Interleukin-6 and Interleukin-10 Gene Polymorphisms in Patients with Chronic Periodontitis and Response to Treatment after 3 Years

Polimorfizam gena za interleukin-6 i interleukin-10 kod pacijenata s kroničnim parodontitisom te odgovor na liječenje nakon tri godine

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Abstract
Objective: The aim of this study was to investigate whether genetic susceptibility to chronic periodontitis, conferred by the presence of the IL-6 -572GG genotype or the IL-10 -592A allele, influences the outcomes following a non-surgical periodontal therapy (NSPT) over a long period of time. Material and methods: Thirty-seven chronic periodontitis patients were divided into two groups according to genotype as susceptible (SCP) and non-susceptible (NSCP). All subjects were clinically evaluated at baseline and 3 years following NSPT. Blood samples were collected at baseline from the individuals who fulfilled the inclusion criteria. All participants received NSPT from a single periodontist who was blind to the genotype status of each patient. A statistical analysis was performed by comparing the variables between groups using the Mann-Whitney U test and between baseline and 3 years for each group using the Wilcoxon test. Results: The mean age of the population was estimated to be 47.68±8.64 years and it included 51.4% females, 48.6% smokers, and 45.9% alcohol consumers. Following a genetic analysis, 70.3% of patients were homozygous carriers of the IL-6 -572G (IL-6 SCP), and 46.0% of them were carriers of the IL-10 -592A allele (IL-10 SCP). NSPT reduced all studied parameters (probing depth, attachment loss, bleeding on probing, percentage of sites with 4-6mm and ≥7mm pocket depth and attachment loss) to all participants, but the treatment outcome was not associated with the genotype. The SCP and NSCP individuals showed similar clinical parameters at baseline and at 3 years. Conclusions: Within the limitations of this 3-year prospective cohort study in Caucasians diagnosed with chronic periodontitis, individuals susceptible to periodontal disease as determined by the presence of the IL-6 -572GG genotype or the IL-10 -592A allele showed similar treatment outcome following NSPT.

Introduction
Periodontitis is a non-communicable multifactorial inflammatory disease associated with dysbiotic plaque biofilms resulting in progressive destruction of the tooth-supporting tissues and eventually tooth loss (1). Periodontal disease onset and progression are a result of the interaction between the dysbiosis of the commensal oral microbiota and the host response (2). In the 2017 World Workshop on the Classification of Periodontal and Peri-implant Diseases and Conditions it was recognized that population subgroups may exhibit

Uvod
Parodontitis je nezarazna multifaktorijska upalna bolest povezana s biofilmom s disbiotičkim plakom, što rezultira progresivnom uništavanjem tkiva koje podupire zub i na kraju uzrokuje njegov gubitak (1). Pojava i progresija parodontitne bolesti rezultat su interakcije između disbioze komensalne oralne mikrobiote i odgovora domaćina (2). Na Svjetskoj radionici o klasifikaciji parodontitnih i peri-implantantnih bolesti i uvjeta, održanoj 2017. godine, istaknuto je da populacijske podskupine mogu pokazati različi-
it distinct disease conditions due to differences with respect to disease susceptibility and exposure (1).

Susceptibility to periodontal disease and response to treatment vary among individuals and depend on different factors. Disease susceptibility depends on environmental and host risk factors, either modifiable such as smoking, diabetes mellitus, obesity and oral hygiene or unmodifiable including genetic predisposition (3). In a study based on 110 pairs of adult twins, 38-82% of the population variance for periodontal clinical parameters may be attributed to heredity of genetic factors highlighting the role of host genetic influences (4). In recent decades, multiple studies have examined the association between gene polymorphisms and the risk of periodontitis development (5).

