Relationship Between Crevicular Aspartate Aminotransferase Levels and Periodontal Disease Progression

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Background: Aspartate aminotransferase (AST), an enzyme released from necrotic cells, has been identified in gingival crevicular fluid (GCF), and elevated levels are associated with periodontal tissue destruction. The aim of this study was to examine the relationship between elevated GCF levels of AST and periodontal disease progression.

Methods: Over a 12-month period, 8 to 10 interproximal sites in 41 periodontitis subjects (PS) and 15 healthy subjects (HS) were monitored. Clinical measurements included relative attachment level (RAL), probing depth, and bleeding on probing (BOP). Semiquantitative levels of GCF AST (<800 μIU, ≥800 μIU, and ≥1,200 μIU) were determined using a chairside assay. At the 6- and 12-month visits, scaling and root planing and prophylaxis were performed in the PS and HS, respectively. Sensitivity, specificity, positive predictive values (PPV), and negative predictive values (NPV) were calculated for 2 diagnostic criteria (AST ≥800 μIU, AST ≥1,200 μIU) utilizing 4 thresholds of disease progression as determined by 2 methods (absolute change in relative attachment level and cumulative sum [CUSUM]).

Results: The percentage of sites exhibiting AST ≥800 μIU, AST ≥1,200 μIU, and BOP in the PS was significantly (P <0.02) lower at 6 and 12 months compared to baseline. The use of crevicular AST activity to monitor periodontal disease progression was associated with many false-positive results. Overall, low specificities, PPV, and odds ratios were demonstrated by the assay when using 2 diagnostic criteria and 4 thresholds of disease progression. The high NPV suggest that a negative AST test result was indicative of a periodontally stable site.

Conclusions: These results demonstrate that elevated levels of AST were present at sites that did not subsequently exhibit disease progression. The high prevalence of AST-positive sites due to gingival inflammation diminished the test's ability to discriminate between progressive and stable, but inflamed, sites. *J Periodontol 2001;72:17-24.*

KEY WORDS

Aspartate aminotransferase; gingival crevicular fluid/analysis; periodontal diseases/diagnosis; disease progression.

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Current methods used to assess periodontal health include the utilization of periodontal probes and radiography. Both methods identify past tissue destruction, but provide no information regarding sites actively undergoing disease progression or identifying sites at risk of attachment loss.[1] Biochemical markers in gingival crevicular fluid (GCF) associated with the anatomic events of periodontitis have been investigated as potential methods to identify and predict future disease progression.[2-5] One host-derived enzyme that has been extensively studied in both animal[6-8] and human[9-13] investigations is aspartate aminotransferase (AST). The results of these studies indicate that elevated levels of AST are identified at sites experiencing gingival inflammation,[10,12] sites exhibiting a history of past attachment loss, and at sites actively undergoing disease progression.[13] In addition, the highest levels of AST appear to be at sites experiencing active tissue breakdown.[13] While elevated AST levels have been identified at sites undergoing periodontal tissue destruction (i.e., gingival inflammation, attachment loss), the ability of this marker to discern between stable and progressive sites has not yet been elucidated. The aim of the present study was to use a recently developed chairside assay for monitoring AST levels in GCF to examine the relationship between elevated AST levels and periodontal disease progression.

MATERIALS AND METHODS

Study Population

Fifty-three subjects exhibiting moderate to severe chronic periodontitis and 15 periodontally healthy controls were recruited. Eligible participants had not received any periodontal therapy for a minimum of 6 months and no antibiotic treatment for at least 3 months prior to study enrollment. Each individual was monitored at 8 to 10 interproximal sites. The sites monitored in the periodontitis subjects (PS) exhibited probing depths ≥5 mm and ≤8 mm as determined by manual probing, bleeding on probing, and bone loss as manifested by a distance of ≥3 mm from the cemento-enamel junction to the alveolar crest on bitewing radiographs. In contrast, the sites monitored in the 15 healthy subjects (HS) exhibited probing depth ≤3 mm, no evidence of bone loss, and no bleeding on probing at the screening examination. Thus, sites exhibiting periodontal attachment loss and periodontal health were not from the same subjects. The sites selected may have been in one or both arches. This study was approved by the Institutional Review Board at the Harvard Medical School and informed consent was obtained in writing from each subject prior to study commencement.

