) comorbidities that may be associated with both history of lung obstruction and being edentulous were also examined using data from Visit 4. Other potential confounders examined included race and examination center, ethnicity, education level, income, frequency of dental visits, diabetes, body mass index, alcohol use, and medication utilization. These data were extracted from Visit 4.

Data Analysis

Mulitivariate logistic regression was used to examine the association between COPD and edentulous status. This was followed by a logistic regression analysis of the dentate subjects comparing the COPD prevalence and severity of dentate patients without periodontal disease to that of dentate patients with periodontal disease. The exposure variable, which is lung obstruction, was examined as both a dichotomous variable (e.g., positive prior COPD vs. no COPD) and by logistic models using nominal variables (e.g., no lung disease, restricted disease, GOLD 0, Stage I, Stage II, Stage III, and Stage IV) based upon spirometry data collected as part of the ARIC examination. For the no COPD or GOLD reference group we included: subjects with and without chronic respiratory symptoms with no lung function abnormality, and subjects with GOLD 0 and restricted disease. Multiple regression models were used to control for confounding. When adjusting for potential confounding variables we included in certain models variables that are known to modify either periodontal disease status or COPD , including Body mass index and smokeless tobacco. We developed minimally and fully-adjusted logistical models incorporating significant confounders and effect modifiers to compute odds ratios (OR) and 95% confidence intervals (CI). SAS Version 9.2 (Cary, NC). We also included traditional risk factors for edentulism, periodontal disease and COPD- such as age, even if not statistically significant in this cohort. A p-value of <0.05 was considered statistically significant for this study.

Sample Size and Power Calculations

We knew *a priori* that the ARIC cohort who had spirometry data from Visit 2 included 2,087 edentulous subjects, as determined by questionnaire data at Visit 4. We also had 11,378 dentate subjects with spirometry data at Visit 2, of which 5,155 subjects had a full-mouth periodontal exam completed. Thus, if approximately 9% of the 13,465 subjects (2,087 edentulous and 11,378 dentate) were determined to have COPD, we estimated that we had >99% power to detect a significant difference of 1% at p=0.05 in the prevalence of COPD when comparing edentulous vs. dentate subjects.

RESULTS

ARIC subject participation was based upon the inception cohort of 15,792 subjects. The Visit 4 screenings were broadly divided into 11,378 dentate and 2,087 edentulous subjects who also had spirometry data. These subjects are used for analyses in Tables 1-6 on the relationship between dentate status and COPD. Subjects were excluded (n=2,327) from the original inception participants for incomplete data, dental implants only, and missing Visit 4 screening. Table 7 is based upon the 8,274 subjects eligible for the oral exam, of which 6967 (84.1%) were actually examined. Of those examined, the periodontal portion of the exam was not completed on 174 subjects, resulting in 6,793 subjects with full periodontal data.

The distribution of study subjects according to dentate status and GOLD classification is shown in Table 1. Among the edentulous subjects (2087), there were 591 or 28.3% with COPD (Gold Stages I-IV). With the exception of GOLD I where the prevalence of edentulism was 14.7 percent, the prevalence of edentulous individuals increased from 16.4 percent for GOLD 0 to 35.6% for GOLD III/IV. . The crude odds ratio (not shown in Table 1) for edentulism being associated with prior COPD vs no COPD was 1.62 (95% CI, 1.46-1.80). Approximately 13 percent of individuals with no chronic respiratory symptoms and

no lung function abnormality (i.e. no lung disease) were edentulous. There were 2232 subjects with a prior COPD (19.6%) among 11,378 dentate subjects.

Table 2 presents the prevalence of various subject characteristics according to GOLD classification. In this table, the GOLD reference group for statistical testing combines the following three categories of subjects: no lung disease, GOLD 0, and subjects with chronic respiratory symptoms but no lung function abnormality. The general patterns reflected in Table 2 show that compared to the reference group those subjects in the GOLD III-IV category were much more likely to be edentulous, to smoke, to use smokeless tobacco, to be African American or North Carolina Caucasians, male, and somewhat more likely to have lower levels of income and education, be older and more likely to have chronic heart failure and heart disease.

Table 3 presents multivariate logistic models for the relationship between edentulous /dentate status and GOLD stages using the GOLD reference group described above. In an unadjusted model individuals with GOLD II and GOLD III/IV scores were at significantly higher odds for edentulism that increased with increasing GOLD stage severity (OR=2.06; 95% CI 1.79-2.38 and OR=3.38; 95% CI 2.61-4.39, respectively). Minimally adjusted models (race/center, sex and age) showed similar significant effects for GOLD II and GOLD III/IV with little attenuation. The increased risk of being edentulous for GOLD II and GOLD III/IV categories remain significant, but have slightly lower odds ratios. However, the fully adjusted model showed more attenuation with the odds for being edentulous being 1.3 (1.08-1.62) and 2.5 (1.68-3.63) times greater for GOLD II disease and the most severe category GOLD III/IV, respectively.

Table 4 shows the association between periodontal status and GOLD classifications for the dentate subjects. Because of small cell sizes in the GOLD III and IV groups, we combined them with GOLD II. Using the CDC/AAP classification of periodontal disease, which is based upon clusters of clinical signs, there is a significant positive association between higher GOLD stage and severe periodontal disease ($p<0.0001$). Subjects with GOLD I or GOLD II-IV were more likely to have severe periodontitis than the

reference group. With respect to the individual periodontal variables measured as means or extent scores, individuals with a GOLD classification of I were more likely to have a greater extent of periodontal pocket depths of 4mm or more, greater extent of attachment loss of 3mm. or more, a higher mean attachment loss and a greater extent of plaque in their mouths than the reference group. Those with GOLD scores of II-IV were significantly higher on all periodontal measures and had fewer teeth compared to the reference group.

Logistic models for the association between GOLD status and periodontal status using the AAP/CDC definitions appear in Table 5. As in Table 4, small cell size resulted in grouping the more severe GOLD stages together as GOLD II/III/IV. In general, the odds ratios for severe periodontal disease increased with more severe GOLD stage in the crude, minimally adjusted and fully adjusted models. There is also an increase in odds as the severity of periodontal disease increases for the two GOLD categories shown using the periodontally healthy group as the reference group within each GOLD category. Although adjusting for relevant confounders generally decreased the odds, there was still a statistically significant association between higher GOLD stage and severe periodontal disease in the fully adjusted model (OR=1.41; 95% CI 1.07-1.87).

The relationship between spirometry based GOLD classification and self-reported physician-based diagnosis of bronchitis or emphysema is shown in Table 6. Participants classified as GOLD III/IV were significantly more likely to have self-reported bronchitis or emphysema. There is a trend for a positive association except for the GOLD zero category. Interestingly, 65.9% of subjects with GOLD III/IV report no diagnosis of COPD suggesting that self-report of bronchitis or emphysema is not a strong predictor of GOLD status. In fact, of all subjects reporting a positive diagnosis of bronchitis or emphysema 53% demonstrated no evidence of chronic respiratory symptoms and no lung function abnormality.

DISCUSSION

We found a significant association between prior COPD and edentulism, with evidence of an increasing prevalence of edentulism with increasing GOLD classification. Although there was some reduction in the magnitude of effect in the adjusted models, the association between dentate status and GOLD classification remained significant even in the fully adjusted model, with a 1.3 fold increased odds of being edentulous in the GOLD II category and a 2.5 fold increased odds of being edentulous in the most severe GOLD III/IV category in the fully adjusted regression model. This represents the first report of an association between edentulism and COPD in a population with GOLD measurements.

In the subgroup of dentate subjects, there was a significant association between the GOLD II - IV group vs. the GOLD reference group and prevalent periodontal disease with a significant increase in the odds of entry level and severe periodontal disease in the crude and minimally adjusted models. In the fully adjusted model, only the association between GOLD stage II/III/IV and severe periodontal disease [OR 1.41 (1.07-1.87)] remained significant. This is the first population report to include both full-mouth periodontal examination data as well as Spirometry assessments, thereby providing direct confirmation of the association between severe periodontal disease and COPD, as well as a dose-response relationship between these conditions.

While there is no previous published information available about the association between edentulism status and COPD, there is evidence in the literature of an association between periodontal disease and COPD, consistent with the findings of the current study [5,6,7]. The results of this investigation were based upon standardized pulmonary function tests and suggest that studies that are based upon self-reported diagnoses can potentially result in significant misclassification error. Our data shown in Table 6 suggest that of the 12,297 subjects reporting no diagnosis, 2,390 subjects or 19.4% were classified as GOLD I-IV.

Among those 433 subjects with GOLD I-IV the positive predictive rate was only 15.3%. These findings suggest that an important strength of the current study was the classification of disease based on an objective biological measure (e.g., spirometry) rather than a self-reported measure.

Additional strengths of the current study include the large sample size, the inclusion of African Americans providing some racial diversity of the sample, the use of a full-mouth examination protocol and the collection of information about key confounding variables, including but not limited to: tobacco use, hypertension, diabetes, and income. Furthermore, the outcomes of interest, edentulism and periodontal disease, were evaluated using a comprehensive oral examination at Visit 4.

