Periodontitis Prevalence in ulcerative Colitis & Crohn's disease (PPCC) patients: A case-control study

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Author contribution

KB, CB, AS conceptualization; KB, JB, AS organization, execution, and data collection. KB, NP, AS data analysis, interpretation, KB, CB, JB, BK, AS manuscript drafting.

Data availability statement

The data are available by the authors upon reasonable request.

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Abstract

Aim

The aim of this questionnaire-based, case-control study was to assess whether self-reported oral health and periodontitis in ulcerative colitis (UC) and Crohn's disease (CD) patients differ from that in matched controls without inflammatory bowel disease (IBD).

Methods

A survey including questions on general anamnestic information, IBD diagnosis, and oral health was distributed online. Self-perceived overall health of teeth and gums, severe periodontitis, and tooth loss were defined as outcome parameters.

Results

Analyses were based on answers from 1108 IBD patients and 3429 controls. IBD patients reported significantly worse oral health and more periodontal problems compared to controls. Regression analyses corrected for relevant confounders showed for UC and CD patients significantly increased odds for fair or poor self-perceived overall health of teeth and gums (OR 2.147 and 2.736, respectively) and for severe periodontitis (OR 1.739 and 2.574, respectively) compared to controls; CD patients presented additionally 91% higher odds for having < 20 remaining teeth.

Conclusions

UC and CD patients have significantly increased odds for worse self-perceived oral health and severe periodontitis compared to controls, with CD patients being more severely affected and losing more teeth. It is strongly recommended that IBD patients are kept under close surveillance to prevent periodontitis development and/or mitigate its progression.

Keywords

Case-control study; Crohn's disease; inflammatory bowel disease; periodontal disease; ulcerative colitis.

Clinical Relevance

Scientific rationale for the study

The etiopathogenesis of inflammatory bowel diseases (IBD) has similarities to that of periodontitis and previous studies have indicated an association between both diseases.

Principal findings

Based on answers of 1108 cases and 3429 matched controls, IBD patients had higher odds for worse self-perceived oral health and for severe periodontitis compared to controls. Patients with Crohn's disease were those most affected and had also significantly fewer teeth than the controls.

Practical implications

It is strongly recommended that patients with IBD are kept under close surveillance to prevent periodontitis and/or mitigate its progression and tooth loss.

Introduction

The etiopathogenesis of inflammatory bowel diseases [IBD, i.e., Ulcerative Colitis (UC) or Crohn's disease (CD)] appears in many aspects similar to that of periodontitis. Both diseases involve an excessive inflammatory response in the intestinal or oral mucosa, respectively, to a microbial trigger in a susceptible host. This response is characterized by massive tissue infiltration by neutrophils, as first line defense mechanism, which at the same time causes tissue destruction (Cho 2008; Graves 2008; Indriolo et al. 2011; Bartold & Van Dyke 2013; Bertl et al. 2016; de Souza & Fiocchi 2016). Additionally, both diseases share common risk factors (e.g., poor oral hygiene, smoking, diet, psychosocial stress, etc.) (Genco & Borgnakke 2013; Ananthakrishnan et al. 2014; Martin et al. 2015; Racine et al. 2016; Li et al. 2021).

It has been reported that patients being diagnosed with IBD present higher prevalence and/or severity of periodontitis compared to controls without IBD [see reviews: (Agossa et al. 2017; Papageorgiou et al. 2017; She et al. 2020; Agossa et al. 2021; Lorenzo-Pouso et al. 2021; Nijakowski et al. 2021; Zhang et al. 2021)]. Specifically, in small-sized cross-sectional studies, IBD patients presented with increased probing pocket depths, more clinical attachment loss, and/or increased gingival bleeding tendency, compared to subjects without IBD (Brito et al. 2008; Habashneh et al. 2012; Vavricka et al. 2013; Slebioda et al. 2014; Koutsochristou et al. 2015; Schmidt et al. 2018; Zhang et al. 2020). Further, differences in the oral microflora have been reported that may partly be due to specific characteristics of IBD patients, e.g., IBD patients harbor higher numbers of bacteria related to opportunistic infections compared to non-IBD subjects (Van Dyke et al. 1986; Stein et al. 2010; Docktor et al. 2012; Brito et al. 2013; Said et al. 2014; Schmidt et al. 2018; Xun et al. 2018). Furthermore, it has been very recently reported that the gut microbiome of IBD patients – compared to the gut microbiome of IBD-free controls – is significantly more alike to the oral microbiome (Imai et al. 2021). Recent registry-based, large-scale studies of Asian populations, have also indicated a potential bi-directional relationship, i.e., suffering from IBD significantly increased the risk to develop periodontitis, while being diagnosed with periodontitis significantly increased the risk to develop IBD (Chi et al. 2018; Lin et al. 2018; Kang et al. 2020).

The incidence of IBD is increasing worldwide, while in Europe more than 3 million people are suffering from it, with northern European countries appearing more affected compared to those in the south (Burisch & Munkholm 2015; Zhao et al. 2021). Considering the known impact of periodontitis on quality of life and on the systemic health, as well as its financial burden on the personal and societal level (The Economist Intelligence Unit 2021), it is of importance to know whether IBD patients are more prone to periodontitis; however, there is paucity of data from Europe on this topic. The aim of the present questionnaire-based, case-control study was to assess on a large-scale whether self-perceived overall

health of teeth and gums, severe periodontitis, and tooth loss in UC and CD patients differs from that in matched controls without IBD.