Study Design

A masked, controlled design with a single treatment arm was utilized. Neither the subjects nor clinical examiner knew the results of the AST assay. Likewise, the examiner responsible for recording the AST assay results was masked in regards to the subject's periodontal condition. Over a 12-month period, 8 to 10 interproximal sites were monitored in PS and HS, monthly and quarterly, respectively (Fig. 1). The parameters monitored included determination of GCF AST level using a rapid chairside assay,¶ and clinical measurements including probing depth (PD), bleeding on probing (BOP), and relative attachment level (RAL).

At the 6- and 12-month visits, scaling and root planing was performed in the periodontitis subjects. Both hand and ultrasonic instrumentation were utilized. A maximum of 2 sessions with no time limitations was allowed to complete each subject. Local anesthetic was used at the discretion of the clinician. Periodontally healthy subjects received a dental prophylaxis at 6 and 12 months.

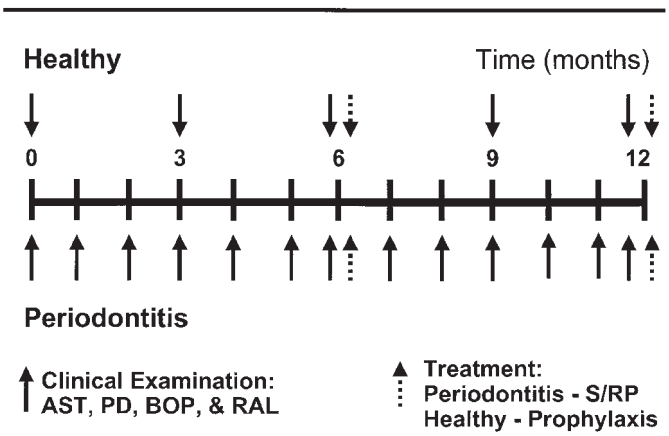

Figure 1.
Study design.

Clinical Measurements and Calibration

Probing depth was recorded with an automated probe# that utilized a controlled force of 20 g. A dichotomous evaluation of bleeding on probing (+ or −) was recorded. Relative attachment level was measured utilizing an automated probe** that used an occlusal disk as the reference landmark. For both probing depth and RAL, 2 passes were performed to obtain a mean value. If a difference of ≥0.5 mm existed, a third pass was recorded, and the median value was used. The presence of bleeding on probing was determined 10 seconds after completing the initial probing depth measurement. A single examiner completed all of the clinical measurements performed in this study.

A calibration exercise was conducted to assess intra-examiner reliability. For this exercise, a subset of 10 periodontitis subjects from the trial was examined twice 7 days apart. The 10 subjects contributed a total of 82 interproximal sites for this calibration study. Two passes were performed at each site at each visit. The examiner's repeatability and measurement of agreement within 0.5 mm and 1 mm utilizing the automated disk probe were calculated to assess intra-examiner reliability. The examiner's relative attachment level measurements between the 2 visits demonstrated 86.7% and 100% agreement within 0.5 mm and 1 mm, respectively. The examiner's repeatability utilizing the automated disk probe was estimated at 0.58 mm, which represents the pooled estimate of the standard deviation.

Biochemical Monitoring (AST)

Gingival crevicular fluid was harvested for AST analysis prior to any clinical measurements. Each site was air-dried and a methylcellulose paper strip†† was inserted gently at the margin of the sulcus and removed after 30 seconds. The amount of AST present on the collected strip was semiquantitatively (<800 μIU, ≥800 μIU, and ≥1,200 μIU) determined using a rapid chairside assay.¶ The assay is based on a colorimetric reaction in which an examiner compares 2 positive control wells of known AST level (i.e., 800 μIU, 1,200 μIU)

¶ PocketWatch, Pacific Pharmaceuticals, Inc., San Diego, CA.
# Florida Probe Corporation, Gainesville, FL.
** Florida Disc Probe Corporation.
†† Pro-Flow, Inc., Amityville, NY.

to test wells which contain the paper strips impregnated with gingival crevicular fluid from the sites under investigation. If the color was equal to or lighter (more pink) than the positive controls, the result was considered positive. The test was scored positive or negative for the AST 1,200 μIU control first, followed by the 800 μIU control. At room temperature, the AST 800 μIU comparison was scored between 8 and 15 minutes.