The current study must also be considered in light of certain limitations. First, the design of the current study does not allow us to determine the directionality or temporality of any association found. It has been reported previously that the dental ARIC sub-sample is healthier than the greater ARIC sample and that the edentulous subjects within the ARIC dataset have overall poorer health,[9] as compared to the ARIC dental sample. Thus, it is possible that the observed relationship between both edentulism and periodontal disease with prior COPD may be due in part to shared risk factors. There is also the potential bias due to differential loss to follow-up prior to Visit 4. The current study included only those subjects with dental history information at Visit 4. Finally, it is possible that participants with COPD may have been more likely to be lost to follow-up (compared to participants without COPD) or that participants with more severe COPD may have had a lower probability of surviving to Visit 4 than participants with mild COPD or normal lung function. There are no data in this report to mechanistically link edentulism with increased risk for COPD. Previous studies of periodontal disease associations with COPD have discussed the potential role of periodontal infection serving as a chronic repository of pathogenic oral organisms that could be aspirated into the airway to challenge the lungs[6]. Periodontal infections are also associated with increases in systemic markers of inflammation including biomarkers such as C-reactive protein (CRP)[13]. By analogy, edentulism is commonly associated with denture infections (denture mucositis)

which induce mucosal inflammation and unclean dentures can also pose as a chronic reservoir of oral pathogens. However, the potential role of denture-based infection as a potential risk factor for COPD remains to be elucidated.

CONCLUSIONS

Edentulism was associated with prior COPD, with an incremental effect observed with increasing GOLD classification. Additionally, among dentate individuals, severe periodontal disease was associated with GOLD classification. This is one of the first analyses of COPD and dentate status, and expands upon the available literature regarding periodontal disease and COPD. Further research is warranted to explore the relationship of edentulism and periodontal disease with COPD.

Conflict of Interest

There are no potential conflicts of interest that exist with any companies/organizations whose products or services may be discussed in this article.

Source of Funding

This work was supported by a grant from GlaxoSmithKline and we declare that the sponsor had no role in the study design, collection, analysis and interpretation of data; in the writing of the manuscript; and in the decision to submit the manuscript for publication.

Responsibility for Data

This is to verify that we have full access to all the data in this study and take full responsibility for the integrity of the data and accuracy of the data analysis, including and especially any adverse effects.

Abbreviations:

AAP/CDC – American Association of Periodontology/Center for Disease Control

ARIC – Atherosclerosis Risk in Communities
CHF – Congestive Heart Failure
CI – Confidence Intervals
COPD – Chronic Obstructive Pulmonary Disease
CVD – Cardiovascular Disease
D-ARIC – Dental Atherosclerosis Risk in Communities
FEV – Forced Expiratory Volume
FVC – Forced Vital Capacity
GOLD – Global Initiative for Chronic Obstructive Lung Disease
MAL – Mean Attachment Loss
NHANES – National Health and Nutrition Examination Survey
OR – Odds Ratio
SES – Social Economic Status
WHO – World Health Organization

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Table 1. Dentate Status by GOLD Stage

	No Chronic Respiratory Symptoms & No Lung Function Abnormality	Restricted Disease (FEV_1/FVC≥0.7 and FVC<80% predicted)	GOLD 0 (Chronic Respiratory Symptoms & No Lung Function Abnormality)	GOLD I	GOLD II	GOLD III/IV	p-value*
Edentulous	1294 (13.3%)	151 (24.6%)	51 (16.4%)	208 (14.7%)	290 (25.2%)	93 (35.6%)	
Dentate	8422 (86.7%)	464 (75.5%)	260 (83.6%)	1204 (85.3%)	860 (74.8%)	168 (64.4%)	<0.0001

*Chisq

Table 2. Demographics by GOLD Stage

	GOLD Reference*	GOLD I	GOLD II	GOLD III/IV	p-value**
Edentulous	1496 (14.1%)	208 (14.7%)	290 (25.2%)	93 (35.6%)	
Dentate	9146 (85.9%)	1204 (85.3%)	860 (74.8%)	168 (64.4%)	<0.0001
Race/Center					
MS African Americans	2654 (25.1%)	191 (13.6%)	196 (17.1%)	73 (28.4%)	
NC African Americans	285 (2.7%)	35 (2.5%)	27 (2.4%)	11 (4.3%)	
NC White	2211 (20.9%)	401 (28.5%)	344 (30.0%)	84 (32.7%)	
Washington Co, MD	2680 (25.3%)	350 (24.9%)	337 (29.4%)	56 (21.8%)	
Surburban Minneapolis	2747 (26.0%)	430 (30.6%)	243 (21.2%)	33 (12.8%)	<0.0001
Female	6344 (59.6%)	684 (48.4%)	457 (39.7%)	125 (47.9%)	
Male	4298 (40.4%)	728 (51.6%)	693 (60.3%)	136 (52.1%)	<0.0001
Mean Age (StdDev)	62.4 (5.59)	64.2 (5.69)	64.9 (5.57)	64.2 (5.70)	<0.0001
Mean BMI (StdDev)	29.2 (5.68)	27.1 (4.81)	27.6 (5.34)	27.3 (6.16)	<0.0001
Diabetes (Yes)	1573 (17.4%)	132 (10.8%)	179 (19.7%)	36 (20.7%)	
No	7486 (82.6%)	1090 (89.2%)	732 (80.4%)	138 (79.3%)	<0.0001
Hypertension (Yes)	3591 (39.4%)	388 (31.9%)	374 (40.7%)	74 (41.8%)	
No	5535 (60.7%)	829 (68.1%)	545 (59.3%)	103 (58.2%)	<0.0001
Income (Low)	2718 (31.1%)	365 (31.2%)	321 (37.2%)	72 (41.6%)	
Medium	3071 (35.2%)	440 (37.6%)	316 (36.7%)	59 (34.1%)	
High	2945 (33.7%)	366 (31.3%)	225 (26.1%)	42 (24.3%)	<0.0001
Education (Basic)	2226 (21.0%)	291 (20.6%)	332 (28.9%)	93 (35.8%)	
Intermediate	4360 (41.0%)	564 (40.0%)	480 (41.8%)	101 (38.9%)	
Advanced	4038 (38.0%)	556 (39.4%)	336 (29.3%)	66 (25.4%)	<0.0001
Alcohol Use (Yes)	4404 (48.4%)	657 (53.9%)	463 (51.1%)	78 (44.3%)	
No	4695 (51.6%)	561 (46.1%)	444 (49.0%)	98 (55.7%)	0.001
Smoke (Current, Heavy)	748 (8.6%)	191 (16.4%)	256 (29.8%)	33 (20.6%)	
Current, Light	245 (2.8%)	34 (2.9%)	15 (1.7%)	1 (0.6%)	
Former, Heavy	1304 (14.9%)	309 (26.5%)	339 (39.4%)	76 (47.5%)	
Former, Light	1981 (22.7%)	228 (19.6%)	100 (11.6%)	17 (10.6%)	
Never	4448 (51.0%)	403 (34.6%)	150 (17.4%)	33 (20.6%)	<0.0001
Smokeless Tobacco (Yes)	699 (7.7%)	131 (10.8%)	138 (15.2%)	34 (19.3%)	
No	8401 (92.3%)	1088 (89.3%)	769 (84.8%)	142 (80.7%)	<0.0001
Coronary Heart Disease (Yes)	718 (6.9%)	106 (7.6%)	159 (14.2%)	31 (13.0%)	
No	9727 (93.1%)	1281 (92.4%)	963 (85.8%)	208 (87.0%)	<0.0001
Congestive Heart Failure (Yes)	191 (2.1%)	25 (2.1%)	41 (4.6%)	9 (5.1%)	
No	8878 (97.9%)	1194 (98.0%)	861 (95.5%)	166 (94.9%)	<0.0001

*GOLD Reference: No Chronic Respiratory Symptoms & No Lung Function Abnormality + GOLD Zero (Chronic Respiratory Symptoms & No Lung Function Abnormality) + Restrictive (FEV1/FVC >= 0.70 and FVC < 80% predicted)

**Chisq or t-test

Table 3: Generalized Logits Models: Association between edentulism and GOLD Stages as compared to dentate subjects

	GOLD Reference*	GOLD I	GOLD II	GOLD III/IV
Model 1 Crude				
Edentulous	Reference	1.06 (0.90-1.24)	**2.06 (1.79-2.38)**	**3.38 (2.61-**
Model 2 Minimally Adjusted**				
Edentulous	Reference	1.12 (0.93-1.34)	**1.92 (1.61-2.28)**	**3.17 (2.28-**
Model 3 Fully Adjusted ****				
Edentulous	Reference	1.05 (0.86-1.28)	**1.32 (1.08-1.62)**	**2.47 (1.68-**

*GOLD Reference: No Chronic Respiratory Symptoms & No Lung Function Abnormality + GOLD Zero (Chronic Respiratory Symptoms & No Lung Function Abnormality) + Restrictive (FEV1/FVC >= 0.70 and FVC < 80% predicted)

**Model 2 is minimally adjusted for race/center (5-level), male, age (years)

***Model 3 is fully adjusted for race/center (5-level), male, age (years), diabetes, hypertension, smoking (5-levels), smokeless tobacco, alcohol, income (3-level), education (3-level), CFH and CHD

Table 4. Periodontal measures among the 5,155 dentate subjects by GOLD stages

	GOLD Reference*	GOLD I	GOLD II/III/IV	Overall p-value
CDC/AAP Definition				
Healthy N (SD)	2378 (43.0%)	281 (38.1%)	151 (28.5%)	
Entry N (SD)	2271 (41.1%)	295 (40.0%)	233 (44.1%)	
Severe N (SD)	878 (15.9%)	161 (21.9%)	145 (27.4%)	<0.0001
Mean (StdDev)				
Extent PD >=4mm	7.05 (11.3)	8.12 (12.3)[a]	9.66 (14.8)[d]	<0.0001
Mean PD	1.89 (0.56)	1.94 (0.61)	2.03 (0.74)[d]	<0.0001
Extent AL >=3mm	21.7 (21.8)	27.6 (26.0)[d]	34.3 (28.7)[d]	<0.0001
Mean AL	1.72 (0.96)	1.94 (1.15)[d]	2.29 (1.43)[d]	<0.0001
Extent BOP	25.2 (23.4)	25.1 (24.3)	27.7 (26.4)[a]	0.07
Extent PQ >=1	42.5 (38.3)	39.3 (37.7)[a]	49.9 (39.3)[d]	<0.0001
Number of Teeth	22.0 (6.99)	21.5 (7.26)	18.8 (8.09)[d]	<0.0001

