J Clin Periodontol 2006; 33: 663–670 doi: 10.1111/j.1600-051X.2006.00966.x

Journal of Clinical Periodontology

Prognostic factors in the treatment of generalized aggressive periodontitis: I. Clinical features and initial outcome

Francis J. Hughes[1], Mahnaz Syed[1], Bindhu Koshy[1], Valeria Marinho[1], Nagihan Bostanci[1], Ian J. McKay[1], Michael A. Curtis[2], Raymond E. Croucher[1], Wagner Marcenes[1]

[1]Collaborative Group in Risk Factors for Periodontal Disease. Institute of Dentistry; and [2]Institute for Cell & Molecular Sciences, Barts and The London, Queen Mary's School of Medicine and Dentistry, Turner Street, London E1 2AD, UK.

Hughes FJ, Syed M, Koshy B, Marinho V, Bostanci N, McKay IJ, Curtis MA, Croucher RE, Marcenes W. Prognostic factors in the treatment of generalized aggressive periodontitis: I. Clinical features and initial outcome. J Clin Periodontol 2006; 33: 663–670. doi: 10.1111/j.1600-051X.2006.00966.x.

Abstract

Aims: The aims of this study were to investigate prognostic factors for initial response to non-surgical periodontal treatment for generalized aggressive periodontitis.

Methods: Seventy-nine patients with generalized aggressive periodontitis were included in this prospective follow-up intervention study. Patients' clinical and demographic parameters were collected at baseline and 10 weeks following a standard course of treatment (four visits of non-surgical root surface debridement together with OHI as required). The relationship between clinical variables and treatment outcome were analysed at site-specific level by χ^2 analysis and for patient-specific variables by logistic regression.

Results: In general, there was a good response to the treatment provided. In deep sites the mean pocket depth reduction was 2.11 ± 2.01 mm. Site-specific analysis showed that the presence of plaque had a small but significant predictive effect on outcome (odds ratio 1.4). Sites on teeth with grade II/III mobility showed a significantly reduced response to treatment.

Twenty-five patients were classified as ''non-responders''. Current smoking was strongly associated with non-responding patients (odds ratio 3.8) in a logistic regression model; plaque, baseline bleeding and initial pocket depth were not significantly associated with treatment outcomes.

Conclusions: Overall, the results emphasize the importance of smoking as a negative prognostic factor, and suggest that treatment outcomes may be determined by a wide range of different determinants requiring further study.

Key words: aggressive periodontitis; prognosis; smoking; treatment

Accepted for publication 25 May 2006

There are many studies which demonstrate the efficacy of non-surgical therapies for the management of periodontitis (Badersten et al. 1981, 1984, Pihlstrom et al. 1983, Lindhe et al. 1984, Hujoel et al. 2000, Heitz-Mayfield et al. 2002, Tunkel et al. 2002, Van der Weijden & Timmerman 2002). Most of these studies have described the non-surgical management of chronic periodontitis, and there are rather fewer studies which have restricted therapy to patients with aggressive or early onset periodontitis (Kamma & Baehni 2003; D'Aiuto, et al. 2005). Despite the general effectiveness of this therapy, studies typically describe a range of responses including some patients and some sites which do not respond to therapy (Hirschfeld & Wasserman 1978, Claffey & Egelberg 1994, Claffey et al. 1996). These observations are made daily by periodontists during their normal clinical treatment; the recognition and management of sites and patients, which do not respond to mechanical therapies represents a major challenge for the clinician.

Clinically, prognostic judgements are made following assessment of parameters such as initial pocket depth,

presence of plaque or bleeding, presence of furcations and the site of the lesion (Persson et al. 2003a). Previous studies of clinical prognostic factors suggest, in fact, that these clinical parameters are relatively poor predictors of prognosis of individual patients or sites, particularly in the short term (Claffey et al. 1990, Claffey 1991). There is thus considerable interest in improving the assessment and prognosis for individual patients, and understanding the mechanisms which may determine treatment outcome (Persson et al. 2003b).

Periodontitis is a chronic disease of complex aetiology and its susceptibility may be determined by a variety of risk factors, which may include specific factors within the oral microflora, smoking, genetic factors and psychosocial and behavioural factors. Many of these factors may also be significant determinants of treatment response and outcome. For example, classic studies have highlighted the importance of plaque control as a determinant of treatment outcome (Lindhe et al. 1984) and microbiological studies have suggested that persistence of specific micro organisms such as *Poryphyromonas gingivalis* and *Actinobacillus actinomycetemcomitans* may also be associated with poor treatment outcomes. In recent years, it has become increasingly apparent that smoking is not only a major risk factor of periodontal disease but has a significant detrimental affect on treatment response (Bergstrom 2004). Although there is currently considerable interest in the role of genetic factors in the aetiology of periodontal disease there are, as yet, relatively few studies, which describe the effects of specific genotypes on treatment outcome. Likewise, a number of studies have described the role of psychosocial factors on the aetiology of periodontal disease and suggest that they may act via modulation of both behaviours and of the host response (Croucher et al. 1997). It is likely that psychosocial factors may also influence prognosis both by direct effects on host responses and by affecting patient behaviours (Croucher et al. 1997).

