Changes in Third Molar and Nonthird Molar Periodontal Pathology Over Time

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Purpose: The purpose of this study was to assess changes in periodontal probing depth (PD) over time for third molar and nonthird molar regions in young adults.

Patients and Methods: The data were obtained from healthy subjects with 4 asymptomatic third molars, enrolled in an IRB-approved longitudinal trial. Demographic and oral health data were collected at baseline. Full-mouth PD, 6 sites per tooth, was conducted to determine periodontal status at baseline and at longest follow-up. The third molar region was defined as the PD for 6 sites around the third molars and the 2 sites on the distal of the second molars. The nonthird molar region was defined as the remainder of the PD sites in the mouth. The primary outcome measures for this study were the occurrence of a PD greater than or equal to 4 mm and the increase in PD of at least 2 mm in the third molar and nonthird molar regions. Changes from enrollment to longest follow-up were compared by the binomial or McNemar's test. Level of significance was .05.

Results: Data from 195 subjects were available, and the median follow-up was 5.9 years (interquartile range [IQ], 4.6 to 6.9 years). Median age at enrollment was 26.2 years (IQ, 22.0 to 34.0 years); 52% were female, 84% were Caucasian, and 10% were African American. The proportion of subjects with at least 1 involved site in nonthird molars increased significantly from baseline to follow-up, 36% to 49% ($P < .01$), reflecting mostly changes in mandibular nonthird molars, 33% to 48% ($P < .01$). Of the 122 subjects who presented at baseline with at least 1 PD greater than or equal to 4 mm in the third molar region, the proportion of subjects with at least 1 involved site in nonthird molars increased significantly from baseline to follow-up, 48% to 59% ($P = .05$), also reflecting mostly changes in mandibular nonthird molars, 44% to 59% ($P = .05$).

Conclusion: In this unique longitudinal clinical study of early periodontal disease in young adults, periodontal pathology worsened over time for nonthird molars. This was more likely if PD greater than or equal to 4 mm was detected in the third molar region.

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Clinicians have implicated the molar regions of the mouth as clinical sites for the initiation of periodontal pathology, although data confirming this notion in young adults are limited. Blakey et al have reported that asymptomatic periodontal disease, defined as at least 1 periodontal probing depth (PD) greater than or equal to 5 mm, was detected in the third molar region at baseline in a quarter of young adults enrolled in a longitudinal trial.[1] Few subjects had PD greater than or equal to 5 mm affecting teeth more anterior in the mouth. Over a median 2.2-year follow-up, periodontal pathology worsened for a quarter of the subjects, defined as an increase in PD greater than or equal to 2 mm in the third molar region.[2] This periodontal progression was significantly more likely if baseline PD in the third molar region was greater than or equal to 4 mm, or if baseline subject level "orange" and "red" cluster periodontal pathogens were detected in amounts greater than or equal to 10^5.[3]

If the perceptions about the initiation of periodontal pathology are accurate, it would be expected that the proportion of subjects with periodontal disease in the nonthird molar region would increase significantly over time in those subjects with periodontal disease in the third molar region at baseline. To assess the relationship between third molar and nonthird molar periodontal pathology, this study was designed to analyze changes in periodontal probing depth in the young adults enrolled in our longitudinal study.

Patients and Methods

The data for these analyses are from subjects with 4 asymptomatic third molars enrolled in an IRB-approved longitudinal trial at 2 academic clinical centers, the University of Kentucky and the University of North Carolina. Inclusion criteria for the trial dictated that subjects be healthy (American Society of Anesthesiologists I, II), be between the ages of 14 and 45 years, and have 4 asymptomatic third molars with adjacent second molars. Subjects with the most severe form of periodontal disease (American Academy of Periodontology IV), or who had taken antibiotics within 3 months prior to enrollment were excluded from participation. Subjects were enrolled over a 4-year period ending in 2002.

Demographic data and data assessing oral health were collected from each subject at baseline and at follow-up examinations. Enrolled subjects had a dental prophylaxis after data collection at each visit. This ensured a minimal level of periodontal care for all subjects in the study, although study subjects were encouraged to continue to receive routine dental care from their dentist. To be included in these analyses, subjects had to have had a follow-up examination at least 4 years after enrollment.

