Relationship between chronic gingivitis and subsequent depression in 13,088 patients followed in general practices

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Running title: Chronic gingivitis and subsequent depression

Abstract

Goal: The aim of this study was to analyze the association between chronic gingivitis and subsequent depression in patients aged ≥14 years who were followed up in general practices in the UK.

Methods: This study included patients aged ≥14 years who had received an initial diagnosis of chronic gingivitis in one of 256 general practices in the United Kingdom between January 2000 and December 2016 (index date). Patients without chronic gingivitis were matched (1:1) to those with chronic gingivitis by sex, age, index year, treating physician, and Charlson Comorbidity Index (CCI). For patients without chronic gingivitis, the index date was a randomly selected visit date between 2000 and 2016. The association between chronic gingivitis and the incidence of depression was investigated using Kaplan-Meier curves and Cox regression analyses.

Results: This study included 6,544 patients with chronic gingivitis and 6,544 patients without chronic gingivitis [49.2% were women; mean (standard deviation) age 40.3 (19.1) years]. A total of 16.3% of individuals with chronic gingivitis and 8.8% of those without chronic gingivitis received an initial diagnosis of depression within 10 years of the index date (log-rank p-value<0.001). There was a positive and significant association between chronic gingivitis and depression in the overall sample [hazard ratio (HR)=1.82, 95% confidence interval (CI)=1.55-2.48]. These findings were corroborated in men and women and in all age groups with the exception of patients aged >65 years.

Conclusions: Our study demonstrated an association between chronic gingivitis and subsequent depression.

Keywords: chronic gingivitis; depression; retrospective cohort study; United Kingdom

Introduction

Gingivitis is a reversible inflammation that is limited locally to the gingiva. It does not spread via the periodontal attachment. The origin of gingivitis may lie in several predisposing factors that promote plaque accumulation (including xerostomia), as well as a number of systemic risk factors (including smoking, hyperglycemia, hormones). Typical signs of gingivitis are redness, swelling, halitosis, and bleeding when gently probed. Untreated gingivitis is a preliminary stage of periodontitis [1, 2]. Periodontal disease has a high prevalence of 20-50% worldwide [3].

Symptoms of gingivitis such as halitosis can have a negative impact on quality of life: it may give rise to social and occupational limitations, including the development of social anxiety disorders [4]. This can adversely affect social interactions [5].

A number of studies have already shown that depression influences periodontal disease [6]. It has been shown that mental health can have a negative impact on oral health [7] and that biological components and behavioral mechanisms that are connected with depression can have an adverse effect on periodontal health [6]. Little is known about the reverse association, however. Indeed, to the best of our knowledge, there is only one Taiwanese cohort study that has investigated periodontal disease as a risk factor for subsequent depression [8].

Our aim is to investigate whether there is an association between chronic gingivitis and subsequent depression in a group of patients observed over a period of 10 years in the United Kingdom. As the prevalence of depression is high in the UK, with 19.7% of the population (≥16 years) documented as exhibiting depressive symptoms in 2014 [9], investigating the risk factors for this condition is particularly important in the UK.

Methods

Database

This study was based on data from the Disease Analyzer database (IQVIA), which contains drug prescriptions, diagnoses, and basic medical and demographic data obtained directly and in anonymous format from computer systems used in the practices of general practitioners and specialists [10]. Diagnoses, prescriptions, and the quality of reported data are monitored regularly by IQVIA based on a number of criteria (e.g., completeness of documentation, linkage between diagnoses and prescriptions). In the United Kingdom, the sampling method for the Disease Analyzer database was based on statistics from all doctors in the United Kingdom.

These statistics were used to determine the panel composition according to the following strata: region, community size category, and age of physician [11].