Polymorphisms in the promoter region of the Interleukin (IL)-6 gene affect the transcription and expression of IL-6 in individuals leading to the up-regulation of IL-6 levels in serum (6) and gingival tissues (7). Similarly, polymorphisms in the promoter region of the IL-10 gene may change the expression of IL-10 in response to inflammatory disease, thus influencing the disease outcome (8,9). A meta-analyses aimed to determine whether IL-6 and IL-10 polymorphisms confer susceptibility to periodontitis have indicated a significant association between the IL-6 -572 G allele and IL-10 -592 A allele and AA genotype with chronic periodontitis (10-13).

The treatment of periodontitis aims to arrest disease progression by reducing the bacterial load, in order to reduce the risk of tooth loss and to prevent the disease recurrence (14). A reasonable endpoint of non-surgical periodontal treatment should include the absence of clinical signs of gingival inflammation, shallow pocket depth and low levels of plaque accumulation. Studies have demonstrated that periodontal treatment can lead to positive clinical outcomes and a supportive periodontal therapy is effective in maintaining periodontal health and preventing a long-term tooth loss (15-17).

Although periodontal therapy is highly predictable, a patient- and tooth-related factors have been associated with tooth loss and further disease progression during supportive periodontal therapy including age, smoking, systemic conditions and genetics (18,19). Rapid progression from gingivitis to periodontitis has been detected in 10-15% of the population and 8-12% of patients within a population exhibit a number of sites that do not respond to a routine periodontal treatment (20,21). Identifying host-related factors such as gene polymorphisms associated with the development and progression of periodontal diseases may lead to early recognition of patients unresponsive to periodontal treatment (22).

Although environmental factors have been widely investigated as possible predictors of disease progression in individuals who received periodontal therapy, information concerning genetic factors is scarce.

A meta-analysis that examined the effects of several susceptible genotypes to chronic periodontitis with the periodontal treatment outcome and tooth loss concluded that pocket depth reduction in the first three and six months after a non-surgical periodontal therapy was associated with susceptible genotypes (23). However, the number of available studies was insufficient to draw clear conclusions and further studies are ta stanja iste bolesti zbog razlika uvjetovanih osjetljivošću i izloženosti bolesti (1).

Osjetljivost na parodontalnu bolest i odgovor na liječenje razlikuju se od pojedinaca do pojedinca i ovise o različitim čimbenicima. Osjetljivost ovisi o čimbenicima rizika kad je riječ o okolišu i domaćinu, bilo da je promjenjiva poput pušenja, dijabetesa melitusa, pretilosti i oralne higijene, ili ne-promjenjiva, uključujući i genetsku predispoziciju (3). U istraživanju na temelju 110 parova odraslih blizanaca, od 38 do 82 % opaženih varijanaca populacije za parodontalne kliničke parametre može se pripisati nasljedivanju čimbenika koji ističu ulogu genetskih utjecaja domaćina (4). Tijekom posljednjih desetljeća u više su istraživanja autori proučavali povezanost izmedu polimorfizama gena i rizika od razvoja parodontitisa (5).

Polimorfizmi u promotornoj regiji gena interleukina II (IL) utječu na transkripciju i ekspresiju IL-6 kod pojedinaca, što potiče porast regulacije razine IL-6 u serumu (6) i gingivnom tkivu (7). Slično tome, polimorfizmi u promotornoj regiji gena IL-10 mogu promijeniti njegovu ekspresiju kao odgovor na upalnu bolest i tako utjecati na konačni rezultat (8,9). U metaanalizama u kojima se željelo ustanoviti omogućuju li polimorfizmi IL-6 i IL-10 osjetljivost na parodontitis, pokazala se značajna povezanost alela IL-6-572 G i genotipa IL-10-592 A AA s kroničnim parodontitismom (10 – 13).

Svrha liječenja parodontitisa jest zaustaviti progresiju bolesti smanjenjem bakterijskog opterećenja kako bi se smašnjo rizik od gubitka zuba i spriječio ponovni nastanak bolesti (14). Razumna krajnja točka nekiurškoga parodontalnog liječenja trebala bi uključivati odsutnost kliničkih znakova upale gingive, plitke džepove i nisku razinu nakupljanja plaka. Istraživanja su pokazala da se parodontološkim liječenjem mogu postići pozitivni klinički ishodi, a potporna terapija učinkovita je u održavanju zdravlja parodonta i sprječavanju dugoročnog gubitka zuba (15 – 17).