Materials and Methods

Population details and distribution of the questionnaire

The present questionnaire-based case-control study (Periodontitis Prevalence in ulcerative Colitis & Crohn's disease patients: the PPCC study) was conducted in Denmark and included IBD patients and matched controls (i.e., not diagnosed with IBD) in a 1:3 ratio. The ratio of 1:3 was chosen to achieve at least a power of 80% assuming alpha of 0.05, a correlation coefficient between cases and controls of 0.2, an odds ratio (OR) of 3, and a prevalence of exposure (i.e., presence of periodontitis) in controls of 0.2 (Hennessy et al. 1999). This represented a quite conservative assumption, as the calculation is based on a small number of cases (n = 50) and any increase in the number of cases results in a higher power. A web-based survey tool (Sunet Survey) was used, allowing anonymous response to the questionnaire. Information about the study was distributed to all members of the Danish Colitis-Crohn Association (CCF) (www.ccf.dk; 4200 IBD patients) via email, homepage, and social media. The survey remained open receiving responses for a period of 6 months (i.e., from November 2018 to April 2019), and CCF members received 3 reminders in total. Thereafter, potential controls were identified from the database of Statistics Denmark (www.dst.dk), a state-owned institute under the Danish Ministry of the Interior and Housing. These were matched to the IBD patients according to a) gender, b) age, c) education (up to high school / higher education up to 3 years / higher education > 3 years), d) income after taxes (< 10000 DKK / ≥ 10000 DKK), and e) living area (city / non-city). The matching based on this database a priori excluded citizens with a UC or CD diagnosis, i.e., data of controls were linked to the National Patient Registry using the unique Danish ID-number, which includes information on all diagnoses, procedures, and treatments of citizens in the public Danish health care system. Based on previous experience of Statistics Denmark, and an expected age-dependent response rate in similar type of surveys of 25 to 33%, 9 to 12 controls were matched to each IBD case. The identified potential controls received information about the study directly via email in the national official communication platform (www.e-boks.com), but their answers were treated anonymously. The online platform remained open receiving responses for a period of 6 months (i.e., from July 2020 to December 2020), and the identified controls received 3 reminders in total. No ethical approval was required for this type of study in Denmark.

Content of the questionnaire

The questionnaire included questions on general information (i.e., age, gender, body height and weight, smoking status, systemic diseases, living area, education, and income after taxes), oral health related

questions (i.e., number of teeth, state of teeth and gums), as well as questions previously recommended for self-reported surveillance of periodontitis (Eke et al. 2013). The questionnaire sent out to the cases additionally included a question on the IBD diagnosis (i.e., UC, CD, or unclassified IBD). Other parts of the questionnaire, such as IBD-specific questionnaires and questions on oral health-related quality of life, oral lesions, details on recent dental visits, etc. will be reported elsewhere. All information and questions were provided in Danish. Based on the provided answers the body mass index (BMI) was calculated. Further, based on 5 questions for self-reported surveillance of periodontitis, age, and smoking status, the Periodontal Screening Score (PESS) (Carra et al. 2018), previously validated for identifying severe periodontitis cases, was calculated. PESS ≥ 5 is indicative for severe periodontitis (Carra et al. 2018).

Statistical analysis

Frequency distribution for categorical variables and means (standard deviations), medians and interquartile ranges for continuous variables are reported for IBD patients and controls, and separately for UC and CD patients. Patients indicating that they had unclassified IBD were grouped with UC, whereas patients reporting to be diagnosed with both UC and CD were excluded from any secondary analyses involving only the cases. To test any differences between controls and IBD patients or between UC and CD patients, either Fisher's exact test or chi-squared test was applied for categorical parameters (i.e., chi-squared test was applied if each cell presented with a frequency > 5, otherwise Fisher's exact test was used) and for continuous variables either an independent *t*-test (for normally distributed data) or a Mann Whitney-U test (for non-normally distributed data). Normality of the data was controlled graphically by Q-Q-plots and by the Shapiro-Wilk test. The following 3 parameters were defined as primary outcome variables: 1) self-perceived overall health of teeth and gums (dichotomous outcome parameter; excellent / very good / good versus fair / poor), 2) PESS ≥ 5 (dichotomous outcome parameter; PESS 1-4 versus PESS ≥ 5), and 3) tooth number (dichotomous outcome parameter; ≥ 20 teeth versus 10 to 19 teeth / 1 to 9 teeth / edentulous). Patient group (control / UC / CD) was defined as the main predictor and age, gender, and smoking status (never / former / current) as a priori confounders. In a first step, for each of the primary outcome variables, a binary logistic regression analysis including the main predictor and the a priori confounders was constructed as a base model. In a second step the following potential confounders were added one at the time to the base model: diabetes; osteoporosis; rheumatoid arthritis; ankylosing spondylitis; psoriasis; depression; high cholesterol; cardiovascular disease; asthma; chronic obstructive pulmonary disease; living area (city / suburban area / countryside); education (no school or primary school / high school / higher education up to 3 years / higher education up to 6 years and/or PhD); income after taxes (< 5000 DKK / 5000 to < 10000 DKK / 10000 to < 20000 DKK / ≥ 20000 DKK); BMI; and PESS ≥ 5 and/or tooth number, depending

on the primary outcome parameter of the specific regression analysis. All confounders changing the OR of the main predictor (i.e., patient group) by ≥ 10% were added in the base model to construct the final model. Statistical analysis was performed with STATA/IC 17.0 for Mac and a p-value ≤ 0.05 was considered as statistically significant.

