Aggressive Periodontitis: 5-Year Follow-Up of Treatment

Rainer Buchmann,* Martha E. Nunn,† Thomas E. Van Dyke,‡ and Dieter E. Lange§

Background: *The hypothesis that in subjects with aggressive periodontitis, a long-term stability of periodontal health can be achieved following comprehensive mechanical/surgical and systemic antimicrobial therapy was tested in this prospective study.*

Methods: *Thirteen patients (36.9 ± 7.4 years) with aggressive periodontitis were monitored before and up to 5 years following periodontal therapy. Clinical attachment levels (CAL) were assessed pretherapy, and at 3 months following completion of active periodontal therapy supplemented by amoxicillin plus metronidazole. All subjects were subsequently enrolled in a maintenance program and provided with supportive periodontal therapy with 3 to 4 appointments annually. Reexaminations were performed after 6 months and 1, 2, 3, 4, and 5 years. The data were analyzed using the method of generalized estimating equations (GEE) for CAL changes from baseline to the 3-month visit, and from completion of periodontal therapy to each annual visit up to the 5-year follow-up reappointment.*

Results: *During the 5-year study, all subjects strongly benefited from periodontal treatment. Between baseline and the 3-month reexamination, the CAL levels revealed a significant decrease of 2.23 mm (95% confidence interval [CI]: 1.77 to 2.69 mm; P ≤0.001). At the 5-year maintenance visit, the CAL changes ranged from –0.04 to +0.29 mm with no further statistically significant periodontal breakdown (P >0.05). Five years after surgery, 3.2% of the treated sites demonstrated a further CAL gain ≥3 mm. A stabilization (CAL –2 to +2 mm) occurred in 94.6% of the cases. The number of periodontal sites experiencing a breakdown varied from 5.3% at 6 months to 2.2% at 5 years.*

Conclusions: *In aggressive periodontitis, comprehensive mechanical/surgical and antimicrobial therapy is an appropriate treatment regimen for long-term stabilization of periodontal health. In this study, periodontal disease progression was successfully arrested in 95% of the initially compromised lesions, while 2% to 5% experienced discrete or recurrent episodes of loss of periodontal support.* J Periodontol 2002;73: 675-683.

KEY WORDS

Periodontal diseases/surgery; periodontal diseases/therapy; periodontal attachment loss/therapy; follow-up studies.

Aggressive periodontitis encompasses a distinct type of periodontal disease and affects people who, in most cases, otherwise appear healthy. The amplified host response to microbial infection causes severe damage of periodontal tissues with harmful side effects, particularly for cardiovascular and other neutrophil-generated diseases that have not yet been fully investigated.[1] When longitudinally monitored, additional attachment loss can be demonstrated at one or more sites, despite well-executed therapeutic and patient efforts to stop disease progression.[2,3] Initial periodontal scaling and root planing (SRP) treatment alone is often ineffective and should be supplemented by antimicrobial therapy.[3]

In advanced periodontal disease, an inappropriate amplified recruitment of neutrophils creates noxious inflammatory responses with deleterious effects on oral and periodontal disease conditions.[4] Fundamental evidence from multi-center studies indicates that both non-surgical and surgical approaches to periodontal disease promote the resolution of disease, aimed at pocket reduction and the maintenance of reasonable attachment levels.[5,6] It is accepted that the use of metronidazole and amoxicillin is advantageous in rapidly lowering periodontal pathogen counts when accompanied by SRP.[7,8] Recently, a 2-step enhanced root planing procedure was proposed with antibiotics administered after completion of initial therapy.[9] These data suggest that amoxicillin plus metronidazole in a non-surgical treatment setting may represent the sole approach to resolving periodontal infection. Evidence obtained from short time trials with a final evaluation performed 3 to 36 months following termination of active therapy confirms this assumption.[10-12]

* Private practice, Hamm, Westfalen, Germany; previously, Department of Periodontology and Oral Biology, Goldman School of Dental Medicine, Boston University, Boston, MA.
† Department of Health Policy and Health Services Research.
‡ Department of Periodontology and Oral Biology.
§ Department of Periodontology, School of Dental Medicine, University of Münster, Germany.

Reports from long-term surveys of periodontal therapy document that microbiota residing in root-adherent biofilms left due to inadequate instrumentation during non-surgical treatment are not affected by adjunctive antibiotic therapy, and require surgical intervention to completely arrest periodontal disease.[13] Although clinical studies have generally failed to demonstrate an advantage of surgical procedures over root planing alone,[14-17] comparisons are limited due to variation in patient susceptibility, defect type, and evidence of deterioration.[18]

Stabilization and gain of clinical attachment are recognized as major outcome assessments. The rate of periodontal disease progression varies between patient groups, disease type, and severity.[19] The incidence of breakdown sites defined by radiographic evidence of alveolar bone loss or deterioration of probing attachment levels averages, on a site level, between 1.2% to 8.6% in an untreated population group[20] and between 2% to 4% in treated patients with previous periodontal disease, regardless of the treatment modality.[13,16] Multiple variables, such as the threshold level for breakdown sites, the initial disease site category, and the time span allowing for periodontal deterioration must be carefully considered when evaluating the disease progression rate in clinical studies.

