Discrepancy of Clinical Parameters between the First and Second Molars Can Help to Differentiate Subjects with Aggressive Periodontitis from Chronic Periodontitis: a Cross-sectional Study Based on a Large Chinese Population

Jian JIAO, Jing Ren ZHAO, Li ZHANG, Dong SHI, Rui Fang LU, Huan Xin MENG

Objective: To explore associations between mean discrepancy values for the first and second molars (MDVFSs) and generalised aggressive periodontitis (GAgP) using hospital-based periodontal examination records from a large Chinese population.

Methods: Data from consecutive patients diagnosed as having chronic periodontitis (CP, n = 51,849) and GAgP (n = 2,706) were included. Patient ages, gender, smoking status, mean full-mouth probing depth (PD), and mean full-mouth attachment loss (AL), as well as MDVFSs for PD and AL, were extracted. Multivariate linear regression was used to test associations between MDVFSs and GAgP.

Results: After multivariate risk adjustment for potential confounding factors (age, smoking status, and mean PD and AL), the MDVFSs for PD (OR = 2.20, 95%CI: 2.04 to 2.38, P < 0.001) and AL (OR = 1.51, 95%CI: 1.44 to 1.59, P < 0.001) were significantly associated with GAgP. The probability of GAgP was associated with MDVFS for PD falling between 0 mm and 2.5 mm (OR = 4.55, 95%CI: 4.01 to 5.17) and MDVFS for AL falling between 0 mm and 3.5 mm (OR = 2.01, 95%CI: 1.86 to 2.16, P < 0.001).

Conclusion: This study revealed associations between MDVFSs and GAgP, demonstrating that MDVFSs can serve as promising auxiliary references for the differential diagnosis between CP and GAgP.

Key words: aggressive periodontitis, chronic periodontitis, diagnosis


Chronic periodontitis (CP) and aggressive periodontitis (AgP) are the two major forms of periodontitis. Clinically, they differ in many aspects, such as rates of progression, age of disease onset, patterns of periodontal destruction, clinical signs of gingival inflammation, and the relative abundance of dental plaque and calculus.1 Most clinicians and scientists consider that there is no specific pattern of periodontal damage to the number and types of teeth involved for patients with CP and patients with generalised aggressive periodontitis (GAgP)1-3. However, an analysis of periodontal examination data from 34,677 patients with periodontal disease who visited the Department of Periodontology, Peking University School, and Hospital of Stomatology, between 2012 and 2017 revealed differences in tooth-specific characteristics between subjects with CP and those with GAgP.4 In patients with CP, the mean probing depth (PD) and attachment loss (AL) of the first molars tended to be smaller than those of the second molars. By contrast, the mean PD and AL of the first

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molars tended to be greater than those of the second molars in patients with GAgP.

Based on the findings above, the purpose of the present study is to explore associations between the discrepancy of clinical parameters between first molar sand second molars and GAgP by examining data from hospital-based periodontal examination records from a large Chinese population, and to investigate the potential value of the discrepancy to the differential diagnosis between chronic periodontitis and aggressive periodontitis. The hypothesis of the present study was that mean discrepancy values between the first molars and the second molars (MDVFS) of PD and AL were associated to GAgP.

Materials and methods

Study population
Consecutive patients who visited the Department of Periodontology, Peking University School and Hospital of Stomatolgy between January 2007 and January 2015 were involved in this retrospective cross-sectional study.

No informed consent was required since the data were anonymous. The study was approved by the Ethics Committee of the Peking University School and Hospital of Stomatology (approval number: PKUSSIRB-201310066). All protocols were performed in accordance with approved guidelines and regulations.

The inclusion criteria were: i) patients diagnosed with CP or GAgP according to the classification proposed at the International Workshop for the Classification of Periodontal Diseases and Conditions in 19992, ii) aged between 12 ~ 80 years old, iii) at least one pair of first and second molars in the same quadrant and iv) systemically healthy.

The exclusion criteria were: i) patients diagnosed with diseases other than CP or GAgP, ii) younger than 12 years old or over 80 years old, iii) no pair of first and second molars in the same quadrant and iv) systemically compromised (e.g. acquired immune deficiency syndrome; diabetes mellitus; nephrosis; hepatopathy; hypertension; neutropenia etc.) or pregnancy or under medication known to affect periodontium.