Iako je parodontološka terapija vrlo predvidiva, čimbenici koji su povezani s pacijentima i zubom statistički su značajno povezani s gubitkom zuba i daljnjim napredovanjem bolesti tijekom liječenja, uključujući dob, pušenje, sistemska stanja i genetiku (18, 19). Brza progresija gingivitisa u parodontitis otkrivena je kod 10 do 15 % populacije, a od 8 do 12 % pacijenata u sklopu populacije ima brojna mjesta koja ne reagiraju na rutinsko parodontološko liječenje (20, 21).

Utvrđivanje čimbenika povezanih s domaćinom, poput genetskih polimorfizama povezanih s pojavom i progresijom parodontalnih bolesti, može pomoći da se rano uoče pacijenti koji ne reagiraju na liječenje (22). Iako su okolišni čimbenici široko istraženi kao mogući prediktor progresije bolesti kod pojedinaca koji su primali parodontološku terapiju, informacija o genetskim čimbenicima je malo.

U metaanalizi, u kojoj su se ispitivali učinci nekoliko osjetljivih genotipova na kronični parodontitis s ishodom parodontološkog liječenja i gubitkom zuba, zaključeno je da je smanjenje dubine džepa u prva tri mjeseca i šest mjeseci po liječenju nekiurške parodontološke terapije povezano s osjetljivim genotipovima (23). No broj dostupnih istraživanja nije bio dovoljan za nedvojbenе zaključke pa su potrebna daljnja istraživanja (21). U prospektivnoj studiji s kratkim raz-
needed (21). In a prospective study with a short follow-up pe-
period (45 days following non-surgical periodontal therapy), IL-
6 -572 G/C and IL-10 -592 C/A polymorphisms did not in-
fluence the treatment outcome of chronic periodontitis (24).
Additional methodologically sound studies are needed to con-
tribute to the prediction of periodontal treatment response.

There is still lack of long-term data regarding the treatment
outcome and disease susceptibility in patients with chronic
periodontitis. To the best of our knowledge, there are current-
ly no published clinical studies that evaluate the effect of gene
polymorphisms on the outcome of non-surgical periodontal
therapy over a long period of time. Hence, the aim of this study
was to investigate whether genetic susceptibility to chronic
periodontitis, conferred by the presence of the IL-6 -572GG
genotype or the IL-10 -592A allele, influences the clinical out-
comes of non-surgical long-term periodontal therapy.

Material and methods

This prospective cohort study included consecutive
chronic periodontitis patients from a private practice limit-
ed to Periodontics and Implant Dentistry in Thessaloni-
ki, Greece between September 2014 and June 2015. All el-
igible patients consented to the study protocols. Out of 68
treated subjects, 67 were re-evaluated 45 days following the
treatment and the results of the analysis have been published
separately (24). The subjects were encouraged to attend sup-
portive periodontal therapy on a 3- or 4- month recall pro-
tocol based on their individual needs. A total of 37 out of 67
re-evaluated at 45 days patients presented at their 3-year fol-
low-up appointment. The remaining 30 subjects moved away
from the area, did not attend a number or all of the mainte-
nance appointments, or had a surgical periodontal treatment
as part of their treatment plan.

Patients were included in the study on the basis of the fol-
lowing inclusion criteria:

a. Diagnosis of chronic periodontitis based on the 1999
classification system for periodontal disease (25). Two
or more non-adjacent sites with interproximal clinical
attachment loss (CAL) ≥ 3 mm, probing pocket depth
(PPD) ≥ 5 mm and bleeding on probing (BOP).

b. Attendance of supportive periodontal therapy on a 3-4
month recall protocol.

c. Completion of periodontal re-evaluation 3 years follow-
ing the active periodontal treatment.

d. Systemic health.

e. Age of 30-70 years.

f. Presence of ≥ 16 teeth at initial appointment.