A meta-analysis of treatment for chronic periodontal disease from 5 published randomized controlled trials (RCT) reported the efficacy of periodontal therapy by clinical attachment levels for different probing depths 1 year after treatment.[15] It was documented that, for all categories of periodontal disease, the average CAL gain was similar (between 0.2 to 0.8 mm) except for advanced disease severity with PD ≥7 mm, where surgical treatment was, to some extent, advantageous. These findings favor non-surgical treatment approaches in patients with mild or moderate periodontal disease. In severe periodontitis with advanced loss of tissue support, resolution of disease by surgical procedures is recommended. It would advance our understanding of periodontal disease if it were determined that these treatment approaches could be successfully applied to aggressive periodontal disease.

Thus, in the present investigation, the hypothesis that a long-term stability of periodontal health can be achieved following comprehensive mechanical/surgical and systemic antimicrobial therapy in aggressive periodontitis patients was tested.

MATERIALS AND METHODS

Study Population

The data for this study were obtained from 13 patients (4 females, 9 males; average age, 36.9 ± 7.4 years; range, 26 to 46 years) from the Department of Periodontology, University of Münster, with aggressive periodontal disease[2] and evidence of prior attachment loss. All subjects had at least 22 teeth present. Patients selected to enter into the study were screened for periodontal disease by radiographic evidence of intrabony defects exceeding more than 50% of the root length and probing depths >5 mm at more than 8 sites within each quadrant. Initial microbial testing evidenced the presence of *Actinobacillus actinomycetemcomitans* in subgingival plaque samples with concentrations exceeding more than 10^4 colony-forming units/ml. Exclusion criteria included smoking, pregnancy, periodontal therapy or antibiotics in the previous 6 months, any systemic condition that might affect the progression or treatment of periodontitis, and the need for premedication for therapy. Throughout the study, patients were requested to report to the principal investigator any orofacial or medical infection where antibiotics were administered. No subject with localized juvenile periodontitis or acute necrotizing ulcerative gingivitis was included in the study. Table 1 presents the baseline demographic and clinical characteristics of the 13 periodontal patients enrolled in the study.

Periodontal Examinations

Subjects were screened for suitability and, if they accepted, asked to sign informed consent forms. The patients were examined at baseline, 3 months after completion of active therapy, and 6, 12, 24, 36, 48, and 60 months during the maintenance period. Probing depths (PD) as the distance between the gingival margin and the bottom of the periodontal pocket as well as clinical attachment levels (CAL) as the distance from the cemento-enamel junction (CEJ) to the clinical base of the periodontal pocket were taken at 6 sites per tooth (buccal: mb/b/db; lingual: dl/l/ml) using a straight rigid periodontal probe with a 3-3-2-3 mm calibration and a 0.4 mm diameter tip. The PD and CAL measurements (reproducibility ±1 mm greater than 95%) were performed by the same calibrated examiner throughout the study. Bleeding on probing (BOP) was recorded dichotomously at 4 surfaces around each tooth. The presence of supragingival plaque was assessed at 4 sites per tooth accord-

Table 1.

Baseline Demographic and Clinical Characteristics of Study Population

Variable	Women	Men	Total
Age at baseline (years)	38.8 ± 7.7	36.0 ± 7.6	36.9 ± 7.4
Number of sites examined	32	68	100
% sites with CAL (N)			
<4 mm	0.0 (0)	1.5 (1)	1.0 (1)
4-6 mm	9.4 (3)	23.5 (16)	19.0 (19)
>6 mm	90.6 (29)	75.0 (51)	80.0 (80)
% sites with GI (N)			
GI = 0	0.0 (0)	2.9 (2)	2.0 (2)
GI = 1	18.8 (6)	5.9 (4)	10.0 (10)
GI = 2	40.6 (13)	50.0 (34)	47.0 (47)
GI = 3	40.6 (13)	41.2 (28)	41.0 (41)

ing to the plaque index (PI).[21] The gingival conditions were visually examined at 4 surfaces per tooth using the gingival index (GI).[22] Here, we focus the data presentation on the analysis of the clinical attachment levels as the primary outcome variable.

Periodontal Site Selection

In each of the 13 individuals, a total of 8 teeth (2 per quadrant) with interapproximate bone loss >50% of the rooth length were selected for periodontal examination. For computation of CAL changes, the most deteriorated site per tooth was chosen. Single subjects presented teeth that were recorded initially, but could not be maintained during the 5-year trial. Since those sites exited the complete study, 99 sites were examined on average. The mean contribution per patient was 7.6 sites.

