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EPIDEMIOLOGY (COHORT STUDY OR CASE–CONTROL STUDY)

Clinical performance of non-surgical periodontal therapy in a large Chinese population with generalized aggressive periodontitis

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Abstract

Aim: This study aimed to evaluate clinical performance of non-surgical periodontal treatment (NSPT) and its influential factors in a large Chinese population with generalized aggressive periodontitis (GAgP).

Material and Methods: Longitudinal periodontal examination data of 1,004 GAgP patients (numbers of patients with observation periods 6 weeks~, 3 months~, 6 months~, 1 year~, 3 years~ and >5 years were 203, 310, 193, 205, 70 and 23, respectively) were extracted from a hospital-based electronic periodontal charting record system and analysed by multilevel analysis.

Results: Mean probing depth (PD) and attachment loss (AL) reductions at patient level were 1.17 mm and 1.07 mm, respectively. Multilevel analysis demonstrated PD reductions after maintenance were mainly influenced by frequency of supportive periodontal treatment (FSPT), gender, adjunctive systemic use of antibiotics, baseline mobility, tooth type and baseline PD and bleeding index reductions were mainly influenced by FSPT, adjunctive systemic use of antibiotics, baseline AL, baseline mobility, tooth type and baseline PD.

Conclusion: The clinical performance of NSPT on patients with GAgP was proved in the large Chinese population. Outcomes of NSPT were mainly influenced by FSPT, adjunctive systemic use of antibiotics, baseline mobility, tooth type and baseline PD.

KEYWORDS
aggressive periodontitis, antibiotic, clinical performance, non-surgical periodontal therapy, real-world study

1 | INTRODUCTION

Aggressive periodontitis (AgP) is a group of severe forms of periodontitis occurring early in life with rapid periodontal destruction and tendency to cluster within families (Albandar, 2014a,b; Armitage, 1999, 2004).

The overall treatment concepts and goals of aggressive periodontitis are very similar to chronic periodontitis (CP). Therefore, treatment of AgP always centres on effective and thorough plaque control by non-surgical periodontal therapy (NSPT) and access surgery to halt periodontal destruction or regain periodontal attachment by regenerative surgery (Aimetti, Romano, Guzzi, & Carnevale,

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2012; Deas & Mealey, 2010; Teughels, Dhondt, Dekeyser, & Quirynen, 2014).

Although the therapeutic effect of NSPT on CP patients is well researched (Hung & Douglass, 2002; Trombelli, Franceschetti, & Farina, 2015; Van der Weijden & Timmerman, 2002), information about treatment outcomes of NSPT on patients with generalized aggressive periodontitis (GAgP) and their long-term stability is still limited (Teughels et al., 2014). Several studies reported the clinical parameter changes by non-surgical root debridement alone. For patients with GAgP, PD reductions after treatment ranged from 0.4 mm to 2.1 mm for a 2 to 4 months' period of observation and clinical attachment gain ranged from 0.2 mm to 1.0 mm for a 6 months to 2 years' period of observation (Aimetti et al., 2012; Baltacioglu, Aslan, Sarac, Saybak, & Yuva, 2011; Casarin et al., 2012; Guerrero et al., 2005; Haas et al., 2008; Heller et al., 2011; Hughes et al., 2006; Mestnik et al., 2010; Purucker, Mertes, Goodson, & Bernimoulin, 2001; Sakellari, Vouros, & Konstantinidis, 2003; Sigusch, Beier, Klinger, Pfister, & Glockmann, 2001; Varela et al., 2011; Xajigeorgiou, Sakellari, Slini, Baka, & Konstantinidis, 2006; Yek et al., 2010). However, the sample size of most of these studies was from 10 to 20, and their outcomes fell within a relatively large range.

A study reporting long-term survival rates of questionable and hopeless teeth in patients with AgP and CP showed that AgP patients reacted similarly to CP patients on periodontal treatment (Graetz et al., 2011). However, some other studies (Mestnik et al., 2010; Rabelo et al., 2015; Slots and Research, Science and Therapy Committee, 2004; Tonetti & Mombelli, 1999; Xajigeorgiou et al., 2006) and a literature review (Armitage, 1999) indicated that treatment outcomes of conventional mechanical root surface debridement for subjects with AgP may be less predictable than CP and a study even showed that 25 out of 79 (31.65%) patients with GAgP did not respond to treatment (Hughes et al., 2006). Therefore, adjunctive antibiotic treatments were suggested by scientists and clinicians. Randomized clinical trials (RCTs) showed that the additional reductions of probing depth (PD) and attachment loss (AL) ranged from -0.26 mm to 1.16 mm and 0.30 mm to 1.05 mm, respectively (Aimetti et al., 2012; Baltacioglu et al., 2011; Beliveau et al., 2012; Casarin et al., 2012; Emingil et al., 2012; Griffiths et al., 2011; Guerrero et al., 2005; Haas et al., 2008; Heller et al., 2011; de Lima Oliveira et al., 2012; Mestnik et al., 2010, 2012; Moreno Villagrana & Gomez Clavel, 2012; Palmer, Watts, & Wilson, 1996; Purucker et al., 2001; Sakellari et al., 2003; Sigusch et al., 2001; Silva-Senem et al., 2013; Varela et al., 2011; Xajigeorgiou et al., 2006; Yek et al., 2010). A systematic review and Bayesian Network meta-analysis, to evaluate the benefit of adjunctive use of systemic antibiotic on the treatment outcomes of AgP, showed that significantly greater attachment level gain (mean differences were 1.08 mm and 0.45 mm for SRP + metronidazole and SRP + amoxicillin + metronidazole, respectively) and PD reductions (mean differences were 1.05 mm and 0.53 mm for SRP + metronidazole and SRP + amoxicillin + metronidazole, respectively) were found for test group than control group (Rabelo et al., 2015).

It should be noted that, however, most of studies mentioned above and included in the meta-analysis (Rabelo et al., 2015) were with a relatively small sample size (<20), heterogeneity and unclear or high risk of bias. Additionally, the overwhelming majority of the results mentioned above were from clinical trials but not the real clinical circumstances. Data about effectiveness, the extent of a beneficial outcome produced by an intervention under practical circumstances, of NSPT and adjunctive systemic antibiotic therapy to the mechanical treatment on subjects with GAgP were still lacking. Therefore, the aim of the present study is to evaluate the clinical performance of NSPT and its influential factors on a large Chinese cohort of over 1,000 subjects with GAgP.