The exclusion criteria consisted of:

a. Any periodontal treatment within the last 12 months
from the study initiation.

b. Poor attendance of follow-up/recall appointments (fail-
ure to attend the recommended supportive periodontal
therapy 3-4 month recall protocol).

c. Lack of data at the follow-up examination 3 years after
active periodontal treatment.

d. Need for periodontal surgery (resective or regenerative)
following the non-surgical periodontal therapy.

dobrjem praćenja (45 dana poslije nekirurške parodontolo-
ške terapije), polimorfizmi IL-6 -572 G/C i IL-10 -592 C/A
nisu utjecali na ishod liječenja kroničnog parodontitisa (24).
Potrebne su dodatne metodološki ispravne studije da bi se
pridonijelo predviđanju reakcije na parodontološko liječenje.

Još uvijek nedostaju dugoročni podatci o ishodu liječenja
i osjetljivosti na bolest kod pacijenata s kroničnim parodon-
titisom. Koliko nam je poznato, trenutačno nema objavlj-
jenih kliničkih istraživanja u kojima autori procjenjuju utjecaj
genetskih polimorfizama na ishod nekirurške parodontološ-
ke terapije tijekom duljeg razdoblja. Dakle, cilj ovog istraži-
vanja bio je istražiti utječe li genetska osjetljivost na kronični
parodontitis, dodijeljena prisutnošću genotipa IL-6 -572GG
ili alela IL-10 -592A, na dugoročne kliničke rezultate neki-
rurške parodontološke terapije.

Materijali i metode

U ovo prospektivno kohortno istraživanje bili su izme-
du rujna 2014. i lipnja 2015. uključeni pacijenti s kronič-
nim parodonttitisom iz privatne prakse ograničenе na paro-
dontošku terapiju i stomatologiju implantata u Solunu u
Grčkoj. Svi odgovarajući pacijenti pristali su na protokol
istraživanja. Od 68 liječenih ispitanika, 67 je ponovno pro-
čijenjeno 45 dana poslije tretmana, a rezultate analize objav-
ljeni su odvojeno (24). Ispitanici su poticani da sudjeluju u
podupiručnoj parodontološkoj terapiji i na 3-mjesečno do
4-mjesečni protokol ponovnog pozivanja na temelju njihovih
individualnih potreba. Ukupno 37, od 67 osoba procjen-
enih 45 dana poslije terapije, pravčeno je i procijenjeno
tijekom njihovih trogodišnjih kontrola. Preostalih 30 napu-
stilo je područje i/ili nije došlo na određeni broj termina ili
uprje nisu dolazili, ili su isključeni zato što su bili podvrg-
jeni kirurškom parodontološkom liječenju u sklopu njihov-
og plana liječenja.

Pacijenti su bili uključeni u studiju na temelju sljedećih
kriterija:

a. dijagnoze kroničnog parodontitisa postavljene na temelju
klasifikacijskog sustava za parodontnu bolest iz 1999. go-
dine (25); dva ili više susjednih mjesta s interproksimal-
nim gubitkom kliničkoga epitelnog pripoja (CAL) ≥ 3
mm, dubinom sondiranja džepova (PPD) ≥ 5 mm i kva-
renjem poslije sondiranja (BOP).

b. sudjelovanja u potpornoj parodontološkoj terapiji na te-
melju 3-mjesečnog i 4-mjesečnog protokola kontrolnih
pregleda

c. završetka ponovne procjene parodonta tri godine nakon
aktivnoga parodontološkog liječenja

d. zadovoljavajućeg općeg zdravlja

e. dob ili između 30 i 70 godina

f. prisutnosti ≥ 16 zuba u prvom terminu.