There is a relative lack of prognostic information specifically in the management of aggressive periodontitis however, and in order to investigate possible prognostic factors which may affect treatment responses in aggressive periodontitis we have conducted a multidisciplinary study to determine the possible relative role of clinical, behavioural, microbiological, psychosocial and genetic factors on the response to a standardized non-surgical treatment in subjects with generalized aggressive periodontitis. Here we describe our initial findings, which include a description of patient cohort and treatment responses, together with an investigation of the predictive role of clinical parameters in determining initial outcome. Specifically the aim of the study reported here is to test the hypothesis that clinical parameters and patient characteristics may predict poor initial response to non-surgical treatment in patients with generalized AgP.

Material and Methods

Overview

The study was a longitudinal intervention study in patients with generalized aggressive periodontitis who received a standardized course of non-surgical treatment and were followed up prospectively to determine treatment outcomes 10 weeks post-operatively. Protocols for this study were approved by the East London and City Health Authority Local Research Ethics Committee. All participants signed a written consent form.

Patient cohort

Patients were recruited from the new referrals clinic, The Dental Teaching Hospital, Barts and The London NHS Trust following assessment by a consultant periodontist. Patients with a clinical diagnosis of aggressive periodontitis with attachment loss of greater than 6 mm affecting a minimum of six teeth between the ages of 18 and 40 years old were eligible for inclusion in this study. Exclusion criteria were patients with a history of periodontal treatment or antimicrobial therapy within the previous 6 months, affected by any systemic condition likely to affect the periodontal tissues (including pregnancy), or were taking any medication which might have the same effects. All patients included in the study had sites exhibiting 6 mm clinical attachment loss (CAL) affecting more than two teeth in addition to incisors and first molars.

Initially, a minimum sample size of 126 patients was proposed to demonstrate a 2.5-fold difference in treatment failure at the patient level between exposed and unexposed groups. This was assuming 15% dropout, no more than 70% frequency of exposure to distress, no less than 20% frequency of poor response to the periodontal treatment among unexposed, with 80% power at the 95% confidence level.

Calculations of power of the study were performed based on an analysis of a single patient-level parameter showing a 20% difference between responding and non-responding patients, assuming 30% of the subjects were in the non-responding group. Using this estimate, a minimum number of 75 completed subjects was required to give an α value of 0.05 with 80% power.

Study protocol

At baseline subjects received a full clinical assessment. Full mouth 6-point probing depths, and recession measured from the cemento-enamel junction were recorded in 0.2 mm increments using an electronic probe (Florida probe™, Florida Probe, Gainsville, FL, USA) and clinical attachment levels also calculated by addition of probing depth with recession measurements. The presence or absence of plaque, bleeding on probing, and suppuration was recorded for all sites. The presence of furcation lesions and mobility were also recorded for all teeth. Samples of gingival crevicular fluid from six affected sites were taken using Periostrip paper, and microbiological samples were taken from three deep sites and three shallow sites using paper points, which were then placed immediately into anaerobic transport medium. A 10 ml venous blood sample was also taken from each patient. The patients were then asked to complete an inventory to assess life events and behavioural factors, and their full smoking history was obtained. This was supplemented with a measurement of carbon monoxide in expired air by Smokerlyzer™ as an objective estimate of smoking behaviour. All demographic data and clinical measurements were recorded electronically using the Florida Probe database software. Other information including smoking history were recorded on paper clinical record forms.

Patients received four visits of non-surgical periodontal treatment of 30 min duration each at weekly intervals. At these appointments, patients received oral hygiene instruction and full mouth subgingival scaling and debridement using hand and ultrasonic instrumentation, one quad-

Table 1. Details of subjects who completed the study and included in subsequent data analyses

Age	Mean 34.18	SD 5	Range 20–40
Sex	Male 28	Female 51	
Smoking	Non-smokers 59	Smokers 20	
No. of deep sites	Mean 23.98	SD 14.68	Range 7–103
No. of missing teeth*	Mean 1.74	SD 1.97	Range 0–7

*Excluding third molars and first premolar pairs, previously extracted for orthodontic purposes.

rant at a time, using local anaesthesia where necessary. This was carried out by one of two experience periodontists (authors M.S. and B.K.) and on completion of treatment patients were then seen 10 weeks later for a further clinical examination including recording of all variables assessed at baseline.

In order to assess intra- and inter-examiner reproducibility, 11 patients were subjected to re-measurement of 2 quadrants for probing depths, recession, plaque and bleeding on the same day. four of these repeat measurements were carried out by the same examiner, and seven by the alternate examiner. A total of 640 sites were included in the reproducibility study.

Data entry and analysis

Demographic and clinical data stored in the Florida Probe™ database were exported directly for analyses. Other trial information including smoking history were recorded in hard copy on paper clinical record forms and data subsequently entered manually into the study database. Data were exported to SPSS for statistical analyses. Analyses were carried out separately for site-specific and patient-specific outcomes.

Site-specific analysis

Site-specific analyses were carried out in order to investigate the relationship between clinical parameters at individual sites and their clinical outcomes. Outcome measures were analysed on deep sites only, as defined by those showing a minimum probing pocket depth of 5 mm at baseline. The primary outcome measure to determine response to treatment for site-specific analyses was change in pocket depth, as calculated by comparing pre- and post-operative measurements. Responding sites were defined as those showing at least 2 mm reduction in probing pocket depth post-operatively; non-responding sites were defined as those showing no improvement or deterioration in the probing pocket depth post-operatively. Sites showing smaller improvements in pocket depth in response to treatment were omitted from these site-specific analyses. Explanatory variables (potential prognostic factors) tested included presence of plaque and bleeding at baseline and at follow-up, baseline pocket depth, recession and CAL, the presence of mobility or furcation involvement at baseline, and single-rooted *versus* multi-rooted teeth. The predictive power of explanatory variables was measured by χ^2 contingency tables; differences in pocket depths and recession between groups was measured by Mann–Whitney *U*-tests.