[a] = p<0.05, b=p<0.01, c=p<0.001, d=p<0.0001,

All superscripted p values are compared to reference group by Chi square or GLM

Table 5: Generalized Logits Models: Periodontal status (CDC/AAP Definition) by GOLD stages

	GOLD I	GOLD II/III/IV
Model 1 Crude		
Healthy	Reference	Reference
Entry	1.10 (0.92-1.31)	**1.62 (1.31-2.00)**
Severe	**1.55 (1.26-1.91)**	**2.60 (2.05-3.31)**
Model 2 Minimally Adjusted*		
Healthy	Reference	Reference
Entry	0.99 (0.83-1.19)	**1.42 (1.14-1.77)**
Severe	**1.46 (1.17-1.82)**	**2.17 (1.67-2.80)**
Model 3 Fully Adjusted **		
Healthy	Reference	Reference
Entry	0.95 (0.79-1.14)	1.10 (0.87-1.39)
Severe	1.23 (0.97-1.55)	**1.41 (1.07-1.87)**

*Model 2 is minimally adjusted for race/center (5-level), male, age (years)

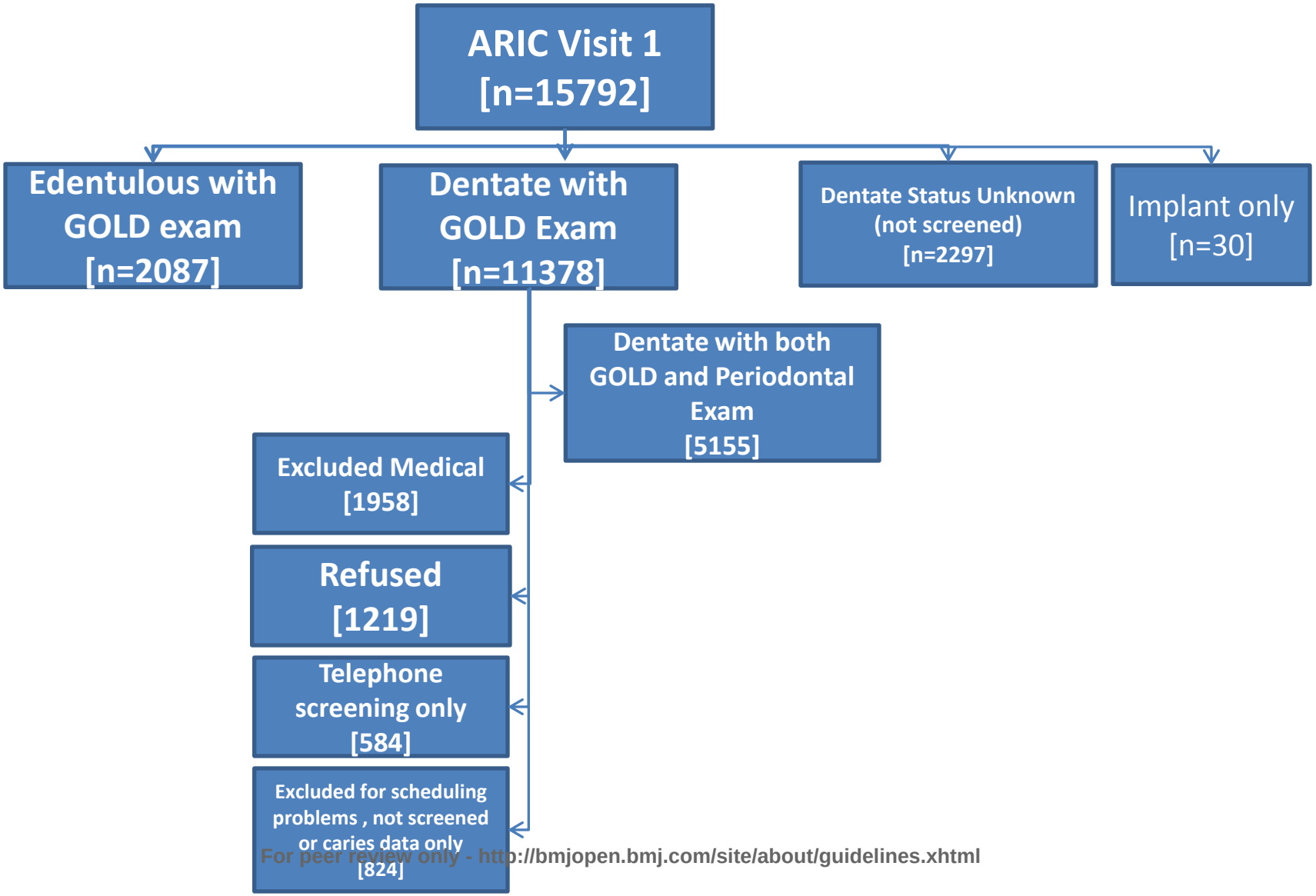
**Model 3 is fully adjusted for race/center (5-level), male, age (years), diabetes, hypertension, smoking (5-levels), smokeless tobacco, alcohol, income (3-level), education (3-level)

Table 6: Self reported physician diagnosis of bronchitis or emphysema according to GOLD stages .

	No Chronic Respiratory Symptoms & No Lung Function Abnormality	**GOLD Zero (Chronic Respiratory Symptoms & No Lung Function Abnormality)**	**Restricted Disease (FEV_1/FVC≥0.7 and FVC<80% predicted)**	**GOLD I**	**GOLD II**	**GOLD III/IV**	**p-value[a]**
Self Report (Yes)	633 (6.5%)	65 (20.9%)	64 (10.4%)	143 (10.1%)	201 (17.5%)	89 (34.1%)	
No	9083 (93.5%)	246 (79.1%)	551 (89.6%)	1269 (89.7%)	949 (82.5%)	172 (65.9%)	<0.0001

a) Chi square

Participant Flow Diagram



BMJ open

Obstructive Lung Disease and Edentulism in the Atherosclerosis Risk in Communities(ARIC) Study

Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2012-001615.R1
Article Type:	Research
Date Submitted by the Author:	17-Oct-2012
Complete List of Authors:	Offenbacher, Steven; Univ of NC School of Dentistry/NC Oral Health Institute/Koury Oral Health Sciences, Periodontology Beck, James; Univ of NC School of Dentistry/NC Oral Health Institute/Koury Oral Health Sciences, Dental Ecology; Univ of NC School of Dentistry/NC Oral Health Institute/Koury Oral Health Sciences, Dental Ecology Barros, Silvana; Univ of NC School of Dentistry/NC Oral Health Institute/Koury Oral Health Sciences, Periodontology Suruki, Robert; Worldwide Epidemiology, GlaxoSmithKline R&D Loewy, Zvi; Touro College of Pharmacy, Pharmaceutical and Biomedical Sciences
Primary Subject Heading:	Dentistry and oral medicine
Secondary Subject Heading:	Respiratory medicine, Cardiovascular medicine
Keywords:	Pulmonary disease, Edentulism, Chronic Obstructive disease, bronchitis

Word Count: 2763

OBSTRUCTIVE AIRWAY DISEASE AND EDENTULISM IN THE ATHEROSCLEROSIS RISK IN COMMUNITIES (ARIC) STUDY

Running Title: COPD and Edentulism

Keywords: pulmonary disease, edentulism, chronic obstructive pulmonary disease, bronchitis

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Abstract:

Objectives: We examined the potential association between prior COPD and edentulism, and whether the association varied by COPD severity using data from the Dental ARIC Study. **Design**: Cross-sectional **Setting**: Community dwelling subjects from four US communities. **Participants and Measurements**: Cases were identified as edentulous (without teeth) and subjects with one or more natural teeth were identified as dentate. COPD cases were defined by spirometry measurements that showed the ratio of forced expiratory volume (one second) to vital capacity to be less than 0.7. The severity of COPD cases was also scored using a modified Global Initiative for Chronic Obstructive Lung Disease classification criteria (GOLD scoring I-IV). Multiple-logistic regression was used to examine the association between COPD and edentulism, while adjusting for age, gender, center/race, ethnicity, education level, income, diabetes, hypertension, coronary heart disease and congestive heart failure, body mass index, smoking, smokeless tobacco use and alcohol consumption.

Results: 13,465 participants were included in this analysis (2,087 edentulous; 11,378 dentate). Approximately 28.3% of edentulous participants had prior COPD compared to 19.6% among dentate participants ($p<0.0001$). After adjustment for potential confounders, we observed a 1.3(1.08-1.62) and 2.5(1.68-3.63) fold increased risk of edentulism among GOLD II and GOLD III/IV COPD, respectively, as compared to the non-COPD/dentate referent. Given the short period of time between the measurements of COPD (Visit2) and dentate status (Visit4) relative to the natural history of both diseases, neither temporality nor insight as to the directionality of the association can be ascertained.

Conclusion: We found a statistically significant association between prior COPD and edentulism, with evidence of a positive incremental effect seen with increasing GOLD classification.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is currently the fifth leading cause of death world-wide, and is expected to rise to fourth place in 2030.[1] Although COPD has a heterogeneous clinical presentation primarily characterized by airflow limitation, generally associated with an abnormal inflammatory response of the lungs[2] , it is also often associated with a significant systemic inflammatory response[3] which has been correlated with adverse clinical effects[3,4].