The process of patient selection and screening is presented in Figure 1.

Data extraction

The following periodontal parameters were extracted from the electronic records at the patient’s initial visit: i) age at initial visit, ii) gender (male vs female), iii) smoking status (non-smoker vs smoker), iv) full-mouth mean PD, iv) full-mouth mean AL, v) mean PD of the first molar or the second molar included for analysis, vi) mean PD of the first molar or the second molar included for analysis, vii) whether the first molar or the second molar included for analysis was lost or not, viii) MDVFS of PD, calculating by the subtraction between mean PD of the first molar and mean PD of the second molar in the same quadrant and ix) MDVFS of AL, calculating by the subtraction between mean AL of the first molar and mean AL of the second molar in the same quadrant.

Statistical analysis

The statistical analysis was performed with R (http://www.R-project.org) and EmpowerStats (www.empowerstats.com; X&Y solutions, Boston, MA, USA) software. Firstly, the distribution of continuous variables between CP and GAgP was compared by t test (for normal distributions) or the Kruskal–Wallis rank sum test (for non-normal distributions), while that of categorical
Table 1  Demographic data and main periodontal parameters of included subjects.

<table>
<thead>
<tr>
<th></th>
<th>CP</th>
<th>AgP</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>27,489 (53.02%)</td>
<td>1,471 (54.36%)</td>
<td>0.169</td>
</tr>
<tr>
<td>Male</td>
<td>24,360 (46.98%)</td>
<td>1,235 (45.64%)</td>
<td></td>
</tr>
<tr>
<td>Smoking status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-smoker</td>
<td>41,307 (79.67%)</td>
<td>2,233 (82.52%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Smoker</td>
<td>10,542 (20.33%)</td>
<td>473 (17.48%)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>51,849</td>
<td>2,706</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>44.33 ± 13.57</td>
<td>30.74 ± 5.76</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Mean PD on subject level (mm)</td>
<td>3.37 ± 0.80</td>
<td>4.40 ± 1.04</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Mean AL on subject level (mm)</td>
<td>3.66 ± 1.07</td>
<td>4.80 ± 1.22</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>MDVFS (mean PD, mm)</td>
<td>-0.23 ± 0.53</td>
<td>0.19 ± 0.77</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>MDVFS (mean AL, mm)</td>
<td>-0.05 ± 0.79</td>
<td>0.57 ± 1.13</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

Mean ± SD or N (percentage).
CP: Chronic periodontitis; AgP: Aggressive periodontitis; PD: probing depth; AL: attachment loss; MDVFS: mean discrepancy value between first and second molars.

Table 2  Univariate logistic regressions between candidate confounding factors or factors of interest and the diagnosis of aggressive periodontitis (chronic periodontitis as referent).

<table>
<thead>
<tr>
<th></th>
<th>OR</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>0.95</td>
<td>(0.88, 1.02)</td>
<td>0.169</td>
</tr>
<tr>
<td>Smoking status</td>
<td>0.83</td>
<td>(0.75, 0.92)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Age</td>
<td>0.90</td>
<td>(0.90, 0.91)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Mean PD on subject level (mm)</td>
<td>1.94</td>
<td>(1.89, 1.99)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Mean AL on subject level (mm)</td>
<td>2.94</td>
<td>(2.83, 3.05)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>MDVFS (mean PD, mm)</td>
<td>3.40</td>
<td>(3.19, 3.63)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>MDVFS (mean AL, mm)</td>
<td>1.89</td>
<td>(1.82, 1.96)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

PD: probing depth; AL: attachment loss; MDVFS: mean discrepancy value between first and second molars.

variables was compared using the $\chi^2$ test (Table 1). Secondly, univariate logistic regression models were used to test for correlations of the MDVFS for PD, that for AL, and other covariates with GAgP (Table 2). Thirdly, multivariate logistic regression models were used to evaluate whether the MDVFSs for PD and AL were associated with GAgP, with adjustment for potential confounding factors identified in the univariate analysis (Table 3). We then explored the relationships between GAgP and the MDVFSs for PD and AL, respectively, using smoothing plots with adjustment for potential confounders (Fig 2). We further applied two three-piecewise logistic regression models to examine the threshold effects of the MDVFSs for PD and AL on GAgP according to the
smoothing plot results (Table 3). A two-sided $P$ value of $< 0.05$ was considered significant.