Periodontal Treatment

All individuals were enrolled in an individual oral hygiene program with repeated motivation and instruction in self-performed oral hygiene and a weekly prophylaxis (3 to 4 sessions) prior to surgery. Surgical periodontal therapy was applied to all subjects. Subgingival SRP was performed under local anesthesia[§] at sites with PD >4 mm. Sites with PD ≥6 mm were accessed using the modified Widman technique (4 to 6 sessions). Among the 100 sites examined initially (Table 1), 14 sites received SRP, and 86 sites were subjected to Widman flap surgery. After intrasulcular incision, a mucoperiosteal flap was raised beyond the mucogingival border to access the periodontal defect. Following removal of the interradicular inflammatory granulation tissue, the denuded root surfaces were mechanically scaled, root planed, and repeatedly rinsed with 0.1% chlorhexidine digluconate solution.[‖] No osseous surgery was carried out. Flaps were replaced as close as possible to their initial position to completely cover the periodontal defect and fixed with interdental sutures. Systemic 3 × 500 mg/day amoxicillin[¶] and 3 × 250 mg/day metronidazole[#] were prescribed for 7 days during SRP and surgical periodontal therapy to eliminate *A. actinomycetemcomitans* from the subgingival environment and the oral cavity.[10] The postsurgical follow-up included suture removal and a careful cleaning of the treated periodontal sites 1 week post-therapy. During the first and second postoperative weeks, a 0.1% chlorhexidine digluconate solution was prescribed for twice daily 2 minute rinses.

Maintenance

The patients were enrolled in a regularly scheduled maintenance program. During the first year, subjects were monitored in 3- to 6-month recall intervals, which included repeated oral hygiene instructions and a full-mouth tooth cleaning with a polishing agent[**] according to their individual needs. At each visit, additional subgingival instrumentation was performed under local anesthesia at periodontal sites that revealed >4 mm PD and positive BOP scores. All patients were regularly screened for caries and radiographically examined to evaluate the crestal bone height and to detect early periapical lesions. Individuals needing further prosthodontic or implant treatment were referred to a specialist 6 months after periodontal therapy.

The full range of periodontal parameters was assessed as described above at baseline and 3 months after surgical periodontal therapy. Thereafter, all subjects were completely reexamined 6, 12, 24, 36, 48, and 60 months following periodontal therapy. All clinical measurements were taken by the first author (RB). Periodontal sites replaced with dental crowns during the maintenance period were excluded from recording.

Statistical Analysis

The data analysis and statistical tests were evaluated on a site level using the method of generalized estimating equations (GEE) assuming an exchangeable

§ Xylocain Spezial 2%, Astra Chemicals, Mölndal/Göteborg, Sweden.
‖ Chlorhexamed fluid, Procter & Gamble, Schwalbach, Germany.
¶ Ratiopharm GmbH, Blaubeuren, Germany.
# Artesan GmbH, Lüchow, Germany.
** Oralust, Oral-B Laboratories, Kronberg im Taunus, Germany.

working correlation. In addition, data were analyzed on a patient level basis to verify the results because of the relatively small sample size.[19,23] CAL changes were analyzed from baseline to completion of active therapy (3 months), and then compared to each of the 5-year follow-up reappointments. Site level changes in CAL were analyzed using GEE, while patient level changes in CAL were subjected to the Wilcoxon signed rank test. To calculate breakdown sites, we employed a threshold of ≥3 mm.[24] Statistical significance was considered at an $\alpha = 0.05$.

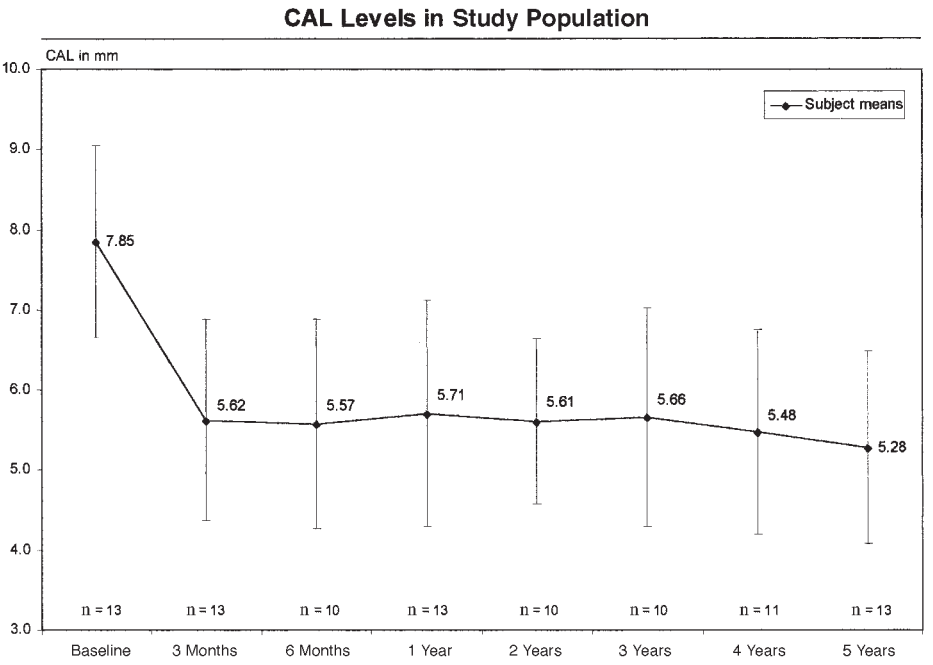

Figure 1.
CAL in aggressive periodontitis.