Over the past decade there has been an increased interest in the link between respiratory diseases and oral infection. Higher levels of tooth-associated microorganisms (plaque) and periodontal disease have been associated with COPD [5,6,7]. Recently, in a very comprehensive oral microbiology study, high levels of diverse microbes- including several implicated in COPD and denture stomatitis- were identified on previously worn dentures[8] .Thus both the teeth and the dentures are non-desquamating oral surfaces that allow the oral biofilm to emerge eliciting periodontal disease or denture stomatitis, respectively. This raises the question as to whether denture-associated microbes may contribute to COPD in a manner analogous to that similar to periodontal organisms. Because oral infections and denture-based sources of sepsis are both treatable and preventable, the potential association of high microbial burden of oral origin to COPD may represent modifiable risk factors that may potentially improve respiratory-related morbidity. It has been suggested by Garcia and colleagues [7] that the observed association between oral health and COPD may be due to aspiration of oral pathogens, or a common underlying host susceptibility trait that places individuals at risk for both conditions such as an exaggerated inflammatory response that is triggered by oral microbes.

Although numerous studies have examined the association between oral health and respiratory diseases in dentate individuals, the published literature are scant with respect to studies that have examined the association between edentulism and COPD status/severity. We undertook the current study to examine the potential association between COPD and edentulism using data from the Atherosclerosis Risk in

Communities (ARIC) Study. We hypothesized that edentulism would be associated with a diagnosis of COPD and display a higher prevalence with more spirometry categories of COPD. These data include not only dentate status and full-mouth periodontal examination measurements, but also includes results from direct pulmonary function tests and symptomology assessments that enabled us to classify the levels of COPD present.

METHODS

We sought to test the hypothesis that the prevalence of edentulism was greater among individuals with a reported history of lung disease, (i.e. COPD) and that the association with edentulism varied by COPD severity as determined by a modified Global Initiative for Chronic Obstructive Lung disease (GOLD) criteria. Our second hypothesis was that among dentate subjects there was a difference in the prevalence of periodontal disease according to the severity of COPD as measured by GOLD criteria.

Study Population and Study Design

The entire cohort from the ARIC study was 15,792 and the available dental cohort Dental Atherosclerosis Risk in Communities (D-ARIC) data were used to study participants with both a periodontal examination and completed spirometry data. The cohort selection process and reasons for exclusion appear in Figure 1. Descriptions of the cohort and the periodontal examination procedure have been described previously [9]. Eligible participants were all aged 45-64 at study entry (i.e., Visit 1) and had spirometry measurements at Visit 2 (3 years later) and periodontal examinations at D-ARIC Visit 4 (6 years from visit 2).

Case Definitions

Edentulism case definitions were defined as study participants without any natural teeth or implants. Participants with one or more natural teeth (comprising 11,378 subjects) were selected as the dentate subjects. The absence, presence or severity of periodontal disease among dentate subjects was determined

using the joint American Association of Periodontology/Center for Disease Control (AAP/CDC) consensus definitions of Health, Early and Advanced disease.[10]

This investigation represents the first report that uses actual pulmonary function data to assess lung function as an exposure related to edentulism or periodontal disease. The measured exposure of pulmonary function was classified both as a dichotomous (e.g., COPD vs. no COPD) and ordinal categorical variable (e.g., no lung disease, restrictive disease, COPD GOLD Stage I, Stage II, Stage III, and Stage IV), using the following criteria.

Airway obstruction

Dichotomous variable (COPD/no COPD)—Prior airway obstruction (or COPD) was defined based on spirometry measurements collected during Visit 2. Participants with a ratio of forced expiratory volume in one second (FEV_1) and forced vital capacity (FVC) less than 0.7 were determined to have airway obstruction consistent with COPD.

Ordinal categorical variable (COPD GOLD Stage)—Severity of COPD was also examined in this study among COPD participants using a modification of the spirometry-based criteria for severity outlined in the GOLD guidelines.[11,12]

GOLD Stage	Spirometry Criteria
No lung disease	$FEV_1/FVC \geq 0.7$ and $FEV_1 \geq 80\%$ predicted
Restrictive disease	$FEV_1/FVC \geq 0.7$ and $FVC < 80\%$ predicted
Stage 0	Presence of respiratory symptoms in the absence of any lung function abnormality; and no lung disease
Stage I	$FEV_1/FVC < 0.7$ and $FEV_1 \geq 80\%$ predicted
Stage II	$FEV_1/FVC < 0.7$ and $50\% \leq FEV_1 < 80\%$ predicted
Stage III	$FEV_1/FVC < 0.7$ and $30\% \leq FEV_1 < 50\%$ predicted
Stage IV	$FEV_1/FVC < 0.7$ and $FEV_1 < 30\%$ predicted

Variables of Interest

Smoking data (both for cigarettes and cigars) collected during Visit 4 were used to adjust for the confounding effect of smoking on the relationship between airway obstruction (COPD) and being edentulous. Smoking was treated as a five-level categorical variable, as described in detail previously [7]. Cardiovascular disease (CVD) comorbidities that may be associated with both history of airway obstruction and being edentulous were also examined using data from Visit 4. Other potential confounders examined included race and examination center, ethnicity, education level, income, frequency of dental visits, diabetes, body mass index, alcohol use, and medication utilization. These data were extracted from Visit 4.

Data Analysis

Mulitivariate logistic regression was used to examine the association between COPD and edentulous status. This was followed by a logistic regression analysis of the dentate subjects comparing the COPD prevalence and severity of dentate patients without periodontal disease to that of dentate patients with periodontal disease. The exposure variable, which is airway obstruction, was examined as both a dichotomous variable (e.g., positive prior COPD vs. no COPD) and by logistic models using nominal variables (e.g., no lung disease, restrictive disease, GOLD 0, Stage I, Stage II, Stage III, and Stage IV) based upon spirometry data collected as part of the ARIC examination. For the no COPD or GOLD reference group we included: subjects with and without chronic respiratory symptoms with no lung function abnormality, and subjects with GOLD 0 and restrictive disease. Multiple regression models were used to control for confounding. When adjusting for potential confounding variables we included in certain models variables that are known to modify either periodontal disease status or COPD , including Body mass index and smokeless tobacco. We developed minimally and fully-adjusted logistical models incorporating significant confounders and effect modifiers to compute odds ratios (OR) and 95% confidence intervals (CI). SAS Version 9.2 (Cary, NC). We also included traditional risk factors for

edentulism, periodontal disease and COPD- such as age, even if not statistically significant in this cohort. A p-value of <0.05 was considered statistically significant for this study.

Sample Size and Power Calculations

We knew *a priori* that the ARIC cohort who had spirometry data from Visit 2 included 2,087 edentulous subjects, as determined by questionnaire data at Visit 4. We also had 11,378 dentate subjects with spirometry data at Visit 2, of which 5,155 subjects had a full-mouth periodontal exam completed. Thus, if approximately 9% of the 13,465 subjects (2,087 edentulous and 11,378 dentate) were determined to have COPD, we estimated that we had >99% power to detect a significant difference of 1% at p=0.05 in the prevalence of COPD when comparing edentulous vs. dentate subjects.

RESULTS

ARIC subject participation was based upon the inception cohort of 15,792 subjects. The Visit 4 screenings were broadly divided into 11,378 dentate and 2,087 edentulous subjects who also had spirometry data. These subjects are used for analyses in Tables 1-6 on the relationship between dentate status and COPD. Subjects were excluded (n=2,327) from the original inception participants for incomplete data, dental implants only, and missing Visit 4 screening. Table 7 is based upon the 8,274 subjects eligible for the oral exam, of which 6967 (84.1%) were actually examined. Of those examined, the periodontal portion of the exam was not completed on 174 subjects, resulting in 6,793 subjects with full periodontal data.

The distribution of study subjects according to dentate status and GOLD classification is shown in Table 1. Among the edentulous subjects (2087), there were 591 or 28.3% with COPD (Gold Stages I-IV). With the exception of GOLD I where the prevalence of edentulism was 14.7 percent, the prevalence of edentulous individuals increased from 16.4 percent for GOLD 0 to 35.6% for GOLD III/IV. . The crude odds ratio (not shown in Table 1) for edentulism being associated with prior COPD vs no COPD was 1.62

(95% CI, 1.46-1.80). Approximately 13 percent of individuals with no chronic respiratory symptoms and no lung function abnormality (i.e. no lung disease) were edentulous. There were 2232 subjects with a prior COPD (19.6%) among 11,378 dentate subjects.

Table 2 presents the prevalence of various subject characteristics according to GOLD classification. In this table, the GOLD reference group for statistical testing combines the following three categories of subjects: no lung disease, GOLD 0, and subjects with chronic respiratory symptoms but no lung function abnormality. The general patterns reflected in Table 2 show that compared to the reference group those subjects in the GOLD III-IV category were much more likely to be edentulous, to smoke, to use smokeless tobacco, to be African American or North Carolina Caucasians, male, and somewhat more likely to have lower levels of income and education, be older and more likely to have chronic heart failure and heart disease.

Table 3 presents multivariate logistic models for the relationship between edentulous /dentate status and GOLD stages using the GOLD reference group described above. In an unadjusted model individuals with GOLD II and GOLD III/IV scores were at significantly higher odds for edentulism that increased with increasing GOLD stage severity (OR=2.06; 95% CI 1.79-2.38 and OR=3.38; 95% CI 2.61-4.39, respectively). Minimally adjusted models (race/center, sex and age) showed similar significant effects for GOLD II and GOLD III/IV with little attenuation. The increased risk of being edentulous for GOLD II and GOLD III/IV categories remain significant, but have slightly lower odds ratios. However, the fully adjusted model showed more attenuation with the odds for being edentulous being 1.3 (1.08-1.62) and 2.5 (1.68-3.63) times greater for GOLD II disease and the most severe category GOLD III/IV, respectively.