Results

In total, 51,849 (95.04%) patients with CP and 2,706 (4.96%) patients with GAgP were included in this study. Table 1 lists the demographic and clinical characteristics of the subjects. There was no significant difference in the distribution of male and female patients between the CP and GAgP groups. The GAgP group contained a larger proportion of smokers than the CP group (20.33% vs 17.48%, $P < 0.001$). At the time of their initial visit, patients in the GAgP group were significantly younger than those in the CP group (30.73 mm vs 44.33 years, $P < 0.001$). Full-mouth mean PD and AL were significantly larger in the GAgP group than in the CP group (4.40 mm vs 3.37 mm and 4.80 mm vs 3.66 mm, respectively; both $P < 0.001$). Similarly, mean PD and AL of both the first and second molars included in the analysis were larger in the GAgP group than in the CP group (5.18 mm vs 3.93 mm and 4.98 mm vs 4.17 mm, respectively; both $P < 0.001$). Subjects with GAgP had lost fewer first and second molars than subjects with CP (0.32 vs 0.44 and 0.20 vs 0.44, respectively; both $P < 0.001$). The numbers of first and second molars lost differed significantly among patients with GAgP (0.32 vs 0.20, $P < 0.001$), but not among those with CP. Additionally, significantly greater MDVFSs for PD and AL were found in the GAgP group compared with the CP group (0.19 mm vs -0.23 mm and 0.57 mm vs -0.05 mm, respectively; both $P < 0.001$).

The univariate regression analyses revealed that the MDVFSs for PD [odds ratio (OR) 3.40, 95% confidence interval (CI) 3.19 to 3.63, $P < 0.001$] and AL (OR 1.89, 95% CI 1.82 to 1.96, $P < 0.001$) were associated significantly with GAgP. Additionally, smoking status (OR 0.83, 95% CI 0.75 to 0.92, $P < 0.001$), patient age (OR 0.90, 95% CI 0.90 to 0.91, $P < 0.001$), mean full-mouth PD (OR 1.94, 95% CI 1.89 to 1.99, $P < 0.001$), and mean full-mouth AL (OR 2.94, 95% CI 2.83 to 3.05, $P < 0.001$) were associated with GAgP (Table 2).

After adjusting for potential confounders, MDVFSs for PD (OR 2.20, 95% CI 2.04 to 2.38, $P < 0.001$) and AL (OR 1.51, 95% CI 1.44 to 1.59, $P < 0.001$) were associated significantly with GAgP (Table 3). After further adjustment for factors potentially related to GAgP, including age, smoking status, and mean PD and AL, nonlinear relationships were observed between MDVFSs for PD and AL and GAgP (Fig 2). Generally, the probability of GAgP increased with the MDVFSs. Additionally, the smoothing plots showed clear inflection points (0 mm and 2.5 mm for MDVFS for PD and 0 mm and 3.5 mm for the MDVFS for AL). The probability of GAgP was associated with MDVFSs for PD falling between 0 mm and 2.5 mm (OR 5.84, 95% CI 5.32 to 6.40, $P < 0.001$), but not with values falling outside this range. Similarly, the probability of GAgP was associated with MDVFS for AL falling between 0 mm and 3.5 mm (OR 2.25, 95% CI 2.14 to 2.37, $P < 0.001$).

### Table 3

Multivariate logistic regressions and their stratified analysis between factors of interest and the diagnosis of aggressive periodontitis (chronic periodontitis as referent).