Because White et al and Lieff et al have documented the association between increased PD and the detection of higher levels of periodontal pathogens, full-mouth periodontal probing, 6 sites per tooth, was considered a reliable measure of periodontal pathology and conducted as a measure of clinical periodontal status at baseline and follow-up.[3,4]

The oral cavity was divided into third molar and nonthird molar regions. The third molar region included the 6 third molar probing sites and the 2 distal probing sites of the second molars (maximum of 16 sites per jaw). The nonthird molar region included all remaining probing sites (maximum of 80 sites per jaw).

The primary outcome measures for this study were subject level changes in PD over time in the third molar and in nonthird molar regions. The maximum recorded PD, rounded to the lower whole number, was used to indicate the presence or absence of 3 subject-level aggregated measures considered of clinical significance in each jaw and oral region: *1*) the presence/absence of at least 1 PD greater than or equal to 4 mm; *2*) the presence/absence of at least 4 PD greater than or equal to 4 mm; and *3*) the presence/absence of an increase in PD greater than or equal to 2 mm from baseline to longest follow-up.[1-5]

Outcomes for the maxilla and mandible were analyzed separately because Blakey et al reported significant differences by jaw for PD at baseline.[1] An increase in PD greater than or equal to 2 mm from baseline to longest follow-up was considered progression of periodontal disease or worsening of periodontal pathology.[2] Having at least 4 PD greater than or equal to 4 mm detected around third molars was considered indicative of systemic exposure to periodontal pathogens, as suggested by Moss et al.[5]

Because White et al reported greater odds of periodontal progression in the third molar region if baseline PD was greater than or equal to 4 mm, data from subjects with and without third molar PD greater than or equal to 4 mm at baseline were analyzed separately as possible risk indicators of worsening periodontal status.[3]

Changes from baseline to longest follow-up were compared by McNemar's test or the binomial test for a single proportion when the baseline percentage was 0. Analyses were done separately for subjects at baseline who had no sites with greater than or equal to 4 mm PD in the third molar region and those with at least 1 site with greater than or equal to 4 mm PD in the third molar region. Level of significance was set at .05.

Results

Data from 195 subjects with follow-up at least 4 years after enrollment were available for analysis

Table 1. DEMOGRAPHIC CHARACTERISTICS AT BASELINE OF SUBJECTS WITH ASYMPTOMATIC THIRD MOLARS AND AT LEAST 4-YEAR FOLLOW-UP FOR DATA COLLECTION (n = 195) AND A COMPARISON BETWEEN THOSE SUBJECTS AT BASELINE WITH ALL PD <4 mm IN THE THIRD MOLAR REGION (n = 73) AND THOSE WITH AT LEAST 1 THIRD MOLAR SITE WITH PD ≥4 mm (n = 122)

	All Subjects		All Third Molar PD <4 mm		At Least 1 Third Molar PD ≥4 mm		
	n	%	n	%	n	%	*P* Value
Female	102	52	44	61	58	48	
Male	93	48	29	39	64	52	.08
Caucasian	162	83					
African American	21	11	4	2	17	9	.07
Other	12	6					
Median age in years at enrollment	26.3 IQ 22.0-34.0		24.1 IQ 19.2-32.6		28.2 IQ 22.9-34.9		.009
Median follow-up in years	5.9 IQ 4.6-6.9		5.3 IQ 4.3-6.4		6.1 IQ 5.0-6.9		.03

Abbreviation: IQ, interquartile range.

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(Table 1). Median follow-up was 5.9 years (interquartile range [IQ], 4.6 to 6.9 years). Median age at enrollment was 26.3 years (IQ, 22.0 to 34.0 years). More subjects were female (52%) and Caucasian (83%).

All third molars were removed in 40 subjects (20% of those studied) between baseline and longest follow-up. For these subjects, outcomes for the third molar region were predicated on the PD from the distal of the second molars at longest follow-up and on the third molar PD at the examination closest to the third molar removal. At baseline, 57% of those who had third molars removed had at least 1 probing site in the third molar region with a PD greater than or equal to 4 mm.

