

ORIGINAL ARTICLE

Periodontitis prevalence in patients with ulcerative colitis and Crohn's disease - PPCC: A case-control study

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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 patients with ulcerative colitis (UC) and Crohn's disease (CD) differ from those in matched controls without inflammatory bowel disease (IBD).

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

Conclusion: Patients with UC and CD have significantly increased odds for worse self-perceived oral health and severe periodontitis compared to controls, with the former being more severely affected and losing more teeth. It is strongly recommended that patients with IBD 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 study: The aetiopathogenesis of inflammatory bowel diseases (IBD) has similarities to that of periodontitis, and previous studies have indicated an association between both diseases.

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Principal findings: Based on the answers of 1108 cases and 3429 matched controls, patients with IBD 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.

1 | INTRODUCTION

The aetiopathogenesis of inflammatory bowel diseases (IBD; i.e., ulcerative colitis [UC] and 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 defence 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; Ananthkrishnan 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 by 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; Y. Zhang et al., 2021). Specifically, in small-sized cross-sectional studies, patients with IBD 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; Sleboda et al., 2014; Koutsochristou et al., 2015; Schmidt et al., 2018; L. Zhang et al., 2020). Further, differences in the oral microflora have been reported, which may partly be due to specific characteristics of IBD patients: for example, IBD patients harbour 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 that of IBD-free controls—is significantly more like the oral microbiome (Imai et al., 2021). Recent registry-based, large-scale studies of Asian populations have also indicated a potential bi-directional relationship, that is, those suffering from IBD are at significantly increased 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. In Europe, more than 1.3 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 the quality of life and on the systemic health, as well as its financial burden at 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 differ from those in matched controls without IBD.

2 | MATERIALS AND METHODS

2.1 | 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 an 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 represents a very 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 for receiving responses for a period of 6 months (i.e., from November 2018 to April 2019), and CCF members received three 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 (10,000 DKK/≥10,000 DKK), and (e) living area (city/non-city). The matching based on this database a priori excluded citizens with a UC or CD diagnosis, that is, 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 healthcare system. Based on previous experience of Statistics Denmark, and an expected age-dependent response rate in similar

type of surveys of 25%–33%, 9–12 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 for receiving responses for a period of 6 months (i.e., from July 2020 to December 2020), and the identified controls received three reminders in total. No ethical approval is required for this type of study in Denmark.

2.2 | 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 IBD diagnosis (i.e., UC, CD, or unclassified IBD). Other parts of the questionnaire, such as IBD-specific questions and questions on oral-health-related quality of life, oral lesions, details on recent dental visits, and so on, 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 five questions for self-reported surveillance of periodontitis, age, and smoking status, the Periodontal Screening Score (PESS) (Carra et al., 2018), which had been previously validated for identifying severe periodontitis cases, was calculated. PESS ≥ 5 is indicative for severe periodontitis (Carra et al., 2018).

2.3 | Statistical analysis

Frequency distribution for categorical variables and means, standard deviations (SDs), medians, and interquartile ranges for continuous variables are reported for IBD patients and controls and separately for UC and CD patients. Patients who indicated 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 three parameters were defined as the primary outcome variables: (1) self-perceived overall health of teeth and gums (dichotomous outcome parameter; excellent/very good/good vs. fair/poor); (2) PESS ≥ 5 (dichotomous outcome parameter; PESS 1–4 vs. PESS ≥ 5); and (3) number of teeth (dichotomous outcome parameter; ≥ 20 teeth vs. 10–19 teeth/1–9

teeth/edentulous). Patient group (control/UC/CD) was defined as the main predictor, whereas age, gender, and smoking status (never/former/current) were defined 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 conducted 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– $< 10,000$ DKK/10,000– $< 20,000$ DKK/ $\geq 20,000$ 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 $\geq 10\%$ 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.

3 | RESULTS

3.1 | Response rate

Within 6 months, 1108 IBD patients responded to the survey (response rate based on the known number of CCF members: 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, 12,949 potential controls were matched and contacted; within a period of 6 months, 3429 eligible answers of controls were received (response rate: 26.5%).