Study population

This study included patients who had received an initial diagnosis of chronic gingivitis (ICD-10: K05.1) in one of 256 general practices including 1,721 physicians in the United Kingdom between January 2000 and December 2016 (index date). Inclusion criteria were as follows: age ≥14 years on the index date (as no complete data are available for children <14) with no diagnosis of schizophrenia, schizotypal, delusional, and other non-mood psychotic disorders (ICD-10: F20-29), mood disorders (ICD-10: F30-39) or anxiety, dissociative, stress-related, somatoform and other nonpsychotic mental disorders (ICD-10: F40-48) and no prescription for antidepressants (ATC: N06A) documented prior to the index date.

After applying similar inclusion criteria, patients without chronic gingivitis were matched (1:1) to those with chronic gingivitis by sex, age, index year, treating physician, and Charlson Comorbidity Index (CCI). The CCI describes 22 comorbid conditions where each condition is assigned a score from 1 to 6 depending on the risk of mortality. Clinical conditions and associated scores in the CCI are as follows: myocardial infarction, congestive heart failure, peripheral vascular disease, dementia, cerebrovascular disease, chronic lung disease, connective tissue disease, ulcer, chronic liver disease, diabetes, hemiplegia, moderate or severe kidney disease, diabetes with end-organ damage, tumor, leukemia, lymphoma, moderate or severe liver disease, malignant tumor, metastasis, and AIDS (Quan et al. 2005). Thus, the CCI is a proxy of comorbidity, with higher scores indicating higher comorbidity profiles. For patients without chronic gingivitis, the index date was a randomly selected visit date between January 2000 and December 2016 (Figure 1).

Study outcome and statistical analyses

The study outcome was the cumulative incidence of depression (ICD-10: F32, F33) in patients with chronic gingivitis compared to patients without chronic gingivitis. Baseline characteristics (i.e. sex, age, CCI) were compared for patients with and those without chronic gingivitis using chi-squared tests for sex and Wilcoxon tests for age and CCI. Kaplan-Meier curves were also used to analyze the incidence of depression in the overall sample and by sex and age group (14-30, 31-50, 51-65, >65 years). Finally, the association between chronic gingivitis and depression was studied with Cox regression models in the overall population and also by sex and age group. Since patients with and without chronic gingivitis were matched by age, sex, and CCI, the Cox regression analyses were not adjusted for these variables. The results of the Cox regression analyses are presented as hazard ratios (HRs) with 95% confidence intervals (CIs).

P-values of less than 0.05 were considered statistically significant. All analyses were performed using SAS 9.4 (SAS Institute, Cray, USA).

Results

This study included 6,544 patients with chronic gingivitis and 6,544 patients without chronic gingivitis. The proportion of women in the population was 49.2%, and the mean (standard deviation) age was 40.3 (19.1) years (Table 1). After 10 years of follow-up, 16.3% of individuals with chronic gingivitis and 8.8% of those without chronic gingivitis had received an initial diagnosis of depression (log-rank p-value<0.001; Figure 2). The results of the Cox Regression analyses are displayed in Table 2. Overall, there was a positive and significant association between chronic gingivitis and depression (HR=1.82; 95% CI=1.58-2.08). These findings were corroborated in men (HR=1.96; 95% CI=1.55-2.48) and women (HR=1.74; 95% CI=1.47-2.06). The strength of the association varied across the different groups with HRs ranging from 1.44 in individuals aged 14-20 to 2.04 in those aged 36-50 and 51-65 years. The association between chronic gingivitis and depression was not statistically significant in individuals aged >65 years (p=0.122) (Table 2).

Discussion

As our study is the first to investigate whether there is an association between chronic gingivitis and subsequent depression in the United Kingdom, there is a dearth of comparable literature. Only one cohort study in Taiwan has investigated the association between periodontitis and subsequent depression. This study found that there was a relationship between the two [8]. Gingivitis and periodontitis are clinically distinct: Gingivitis is the preliminary stage and a prerequisite for the development of periodontitis [1]. Our study investigated the precursor stage and shows that of the 6,544 patients from both sides examined, 16.3% of patients with chronic gingivitis and 8.8% of patients without chronic gingivitis were diagnosed with initial depression. The incidence of depression was therefore higher in the gingivitis group. This is consistent with the findings of the cohort study that investigated periodontitis as a risk factor. In that study, the incidence of depression in the periodontitis group was also almost twice as high as in the non-periodontitis group [8].