Clinical Relevance

Scientific rationale for the study: AgP was considered as a type of periodontitis with poor response to treatment, however, evidence of the clinical performance of NSPT on subjects with AgP and its influential factors was limited.
Principal findings: Clinical performance of NSPT in Chinese patients with GAgP was proved by multilevel analysis. Response to NSPT of GAgP subjects was similar to that of CP. It was mainly influenced by the FSPT, adjunctive systemic use of antibiotics, baseline mobility, tooth type and baseline PD.
Practical implications: NSPT is also effective in subjects with GAgP. Effect of NSPT on their teeth with extremely severe periodontal breakdown may be limited.

2 | MATERIAL AND METHODS

2.1 | Study population

Patients who had received NSPT in the Department of Periodontology, Peking University School and Hospital of Stomatology and had at least one periodontal re-evaluation record from January 2007 to January 2015 were included in this retrospective study.

The study was approved by the Ethics Committee of the Peking University School and Hospital of Stomatology (approval number: PKUSSIRB-201310066). All protocols were performed in accordance with approved guidelines and regulations. Informed consent was obtained from all subjects.

Inclusion criteria were:

- Adults diagnosed as GAgP according to the classification proposed at the International Workshop for the Classification of Periodontal Diseases and Conditions in 1999 (Armitage, 1999);
- The onset of periodontal destruction was before 35 years old;
- At least eight teeth, had PD > 5 mm and AL > 3 mm and at least three of them were not the first molars or incisors;

- The clinical diagnosis was confirmed by evidence of inter-proximal bone loss on full-mouth periapical radiographs;
- Patients with a follow-up of at least 6 weeks (only patients with a follow-up of at least 3 months were included for the analysis of tooth loss).

Other referenced criteria for GAgP (The followings were important factors for the diagnosis but patients had no need to meet all the criteria).

- Patients had rapid AL and alveolar bone resorption;
- Patients had family aggregation;
- Patients had progression and imbalanced relationship between local irritation and periodontal destruction.

Exclusion criteria were:

- Systemic disease, pregnancy or under medication affecting periodontium;
- Periodontal surgery history.

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

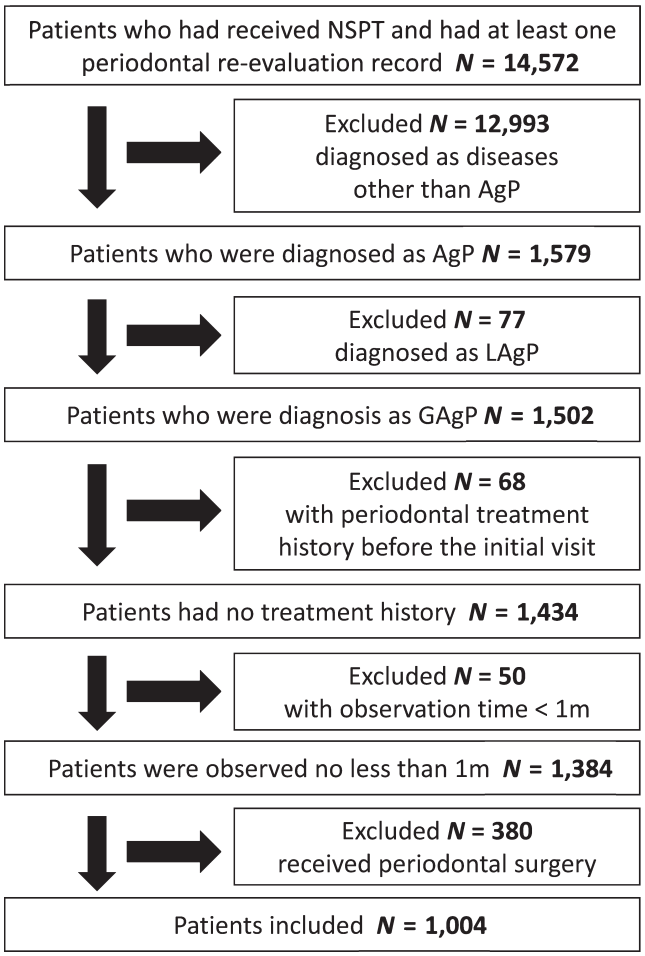


FIGURE 1 Flow chart of patients' selection and screening

2.2 | Data extraction

The following patient-related parameters assessed at the initial visit (T0) and the last evaluation (T1) were extracted from the electronic periodontal charting record system for analysis: (a) patient level: age, frequency of supportive periodontal treatment (FSPT, irregular versus regular), gender (male versus female), observation period, smoking status (non-smoker classified as patients who did not smoke at the initial visit, ex-smoker classified as patients who quitted smoking during NSPT and smoker classified as patients who still smoked at the last visit) (Jiao et al., 2017), adjunctive systemic use of antibiotics (with versus without); (b) tooth level: Mazza bleeding index (BI) (0~5) (Mazza, Newman, & Sims, 1981), tooth mobility (0~III°) (Lang & Lindhe, 2015), AL (measured by the distance from the cementoenamel junction to the bottom of the periodontal pocket. The greatest AL of buccal and lingual surfaces of each tooth was recorded and mean AL of buccal and lingual were computed), tooth type (molars versus non-molars); (c) site level: PD (six sites). Tooth and site level data from the third molars and teeth lost during NSPT were excluded.

2.3 | Periodontal examinations and treatments

Full-mouth periodontal chartings and treatments were performed by qualified clinical periodontists who were systematically trained and calibrated in pre-clinical programmes. NSPT, involving oral hygiene instruction (OHI), scaling and root planing (SRP) using ultrasonic scalers and hand instruments for sites with PD ≥ 4 mm, was performed after the initial examination. Adjunctive systemic use of antibiotics was carried out in some AgP patients after SRP. Whether systemic antibiotics were administrated and the medicine regimes were decided by advices of periodontists and decisions of patients. Systemic administration of amoxicillin (500 mg 3× for 7 days) and metronidazole (200 mg 3× for 7 days) was the most common regime for GAgP patients. Azithromycin (500 mg 1× for 5 days) or roxithromycin (150 mg 2× for 6 days) was administrated as alternatives to amoxicillin when patients were allergic to amoxicillin. Tinidazole (1,000 mg 1× for 3 days) was occasionally prescribed as an alternative medicine of metronidazole. SRPs were finished within 2–4 appointments and OHI was enforced at every appointment. The first re-evaluation was performed 6 weeks after the initial treatment. For supportive periodontal treatment (SPT), full-mouth periodontal charting, OHI reinforcement, prophylaxis scaling and SRP for residual pockets with PD ≥ 4 mm sites were performed at an interval of 3 months. In total, 21 periodontists had performed examinations and treatments for the patients during the study period.