RESULTS

CAL levels in 13 patients indicated a significant treatment-induced decrease from 7.85 mm (GEE mean 7.8 mm) at baseline to a subject mean of 5.62 mm (GEE mean 5.57 mm) following completion of active treatment. From 6 months to 5 years, a stabilization occurred resulting in a subject mean of 5.28 mm (GEE mean 5.28 mm) at the 5-year reexamination (Fig. 1). During the 5 years, the patients experienced individual patterns of CAL changes. Some patients underwent varying amounts of relapses (negative CAL changes) at individual reexamination visits. However, the comparison of CAL changes from baseline to 5 years indicated a statistically significant overall improvement for the 13 patients (Wilcoxon signed rank test; $P<0.05$; Table 2). Single increments of CAL change (deterioration) during maintenance did not affect the 5-year CAL changes from baseline. After some relapses at the 3-year appointment, the CAL changes tended to improve toward the 5-year reexamination, with a final subject mean change of 2.57 mm from baseline (GEE mean 2.53 mm). The subject median CAL changes exhibited no significant differences from surgery completion (0.0 to 0.25 mm). Similarly, no significant changes from 3 months up to 4 years were noted when the data were subjected to GEE. However, using GEE, a statistically significant increase of 0.29 mm in CAL from 3 months to 5 years was observed ($P = 0.02$), although on a patient level, no significant change in CAL could be demonstrated.

When the CAL changes were related to categories of initial PD representing disease severity at baseline, no significant improvement was observed in 3 sites with PD 1 to 3 mm; in contrast, at sites with initial PD 4 to 6 mm (52%) and ≥7 mm (44%), marked clinical responses occurred with no further changes during the 5-year period. Moreover, at the 5-year visit, the CAL changes from baseline were as pronounced as after completion of therapy (3 months), since they did not differ statistically (Table 3).

All sites responded to comprehensive surgical and antimicrobial therapy (baseline to 3 months), with most frequent CAL gains between 1 and 2 mm (55.6%). CAL changes ≥3 mm (37.3%) were less pronounced. At single periodontal sites, the treatment-induced CAL gain reached +7 mm. No measurable CAL changes were noticed at 7 treated sites (7.1%). Following the 6-month appointment, CAL changes ranged between –4 and +4 mm, indicating that single sites underwent further periodontal improvement or deterioration (Tables 4 and 5).

In order not to underestimate the number of active sites,[23] we employed a threshold of ≥3 mm as the cut-off for sites undergoing further periodontal break-

Table 2.

Mean CAL Changes for Study Population; Changes (mm) From Baseline to 3 Months, and at 6, 12, 24, 36, 48, and 60 Months Compared to 3 Months (surgery completion)

			CAL Changes							
Subject/Gender	Age	Initial CAL	Baseline-3 Months	6 Months	1 Year	2 Years	3 Years	4 Years	5 Years	Baseline-5 Years
1/m	31	5.88	1.13	0.88	–0.13	0.32	0.32	0.89	0.18	1.30
2/m	31	6.88	2.38	0.00	–0.25	—	—	0.50	0.63	3.00
3/m	32	7.67	2.00	—	0.17	0.00	—	–0.08	0.67	2.67
4/f	46	8.25	2.13	0.50	0.50	—	0.38	0.50	0.25	2.38
5/m	43	9.75	2.75	–0.75	–0.38	–1.00	–0.25	–0.13	1.13	3.88
6/m	44	8.63	1.88	–0.11	–2.08	1.18	–0.39	0.04	–0.11	1.77
7/m	42	7.75	2.89	—	0.43	0.57	—	0.43	0.57	3.46
8/m	26	5.88	2.13	–0.13	–0.25	–0.50	–0.38	—	–0.13	2.00
9/f	39	7.50	2.38	—	0.25	–0.47	0.13	–0.38	–0.21	2.17
10/m	29	8.50	2.38	0.27	0.38	0.00	0.50	—	0.25	2.63
11/f	42	8.25	4.38	0.13	0.00	0.13	0.50	0.38	0.63	5.00
12/f	28	7.50	2.13	–0.25	–0.25	–0.13	–0.50	–0.13	–0.13	2.00
13/m	46	9.67	0.50	0.00	0.50	—	–0.67	–0.50	0.67	1.17
Subject (N)			13	10	13	10	10	11	13	13
Subject mean			2.23	0.05	–0.09	0.01	–0.04	0.14	0.34	2.57
Subject SD			0.91	0.44	0.68	0.61	0.45	0.43	0.41	1.06
Subject median			2.13	0.0	0.0	0.0	–0.06	0.04	0.25	2.38
P value*			—	0.005†	0.400	0.463	0.374	0.161	0.327	0.002†