We found that the association varies between the different age groups and is strongest among 21-35-year-olds and 36-50-year-olds. Our results were reflected to some extent in a South Korean cross-sectional study in which self-reported depression was most strongly associated

with periodontal disease in the 20-29 age group [12]. It seems that there is a strong association among young adults.

There are numerous reasons why chronic gingivitis may be related to subsequent depression. Gingivitis is characterized by an immunoinflammatory host response [1], which may be linked to neuroinflammation and impaired serotonin synthesis [8]. Restrictions in oral hygiene and the wearing of prostheses as well as pain and halitosis may be associated with depressive symptoms [1, 13]. Halitosis is considered one of the least attractive aspects of social interactions [14] and may give rise to social and occupational limitations [4]. A social anxiety disorder that has developed in an individual with halitosis may persist after successful halitosis treatment [15]. Halitosis may be one of the symptoms of gingivitis that is most strongly associated with subsequent depression. There are studies that show that halitosis patients have symptoms of depression and that there is a connection between the two [16]. People with depressive symptoms may also be less concerned about dental care.

Many studies have demonstrated that there is a connection between periodontitis and diabetes [1, 17] as well as cardiovascular disease [18]. Both diabetes and cardiovascular disease could play a mediating role between chronic gingivitis and depression.

Clinical implications and future research

The connection between these two diseases warrants increasing attention from GPs, and it is important to understand that both can influence each other. It is expected that the prevalence of depression will continue to rise over the next few years until it becomes the most common disease worldwide [19]. It is therefore important to identify and treat potential risk factors. Patients should also be examined for gingivitis by general practitioners. The link between oral diseases and general diseases should be given more attention in general practice. Due to the lack of consensus on the connection between the two disease areas, studies should be conducted in the future to investigate the influence of periodontal disease on subsequent depression and focus on the causes.

Strengths and limitations

The strengths of this study are the number of patients and general practices available for analysis and the length of the follow-up period. Our study is the only one in which gingivitis is examined as a risk factor for later depression. However, as there are also several limitations, the study results should be interpreted with caution. Firstly, the diagnoses were based solely on ICD-10 codes. Had more information on the severity of the condition been available, this might have allowed for more detailed statistical analyses. Secondly, because chronic gingivitis

is a dental diagnosis, the documentation of this diagnosis by GPs may not be complete. Thirdly, this study include only adult patients and no children and adolescents. Fourth, since dental diseases are treated by dentists, the influence of therapy on the association between gingivitis and depression could not be investigated. Fifth, there was no diagnosis of halitosis, which is a common symptom of gingivitis and may be an important factor in the relationship between gingivitis and depression. Finally, no information was available on behavioral and social factors (e.g., physical activity, alcohol consumption, family situation), although these factors may play an important role in the relationship between gingivitis and depression.

Conclusions

Our study shows that chronic gingivitis is significantly associated with subsequent depression. Further studies are needed to gain a better understanding of the relationship between tooth disorders and depression.