Results

Response rate

Within 6 months, 1108 IBD patients responded to the survey (response rate based on the known number of CCF member: 26.4%); 538 patients reported to be diagnosed with UC, 527 with CD, 28 with unclassified IBD, and 15 with both UC and CD. Based on this sample of cases, 12949 potential controls were matched and contacted; within a period of 6 months, 3429 eligible answers of controls were received (response rate: 26.5%).

General characteristics

The general characteristics of IBD patients and controls are displayed in Table 1. Age (48.0 vs. 48.9 years, respectively), income (61.0 vs. 61.2%, respectively, ≥ 10000 DKK), and BMI (26.2 vs. 26.3, respectively) were similar between IBD patients and controls. Some variation was observed, regarding gender and education, but the differences were only up to 5 and 7%, respectively, within the subcategories. A large difference between IBD patients and controls was observed in regards with the living area (i.e., 48.3 vs. 28.6%, respectively, living in a city). Hence, although the invited 12949 potential controls were matched to the IBD patients, those finally answering and included, resulted in a control group including relatively more females, and individuals with a high education and living on the countryside, compared to the IBD group. Further, controls had a higher percentage of never smokers (53.1 vs. 42.0%, respectively), while the percentage of current smokers was comparable in controls and IBD patients (14.0 vs. 16.5%, respectively). Finally, IBD patients presented a significantly higher percentage for most of the assessed systemic diseases.

In Appendix S1 IBD patients are split into those diagnosed with UC or CD; patients with CD included a significantly higher number of females, current smokers, and patients with psoriasis, but were significantly younger, had less frequently high cholesterol, and lower income.

Dental and periodontal characteristics

The self-reported dental and periodontal characteristics of IBD patients and controls are displayed in Table 2. Overall, IBD patients indicated having a worse oral health status compared to controls. Specifically, the percentage of IBD patients perceiving the state of their teeth and gums as poor or very

poor was about 3-times higher than that in the controls, and 15.7% of the IBD patients vs. only 9.7% of the controls had less than 20 remaining teeth. The responses to the questions of the tool for self-reported surveillance of periodontitis indicated significantly more periodontal problems among IBD patients, i.e., the percentage of IBD patients indicating periodontal problems was about twice as high than that in the controls for most of the questions. Finally, a significantly higher percentage of the IBD patients had, compared to controls, a PESS ≥ 5 (31.8 vs. 19.9%, respectively) and ≥ 9 (6.8 vs. 2.8%, respectively).

In Table 3, IBD patients are split into those diagnosed with UC or CD. Patients with CD perceived more often state of the teeth and gums as poor or very poor and had significantly fewer teeth, compared to UC patients. Further, patients with CD were significantly more often thinking they might have gum disease, perceiving the overall health of their teeth and gums as fair or poor, and having recently bleeding gums.

Self-perceived overall health of teeth and gums (Table 4)

In the base model diagnosis of UC and CD significantly increased the odds for perceiving a fair or poor state of the overall health of teeth and gums by 2.3- and 3.2-times, respectively. Only PESS ≥ 5 changed these odds by ≥ 10% and was added to the final model. Correcting for self-perceived severe periodontitis slightly reduced the odds, but diagnosis of UC (OR 2.15, 95% CI 1.73-2.67) and CD (OR 2.74, 95% CI 2.20-3.41) remained highly significant and increased the odds to perceive a fair or poor state of the overall health of teeth and gums. Further, PESS ≥ 5 (OR 18.86, 95% CI 15.09-23.57) and former smoking (OR 1.23, 95% CI 1.03-1.48) significantly increased the odds for perceiving a fair or poor state of the overall health of teeth and gums, while a higher age significantly reduced the odds (OR 0.95, 95% CI 0.94-0.96).

PESS ≥ 5 (Table 5)

In the base model diagnosis of UC and CD significantly increased the odds for having a PESS ≥ 5 and these odds were not changed by ≥ 10% by any of the potential confounders, i.e., the base and final model were identical. Specifically, diagnosis of UC (OR 1.74, 95% CI 1.36-2.22) and CD (OR 2.57, 95% CI 2.00-3.32), a higher age (OR 1.12, 95% CI 1.11-1.13), and former (OR 1.97, 95% CI 1.62-2.39) and current smoking (OR 13.39, 95% CI 10.49-17.08) significantly increased the odds for having a PESS ≥ 5.

Tooth number (Table 6)

In the base model diagnosis of CD significantly increased the odds to have less than 20 teeth by 2.3-times. Only PESS ≥ 5 changed these odds by ≥ 10% and was added to the final model. Correcting for self-perceived severe periodontitis slightly reduced the odds, but diagnosis of CD (OR 1.91, 95% CI 1.46-

2.51) remained highly significant and increased the odds to have less than 20 teeth. Further, PESS ≥ 5 (OR 3.44, 95% CI 2.72-4.34), a higher age (OR 1.04, 95% CI 1.03-1.05), and former (OR 1.54, 95% CI 1.21-1.95) and current smoking (OR 2.29, 95% CI 1.72-3.05) significantly increased the odds to have less than 20 teeth.

