



Tooth loss and alveolar bone crest loss during supportive periodontal therapy in patients with generalized aggressive periodontitis: retrospective study with follow-up of 8 to 15 years

Journal:	<i>Journal of Clinical Periodontology</i>
Manuscript ID	CPE-03-16-6255.R2
Manuscript Type:	Epidemiology (Cohort study or case-control study)
Date Submitted by the Author:	n/a
Complete List of Authors:	Díaz-Faes, Lucía; University of Granada, Periodontology Guerrero, Adrian; Private Periodontal Practice; University of Barcelona, Graduate Comprehensive Dentistry Magán-Fernández, Antonio; University of Granada, Periodontology Bravo, Manuel; School of Dentistry, University of Granada, Preventive and Community Dentistry Mesa, Francisco; University of Granada, Periodontology
Topic:	Treatment
Keywords:	Retrospective studies, Aggressive periodontitis, Tooth loss, Alveolar bone loss, Smoking
Main Methodology:	Epidemiology

SCHOLARONE™
Manuscripts

1
2
3 **Tooth loss and alveolar bone crest loss during supportive periodontal therapy in**
4 **patients with generalized aggressive periodontitis: retrospective study with follow-**
5 **up of 8 to 15 years**
6
7
8
9

10
11
12
13 Lucía Díaz-Faes¹, Adrián Guerrero², Antonio Magán-Fernández¹, Manuel Bravo³,
14 Francisco Mesa¹.
15
16

17
18
19
20
21 1 Periodontology Department, School of Dentistry, University of Granada, Spain.

22
23 2 Private practice in Periodontology "Clínica Guerrero" Marbella, Spain.

24
25 3 Department of Preventive Dentistry and Epidemiology, School of Dentistry, University of
26 Granada, Spain.
27
28

29
30
31
32 **Running head:** Tooth loss in generalized aggressive periodontitis
33

34
35 **Keywords:** Retrospective studies, aggressive periodontitis, tooth loss, alveolar bone
36 loss, smoking.
37
38

39
40
41
42 ***Correspondence to:**

43
44
45 Dr. Francisco Mesa Aguado

46
47 Departamento de Estomatología

48 Facultad de Odontología, Universidad de Granada

49 Campus de Cartuja S/N

50 18071, Granada

51
52
53
54
55
56
57 Tel. +34 958240654; Email: fmesa@ugr.es
58
59
60

ABSTRACT

Aim: To determine the incidence of tooth loss in patients with generalized aggressive periodontitis (GAgP) during supportive periodontal therapy (SPT), identify tooth loss risk factors, and quantify alveolar crest height changes on periapical x-ray during follow-up.

Material and Methods: This retrospective study included 25 GAgP patients with 656 teeth after periodontal treatment (baseline). Data were gathered on sociodemographic, periodontal, and radiological variables at baseline and at the end of follow-up. Linear regression models were used to assess the association of risk factors with tooth loss.

Results: Twenty-eight teeth were extracted during SPT. The mean tooth loss per patient was 1.12 ± 2.01 for all causes and 0.9 ± 2.0 for periodontal disease after a mean follow-up of 10.9 ± 2 years. Clinical variables were improved at the end of follow-up, with a mean reduction of -1 ± 0.8 mm in probing pocket depth (-0.7 to -1.3 , 95%CI) and -0.6 ± 0.9 mm in clinical attachment loss (-0.9 to -0.2 , 95%CI). Mean alveolar bone crest loss at the end of follow-up was 0.36 ± 0.56 mm (0.10 to 0.61 , 95%CI). Smoking was associated with tooth loss ($p=0.052$).

Conclusions: Tooth loss rate was low in GAgP in a regular supportive care program. Clinical variables improved and bone loss was minimal over time. Smoking was associated with tooth loss.

CLINICAL RELEVANCE

Scientific rationale for the study:

Few long-term studies have addressed tooth loss and its related risk factors in GAgP patients receiving regular SPT.

Principal findings:

The results of active GAgP treatment remained stable over time and even improved PPD and CAL, contributing to ensure tooth survival. Smoking was associated with tooth loss.

Practical implications:

A larger number of SPT visits and/or full compliance with STP do not appear to avoid the loss of teeth with worse initial periodontal status. Efforts to support patients in quitting tobacco may contribute to tooth stability in GAgP.

CONFLICT OF INTEREST AND SOURCE OF FUNDING

The authors have stated explicitly that there are no conflicts of interest in connection with this article. This study was self-funded by research group CTS-583 (University of Granada).

INTRODUCTION

Aggressive periodontitis (AgP) affects young people with a non-contributory medical history and self-reported familiar aggregation and is characterized by a rapid attachment loss and bone destruction (Lang et al. 1999). The prevalence ranges between 0.1 and 0.2% in Caucasians and between 1 and 5% in African and Afro-American populations (Susin et al. 2014). Generalized aggressive periodontitis (GAgP) usually affects subjects under 30 years of age but can appear in older individuals. It is defined by generalized interproximal attachment loss involving at least three permanent teeth other than first molars and incisors (Lang et al. 1999).

Supportive Periodontal Therapy (SPT), an extension of active periodontal therapy, is performed at programmed intervals to assist periodontal patients in maintaining oral health (AAP 2000). Disease progression is rapid in patients with untreated aggressive forms of periodontitis, who have a higher risk of relapse during SPT (Teughels et al. 2014) but do not lose more teeth than do chronic periodontitis patients over the long term (Graetz et al. 2011). There has been limited investigation into long-term treatment and maintenance outcomes in GAgP patients (Nibali et al. 2013), with clinical studies on tooth loss over a 5-year follow-up period in 25 patients (Kamma and Baehni 2003), a 6-year period in 64 patients (Brown et al. 1996), and a mean of 10 years in 84 patients (Baumer et al. 2011). Various authors have associated tooth loss in periodontitis with alveolar bone crest loss (Dannewitz et al. 2006, Faggion et al. 2007, Pretzl et al. 2008). Alveolar crest loss was described by Bäumer *et al.* as the most important prognostic factor for tooth loss during SPT in AgP patients (Baumer et al. 2011). The baseline clinical status of teeth has been considered an essential predictive factor for long-term tooth loss (Graetz et al. 2011), and tooth loss has been related to non-compliance with periodontal maintenance programs (Axelsson and Lindhe 1981, Lee et al. 2015). It has

1
2
3 also been reported that risk factors have a similar influence on long-term tooth
4
5 prognosis in both chronic and aggressive periodontitis (Pretzl et al. 2008).
6
7

8 In a recent systematic review of 16 studies, Nibali et al. (Nibali et al. 2013) reported that
9
10 the average tooth loss in AgP during maintenance therapy after initial treatment was
11
12 0.09 teeth per year and that the annual tooth loss was lower in localized (0.05 teeth) than
13
14 in generalized (0.14 teeth) forms. However, 91% of the tooth losses (358 teeth) were in
15
16 only 38% of the patients, with 16% losing only one tooth during the follow-up and 46%
17
18 losing none.
19
20

21
22 The objective of this retrospective study was to determine the incidence of tooth loss in
23
24 GAgP patients undergoing long-term SPT and to identify clinical variables associated
25
26 with losses.
27
28
29
30
31