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Tables and Figures

Figure 1. Selection of study patients

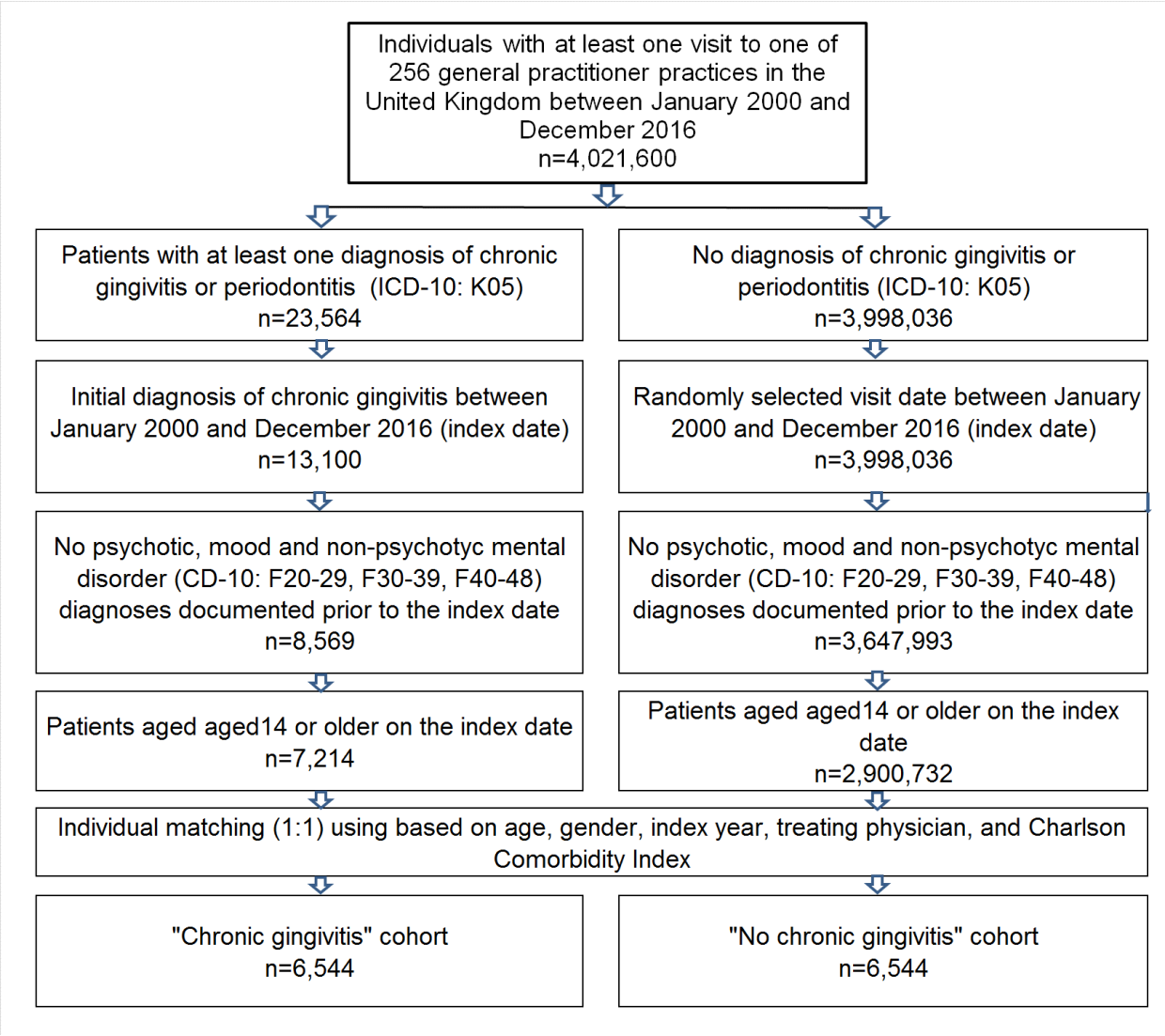

Figure 2. Cumulative incidence of depression in patients with or without chronic gingivitis in the 10 years following the index date