* Wilcoxon signed rank test.
† Significant after adjustment to Bonferroni.

down. Our results clearly demonstrate the efficacy of the treatment approach, since following surgery (3 months), the percentage of stable sites was between 91.8% and 95%. During the recorded intervals, active sites that underwent disease progression consistently ranged between 1.4% and 5.3%. In addition, there was a small decrease in the number of breakdown sites from 5.3% after periodontal therapy to 2.2% at the final 5-year evaluation. It is interesting to note that during the maintenance period, 2% to 4% of the sites experienced further CAL gain compared to following surgery due to repeated instrumentation with continuous tissue remodeling (Table 5, Fig. 2).

DISCUSSION

It has been suggested that periodontal patients, particularly those with severe inflammation,[8,25] benefit from supportive systemic amoxicillin and metronidazole (A+M) therapy.[10] The findings of the present study demonstrate that patients with aggressive periodontitis undergo rapid resolution of disease following comprehensive mechanical/surgical and antimicrobial periodontal therapy, resulting in CAL changes

Table 3.

CAL Changes (mm) for Various PD After Surgery and Changes From Surgery (3 months) to Each Reexamination Visit

	CAL Changes							
PD (mm)	Baseline-3 Months	6 Months*	1 Year	2 Years	3 Years	4 Years	5 Years	Baseline-5 Years
1-3								
N	3	3	3	2	2	3	3	3
Mean	0.33	0.0	–0.67	0.50	0.50	0.0	0.0	0.33
SD	1.15	1.0	1.15	0.71	0.71	1.0	1.0	0.58
Median	1.0	0.0	0.0	0.5	0.5	0.0	0.0	0.0
P value*	—	0.317	0.157	1.000	1.000	1.000	1.000	1.000
4-6								
N	52	38	52	35	37	41	49	49
Mean	1.67	–0.11	0.06	–0.14	0.22	–0.17	–0.29	1.92
SD	1.06	1.20	1.23	1.31	1.36	1.32	1.22	1.35
Median	2.0	0.0	0.0	0.0	0.0	0.0	0.0	2.0
P value*	—	0.0001†	0.073	0.690	0.049	0.909	0.602	0.076
≥7								
N	44	35	43	35	35	33	41	41
Mean	3.00	–0.09	0.09	0.26	–0.09	–0.06	–0.32	3.39
SD	1.58	1.36	1.48	1.22	1.52	1.25	1.29	1.73
Median	3.0	0.0	0.0	0.0	0.0	0.0	0.0	3.0
P value*	—	0.0001†	0.854	0.674	0.228	0.379	0.149	0.110
Total								
N	99	76	98	72	74	77	93	93
Mean	2.22	–0.09	0.05	0.07	0.08	–0.12	–0.29	2.52
SD	1.05	1.26	1.33	1.26	1.42	1.27	1.24	1.72
Median	2.0	0.0	0.0	0.0	0.0	0.0	0.0	2.0
P value*	—	0.0001†	0.254	0.538	0.607	0.533	0.168	0.019

* Wilcoxon signed rank test.
† Significant after adjustment to Bonferroni.

of 2.2 mm after active therapy. In a non-surgical setting (SRP combined with systemic A+M therapy treatment), responses yielded a decrease of only 1.4 mm.[25] In a recent double-blind placebo controlled study, the average CAL changes following SRP plus A+M therapy were 0.7 to 0.9 mm for PD between 4 to 6 mm, and 1.5 to 2.0 mm in PD ≥7 mm.[8] Even after repeated SRP supplemented by systemic antibiotics, the mean CAL changes reached 1.2 to 1.7 mm after 6 months.[9] After 5 years, we demonstrated consistently enhanced treatment responses of 1.9 mm at sites with initial PD 4 to 6 mm, and 3.4 mm at sites with advanced tissue destruction of ≥7 mm. It is conceivable that the sustained CAL outcomes of SRP sites with initial 4 to 6 mm PD located adjacent to a surgically treated defect might have been affected by the surgery and do not represent true SRP sites.

The modified Widman surgical approach to sites with PD >6 mm is advantageous over SRP alone as the resolution of disease becomes more efficacious. Moreover, in aggressive periodontitis, a subgingival recolonization with *A. actinomycetemcomitans* has been documented as a frequent event.[26] Compared to chronic periodontitis, where elimination of *A. actinomycetemcomitans* after SRP plus A+M is more likely,[10] the treatment outcomes in aggressive periodontitis are superior. Due to the prolonged duration of the study, single patients could not be recruited at the 6-month to 4-year intervals as outlined in Table 2. Since all subjects presented at the 5-year visit with CAL changes that are well in the range of stud-

Table 4.