Table 4 shows the association between periodontal status and GOLD classifications for the dentate subjects. Because of small cell sizes in the GOLD III and IV groups, we combined them with GOLD II. Using the CDC/AAP classification of periodontal disease, which is based upon clusters of clinical signs, there is a significant positive association between higher GOLD stage and severe periodontal disease

(p<0.0001). Subjects with GOLD I or GOLD II-IV were more likely to have severe periodontitis than the reference group. With respect to the individual periodontal variables measured as means or extent scores, individuals with a GOLD classification of I were more likely to have a greater extent of periodontal pocket depths of 4mm or more, greater extent of attachment loss of 3mm. or more, a higher mean attachment loss and a greater extent of plaque in their mouths than the reference group. Those with GOLD scores of II-IV were significantly higher on all periodontal measures and had fewer teeth compared to the reference group.

Logistic models for the association between GOLD status and periodontal status using the AAP/CDC definitions appear in Table 5. As in Table 4, small cell size resulted in grouping the more severe GOLD stages together as GOLD II/III/IV. In general, the odds ratios for severe periodontal disease increased with more severe GOLD stage in the crude, minimally adjusted and fully adjusted models. There is also an increase in odds as the severity of periodontal disease increases for the two GOLD categories shown using the periodontally healthy group as the reference group within each GOLD category. Although adjusting for relevant confounders generally decreased the odds, there was still a statistically significant association between higher GOLD stage and severe periodontal disease in the fully adjusted model (OR=1.41; 95% CI 1.07-1.87).

The relationship between spirometry based GOLD classification and self-reported physician-based diagnosis of bronchitis or emphysema is shown in Table 6. Participants classified as GOLD III/IV were significantly more likely to have self-reported bronchitis or emphysema. There is a trend for a positive association except for the GOLD zero category. Interestingly, 65.9% of subjects with GOLD III/IV report no diagnosis of COPD suggesting that self-report of bronchitis or emphysema is not a strong predictor of GOLD status. In fact, of all subjects reporting a positive diagnosis of bronchitis or emphysema 53% demonstrated no evidence of chronic respiratory symptoms and no lung function abnormality.

DISCUSSION

We found a statistically significant association between prior COPD and edentulism, with evidence of an increasing prevalence of edentulism with increasing GOLD classification. Although there was some reduction in the magnitude of effect in the adjusted models, the association between dentate status and GOLD classification remained statistically significant even in the fully adjusted model, with a 1.3 fold increased odds of being edentulous in the GOLD II category and a 2.5 fold increased odds of being edentulous in the most severe GOLD III/IV category in the fully adjusted regression model. This represents the first report of an association between edentulism and COPD in a population with GOLD measurements.

In the subgroup of dentate subjects, there was a significant association between the GOLD II - IV group vs. the GOLD reference group and prevalent periodontal disease with a statistically significant increase in the odds of entry level and severe periodontal disease in the crude and minimally adjusted models. In the fully adjusted model, only the association between GOLD stage II/III/IV and severe periodontal disease [OR 1.41 (1.07-1.87)] remained statistically significant. This is the first population report to include both full-mouth periodontal examination data as well as Spirometry assessments, thereby providing direct confirmation of the association between severe periodontal disease and COPD, as well as a dose-response relationship between these conditions.

While there is no previous published information available about the association between edentulism status and COPD, there is evidence in the literature of an association between periodontal disease and COPD, consistent with the findings of the current study [5,6,7]. The results of this investigation were based upon standardized pulmonary function tests and suggest that studies that are based upon self-reported

diagnoses can potentially result in statistically significant misclassification error. Our data shown in Table 6 suggest that of the 12,297 subjects reporting no diagnosis, 2,390 subjects or 19.4% were classified as GOLD I-IV. Among those 433 subjects with GOLD I-IV the positive predictive rate was only 15.3%. These findings suggest that an important strength of the current study was the classification of disease based on an objective biological measure (e.g., spirometry) rather than a self-reported measure.

Additional strengths of the current study include the large sample size, the inclusion of African Americans providing some racial diversity of the sample, the use of a full-mouth examination protocol and the collection of information about key confounding variables, including but not limited to: tobacco use, hypertension, diabetes, and income. Furthermore, the outcomes of interest, edentulism and periodontal disease, were evaluated using a comprehensive oral examination at Visit 4.

The current study must also be considered in light of certain limitations. First, the design of the current study does not allow us to determine the directionality or temporality of any association found. It has been reported previously that the dental ARIC sub-sample is healthier than the greater ARIC sample and that the edentulous subjects within the ARIC dataset have overall poorer health,[9] as compared to the ARIC dental sample. Thus, it is possible that the observed relationship between both edentulism and periodontal disease with prior COPD may be due in part to shared risk factors. There is also the potential bias due to differential loss to follow-up prior to Visit 4. The current study included only those subjects with dental history information at Visit 4. Finally, it is possible that participants with COPD may have been more likely to be lost to follow-up (compared to participants without COPD) or that participants with more severe COPD may have had a lower probability of surviving to Visit 4 than participants with mild COPD or normal lung function. There are no data in this report to mechanistically link edentulism with increased risk for COPD. Previous studies of periodontal disease associations with COPD have discussed the potential role of periodontal infection serving as a chronic repository of pathogenic oral organisms that could be aspirated into the airway to challenge the lungs[6]. Periodontal infections are also associated

with increases in systemic markers of inflammation including biomarkers such as C-reactive protein (CRP)[13]. By analogy, edentulism is commonly associated with denture infections (denture mucositis) which induce mucosal inflammation and unclean dentures can also pose as a chronic reservoir of oral pathogens. However, the potential role of denture-based infection as a potential risk factor for COPD remains to be elucidated.

CONCLUSIONS

Edentulism was associated with prior COPD, with an incremental effect observed with increasing GOLD classification. Additionally, among dentate individuals, severe periodontal disease was associated with GOLD classification. This is one of the first analyses of COPD and dentate status, and expands upon the available literature regarding periodontal disease and COPD. Further research is warranted to explore the relationship of edentulism and periodontal disease with COPD.

Conflict of Interest

There are no potential conflicts of interest that exist with any companies/organizations whose products or services may be discussed in this article.

Source of Funding

This work was supported by a grant from GlaxoSmithKline and we declare that the sponsor had no role in the study design, collection, analysis and interpretation of data; in the writing of the manuscript; and in the decision to submit the manuscript for publication.

Responsibility for Data

This is to verify that we have full access to all the data in this study and take full responsibility for the integrity of the data and accuracy of the data analysis, including and especially any adverse effects.

Abbreviations:

AAP/CDC – American Association of Periodontology/Center for Disease Control
ARIC – Atherosclerosis Risk in Communities
CHF – Congestive Heart Failure
CI – Confidence Intervals
COPD – Chronic Obstructive Pulmonary Disease
CVD – Cardiovascular Disease
D-ARIC – Dental Atherosclerosis Risk in Communities
FEV – Forced Expiratory Volume
FVC – Forced Vital Capacity
GOLD – Global Initiative for Chronic Obstructive Lung Disease
MAL – Mean Attachment Loss
NHANES – National Health and Nutrition Examination Survey
OR – Odds Ratio
SES – Social Economic Status
WHO – World Health Organization

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Table 1. Dentate Status by GOLD Stage

	No Chronic Respiratory Symptoms & No Lung Function Abnormality	Restrictive Disease ($FEV_1/FVC \geq 0.7$ and $FVC < 80\%$ predicted)	GOLD 0 (Chronic Respiratory Symptoms & No Lung Function Abnormality)	GOLD I	GOLD II	GOLD III/IV	p-value*
Edentulous	1294 (13.3%)	151 (24.6%)	51 (16.4%)	208 (14.7%)	290 (25.2%)	93 (35.6%)	
Dentate	8422 (86.7%)	464 (75.5%)	260 (83.6%)	1204 (85.3%)	860 (74.8%)	168 (64.4%)	<0.0001