<table>
<thead>
<tr>
<th></th>
<th>Non-adjusted</th>
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<th>Adjusted</th>
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<tbody>
<tr>
<td></td>
<td>OR  95%CI</td>
<td>$P$</td>
<td>OR  95%CI</td>
<td>$P$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MDVFS (mean PD, mm)</td>
<td>3.40 (3.19, 3.63)</td>
<td>$&lt; 0.001$</td>
<td>2.20 (2.04, 2.38)</td>
<td>$&lt; 0.001$</td>
<td></td>
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<tr>
<td>&lt; 0</td>
<td>1.34 (1.17, 1.52)</td>
<td>$&lt; 0.001$</td>
<td>0.91 (0.79, 1.05)</td>
<td>0.186</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 – 2.5</td>
<td>5.84 (5.32, 6.40)</td>
<td>$&lt; 0.001$</td>
<td>4.55 (4.01, 5.17)</td>
<td>$&lt; 0.001$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 2.5</td>
<td>0.49 (0.10, 2.39)</td>
<td>0.374</td>
<td>0.23 (0.02, 2.59)</td>
<td>0.233</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MDVFS (mean AL, mm)</td>
<td>1.89 (1.82, 1.96)</td>
<td>$&lt; 0.001$</td>
<td>1.51 (1.44, 1.59)</td>
<td>$&lt; 0.001$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 0</td>
<td>1.51 (1.32, 1.73)</td>
<td>$&lt; 0.001$</td>
<td>0.87 (0.76, 1.01)</td>
<td>0.060</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 – 3.5</td>
<td>2.25 (2.14, 2.37)</td>
<td>$&lt; 0.001$</td>
<td>2.01 (1.86, 2.16)</td>
<td>$&lt; 0.001$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 3.5</td>
<td>0.85 (0.54, 1.35)</td>
<td>0.496</td>
<td>0.82 (0.42, 1.61)</td>
<td>0.562</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

PD: probing depth; AL: attachment loss; MDVFS: mean discrepancy value between first and second molars.

* Adjusted by age, smoking status, mean PD on subject level.

# Adjusted by age, smoking status, mean AL on subject level.
but not with values falling outside this range (Table 3).

Discussion

In general, the results of the present study indicated that MDVFSs are associated with GAgP. In the univariate analysis, the OR for GAgP of the MDVFS for PD was greater than that of mean full-mouth PD. The associations between MDVFSs and GAgP revealed the potential value of MDVFSs in the differential diagnosis between CP and GAgP.

Smoothing plots showed that the relationships between GAgP and the MDVFSs for PD and AL were nonlinear (Fig 2). When the MDVFS was < 0 mm, periodontal destruction of the first molar was not greater than that of the second molar, and the association between the MDVFS and GAgP was therefore insignificant (Table 3). Therefore, the diagnostic value of the MDVFS is limited for patients with more advanced disease in the second molars than in the first molars, and clinicians should make appropriate diagnosis based on comprehensive consideration of patients’ histories and clinical examination findings in these cases.

However, when the MDVFS exceeded 0 mm, and especially when the MDVFS for PD was ≤ 2.5 mm and for AL was ≤ 3.5 mm, it was associated significantly with GAgP (Table 3). In such cases, clinicians should recognize the probability that patients have GAgP. Our study found that the probability of GAgP increased by more than three times and one time, respectively, with 1 mm increases in PD and AL values (Table 3). Moreover, MDVFSs that exceeded the identified inflection points (2.5 mm for PD and 3.5 mm for AL) were not associated with GAgP in this study. This lack of association might be attributable to the small sample of patients with AgP, with such MDVFSs and/or bias caused by the retrospective nature of the study.

Currently, diagnosis of AgP is mainly reliant on patient history, as well as clinical and radiographic examinations. However, history and clinical assessments sometimes fail to provide a clear discrimination of CP and AgP. Almost all the processing of history taking is retrospective and incomplete and false information may challenge the precision of diagnosis. Firstly, one of the main points of diagnosis of AgP is the rate of the progression of the disease. However, longitude records of patients are needed to estimate the rate of progression, which is always inaccessible for patients at the initial visit. Moreover, progression velocity may also be influenced by environmental factors, such as oral hygiene or smoking, and clinicians seem very subjective and have different understanding on the high rate of progression of AgP. Secondly, early onset of the disease is another diagnostic reference of AgP. However, for patients from an area where adequate dental care was inaccessible, or patients with no dental health care awareness, they may visit for periodontal treatment.
at a very advanced stage\textsuperscript{23,24}. The difficulty in getting definite onset time of the disease may also hinder an accurate diagnosis. Thirdly, it may sometimes be difficult to confirm whether there is a familial aggregation of AgP in the patient’s core family. In addition, not every subject with AgP has a definite positive finding of a family history. A study that involved 27 probands with AgP and their relatives showed that only 8% examined relatives were affected with AgP\textsuperscript{25}.