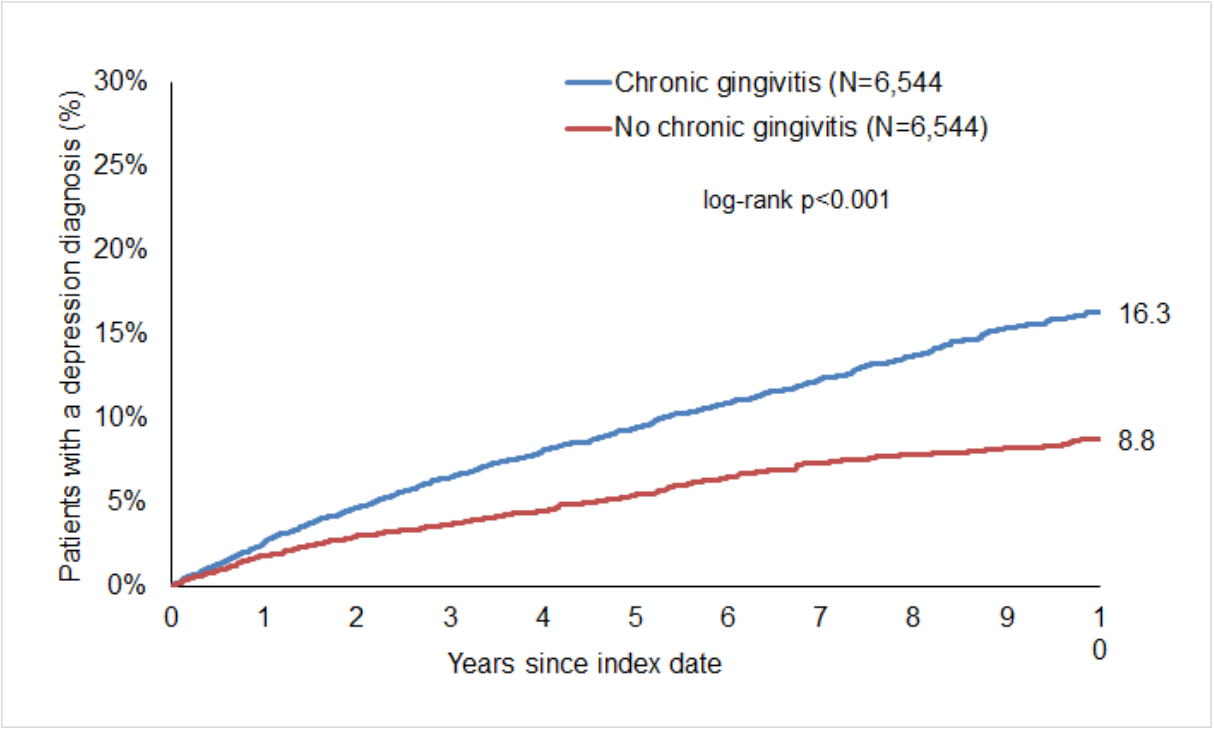

Table 1. Baseline characteristics of study patients after 1:1 matching

Variable	Patients with chronic gingivitis (N=6,544)	Patients without chronic gingivitis (N=6,544)	P-value
Men	3,321 (50.8)	3,321 (50.8)	1.000
Women	3,223 (49.2)	3,223 (49.2)	
Age in years (mean, SD)	40.3 (19.1)	40.3 (19.1)	1.000
Age 14-20 years	967 (14.8)	967 (14.8)	1.000
Age 21-35 years	2,240 (34.2)	2,240 (34.2)	1.000
Age 36-50 years	1,403 (21.4)	1,403 (21.4)	
Age 51-65 years	1,056 (16.1)	1,056 (16.1)	
Age >65 years	878 (13.4)	878 (13.4)	
Charlson Comorbidity Index (Mean, SD)	0.4 (0.8)	0.4 (0.8)	1.000

Data are absolute numbers and percentages unless otherwise specified. SD=Standard deviation

Table 2. Association between chronic gingivitis and the incidence of depression in patients followed for up to 10 years in general practices in the United Kingdom

Population	Proportion in patients with chronic gingivitis	Proportion in patients without chronic gingivitis	Hazard ratio (95% confidence interval)	P-value
Overall	16.3	8.8	1.82 (1.58-2.08)	<0.001
Men	13.1	5.9	1.96 (1.55-2.48)	<0.001
Women	19.3	11.6	1.74 (1.47-2.06)	<0.001
Age 14-20 years	19.1	16.0	1.44 (1.07-1.94)	0.016
Age 21-35 years	19.6	8.9	2.04 (1.62-2.56)	<0.001
Age 36-50 years	16.9	7.1	2.04 (1.52-2.75)	<0.001
Age 51-65 years	10.1	6.0	1.79 (1.18-2.71)	0.006
Age >65 years	11.6	7.3	1.41 (0.91-2.18)	0.122