Discussion

The present large-scale, case-control, questionnaire-based study, using a specific validated tool to assess the association of periodontitis with IBD, is the first of its kind in a European population. The results of the study showed that patients suffering from IBD had significantly higher odds for perceiving the overall health of their teeth and gums as worse and for having severe periodontitis. Patients diagnosed with CD presented even higher odds for these issues, compared to those with UC, and additionally presented significantly higher odds for having lost more teeth compared to matched controls without IBD. These results confirm those of previous studies where an association between periodontitis and IBD was suggested. In one of the first systematic reviews summarizing the studies available at that time, i.e., generally small-sized ones with < 200 IBD patients each, an OR of 5.1 and 4.0 was calculated for patients with UC or CD, respectively, to also have periodontitis (Papageorgiou et al. 2017). In more recent reviews including already studies with larger samples the OR ranged between 2 to 3 (Nijakowski et al. 2021; Zhang et al. 2021), and, if the first large-scale, registry-based, cohort study with > 135000 Taiwanese (Lin et al. 2018) was taken into account, the risk ratio to also have periodontitis ranged between 3 and 4 (Lorenzo-Pouso et al. 2021).

In the present study, periodontitis was identified using the recently suggested Periodontal Screening Score (PESS) (Carra et al. 2018), which is based on a validated set of questions for self-reported surveillance of periodontitis (Eke et al. 2013), age, and smoking status. The PESS has recently been validated to show a moderate-to-high accuracy in identifying severe cases. Specifically, with a cut-off level of PESS ≥ 5, a sensitivity and specificity of 79 and 75%, respectively, and correct classification of 77% of the cases with severe periodontitis [i.e., ≥ 2 interproximal sites with ≥ 6 mm attachment level (not on the same tooth) and ≥ 1 interproximal site with ≥ 5 mm probing pocket depth] was demonstrated (Carra et al. 2018). Here, the fraction of IBD patients having a PESS ≥ 5 was about 1.5-times higher than that in the non-IBD subjects (i.e., 31.8 vs. 19.9%, respectively). This is comparable to what was presented in a recent clinical trial (Zhang et al. 2020) including almost 400 IBD patients and showing a periodontitis prevalence of 37.5%. Likewise, when considering all the questions of the tool for self-reported surveillance of periodontitis (Eke et al. 2013), the fraction of IBD patients indicating periodontal problems in the present study was about twice as high as in the non-IBD subjects, and CD patients additionally presented a 83% higher odds to have less than 20 remaining teeth compared to

controls. Thus, it appears understandable, that UC and CD patients significantly more often perceived their overall health of teeth and gums as fair or poor (OR 2.2 and 2.7, respectively) compared to controls. This finding is well in agreement with previous studies reporting that IBD patients show higher rates of tooth loss, judge that their oral health as worse, and have greater dental treatment needs compared to others of the same age (Rikardsson et al. 2009; Vavricka et al. 2013; Zhang et al. 2020; Tan et al. 2021). In this context, increased rate of tooth loss may reflect higher periodontal disease severity, faster progression, and/or inferior treatment response in IBD patients, but may also be due to caries and/or endodontic problems. Indeed, increased caries activity and need of fillings/dental treatment has been previously reported as a frequent problem of IBD patients (Grössner-Schreiber et al. 2006; Brito et al. 2008; Rikardsson et al. 2009; Slebioda et al. 2014; Johannsen et al. 2015; Koutsochristou et al. 2015; Schmidt et al. 2018; Zhang et al. 2020; Tan et al. 2021). Nevertheless, although self-reporting of the number of remaining teeth has been proven reliable (i.e., reported differences between clinical assessment and self-reporting range from 0.1 to 1.5 teeth) (Buhlin et al. 2002; Matsui et al. 2016; Similä et al. 2018; Ueno et al. 2018), any information about the reasons for tooth loss was considered unreliable and no attempt was made in the present study to obtain such information.

In the above-mentioned study from the National Health Insurance Research Database of Taiwan (Lin et al. 2018), periodontitis patients had a 1.6-times higher risk to develop UC; however, no significant risk for developing CD was detected. Similarly, in another recent registry-based, large-scale, cohort study, again from an Asian population (Korea) (Kang et al. 2020), periodontitis patients had a 1.1-times higher risk to develop UC – but not CD – during a mean follow-up of 7 years, and the risk to develop UC was specifically increased (i.e., 1.9-times higher) among smokers ≥ 65 years of age compared to similarly aged non-smokers. The difference between the present study, where both IBD entities were associated with significantly higher odds for self-reported severe periodontitis compared to controls, and the above-mentioned studies, where only UC was significantly associated with periodontitis may at least partly be due to different study designs and age-dependent features of IBD. Specifically, although CD and UC can be diagnosed at any age, the incidence peaks in most populations below 40 years of age, with CD being diagnosed, on average, 5 to 10 years earlier than UC. Furthermore, UC shows a second incidence peak in the sixth or seventh decade of life (Johnston & Logan 2008; Burisch & Munkholm 2015). The Asian studies included only patients who had been diagnosed with periodontitis and without IBD at baseline, and about two thirds of the study patients were at baseline > 40 years of age (Lin et al. 2018; Kang et al. 2020). Thus, it is likely that these two studies included persons with a higher propensity to UC (due to older age) rather than to CD. Interestingly, in another Taiwanese cohort study, using again the National Health Insurance Research Database, CD patients showed a hazard ratio of 1.4 to develop subsequently periodontitis compared to persons not suffering from CD (Chi et al. 2018). It appears thus