Frequency Distribution of CAL Changes (mean ± SD)

Time	CAL Change (mm)	Frequency Distribution of CAL Changes									
		N	≥ – 4	–3	–2	–1	0	+1	+2	+3	≥ + 4
Baseline-3 months	2.23 ± 0.9	%	—	—	—	2.0	5.1	29.3	26.3	18.2	19.1
		(99)	—	—	—	(2)	(5)	(29)	(26)	(18)	(19)
At 6 months	0.05 ± 0.4	%	—	5.3	5.3	2.4	36.8	23.7	5.1	—	1.3
		(76)	—	(4)	(4)	(17)	(28)	(18)	(4)	—	(1)
At 1 year	–0.09 ± 0.7	%	—	2.0	9.2	21.4	35.7	16.3	12.2	2.0	1.0
		(98)	—	(2)	(9)	(21)	(35)	(16)	(12)	(2)	(1)
At 2 years	0.01 ± 0.6	%	1.4	—	8.3	19.4	34.7	27.8	4.2	4.2	—
		(72)	(1)	—	(6)	(14)	(25)	(20)	(3)	(3)	—
At 3 years	–0.04 ± 0.5	%	—	4.1	12.2	6.8	43.2	23.0	6.8	2.7	1.4
		(74)	—	(3)	(9)	(5)	(32)	(17)	(5)	(2)	(1)
At 4 years	0.14 ± 0.4	%	—	3.9	7.8	22.1	42.9	11.7	9.1	2.6	—
		(77)	—	(3)	(6)	(17)	(33)	(9)	(7)	(2)	—
At 5 years	0.34 ± 0.4	%	—	2.2	16.1	20.4	40.9	14.0	3.2	3.2	—
		(93)	—	(2)	(15)	(19)	(38)	(13)	(3)	(3)	—

ies discussed herein, we suggest that the drop-outs in our investigation (15.4% to 23.1%) did not affect the overall results.

Both patient and site level analysis yielded similar results throughout, with the exception of CAL changes from 3 months to 5 years where the site level approach utilizing GEE displayed a significant increase in CAL, while the patient level comparison using Wilcoxon signed rank test revealed no significant differences. One reasonable explanation is that GEE is subject to bias in small samples, so that the small sample size used in this case may have led to inaccurate results. In addition, the increase in CAL noted (0.29 mm) from 3 months to 5 years is well within the range of –2 to +2 mm that would normally indicate no clinically significant change outside of the range of measurement error.

In a 5-year documentation of clinical responses to recurrent periodontitis after SRP plus amoxicillin or metronidazole therapy, disease progression during the first 3 years was prevented in 14 of 17 subjects (82%).[13] From 3 to 5 years, an additional 6 patients underwent rapid attachment loss, while only 5 of 17 patients (29%) yielded stable CAL levels.[13] From these findings, SRP in patients with advanced periodontal disease was considered to show lack of efficacy, especially at sites where the access to microbial deposits and the removal of biofilm-coated microorganisms on root cementum were limited. The CAL changes over the 5-year period ranged between +0.3 and –0.3 mm, exceeding by far those observed in our study. In a prospective 5-year follow-up study where root planing was compared to flap surgery, it was documented that intraosseous defects cannot be maintained by SRP alone and require surgical intervention.[18] These findings, together with our results, support the hypothesis that, in a long-term perspective, the efficacy of periodontal therapy in severe conditions predominantly depends on an appropriate surgical management of periodontal defects combined with an adequate reinstrumentation during maintenance care.

Breakdown sites were examined using threshold methods[24] and mean and site-based changes.[23] The incidence of periodontal sites experiencing disease progression remained markedly low, ranging from 5.3% after periodontal therapy to 2.2% at the final 5-year reevaluation. The number of failing sites in our study corresponds with data from a 7-year evaluation of periodontal therapy where the annual incidence of breakdown sites was 1.9% following modified Widman flap surgery for initial PD 5 to 6 mm, and

Table 5.

Frequency of CAL Changes Employing a Threshold of ≥3 mm

		Frequency Distribution of CAL Change		
Time	Total	Category*	%	N
Baseline-3 months	99	≥ + 3 mm (B)	37.3	(37)
		–2 to +2 mm (S)	62.7	(62)
		≥ – 3 mm (W)	—	(—)
At 6 months	76	≥ + 3 mm (B)	1.3	(1)
		–2 to +2 mm (S)	93.4	(71)
		≥ – 3 mm (W)	5.3	(4)
At 1 year	98	≥ + 3 mm (B)	3.0	(3)
		–2 to +2 mm (S)	95.0	(93)
		≥ – 3 mm (W)	2.0	(2)
At 2 years	72	≥ + 3 mm (B)	4.2	(3)
		–2 to +2 mm (S)	94.4	(68)
		≥ – 3 mm (W)	1.4	(1)
At 3 years	74	≥ + 3 mm (B)	4.1	(3)
		–2 to +2 mm (S)	91.8	(68)
		≥ – 3 mm (W)	4.1	(3)
At 4 years	77	≥ + 3 mm (B)	2.6	(2)
		–2 to +2 mm (S)	93.5	(72)
		≥ – 3 mm (W)	3.9	(3)
At 5 years	93	≥ + 3 mm (B)	3.2	(3)
		–2 to +2 mm (S)	94.6	(88)
		≥ – 3 mm (W)	2.2	(2)

*B = better; S = same; W = worse.