Statistical Analysis

Disease progression at individual sites over the 6-month pretreatment period was determined by 2 different methods: absolute change and cumulative sum (CUSUM). The absolute change method employed a change in RAL between the baseline and 6-month visit utilizing 3 different thresholds for attachment level change based upon examiner repeatability of RAL measurements using the automated disk probe. Repeatability was estimated as the pooled estimate of the standard deviation (SD) as determined from the calibration study described above. Analysis of variance was utilized to calculate the root mean square error, which is the pooled estimate of the standard deviation. This calculation has been previously recommended as an unbiased estimate of examiner error.[14] The estimated value from the calibration study was SD = 0.58 mm.

The absolute change method designated a change in relative attachment level at greater than or equal to 1 SD, 2 SD, or 3 SD between the baseline and 6-month visit as a significant event. Thus, if a site exhibited a change in RAL between the baseline and 6-month visit ≥0.58 mm, 1.16 mm, or 1.74 mm, it was categorized as having exhibited disease progression.

The second method employed was the CUSUM method,[15] which utilized all 7 monitoring visits to identify changes in relative attachment level. In the CUSUM method, differences from baseline are computed for each observation and the differences are added to obtain a sequence of sums, which increase or decrease with the number of positive or negative changes. If the rate of increase or decrease surpasses a predetermined critical value, a change is declared. Decision limits for the CUSUM method were set with a mask half-height of 2.5 SD and a mask slope of 1.0 SD following conventions established by the British Standards Institution.[16] If a positive trend (increasing relative attachment loss) was detected at any interval between visits 0 and 6, an individual site was categorized as progressing. Both the absolute change and CUSUM methods were performed on the periodontitis subjects to estimate the incidence of disease progression over the 6-month period. As previously reported,[17] utilizing the CUSUM method, 49 of 411 sites (11.9%) demonstrated progression over the 6-month pretreatment period. When attachment level changes ≥0.58 mm, ≥1.16 mm, and ≥1.74 mm were used to identify disease progression, the percentage of sites exhibiting deterioration was 19.5%, 8.8%, and 2.9%, respectively.

The percentages of AST ≥800 μIU, AST ≥1,200 μIU, and BOP-positive sites were calculated for each visit. The change in the proportion of AST ≥800 μIU, AST ≥1,200 μIU, and BOP-positive sites between visits 0 to 6, 0 to 12, and 6 to 12 was tested utilizing a Mantel-Haenszel statistic with one degree of freedom employing a stratified analysis which controlled for subject.

Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were determined for each of 3 diagnostic criteria (AST ≥800 μIU, AST ≥1,200 μIU, and BOP) by using the 4 measures of disease progression (CUSUM, RAL ≥0.58 mm, ≥1.16 mm, and ≥1.74 mm). The presented proportions for sensitivity, specificity, PPV, and NPV are maximum likelihood estimates from the correlated binomial model (custom statistical program). Confidence limits around the proportion (95%) are provided except in those cases where the estimate of P was near the sample-based bounds employed by the method.[18,19] In 3 cases when there was a single, multisite subject, the standard binomial model was employed to provide estimates and confidence limits.

The overall association between diagnostic criteria and categorization of disease progression was estimated and tested by employing a stratified analysis using the Mantel-Haenszel method.[20] The statistical significance of the overall association was tested ($\alpha = 0.05$). The odds ratio and corresponding chi-square statistic are calculated from the 2×2 subtables for those subjects with 2 levels for both the diagnostic (row) and disease progression (column) variables (i.e., no zero row or column totals). The odds ratio is a measure of relative risk. Confidence limits around the estimate of the odds ratio (95%) are provided.

RESULTS

Study Population Demographics

Fifty-three periodontitis subjects were initially recruited for the study. During the 6-month pretreatment period, 6 were terminated due to poor compliance and 1 due to a diagnosis of leukemia. The pretreatment results represent 411 interproximal sites in 46 periodontitis subjects who completed the first 6 months of the trial. During the 6-month post-treatment period, 5 additional subjects were terminated: 3 due to poor compliance, 1 due to a diagnosis of tuberculosis, and one due to pregnancy. Therefore, the post-treatment results represent 366 interproximal sites in 41 subjects who completed the trial. The mean age was 48 years old and the percentage of males was 39%. The percentage of smokers among the PS was 17%.