32 **MATERIALS AND METHODS**

33 *Study design*

34
35
36 A retrospective observational study was performed in consecutive patients undergoing
37
38 treatment for GAgP in a periodontal private practice clinic in Málaga, Spain, who were
39
40 reevaluated between October 2013 and March 2014. STROBE (Strengthening the
41
42 Reporting of Observational Studies in Epidemiology) guidelines were followed (von
43
44 Elm et al. 2008). The study was approved by the Research Ethics Committee of the
45
46 provincial health service (# PI03/11/13) and conducted in accordance with CIOMS
47
48 ethical guidelines and the Helsinki Declaration.
49
50
51
52
53
54
55
56
57
58
59
60

Study Participants

Data were retrieved from the database of the periodontal clinic on all patients with a diagnosis of early-onset periodontitis, rapidly progressive periodontitis, juvenile periodontitis, or GAgP. Study inclusion criteria were: age up to 35 years at the diagnosis and at least 18 years at re-examination., completion of active treatment, current receipt of SPT, minimum follow-up time of ≥ 8 years, presence of > 20 teeth at the time of diagnosis, and complete x-ray series and periodontal records at the diagnosis and at the end of the study. Exclusion criteria were the presence of systemic disease or pregnancy. The study coordinator (L.D-F) telephoned patients meeting the eligibility criteria and invited them to participate in the study. Patients who gave their consent then underwent a complete periodontal examination (full medical and dental history, intra-oral examination, and full-mouth periodontal charting), including periapical x-rays. All subjects had received initial periodontal treatment with a combination of oral amoxicillin (500 mg TID for 7 days) and metronidazole (500 mg TID for 7 days); patients allergic to penicillin received metronidazole alone (Guerrero et al. 2005).

Variables

Data were gathered on the age, sex, and smoking habit of patients at the diagnosis and end of the follow-up, classifying them as non-smokers (or ex-smoker for >5 years) or smokers of <10 cig/day, 10-20 cig/day, or >21 cig/day. Tooth loss was the main outcome variable, measured as the difference between the number of teeth after initial periodontal treatment (baseline) and the number of teeth in the final reevaluation. The position and cause of each tooth loss were recorded. Clinical data on periodontal probing pocket depth (PPD) and clinical attachment loss (CAL) were gathered by two experienced and calibrated periodontists (AG at diagnosis and L.D-F at end of follow-

1
2
3 up) using a manual probe (PCPUNC15, Hu-Friedy, Chicago, IL, USA) at six sites per
4
5 tooth (MV, V, DV, ML, L, DL), excluding third molars.
6
7

8 Inter-examiner calibration was measured in a group of 10 GAgP patients not involved in
9
10 the main study. All of them received SPT at least every 6 months at the same
11
12 periodontal private practice clinic. Both examiners measured full-mouth PPD and
13
14 gingival margin recession of the gingival margin in all 10 subjects, with each patient
15
16 being examined on the same day at two different time points (one per examiner). The
17
18 percentage of between-examiner agreement (within +/- 1mm) on CAL measurements
19
20 was 93.62%, considered adequate.
21
22

23
24 The modified binary index of Tonetti et al. was calculated as plaque index (Tonetti
25
26 2002), and the Ainamo and Bay score as bleeding index (Ainamo and Bay 1975). All
27
28 patients were scheduled to receive SPT every 4-6 months, and data were gathered on
29
30 their total number of SPT sessions and compliance with SPT, classifying patients as
31
32 “compliant” if they had attended all SPT appointments during the entire observation
33
34 period.
35
36

37
38 Mesial and distal bone crest loss was measured in all teeth on periapical x-ray series at
39
40 the diagnosis and in the final reevaluation, using a customized film holder with beam
41
42 guiding tool (Rinn Corporation, Dentsply, York, PA, USA) to obtain a repeatable
43
44 exposure in all intraoral x-ray studies, which were always performed with the same
45
46 radiological device (Oraliz AC, Gendex, Dental Systems, Milan, Italy). The loss was
47
48 calculated as the difference between these time points in the distance from the
49
50 cementoenamel junction (CEJ) to the bone crest area most in contact with the tooth root
51
52 (Mros and Berglundh 2010). For this purpose, periapical x-rays were digitalized with a
53
54 HP Scanjet G2710 scanner (Hewlett-Packard®, Palo Alto, CA, USA) at a resolution of
55
56
57
58
59
60

1
2
3 600x1200 dpi. The measurements were made by a single calibrated researcher (A. M-
4 F.), who was blinded to the patients' clinical data, using a digital image analysis
5 program (ImageJ 1.48v, NIH, Bethesda, MD, USA). Seven randomly selected x-rays
6
7 were examined twice, two weeks apart, in order to determine intra-examiner
8 reproducibility, obtaining an intraclass correlation coefficient of 0.86, indicating good
9
10 intra-examiner agreement. A distance between alveolar crest and CEJ ≤ 1 mm was not
11
12 considered as loss (Hausmann et al. 1991).
13
14
15
16
17

18 19 *Statistical analysis*

20
21
22 The statistical analyses were performed by a single researcher (M.B.). SPSS v.20.0
23 (IBM Inc., Chicago, IL, USA) was used when the unit of analysis was the patient,
24 performing descriptive statistics (means, standard deviations and percentages) and
25 analytical procedures (95% confidence intervals, Mann-Whitney test, Chi-square,
26 Student's t-test for paired samples, and univariate and multivariate linear regression
27 analysis with periodontal tooth loss as dependent variable). The DESCRIPT procedure
28 in SUDAAN 7.0 (RTI International, Research Triangle Park, NC, USA) was used when
29 the unit of analysis was the tooth site in order to account for clustering (multiple
30 observations within each patient) in standard error and p-value calculations. The
31 statistical tests used are given in Table footnotes
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47

48 **RESULTS**

49
50
51 Out of the 157 patients diagnosed with GAgP, 92 met the study eligibility criteria
52 according to their clinical records. It proved impossible to contact 30 of these patients,
53 and 22 of the remaining 62 patients were subsequently excluded (2 for pregnancy, 3 for
54 diabetes, 1 for death, and 16 for continuing their treatment at another clinic). Out of the
55
56
57
58
59
60

1
2
3 final sample of 40 eligible patients, 25 signed written informed consent to study
4 participation. Table 1 displays the age, sex, smoking habit, SPT visits, compliance with
5 SPT program, and mean study follow-up in years of the patients included in the study.
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

There were no statistical differences in gender, age, number of teeth or smoking habit at baseline between the patients included in the study and the patients lost to follow-up. Seven patients attended all programmed SPT visits, while the remaining 18 patients attended at least one appointment a year. The mean (\pm standard deviation) follow-up period was 10.9 ± 2.0 years. At baseline, 656 teeth were evaluated, recording 22 losses due to periodontal disease (12 maxillary molars, 6 maxillary premolars, 1 anterior maxillary tooth, and 3 anterior mandibular tooth); most of the losses (18) were in three patients (Table 2). 8 teeth were lost in regular SPT and 14 in irregular SPT ($p=0.74$). Eighteen teeth lost were multi-rooted; at baseline, eleven of these had no furcation involvement, five had grade I or II furcation involvement, and two had grade III furcation involvement. In their initial treatment, 12 of the 25 patients received sextant periodontal access surgery, 3 guided tissue regeneration, and 1 a free gingival graft. Three patients required repeated surgery during the follow-up (data not shown). At the end of the follow-up, a significant decrease was observed in mean PPD and CAL values, in the percentage of pockets, and in sites with CAL of 4-6 mm and ≥ 7 mm, and a significant mean increase of 0.36 mm was recorded in the CEJ-bone crest distance (Table 3). Table 4 shows that the mean loss of CEJ-bone distance (alveolar crest height) was 0.53 mm in distal sites and 0.43 mm in mesial sites.