Patient-specific analysis

The primary outcome measure for patient-specific analyses was poor response to treatment of deep pockets ($\geqslant$5 mm at baseline). The percentage of sites for each patient that were designated as non-responding (i.e., showed no improvement following treatment) was determined. The study group were dichotomized into ''responding'' and ''non-responding'' patients, non-responding patients being defined as those with a minimum of 30% of their deep sites that did not respond to the treatment provided. This value was chosen arbitrarily a priori as a clinically significant poor response to treatment. Mean values of measurements of pocket depths, recession and CAL from deep sites were calculated for each individual patient to provide the values for entry into patient-level analyses. Similarly, whole mouth plaque and bleeding scores were calculated for each patient.

The explanatory variables (potential prognostic factors) tested included presence of plaque, bleeding, pocket depth, recession, CAL and smoking status at baseline. The predictive power of these explanatory variables was tested using simple and multiple logistic regressions. Modelling of periodontal clinical parameters is complex because of a relatively high correlation among them (e.g. pocket depth and CAL). The first step on modelling was to carry out a simple logistic regression for each explanatory variable. Two further modelling steps were carried out in the analysis. The decision to remove a variable from the equation was based on both statistical ($p<0.05$) and conceptual considerations. Conceptually, it was decided that CAL, pocket depth and recession should not be forced into the equation as these measures are related. The decision to which variable to keep was based on the comparison of level of statistical significance observed in the univariate data analysis. As multiple regression allows one variable for every 10 participants, we had sufficient power to include eight parameters.

Results

A total of 99 patients were recruited to the study. Of these, 16 patients failed to complete the course of treatment according to the protocol. In addition, four patients who satisfied the original entry criteria for the study (including 6 mm CAL in six teeth) had no pocket depths of 5 mm or greater, and were also excluded. Consequently, the data from 79 patients were available for analysis. These patients had a total of 14,130 sites in 2355 teeth between them. Of these sites 1892 (13.34%) were classified as ''deep sites'', exhibiting a minimum of 5 mm pocket depth at baseline.

After exclusion of third molars and matching pairs of first premolars apparently extracted for orthodontic purposes a total of 127 teeth from 38 patients were missing at baseline examination. A further 18 teeth from 11 patients were extracted after initial assessment and excluded from further analysis.

The initial demographic details for the patient cohort are shown in Table 1. At reassessment visit 10 weeks after completion of treatment there was a mean reduction in bleeding sites from 56% to 22%, and reduction in plaque from 48% to 19%. The mean overall outcomes are shown in Table 2. The mean reduction in pocket depth of deep sites was 2.11 mm, with 1.77 mm gain in clinical attachment level. In shallow sites (those with initial pocket depth of 3 mm or less) there was a mean increase in pocket depth of 0.15 mm and increase in clinical attachment loss of 0.13 mm.

Site-specific outcomes

Of the deep sites, 53.1% (1005 sites) were classified as ''responding sites'',

Table 2. Changes in clinical parameters comparing baseline data to measurements taken 10 weeks after non-surgical treatment

	Baseline	10 weeks post-treatment	Mean change
Bleeding (% sites)	56 ± 30	22 ± 19	− 34%*
Plaque (% sites)	48 ± 16	19 ± 12	− 29%*
All Sites			
Pocket depth (mm)	2.98 ± 1.86	2.58 ± 1.55	0.40 ± 1.66**
Recession (mm)	0.38 ± 1.10	0.55 ± 0.98	− 0.20 ± 0.97**
CAL (mm)	3.38 ± 0.46	3.13 ± 0.33	0.21 ± 1.93**
Deep sites only			
Pocket depth (mm)	6.39 ± 1.06	4.28 ± 2.01	2.11 ± 2.01**
Recession (mm)	0.40 ± 0.96	0.74 ± 1.09	− 0.34 ± 1.04**
CAL (mm)	6.78 ± 1.38	5.02 ± 2.53	1.77 ± 2.15**

Pocket Depths, recession and CAL shown for all sites, and for deep sites only (those showing <5mm pocket depth at baseline)
*$p<0.001$ by χ^2 analysis;
**$p<0.001$ by Mann-Whitney *U*-test.
CAL, clinical attachment loss.

Table 3. Site specific analysis comparing clinical features of deep sites classified as responding or non-responding to non-surgical treatment

	Responding sites	Non-responding sites	Significance level
Baseline bleeding	75.00%	81.16%	$p = 0.12$
Baseline plaque	51.49%	52.54%	$p = 0.771$
Outcome bleeding	32.20%	62.65%	$p < 0.001$; OR 3.3 95% CI 2.54–4.34
Outcome plaque	21.17%	27.39%	$p = 0.02$; OR 1.4 95% CI 1.04–1.87

	mean	SD	mean	SD	
Baseline pocket depth	6.52	1.15	6.32	1.00	$p = 0.01$
Baseline recession	0.37	0.84	0.51	1.10	NS
Baseline CAL	6.85	1.41	6.83	1.41	NS
Outcome pocket depth	2.94	1.21	7.22	1.28	ND
Outcome recession	0.71	1.26	0.41	1.05	ND
Outcome CAL	3.63	1.76	7.64	1.54	ND
Presence of mobility	32.72%		38.32%		NS
Furcation	5.8%		7.87%		NS
Single rooted teeth	54.09%		11.80%		NS
Multi-rooted teeth	52.01%		16.04%		