For the entire sample, the percentage of subjects with at least 1 third molar region PD greater than or equal to 4 mm increased minimally from baseline to follow-up, 63% to 64% (Table 2). During the same time frame, the percentage of subjects with a nonthird molar PD greater than or equal to 4 mm increased significantly, 36% to 49% ($P = .005$), reflecting chiefly changes in mandibular nonthird molars, 33% to 48% of subjects ($P = .0008$). Perhaps more important clinically, a significant increase from baseline to follow-up occurred in the proportion of subjects who met the criterion of at least 4 sites with PD greater than or equal to 4 mm in the third molar and in the nonthird molar region, 27% to 37% ($P = .006$) and 14% to 21% ($P = .04$), respectively. Significant changes in the mandible accounted for the increase, 23% to 33% ($P = .008$) and 11% to 19% ($P = .007$) of subjects, for the third molar and nonthird molar regions, respectively.

A more accurate clinical picture of the changes over time was obtained by analyses done separately for those subjects who, at baseline, had no sites with

Table 2. PERCENTAGE OF SUBJECTS, BY JAW AND REGION AT BASELINE AND LONGEST FOLLOW-UP, WITH AT LEAST 1 PERIODONTAL PROBING SITE ≥4 mm, (n = 195)

	At Least 1 Site With PD ≥4 mm			At Least 4 Sites With PD ≥4 mm		
	Baseline	Follow-Up	*P* Value	Baseline	Follow-Up	*P* Value
Maxilla						
Third molar region	17%	21%	.4	7%	7%	.7
Nonthird molar region	15%	15%	1.0	5%	8%	.2
Mandible						
Third molar region	61%	61%	1.0	23%	33%	.008
Nonthird molar region	33%	48%	.001	11%	19%	.007
Subject level						
Third molar region	63%	64%	.8	27%	37%	.006
Nonthird molar region	36%	49%	.005	14%	21%	.04

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Table 3. PERCENTAGE OF SUBJECTS WHO, AT BASELINE, HAD <4 mm PERIODONTAL PROBING DEPTHS FOR ALL THIRD MOLAR REGION SITES (n = 73), BY JAW AND REGION AT BASELINE AND FOLLOW-UP

	At Least 1 Site With PD ≥4 mm			At Least 4 Sites With PD ≥4 mm		
	Baseline	Follow-Up	*P* Value	Baseline	Follow-Up	*P* Value
Maxilla						
Third molar region	0%	7%	.5	0%	1%	.9
Nonthird molar region	8%	10%	.8	0%	3%	.8
Mandible						
Third molar region	0%	37%	.0001	0%	11%	.3
Nonthird molar region	15%	29%	.04	1%	14%	.007
Subject level						
Third molar region	0%	40%	.0001	0%	12%	.3
Nonthird molar region	18%	32%	.04	5%	15%	.05

P values for third molar region from binomial test; for nonthird molar region from McNemar's test.

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PD greater than or equal to 4 mm in the third molar region (n = 73) and those with at least 1 site with PD greater than or equal to 4 mm in the third molar region (n = 122). Significant differences were found for age ($P = .009$) and median follow-up ($P = .03$) (Table 1). Subjects with no periodontally involved third molars at baseline were younger (24.1 vs 28.2 years on average) and had been followed for a shorter period of time (5.3 vs 6.1 years on average). Although not statistically significant, the percentage of males and the percentage of African Americans with third molar region PD greater than or equal to 4 mm were higher.

For those with no third molar region PD greater than or equal to 4 mm at baseline, the percentage of subjects with at least 1 PD greater than or equal to 4 mm in the third molar region at follow-up was 40%, with mandibular sites being the primary contributors (37%) (Table 3). Twelve percent had at least 4 sites with PD greater than or equal to 4 mm in the third molar region at follow-up.