The mean (\pm sd) number of lost teeth was 1.62 ± 2.57 in smokers ($n=13$) and 0.08 ± 0.29 in non-smokers ($n=12$), giving a $p=0.052$ (Table 5). The smallest alveolar crest height loss was in incisors and maxillary canines and the largest was in maxillary and mandibular molars. There was no significant difference ($p=0.318$) in the mean (\pm SD) number of

1
2
3 SPT visits/year between the 18 patients with no tooth loss (1.1 ± 0.6) and the 7 with tooth
4 loss (1.5 ± 0.8) (data not shown). Table 5 exhibits six linear regression models
5 constructed with variables considered to be associated with periodontal tooth loss.
6
7
8
9
10 When all six variables were tested together in a backward multivariate regression
11 model, all variables except tobacco (1.53 ± 0.75 , $p=0.052$) were excluded from the
12 model.
13
14
15

16 17 **DISCUSSION**

18
19
20 In this series of GAgP patients undergoing SPT, the mean tooth loss was 1.12 ± 2.01 per
21 patient for total causes and 0.9 ± 2.0 for periodontal causes after a mean follow up of
22 10.9 years. The annual tooth loss per patient, assuming a constant loss rate, was $0.10 \pm$
23 0.18 , similar to the annual losses published by Nibali et al. in their meta-analysis (0.14)
24 (Nibali et al. 2013) and by Albandar et al. (0.08) (Albandar et al. 1996); Kamma et al.
25 (0.21) (Kamma and Baehni 2003), and Bäumer et al. (0.15) (Baumer et al. 2011).
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
61
62
63
64
65
66
67
68
69
70
71
72
73
74
75
76
77
78
79
80
81
82
83
84
85
86
87
88
89
90
91
92
93
94
95
96
97
98
99
100
101
102
103
104
105
106
107
108
109
110
111
112
113
114
115
116
117
118
119
120
121
122
123
124
125
126
127
128
129
130
131
132
133
134
135
136
137
138
139
140
141
142
143
144
145
146
147
148
149
150
151
152
153
154
155
156
157
158
159
160
161
162
163
164
165
166
167
168
169
170
171
172
173
174
175
176
177
178
179
180
181
182
183
184
185
186
187
188
189
190
191
192
193
194
195
196
197
198
199
200
201
202
203
204
205
206
207
208
209
210
211
212
213
214
215
216
217
218
219
220
221
222
223
224
225
226
227
228
229
230
231
232
233
234
235
236
237
238
239
240
241
242
243
244
245
246
247
248
249
250
251
252
253
254
255
256
257
258
259
260
261
262
263
264
265
266
267
268
269
270
271
272
273
274
275
276
277
278
279
280
281
282
283
284
285
286
287
288
289
290
291
292
293
294
295
296
297
298
299
300
301
302
303
304
305
306
307
308
309
310
311
312
313
314
315
316
317
318
319
320
321
322
323
324
325
326
327
328
329
330
331
332
333
334
335
336
337
338
339
340
341
342
343
344
345
346
347
348
349
350
351
352
353
354
355
356
357
358
359
360
361
362
363
364
365
366
367
368
369
370
371
372
373
374
375
376
377
378
379
380
381
382
383
384
385
386
387
388
389
390
391
392
393
394
395
396
397
398
399
400
401
402
403
404
405
406
407
408
409
410
411
412
413
414
415
416
417
418
419
420
421
422
423
424
425
426
427
428
429
430
431
432
433
434
435
436
437
438
439
440
441
442
443
444
445
446
447
448
449
450
451
452
453
454
455
456
457
458
459
460
461
462
463
464
465
466
467
468
469
470
471
472
473
474
475
476
477
478
479
480
481
482
483
484
485
486
487
488
489
490
491
492
493
494
495
496
497
498
499
500
501
502
503
504
505
506
507
508
509
510
511
512
513
514
515
516
517
518
519
520
521
522
523
524
525
526
527
528
529
530
531
532
533
534
535
536
537
538
539
540
541
542
543
544
545
546
547
548
549
550
551
552
553
554
555
556
557
558
559
560
561
562
563
564
565
566
567
568
569
570
571
572
573
574
575
576
577
578
579
580
581
582
583
584
585
586
587
588
589
590
591
592
593
594
595
596
597
598
599
600
601
602
603
604
605
606
607
608
609
610
611
612
613
614
615
616
617
618
619
620
621
622
623
624
625
626
627
628
629
630
631
632
633
634
635
636
637
638
639
640
641
642
643
644
645
646
647
648
649
650
651
652
653
654
655
656
657
658
659
660
661
662
663
664
665
666
667
668
669
670
671
672
673
674
675
676
677
678
679
680
681
682
683
684
685
686
687
688
689
690
691
692
693
694
695
696
697
698
699
700
701
702
703
704
705
706
707
708
709
710
711
712
713
714
715
716
717
718
719
720
721
722
723
724
725
726
727
728
729
730
731
732
733
734
735
736
737
738
739
740
741
742
743
744
745
746
747
748
749
750
751
752
753
754
755
756
757
758
759
760
761
762
763
764
765
766
767
768
769
770
771
772
773
774
775
776
777
778
779
780
781
782
783
784
785
786
787
788
789
790
791
792
793
794
795
796
797
798
799
800
801
802
803
804
805
806
807
808
809
810
811
812
813
814
815
816
817
818
819
820
821
822
823
824
825
826
827
828
829
830
831
832
833
834
835
836
837
838
839
840
841
842
843
844
845
846
847
848
849
850
851
852
853
854
855
856
857
858
859
860
861
862
863
864
865
866
867
868
869
870
871
872
873
874
875
876
877
878
879
880
881
882
883
884
885
886
887
888
889
890
891
892
893
894
895
896
897
898
899
900
901
902
903
904
905
906
907
908
909
910
911
912
913
914
915
916
917
918
919
920
921
922
923
924
925
926
927
928
929
930
931
932
933
934
935
936
937
938
939
940
941
942
943
944
945
946
947
948
949
950
951
952
953
954
955
956
957
958
959
960
961
962
963
964
965
966
967
968
969
970
971
972
973
974
975
976
977
978
979
980
981
982
983
984
985
986
987
988
989
990
991
992
993
994
995
996
997
998
999
1000

Waerhaug et al., Saxén et al., and Graetz et al., who did not differentiate between
generalized and localized AgP, also observed comparable losses of 0.14, 0.11, and 0.13
respectively (Waerhaug 1977, Saxen et al. 1986, Graetz et al. 2011). However, Dopico
et al. recently described a higher loss rate for AgP patients **not under strict SPT** of 0.27
teeth per patient/year after a mean follow-up of 6.97 years (Dopico et al. 2016). The
main cause of tooth loss in the present study was periodontal, although 72% of the
participants lost no teeth due to periodontal causes. As in previous studies, a small
proportion of the participants were responsible for the majority of tooth losses (Baumer
et al. 2011). Among the teeth lost during the follow up, 82% were multi-rooted (12
molar, and 6 maxillary premolars), consistent with previous reports in both AgP and
chronic periodontitis (Ng et al. 2011, Salvi et al. 2014). Thus, Ng et al. found an OR of

1
2
3 4.7 for the loss of multi-rooted versus single-rooted teeth in patients receiving SPT (Ng
4
5 et al. 2011). Dannewitz et al. attributed the greater loss of maxillary molars during SPT
6
7 to their complex anatomy and higher prevalence of **furcation defects** (Dannewitz et al.
8
9 2006).