Instead of only including patients under 35 years old to allow comparison of patients with CP and GAgP within the same age band, subjects over 35 years old with CP were also included in the present study. Including these patients was mainly because analysing patients with CP from a large age range may better reflect the nature of patients with CP, rather than young patients with CP. In addition, a significantly greater mean number of tooth losses were found in the CP group compared with the GAgP group, due to the fact that many patients in the CP group were elderly subjects with advanced periodontal destruction and loss of many teeth.

The present study indicates a new way of differentiating GAgP from CP: tooth specificity. The fact that more advanced periodontal damage in the first molars than in the second molars can work as an auxiliary reference of AgP diagnosis. Moreover, instead of complex and costly laboratory examinations, clinicians can get extra diagnostic information simply by using a periodontal probe for measurement. Moreover, for a patient over 35 years old with generalised severe periodontal damage, it is hard to figure out whether the patient is GAgP or CP. MDVFS may be a useful tool for auxiliary diagnosis.

However, as the present study was merely a pilot study, more precise analysis, such as exploring the cutting point of MDVFS, or its sensitivity and specificity for a diagnostic test was needed. In addition, radiographic measurements should be performed to test whether a discrepancy between alveolar bone loss of the first and second molars is associated to GAgP.

The association between MDVFS and GAgP can be explained by the following reasons. Firstly, periodontal damage of the first molar is an important reference of diagnosis of localised aggressive periodontitis (LAgP)\textsuperscript{2}, and some academics hold that patients with GAgP always developed from patients with LAgP\textsuperscript{1,26}. Therefore, first molars are the most commonly and severely involved teeth in the entire dentition. Secondly it is well known that the first molar is the first permanent tooth to erupt in the mouth, while the second molar is the last one to erupt\textsuperscript{27}. Several researchers reported that periodontal destruction may also start immediately after the eruption of the teeth\textsuperscript{3,7,8,15}. Therefore, the high rate of regression and the difference of eruption timing might result in the discrepancy of periodontal parameters between the first and second molars.

This study shares limitations with all retrospective studies. Differences in population characteristics and confounding factors may have introduced bias, compromising the validity of the outcomes\textsuperscript{28}. However, the inclusion of a large sample renders the results of the present study resistant to random errors, and thus more reliable. Additionally, data from patients lacking molar pairs in the same quadrant were excluded from the analysis. The results of the present study show that young adults with GAgP have lost more first than second molars (Table 1). Therefore, the exclusion of data from unpaired molars may have led to underestimation of the strength of associations, but not of their validity.

**Conclusion**

This hospital-based cross-sectional study revealed associations between MDVFSs and GAgP in a large Chinese population. MDVFS for PD falling between 0 mm and 2.5 mm and that of AL falling between 0 mm and 3.5 mm were associated positively with GAgP and MDVFSs can serve as promising auxiliary references for the differential diagnosis between CP and GAgP.

**Acknowledgements**

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**Conflicts of interest**

The authors reported no conflicts of interest related to this study.

**Author contribution**

Dr Jian JIAO designed the study, collected and analysed data and prepared the manuscript; Drs Jing Ren ZHAO and Li ZHANG designed the study; Dr Dong SHI collected data; Dr Rui Fang LU analysed data; Dr Huan Xin MENG critically revised the manuscript.

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References


Erratum

Gao et al, for their paper entitled “Optimal Matrix Preparation Methods for Matrix-assisted Laser Desorption/Ionization Time-of-flight Mass Spectrometry Profiling of Low Molecular Weight Peptides in Human Saliva and Serum Samples”, published in the Chinese Journal of Dental Research (CJDR) 2018;21:51–61, have stated that Tables 1 and 2 in their paper were mostly modified from tables in the paper by Penno et al, published in Rapid Communications in MassSpectrometry (RCM) 2009;23:2656–2662. The authors apologise for failing to provide the proper citation and the statement for the modification.