The 1892 of deep sites (>5 mm) were subdivided on the basis of their response to treatment. Sites classified as responding ($n = 1006$) showed a reduction in pocket depth of greater than 2 mm whilst non-responding sites ($n = 306$) showed either no improvement or deterioration in pocket depth. The data below excludes the 579 sites that responded by between 0 and 2 mm. Predictive values of plaque, bleeding mobility, furcations and tooth type tested by χ^2 analysis; other parameters compared by Mann–Whitney *U*-test.
CAL, clinical attachment loss; NS, not significant; ND, not done; CI, cinfidence interval.

showing a reduction in pocket depth of 2 mm or more. 16.6% (306 sites) of the deep sites were classified as non-responding, showing no improvement in pocket depth or deterioration. The number of sites with pocket depth of greater than 5 mm was reduced from 1892 to 630 sites, a reduction of 67%.

Table 3 provides a summary of clinical features of sites classified as responding or non-responding. The presence of plaque at a site at baseline had no predictive ability to distinguish between responding or non-responding sites; the presence of plaque at outcome assessment had a small but significant association with non-responding sites (odds ratio 1.4). Bleeding sites at baseline did not have any significant predictive ability on outcome. There was a significant reduction in bleeding on probing following treatment in responding sites compared with non-responding sites. Non-responding sites had a slightly decreased mean pocket depth at baseline although there was no difference in the recession or clinical attachment level. There was no difference in response between sites from single rooted *versus* those from multi-rooted teeth. Also, there was no difference between the outcome of sites with furcation involvement, or from sites on teeth with the presence of mobility. However, furcation involvements and mobility were analysed further by severity scores, as seen in Table 4, which provides a more detailed summary of outcome of all deep sites where there was mobility or furcation involvement. This demonstrates an overall poorer outcome in sites from teeth with increased mobility in those teeth with grade 2 or 3 mobility scores. However the overall numbers with these scores was proportionately quite small (10.2%).

Patient specific outcomes

The outcome for each individual patient, ranked by the percentage of non-responding sites in each patient is shown in Fig. 1. Fifty-four of the patients were classed as ''responders'' and 25 classified as ''non-responders''. The features of responding and non-responding patients are shown in Table 5. Table 6 shows the outcome of logistic regression analysis of parameters from this data set, showing both the unadjusted and adjusted odds ratios.

Univariate analyses demonstrated that smoking status ($p = 0.045$) and baseline CAL ($p = 0.017$) were statistically associated with response to treatment. Other explanatory variables tested were not of statistical significance. Therefore baseline pocket depth, recession and bleeding were excluded from the next step of modelling for conceptual and statistical reasons. Despite the lack of statistical significance it was decided to force baseline plaque into the model because of its conceptual relevance, as well as age (Level 2). Small changes in the odds ratios suggested that statistical significant explanatory variables in the model (smoking and CAL) were independent of age and plaque levels. In addition, smoking and CAL appear to be independently related to the response to treatment. Finally, a multiple regression analysis was carried out including the statistically significant predictors adjusted by age (Level 3).

Table 4. Effects of severity of mobility and furcation involvement on outcome of deep sites following non-surgical periodontal therapy

Mobility	Grade2/3 $n = 194$		Grade 1 $N = 486$		Grade 0 $N = 1212$		p
	Mean	SD	Mean	SD	mean	SD	
PD change	1.27*	2.22	2.24	1.93	2.19	1.99	< 0.001
Recession change	− 0.37	1.76	− 0.41*	1.01	− 0.22	0.75	<0.001

Furcations	Grade 2/3 $n = 71$		Grade 1 $N = 56$		Grade 0 $n = 1765$		p
	Mean	SD	Mean	SD	mean	SD	
PD change	1.79	1.86	1.71	1.60	2.14	2.03	0.118
Recession change	− 0.49	1.41	− 0.211	0.88	− 0.28	0.98	0.186

Deep sites were divided according to the severity of mobility present at their tooth, and to presence and severity of furcation involvement. The mean (and SD) change in PD and recession was calculated for each group. Differences tested by one-way ANOVA and Bonferroni's multiple comparisons test.
CAL, clinical attachment loss; PD, pocket depth.

These results demonstrate that smokers had an increased risk of poor response to treatment with an odds ratio of greater than 3. Poorer outcome was also significantly associated with increased CAL, although not for pocket depth or recession. Age, levels of plaque and bleeding at baseline were not significantly associated with treatment outcome.

In addition, we also tested the predictive power of plaque levels at follow-up ($p = 0.8$), and change in plaque levels from baseline to follow-up assessment ($p = 0.4$). These associations were not of statistical significance ($p > 0.05$). The lack of association between plaque levels and response to treatment may be because of small variation in plaque levels between participants.

Reproducibility

Studies of reproducibility of measurements suggested good correspondence, with small levels of both intra- and inter-examiner reproducibility. For measurements of plaque 86.7% of re-examination of sites corresponded with the original recording and for bleeding 87.5%. The distribution of repeat measurements for pocket depth and recession is shown in Fig. 2. Eighty-four percent of pocket depth measurements were within 1 mm of the original measurement and 94% of measurements were within 2 mm of the original measurement. For gingival recession 98% of measurements were within 2 mm of the original measurement.