2.4 | Statistical analysis

The primary outcomes included PD, AL, bleeding status change after NSPT. The secondary outcomes included the number of tooth loss and non-response rate to NSPT. The data were analysed by IBM

TABLE 1 Study population characteristics and patient-related factors under study

Category	*N*	%	Mean (*SD*)	Range
Age at T0 (years)	—	—	30.68 (4.97)	18.05~43.55
Supportive periodontal treatment				
Regular	850	84.66	—	—
Irregular	154	15.34	—	—
Gender				
Female	544	54.18	—	—
Male	460	45.82	—	—
Observation period (years)	—	—	1.06 (1.27)	0.12~6.75
Smoking				
Non-smoker	784	78.09	—	—
Ex-smoker	102	10.16	—	—
Smoker	118	11.75	—	—
Systemic antibiotics				
Without	824	82.07	—	—
With	180	17.93	—	—
Total	1,004	100.00	—	—

Note. T0, the initial visit.

SPSS Statistics 20 software (IBM Corp. 2011; NY; USA) and statistical graphs were performed with R (http://www.R-project.org) and EmpowerStats software (www.empowerstats.com, X&Y solutions, Inc.Boston MA).

At first, comparisons of data distribution of different groups were performed using the *t* test or ANOVA (normal distribution) for continuous variables [age, observation period, PD, BOP (percentage of bleeding on probing)%, BOP positive equals to BI and AL) and Chi-square test for categorical data (FSPT, gender, smoking status, systemic antibiotics using) at patient level. In addition, the mean number of tooth loss and number of tooth loss per year for subjects with different observation time had been computed. Then we explored the relationship between independent variables (PD, BOP%, AL, non-response rate and number of tooth loss) at patient level and dependent variables (observation period) by FSPT, systemic antibiotics using and smoking status after adjusting for influential factors, which was illustrated by smoothing plot based on generalized additive models. Besides, multilevel (patient at level 1, tooth at level 2 and site at level 3) analysis was adopted to analyse PD reductions at site level and BI reductions at tooth level. Subsequently, 11 independent variables (introduced in data extraction) were included in the multilevel regression models. The significance of the models was checked by F test. The level of significance was set at $p \leq 0.05$.

In order to assess the treatment response of deep sites (PD ≥ 5 mm), responding sites were defined as those showing at least 2 mm PD reduction and non-responding sites were defined as those showing no improvement or deterioration of PD after treatment (It should be noted that sites showing 1 mm PD reduction was categorized neither responding nor non-responding sites). Similarly, patients were also divided into responding and non-responding patients and non-responding patients were defined as those with at least 30% of their deep sites that did not respond to NSPT (Hughes et al., 2006). Then percentages of responding and non-responding patients/sites were computed.

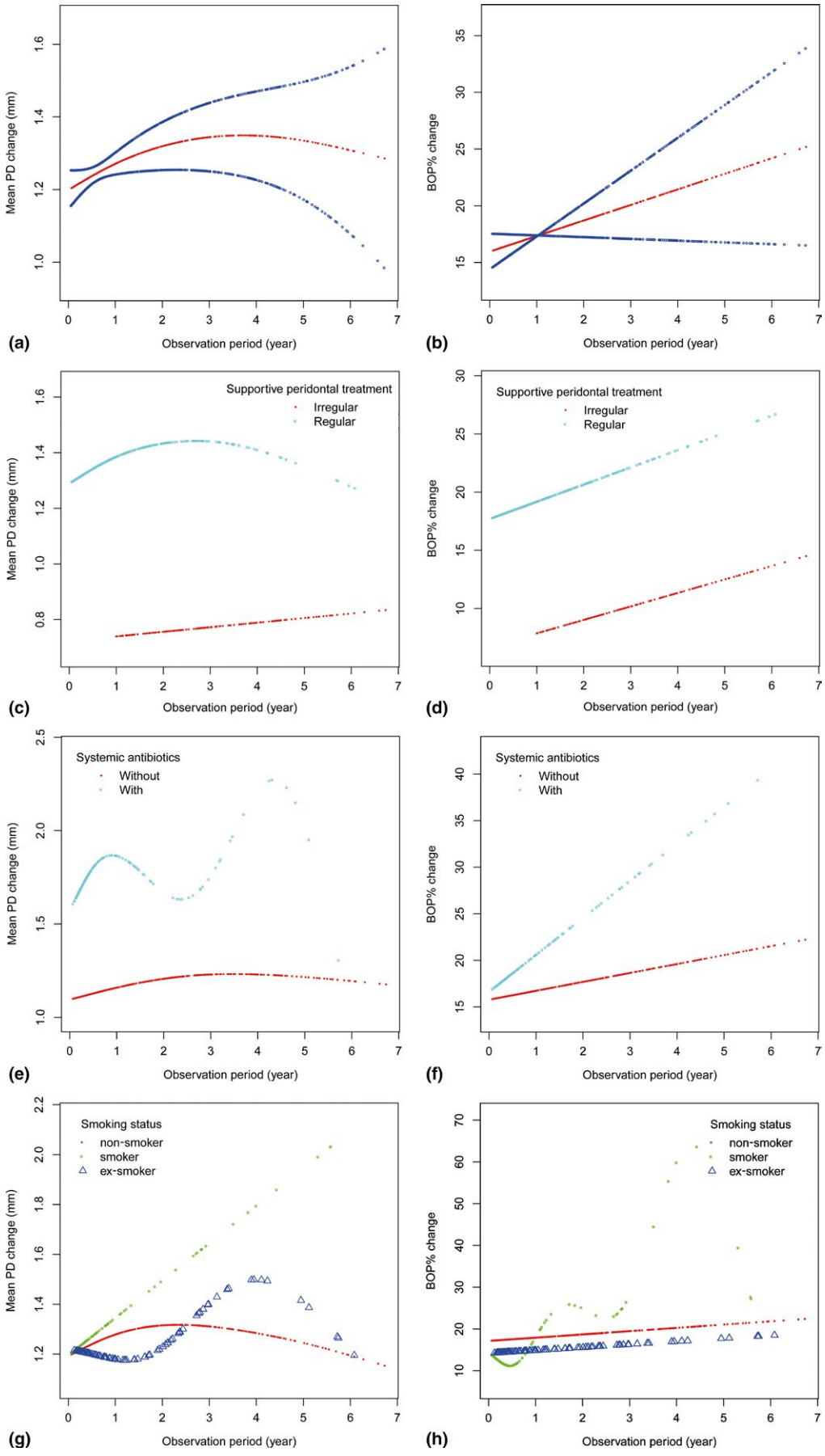
The material and methods used in this study were similar to a study about the clinical performance of NSPT on CP (Jiao et al., 2017).