Fifteen periodontally healthy subjects (139 interproximal sites) were recruited and completed the study. The mean age was 26.6 years old and the percentage of males 40%. The percentage of smokers was 0.07%. The periodontitis subjects were significantly older (48 years versus 26.6 years) and consisted of a higher percentage of smokers (17% versus 0.07%) compared to the periodontally healthy subjects (P <0.05).

Distribution of AST ≥800 µIU, AST ≥1,200 µIU, and BOP-Positive Sites

Figure 2 demonstrates the percentage of AST ≥800 µIU, AST ≥1,200 µIU, and BOP-positive sites at baseline and at 6 and 12 months in the PS group. The percentage of sites exhibiting elevated AST activity and BOP decreased significantly (P <0.01) during the first 6 months of the trial despite no treatment. After scaling and root planing was completed at the 6-month visit, a significant reduction was observed again among all 3 diagnostic parameters at the 12-month visit (P <0.02). The periodontally healthy subjects exhibited AST activity of ≥800 µIU and ≥1,200 µIU at 17.27% and 7.19% sites, respectively, at baseline (Fig. 3). No significant differences were noted in the percentage of AST-positive sites for either threshold at the 6- and 12-month visits. While the percentage of AST-positive sites in the periodontally healthy subjects remained relatively constant during the study, the percentage of sites that exhibited BOP significantly increased from visits 0 to 6 and 6 to 12 (P <0.01, P <0.05, respectively). At study completion, 15.83% of the sites exhibited bleeding on probing (Fig. 3). The periodontitis subjects exhibited a significantly greater percentage (P <0.01) of AST-positive results throughout the pre- and post-treatment period compared to the healthy subjects.

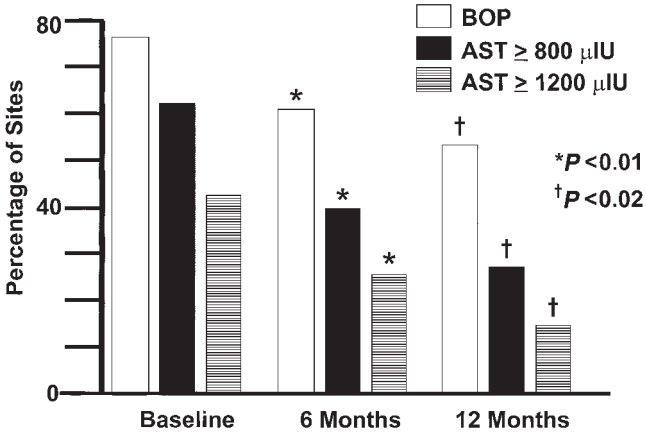

Figure 2.
Percentage of bleeding on probing, AST ≥800 µIU, and AST ≥1,200 µIU positive sites in periodontitis subjects.

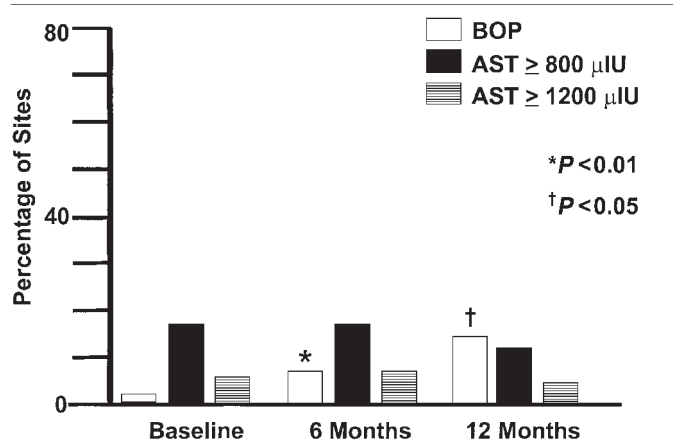

Figure 3.
Percentage of bleeding on probing, AST ≥800 µIU, and AST ≥1,200 µIU positive sites in healthy subjects.

Diagnostic Characteristics of AST Assay

Table 1 demonstrates the sensitivity and specificity of the AST assay and BOP utilizing change in attachment level measurements as the gold standard for periodontal disease progression. When a strict threshold for disease progression was utilized (RAL ≥1.74 mm), the AST ≥800 µIU threshold exhibited a 91.7% sensitivity. However, the specificity was quite low at 34.5%. As expected, at the higher threshold of AST ≥1,200 µIU, the sensitivity decreased to 58.3%, and the specificity increased to 55.7%. Bleeding on probing demonstrated a sensitivity similar to the AST ≥800 µIU threshold. However, the specificity values were extremely low, which is likely due to the high number of false-positive results.