3.2 | 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, $\geq 10,000$ 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 with regard to the living area (i.e., 48.3% vs. 28.6%, respectively, living in a city). Hence, although the invited 12,949 potential controls were matched to the IBD patients, those finally answering and included resulted in a control group that included more females and individuals with a high education and living in 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.

TABLE 1 Self-reported general characteristics of the inflammatory bowel disease (IBD) patients ($n = 1108$) and controls ($n = 3429$)

Parameter	IBD patients	Controls	<i>p</i> -Value
Gender (n [%])			
Female	825 (74.5)	2714 (79.1)	.001
Male	283 (25.5)	715 (20.9)	
Age			
Mean (SD)	48.0 (14.8)	48.9 (13.3)	.068 ^a
Median (Q1; Q3)	49 (37; 59)	50 (40; 57)	
BMI			
Mean (SD)	26.2 (5.4)	26.3 (5.4)	.761 ^b
Median (Q1; Q3)	25.3 (22.4; 29.1)	25.2 (22.6; 29.0)	
Smoking (n [%])			
Never	465 (42.0)	1820 (53.1)	<.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)	.077
Osteoporosis	75 (6.8)	53 (1.6)	<.001
Rheumatoid arthritis	49 (4.4)	45 (1.3)	<.001
Ankylosing spondylitis	30 (2.7)	11 (0.3)	<.001
Psoriasis	64 (5.8)	80 (2.3)	<.001
Depression	89 (8.0)	157 (4.6)	<.001
High cholesterol	73 (6.6)	147 (4.3)	.002
Cardiovascular disease	143 (12.9)	262 (7.6)	<.001
Asthma	92 (8.3)	190 (5.5)	.001
COPD	15 (1.4)	26 (0.8)	.069
Living area (n [%])			
City	535 (48.3)	980 (28.6)	<.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)	<.001^c
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)	.274
5000–<10,000 DKK	303 (27.3)	980 (28.6)	
10,000–<20,000 DKK	413 (37.3)	1223 (35.7)	
≥20,000 DKK	262 (23.7)	874 (25.5)	

Note: Bold values indicate statistical significance.

Abbreviations: BMI, body mass index; COPD, chronic obstructive pulmonary disease; DKK, Danish crowns; Q1/Q3, first/third quartile; SD, standard deviation.

^a*p*-value relates to the mean values, and independent *t*-test was applied.

^b*p*-value relates to the median values, and Mann–Whitney *U*-test was applied.

^cCalculation of the Fisher's exact test was not possible for these data, and *p*-value is based on chi-squared test.

TABLE 2 Self-reported dental and periodontal characteristics of the inflammatory bowel disease (IBD) patients ($n = 1108$) and controls ($n = 3429$)

Parameter	IBD patients	Controls	p-Value
Tooth number (n [%])			
Edentulous	6 (0.5)	23 (0.7)	<.001
1–9 teeth	14 (1.3)	59 (1.7)	
10–19 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)	<.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)	
Do not know	7 (0.6)	14 (0.4)	
State of the gums (n [%])			
Excellent	101 (9.1)	498 (14.5)	<.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)	
Do not know	9 (0.8)	18 (0.5)	
Do you think you might have gum disease? (n [%])			
Yes	330 (29.8)	561 (16.3)	<.001
No	673 (60.7)	2526 (73.7)	
Do not 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)	<.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)	
Do not 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)	<.001
No	760 (68.6)	2538 (74.0)	
Do not 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)	<.001
No	894 (80.7)	3093 (90.2)	
Do not 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)	<.001
No	952 (85.9)	3157 (92.1)	
Do not know	52 (4.7)	111 (3.2)	

TABLE 2 (Continued)