Discussion

There are many studies which have described the overall effectiveness of non-surgical treatment in managing periodontal disease (Badersten et al. 1981, 1984, Pihlstrom et al. 1983, Lindhe et al. 1984). However, it has been recognized that responses to treatment vary considerably and that some patients and some sites will do noticeably worse than others. The factors which may affect outcome are thus of considerable importance in assessing prognosis and considering treatment options for individual patients and sites. This study describes the initial findings of a larger study which aims to investigate a wider range of potential prognostic factors including microbiological, genetic, behavioural and psychosocial factors in influencing treatment outcome.

There are surprisingly few studies which have specifically investigated outcome of non-surgical treatments in patients with generalized aggressive periodontitis or generalized early onset disease. The data from the current study show that, similarly to treatment of chronic periodontitis, non-surgical treatment can be a highly effective treatment for many patients and sites affected by aggressive periodontitis. Overall, the treatment reduced the number of sites showing more than 5 mm probing pocket depth by 67%. This is a clinically relevant measure as this pocket depth is often considered following initial therapy when assessing the need for surgical or other further treatments. The use of adjunctive antimicrobials in the management of patients with generalized aggressive periodontitis is not addressed in this study, although the overall good responses to mechanical debridement therapy seen here suggest at best that adjunctive antimicrobials might be useful in a subgroup of subjects with AgP. Although the evidence for the use of antimicrobials in the management of AgP is equivocal, some studies have nevertheless described significant additional benefits overall from such a treatment regimen (Sigusch et al. 2001, Herrera et al. 2002, Hung & Douglass 2002, Kamma & Baehni 2003). In a further recent study of treatment of generalized aggressive periodontitis, non-surgical treatment alone, similar to that carried out here, reported a reduction of deep pockets by 54%, whereas use of adjunctive amoxicillin and metronidazole increased this figure to 74% (Guerrero et al. 2005).

The findings presented here also support the findings of previous studies of clinical prognostic factors in the outcome of treatment of chronic periodontitis, although these studies are not strictly comparable with the present study which reports only initial outcomes of therapy after 10 weeks post-therapy (Claffey et al. 1990, Claffey 1991). Previous studies have suggested that the presence of bleeding and plaque at specific sites are of limited or no prognostic value, and whilst the presence of severe mobility was associated with a worse treatment outcome, in the current study these teeth accounted for a relatively small number of the poorly responding sites overall. There were too few sites recorded as showing suppuration at baseline to be able to analyse this parameter as a possible prognostic factor. The weak association between initial pocket depth and response of sites has been reported in other studies but recent analyses suggest that this may be the result of mathematical coupling of data rather than a true clinically significant effect (Tu et al. 2002).

There are potentially a number of different ways of describing response or non-response to treatment. In assessing response of specific sites, we have taken a reduction in pocket depth of a minimum of 2 mm as a ''responding site''. Although it is recognized that this excludes a number of sites which have, in fact, shown improvement, by dichotomizing data in this way it was possible to analyse sites which show

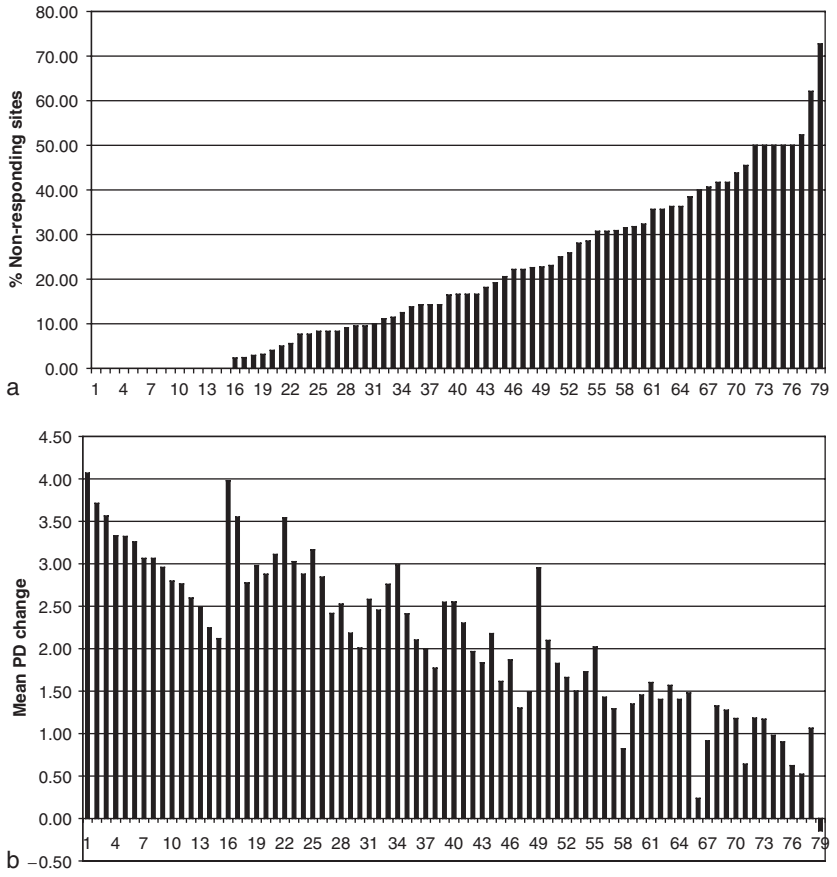

Fig. 1. Outcomes of individual patients ranked by their percentage of non-responding sites. (a) Percentage of non-responding sites. (b) Corresponding values for mean changes in pocket depth of deep sites.