clear that periodontitis is strongly associated with IBD, and it may even be that there is a bilateral direction, i.e., that presence of the one disease increases the risk for development of the other and/or when both present, they aggravate each other. Indeed, it has been recently shown in preclinical in vivo experiments that oral bacterial species, found in abundance in periodontitis, can both directly and indirectly exacerbate inflammatory responses in the gut (Jia et al. 2020; Kitamoto et al. 2020; Tsuzuno et al. 2021). In perspective, a similar type of bi-directional association, has been shown between periodontitis and diabetes (Borgnakke 2019), and is suggested for other systemic conditions, e.g., rheumatoid arthritis, obesity (Lopez-Oliva et al. 2019; Jepsen et al. 2020). Here, IBD patients presented indeed with a higher frequency of other systemic diseases, such as rheumatoid arthritis, ankylosing spondylitis, psoriasis, cardiovascular diseases, etc. compared to the controls. This finding has been apprehended (Bernstein et al. 2005; Burisch et al. 2019), and therefore these conditions were considered in the statistical analysis as potential confounders; however, none of these co-morbidities significantly altered the effect of IBD on any of the outcome parameters. Further, despite the good matching at the time of reaching out to the controls (i.e., matching was performed between the group of IBD patients and the invited controls), the IBD patients and the finally included controls differed significantly in some aspects. Specifically, the control group included less men (20.9 vs. 25.5%), fewer controls were living in a city (28.6 vs. 48.3%), and more controls had a higher education up to 6 years and/or PhD (37.5 vs 30.7%). Nevertheless, these factors were considered in the statistical analyses as potential confounders but did not alter the effect of IBD on any of the outcome parameters.

In perspective, the present questionnaire-based case-control study comes with some inevitable limitations. Specifically, the control group included relatively more females, and individuals with a high education and living on the countryside, compared to the IBD group. This discrepancy may partly be due to the relatively low response rate observed in this group (i.e., 26.5%). However, this response rate compares well to that in the IBD cases and is within the range of similar type of surveys previously conducted by Statistics Denmark (i.e., between 25 to 33%), which was also the basis for inviting 13000 matched potential controls. Furthermore, according to the study design treating all answers anonymously, it was not possible to compare the non-responders to the responders. Finally, since no clinical examination was performed, it was not possible to assess the possible impact of periodontitis stage and extent on IBD presence/activity/severity and vice versa.

In conclusion, the present results support the notion that UC and CD patients have significantly increased odds for fair or poor self-perceived overall health of teeth and gums and severe periodontitis; CD patients seem more severely affected and to lose more teeth. It is therefore strongly recommended

that IBD patients are kept under close surveillance to prevent periodontitis development and/or mitigate its progression and tooth loss.

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Table legends

Table 1. Self-reported general characteristics of the IBD patients (n = 1108) and controls (n = 3429).

Table 2. Self-reported dental and periodontal characteristics of the IBD patients (n = 1108) and controls (n = 3429).

Table 3. Self-reported dental and periodontal characteristics of the patients with ulcerative colitis (including unclassified inflammatory bowel disease; n = 566) and Crohn's disease (n = 527).

Table 4. Results of the binary logistic regression analyses for the dichotomous outcome parameter "self-perceived overall health of teeth and gums"; an OR > 1 indicates higher odds for perceiving the overall health of teeth and gums as fair or poor. Age, gender, and smoking status were defined as a priori confounders.

Table 5. Results of the binary logistic regression analyses for the dichotomous outcome parameter "PESS ≥ 5"; an OR > 1 indicates higher odds for a PESS ≥ 5 (i.e., presence of self-reported severe periodontitis). Age, gender, and smoking status were defined as a priori confounders.

Table 6. Results of the binary logistic regression analyses for the dichotomous outcome parameter "tooth number"; an OR > 1 indicates higher odds to have less than 20 teeth. Age, gender, and smoking status were defined as a priori confounders.

Appendix legends

Appendix S1. Self-reported general characteristics of the patients with ulcerative colitis (including unclassified inflammatory bowel disease; n = 566) and Crohn's disease (n = 527).

Table 1. Self-reported general characteristics of the IBD patients (n = 1108) and controls (n = 3429).

Parameter		**IBD patients**	**Controls**	**p-value**
Gender [n (%)]	*Female*	825 (74.5)	2714 (79.1)	**0.001**
	Male	283 (25.5)	715 (20.9)	
Age	*Mean (S.D.)*	48.0 (14.8)	48.9 (13.3)	0.068[1]
	Median (Q1; Q3)	49 (37; 59)	50 (40; 57)	
BMI	*Mean (S.D.)*	26.2 (5.4)	26.3 (5.4)	0.761[2]
	Median (Q1; Q3)	25.3 (22.4; 29.1)	25.2 (22.6; 29.0)	
Smoking [n (%)]	*Never*	465 (42.0)	1820 (53.1)	**< 0.001**
	Former	460 (41.5)	1129 (32.9)	
	Current	183 (16.5)	480 (14.0)	
Systemic diseases [present; n (%)]	*Diabetes*	40 (3.6)	89 (2.6)	0.077
	Osteoporosis	75 (6.8)	53 (1.6)	**< 0.001**
	Rheumatoid arthritis	49 (4.4)	45 (1.3)	**< 0.001**
	Ankylosing spondylitis	30 (2.7)	11 (0.3)	**< 0.001**
	Psoriasis	64 (5.8)	80 (2.3)	**< 0.001**
	Depression	89 (8.0)	157 (4.6)	**< 0.001**
	High cholesterol	73 (6.6)	147 (4.3)	**0.002**
	Cardiovascular disease	143 (12.9)	262 (7.6)	**< 0.001**
	Asthma	92 (8.3)	190 (5.5)	**0.001**
	COPD	15 (1.4)	26 (0.8)	0.069
Living area [n (%)]	*City*	535 (48.3)	980 (28.6)	**< 0.001**
	Suburban area	370 (33.4)	905 (26.4)	
	Countryside	203 (18.3)	1544 (45.0)	
Education [n (%)]	*No school*	1 (0.1)	19 (0.5)	**< 0.001**[3]
	Primary school	157 (14.2)	410 (12.0)	
	High school	108 (9.8)	260 (7.6)	
	Higher education up to 3 years	501 (45.2)	1454 (42.4)	
	Higher education up to 6 years	324 (29.2)	1219 (35.5)	
	PhD	17 (1.5)	67 (2.0)	
Income [n (%)]	*< 5000 DKK*	130 (11.7)	352 (10.2)	0.274
	5000 to < 10000 DKK	303 (27.3)	980 (28.6)	
	10000 to < 20000 DKK	413 (37.3)	1223 (35.7)	
	≥ 20000 DKK	262 (23.7)	874 (25.5)	