Kriteriji za isključenje bili su:

a. svako parodontološko liječenje u posljednjih 12 mjeseci
od početka ispitivanja

b. rijetko dolaženje ili nedolaženje na kontrole (neuspjeh u
preporučenoj potpornoj parodontološkoj terapiji 3-mje-
sečne i 4-mjesečne kontrole)
Clinical examination and periodontal therapy

Details of the clinical examination and treatment sequence were described previously (24). In brief, the periodontal status was assessed including PPD, CAL and BOP by an independent, blinded to the genetic analysis and calibrated (intra-examiner agreement=0.88) periodontist (E.D). The clinical examination was performed using a manual periodontal probe (15 UNC probe, Hu-Friedy, Chicago, IL, USA) at six sites per tooth apart from third molars. All patients enrolled in the study were treated according to a comprehensive periodontal treatment plan including case presentation, oral hygiene instructions and non-surgical periodontal therapy under local anesthesia. Hand instruments (Hu-Friedy, Chicago, USA) and ultrasonic scalers (KaVo SONOSoft LUX, Kavo, Germany) were utilized.

The treated patients were re-assessed at 6 weeks following the non-surgical periodontal therapy and clinical examination was completed by the same clinical examiner as carried out at the baseline examination. Supportive periodontal therapy was scheduled on a 3-4 month basis including assessment of PPD, CAL and BOP, re-instruction and re-motivation for effective plaque control, professional tooth cleaning with hand instruments and ultrasonic scalers, and subgingival instrumentation in areas with PPD ≥ 5 mm. The last clinical examination was performed at 3 years following the active periodontal treatment.

Study groups

The recruited individuals were grouped based on the IL-6 -572 G/C and IL-10 -592 C/A polymorphisms: IL-6 SCP: Susceptible to chronic periodontitis conferred by the presence of the IL-6 -572GG genotype; IL-10 SCP: Susceptible to chronic periodontitis conferred by the presence of the IL-10 -592A allele; IL-6 NSCP: Non-susceptible to chronic periodontitis carrying the non-susceptible genotype IL-6 -572C/C allele; IL-10 NSCP: Non-susceptible to chronic periodontitis carrying the non-susceptible genotype IL-10 -592CC genotype.

Blood samples and genotyping

Blood drops collected from each patient were used to extract genomic DNA using a commercially available genomic DNA isolation kit following the manufacturer’s instructions (QIAamp, DNA mini blood kit, QIAGEN, Germany). Genotyping of IL-6 -572 G/C (rs1800796) and IL-10 -592 C/A (rs1800872) polymorphisms were determined by polymerase chain reaction and restriction fragment length polymorphism techniques in a final volume of 25 ul using a stan-

Klinički pregled i parodontološka terapija

Pojednosti o kliničkom pregledu i redoslijedu liječenja već su opisane (24). Ukratko, parodontni status procijenjen je uključujući PPD, CAL i BOP, a obavio ga je neovisna, slijet za genetsku analizu i kalibriran specijalist parodontologije E. D. (podudarnost unutar ispitivača = 0,88) Klinički pregled obavljen je ručnom parodontnom sondom (15 UNC sonda, Hu-Friedy, Chicago, IL, SAD) na šest mjesta po zubu, osim trećih krunjaka. Svi pacijenti uključeni u istraživanje liječeni su prema sveobuhvatnom parodontološkom planu liječenja, uključujući prikaz slučaja, upute za oralnu higijenu i nekri uršku terapiju pod lokalnom anestezijom. Korišteni su ručni instrumenti (Hu-Friedy, Chicago, SAD) i ultrazvučni stručnja (KaVo SONOSoft LUX, Kavo, Njemačka).

Liječeni pacijenti ponovno su procijenjeni šest tjedana nakon nekri urške parodontološke terapije, a klinički pregled obavio je isti klinički ispitivač kao i tijekom inicijalnog pregleda. Određena je potporna parodontološka terapija u intervalima od 3 do 4 mjeseca, uključujući procjenu PPD-a, CAL-a i BOP-a, ponovno upućivanje i ponovna motivacija za učinkovitu kontrolu plaka, profesionalno čišćenje zuba ručnim instrumentima i ultrazvučnim stručnjacima te subg in givno instrumentiranje u područjima s PPD-om ≥ 5 mm. Završni klinički pregled obavljen je tri godine poslije aktivnoga parodontološkog liječenja.