3 | RESULTS

3.1 | Study population

According to the selecting criteria and exclusion criteria, 1,004 patients were involved. The mean age of included patients was

FIGURE 2 Relationships between changes of probing depth (dependent variable) and percentage of bleeding on probing (dependent variable) at patient level before and after non-surgical periodontal treatment and observation period (independent variable) in subjects with different frequency of supportive periodontal treatment (c and d), systemic antibiotics using (e and f) and smoking status (g and h) by smoothing plots based on generalized additive models. To eliminate the influence of different baseline periodontal parameters in subgroups and make the data comparable, adjusting of influential factors (baseline age, gender, mean baseline probing depths, mean baseline "percentage of bleeding on probing", mean baseline attachment loss, frequency of supportive periodontal treatment, systemic antibiotics using and smoking status) was performed. Red lines of (a) and (b) were mean of the dependent parameters and blue ones were their 95% confidential intervals


Mean PD change (mm)
BOP% change
Observation period (year)
(a)
(b)
Supportive peridontal treatment
Irregular
Regular
(c)
(d)
Systemic antibiotics
Without
With
(e)
(f)
Smoking status
non-smoker
smoker
ex-smoker
(g)
(h)

30.48 years old and the mean observation period was 1.11 years. Numbers of patients with observation periods 6 weeks~, 3 months~, 6 months~, 1 year~, 3 years~ and >5 years were 203, 310, 193, 205, 70 and 23, respectively. Detail information about the study population characteristics and patient-related factors is shown in Table 1.

3.2 | Changes of clinical parameters at patient level

At patient level, mean PD and AL reduced significantly by 1.17 mm and 1.07 mm respectively. Non-linear smoothing plots were made to illustrate the change of PD, BOP%, AL and non-response rate of NSPT by different observation periods (Figure 2 and 3). Slightly trends of increase in PD and non-response rate and slightly trends of decrease in AL were found as observation period went by. BOP% increase steadily over the observation time. However, approximate significance of smooth terms showed that the changes of the parameters by observation period were not significant. When comparing the differences of the periodontal parameter changes with observation time between patients with regular and irregular SPT, regular patients had significantly higher PD, BOP% and AL changes and lower non-response rate than irregular patients. When comparing the differences of the periodontal parameter changes with observation time between patients with systemic antibiotics using and ones without using, patients with systemic antibiotics using had significantly higher PD, BOP% and AL change and lower non-response rate than irregular patients. When comparing the differences of the periodontal parameter changes with observation time between patients with different smoking status, no significant difference was detected.

Totally, 801 subjects with observation period more than 3 months were included for analysing number of tooth loss during NSPT (involving active periodontal treatment, i.e., APT and SPT) and 37.2% (298 out of 801) of them was with a long-term observation (more than 1 year). Mean number of tooth loss was 0.57 for all the patients and ranged from 0.58 to 0.96 for patients with different observation period. Mean annualized number of tooth loss was 1.05 for all the patients and ranged from 0.86 to 1.51 for patients with different observation period (Supporting Information Table S4). Relationship between number of tooth loss during NSPT and observation period was shown in Figure 4.

Slightly trends of increase in number of tooth loss were found as observation period went by and the estimate of observation period, i.e., one of the independent variables of the generalized addictive model was 0.097 which showed that the annualized number of tooth loss was approximately 0.1 during SPT.