Parameter	IBD patients	Controls	p-Value
During the past 3 months, have you noticed a tooth that does not look right? (n [%])			
Yes	148 (13.4)	233 (6.8)	<.001
No	912 (82.3)	3138 (91.5)	
Do not 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)	.389
1–7 times	925 (83.5)	2824 (82.4)	
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 [%])			
Never	961 (86.7)	3069 (89.5)	.011
1–7 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)	.218
No	452 (40.8)	1373 (40.0)	
Do not know	173 (15.6)	613 (17.9)	
Have your gums bled recently, for example, when brushing your teeth? (n [%])			
Yes	375 (33.8)	681 (19.9)	<.001
No	733 (66.2)	2748 (80.1)	
Do you have food impaction between your teeth? (n [%])			
Yes	613 (55.3)	1537 (44.8)	<.001
No	495 (44.7)	1892 (55.2)	
Do you notice your teeth getting longer? (n [%])			
Yes	216 (19.5)	463 (13.5)	<.001
No	892 (80.5)	2966 (86.5)	
PESS ^a			
Mean (SD)	3.7 (2.7)	3.1 (2.2)	<.001^b
Median (Q1; Q3)	4 (2; 5)	3 (2; 4)	
PESS (n [%]) ^a			
1–4	753 (68.3)	2730 (80.2)	<.001
5–8	274 (24.9)	580 (17.0)	
9–13	75 (6.8)	94 (2.8)	
PESS ≥ 5 (yes; n [%]) ^c	352 (31.8)	681 (19.9)	<.001

Note: Bold values indicate statistical significance.

Abbreviations: PESS, periodontal screening score; Q1/Q3, first/third quartile; SD, standard deviation.

^aBased on 3404 controls and 1102 cases.

^bp-Value relates to the median values, and Mann-Whitney U-test was applied.

^cBased on 3419 controls and 1107 cases.

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 had lower income.

3.3 | 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 versus 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, that is, the percentage of IBD patients indicating periodontal problems was about twice as high as that in the controls for most of the questions. Finally, a significantly higher percentage of the IBD patients

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	<i>p</i> -Value
Tooth number (<i>n</i> [%])			
Edentulous	0 (0.0)	6 (1.2)	.003 ^a
1–9 teeth	7 (1.2)	7 (1.3)	
10–19 teeth	64 (11.3)	87 (16.5)	
≥20 teeth	495 (87.5)	427 (81.0)	
State of the teeth (<i>n</i> [%])			
Excellent	74 (13.1)	48 (9.1)	<.001 ^b
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)	
Do not know	3 (0.5)	4 (0.8)	
State of the gums (<i>n</i> [%])			
Excellent	61 (10.8)	40 (7.6)	.001 ^b
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)	
Do not know	3 (0.5)	6 (1.1)	
Do you think you might have gum disease? (<i>n</i> [%])			
Yes	146 (25.8)	178 (33.8)	.014
No	365 (64.5)	300 (56.9)	
Do not know	55 (9.7)	49 (9.3)	
Overall, how would you rate the health of your teeth and gums? (<i>n</i> [%])			
Excellent	64 (11.3)	34 (6.5)	<.001 ^a
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)	
Do not 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”? (<i>n</i> [%])			
Yes	134 (23.7)	125 (23.7)	.583
No	393 (69.4)	357 (67.8)	
Do not know	39 (6.9)	45 (8.5)	
Have you ever had any teeth become loose on their own, without an injury? (<i>n</i> [%])			
Yes	73 (12.9)	87 (16.5)	.222
No	469 (82.9)	416 (78.9)	
Do not know	24 (4.2)	24 (4.6)	
Have you ever been told by a dental professional that you lost bone around your teeth? (<i>n</i> [%])			
Yes	50 (8.8)	52 (9.9)	.008
No	500 (88.4)	440 (83.5)	
Do not know	16 (2.8)	35 (6.6)	

TABLE 3 (Continued)