Skupine ispitanika

Odabrani pojedinci grupirani su na osnovi polimorfizama IL-6 -572 G/C i IL-10 -592 C/A: skupina IL-6 SCP: sudionicima podložima na kronični parodontitis dodijeljen je status na temelju prisutnosti genotipa IL-6 -572GG; skupina IL-10 SCP: sudionicima podložima na kronični parodontitis koji je potvrđen i prisutnošću alela IL-10 -592A; podskupina IL-6 NSCP: sudionicima otpornima na kronični parodontitis dodijeljen je status jer su nositelji neosjetljivog genotipa IL-6 -572C; podskupina s alelom IL-10 NSCP: sudionicim neosjetljivim na kronični parodontitis su i nositelji neosjetljivog genotipa IL-10 -592CC.

Uzorci krvi i genotipizacija

Prikupljene su kapi krvi od svakog pacijenta i korištene za vađenje genomske DNK s pomoću komercijalno dostupnog kompleta za gensku izolaciju u skladu s uputama proizvođača (QIAamp, DNA miniset za krv, QIAGEN, Njemačka). Genotipizacija polimorfizama IL-6-572 G/C (rs1800796) i IL-10-592 C/A (rs1800872) određena je tehnikom lančane reakcije polimeraze i polimorfizmom duljine ograničenja, u konačnom volumenu od 25 ul, koristeći se standardnim već
standard protocol which was described previously (24). The IL-6 and IL-10 polymorphisms were determined by using primers to generate a PCR product which was then digested and separated on polyacrylamide gels stained with silver nitrate (24).

Statistical analysis

The aim of this study was to assess the treatment outcome following non-surgical periodontal therapy between susceptible and non-susceptible individuals to periodontitis. PPD was considered the primary outcome and the sample size calculation was performed on the basis of a minimum difference of 1 mm in the mean full-mouth PPD values of each patient and a standard deviation of 0.5 mm. Aiming to achieve a 95% power of the study, it was determined that 6 individuals per group would be essential. The distribution of the clinical parameters was tested for normality using the Shapiro-Wilk test. The chi-square test was utilized to determine whether the SCP and NSCP groups were composed of similar proportions as regards to gender, smoking status and alcohol consumption while the Mann-Whitney U test was used for age and the number of teeth. To determine the differences between the timepoints (baseline and 3 years) for each group, the Wilcoxon test was used. The Mann-Whitney test was utilized to compare SCP and NSCP groups at baseline and 3 years. A multiple logistic regression analysis was used to identify possible associations between the genotypes, clinical and demographic parameters. To avoid biased results from multiple comparisons, the results were adjusted according to the Bonferroni correction for the 8 variables analyzed. P-value < 0.05 was considered statistically significant. The statistical analysis was completed using SPSS v.24.0, IBM, Armonk, NY, USA.

Results

The population investigated in this study comprised a total of 37 Caucasians with a mean age of 47.68 ± 8.64 and a diagnosis of chronic periodontitis. It was divided into groups of similar age according to their genotype. The demographic characteristics of the study population are presented in Table 1. The IL-6 SCP and NSCP groups demonstrated similar smoking (p = 0.64) and alcohol consumption (p = 0.50) habits with no significant differences in regards to the mean number of teeth present (p = 0.11). Smoking habits remained unchanged throughout the study duration. In the examined population, more male participants were susceptible to periodontal disease than females (p = 0.02). No differences were found between the IL-10 groups with respect to age (p = 0.30), gender (p = 0.86), alcohol consumption (p = 0.90) and number of teeth (p = 0.96), whereas non-smokers were more likely to be susceptible to periodontal disease (p = 0.03).