3.3 | Changes of clinical parameters at tooth and site level

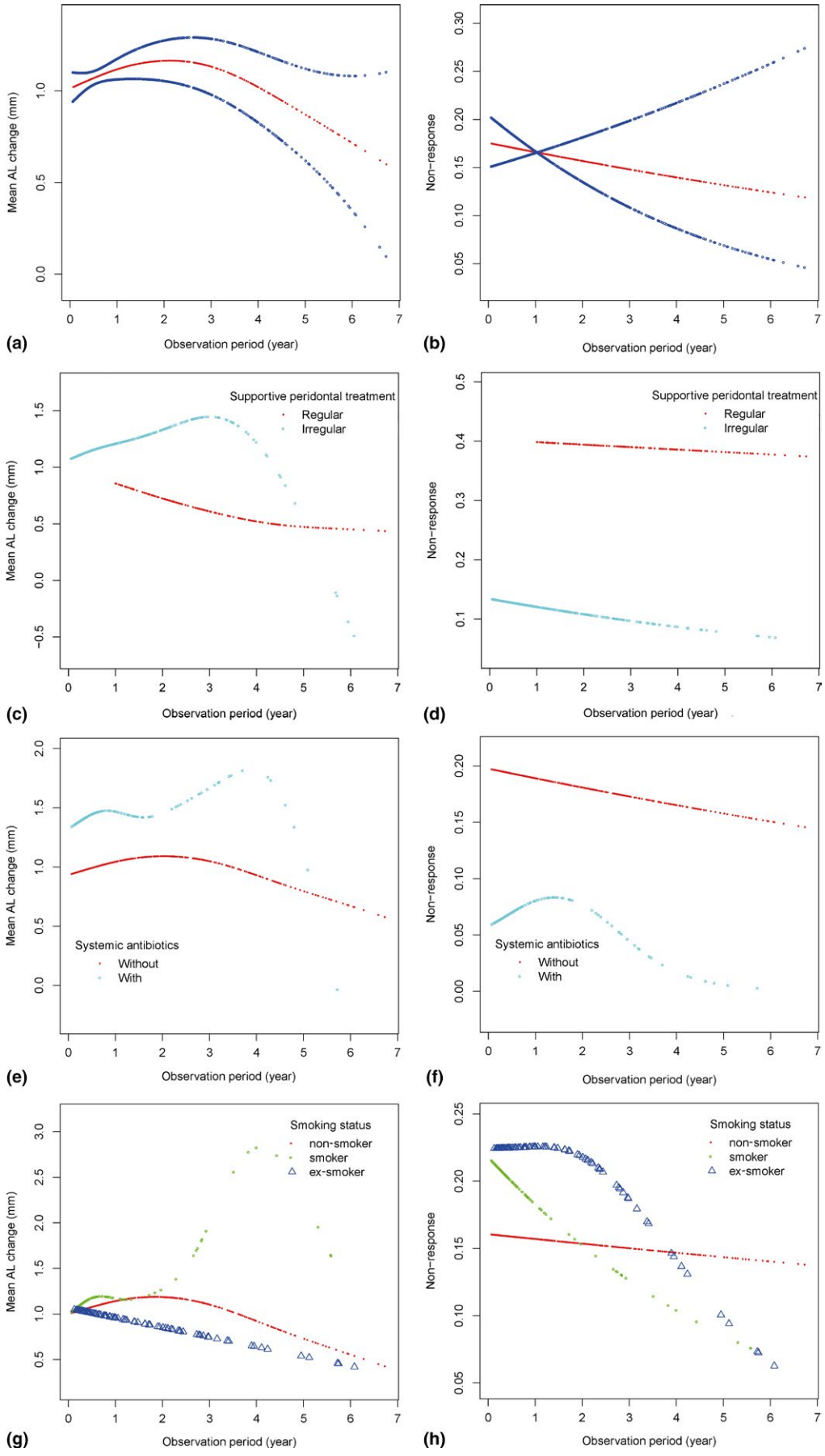
A total of 25,441 teeth and 152,646 sites were included for analysis of PD and BI changes after NSPT. The overall mean PD reductions for all sites and for sites with baseline PD ≥ 5 mm were 1.14 mm and 2.02 mm, respectively; percentage of sites with PD < 4 mm raised from 38.58% to 72.30%. After NSPT, percentages of BI reduction at tooth level for all teeth and for teeth with baseline PD ≥ 5 mm were 66.24% and 71.26%, respectively and percentage of teeth with BOP negative was 16.96%. The percentage of responding sites was 38.48% and non-responding sites was 35.75% (percentage of sites with 1 mm PD reduction was 25.77%).

The Variance Components models showed that significant variations existed at all the levels of the multilevel structure. For PD reduction, both for all sites and for sites with PD ≥ 5 mm, site level variations contributed the most to the total variations while tooth level variations contributed the least to the total variations. When it comes to BI reduction, both for all teeth and teeth with baseline PD ≥ 5 mm, patient level variations contributed more to the total variations than tooth-level variations (Table 2 and 3).

Multilevel linear regression analysis of PD reductions for all sites and sites with baseline PD ≥ 5 mm and BI reductions for all teeth and teeth with baseline PD ≥ 5 mm were presented in Table 2 and 3, respectively. For the linear regression models, coefficient of continuous variables meant the change of dependent variable (PD) when the independent change 1 unit (for example, coefficient of variable baseline PD meant when baseline PD increased 1 mm the PD reduction increased 0.598 mm) and coefficient of categorical variables meant the difference of dependent variable (PD) compared with the reference (for example, coefficient of variable FSPT meant that the 0.428 mm less PD reduction was found in a patient with irregular SPT than that of a patient with regular SPT). For the logistic regression models, odds ratio (OR) of continuous variables meant the increase in OR of dependent variable (BI reduction) when the independent change 1 unit (for example, OR of variable baseline mean PD meant when baseline PD increased 1 mm the probability of BI reduction increase 0.762 times/decrease 1.312 times) and OR of categorical variables meant the difference of dependent variable (PD) compared with the reference (for example, coefficient of variable SPT meant that the OR between irregular and regular patients was 0.272).

Results showed that NSPT, gender, adjunctive systemic use of antibiotics (patient level), baseline mobility, tooth type (tooth level) and baseline PD (site level) were significantly associated with PD reduction for all sites and sites with initial PD ≥ 5 mm.

FIGURE 3 Relationships between changes of attachment loss (dependent variable) and non-response rate (dependent variable) at patient level before and after non-surgical periodontal treatment and observation period (independent variable) in subjects with different frequency of supportive periodontal treatment (c and d), systemic antibiotics using (e and f) and smoking status (g and h) by smoothing plots based on generalized additive models. To eliminate the influence of different baseline periodontal parameters in subgroups and make the data comparable, adjusting of influential factors (baseline age, gender, mean baseline probing depths, mean baseline BOP%, mean baseline attachment loss, frequency of supportive periodontal treatment, systemic antibiotics using and smoking status) was performed. Red lines of (a) and (b) were mean of the dependent parameters and blue ones were their 95% confidential intervals


Mean AL change (mm)
Observation period (year)
(a)
Non−response
Observation period (year)
(b)
Supportive peridontal treatment
Regular
Irregular
Mean AL change (mm)
Observation period (year)
(c)
Supportive peridontal treatment
Regular
Irregular
Non−response
Observation period (year)
(d)
Systemic antibiotics
Without
With
Mean AL change (mm)
Observation period (year)
(e)
Systemic antibiotics
Without
With
Non−response
Observation period (year)
(f)
Smoking status
non-smoker
smoker
ex-smoker
Mean AL change (mm)
Observation period (year)
(g)
Smoking status
non-smoker
smoker
ex-smoker
Non−response
Observation period (year)
(h)