10
11
12 **In our study, we analyzed 3168 sites, and 4.2% of these had pockets ≥ 7 mm deep at**
13 **baseline (134 pockets ≥ 7 mm), and the number of sites with CAL loss ≥ 7 mm was much**
14 **higher (241). The average PPD at baseline was 3.7 mm, with a 43% of healthy sites at**
15 **baseline (≤ 3 mm). This result is within the range of previous baseline periodontal status**
16 **reported by other studies. Monteiro et al. and Hughes et al. reported a mean PPD of 2.7**
17 **and 2.98 mm respectively, while Haas et al. published a mean PPD at baseline of 4.7mm**
18 **in GAgP (Monteiro et al. 2015, Hughes et al. 2006b, Haas et al. 2008).**
19
20
21
22
23
24
25
26
27

28
29 A systematic review of 13 retrospective cohort studies associated age, smoking, and
30
31 baseline prognosis with tooth loss after SPT for at least 5 years; however, the authors
32
33 did not reach definitive conclusions due to the heterogeneity among studies, problems
34
35 with the categorization of smoking, and the need to subdivide patients by periodontitis
36
37 type (Chambrone et al. 2010). A progressive increase in tooth loss with higher age in
38
39 the general population can also be due to fractures resulting from the presence of dental
40
41 fillings, endodontically-treated teeth or dental traumatism (Schiffner et al. 2009). In
42
43 our GAgP patients, the mean age was only 30 years, but six teeth were lost for these
44
45 reasons.
46
47

48
49 Epidemiological and clinical studies have confirmed tobacco smoking as a major risk
50
51 factor in periodontitis and, therefore, in tooth loss (Palmer et al. 2005). It has been
52
53 reported that periodontal treatment outcomes are worse in smokers (Hughes et al.
54
55 2006a), and smoking has been associated with higher long-term tooth loss rates (Konig
56
57
58
59
60

1
2
3 et al. 2002). Smoking was also related to tooth loss in the present study. Thus, out of the
4
5 22 teeth lost for periodontal causes, 21 (95.5%) were from patients who were smokers
6
7 at their diagnosis, and 14 (63.6%) were from patients who were smokers at the end of
8
9 the follow-up. Linear regression confirmed this relationship. Smoking has several
10
11 harmful effects on periodontal tissue, including alterations in gingival vasculature and
12
13 the impairment of neutrophil and fibroblast functions (Palmer et al. 2005).

14
15
16 Sigusch et al. and Haas et al. found that scaling and root planning in GAgP patients
17
18 stabilized the disease for 6 months, followed by a clinical worsening and disease
19
20 recurrence (Sigusch et al. 2001, Haas et al. 2008). In contrast, good long-term outcomes
21
22 were obtained in the present patients after SPT for a mean of almost 11 years, with a
23
24 reduction in mean PPD of 1 ± 0.8 mm and a gain in CAL of 0.6 ± 0.9 mm. These values
25
26 are not in agreement with the results compiled in a review by Teughels et al, in which
27
28 relapse and progression of the disease were observed at 6 months after the treatment of
29
30 GAgP patients despite their receipt of SPT (Teughels et al. 2014).

31
32
33
34
35 No published data appear to be available on absolute changes (in mm) in the alveolar
36
37 crest height of GAgP patients **in regular SPT** over the short or long-term. In the present
38
39 study, a mean alveolar crest loss of 0.36 ± 0.56 mm was found between baseline and the
40
41 end of the follow-up. **Onabolu et al. found that AgP (both generalized and localized**
42
43 **forms) showed rate of bone loss of 0.31 mm/year, higher than the results of our study,**
44
45 **but in patients not under regular SPT, using panoramic and bitewing apart from**
46
47 **periapical radiographs (Onabolu et al. 2015).** A loss of 1 mm every 10 years was
48
49 observed by Wennström et al. in chronic periodontitis patients under SPT (Wennstrom
50
51 et al. 1993). The greatest height loss was observed in mandibular and maxillary molars,
52
53 likely due to the more difficult access to these teeth for maintenance and hygiene
54
55 procedures and the presence of **furcation defects**. The lowest height loss was in
56
57
58
59
60

1
2
3 maxillary incisors and canines, which are much easier to access and may receive more
4
5 attention as the most visible teeth. Bäumer et al. found an association between alveolar
6
7 crest loss and tooth loss in localized and generalized AgP (Baumer et al. 2011). Unlike
8
9 in the present study, they reported bone loss as percentages and used panoramic x-rays,
10
11 which can offer distorted images of posterior segments. It is well-known that periapical
12
13 radiography is a superior technique for measuring alveolar crest loss (Zaki et al. 2015).
14
15

16
17 Patients who had abandoned SPT for several years were excluded from this study, as
18
19 recommended by Salvi et al. (Salvi et al. 2014). Our finding of a larger number of SPT
20
21 visits by the patients who lost teeth than by those who did not is likely attributable to the
22
23 more frequent treatment sessions required by more severe patients. The effect of SPT on
24
25 tooth loss is controversial, with some authors finding a reduction in tooth loss with
26
27 regular SPT (McFall 1982, Fardal et al. 2004, Faggion et al. 2007, Matuliene et al.
28
29 2008) but others finding no difference between patients receiving and not receiving
30
31 programmed SPT (Baumer et al. 2011, Dannewitz et al. 2016). The key factor for tooth
32
33 preservation is the compliance of patients with their SPT program, which should be
34
35 individualized (Axelsson and Lindhe 1981). However, linear regression analysis
36
37 showed that tooth loss in our study was not associated with either the number of SPT
38
39 visits or with SPT compliance. A recent meta-analysis reported a lesser tooth loss with
40
41 better SPT compliance, but no distinction was made among different types of
42
43 periodontitis and the results were highly heterogeneous, attributed to confounding
44
45 variables that can also affect tooth loss, such as the quality of the SPT and the
46
47 socioeconomic level of patients, among other unidentified factors (Lee et al. 2015).
48
49 Thus, in the present study, the baseline clinical status was significantly worse for the
50
51 teeth that were subsequently lost than for those that were preserved, which would have
52
53 acted as a confounder in the relationship between SPT attendance and tooth loss. It is
54
55
56
57
58
59
60

1
2
3 evidently important to diagnose and treat the disease as early as possible. Nevertheless,
4
5 we highlight the good outcomes obtained after a mean of 10.9 years under SPT in the
6
7 present patients, all of whom attended at least once a year, with an improvement in
8
9 mean PPD and CAL values.
10

11
12 Study limitations include the small sample size, although our evaluation included 656
13
14 teeth, 3,168 clinical sites, and 713 radiological sites (measured twice). In order to
15
16 explain risk factors, the small number of patients included in this study causes low
17
18 statistical power, particularly for multivariate analyses. We also treated the mean
19
20 alveolar crest height loss as constant over time in computing annual rates, a common
21
22 assumption in the literature when measurements at intermediate intervals are not
23
24 available (Pjetursson et al. 2014). Potential selection bias was controlled by ensuring that the
25
26 baseline characteristics of the patients lost to follow-up did not differ from those who were
27
28 finally included in the study. Finally, a complete radiological assessment was not always
29
30 possible, because the quality of some x-rays were inadequate for alveolar crest height
31
32 measurement with the software used
33
34
35
36