Clinical outcomes of periodontal treatment and IL-6 genotype

The clinical parameters of the IL-6 SCP and NSCP patients at baseline and 3 years following periodontal therapy are shown in Table 2. All clinical variables of the SCP and NSCP groups were similar at baseline irrespective of the genotype (p = 0.05) and all decreased significantly three years following a non-surgical periodontal treatment in both groups.

opisanim protokolum (24). Polimorfizmi IL-6 i IL-10 određeni su korištenjem primjera za generiranje PCR produkta koji se zatim digestirao i odvojio elektroforezom na poliakrilamidne gelove obojeni srebrnim nitratom (24).

Statistička analiza

Svrha ovog istraživanja bila je procijeniti ishod liječenja nakon nekirurške parodontološke terapije između osjetljivih i osoba otpornih na parodontitis. PPD je smatran priručnim ishodom, a razlikovanje veličine uzorka provedeno je na temelju minimalne razlike od 1 mm u srednjim vrijednostima PPD-a za cijelu usta svakog pacijenta i standardnog odstupanja od 0.5 mm. Kako bi se postiglo 95% snage testa, utvrđeno je da u svakoj skupini mora biti šest pojedinaca. Raspoljed kliničkih parametara testiran je na normalnost korištenjem Shapiro-Wilkova testa. Hi-kvadrat test utoprjeđen je da se utvrdi jesu li SCP i NSCP skupine bile slične u omjeru kada je riječ o spolu, pušačkom statusu i konzumaciji alkohola, a Mann-Whitneyjevim U-testom određivali su se dob i broj zuba. Da bi se ustanovile razlike između vremenskih točaka (ishodišnja vrijednost i poslije tri godine), za svaku skupinu korišten je Wilcoxonov test. Mann-Whitneyjev test promijenjen je za usporedbu SCP i NSCP skupina na početnom početnoj točki i nakon tri godine. Za analizu mogućih povezanosti genotipa te kliničkih i demografskih parametara korištena je višestruka logistička regresijska analiza. Da bi se izbjegli prirusti rezultati iz više usporedbi, za osam analiziranih varijabli rezultati su prilagođeni prema Bonferronijevoj korekciji. P-vrijednost < 0.05 smatrala se statistički značajnom. Statistička analiza objavljena je u sustavu SPSS v.24.0, IBM, Armonk, NY, SAD.

Rezultati

Populacija uključena u ovo istraživanje sastojala se od ukupno 37 bijelaca prosječne dobi od 47.68 ± 8.64 godina i s dijagnozom kroničnog parodontitisa. Podijeljeni su u skupine slične prema dob i ustanovljenom genotipu. Demografska obilježja ispitivane populacije prikazana su u tablici 1. Za skupine IL-6 SCP i NSCP zabilježene su slične navike kad je riječ o pušenju (p = 0.64) i konzumaciji alkohola (p = 0.50), bez značajnih razlika s obzirom na srednji broj prisutnih zuba (p = 0.11). Navike pušenja su tijekom provedbe studije ostale nepromijenjene. U ispitivanoj populaciji više je muškaraca bilo podložno parodontnoj bolesti u odnosu prema ženama (p = 0.02). Nisu pronađene razlike između IL-10 skupina s obzirom na dob (p = 0.30), spol (p = 0.86), konzumaciju alkohola (p = 0.90) i broj zuba (p = 0.96), dok su nepušački vjerojatno bili osjetljiviji na parodontnu bolest (p = 0.03).