3.8% for initial PD ≥7 mm.[16] When a stepwise approach to determine attachment level changes was utilized, disease progression in established periodontitis was detected in 8.3% of periodontal sites over a 9-month period.[19] In another setting to define clinical attachment loss, the so-called incidence density (time to event) analytic strategy, the annual rate for active sites with a selected cut-off >3 mm was 2.1%.[27] Hence, although the threshold approach to define attachment loss applied to our database might result in some over- or underestimation of the number of breakdown sites,[23] the present findings indicate that the rate of progressing sites in treated aggressive periodontitis is similar to chronic periodontal disease once the disease is resolved by treatment means reported herein.

Our results provide support for the hypothesis that a consistent resolution of aggressive periodontal disease as evidenced by the decrease of CAL can be achieved utilizing a mechanical/surgical and antimicrobial treatment approach. Since aggressive periodontal inflammation is characterized by an upregulation of neutrophil recruitment that initiates severe injuries at multiple periodontal sites,[6] treatment principles should comprise both the surgical remodeling of long-term inflammatory altered periodontal tissues plus the control of periodontal bacteria eliciting leukocyte recruitment by systemic administration of antibiotics. These observations agree with findings from a meta-analysis of periodontal treatment[14] that favors surgical therapy in advanced disease severity settings, and when the major outcome is aimed at improvement of clinical attachment levels.

Within the limitations of our study, the following conclusions may be drawn: 1) in aggressive periodontitis, comprehensive mechanical/surgical and antimicrobial therapy is an appropriate treatment regimen for long-term stabilization of periodontal health, and 2) periodontal disease progression can be suc-

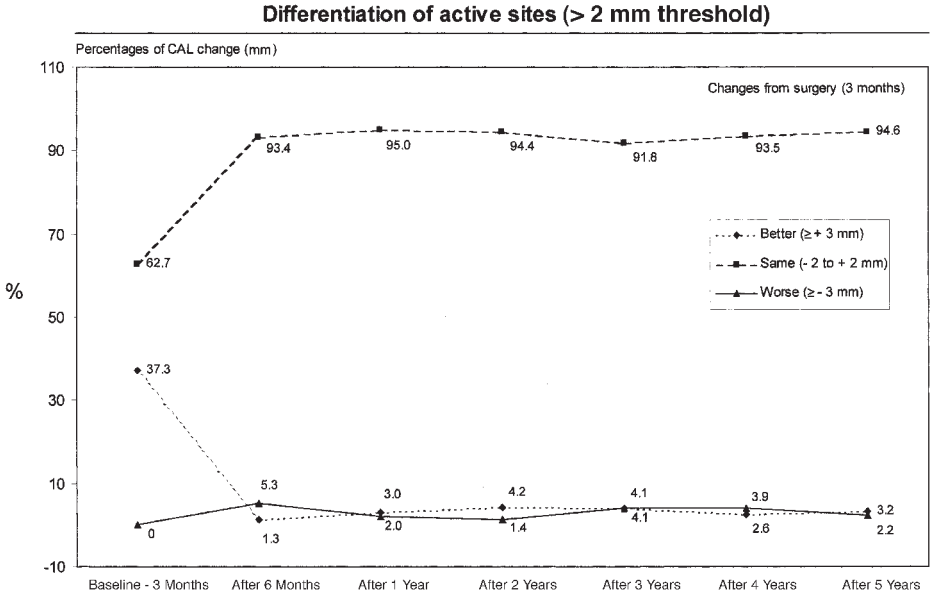

Figure 2.
Periodontal breakdown sites during the 5-year trial.

cessfully arrested in 95% of the initially compromised lesions, while 2% to 5% elicited discrete or recurrent episodes of loss of periodontal support.

ACKNOWLEDGMENTS

The authors appreciate the encouragement of Prof. Dr. T.F. Flemmig to develop this study.