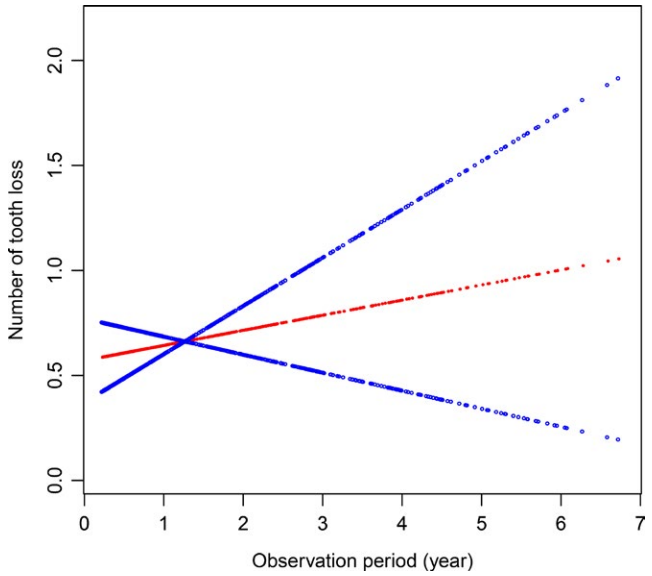


FIGURE 4 Relationships between number of tooth loss (dependent variable) during non-surgical periodontal treatment and observation period (independent variable) by smoothing plots based on generalized additive models. To eliminate the influence of different baseline periodontal parameters in subjects with various observation period and make the data comparable, adjusting of influential factors (baseline age, gender, mean baseline probing depths, mean baseline BOP%, mean baseline attachment loss, frequency of supportive periodontal treatment, systemic antibiotics using and smoking status) was performed. Only data of subjects with observation time more than 3 months were included for analysis. The estimated number of annual tooth loss was 0.09 per year. Red line was mean of the dependent parameter and blue one was 95% confidential intervals

Baseline age and baseline AL were also significantly associated with PD reductions for all sites and sites with baseline PD ≥ 5 mm but their coefficient values were too small (<0.1) to have clinically significant effects. After the inclusion of the variables, the total variances of models reduced at each level. When it comes to BI, FSPT, adjunctive systemic use of antibiotics (patient level), baseline AL, baseline mobility, tooth type and baseline PD (tooth level) were significantly associated with PD reductions for all sites and sites with baseline PD ≥ 5 mm. All the models constructed in the present study were evaluated by *F* test. The results showed that the *p* values were all <0.05, which means the quality of models was good.

4 | DISCUSSION

The clinical performance of NSPT on subjects with GAgP was proved in this large sample retrospective cohort of Chinese patients. After NSPT, average PD reductions were 1.17 mm and 1.14 mm for patient level and site level, respectively (Figure 2 and Supporting Information Table S3). There were also over 65% of teeth whose BI reduced.

Several previous studies have assessed treatment outcomes of AgP. PD reductions after NSPT varied from 0.1 mm to 2.1 mm for all sites and 1.2 mm to 2.7 mm for deep pockets among different studies with relatively large heterogeneity (Aimetti et al., 2012; Asikainen, Jousimies-Somer, Kanervo, & Saxen, 1990; Baltacioglu et al., 2011; Casarin et al., 2012; Guerrero et al., 2005; Gunsolley et al., 1995; Haas et al., 2008; Heller et al., 2011; Kornman & Robertson, 1985; Mestnik et al., 2010; Purucker et al., 2001; Sakellari et al., 2003; Saxen & Asikainen, 1993; Sigusch et al., 2001; Slots & Rosling, 1983; Unsal, Walsh, & Akkaya, 1995; Varela et al., 2011; Xajigeorgiou et al., 2006; Yek et al., 2010). PD reductions after treatment of the present study were greater than that of most of the studies mentioned above. This is partially due to worse periodontal condition of Chinese patients with GAgP. Unfortunately, oral hygiene of Chinese patients is worse and their awareness of periodontal diseases is less sufficient, in general, than subjects from developed countries. This fact might result from that treatments for subjects with GAgP were initiated at more advanced stage of the disease and ethnic difference in genetics, e.g., genotype frequencies of polymorphisms vitamin D receptor gene (Deng et al., 2011), and microbiology, e.g., the presence of *Aggregatibacter actinomycetemcomitans* between Chinese and Caucasians (Han et al., 1991; Ishikawa, Kawashima, Oda, Iwata, & Arakawa, 2002; Kononen & Muller, 2014; Li, Feng, et al., 2015).

Moreover, varied treatment outcomes among studies may also be attributed to various strategies of subject selection. In a RCT, the inclusion criteria are often strict and only selective subjects can be recruited. This pragmatic effectiveness study with over 1,000 patients included, however, conducted in individuals of huge heterogeneity and almost all accessible data of candidates were analysed. Therefore, results of this study may be better extrapolated to the clinical practice.

The annualized number of tooth loss of the present study (1.05 per year) was much higher than those of other studies or meta-analysis concerning long-term prognosis of AgP (ranging from 0.09 to 0.27 per year) (Angst 2013; Baumer et al., 2011; Diaz-Faes, Guerrero, Magan-Fernandez, Bravo, & Mesa, 2016; Dopico, Nibali, & Donos, 2016; Graetz et al., 2017; Nibali, Farias, Vajgel, Tu, & Donos, 2013). The primary reason is that the number reported above was the sum of teeth lost during both APT and SPT instead of SPT only reported in previous studies mentioned above. In addition, decisions of tooth extraction may be influenced by many factors such as the patients' attitude and the instruction by periodontists. In our country, patients may be more reluctant to have their teeth extracted due to culture and insurance policy. Besides, reasons for tooth loss were not recorded in the EPCRS which may overestimate the tooth loss due to periodontal reasons. In the present study, the annualized number of tooth loss during SPT can be estimated by the gradient of the smoothing plot (Figure 4). The estimated number of annual tooth loss was 0.097 per year, which was consistent to those reported by previous study (Angst 2013; Baumer et al., 2011; Diaz-Faes et al., 2016; Dopico et al., 2016; Graetz et al., 2017; Nibali et al., 2013). In our future research, the influential factors of periodontal tooth loss of AgP patients will be explored in detail.