Table 2 demonstrates the PPV, NPV, and overall agreement for both the AST assay and BOP. Overall, the AST assay at both thresholds consistently demonstrated low PPV and high NPV regardless of the method used to define progression. As a result of the low PPV, the overall agreement for the assay was weak.

The association between a positive AST test result at baseline and the risk of disease progression over the following 6 months was evaluated by calculating an odds ratio at the different thresholds of disease progression defined previously (Table 3). The significance of that association was assessed utilizing a test of overall association. The greatest association was found at RAL ≥1.74 mm where the AST ≥800 µIU threshold demonstrated an odds ratio of 12.58. This finding is not truly significant as evidenced by a marginal overall association (P = 0.06) and large 95% confidence limits. In summary, there was a relatively weak association between a site exhibiting elevated baseline AST levels and subsequently experiencing attachment loss over the next 6 months.

Table 1.

Diagnostic Characteristics of AST Assay: Sensitivity and Specificity*

Comparison	Sensitivity		Specificity	
	P	95% Confidence Limits	*P*	95% Confidence Limits
AST ≥800 μIU vs. CUSUM	74.5%	(60.6%, 88.4%)	36.2%	(29.7%, 42.6%)
AST ≥1200 μIU vs. CUSUM	54.1%	(38.5%, 69.7%)	57.2%	(50.7%, 63.7%)
BOP vs. CUSUM	84.2%†		22.5%	(16.8%, 28.3%)
AST ≥800 μIU vs. RAL ≥0.58 mm	65.5%	(53.1%, 77.9%)	36.1%	(30.1%, 42.0%)
AST ≥1200 μIU vs. RAL ≥0.58 mm	46.1%	(33.2%, 58.9%)	55.6%	(47.9%, 63.3%)
BOP vs. RAL ≥0.58 mm	81.0%	(71.9%, 90.1%)	23.8%	(18.2%, 29.4%)
AST ≥800 μIU vs. RAL ≥1.16 mm	71.2%†		34.7%	(28.5%, 41.0%)
AST ≥1200 μIU vs. RAL ≥1.16 mm	48.3%	(29.0%, 67.5%)	57.3%	(50.9%, 63.8%)
BOP vs. RAL ≥1.16 mm	75.5%†		21.9%	(16.6%, 27.3%)
AST ≥800 μIU vs. RAL ≥1.74 mm	91.7%‡	(76.0%, 100%)	34.5%	(28.8%, 40.3%)
AST ≥1200 μIU vs. RAL ≥1.74 mm	58.3%‡	(30.4%, 86.2%)	55.7%	(49.1%, 62.3%)
BOP vs. RAL ≥1.74 mm	91.7%‡	(76.0%, 100%)	22.8%	(17.6%, 28.1%)

* Sensitivity and specificity are maximum likelihood estimates from the correlated binomial model. In those cases designated (†) where the estimate of ρ was near the sample-based bounds employed by the method, the confidence limits are not presented. In those cases designated (‡) with a single multisite patient, the standard binomial model is employed to provide estimates and confidence limits.

DISCUSSION

Accurate detection of periodontal sites exhibiting disease progression or those at risk of future deterioration has proven difficult. The development of chairside tests for host mediators associated with the anatomic events of periodontitis may serve as useful methods for identifying and predicting future progression. The aim of this study was to examine the relationship between elevated levels of AST in gingival crevicular fluid and periodontal disease progression over a 6-month period in untreated periodontitis subjects.

The diseased sites exhibited a significantly greater percentage of AST-positive results throughout the pre- and post-treatment period compared to the healthy sites. Imrey et al. also reported a substantial relationship between AST levels and clinical indices at the patient level, demonstrating that patients with more severe periodontitis exhibited higher AST levels.[9] In contrast to Imrey et al., who utilized only periodontitis subjects, the present study included a periodontally healthy cohort. Overall, these findings suggest that the AST assay results correlate with traditional clinical indices.