37
38 This retrospective study, along with the one by Graetz et al. (Graetz et al. 2011), are the
39
40 longest follow-up of GAgP patients published to date. A low tooth loss rate was
41
42 obtained in the patients, who were on a regular supportive care program for a mean of
43
44 almost 11 years, while clinical periodontal variables improved and alveolar crest loss
45
46 was minimal. Smoking was associated with tooth loss.
47
48

49 50 **ACKNOWLEDGEMENTS**

51
52 The authors are grateful to Richard Davies, professional translator, for his assistance
53
54 with the English version of the manuscript.
55
56
57
58
59
60

REFERENCES

- 1
2
3
4
5 AAP (2000) Parameter on aggressive periodontitis. American Academy of Periodontology.
6 *Journal of periodontology* **71**, 867-869. doi:10.1902/jop.2000.71.5-S.867.
7
- 8 Ainamo, J. & Bay, I. (1975) Problems and proposals for recording gingivitis and plaque.
9 *International dental journal* **25**, 229-235.
10
- 11 Albandar, J. M., Brown, L. J. & Loe, H. (1996) Dental caries and tooth loss in adolescents with
12 early-onset periodontitis. *Journal of periodontology* **67**, 960-967.
13 doi:10.1902/jop.1996.67.10.960.
14
- 15 Axelsson, P. & Lindhe, J. (1981) The significance of maintenance care in the treatment of
16 periodontal disease. *Journal of clinical periodontology* **8**, 281-294.
17
- 18 Baumer, A., Pretzl, B., Cosgarea, R., Kim, T. S., Reitmeir, P., Eickholz, P. & Dannewitz, B.
19 (2011) Tooth loss in aggressive periodontitis after active periodontal therapy: patient-
20 related and tooth-related prognostic factors. *Journal of clinical periodontology* **38**, 644-
21 651. doi:10.1111/j.1600-051X.2011.01733.x.
22
- 23 Brown, L. J., Albandar, J. M., Brunelle, J. A. & Loe, H. (1996) Early-onset periodontitis:
24 progression of attachment loss during 6 years. *Journal of periodontology* **67**, 968-975.
25 doi:10.1902/jop.1996.67.10.968.
26
- 27 Chambrone, L., Chambrone, D., Lima, L. A. & Chambrone, L. A. (2010) Predictors of tooth
28 loss during long-term periodontal maintenance: a systematic review of observational
29 studies. *Journal of clinical periodontology* **37**, 675-684. doi:10.1111/j.1600-
30 051X.2010.01587.x.
31
- 32 Dannewitz, B., Krieger, J. K., Husing, J. & Eickholz, P. (2006) Loss of molars in periodontally
33 treated patients: a retrospective analysis five years or more after active periodontal
34 treatment. *Journal of clinical periodontology* **33**, 53-61. doi:10.1111/j.1600-
35 051X.2005.00858.x.
36
- 37 Dannewitz, B., Zeidler, A., Husing, J., Saure, D., Pfefferle, T., Eickholz, P. & Pretzl, B. (2016)
38 Loss of molars in periodontally treated patients: results 10 years and more after active
39 periodontal therapy. *Journal of clinical periodontology* **43**, 53-62.
40 doi:10.1111/jcpe.12488.
41
- 42 Dopico, J., Nibali, L. & Donos, N. (2016) Disease progression in aggressive periodontitis
43 patients. A Retrospective Study. *Journal of clinical periodontology* **43**, 531-537.
44 doi:10.1111/jcpe.12533.
45
- 46 Faggion, C. M., Jr., Petersilka, G., Lange, D. E., Gerss, J. & Flemmig, T. F. (2007) Prognostic
47 model for tooth survival in patients treated for periodontitis. *Journal of clinical*
48 *periodontology* **34**, 226-231. doi:10.1111/j.1600-051X.2006.01045.x.
49
- 50 Fardal, O., Johannessen, A. C. & Linden, G. J. (2004) Tooth loss during maintenance following
51 periodontal treatment in a periodontal practice in Norway. *Journal of clinical*
52 *periodontology* **31**, 550-555. doi:10.1111/j.1600-051X.2004.00519.x.
53
- 54 Graetz, C., Dorfer, C. E., Kahl, M., Kocher, T., Fawzy El-Sayed, K., Wiebe, J. F., Gomer, K. &
55 Ruhling, A. (2011) Retention of questionable and hopeless teeth in compliant patients
56 treated for aggressive periodontitis. *Journal of clinical periodontology* **38**, 707-714.
57 doi:10.1111/j.1600-051X.2011.01743.x.
58
59
60

- 1
2
3 Guerrero, A., Griffiths, G. S., Nibali, L., Suvan, J., Moles, D. R., Laurell, L. & Tonetti, M. S.
4 (2005) Adjunctive benefits of systemic amoxicillin and metronidazole in non-surgical
5 treatment of generalized aggressive periodontitis: a randomized placebo-controlled
6 clinical trial. *Journal of clinical periodontology* **32**, 1096-1107. doi:10.1111/j.1600-
7 051X.2005.00814.x.
8
- 9 Haas, A. N., de Castro, G. D., Moreno, T., Susin, C., Albandar, J. M., Oppermann, R. V. &
10 Rosing, C. K. (2008) Azithromycin as an adjunctive treatment of aggressive
11 periodontitis: 12-months randomized clinical trial. *Journal of clinical periodontology*
12 **35**, 696-704. doi:10.1111/j.1600-051X.2008.01254.x.
13
- 14 Hausmann, E., Allen, K. & Clerehugh, V. (1991) What alveolar crest level on a bite-wing
15 radiograph represents bone loss? *Journal of periodontology* **62**, 570-572.
16 doi:10.1902/jop.1991.62.9.570.
17
- 18 Hughes, F. J., Syed, M., Koshy, B., Bostanci, N., McKay, I. J., Curtis, M. A., Marcenes, W. &
19 Croucher, R. E. (2006a) Prognostic factors in the treatment of generalized aggressive
20 periodontitis: II. Effects of smoking on initial outcome. *Journal of clinical*
21 *periodontology* **33**, 671-676. doi:10.1111/j.1600-051X.2006.00965.x.
22
- 23 Hughes, F. J., Syed, M., Koshy, B., Marinho, V., Bostanci, N., McKay, I. J., Curtis, M. A.,
24 Croucher, R. E. & Marcenes, W. (2006b) Prognostic factors in the treatment of
25 generalized aggressive periodontitis: I. Clinical features and initial outcome. *Journal of*
26 *clinical periodontology* **33**, 663-670. doi:10.1111/j.1600-051X.2006.00966.x.
27
- 28 Kamma, J. J. & Baehni, P. C. (2003) Five-year maintenance follow-up of early-onset
29 periodontitis patients. *Journal of clinical periodontology* **30**, 562-572.
30
- 31 Konig, J., Plagmann, H. C., Ruhling, A. & Kocher, T. (2002) Tooth loss and pocket probing
32 depths in compliant periodontally treated patients: a retrospective analysis. *Journal of*
33 *clinical periodontology* **29**, 1092-1100.
34
- 35 Lang, N. P., Bartold, P. M., Cullinan, M. P., Jeffcoat, M., Mombelli, A., Murakami, S., Page,
36 R., Papapanou, P. N., Tonetti, M. & Van Dyke, T. (1999) Consensus Report:
37 Aggressive Periodontitis. *Annals of Periodontology* **4**, 53.
38 doi:10.1902/annals.1999.4.1.53.
39
- 40 Lee, C. T., Huang, H. Y., Sun, T. C. & Karimbux, N. (2015) Impact of Patient Compliance on
41 Tooth Loss during Supportive Periodontal Therapy: A Systematic Review and Meta-
42 analysis. *Journal of dental research* **94**, 777-786. doi:10.1177/0022034515578910.
43
- 44 Matuliene, G., Pjetursson, B. E., Salvi, G. E., Schmidlin, K., Bragger, U., Zwahlen, M. & Lang,
45 N. P. (2008) Influence of residual pockets on progression of periodontitis and tooth
46 loss: results after 11 years of maintenance. *Journal of clinical periodontology* **35**, 685-
47 695. doi:10.1111/j.1600-051X.2008.01245.x.
48
- 49 McFall, W. T., Jr. (1982) Tooth loss in 100 treated patients with periodontal disease. A long-
50 term study. *Journal of periodontology* **53**, 539-549. doi:10.1902/jop.1982.53.9.539.
51
- 52 Monteiro, M., Casati, M. Z., Taiete, T., Vale, H. F., Nociti, F. H., Jr., Sallum, E. A., Silverio, K.
53 G. & Casarin, R. C. (2015) Periodontal clinical and microbiological characteristics in
54 healthy versus generalized aggressive periodontitis families. *Journal of clinical*
55 *periodontology* **42**, 914-921. doi:10.1111/jcpe.12459.
56
57
58
59
60