Table 5. Patient-level analysis: Comparison of clinical and other parameters in responding patients and non-responding patients

	Non-Responders		Responders	
	mean	SD	mean	SD
Smoker (%)	40		18.5	
Age	33.24	5.58	34.53	4.84
Total deep sites	23.84	14.68	24.02	21.57
Non-responding sites	17.95	12.49	5.70	6.79
% non-responding	42.44	10.46	10.01	8.98
Baseline bleeding	53.69%	33.53%	58.02%	29.11%
Baseline plaque	48.76%	16.98%	49.12%	13.57%
Baseline pocket depth	6.39	0.61	6.20	0.49
Baseline recession	0.51	0.54	0.23	0.65
Baseline CAL	6.90	0.79	6.42	0.75
Outcome bleeding	28.12%	24.33%	19.76%	14.02%
Outcome plaque	21.19%	17.47%	17.38%	9.16%
Outcome pocket depth	5.28	0.75	3.61	0.81
Outcome recession	0.67	0.72	0.46	0.75
Outcome CAL	5.95	1.03	4.07	1.05

Responders were classified as those showing less than 30% of sites which did not show any response to treatment; Non-responders had more than 30% of sites which did not show any response to treatment.

CAL, clinical attachment loss.

clear and definitive responses compared with those non-responding sites.

Periodontal disease is a site-specific disease and responses to treatment will vary in different sites in the same patient, making the assessment of overall response in a patient methodologically problematic. Rather than assessing mean pocket reduction as a measure of response to treatment for a given patient, this study used the number and percentage of sites in each patient that failed to respond as a more clinically relevant measure of assessing overall treatment outcome for each patient. Although patient outcomes assessed in this way correspond fairly closely to mean changes in pocket depth (Fig. 1) there was by no means an absolute agreement in assessment of treatment outcome in these patients using the different methods, underlining the importance of carefully considering the method of estimation of overall response at the patient level.

In our study, a range of possible indicators of poorly responding patients were evaluated. These variables included the age of patient, pocket depth, recession, baseline plaque levels, bleeding on probing and smoking. When analysed separately it is clear that only two of these factors, namely CAL and smoking, appear to be related to response to treatment. To assess for possible interactions a multiple logistical regression analysis was then performed. This confirmed that these two factors were significantly correlated with a poor response to treatment. Although the initial statistical analysis suggested that levels of plaque (and the related measure of bleeding on probing) was not related to response to treatment this factor was forced into the multiple logistical regression model. A comparison of the statistical outcome with and without including levels of plaque (Table 6) shows it makes no difference to the overall result, demonstrating that initial plaque levels were not associated with outcome; similarly post-treatment plaque levels were not associated with outcome.

The initial calculation of required sample size assumed a 15% dropout ($n = 19$) but in the end the original target numbers were not full met. This may have reduced the power of the tests, and the presence of borderline levels of significance in the patient-specific analyses might thus imply a type 2 error. However, as there was no borderline level of significance it is unlikely that this may have affected the final outcome of the results.

As this study presents only our initial findings of a larger study of prognostic factors of treatment outcome we are aware of some of the limitations in the interpretation of the data presented here.

Firstly, at this stage only initial outcome of treatment has been assessed 10 weeks following completion of non-surgical treatment. However, this is a clinically relevant question given that requirements for surgery and other therapies are generally assessed following completion of cause-related therapy. We plan further follow up of these patients beyond 12 months including description of outcomes after further more complex therapy including surgery which has been scheduled in a number of patients. Furthermore, the data presented here which show a relatively poor correlation of clinical parameters with treatment outcome reinforce the suggestion that prognosis may be dependent on a wide range of factors which depend not only on the initial clinical status but also on behavioural, microbiological and genetic factors. Consequently, in this initial report we have not carried out any attempts at multilevel analysis to assess the relative contribution of site-specific, tooth-specific and patient-specific factors on outcome. However, in a recent study it was suggested that site-specific factors may be the major determinant of initial outcomes of treatment in severe periodontitis, emphasising the need for this approach for further analysis of our data (D'Aiuto et al. 2005). In particular, although the data here suggests smoking is a major factor in determining poorer outcome we have analysed this in more detail in a further manuscript (Hughes et al. 2006), and intend to carry out further analyses using multilevel modelling which will include behavioural, microbiological and genetic factors.

Overall, although the data supports the use of non-surgical periodontal therapy on management of patients with generalized aggressive periodontitis, the poor correlation between clinical prognostic factors and outcome are supportive of the need for broader analysis of this patient group in order to model the relative effects of a range of additional putative prognostic factors and treatment outcome.