TABLE 2 Multilevel linear regression analysis of PD reductions for all sites and sites with baseline PD ≥ 5 mm

	All sites			PD ≥ 5 mm at T0		
	Coefficient	SE	*p*	Coefficient	SE	*p*
Intercept	−0.657	0.145	**<0.001**	−0.092	0.261	0.725
Patient level						
Age at T0	−0.022	0.004	**<0.001**	−0.028	0.005	**<0.001**
SPT (irregular versus regular)	−0.428	0.068	**<0.001**	−0.596	0.090	**<0.001**
Gender (male versus female)	−0.113	0.038	**0.003**	−0.131	0.050	**0.008**
Non-smoker (reference)						
Smoker	−0.060	0.059	0.310	−0.085	0.077	0.267
Ex-smoker	0.034	0.061	0.582	−0.010	0.080	0.897
Observation period[a]	0.022	0.019	0.252	0.054	0.026	**0.036**
Systemic antibiotics (with versus without)	0.175	0.048	**<0.001**	0.257	0.062	**<0.001**
Tooth level						
AL at T0	0.019	0.003	**<0.001**	−0.003	0.006	0.558
Degree 0 of mobility (reference)						
Degree III	−0.163	0.024	**<0.001**	−0.171	0.032	**<0.001**
Degree II	0.014	0.013	0.264	0.018	0.018	0.313
Degree I	0.018	0.009	**0.048**	0.006	0.014	0.697
BI at T0 = 0 (reference)						
BI at T0 = 4	0.043	0.088	0.628	−0.250	0.211	0.236
BI at T0 = 3	−0.013	0.088	0.881	−0.306	0.211	0.147
BI at T0 = 2	−0.015	0.087	0.861	−0.339	0.210	0.107
BI at T0 = 1	0.068	0.088	0.442	−0.324	0.215	0.131
Tooth types (molars versus non-molars)	−0.692	0.008	**<0.001**	−0.822	0.012	**<0.001**
Site level						
PD at T0	0.598	0.002	**<0.001**	0.613	0.004	**<0.001**
Variance						
Patient level	0.319	0.015	**<0.001**	0.528	0.025	**<0.001**
Tooth level	0.153	0.003	**<0.001**	0.239	0.005	**<0.001**
Site level	0.759	0.003	**<0.001**	0.994	0.006	**<0.001**

Notes. BI, bleeding index; SPT, supportive periodontal treatment; PD, Probing depth; T0, the initial visit, above models were evaluated test by *F* test, $p < 0.001$.

[a]Data of patients with observation time more than 6 weeks were included.

Patients in the present study with various observation periods may have different baseline parameters. A direct comparison between parameter changes of patients with different observation period was unreasonable. Therefore, adjustments of confounding factors were performed and smoothing plots were made to illustrate the change of parameters as time went by (Figure 2). However, both results from three levels showed that the periodontal parameters seemed not dramatically change with time (Figure 2 and Table 2 and 3).

Conventional view was that AgP may respond unpredictably to mechanical treatment (Mestnik et al., 2012; Rabelo et al., 2015; Slots and Research, Science and Therapy Committee, 2004; Xajigeorgiou et al., 2006). A study to evaluate the response to periodontal treatment of patients with AgP showed that there was a good response to the treatment generally.

However, there were still over 30% of the patients and 16.6% of deep sites were non-responding to mechanical treatment and the non-response patients and sites were mainly associated with

TABLE 3 Multilevel logistic regression analysis of BI reductions for all teeth and teeth with baseline PD ≥ 5 mm

	All teeth			PD ≥ 5 mm at T0		
	Odds ratio	*SE*	*p*	Odds ratio	*SE*	*p*
Intercept	0.000	15.082	0.384	0.000	41.440	0.708
Patient level						
Age at T0	0.988	0.017	0.451	0.984	0.018	0.367
SPT (irregular versus regular)	0.272	0.303	**<0.001**	0.268	0.328	**<0.001**
Gender (male versus female)	0.815	0.169	0.229	0.889	0.182	0.517
Observation period[a]		0.086	0.278		0.093	0.333
Non-smoker (reference)	0.799	0.260	0.386	0.746	0.280	0.294
Smoker	0.734	0.270	0.253	0.658	0.292	0.151
Ex-smoker	1.097	0.086	0.278	1.094	0.093	0.333
Systemic antibiotics (with versus without)	2.507	0.213	**<0.001**	2.396	0.229	**<0.001**
Tooth level						
Attachment loss at T0	0.874	0.013	**<0.001**	0.839	0.015	**<0.001**
Degree 0 of mobility (reference)						
Degree III	0.550	0.056	**<0.001**	0.505	0.059	**<0.001**
Degree II	0.846	0.031	**<0.001**	0.825	0.034	**<0.001**
Degree I	0.998	0.024	0.940	0.986	0.026	0.586
BI at T0 = 0 (reference)						
BI at T0 = 4	2.1E + 08	15.073	0.204	2.3E+09	41.436	0.603
BI at T0 = 3	1.6E + 07	15.073	0.272	1.5E+08	41.436	0.650
BI at T0 = 2	7.8E + 05	15.073	0.368	6.2E+06	41.436	0.706
BI at T0 = 1	1.5E + 04	15.072	0.522	7.9E+04	41.436	0.786
Tooth types (molars versus non-molars)	0.401	0.021	**<0.001**	0.399	0.022	**<0.001**
PD at T0	0.762	0.016	**<0.001**	0.836	0.019	**<0.001**
Variance						
Patient level	4.6E + 02	0.310	**<0.001**	1.1E+03	0.361	**<0.001**
Tooth level	1.000	—	—	1.000	—	—

Notes. BI, bleeding index; SPT, supportive periodontal treatment; PD, Probing depth; T0, the initial visit, above models were evaluated test by *F* test, $p < 0.001$.

[a]Data of patients with observation time more than 6 weeks were included.

current smoking (Hughes et al., 2006). Moreover, there was also a study reported that AgP patients reacted similarly to CP patients on periodontal treatment (Graetz et al., 2011). In the present study, percentages of non-responding patients and sites were lower than those from study by Hughes et al. Comparing results of NSPT on subjects with GAgP with results on a cohort in subjects with CP (Jiao et al., 2017), the improvement after treatment in patients with GAgP may be even better than that of CP: Firstly, mean PD reduction at site level of GAgP patients for all sites was greater than that of CP patients (1.17 mm versus 0.65 mm); Secondly, multilevel analysis, which adjusted many influential factors of NSPT also showed that interceptions of the models in patients with GAgP, both for all sites and baseline deep sites, were greater than that of CP patients. Better response to NSPT of patient with GAgP may be attributed to the genetic (Deng et al., 2011; Li et al., 2004) and/or microbial diversity (Han et al., 1991; Li, Feng, et al., 2015; Li, Xu, et al., 2015) of the two diseases and better wound healing in patients with GAgP whose mean age was younger than that of CP.