[1] p-value relates to the mean values and independent t-test was applied.

[2] p-value relates to the median values and Mann Whitney-U test was applied.

[3] Calculation of the Fisher's exact test was not possible for these data and p-value is based on chi-squared test.

Bold values indicate statistical significance.

BMI, body mass index; COPD, chronic obstructive pulmonary disease; DKK, danish crowns; Q1/Q3, first/third quartile; S.D., standard deviation.

Table 2. Self-reported dental and periodontal characteristics of the IBD patients (n = 1108) and controls (n = 3429).

Parameter		**IBD patients**	Controls	p-value
Tooth number [n (%)]	*Edentulous*	6 (0.5)	23 (0.7)	**< 0.001**
	1 to 9 teeth	14 (1.3)	59 (1.7)	
	10 to 19 teeth	154 (13.9)	251 (7.3)	
	≥ 20 teeth	934 (84.3)	3096 (90.3)	
State of the teeth [n (%)]	*Excellent*	122 (11.0)	526 (15.3)	**< 0.001**
	Very good	252 (22.7)	1124 (32.8)	
	Good	190 (17.2)	756 (22.1)	
	Average	287 (25.9)	758 (22.1)	
	Poor	187 (16.9)	195 (5.7)	
	Very poor	63 (5.7)	56 (1.6)	
	Don't know	7 (0.6)	14 (0.4)	
State of the gums [n (%)]	*Excellent*	101 (9.1)	498 (14.5)	**< 0.001**
	Very good	229 (20.7)	1090 (31.8)	
	Good	191 (17.2)	733 (21.4)	
	Average	316 (28.5)	817 (23.8)	
	Poor	217 (19.6)	235 (6.9)	
	Very poor	45 (4.1)	38 (1.1)	
	Don't know	9 (0.8)	18 (0.5)	
Do you think you might have gum disease? [n (%)]	*Yes*	330 (29.8)	561 (16.3)	**< 0.001**
	No	673 (60.7)	2526 (73.7)	
	Don't know	105 (9.5)	342 (10.0)	
Overall, how would you rate the health of your teeth and gums? [n (%)]	*Excellent*	98 (8.8)	439 (12.8)	**< 0.001**
	Very good	261 (23.6)	1267 (37.0)	
	Good	280 (25.3)	1008 (29.4)	
	Fair	274 (24.7)	507 (14.8)	
	Poor	189 (17.1)	183 (5.3)	
	Don't know	6 (0.5)	25 (0.7)	
Have you ever had treatment for gum disease such as scaling and root planing, sometimes called "deep cleaning"? [n (%)]	*Yes*	264 (23.8)	613 (17.9)	**< 0.001**
	No	760 (68.6)	2538 (74.0)	
	Don't know	84 (7.6)	278 (8.1)	
Have you ever had any teeth become loose on their own, without an injury? [n (%)]	*Yes*	163 (14.7)	231 (6.7)	**< 0.001**
	No	894 (80.7)	3093 (90.2)	
	Don't know	51 (4.6)	105 (3.1)	
Have you ever been told by a dental professional that you lost bone around your teeth? [n (%)]	*Yes*	104 (9.4)	161 (4.7)	**< 0.001**
	No	952 (85.9)	3157 (92.1)	
	Don't know	52 (4.7)	111 (3.2)	
During the past 3 months, have you noticed a tooth that doesn't look right? [n (%)]	*Yes*	148 (13.4)	233 (6.8)	**< 0.001**
	No	912 (82.3)	3138 (91.5)	
	Don't know	48 (4.3)	58 (1.7)	
In the last 7 days, how many times did you use dental floss or any other device to clean between your teeth? [n (%)]	*Never*	183 (16.5)	605 (17.6)	0.389
	1- to 7-times	925 (83.5)	2824 (82.4)	
	Never	961 (86.7)	3069 (89.5)	**0.011**