*Chisq

Table 2. Demographics by GOLD Stage

	GOLD Reference*	GOLD I	GOLD II	GOLD III/IV	p-value**
Edentulous	1496 (14.1%)	208 (14.7%)	290 (25.2%)	93 (35.6%)	
Dentate	9146 (85.9%)	1204 (85.3%)	860 (74.8%)	168 (64.4%)	<0.0001
Race/Center					
MS African Americans	2654 (25.1%)	191 (13.6%)	196 (17.1%)	73 (28.4%)	
NC African Americans	285 (2.7%)	35 (2.5%)	27 (2.4%)	11 (4.3%)	
NC White	2211 (20.9%)	401 (28.5%)	344 (30.0%)	84 (32.7%)	
Washington Co, MD	2680 (25.3%)	350 (24.9%)	337 (29.4%)	56 (21.8%)	
Surburban Minneapolis	2747 (26.0%)	430 (30.6%)	243 (21.2%)	33 (12.8%)	<0.0001
Female	6344 (59.6%)	684 (48.4%)	457 (39.7%)	125 (47.9%)	
Male	4298 (40.4%)	728 (51.6%)	693 (60.3%)	136 (52.1%)	<0.0001
Mean Age (StdDev)	62.4 (5.59)	64.2 (5.69)	64.9 (5.57)	64.2 (5.70)	<0.0001
Mean BMI (StdDev)	29.2 (5.68)	27.1 (4.81)	27.6 (5.34)	27.3 (6.16)	<0.0001
Diabetes (Yes)	1573 (17.4%)	132 (10.8%)	179 (19.7%)	36 (20.7%)	
No	7486 (82.6%)	1090 (89.2%)	732 (80.4%)	138 (79.3%)	<0.0001
Hypertension (Yes)	3591 (39.4%)	388 (31.9%)	374 (40.7%)	74 (41.8%)	
No	5535 (60.7%)	829 (68.1%)	545 (59.3%)	103 (58.2%)	<0.0001
Income (Low)	2718 (31.1%)	365 (31.2%)	321 (37.2%)	72 (41.6%)	
Medium	3071 (35.2%)	440 (37.6%)	316 (36.7%)	59 (34.1%)	
High	2945 (33.7%)	366 (31.3%)	225 (26.1%)	42 (24.3%)	<0.0001
Education (Basic)	2226 (21.0%)	291 (20.6%)	332 (28.9%)	93 (35.8%)	
Intermediate	4360 (41.0%)	564 (40.0%)	480 (41.8%)	101 (38.9%)	
Advanced	4038 (38.0%)	556 (39.4%)	336 (29.3%)	66 (25.4%)	<0.0001
Alcohol Use (Yes)	4404 (48.4%)	657 (53.9%)	463 (51.1%)	78 (44.3%)	
No	4695 (51.6%)	561 (46.1%)	444 (49.0%)	98 (55.7%)	0.001
Smoke (Current, Heavy)	748 (8.6%)	191 (16.4%)	256 (29.8%)	33 (20.6%)	
Current, Light	245 (2.8%)	34 (2.9%)	15 (1.7%)	1 (0.6%)	
Former, Heavy	1304 (14.9%)	309 (26.5%)	339 (39.4%)	76 (47.5%)	
Former, Light	1981 (22.7%)	228 (19.6%)	100 (11.6%)	17 (10.6%)	
Never	4448 (51.0%)	403 (34.6%)	150 (17.4%)	33 (20.6%)	<0.0001
Smokeless Tobacco (Yes)	699 (7.7%)	131 (10.8%)	138 (15.2%)	34 (19.3%)	
No	8401 (92.3%)	1088 (89.3%)	769 (84.8%)	142 (80.7%)	<0.0001
Coronary Heart Disease (Yes)	718 (6.9%)	106 (7.6%)	159 (14.2%)	31 (13.0%)	
No	9727 (93.1%)	1281 (92.4%)	963 (85.8%)	208 (87.0%)	<0.0001
Congestive Heart Failure (Yes)	191 (2.1%)	25 (2.1%)	41 (4.6%)	9 (5.1%)	
No	8878 (97.9%)	1194 (98.0%)	861 (95.5%)	166 (94.9%)	<0.0001

*GOLD Reference: No Chronic Respiratory Symptoms & No Lung Function Abnormality + GOLD Zero (Chronic Respiratory Symptoms & No Lung Function Abnormality) + Restrictive (FEV1/FVC >= 0.70 and FVC < 80% predicted)

**Chisq or t-test

Table 3: Generalized Logits Models: Association between edentulism and GOLD Stages as compared to dentate subjects

	GOLD Reference*	GOLD I	GOLD II	GOLD III/IV
Model 1 Crude				
Edentulous	Reference	1.06 (0.90-1.24)	**2.06 (1.79-2.38)**	**3.38 (2.61-4.39)**
Model 2 Minimally Adjusted**				
Edentulous	Reference	1.12 (0.93-1.34)	**1.92 (1.61-2.28)**	**3.17 (2.28-4.41)**
Model 3 Fully Adjusted ****				
Edentulous	Reference	1.05 (0.86-1.28)	**1.32 (1.08-1.62)**	**2.47 (1.68-3.63)**

*GOLD Reference: No Chronic Respiratory Symptoms & No Lung Function Abnormality + GOLD Zero (Chronic Respiratory Symptoms & No Lung Function Abnormality) + Restrictive (FEV1/FVC >= 0.70 and FVC < 80% predicted)

**Model 2 is minimally adjusted for race/center (5-level), male, age (years)

***Model 3 is fully adjusted for race/center (5-level), male, age (years), diabetes, hypertension, smoking (5-levels), smokeless tobacco, alcohol, income (3-level), education (3-level), CFH and CHD

Table 4. Periodontal measures among the 5,155 dentate subjects by GOLD stages

	GOLD Reference*	GOLD I	GOLD II/III/IV	Overall p-value
CDC/AAP Definition				
Healthy N (SD)	2378 (43.0%)	281 (38.1%)	151 (28.5%)	
Entry N (SD)	2271 (41.1%)	295 (40.0%)	233 (44.1%)	
Severe N (SD)	878 (15.9%)	161 (21.9%)	145 (27.4%)	<0.0001
Mean (StdDev)				
Extent PD >=4mm	7.05 (11.3)	8.12 (12.3)[a]	9.66 (14.8)[d]	<0.0001
Mean PD	1.89 (0.56)	1.94 (0.61)	2.03 (0.74)[d]	<0.0001
Extent AL >=3mm	21.7 (21.8)	27.6 (26.0)[d]	34.3 (28.7)[d]	<0.0001
Mean AL	1.72 (0.96)	1.94 (1.15)[d]	2.29 (1.43)[d]	<0.0001
Extent BOP	25.2 (23.4)	25.1 (24.3)	27.7 (26.4)[a]	0.07
Extent PQ >=1	42.5 (38.3)	39.3 (37.7)[a]	49.9 (39.3)[d]	<0.0001
Number of Teeth	22.0 (6.99)	21.5 (7.26)	18.8 (8.09)[d]	<0.0001

[a] = p<0.05, b=p<0.01, c=p<0.001, d=p<0.0001,
All superscripted p values are compared to reference group by Chi square or GLM

Table 5: Generalized Logits Models: Periodontal status (CDC/AAP Definition) by GOLD stages

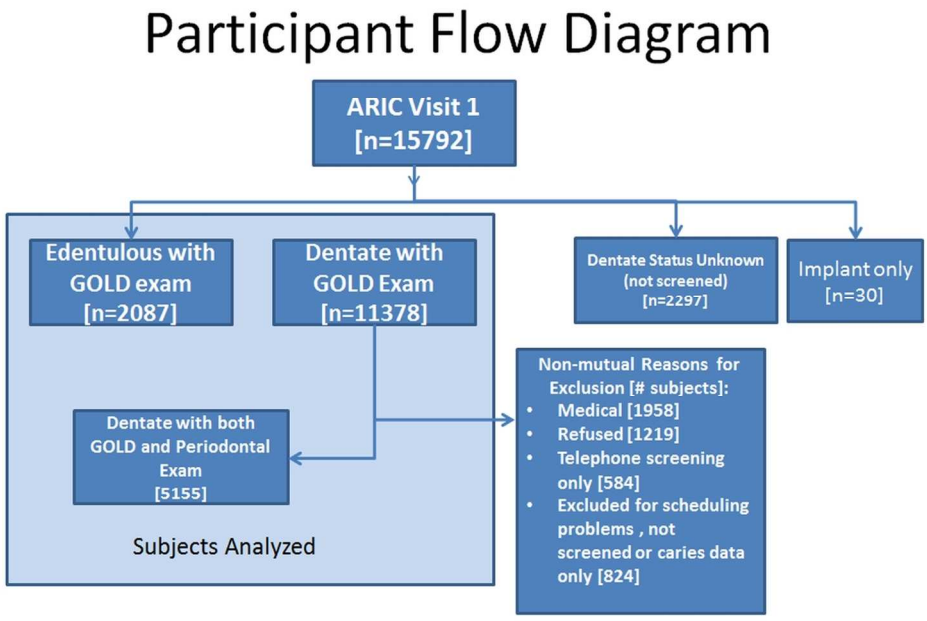
	GOLD I	GOLD II/III/IV
Model 1 Crude		
Healthy	Reference	Reference
Entry	1.10 (0.92-1.31)	**1.62 (1.31-2.00)**
Severe	**1.55 (1.26-1.91)**	**2.60 (2.05-3.31)**
Model 2 Minimally Adjusted*		
Healthy	Reference	Reference
Entry	0.99 (0.83-1.19)	**1.42 (1.14-1.77)**
Severe	**1.46 (1.17-1.82)**	**2.17 (1.67-2.80)**
Model 3 Fully Adjusted **		
Healthy	Reference	Reference
Entry	0.95 (0.79-1.14)	1.10 (0.87-1.39)
Severe	1.23 (0.97-1.55)	**1.41 (1.07-1.87)**

*Model 2 is minimally adjusted for race/center (5-level), male, age (years)
**Model 3 is fully adjusted for race/center (5-level), male, age (years), diabetes, hypertension, smoking (5-levels), smokeless tobacco, alcohol, income (3-level), education (3-level)

Table 6: Self reported physician diagnosis of bronchitis or emphysema according to GOLD stages .

	No Chronic Respiratory Symptoms & No Lung Function Abnormality	**GOLD Zero (Chronic Respiratory Symptoms & No Lung Function Abnormality)**	**Restrictive Disease ($FEV_1/FVC \geq 0.7$ and $FVC < 80\%$ predicted)**	**GOLD I**	**GOLD II**	**GOLD III/IV**	**p-value[a]**
Self Report (Yes)	633 (6.5%)	65 (20.9%)	64 (10.4%)	143 (10.1%)	201 (17.5%)	89 (34.1%)	
No	9083 (93.5%)	246 (79.1%)	551 (89.6%)	1269 (89.7%)	949 (82.5%)	172 (65.9%)	<0.0001

a) Chi square



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Word Count: 29342763

OBSTRUCTIVE AIRWAYLUNG DISEASE AND EDENTULISM IN THE ATHEROSCLEROSIS RISK IN COMMUNITIES (ARIC) STUDY

Running Title: COPD and Edentulism

Keywords: pulmonary disease, edentulism, chronic obstructive pulmonary disease, bronchitis

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Abstract:

Objectives: We examined the potential association between prior COPD and edentulism, and whether the association varied by COPD severity using data from the Dental ARIC Study.