Parameter	Ulcerative colitis	Crohn's disease	p-Value
During the past 3 months, have you noticed a tooth that does not look right? (n [%])			
Yes	65 (11.5)	79 (15.0)	.141
No	479 (84.6)	422 (80.1)	
Do not 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)	.345
1–7 times	467 (82.5)	446 (84.6)	
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 [%])			
Never	495 (87.5)	454 (86.2)	.523
1–7 times	71 (12.5)	73 (13.8)	
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)	.655
No	223 (39.4)	222 (42.1)	
Do not know	91 (16.1)	80 (15.2)	
Have your gums bled recently, for example, when brushing your teeth? (n [%])			
Yes	168 (29.7)	200 (38.0)	.004
No	398 (70.3)	327 (62.0)	
Do you have food impaction between your teeth? (n [%])			
Yes	316 (55.8)	288 (54.7)	.695
No	250 (44.2)	239 (45.3)	
Do you notice your teeth getting longer? (n [%])			
Yes	109 (19.3)	101 (19.2)	.969
No	457 (80.7)	426 (80.8)	
PESS ^c			
Mean (SD)	3.7 (2.7)	3.7 (2.8)	.980 ^d
Median (Q1; Q3)	4 (2; 5)	3 (2; 5)	
PESS (n [%]) ^c			
1–4	395 (69.9)	351 (67.2)	.408
5–8	129 (22.8)	137 (26.3)	
9–13	41 (7.3)	34 (6.5)	
PESS ≥ 5 (yes; n [%]) ^e	171 (30.2)	173 (32.9)	.341

Note: Bold values indicate statistical significance.

Abbreviations: PESS, periodontal screening score; Q1/Q3, first/third quartile; SD, standard deviation.

^aFisher's exact test was applied.

^bCalculation of the Fisher's exact test was not possible for these data, and *p*-value is based on chi-squared test.

^cBased on 565 patients with ulcerative colitis (including unclassified inflammatory bowel disease) and 522 patients with Crohn's disease.

^d*p*-Value relates to the median values, and Mann–Whitney *U*-test was applied.

^eBased on 566 patients with ulcerative colitis (including unclassified inflammatory bowel disease) and 526 patients with Crohn's disease.

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 the 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.

3.4 | Self-perceived overall health of teeth and gums

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% confidence interval [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) (Table 4).

TABLE 4 Results of the binary logistic regression analyses for the dichotomous outcome parameter “self-perceived overall health of teeth and gums”; an odds ratio (OR) >1 indicates higher odds for perceiving the overall health of teeth and gums as fair or poor

Parameter	OR	95% CI		p-Value
		Lower	Upper	
<i>Base model</i>				
Patient group				
Control	Ref.			
Ulcerative colitis	2.348	1.936	2.849	<.001
Crohn's disease	3.210	2.640	3.902	<.001
Age				
Per unit (year)	0.998	0.993	1.003	.390
Gender				
Male	Ref.			
Female	0.980	0.828	1.164	.818
Smoking				
Never	Ref.			
Former	1.449	1.237	1.699	<.001
Current	2.799	2.310	3.392	<.001
<i>Final model</i>				
Patient group				
Control	Ref.			
Ulcerative colitis	2.147	1.726	2.670	<.001
Crohn's disease	2.736	2.195	3.412	<.001
PESS				
<5	Ref.			
≥ 5	18.856	15.087	23.566	<.001
Age				
Per unit (year)	0.950	0.943	0.957	<.001
Gender				
Male	Ref.			
Female	1.020	0.844	1.233	.836
Smoking				
Never	Ref.			
Former	1.233	1.030	1.476	.022
Current	1.072	0.854	1.346	.548

Note: Age, gender, and smoking status were defined as a priori confounders. Bold values indicate significance. Abbreviations: CI, confidence interval; PESS, periodontal screening score.

3.5 | PESS ≥ 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 $\geq 10\%$ by any of the potential confounders, that is, 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 (Table 5).

3.6 | Number of teeth

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 $\geq 10\%$ 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 of having fewer 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 of having fewer than 20 teeth (Table 6).