In the last 7 days, how many times did you use mouthwash or other dental rinse product that you use to treat dental disease or dental problems? [n (%)]	*1- to 7-times*	147 (13.3)	360 (10.5)	
Have your parents or siblings now or in the past had problems with their gums and / or lost their teeth early in life? [n (%)]	*Yes*	483 (43.6)	1443 (42.1)	0.218
	No	452 (40.8)	1373 (40.0)	
	Don't know	173 (15.6)	613 (17.9)	
Have your gums bled recently, e.g., when brushing your teeth? [n (%)]	*Yes*	375 (33.8)	681 (19.9)	**< 0.001**
	No	733 (66.2)	2748 (80.1)	
Do you have food impaction between your teeth? [n (%)]	*Yes*	613 (55.3)	1537 (44.8)	**< 0.001**
	No	495 (44.7)	1892 (55.2)	
Do you notice your teeth getting longer? [n (%)]	*Yes*	216 (19.5)	463 (13.5)	**< 0.001**
	No	892 (80.5)	2966 (86.5)	
PESS[2]	*Mean (S.D.)*	3.7 (2.7)	3.1 (2.2)	**< 0.001**[1]
	Median (Q1; Q3)	4 (2; 5)	3 (2; 4)	
PESS [n (%)][2]	*1 to 4*	753 (68.3)	2730 (80.2)	**< 0.001**
	5 to 8	274 (24.9)	580 (17.0)	
	9 to 13	75 (6.8)	94 (2.8)	
PESS ≥ 5 [yes; n (%)][3]		352 (31.8)	681 (19.9)	**< 0.001**

[1] p-value relates to the median values and Mann Whitney-U test was applied.

[2] Based on 3404 controls and 1102 cases.

[3] Based on 3419 controls and 1107 cases.

Bold values indicate statistical significance.

PESS, periodontal screening score; Q1/Q3, first/third quartile; S.D., standard deviation.

Table 3. Self-reported dental and periodontal characteristics of the patients with ulcerative colitis (including unclassified inflammatory bowel disease; n = 566) and Crohn's disease (n = 527).

Parameter		Ulcerative colitis	Crohn's disease	p-value
Tooth number [n (%)]	*Edentulous*	0 (0.0)	6 (1.2)	**0.003**[1]
	1 to 9 teeth	7 (1.2)	7 (1.3)	
	10 to 19 teeth	64 (11.3)	87 (16.5)	
	≥ 20 teeth	495 (87.5)	427 (81.0)	
State of the teeth [n (%)]	*Excellent*	74 (13.1)	48 (9.1)	**< 0.001**[2]
	Very good	143 (25.3)	106 (20.1)	
	Good	91 (16.1)	95 (18.0)	
	Average	161 (28.4)	123 (23.4)	
	Poor	70 (12.4)	114 (21.6)	
	Very poor	24 (4.2)	37 (7.0)	
	Don't know	3 (0.5)	4 (0.8)	
State of the gums [n (%)]	*Excellent*	61 (10.8)	40 (7.6)	**0.001**[2]
	Very good	141 (24.9)	86 (16.3)	
	Good	89 (15.7)	98 (18.6)	
	Average	159 (28.1)	152 (28.8)	
	Poor	92 (16.3)	122 (23.2)	
	Very poor	21 (3.7)	23 (4.4)	
	Don't know	3 (0.5)	6 (1.1)	
Do you think you might have gum disease? [n (%)]	*Yes*	146 (25.8)	178 (33.8)	**0.014**
	No	365 (64.5)	300 (56.9)	
	Don't know	55 (9.7)	49 (9.3)	
Overall, how would you rate the health of your teeth and gums? [n (%)]	*Excellent*	64 (11.3)	34 (6.5)	**< 0.001**[1]
	Very good	147 (26.0)	112 (21.2)	
	Good	143 (25.3)	133 (25.2)	
	Fair	139 (24.5)	130 (24.7)	
	Poor	72 (12.7)	113 (21.4)	
	Don't know	1 (0.2)	5 (1.0)	
Have you ever had treatment for gum disease such as scaling and root planing, sometimes called "deep cleaning"? [n (%)]	*Yes*	134 (23.7)	125 (23.7)	0.583
	No	393 (69.4)	357 (67.8)	
	Don't know	39 (6.9)	45 (8.5)	
Have you ever had any teeth become loose on their own, without an injury? [n (%)]	*Yes*	73 (12.9)	87 (16.5)	0.222
	No	469 (82.9)	416 (78.9)	
	Don't know	24 (4.2)	24 (4.6)	
Have you ever been told by a dental professional that you lost bone around your teeth? [n (%)]	*Yes*	50 (8.8)	52 (9.9)	**0.008**
	No	500 (88.4)	440 (83.5)	
	Don't know	16 (2.8)	35 (6.6)	
During the past 3 months, have you noticed a tooth that doesn't look right? [n (%)]	*Yes*	65 (11.5)	79 (15.0)	0.141
	No	479 (84.6)	422 (80.1)	
	Don't know	22 (3.9)	26 (4.9)	
In the last 7 days, how many times did you use dental floss or any other device to clean between your teeth? [n (%)]	*Never*	99 (17.5)	81 (15.4)	0.345
	1- to 7-times	467 (82.5)	446 (84.6)	
In the last 7 days, how many times did you use mouthwash or other dental rinse	*Never*	495 (87.5)	454 (86.2)	0.523
	1- to 7-times	71 (12.5)	73 (13.8)	

product that you use to treat dental disease or dental problems? [n (%)]				
Have your parents or siblings now or in the past had problems with their gums and / or lost their teeth early in life? [n (%)]	*Yes*	252 (44.5)	225 (42.7)	0.655
	No	223 (39.4)	222 (42.1)	
	Don't know	91 (16.1)	80 (15.2)	
Have your gums bled recently, e.g., when brushing your teeth? [n (%)]	*Yes*	168 (29.7)	200 (38.0)	**0.004**
	No	398 (70.3)	327 (62.0)	
Do you have food impaction between your teeth? [n (%)]	*Yes*	316 (55.8)	288 (54.7)	0.695
	No	250 (44.2)	239 (45.3)	
Do you notice your teeth getting longer? [n (%)]	*Yes*	109 (19.3)	101 (19.2)	0.969
	No	457 (80.7)	426 (80.8)	
PESS[4]	*Mean (S.D.)*	3.7 (2.7)	3.7 (2.8)	0.980[3]
	Median (Q1; Q3)	4 (2; 5)	3 (2; 5)	
PESS [n (%)][4]	*1 to 4*	395 (69.9)	351 (67.2)	0.408
	5 to 8	129 (22.8)	137 (26.3)	
	9 to 13	41 (7.3)	34 (6.5)	
PESS ≥ 5 [yes; n (%)][5]		171 (30.2)	173 (32.9)	0.341

[1] Fisher's exact test was applied.