Design: Cross-sectional ~~Case-control~~

Setting: Community dwelling subjects from four US communities.

Participants and Measurements: Cases were identified as edentulous (without teeth) and subjects with one or more natural teeth were identified as dentate. COPD cases were defined by spirometry measurements that showed the ratio of forced expiratory volume (one second) to vital capacity to be less than 0.7. The severity of COPD cases was also scored using a modified Global Initiative for Chronic Obstructive Lung Disease classification criteria (GOLD scoring I-IV). Multiple-logistic regression was used to examine the association between COPD and edentulism, while adjusting for age, gender, center/race, ethnicity, education level, income, diabetes, hypertension, coronary heart disease and congestive heart failure, body mass index, smoking, smokeless tobacco use and alcohol consumption.

Results: 13,465 participants were included in this analysis (2,087 edentulous; 11,378 dentate). Approximately 28.3% of edentulous participants had prior COPD compared to 19.6% among dentate participants ($p<0.0001$). After adjustment for potential confounders, we observed a 1.3(1.08-1.62) and 2.5(1.68-3.63) fold increased risk of edentulism among GOLD II and GOLD III/IV COPD, respectively, as compared to the non-COPD/dentate referent. Given the short period of time between the measurements of COPD (Visit2) and dentate status (Visit4) relative to the natural history of both diseases, neither temporality nor insight as to the directionality of the association can be ascertained.

Conclusion: We found a statistically significant association between prior COPD and edentulism, with evidence of a positive incremental effect seen with increasing GOLD classification.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is currently the fifth leading cause of death world-wide, and is expected to rise to fourth place in 2030.[1] Although COPD has a heterogeneous clinical presentation primarily characterized by airflow limitation, generally associated with an abnormal inflammatory response of the lungs[2] , it is also often associated with a significant systemic inflammatory response[3] which has been correlated with adverse clinical effects[3,4].

Over the past decade there has been an increased interest in the link between respiratory diseases and oral infection. Higher levels of tooth-associated microorganisms (plaque) and periodontal disease have been associated with COPD [5,6,7]. Recently, in a very comprehensive oral microbiology study, high levels of diverse microbes- including several implicated in COPD and denture stomatitis- were identified on previously worn dentures[8] .Thus both the teeth and the dentures are non-desquamating oral surfaces that allow the oral biofilm to emerge eliciting periodontal disease or denture stomatitis, respectively. This raises the question as to whether denture-associated microbes may contribute to COPD in a manner analogous to that similar to periodontal organisms. Because oral infections and denture-based sources of sepsis are both treatable and preventable, the potential association of high microbial burden of oral origin to COPD may represent modifiable risk factors that may potentially improve respiratory-related morbidity. It has been suggested by Garcia and colleagues [7] that the observed association between oral health and COPD may be due to aspiration of oral pathogens, or a common underlying host susceptibility trait that places individuals at risk for both conditions such as an exaggerated inflammatory response that is triggered by oral microbes.

Although numerous studies have examined the association between oral health and respiratory diseases in dentate individuals, the published literature are scant with respect to studies that have examined the association between edentulism and COPD status/severity. We undertook the current study to examine the potential association between COPD and edentulism using data from the Atherosclerosis Risk in

Communities (ARIC) Study. We hypothesized that edentulism would be associated with a diagnosis of COPD and display a higher prevalence with more spirometry categories of COPD. These data include not only dentate status and full-mouth periodontal examination measurements, but also includes results from direct pulmonary function tests and symptomology assessments that enabled us to classify the levels of COPD present.

METHODS

We sought to test the hypothesis that the prevalence of edentulism was greater among individuals with a reported history of lung disease, (i.e. COPD) and that the association with edentulism varied by COPD severity as determined by a modified Global Initiative for Chronic Obstructive Lung disease (GOLD) criteria. Our second hypothesis was that among dentate subjects there was a difference in the prevalence of periodontal disease according to the severity of COPD as measured by GOLD criteria.

Study Population and Study Design

The entire cohort from the ARIC study was 15,792 and the available dental cohort Dental Atherosclerosis Risk in Communities (D-ARIC) data were used to study participants with both a periodontal examination and completed spirometry data. The cohort selection process and reasons for exclusion appear in Figure 1. Descriptions of the cohort and the periodontal examination procedure have been described previously [9]. Eligible participants were all aged 45-64 at study entry (i.e., Visit 1) and had spirometry measurements at Visit 2 (3 years later) and periodontal examinations at D-ARIC Visit 4 (6 years from visit 2).

Case Definitions

Edentulism case definitions were defined as study participants without any natural teeth or implants. Participants with one or more natural teeth (comprising 11,378 subjects) were selected as the dentate subjects. The absence, presence or severity of periodontal disease among dentate subjects was determined

using the joint American Association of Periodontology/Center for Disease Control (AAP/CDC) consensus definitions of Health, Early and Advanced disease.[10]

This investigation represents the first report that uses actual pulmonary function data to assess lung function as an exposure related to edentulism or periodontal disease. The measured exposure of pulmonary function was classified both as a dichotomous (e.g., COPD vs. no COPD) and ordinal categorical variable (e.g., no lung disease, restrictive~~restricted~~ disease, COPD GOLD Stage I, Stage II, Stage III, and Stage IV), using the following criteria.

Airway obstruction

~~Lung Obstruction~~

Dichotomous variable (COPD/no COPD)—Prior airway~~lung~~ obstruction (or COPD) was defined based on spirometry measurements collected during Visit 2. Participants with a ratio of forced expiratory volume in one second (FEV_1) and forced vital capacity (FVC) less than 0.7 were determined to have airway~~lung~~ obstruction consistent with COPD.

Ordinal categorical variable (COPD GOLD Stage)—Severity of COPD was also examined in this study among COPD participants using a modification of the spirometry-based criteria for severity outlined in the GOLD guidelines.[11,12]

GOLD Stage	Spirometry Criteria
No lung disease	$FEV_1/FVC \geq 0.7$ and $FEV_1 \geq 80\%$ predicted
Restrictive~~Restricted~~	$FEV_1/FVC \geq 0.7$ and $FVC < 80\%$ predicted
Stage 0	Presence of respiratory symptoms in the absence of any lung function abnormality; and no lung disease
Stage I	$FEV_1/FVC < 0.7$ and $FEV_1 \geq 80\%$ predicted
Stage II	$FEV_1/FVC < 0.7$ and $50\% \leq FEV_1 < 80\%$ predicted
Stage III	$FEV_1/FVC < 0.7$ and $30\% \leq FEV_1 < 50\%$ predicted

Stage IV	$FEV_1/FVC<0.7$ and $FEV_1<30\%$ predicted

Variables of Interest

Smoking data (both for cigarettes and cigars) collected during Visit 4 were used to adjust for the confounding effect of smoking on the relationship between airway~~lung~~ obstruction (COPD) and being edentulous. Smoking was treated as a five-level categorical variable, as described in detail previously [7]. Cardiovascular disease (CVD) comorbidities that may be associated with both history of airway~~lung~~ obstruction and being edentulous were also examined using data from Visit 4. Other potential confounders examined included race and examination center, ethnicity, education level, income, frequency of dental visits, diabetes, body mass index, alcohol use, and medication utilization. These data were extracted from Visit 4.

Data Analysis

Mulitivariate logistic regression was used to examine the association between COPD and edentulous status. This was followed by a logistic regression analysis of the dentate subjects comparing the COPD prevalence and severity of dentate patients without periodontal disease to that of dentate patients with periodontal disease. The exposure variable, which is airway~~lung~~ obstruction, was examined as both a dichotomous variable (e.g., positive prior COPD vs. no COPD) and by logistic models using nominal variables (e.g., no lung disease, restrictive~~restricted~~ disease, GOLD 0, Stage I, Stage II, Stage III, and Stage IV) based upon spirometry data collected as part of the ARIC examination. For the no COPD or GOLD reference group we included: subjects with and without chronic respiratory symptoms with no lung function abnormality, and subjects with GOLD 0 and restrictive~~restricted~~ disease. Multiple regression models were used to control for confounding. When adjusting for potential confounding variables we included in certain models variables that are known to modify either periodontal disease status or COPD , including Body mass index and smokeless tobacco. We developed minimally and fully-

adjusted logistical models incorporating significant confounders and effect modifiers to compute odds ratios (OR) and 95% confidence intervals (CI). SAS Version 9.2 (Cary, NC). We also included traditional risk factors for edentulism, periodontal disease and COPD- such as age, even if not statistically significant in this cohort. A p-value of <0.05 was considered statistically significant for this study.

Sample Size and Power Calculations

We knew *a priori* that the ARIC cohort who had spirometry data from Visit 2 included 2,087 edentulous subjects, as determined by questionnaire data at Visit 4. We also had 11,378 dentate subjects with spirometry data at Visit 2, of which 5,155 subjects had a full-mouth periodontal exam completed. Thus, if approximately 9% of the 13,465 subjects (2,087 edentulous and 11,378 dentate) were determined to have COPD, we estimated that we had >99% power to detect a significant difference of 1% at p=0.05 in the prevalence of COPD when comparing edentulous vs. dentate subjects.