- 1
2
3 Mros, S. T. & Berglundh, T. (2010) Aggressive periodontitis in children: a 14-19-year follow-
4 up. *Journal of clinical periodontology* **37**, 283-287. doi:10.1111/j.1600-
5 051X.2009.01526.x.
6
7 Ng, M. C., Ong, M. M., Lim, L. P., Koh, C. G. & Chan, Y. H. (2011) Tooth loss in compliant
8 and non-compliant periodontally treated patients: 7 years after active periodontal
9 therapy. *Journal of clinical periodontology* **38**, 499-508. doi:10.1111/j.1600-
10 051X.2011.01708.x.
11
12 Nibali, L., Farias, B. C., Vajgel, A., Tu, Y. K. & Donos, N. (2013) Tooth loss in aggressive
13 periodontitis: a systematic review. *Journal of dental research* **92**, 868-875.
14 doi:10.1177/0022034513501878.
15
16 Onabolu, O., Donos, N., Tu, Y. K., Darbar, U. & Nibali, L. (2015) Periodontal progression
17 based on radiographic records: An observational study in chronic and aggressive
18 periodontitis. *Journal of dentistry* **43**, 673-682. doi:10.1016/j.jdent.2015.02.005.
19
20 Palmer, R. M., Wilson, R. F., Hasan, A. S. & Scott, D. A. (2005) Mechanisms of action of
21 environmental factors--tobacco smoking. *Journal of clinical periodontology* **32 Suppl**
22 **6**, 180-195. doi:10.1111/j.1600-051X.2005.00786.x.
23
24 Pjetursson, B. E., Asgeirsson, A. G., Zwahlen, M. & Sailer, I. (2014) Improvements in implant
25 dentistry over the last decade: comparison of survival and complication rates in older
26 and newer publications. *The International journal of oral & maxillofacial implants* **29**
27 **Suppl**, 308-324. doi:10.11607/jomi.2014suppl.g5.2.
28
29 Pretzl, B., Kaltschmitt, J., Kim, T. S., Reitmeir, P. & Eickholz, P. (2008) Tooth loss after active
30 periodontal therapy. 2: tooth-related factors. *Journal of clinical periodontology* **35**, 175-
31 182. doi:10.1111/j.1600-051X.2007.01182.x.
32
33 Salvi, G. E., Mischler, D. C., Schmidlin, K., Matuliene, G., Pjetursson, B. E., Bragger, U. &
34 Lang, N. P. (2014) Risk factors associated with the longevity of multi-rooted teeth.
35 Long-term outcomes after active and supportive periodontal therapy. *Journal of clinical*
36 *periodontology* **41**, 701-707. doi:10.1111/jcpe.12266.
37
38 Saxen, L., Asikainen, S., Sandholm, L. & Kari, K. (1986) Treatment of juvenile periodontitis
39 without antibiotics. A follow-up study. *Journal of clinical periodontology* **13**, 714-719.
40
41 Schiffner, U., Hoffmann, T., Kerschbaum, T. & Micheelis, W. (2009) Oral health in German
42 children, adolescents, adults and senior citizens in 2005. *Community dental health* **26**,
43 18-22.
44
45 Sigusch, B., Beier, M., Klinger, G., Pfister, W. & Glockmann, E. (2001) A 2-step non-surgical
46 procedure and systemic antibiotics in the treatment of rapidly progressive periodontitis.
47 *Journal of periodontology* **72**, 275-283. doi:10.1902/jop.2001.72.3.275.
48
49 Susin, C., Haas, A. N. & Albandar, J. M. (2014) Epidemiology and demographics of aggressive
50 periodontitis. *Periodontol 2000* **65**, 27-45. doi:10.1111/prd.12019.
51
52 Teughels, W., Dhondt, R., Dekeyser, C. & Quirynen, M. (2014) Treatment of aggressive
53 periodontitis. *Periodontol 2000* **65**, 107-133. doi:10.1111/prd.12020.
54
55 Tonetti, M. S. (2002) The future of periodontology: new treatments for a new era. *Journal of the*
56 *International Academy of Periodontology* **4**, 110-114.
57
58
59
60

1
2
3 von Elm, E., Altman, D. G., Egger, M., Pocock, S. J., Gøtzsche, P. C., Vandenbroucke, J. P. &
4 Initiative, S. (2008) The Strengthening the Reporting of Observational Studies in
5 Epidemiology (STROBE) statement: guidelines for reporting observational studies.
6 *Journal of clinical epidemiology* **61**, 344-349. doi:10.1016/j.jclinepi.2007.11.008.
7

8 Waerhaug, J. (1977) Plaque control in the treatment of juvenile periodontitis. *Journal of clinical*
9 *periodontology* **4**, 29-40.
10

11 Wennstrom, J. L., Serino, G., Lindhe, J., Eneroth, L. & Tollskog, G. (1993) Periodontal
12 conditions of adult regular dental care attendants. A 12-year longitudinal study. *Journal*
13 *of clinical periodontology* **20**, 714-722.
14

15 Zaki, H. A., Hoffmann, K. R., Hausmann, E. & Scannapieco, F. A. (2015) Is Radiologic
16 Assessment of Alveolar Crest Height Useful to Monitor Periodontal Disease Activity?
17 *Dent Clin North Am* **59**, 859-872. doi:10.1016/j.cden.2015.06.009.
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Table 1. Patient data (n=25)

Variable		
Age (years), mean±sd	30.8±4.1	
Women, n (%)	17 (68.0)	
Smoking at diagnosis, n (%)		
No or ex-smoker ≥5 years	12	(48.0)
Ex-smoker <5 years	2	(8.0)
<10 cig./day	3	(12.0)
10-19 cig./day	4	(16.0)
≥20 cig./day	4	(16.0)
Smoking at end of follow-up, n (%)		
No or ex-smoker ≥5 years	17	(68.0)
Ex-smoker <5 years	0	-
<10 cig./day	2	(8.0)
10-19 cig./day	4	(16.0)
≥20 cig./day	2	(8.0)
N° SPT visits, mean±sd	12.8±7.7	
Compliant with SPT, n (%)	7 (28.0)	
Follow-up (years), mean±sd	10.9±2.0	
Lost to follow-up patients (n=132)		
Age (years), mean±sd	31.9±4.9	0.279a
Women, n (%)	92 (69.7%)	0.941b
Smokers	64 (48.5%)	0.845b
Teeth at baseline, mean±sd	25.4±2.6	0.145a

a: Mann-Whitney U-test. b: Chi-square test with Yate's correction.