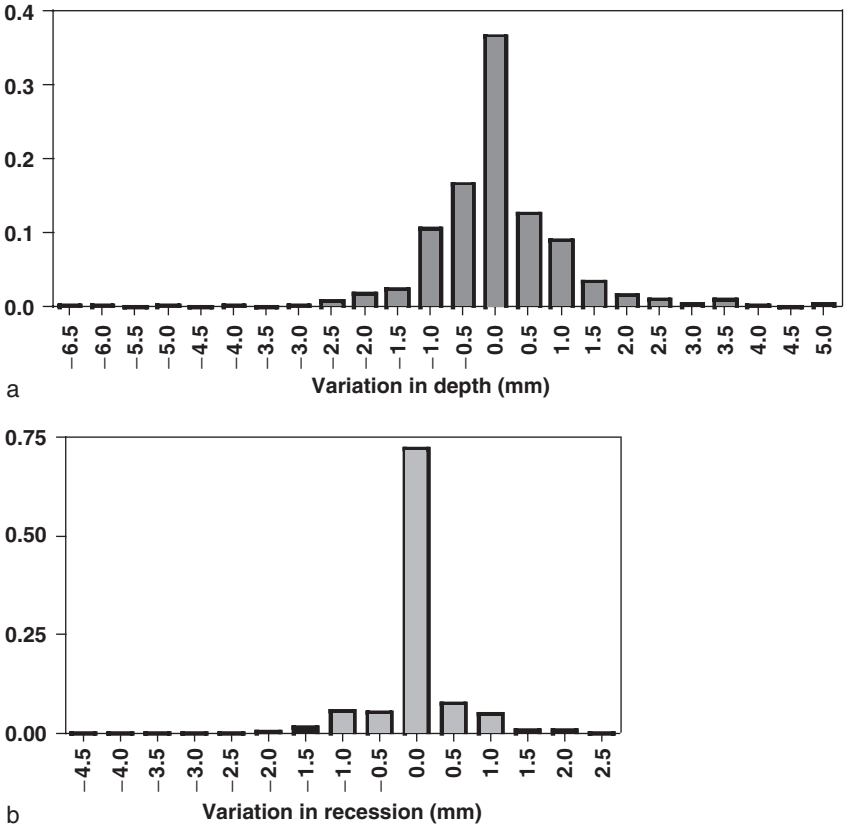

Fig. 2. Results of reproducibility study showing variations in (a) pocket depths and (b) recession between original and repeat measurements.

Acknowledgements

This study was supported by Medical Research Council Co-operative Group Development Grant G9,900,181

Table 6. Logistic regression results for predictor variables for the outcome (dependent variable) ''response to treatment'', expressed firstly as crude (unadjusted) regression coefficients (B)/odds ratios (ORs) with their 95% CIs and significance values, and subsequently expressed as adjusted regression coefficients in the two proposed models/regression equations

	Univariate analysis		Model 1		Model 2	
	unadjusted OR (95% CI)	*p*–value	adjusted OR (95% CI)[1]	*p*–value	adjusted OR (95% CI)[2]	*p*–value
Age	0.95 (0.87–1.05)	0.300	0.92 (0.83–1.03)	0.132	0.92 (0.83–1.02)	0.112
Smoking status						
Non-smoker versus smoker	2.93 (1.02–8.42)	0.045	3.65 (1.15–11.6)	0.028	3.38 (1.09–10.5)	0.035
Baseline CAL (mm)	2.27 (0.23–0.86)	0.017	2.39 (1.18–4.83)	0.016	2.37 (1.18–4.75)	0.015
Baseline PPD (mm)	1.96 (0.8–4.76)	0.140	*			
Baseline recession (mm)	2.40 (0.93–6.20)	0.071	*			
Baseline plaque	2.87 (0.2–41.61)	0.439	3.82 (0.21–69.25)	0.365	*	
Baseline bleeding	0.32 (0.07–1.54)	0.157	*			

Model 1 shows inclusion of significant factors and the forced inclusion of age and plaque; model 2 omits baseline plaque scores.
*Variables not selected.
Model 1: 1st+2nd level.
Model 2: Selected variables from 1st and 2nd level+3rd.
CAL, clinical attachment loss; PPD, periodontal pocket depth.

References

Badersten, A., Nilveus, R. & Egelberg, J. (1981) Effect of nonsurgical periodontal therapy. I. Moderately advanced periodontitis. *Journal of Clinical Periodontology* **8**, 57–72.

Badersten, A., Nilveus, R. & Egelberg, J. (1984) Effect of nonsurgical periodontal therapy. II. Severely advanced periodontitis. *Journal of Clinical Periodontology* **11**, 63–76.

Bergstrom, J. (2004) Tobacco smoking and chronic destructive periodontal disease. *Odontology* **92**, 1–8.

Claffey, N. (1991) Decision making in periodontal therapy. The re-evaluation. *Journal of Clinical Periodontology* **18**, 384–389.

Claffey, N. & Egelberg, J. (1994) Clinical characteristics of periodontal sites with probing attachment loss following initial periodontal treatment. *Journal of Clinical Periodontology* **21**, 670–679.

Claffey, N., Kelly, A., Bergquist, J. & Egelberg, J. (1996) Patterns of attachment loss in advanced periodontitis patients monitored following initial periodontal treatment. *Journal of Clinical Periodontology* **23**, 523–531.

Claffey, N., Nylund, K., Kiger, R., Garrett, S. & Egelberg, J. (1990) Diagnostic predictability of scores of plaque, bleeding, suppuration and probing depth for probing attachment loss 3 1/2 years of observation following initial periodontal therapy. *Journal of Clinical Periodontology* **17**, 108–114.

Croucher, R., Marcenes, W. S., Torres, M. C., Hughes, F. & Sheiham, A. (1997) The relationship between life-events and periodontitis. A case–control study. *Journal of Clinical Periodontology* **24**, 39–43.