RESULTS

ARIC subject participation was based upon the inception cohort of 15,792 subjects. The Visit 4 screenings were broadly divided into 11,378 dentate and 2,087 edentulous subjects who also had spirometry data. These subjects are used for analyses in Tables 1-6 on the relationship between dentate status and COPD. Subjects were excluded (n=2,327) from the original inception participants for incomplete data, dental implants only, and missing Visit 4 screening. Table 7 is based upon the 8,274 subjects eligible for the oral exam, of which 6967 (84.1%) were actually examined. Of those examined, the periodontal portion of the exam was not completed on 174 subjects, resulting in 6,793 subjects with full periodontal data.

The distribution of study subjects according to dentate status and GOLD classification is shown in Table 1. Among the edentulous subjects (2087), there were 591 or 28.3% with COPD (Gold Stages I-IV). With the exception of GOLD I where the prevalence of edentulism was 14.7 percent, the prevalence of

edentulous individuals increased from 16.4 percent for GOLD 0 to 35.6% for GOLD III/IV. . The crude odds ratio (not shown in Table 1) for edentulism being associated with prior COPD vs no COPD was 1.62 (95% CI, 1.46-1.80). Approximately 13 percent of individuals with no chronic respiratory symptoms and no lung function abnormality (i.e. no lung disease) were edentulous. There were 2232 subjects with a prior COPD (19.6%) among 11,378 dentate subjects.

Table 2 presents the prevalence of various subject characteristics according to GOLD classification. In this table, the GOLD reference group for statistical testing combines the following three categories of subjects: no lung disease, GOLD 0, and subjects with chronic respiratory symptoms but no lung function abnormality. The general patterns reflected in Table 2 show that compared to the reference group those subjects in the GOLD III-IV category were much more likely to be edentulous, to smoke, to use smokeless tobacco, to be African American or North Carolina Caucasians, male, and somewhat more likely to have lower levels of income and education, be older and more likely to have chronic heart failure and heart disease.

Table 3 presents multivariate logistic models for the relationship between edentulous /dentate status and GOLD stages using the GOLD reference group described above. In an unadjusted model individuals with GOLD II and GOLD III/IV scores were at significantly higher odds for edentulism that increased with increasing GOLD stage severity (OR=2.06; 95% CI 1.79-2.38 and OR=3.38; 95% CI 2.61-4.39, respectively). Minimally adjusted models (race/center, sex and age) showed similar significant effects for GOLD II and GOLD III/IV with little attenuation. The increased risk of being edentulous for GOLD II and GOLD III/IV categories remain significant, but have slightly lower odds ratios. However, the fully adjusted model showed more attenuation with the odds for being edentulous being 1.3 (1.08-1.62) and 2.5 (1.68-3.63) times greater for GOLD II disease and the most severe category GOLD III/IV, respectively.

Table 4 shows the association between periodontal status and GOLD classifications for the dentate subjects. Because of small cell sizes in the GOLD III and IV groups, we combined them with GOLD II.

Using the CDC/AAP classification of periodontal disease, which is based upon clusters of clinical signs, there is a significant positive association between higher GOLD stage and severe periodontal disease ($p<0.0001$). Subjects with GOLD I or GOLD II-IV were more likely to have severe periodontitis than the reference group. With respect to the individual periodontal variables measured as means or extent scores, individuals with a GOLD classification of I were more likely to have a greater extent of periodontal pocket depths of 4mm or more, greater extent of attachment loss of 3mm. or more, a higher mean attachment loss and a greater extent of plaque in their mouths than the reference group. Those with GOLD scores of II-IV were significantly higher on all periodontal measures and had fewer teeth compared to the reference group.

Logistic models for the association between GOLD status and periodontal status using the AAP/CDC definitions appear in Table 5. As in Table 4, small cell size resulted in grouping the more severe GOLD stages together as GOLD II/III/IV. In general, the odds ratios for severe periodontal disease increased with more severe GOLD stage in the crude, minimally adjusted and fully adjusted models. There is also an increase in odds as the severity of periodontal disease increases for the two GOLD categories shown using the periodontally healthy group as the reference group within each GOLD category. Although adjusting for relevant confounders generally decreased the odds, there was still a statistically significant association between higher GOLD stage and severe periodontal disease in the fully adjusted model (OR=1.41; 95% CI 1.07-1.87).

The relationship between spirometry based GOLD classification and self-reported physician-based diagnosis of bronchitis or emphysema is shown in Table 6. Participants classified as GOLD III/IV were significantly more likely to have self-reported bronchitis or emphysema. There is a trend for a positive association except for the GOLD zero category. Interestingly, 65.9% of subjects with GOLD III/IV report no diagnosis of COPD suggesting that self-report of bronchitis or emphysema is not a strong predictor of GOLD status. In fact, of all subjects reporting a positive diagnosis of bronchitis or

emphysema 53% demonstrated no evidence of chronic respiratory symptoms and no lung function abnormality.

DISCUSSION

We found a statistically significant association between prior COPD and edentulism, with evidence of an increasing prevalence of edentulism with increasing GOLD classification. Although there was some reduction in the magnitude of effect in the adjusted models, the association between dentate status and GOLD classification remained statistically significant even in the fully adjusted model, with a 1.3 fold increased odds of being edentulous in the GOLD II category and a 2.5 fold increased odds of being edentulous in the most severe GOLD III/IV category in the fully adjusted regression model. This represents the first report of an association between edentulism and COPD in a population with GOLD measurements.

In the subgroup of dentate subjects, there was a significant association between the GOLD II - IV group vs. the GOLD reference group and prevalent periodontal disease with a statistically significant increase in the odds of entry level and severe periodontal disease in the crude and minimally adjusted models. In the fully adjusted model, only the association between GOLD stage II/III/IV and severe periodontal disease [OR 1.41 (1.07-1.87)] remained statistically significant. This is the first population report to include both full-mouth periodontal examination data as well as Spirometry assessments, thereby providing direct confirmation of the association between severe periodontal disease and COPD, as well as a dose-response relationship between these conditions.

While there is no previous published information available about the association between edentulism status and COPD, there is evidence in the literature of an association between periodontal disease and

COPD, consistent with the findings of the current study [5,6,7]. The results of this investigation were based upon standardized pulmonary function tests and suggest that studies that are based upon self-reported diagnoses can potentially result in statistically significant misclassification error. Our data shown in Table 6 suggest that of the 12,297 subjects reporting no diagnosis, 2,390 subjects or 19.4% were classified as GOLD I-IV. Among those 433 subjects with GOLD I-IV the positive predictive rate was only 15.3%. These findings suggest that an important strength of the current study was the classification of disease based on an objective biological measure (e.g., spirometry) rather than a self-reported measure.

Additional strengths of the current study include the large sample size, the inclusion of African Americans providing some racial diversity of the sample, the use of a full-mouth examination protocol and the collection of information about key confounding variables, including but not limited to: tobacco use, hypertension, diabetes, and income. Furthermore, the outcomes of interest, edentulism and periodontal disease, were evaluated using a comprehensive oral examination at Visit 4.

The current study must also be considered in light of certain limitations. First, the design of the current study does not allow us to determine the directionality or temporality of any association found. It has been reported previously that the dental ARIC sub-sample is healthier than the greater ARIC sample and that the edentulous subjects within the ARIC dataset have overall poorer health,[9] as compared to the ARIC dental sample. Thus, it is possible that the observed relationship between both edentulism and periodontal disease with prior COPD may be due in part to shared risk factors. There is also the potential bias due to differential loss to follow-up prior to Visit 4. The current study included only those subjects with dental history information at Visit 4. Finally, it is possible that participants with COPD may have been more likely to be lost to follow-up (compared to participants without COPD) or that participants with more severe COPD may have had a lower probability of surviving to Visit 4 than participants with mild COPD or normal lung function. There are no data in this report to mechanistically link edentulism with increased risk for COPD. Previous studies of periodontal disease associations with COPD have discussed

the potential role of periodontal infection serving as a chronic repository of pathogenic oral organisms that could be aspirated into the airway to challenge the lungs[6]. Periodontal infections are also associated with increases in systemic markers of inflammation including biomarkers such as C-reactive protein (CRP)[13]. By analogy, edentulism is commonly associated with denture infections (denture mucositis) which induce mucosal inflammation and unclean dentures can also pose as a chronic reservoir of oral pathogens. However, the potential role of denture-based infection as a potential risk factor for COPD remains to be elucidated.

CONCLUSIONS

Edentulism was associated with prior COPD, with an incremental effect observed with increasing GOLD classification. Additionally, among dentate individuals, severe periodontal disease was associated with GOLD classification. This is one of the first analyses of COPD and dentate status, and expands upon the available literature regarding periodontal disease and COPD. Further research is warranted to explore the relationship of edentulism and periodontal disease with COPD.

Conflict of Interest

There are no potential conflicts of interest that exist with any companies/organizations whose products or services may be discussed in this article.

Source of Funding

This work was supported by a grant from GlaxoSmithKline and we declare that the sponsor had no role in the study design, collection, analysis and interpretation of data; in the writing of the manuscript; and in the decision to submit the manuscript for publication.

Responsibility for Data

This is to verify that we have full access to all the data in this study and take full responsibility for the integrity of the data and accuracy of the data analysis, including and especially any adverse effects.

Abbreviations:

AAP/CDC – American Association of Periodontology/Center for Disease Control
ARIC – Atherosclerosis Risk in Communities
CHF – Congestive Heart Failure
CI – Confidence Intervals
COPD – Chronic Obstructive Pulmonary Disease
CVD – Cardiovascular Disease
D-ARIC – Dental Atherosclerosis Risk in Communities
FEV – Forced Expiratory Volume
FVC – Forced Vital Capacity
GOLD – Global Initiative for Chronic Obstructive Lung Disease
MAL – Mean Attachment Loss
NHANES – National Health and Nutrition Examination Survey
OR – Odds Ratio
SES – Social Economic Status
WHO – World Health Organization

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