TABLE 5 Results of the binary logistic regression analyses for the dichotomous outcome parameter “periodontal screening score (PESS) ≥ 5 ”; an odds ratio (OR) >1 indicates higher odds for a PESS ≥ 5 (i.e., presence of self-reported severe periodontitis)

Parameter	OR	95% CI		p-Value
		Lower	Upper	
<i>Base model/final model^a</i>				
Patient group				
Control	Ref.			
Ulcerative colitis	1.739	1.360	2.224	<.001
Crohn's disease	2.574	1.998	3.316	<.001
Age				
Per unit (year)	1.116	1.107	1.126	<.001
Gender				
Male	Ref.			
Female	1.109	0.908	1.356	.311
Smoking				
Never	Ref.			
Former	1.966	1.620	2.385	<.001
Current	13.386	10.490	17.081	<.001

Note: Age, gender, and smoking status were defined as a priori confounders. Bold values indicate significance.

Abbreviations: CI, confidence interval.

^aNone of the potential confounders changed the OR of the main predictor by $\geq 10\%$, that is, the base and final model are identical.

TABLE 6 Results of the binary logistic regression analyses for the dichotomous outcome parameter “tooth number”; an odds ratio (OR) >1 indicates higher odds to have less than 20 teeth

Parameter	OR	95% CI		p-Value
		Lower	Upper	
<i>Base model</i>				
Patient group				
Control	Ref.			
Ulcerative colitis	1.158	0.867	1.547	.320
Crohn's disease	2.294	1.762	2.985	<.001
Age				
Per unit (year)	1.060	1.052	1.069	<.001
Gender				
Male	Ref.			
Female	0.914	0.730	1.146	.437
Smoking				
Never	Ref.			
Former	1.751	1.390	2.205	<.001
Current	4.038	3.106	5.249	<.001
<i>Final model</i>				
Patient group				
Control	Ref.			
Ulcerative colitis	1.041	0.776	1.398	.788
Crohn's disease	1.913	1.458	2.510	<.001
PESS				
<5	Ref.			
≥5	3.437	2.721	4.340	<.001
Age				
Per unit (year)	1.039	1.029	1.049	<.001
Gender				
Male	Ref.			
Female	0.895	0.711	1.126	.344
Smoking				
Never	Ref.			
Former	1.535	1.212	1.945	<.001
Current	2.292	1.723	3.049	<.001

Note: Age, gender, and smoking status were defined as a priori confounders. Bold values indicate significance. Abbreviations: CI, confidence interval; PESS, periodontal screening score.

4 | DISCUSSION

The present large-scale, questionnaire-based case-control 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, that is, 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 studies with larger samples, the OR ranged between 2 and 3 (Nijakowski et al., 2021; Y. Zhang et al., 2021), and, if the first large-scale, registry-based, cohort study with >135,000 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 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. PESS has recently been validated to show 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 inter-proximal sites with ≥6 mm attachment level [not on the same tooth] and ≥1 inter-proximal site with ≥5 mm probing pocket depth) were 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 (L. 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 <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 in good 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; L. Zhang et al., 2020; Tan et al., 2021). In this context, the 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 hence the need for 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; L. 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, 5–10 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 >40 years of age at baseline (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 relationship, that is, that presence of the one disease increases the risk for the development of the other, and/or when both are present, they aggravate each other. Indeed, it has been recently shown in pre-clinical 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 (Borngnakke, 2019) and suggested for other systemic conditions, for example, rheumatoid arthritis and 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, and so on, 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 comorbidities 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 fewer 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 as well as 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 with that in the IBD cases and is within the range of similar type of surveys previously conducted by Statistics Denmark (i.e., between 25% and 33%), which was also the basis for inviting 13,000 matched potential controls. Furthermore, according to the study design treating all answers anonymously, it was not possible to compare the non-responders with 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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CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

Conceptualization: Kristina Bertl, Corinna Bruckmann, and Andreas Stavropoulos. *Organization, execution and data collection:* Kristina Bertl, Johan Burisch, and Andreas Stavropoulos. *Data analysis, interpretation:* Kristina Bertl, Nikolaos Pandis, and Andreas Stavropoulos. *Manuscript drafting:* Kristina Bertl, Corinna Bruckmann, Johan Burisch, Björn Klinge, and Andreas Stavropoulos.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

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