If subjects had no third molar region PD greater than or equal to 4 mm at baseline, a relatively small percentage had at least 1 site with a PD greater than or equal to 4 mm in the nonthird molar region at baseline (Table 3). A significant increase was evident in the proportion of subjects with at least 1 PD greater than or equal to 4 mm in the nonthird molar region from baseline to follow-up, 18% to 32% ($P = .04$) of subjects, reflecting mostly changes in subjects' mandibular nonthird molars, 15% to 29% ($P = .04$). The maxilla was affected minimally, 10% or less at baseline and follow-up. Similarly, the percentage of subjects with at least 4 sites with PD greater than or equal to 4 mm in nonthird molars was significantly increased at follow-up, 5% to 15% ($P = .05$), again reflecting changes in mandibular nonthird molars, 1% to 14% ($P = .007$). Ten percent of these 73 subjects had at least 1 third molar region probing site that increased at least 2 mm during the follow-up period (data not displayed). None of the nonthird molar region probing sites increased by 2 mm.

Of the 122 subjects who presented at baseline with at least 1 PD greater than or equal to 4 mm in the third molar region, virtually all (98%) had 1 involved site in the mandible (Table 4). The maxilla was affected in fewer subjects, 28%. The number of these subjects with at least 1 PD greater than or equal to 4 mm in the third molar region decreased to 78% at follow-up. In contrast, the proportion of subjects with at least 1 PD greater than or equal to 5 mm detected in the third molar region at baseline, was increased at follow-up, 40% to 47% (data not shown).

For these 122 subjects, the proportion with at least 1 involved site in the nonthird molar region increased significantly from baseline to follow-up, 48% to 59% ($P = .05$). The increase reflected the increase in affected mandibular nonthird molar sites, 44% to 59% ($P = .01$). By follow-up, half of the subjects had at least 4 sites with PD greater than or equal to 4 mm in the third molar region, and one quarter had at least 4 sites with PD greater than or equal to 4 mm in nonthird molars (Table 4). Eleven percent of these subjects had at least 1 third molar region and 1 nonthird molar region probing site increase by at least 2 mm (data not shown).

If no periodontal involvement was detected in the third molar region at baseline, the number of probing sites greater than or equal to 4 mm per subject increased minimally at follow-up (Table 5). At baseline, subjects with at least 1 third molar region PD greater than or equal to 4 mm presented with a median of 3 of a possible 32 probing sites with PD greater than or equal to 4 mm in the third molar region and substantially fewer affected probing sites greater than or equal to 4 mm in the nonthird molar region. The number of probing sites greater than or equal to 4 mm in the mandible was considerably higher than in the

Table 4. PERCENTAGE OF SUBJECTS WHO, AT BASELINE, HAD AT LEAST 1 SITE WITH ≥4 mm PERIODONTAL PROBING DEPTH IN THE THIRD MOLAR REGION (n = 122), BY JAW AND REGION AT BASELINE AND FOLLOW-UP

	At Least 1 Site With PD ≥4 mm			At Least 4 Sites With PD ≥4 mm		
	Baseline	Follow-Up	P Value	Baseline	Follow-Up	P Value
Maxilla						
Third molar region	28%	29%	.9	11%	11%	1.0
Nonthird molar region	19%	18%	.8	7%	10%	.4
Mandible						
Third molar region	98%	75%	<.001	37%	47%	.08
Nonthird molar region	44%	59%	.01	17%	22%	.2
Subject level						
Third molar region	100%	78%	<.001	43%	52%	.09
Nonthird molar region	48%	59%	.05	20%	24%	.3

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maxilla. At follow-up, the most affected subjects, those in the upper quartile, had at least 7 of a possible 32 probing sites and 6 of a possible 16 mandibular probing sites greater than or equal to 4 mm detected in the third molar region (Table 5). Fewer nonthird molar probing sites greater than or equal to 4 mm were detected at follow-up.

Discussion

In these young, asymptomatic adult subjects, the most clinically relevant findings of our study over time were that periodontal pathology was detected more often in the third molar and in nonthird molar regions than clinicians might expect. Two thirds of the 195 study subjects had a third molar region with PD greater than or equal to 4 mm at longest follow-up, most often in the mandible. A finding of at least 1 PD greater than or equal to 4 mm was detected in nonthird molars in half of the 195 study subjects at longest follow-up, more likely if at least 1 third molar region PD greater than or equal to 4 mm was present at baseline. Among subjects with no third molar region periodontal pathology at baseline, 40% developed PD greater than or equal to 4 mm in the third molar region over the study time frame, accompanied by significant changes in nonthird molars. Periodontal pathology largely reflected clinical findings in the mandible for both the third molar and nonthird molar regions and was detected less often in the maxilla in these subjects.