SPT = Supportive Periodontal Therapy; Compliant = attending 100% of programmed visits

Table 2. Tooth loss related variables (n=25)

Variable	n (%)
Teeth at baseline	
Range	22-28
mean±sd	26.2±1.8
Teeth at end of follow-up	
Range	19-28
mean±sd	25.1±3.1
Lost Teeth (Total)	28 (100)
Causes:	
Periodontal	22 (78.6)
Conservative treatment	2 (7.1)
Vertical fracture	1 (3.6)
Orthodontic treatment	3 (10.7)
Distribution of tooth loss among patients	
0	18 (72.0)
1	4 (16.0)
2	0 -
3	0 -
4	0 -
5	1 (4.0)
6	1 (4.0)
7	1 (4.0)
mean±sd	0.9±2.0
95% CI	0.1-1.7

Table 3. Periodontal and bone height variables in 25 patients

Variable	Baseline	Final	Difference		p-value ^a
	mean±sd	mean±sd	mean±sd	95%-CI	
PPD (mm.)	3.7±2.0	2.7±1.5	-1.0±0.8	-0.7 to -1.3	<0.001
% healthy sites (≤3 mm).	42.9±31.0	86.9±10.0	44.0±27.9	32.3 to 55.7	<0.001
% pockets 4-6 mm.	52.9±28.6	12.5±9.5	-40.4±26.1	-51.3 to -29.5	<0.001
% pockets ≥7 mm.	4.2±7.4	0.6±0.9	-3.6±6.9	-6.5 to -0.7	0.023
CAL (mm.)	4.1±1.3	3.6±1.0	-0.6±0.9	-0.9 to -0.2	0.012
% sites ≤3 mm.	39.4±30.4	63.9±21.7	24.5±31.2	11.4 to 37.5	0.001
% sites 4-6 mm.	53.0±25.7	31.4±17.1	-21.6±30.0	-34.1 to -9.1	0.003
% sites ≥7 mm.	7.6±10.9	4.7±7.1	-2.9±7.4	-6.0 to 0.2	0.084
CEJ- Bone crest (mm.)	3.45±1.11	3.81±1.12	0.36±0.56	0.10 to 0.61	0.013

a: Student's t-test for paired samples; p-values were not adjusted for multiple testing

Table 4. Changes in CEJ-bone crest distance

Variable	sites	Initial	Final	Difference	
		mean±sd	mean±sd	mean±sd	95% CI ^a
All sites	713	3.33±1.60	3.81±1.62	0.48±1.13	0.25 - 0.71
Mesial	380	3.33±1.61	3.77±1.64	0.43±1.17	0.19 - 0.68
Distal	333	3.33±1.60	3.86±1.60	0.53±1.09	0.29 - 0.77
Maxillary Incisor +Canine	159	4.10±1.93	4.22±1.65	0.12±1.20	-0.20 - 0.43
Maxillary Premolar	104	2.86±1.26	3.41±1.53	0.56±1.19	0.15 - 0.96
Maxillary Molar	75	3.18±1.49	3.84±1.68	0.65±0.95	0.34 - 0.96
Mandibular Incisor +Canine	180	3.49±1.46	4.05±1.45	0.56±0.99	0.23 - 0.88
Mandibular Premolar	125	2.77±1.22	3.27±1.23	0.50±0.93	0.23 - 0.78
Mandibular Molar	70	3.03±1.62	3.80±2.21	0.77±1.51	0.32 - 1.22

a: 95% confidence interval, calculated using SUDAAN DESCRIPT procedure to account for clustering (multiple sites within teeth and patients). When the 95% CI does not include the value 0, it is interpreted as a statistically significant change between baseline and final observations. Only teeth present at baseline and at the end of the study were included in this analysis.

Table 5. Univariate linear regression analysis of the variables associated with periodontal tooth loss (n=25)

Variable	$\beta \pm se$	p-value
Age (years) mean \pm sd	0.13 \pm 0.10	0.210
Women	-1.28 \pm 0.83	0.136
Smokers	1.53 \pm 0.75	0.052
SPT visits	0.08 \pm 0.05	0.154
Compliance with SPT	0.37 \pm 0.90	0.689
Follow-up (years)	0.17 \pm 0.20	0.408

Only smoking was statistically significant in multivariate regression (not shown).

1
2
3 **Manuscript Title:** Tooth loss and alveolar bone crest loss during supportive periodontal
4 therapy in patients with generalized aggressive periodontitis: retrospective study with follow-up
5 of 8 to 15 years (CPE-03-16-6255.R3).
6
7

8
9 **Associate Editor's Comments to Author:**

10 Thanks for the revisions that were generally appreciated by the referees. Please address the few
11 remaining issues and update your reference list (please see recent relevant papers e.g. in the JCP
12 including online early and accepted manuscripts available on the Journal website.
13
14

15 **Response:** Pubmed and JCP website have been checked for recent papers concerning the topic
16 of this manuscript. Another reference has been included (Monteiro et al 2015).
17
18

19
20 **Reviewer(s)' Comments to Author:**

21
22 Referee: 1

23
24 A cohort of 25 patients who had been treated non-surgically including adjunctive systemic
25 antibiotics for generalised aggressive periodontitis (gAgP) were examined retrospectively. Main
26 outcome was tooth loss during supportive periodontal therapy (SPT). From a total of 656 teeth
27 28 were extracted during SPT. Smoking was marginally associated with increased tooth loss.
28
29 This is the revision of the manuscript on a retrospective cohort study on the relevant issue of
30 tooth retention by periodontal treatment in AgP. The manuscript was improved substantially.
31
32 However, there still are some issues requiring clarification.
33
34
35

- 36
37 1. It is difficult to recruit and follow-up a large cohort of GAgP patients. This explains the
38 small number of patients included in this study. However, this small number causes low
39 power particularly for multivariate analyses trying to explain risk factors (e.g. irregular
40 SPT). The authors may wish to point out this issue clearly in the Discussion section.
41

42 **Response:** We totally agree with the reviewer. We have now included this issue as a
43 limitation in the Discussion section as follows: *"In order to explain risk factors, the small
44 number of patients included in this study, causes low statistical power, particularly for
45 multivariate analyses"*.
46
47
48

- 49
50 2. We all agree that we can retain periodontally compromised teeth for a long time even in
51 gAgP. However, there is quite strong evidence for the benefit of regular SPT. The
52 difference between regular and irregular SPT stronger if the difference between regular and
53 irregular SPT is large. In this small cohort study the difference between SPT frequency in
54 the regular and irregular group is small, is it not?
55
56
57
58
59
60

1
2
3 **Response:** The SPT program was individualized for each patient, with interval between
4 visits of 3 to 6 months. There were patients that attended 4 times/year (regular SPT) and
5 patients that only attended 1 time/year (irregular SPT). We think that this difference in SPT
6 visits is not small.
7
8
9

10 Abstract, Practical implications

- 11
12 3. page 39, lines 30-33: The study failed to show an association between irregular SPT and
13 tooth loss. There were 7 patients attending all scheduled SPT visits (regular SPT) and 18
14 patients attended at least 1 SPT visit per year. The difference between the actual SPT
15 frequencies (regular/irregular) is low and the number of subjects is very low (low test
16 power). Thus, the respective statement on effect of SPT is not sufficiently supported by the
17 data presented.
18
19