Results mentioned above suggest that AgP respond predictably to NSPT and even may respond better than CP. It should be noted that, comparison of treatment outcomes of the two diseases aforementioned was indirect and may be distorted by the uneven disease severity at baseline. Therefore, the results should be interpreted with caution. Prospective studies with matched baseline clinical parameters are needed to test which type of periodontitis responds better to NSPT. Moreover, fundamental researches are also needed to find reasons for the difference in treatment outcomes.

Multilevel analysis also showed that additional PD reduction can be found when adjunctive antibiotic therapy was administrated (0.18 mm and 0.26 mm for all sites and deep sites, respectively, Table 2). The benefit of systemic antibiotic use was slightly less than results from previous RCTs (Aimetti et al., 2012; Baltacioglu et al., 2011; Casarin et al., 2012; Guerrero et al., 2005; Haas et al., 2008; Heller et al., 2011; Li, Xu, et al., 2015; Lu, Feng, Xu, & Meng, 2015; Mestnik et al., 2010; Purucker et al., 2001; Sakellari et al., 2003; Sigusch et al., 2001; Varela et al., 2011; Xajigeorgiou et al., 2006; Yek et al., 2010) but similar to that of meta-analyses (Keestra, Grosjean, Coucke, Quirynen, & Teughels, 2015; Rabelo et al., 2015; Silva-Senem et al., 2013). In the present studies, a multiple factors analysis was applied to minimize influence of other confounding factors and test the effect of a certain factor in turn. Results from the present study suggest that effect of adjunctive antibiotic therapy may not be as great as a dentist's prediction. Furthermore, cost-effectiveness analysis is needed to help clinicians make reasonable decisions.

According to data from the National Oral Health Survey of China carried out in 2005, percentages of periodontally healthy people of 35–44 and 65–74 age groups were only 14.5% and 14.1%, respectively, and prevalence of gum bleeding reached 77.3% and 68%, respectively, for the two age groups (Qi, 2008). Data from our EPCRS showed that over 90% patients received in our department were categorized as severe periodontitis according to CDC/AAP criteria (Eke, 2012). Nevertheless, mean annual dental visits of citizens in Beijing, one of the most developed cities of China, was only 0.34 per year although the situation was improving over time (Meng, 2008). Compared with patients from developed countries, patients from developing countries, such as China, have poorer oral hygiene, higher prevalence and severer extent of periodontal disease, weaker awareness of prevention and regular dental visits, smaller coverage of dental insurance and less chance of receiving professional periodontal therapy in time (Meng, 2008). What is more, severity of patients included in our study were more advanced than those of reported by other studies since Chinese patients often visited in advanced stages of aggressive periodontitis. In addition, for patients with observation period of over 1 year, over half of them were with erratic compliance.

However, results from the present study showed that NSPT also effective for patients with disadvantages mentioned above. The overall PD reduction after NSPT was 1.17 mm and PD ≥ 5 mm (%) reduction was 28.27% after treatment which was even more than most of studies concerning NSPT of GAgP patients. In addition, for patients with erratic compliance who finished NSPT and re-evaluated more than 3 years after treatment, PD also reduced significantly although significantly less than patients with regular frequency of periodontal maintenance. In all conditions, NSPT is an effective and important way of removing biofilms and controlling periodontal infection.

Results from multilevel analysis also indicated the limitation of NSPT on teeth and sites with advanced periodontal destruction, which were supported by the prevalent points in the periodontal field (Lang and Lindhe, 2015). For sites with initially deep pockets, although NSPT was still effective, greater pocket depth reduction and clinical attachment gain were generally obtained by periodontal surgery especially for molars with furcation involvement and/or angular bone defect (Becker et al., 2001; Knowles et al., 1979; Lindhe, Westfelt, Nyman, Socransky, & Haffajee, 1984; Lu et al., 2015). Moreover, for teeth with severe periodontal damage and poor or hopeless prognosis, e.g., with horizontal bone loss involving >2/3 of the root and III° mobility, the clinical performance of NSPT was limited and other treatment regimens should be considered (e.g., periodontal surgery for readily self-cleaning or splinting to stabilize losing teeth for teeth with poor prognoses and extraction for teeth with hopeless prognoses).

The present study has several strengths. Results of this study may better reflect the condition of real dental practice than RCTs owing to heterogeneity of subjects and a large sample size especially for a rare disease such as GAgP. Besides, information for GAgP from the study may be with more reference value for patients from Asia, patients with worse dental care and patients with more advanced periodontal breakdown. However, our study also shared limitations of observational and retrospective studies. Selection and information bias may threaten the validity of the treatment outcomes (Concato, 2012). In addition, it should be noted that patients who were >35 years old but with a clear disease onset age <35 years old and diagnosed as GAgP according to the classification in 1999 were also included in the present study for analysis. However, multilevel analysis showed that age was not an influential factor of clinical performance of NSPT for patient with GAgP. Therefore, the inclusion of GAgP patients of age >35 years may not compromise comparability of the present study with other similar studies.

Moreover, range of the observation period of patients included was from 6 weeks to 7 years, the mean observation period, however, was only about 1 year. This was attributed to the fact that a considerable proportion of included patients were with a short observational period. However, results from the present study showed that the FSPT significantly influenced the clinical performance of NSPT in spite of the fact that the low proportion of patients with long-term observation may decrease the effect of SPT. Furthermore, data of teeth extracted during NSPT was excluded for analysis owing to the fact that paired data were a basic requirement of statistical analysis of the present study. However, the exclusion did influence the final results of the clinical performance of NSPT on patients with GAgP. Results from the present study showed that hopeless teeth may respond worse to NSPT but the treatment may be also effective. Therefore, the exclusion of extracted teeth may reduce

the strength of treatment clinical performance but not the tendency of the results.

5 | CONCLUSION

The clinical performance of NSPT was proved by this hospital-based retrospective study in a large Chinese population with GAgP. Outcomes of NSPT are mainly influenced by baseline PD, tooth type, SPT, adjunctive systemic use of antibiotics and baseline mobility.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interests.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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