From a clinical perspective, our data suggest that periodontal pathology developing over time anterior to the third molar region may incrementally follow periodontal pathology detected in the mandibular third molar region. As displayed in Tables 3 and 4, subjects with nonthird molar probing sites at least 4 mm increased from baseline to longest follow-up,

Table 5. A COMPARISON OF THE DISTRIBUTION OF THE NUMBER OF PROBING SITES PER SUBJECT WITH A PERIODONTAL PROBING DEPTH OF ≥4 mm FOR THOSE WHO, AT BASELINE, HAD NO SITE IN THE THIRD MOLAR REGION WITH A PD ≥4 mm (n = 73) AND THOSE WHO HAD AT LEAST 1 PD ≥4 mm IN THE THIRD MOLAR REGION (n = 122)

	All PD <4 mm in Third Molar Region at Baseline						At Least 1 PD ≥4 mm in Third Molar Region at Baseline					
	Baseline			Follow-Up			Baseline			Follow-Up		
	P25	P50	P75	P25	P50	P75	P25	P50	P75	P25	P50	P75
Maxilla												
Third molar region	0	0	0	0	0	0	0	0	0	0	0	1
Nonthird molar region	0	0	0	0	0	0	0	0	0	0	0	0
Mandible												
Third molar region	0	0	0	0	0	2	1	3	5	1	3	6
Nonthird molar region	0	0	0	0	0	1	0	0	2	0	1	3
Subject level												
Third molar region	0	0	0	0	0	2	1	3	5	1	4	7
Nonthird molar region	0	0	0	0	0	2	0	0	3	0	1	3

Abbreviations: P25, lower quartile; P50, median; P75, upper quartile.

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more likely if third molar PD was greater than or equal to 4 mm. However, these analyses do not show "cause and effect." We plan to explore this topic further, assessing also the relationships between the detection of periodontal pathogens at baseline and changes in periodontal probing depth over time and the impact of third molar removal on periodontal pathology detected in nonthird molars.

Although few in number, other clinical studies of young adults have suggested that third molars were associated with periodontal pathology in nonthird molars. In a US population sample aged 18 to 34 years from the Third National Health and Nutrition Examination Survey (NHANES III), Elter et al reported that a visible third molar was associated with twice the odds of a prevalent PD greater than or equal to 5 mm on the adjacent second molar, while controlling for other factors associated with visible third molars and periodontal disease.[6] No third molar periodontal probing measures were collected from these subjects.

Moss et al have reported that third molar periodontal pathology detected at enrollment in subjects studied over the course of pregnancy, defined as either PD greater than or equal to 4 mm or bleeding on probing around third molars, increased the odds of periodontal disease progression throughout the mouth by postpartum clinical examination, defined as at least 4 probing sites with increased PD greater than or equal to 2 mm with resulting PD greater than or equal to 4 mm.[7]

Do increased periodontal probing depths around third molars represent "pseudopockets," a condition thought to be clinically benign? White et al have reported data on third molar periodontal pathology over time from young adult subjects. At enrollment, periodontal probing depths at least 5 mm in the third molar region were associated with high levels ($\geq 10^5$) of "orange" and "red" cluster periodontal pathogens.[8] Detection of these pathogens at enrollment doubled the odds of periodontal disease progression, an increase in third molar probing depths of at least 2 mm in a 2-year time frame.[3] In the National Institutes of Health-sponsored longitudinal clinical study, Oral Conditions and Pregnancy (OCAP), periodontal probing depths were specifically chosen as risk markers because of the high levels of periodontal pathogens detected at enrollment and the documented risks of systemic exposure to the pathogens.[4] We conclude that "pseudopockets" may not be benign, and increased periodontal probing depths are risk markers for periodontal pathology.