20 **Response:** We think that the statement about the effect of SPT visits on tooth loss is
21 expressed in a non-categorical way and with caution, due to the limitation of a low sample
22 size (this issue is addressed in the discussion section). Nevertheless, our results support this
23 statement.
24
25
26

- 27
28
29 4. page 39, lines 33-36: On page 45, lines 50-53 the authors report that smokers on average
30 lose less teeth (i.e. 0.08 ± 0.29) than non-smokers (i.e. 1.61 ± 2.57). How does this support the
31 statement that quitting tobacco may contribute to tooth stability?
32

33 **Response:** We have checked the statistical analysis and unfortunately there was a problem
34 with codification. The statement has been rewritten as follows: "*The mean (\pm sd) number of
35 lost teeth was 1.62 ± 2.57 in smokers ($n=13$) and 0.08 ± 0.29 in non-smokers ($n=12$), giving a
36 $p=0.052$ (Table 5)."*

37
38
39
40
41 Material & Methods

- 42 5. 3 page 42, lines 11-17: Why limiting age at diagnosis to 18 years at the diagnosis? This is
43 a retrospective study reporting tooth loss 10 years after therapy. Any patient receiving
44 therapy around puberty (approximately 10-13 years) would have been at least 18 10 years
45 after therapy. The inclusion criteria cannot be changed anymore. However, they are not
46 plausible. Plausible would be up to 35 years at diagnosis and at least 18 years at re-
47 examination.
48
49

50 **Response:** We have now added this remark accordingly in materials & methods.
51
52
53
54
55
56
57
58
59
60

6. page 43, lines 39-48: How precise was the distance CEJ to bone crest measured? To the nearest 1 mm or to the nearest 0.1 mm?

Response: The digital image analysis program used (ImageJ®) was set to show measures to the nearest 0.01 mm.

Results

7. How many teeth were lost in the regular and how many in the irregular SPT group? How many SPT visits

Response: Out of the 22 teeth lost due to periodontal disease, 8 teeth were lost in regular SPT and 14 in irregular SPT. This new result has been included in results section

Group	Patients (n)	Teeth lost mean±sd	Total SPT visits mean±sd
SPT irregular	18	0.78±1.77	10.2±6.5
SPT regular	7	1.14±2.61	19.6±6.8
Student's t-test		p= 0.742	p= 0.004

Table 1 shows the mean number of SPT visits during follow-up and the number of patients compliant with SPT.

8. page 45, lines 25-28: Use furcation involvement instead of furcation.

Response: We have used the term “furcation involvement”, as requested by the reviewer.

9. Page 45, lines 40-46: The authors fail to find a correlation between tooth loss and plaque/gingival index at the end of the study and report this explicitly. How should plaque and gingival index at the end of the study influence tooth loss during the 10 years before? If there would be data on mean plaque and gingival index during SPT expecting a correlation would be plausible. However, not for the respective values after tooth loss has occurred. Remove sentence.

Response: This sentence was added in response to a request of another reviewer in R2. Sentence has been removed accordingly from the text as suggested by the actual reviewer.

Discussion

10. page 50, lines 8-15: Undoubtedly, this is a very nice cohort study on gAgP. However, it has its limitations. Bäumer et al. 2011 already reported 71 gAgP patients with a mean of 10.5 years (5-17). Actually, 10.9 years of follow-up is a longer follow-up. However, Graetz et al. 2011 report 32 patients with gAgP with a follow-up of on average 15.3 years which is

1
2
3 definitely longer than the actual study reports. The authors should not ignore that there
4 exists already substantial work. The authors may wish to address this fact in the discussion.

5
6 **Response:** We have now cited the work of Graetz et al. as the study with the longest
7 follow-up period and have changed this paragraph at the end of discussion section: "*This*
8 *retrospective study, along with the one by Graetz et al. (Graetz et al. 2011), are the*
9 *longest follow-up of GAgP patients published to date*".
10
11

12
13
14 Referee: 2

15 The authors carefully considered previous reviewers comments and modified the text
16 accordingly. The paper now acknowledges better the limitations and it is clearer. I have a few
17 additional comments:
18
19

20
21 Results:

- 22
23 1. The authors stated 'The mean (\pm sd) number of lost teeth was 1.61 ± 2.57 in non-smokers
24 ($n=13$) and 0.08 ± 0.29 in smokers ($n=12$), a significant difference ($p=0.049$; Student's t-
25 test).' If that was the case, then smoking would have a protective effect on tooth loss. Please
26 correct.
27
28

29 **Response:** We have checked the statistical analysis and unfortunately there was a problem
30 with codification. The statement has been rewritten as follows: "*The mean (\pm sd) number of*
31 *lost teeth was 1.62 ± 2.57 in smokers ($n=13$) and 0.08 ± 0.29 in non-smokers ($n=12$), giving a*
32 *$p=0.052$ (Table 5).*"
33
34
35

36
37 Discussion:

- 38 2. Please note the Dopico et al. study included patients not undergoing regular SPT. I suggest
39 adding the word 'irregular' to SPT or 'not under strict SPT'
40

41 **Response:** Following the reviewer's recommendation, we have added in discussion "not
42 under strict SPT" when referring to the study of Dopico et al.
43
44

- 45
46 3. 'No published data appear to be available on absolute changes (in mm) in the alveolar crest
47 height of GAgP patients over the short or long-term'. Please refer to the study by Onabolu
48 et al. 2015 for comparison of crestal bone loss in AgP vs. CP not under regular SPT.
49

50 **Response:** Following the reviewer's remark, we have now referred and cited the work of
51 Onabolu et al. We compare our results and highlight the differences between both studies.
52
53

- 54
55 4. 'In this retrospective study, with the longest follow-up of GAgP patients published to
56 date...'. Please compare length of follow-up with the study by Graetz et al. 2011
57
58
59
60

1
2
3 **Response:** We have now cited the work of Graetz et al. as the study with the longest
4 follow-up period and have changed this paragraph at the end of discussion section: “*This*
5 *retrospective study, along with the one by Graetz et al. (Graetz et al. 2011), are the longest*
6 *follow-up of GAgP patients published to date*”.

- 7
8
9
10
11
12 5. Please add a comment on initial disease severity of this patient group (as per my previous
13 comment) to allow comparison with previous longitudinal studies.

14 **Response:** We have found that Average PPD is not frequently reported in AgP studies, but
15 our results are in the range of other published data. We have added in the discussion section
16 a new paragraph on the periodontal conditions at baseline of the patients included in the
17 study and compared it with other baseline conditions reported in GAgP studies:

18 *“In our study, we analyzed 3168 sites, and 4.2% of these had pockets ≥ 7 mm deep at*
19 *baseline (134 pockets ≥ 7 mm), and the number of sites with CAL loss ≥ 7 mm was much*
20 *higher (241). The average PPD at baseline was 3.7 mm, with a 43% of healthy sites at*
21 *baseline (≤ 3 mm). This result is within the range of previous baseline periodontal status*
22 *reported by other studies. Monteiro et al. and Hughes et al. reported a mean PPD of 2.7 and*
23 *2.98 mm respectively, while Haas et al. published a mean PPD at baseline of 4.7mm in GAgP*
24 *(Monteiro et al. 2015, Hughes et al. 2006b, Haas et al. 2008).”*
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60