[2] Calculation of the Fisher's exact test was not possible for these data and p-value is based on chi-squared test.

[3] p-value relates to the median values and Mann Whitney-U test was applied.

[4] Based on 565 patients with ulcerative colitis (including unclassified inflammatory bowel disease) and 522 patients with Crohn's disease.

[5] Based on 566 patients with ulcerative colitis (including unclassified inflammatory bowel disease) and 526 patients with Crohn's disease.

Bold values indicate statistical significance.

PESS, periodontal screening score; Q1/Q3, first/third quartile; S.D., standard deviation.

Table 4. Results of the binary logistic regression analyses for the dichotomous outcome parameter "self-perceived overall health of teeth and gums"; an OR > 1 indicates higher odds for perceiving the overall health of teeth and gums as fair or poor. Age, gender, and smoking status were defined as a priori confounders.

Parameter		OR	95% CI		p-value
			Lower	Upper	
Base model					
Patient group	*Control*	Ref.			
	Ulcerative colitis	**2.348**	1.936	2.849	< 0.001
	Crohn's disease	**3.210**	2.640	3.902	< 0.001
Age	*Per unit (year)*	0.998	0.993	1.003	0.390
Gender	*Male*	Ref.			
	Female	0.980	0.828	1.164	0.818
Smoking	*Never*	Ref.			
	Former	**1.449**	1.237	1.699	< 0.001
	Current	**2.799**	2.310	3.392	< 0.001
Final model					
Patient group	*Control*	Ref.			
	Ulcerative colitis	**2.147**	1.726	2.670	< 0.001
	Crohn's disease	**2.736**	2.195	3.412	< 0.001
PESS	*< 5*	Ref.			
	≥ 5	**18.856**	15.087	23.566	< 0.001
Age	*Per unit (year)*	**0.950**	0.943	0.957	< 0.001
Gender	*Male*	Ref.			
	Female	1.020	0.844	1.233	0.836
Smoking	*Never*	Ref.			
	Former	**1.233**	1.030	1.476	0.022
	Current	1.072	0.854	1.346	0.548

Bold values indicate significance.

CI, confidence interval; OR, odds ratio; PESS, periodontal screening score.

Table 5. Results of the binary logistic regression analyses for the dichotomous outcome parameter "PESS ≥ 5"; an OR > 1 indicates higher odds for a PESS ≥ 5 (i.e., presence of self-reported severe periodontitis). Age, gender, and smoking status were defined as a priori confounders.

Parameter		OR	95% CI		p-value
			Lower	Upper	
Base model / Final model[1]					
Patient group	*Control*	Ref.			
	Ulcerative colitis	**1.739**	1.360	2.224	< 0.001
	Crohn's disease	**2.574**	1.998	3.316	< 0.001
Age	*Per unit (year)*	**1.116**	1.107	1.126	< 0.001
Gender	*Male*	Ref.			
	Female	1.109	0.908	1.356	0.311
Smoking	*Never*	Ref.			
	Former	**1.966**	1.620	2.385	< 0.001
	Current	**13.386**	10.490	17.081	< 0.001

[1] None of the potential confounders changed the OR of the main predictor by ≥ 10%, i.e., the base and final model are identical.

Bold values indicate significance.

CI, confidence interval; OR, odds ratio; PESS, periodontal screening score.

Table 6. Results of the binary logistic regression analyses for the dichotomous outcome parameter "tooth number"; an OR > 1 indicates higher odds to have less than 20 teeth. Age, gender, and smoking status were defined as a priori confounders.

Parameter		OR	95% CI		p-value
			Lower	Upper	
Base model					
Patient group	*Control*	Ref.			
	Ulcerative colitis	1.158	0.867	1.547	0.320
	Crohn's disease	**2.294**	1.762	2.985	< 0.001
Age	*Per unit (year)*	**1.060**	1.052	1.069	< 0.001
Gender	*Male*	Ref.			
	Female	0.914	0.730	1.146	0.437
Smoking	*Never*	Ref.			
	Former	**1.751**	1.390	2.205	< 0.001
	Current	**4.038**	3.106	5.249	< 0.001
Final model					
Patient group	*Control*	Ref.			
	Ulcerative colitis	1.041	0.776	1.398	0.788
	Crohn's disease	**1.913**	1.458	2.510	< 0.001
PESS	*< 5*	Ref.			
	≥ 5	**3.437**	2.721	4.340	< 0.001
Age	*Per unit (year)*	**1.039**	1.029	1.049	< 0.001
Gender	*Male*	Ref.			
	Female	0.895	0.711	1.126	0.344
Smoking	*Never*	Ref.			
	Former	**1.535**	1.212	1.945	< 0.001
	Current	**2.292**	1.723	3.049	< 0.001

Bold values indicate significance.

CI, confidence interval; OR, odds ratio; PESS, periodontal screening score.