These clinical findings are consistent with current biological models of periodontal disease that indicate that the acquisition of recognized periodontal pathogens is critical for the initiation and progression of periodontal pathology.[9] If a patient's neutrophils and the associated immune response cannot control these pathogenic bacteria colonized in the accumulated biofilm on the involved teeth, periodontal tissue destruction detected clinically by increased PD follows.

The detection and quantification of the levels of periodontal pathogens are facilitated by technology using whole chromosomal DNA probes and checkerboard DNA-DNA hybridization. Specific bacterial species, including *P. gingivalis* and *T. forsythus* of the "red cluster," possess virulence traits empowering the microorganisms to bypass the immune defenses of the host patient. These organisms, when detected in high numbers, are risk factors for periodontal disease.[10,11]

In previous publications on the cohort we are studying, elevated subject levels of the gingival crevicular fluid inflammatory mediator, IL-1β, were detected in subjects with increased PD greater than or equal to 5 mm in the third molar region at baseline, suggesting an inflammatory response compatible with early periodontal disease.[12] After a short follow-up, the clinical finding at baseline of at least 1 site in the third molar region of PD greater than or equal to 4 mm led to 20-fold increased odds of a worsening periodontal condition in a third molar region probing site. The data we report here amplify the earlier findings on our study subjects.

In the aggregate, our data suggest that our study subjects have early periodontal disease. Although a third of subjects showed at least 4 sites with PD greater than or equal to 4 mm in the third molar region at follow-up, only one fifth of subjects had 4 or more PD greater than or equal to 4 mm at follow-up in nonthird molars. However, if multiple probing sites greater than or equal to 4 mm are detected, affected individuals are potentially at risk for a systemic inflammatory response to periodontal pathology.

Moss et al have reported that young adult pregnant subjects in OCAP with the more severe levels of periodontal pathology at enrollment less than 26 weeks gestation, those in the highest quartile of third molars with at least 4 PD greater than or equal to 4 mm, had more than double the relative risk of preterm birth, similar to the odds of smoking during pregnancy.[5] Also, this level of third molar periodontal pathology was significantly associated with elevated serum levels of C-reactive protein, an acute phase inflammatory response from the liver, and of the prostaglandin, d8iso, reflecting levels of free-radical formation. The topic will be studied further in our subjects with longer follow-up.

How do we interpret the finding that fewer subjects had third molar region PD greater than or equal to 4 mm at follow-up than at baseline? Each subject in our trial had a dental prophylaxis after data collection at baseline and at each follow-up visit, usually at

yearly intervals. This treatment could have improved the clinical status of some subjects with third molar region PD greater than or equal to 4 mm at baseline. In addition, a "Hawthorne effect" is probable from study participation. Those in the clinical trial may be more aware of their periodontal status and, as a result, may have been more attentive to home care and sought treatment more regularly from their dentist.

However, the proportion of subjects with more severe periodontal pathology detected at baseline did not decrease over time. Subjects with at least 1 PD greater than or equal to 5 mm or at least 4 sites with PD greater than or equal to 4 mm in the third molar region and in nonthird molars were increased at follow-up, suggesting that prophylaxis therapy alone may not be adequate to prevent worsening of periodontal pathology. The timing and effectiveness of the treatment of third molar periodontal pathology by scaling and root planing, perhaps combined with antimicrobial therapy, should be studied further.

Our data demonstrating early periodontal disease in young adult subjects should be interpreted with some caution. Although our study subjects are a diverse group of young adults retaining asymptomatic third molars, they are not a sample representative of the United States population. However, the data we report from our study subjects suggest that a clinical finding of PD greater than or equal to 4 mm in the third molar region should not be ignored.

We urge patients and their dentists to carefully consider treatment options when PD greater than or equal to 4 mm is detected in the third molar region, with or without attachment loss found more often in older populations with periodontal disease. Considering that periodontal pathology in the third molar region is difficult to treat effectively, the more prudent option for most patients with early diagnosed third molar periodontal pathology might be third molar removal. Although this clinical option can be considered rational treatment, it is not tested by our study to date. However, these data do provide the first longitudinal data of early periodontal disease in young adults. Our subsequent analyses, including the impact of third molar removal in affected subjects in our study, may further clarify treatment decisions regarding asymptomatic third molars.

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