REFERENCES

1. Beck JD, Slade G, Offenbacher S. Oral disease, cardiovascular disease and systemic inflammation. *Periodontol 2000* 2000;23:110-120.
2. Armitage GC. Development of a classification system for periodontal diseases and conditions. *Ann Periodontol* 1999;4:1-6.
3. American Academy of Periodontology. Parameter on aggressive periodontitis. *J Periodontol* 2000;71(Suppl.): 867-869.
4. Pouliot M, Clish CB, Petasis NA, Van Dyke TE, Serhan CN. Lipoxin A(4) analogues inhibit leukocyte recruitment to *Porphyromonas gingivalis:* A role for cyclooxygenase-2 and lipoxins in periodontal disease. *Biochem* 2000;39:4761-4768.
5. Cobb C. Nonsurgical pocket therapy: Mechanical. *Ann Periodontol* 1996;1:443-446.
6. Palcanis K. Surgical pocket therapy. *Ann Periodontol* 1996;1:589-616.
7. Feres M, Haffajee AD, Allard K, Som S, Socransky SS. Change in subgingival microbial profiles in adult periodontitis subjects receiving either systemically-administered amoxicillin or metronidazole. *J Clin Periodontol* 2001;28:597-609.
8. Winkel EG, van Winkelhoff AJ, Timmerman MF, van der Velden U, van der Weijden GA. Amoxicillin plus metronidazole in the treatment of adult periodontitis patients. A double-blind placebo-controlled study. *J Clin Periodontol* 2001;28:296-305.
9. Sigusch B, Beier M, Klinger G, Pfister W, Glockmann E. A 2-step non-surgical procedure and systemic antibiotics in the treatment of rapidly progressive periodontitis. *J Periodontol* 2001;72:275-283.
10. Pavicic MJ, van Winkelhoff AJ, Douqué NH, Steures RWR, de Graaff J. Microbiological and clinical effects of metronidazole and amoxicillin in *Actinobacillus actinomycetemcomitans*-associated periodontitis. A 2-year evaluation. *J Clin Periodontol* 1994; 21:107-112.
11. Berglundh T, Krok L, Liljenberg B, Westfelt E, Serino G, Lindhe J. The use of metronidazole and amoxicillin in the treatment of advanced periodontal disease. A prospective, controlled clinical trial. *J Clin Periodontol* 1998;25:354-362.
12. Winkel EG, van Winkelhoff AJ, van der Velden U. Additional clinical and microbiological effects of amoxicillin and metronidazole after initial periodontal therapy. *J Clin Periodontol* 1998;25:857-864.
13. Serino G, Rosling B, Ramberg P, Hellstrom MK, Socransky SS, Lindhe J. The effect of systemic antibiotics in the treatment of patients with recurrent periodontitis. *J Clin Periodontol* 2001;28:411-418.
14. Antczak-Bouckoms A, Joshipura K, Burdick E, Tulloch JF. Meta-analysis of surgical versus non-surgical methods of treatment for periodontal disease. *J Clin Periodontol* 1993;20:259-268.
15. Berkey CS, Antczak-Bouckoms A, Hoaglin DC, Mosteller F, Pihlstrom BL. Multiple-outcomes meta-analysis of treatments for periodontal disease. *J Dent Res* 1995;74:1030-1039.
16. Kaldahl WB, Kalkwarf KL, Patil KD, Molvar MP, Dyer JK. Long-term evaluation of periodontal therapy: II. Incidence of sites breaking down. *J Periodontol* 1996; 67:103-108.
17. Haffajee AD, Cugini MA, Dibart S, Kent RL Jr., Socransky SS. The effect of SRP on the clinical and microbiological parameters of periodontal disease. *J Clin Periodontol* 1997;24:324-334.
18. Renvert S, Nilvéus R, Dahlén G, Slots J, Egelberg J. 5-year follow-up of periodontal osseous defects treated by root planing or flap surgery. *J Clin Periodontol* 1990; 17:356-363.
19. Machtei EE, Norderyd J, Koch G, Dunford R, Grossi S, Genco RJ. The rate of periodontal attachment loss in subjects with established periodontitis. *J Periodontol* 1993;64:713-718.
20. Albandar JM. A 6-year study on the pattern of periodontal disease progression. *J Clin Periodontol* 1990; 17:467-471.
21. Silness J, Löe H. Periodontal disease in pregnancy. II. Correlation between oral hygiene and periodontal condition. *Acta Odontol Scand* 1964;22:121-135.
22. Löe H, Silness J. Periodontal disease in pregnancy. I. Prevalence and severity. *Acta Odontol Scand* 1963;21: 533-551.
23. Machtei EE, Schmidt M, Hausmann E, et al. Outcome variables in periodontal research: Means and threshold-based site changes. *J Periodontol* 2000;71:555-561.
24. DeRouen TA. Biostatistical and methodological issues in demonstrating efficacy of therapeutic agents for periodontal disease. *J Dent Res* 1989;68:1661-1666.
25. van Winkelhoff AJ, Tijhof CJ, de Graaff J. Microbiological and clinical results of metronidazole plus amoxicillin therapy in *Actinobacillus actinomycetemcomitans*-associated periodontitis. *J Periodontol* 1992;63: 52-57.
26. Buchmann R, Müller RF, Heinecke A, Lange DE. *Actinobacillus actinomycetemcomitans* in destructive periodontal disease. Three-year follow-up results. *J Periodontol* 2000;71:444-453.
27. Beck JD, Cusmano L, Green-Helms W, Koch GG, Offenbacher S. A 5-year study of attachment loss in community-dwelling older adults: Incidence density. *J Periodont Res* 1997;32:506-515.

Correspondence: Dr. Rainer Buchmann, Bussardstr. 6, D-59071 Hamm, Germany. E-mail: rainer_buchmann@yahoo.de.

Accepted for publication January 18, 2002.