D'Aiuto, F., Ready, D., Parkar, M. & Tonetti, M. S. (2005) Relative contribution of patient-, tooth-, and site-associated variability on the clinical outcomes of subgingival debridement. I. Probing depths. *Journal of Periodontology* **76**, 398–405.

Guerrero, A., Griffiths, G. S., Nibali, L., Suvan, J., Moles, D. R., Laurell, L. & Tonetti, M. S. (2005) Adjunctive benefits of systemic amoxicillin and metronidazole in non-surgical treatment of generalized aggressive periodontitis: a randomized placebo-controlled clinical trial. *Journal of Clinical Periodontology* **32**, 1096–1107.

Heitz-Mayfield, L. J., Trombelli, L., Heitz, F., Needleman, I. & Moles, D. (2002) A systematic review of the effect of surgical debridement versus non-surgical debridement for the treatment of chronic periodontitis. *Journal of Clinical Periodontology* **29** (Suppl 3), 92–102; discussion 160–102.

Herrera, D., Sanz, M., Jepsen, S., Needleman, I. & Roldan, S. (2002) A systematic review on the effect of systemic antimicrobials as an adjunct to scaling and root planing in periodontitis patients. *Journal of Clinical Periodontology* **29** (Suppl 3), 136–159; discussion 160–132.

Hirschfeld, L. & Wasserman, B. (1978) A long-term survey of tooth loss in 600 treated periodontal patients. *Journal of Periodontology* **49**, 225–237.

Hughes, F. J., Syed, M., Koshy, B., Bostanci, N., McKay, I. J., Curtis, M. A., Marcenes, W. & Croucher, R. E. (2006) Prognostic factors in the treatment of generalised aggressive periodontitis: II. Effects of smoking on initial outcome. *Journal of Clinical Periodontology* **33**, 671–676.

Hujoel, P. P., Leroux, B. G., Selipsky, H. & White, B. A. (2000) Non-surgical periodontal therapy and tooth loss. A cohort study. *Journal of Periodontology* **71**, 736–742.

Hung, H. C. & Douglass, C. W. (2002) Meta-analysis of the effect of scaling and root planing, surgical treatment and antibiotic therapies on periodontal probing depth and attachment loss. *Journal of Clinical Periodontology* **29**, 975–986.

Kamma, J. J. & Baehni, P. C. (2003) Five-year maintenance follow-up of early-onset periodontitis patients. *Journal of Clinical Periodontology* **30**, 562–572.

Lindhe, J., Westfelt, E., Nyman, S., Socransky, S. S. & Haffajee, A. D. (1984) Long-term effect of surgical/non-surgical treatment of periodontal disease. *Journal of Clinical Periodontology* **11**, 448–458.

Persson, G. R., Attstrom, R., Lang, N. P. & Page, R. C. (2003a) Perceived risk of deteriorating periodontal conditions. *Journal of Clinical Periodontology* **30**, 982–989.

Persson, G. R., Mancl, L. A., Martin, J. & Page, R. C. (2003b) Assessing periodontal disease risk: a comparison of clinicians' assessment versus a computerized tool. *Journal of the American Dental Association* **134**, 575–582.

Pihlstrom, B. L., McHugh, R. B., Oliphant, T. H. & Ortiz-Campos, C. (1983) Comparison of surgical and nonsurgical treatment of periodontal disease. A review of current studies and additional results after 61/2 years. *Journal of Clinical Periodontology* **10**, 524–541.

Sigusch, B., Beier, M., Klinger, G., Pfister, W. & Glockmann, E. (2001) A 2-step non-surgical procedure and systemic antibiotics in the treatment of rapidly progressive periodontitis. *J* **72**, 275–283.

Tu, Y. K., Gilthorpe, M. S. & Griffiths, G. S. (2002) Is reduction of pocket probing depth correlated with the baseline value or is it ''mathematical coupling''? *Journal of Dental Resesearch* **81**, 722–726.

Tunkel, J., Heinecke, A. & Flemmig, T. F. (2002) A systematic review of efficacy of machine-driven and manual subgingival debridement in the treatment of chronic periodontitis. *Journal Clinical Periodontology* **29** (Suppl 3), 72–81; discussion 90–71.

Van der Weijden, G. A. & Timmerman, M. F. (2002) A systematic review on the clinical efficacy of subgingival debridement in the treatment of chronic periodontitis. *Journal of Clinical Periodontology* **29** (Suppl 3), 55–71; discussion 90–51.

Address:
Francis J. Hughes
Centre for Adult Oral Health
Institute of Dentistry
Barts and The London, Queen Mary's School of Medicine and Dentistry
Turner Street
London E1 2AD,
UK
Fax +44 (0) 20 7377 7064
E-mail: f.j.hughes@qmul.ac.uk

Clinical summary

Scientific rationale for study: It is well recognized that patients may show different responses to periodontal treatment. The aims of this study were to investigate the prognostic factors that might determine outcome of non-surgical treatment for generalized aggressive periodontitis.

Principal findings: Most patients and most deep sites respond to non-surgical therapy; however a subset of non-responsive patients can be identified. Interestingly, levels of plaque did not appear to determine response of patients but smoking appears to be a key risk factor.

Practical implications: The results emphasize the complexity of factors, including smoking, which may determine how an individual patient will respond to treatment.