The periodontitis subjects exhibited a significant decline in AST-positive sites over both the pre- and post-treatment period. The proportions found in this study 6 months after mechanical therapy are similar to those reported by Persson et al. 28 days after scaling and root planing and prophylaxis in periodontitis and healthy subjects, respectively.[11] It should be noted that a GCF AST level of 800 μIU is approximately 20 times greater than levels found in serum of normal periodontally healthy subjects.[21] Therefore, the finding that both healthy and diseased sites exhibit AST ≥800 μIU in GCF indicates that significant local tissue destruction does occur at healthy and diseased sites. However, this destruction does not necessarily result in clinically significant attachment level changes.

The evaluation of new diagnostic tests for periodontitis is difficult due to the absence of an adequate gold standard to identify true disease. Traditionally, investigators have utilized high thresholds that detect sites exhibiting severe attachment loss, but label many active sites as periodontally stable. If the diagnostic test under investigation is more sensitive than the attachment level change used to identify progression, the test will appear to exhibit a high sensitivity and poor specificity. In an attempt to circumvent this situation, the present study utilized 4 thresholds to identify attachment level changes. As expected, when the high threshold of ≥1.74 mm was used, the AST ≥800 μIU threshold demonstrated a favorable sensitivity of 91.7% and a low specificity of 34.5%. Persson and Page reported that AST ≥800 μIU demonstrated a sensitivity of 93% and specificity of 68% for sites exhibiting an attachment loss ≥2 mm.[22] These investigators utilized the AST value recorded at the visit the attachment loss was identified to calculate the sensitivity and specificity. In contrast, the present study used AST values recorded at baseline to assess the ability of the assay to identify disease progression over a 6-month period. These findings suggest that the AST assay was associated with a large number of false-positive results.

Table 2.

Diagnostic Characteristics of AST Assay: Positive Predictive Value, Negative Predictive Value, and Overall Agreement*

Comparison	Positive Predictive Value		Negative Predictive Value		Overall Agreement
	P	95% Confidence Limits	*P*	95% Confidence Limits	*P*
AST ≥800 µIU vs. CUSUM	12.7%	(7.4%, 18.1%)	91.8%	(87.0%, 96.6%)	42.3%
AST ≥1200 µIU vs. CUSUM	14.0%	(7.7%, 20.4%)	90.2%	(85.9%, 94.4%)	56.7%
BOP vs. CUSUM	13.2%	(8.8%, 17.5%)	91.7%†		31.1%
AST ≥800 µIU vs. RAL ≥0.58 mm	20.5%	(14.9%, 26.1%)	83.1%	(76.8%, 89.4%)	43.6%
AST ≥1200 µIU vs. RAL ≥0.58 mm	20.8%	(14.2%, 27.5%)	82.1%†		55.0%
BOP vs. RAL ≥0.58 mm	20.7%	(15.8%, 25.6%)	84.3%†		35.3%
AST ≥ 800 µIU vs. RAL ≥1.16 mm	9.6%	(5.5%, 13.7%)	92.2%	(86.7%, 97.7%)	40.1%
AST ≥1200 µIU vs. RAL ≥1.16 mm	9.6%	(4.4%, 14.8%)	91.8%	(87.4%, 96.2%)	56.0%
BOP vs. RAL ≥1.16 mm	8.6%	(5.4%, 11.8%)	90.0%	(83.0%, 96.9%)	27.5%
AST ≥800 µIU vs. RAL ≥1.74 mm	4.2%†		99.3%†		38.7%
AST ≥1200 µIU vs. RAL ≥1.74 mm	3.8%	(0.8%, 6.7%)	97.8%†		56.0%
BOP vs. RAL ≥1.74 mm	3.5%†		98.9%†		25.5%

* Positive and negative predictive values are maximum likelihood estimates from the correlated binomial model. In those cases designated (†) where the estimate of ρ was near the sample-based bounds employed by the method, the confidence limits are not presented.

The effect of disease prevalence on predictive values was evident in this study. Overall, the relatively low prevalence of disease progression (2.9% to 19.5%) resulted in low PPV (4.2% to 20.5% for AST ≥800 µIU) and high NPV (83.1% to 99.3% for AST ≥800 µIU). These predictive values suggest that a positive AST assay result would not provide the clinician with any significant diagnostic information since many of the sites with a positive result do not exhibit disease progression. However, the high NPV suggest that a negative test result may be highly indicative of a periodontally stable site. In the present study, the AST assay did not provide significantly more diagnostic information about a site than bleeding on probing.

An odds ratio of 12.58 was found for sites exhibiting AST ≥800 µIU at baseline and subsequently demonstrating RAL of ≥1.74 mm over the following 6-month period. This association was found to be marginally significant ($P = 0.06$). Persson and Page reported a similar odds ratio of 15.4 when evaluating the association between AST ≥800 µIU and a confirmed attachment loss ≥2 mm.[22] Other comparisons utilizing lower thresholds did not exhibit any significant associations with AST-positive results.

In summary, the use of crevicular AST activity to monitor periodontal disease progression was associated with many false-positive results and, therefore, could not discriminate between progressive and non-progressive sites. The high prevalence of sites exhibiting elevated AST activity at baseline, which did not subsequently exhibit progression, was due to the presence of gingival inflammation as evidenced by the high percentage of bleeding on probing sites. It has been previously demonstrated that elevated AST levels occur at sites exhibiting gingival inflammation, and that site and subject variability in AST levels exists.[10,12] As a result, the gingival inflammation may have been a confounding factor, which reduced the ability of the AST assay to identify progressive sites. To avoid this effect, a supragingival scaling provided prior to study commencement may have reduced gingival inflammation without totally disrupting the subgingival environment, enabling disease progression to occur.

AST is a non-specific marker for cell death and tissue destruction. The periodontal diseases are comprised of 2 major conditions (i.e., gingivitis, periodontitis) which both exhibit cell death and loss of tissue. Perhaps it is necessary to identify what cell type is primarily responsible for AST activity in different disease states. Mizuho et al. reported in vitro that human gingival epithelial cells demonstrated significantly higher levels of AST activity compared to other periodontally derived cells, polymorphonuclear leukocytes, and plasma in peripheral blood from patients exhibiting periodontal health.[23] In addition, the type of AST present (mitochondrial or cytoplasmic) may make a difference in assessing disease progression or risk of breakdown. For example,

Table 3.

Diagnostic Characteristics of AST Assay: Odds Ratio and Test of Overall Association

Comparison	Odds Ratio		Overall Association	
	Ratio	95% Confidence Limits	χ^2	*P* Value
AST ≥800 μIU vs. CUSUM	2.00	(.92, 4.34)	3.04	0.08
AST ≥1200 μIU vs. CUSUM	1.44	(.66, 3.14)	0.85	0.36
BOP vs. CUSUM	1.83	(.86, 3.90)	2.45	0.12
AST ≥800 μIU vs. RAL ≥0.58 mm	1.03	(.57, 1.86)	0.01	0.91
AST ≥1200 μIU vs. RAL ≥0.58 mm	.88	(.46, 1.66)	0.16	0.69
BOP vs. RAL ≥0.58 mm	1.41	(.74, 2.69)	1.08	0.30
AST ≥800 μIU vs. RAL ≥1.16 mm	1.36	(.57, 3.26)	0.48	0.49
AST ≥1200 μIU vs. RAL ≥1.16 mm	1.00	(.44, 2.27)	0.00	1.00
BOP vs. RAL ≥1.16 mm	1.02	(.41, 2.53)	0.00	0.96
AST ≥800 μIU vs. RAL ≥1.74 mm	12.58	(.90, 176.78)	3.53	0.06
AST ≥1200 μIU vs. RAL ≥1.74 mm	1.32	(.31, 5.54)	0.14	0.71
BOP vs. RAL ≥1.74 mm	4.97	(.77, 32.27)	2.82	0.09

increased levels of mitochondrial AST following a myocardial infarction indicate that more cell necrosis has occurred, and the prognosis is worsened.[24] Due to the multifactorial etiology of periodontal diseases, the likelihood of one marker discriminating between progressive and non-progressive sites is minimal. Recently, investigators have demonstrated in cross-sectional studies that elevated AST activity was associated with the presence of putative periodontal pathogens including *Porphyromonas gingivalis, Actinobacillus actinomycetemcomitans,* and *Prevotella intermedia.*[25,26] Future studies should therefore examine longitudinally the utilization of elevated GCF AST activity in combination with microbiologic or other host markers to develop patient profiles, which may allow for improved identification of individuals at risk of disease progression.

ACKNOWLEDGMENTS

This study was supported by Pacific Pharmaceuticals, Inc., San Diego, California, and NIDCR grant DE7010. Dr. Reasner is Vice President, Clinical Operations & Data Analysis at Sepracor, Inc., Marlborough, Massachusetts.

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Accepted for publication June 5, 2000.