Klinički ishodi parodontološkog liječenja i genotip IL-6

Klinički parametri IL-6 pacijenata s SCP-om i NSCP-om preoperativno i tri godine nakon parodontološke terapije na- laze se u tablici 2. Sve kliničke varijable SCP i NSCP skupina bile su slične kad je riječ o početnoj vrijednosti, bez obzira na genotip (p > 0.05), i sve su se znatno smanjile poslije trogo- dišnjeg nekiurškog parodontološkog liječenja u objema skupina (SCP i NSCP) (p < 0.05), osim za postotak mjesta...
### Table 1: Demographic characteristics of the study population

| Parameters • Parameteri | SCP (n=26) | NSCP (n=11) | p-value* | SCP (n=17) | NSCP (n=20) | p-value* | Total • Ukupno (n=37) |
|-------------------------|------------|-------------|----------|------------|-------------|----------|----------------------|
| Age • Dob (mean ± SD in years • arit. sredina ± SD u godinama) | 48.31 ± 9.88 | 46.18 ± 4.56 | 0.50 | 49.29 ± 9.18 | 46.30 ± 8.12 | 0.30 | 47.68 ± 8.64 |
| Gender • Spol | 16 (61.5) | 10 (38.5) | 0.02 | 8 (47.1) | 10 (50) | 0.86 | 18 (46.8) |
| Male • Muški (%) | 10 (38.5) | 9 (31.8) | 10 (50) | 9 (45) | 0.30 | 19 (51.4) |
| Female • Ženski (%) | 12 (46.2) | 6 (23.1) | 0.64 | 5 (29.4) | 7 (35) | 0.03 | 19 (51.4) |
| Smoking • Pušenje | 12 (46.2) | 6 (23.1) | 0.64 | 5 (29.4) | 7 (35) | 0.03 | 19 (51.4) |
| Yes • Da (%) | 10 (38.5) | 6 (23.1) | 0.50 | 8 (47.1) | 9 (45) | 0.90 | 17 (45.9) |
| No • Ne (%) | 15 (57.7) | 5 (23.1) | 0.50 | 12 (70.6) | 11 (55) | 0.86 | 18 (48.6) |
| Alcohol consumption • Konzumacija alkohola | 11 (42.3) | 6 (23.1) | 0.50 | 8 (47.1) | 9 (45) | 0.90 | 17 (45.9) |
| Yes • Da (%) | 15 (57.7) | 5 (23.1) | 0.50 | 12 (70.6) | 11 (55) | 0.86 | 18 (48.6) |
| Number of teeth • Broj zuba (mean ± SD • arit. sredina ± SD) | 26.23 ± 1.97 | 25.00 ± 2.28 | 0.11 | 25.88 ± 2.21 | 25.85 ± 2.08 | 0.96 | 25.87 ± 2.11 |

* Mann-Whitney tests were used to compare age and number of teeth between SCP and NSCP groups. Chi-square tests were utilized for comparisons between SCP and NSCP groups with respect to gender, smoking, alcohol consumption. • Mann-Whitneyev test korišten je za usporedbu dobi i broja zuba između grupa SCP i NSCP; hi-kvadrat test korišten je za usporedbu između SCP i NSCP grupa ovisno o spolu, navikama pušenja i konzumaciji alkohola.

### Table 2: Clinical parameters of the IL-6 SCP and NSCP patients at baseline and 3 years following periodontal therapy.

| Clinical parameters • Klinički parametri | SCP (n=26) | NSCP (n=11) | p-value** |
|------------------------------------------|------------|-------------|-----------|
| Full-mouth PPD (mm) • Sveobuhvatno sondiranje PPD-a (mm) | 3.57 (2.21-4.98) | 3.37 (2.68-4.19) | 0.32 |
| Baseline • Preoperativno | 3.39 (2.00-3.71) | 2.21 (2.00-3.21) | 0.29 |
| 3 years • 3 godine | <0.001 | 0.003 |
| Full-mouth BOP (%) • Sveobuhvatno BOP (%) | 100.00 (21.43-100.00) | 100.00 (10.87-100) | 1.00 |
| Baseline • Preoperativno | 8.63 (0-100.00) | 6.52 (0.67-62.50) | 0.56 |
| 3 years • 3 godine | <0.001 | 0.003 |
| p-value* • p-vrijednost* | | | |
| Full-mouth CAL (mm) • Sveobuhvatno CAL (mm) | 3.67 (2.21-5.18) | 3.55 (2.83-4.31) | 0.49 |
| Baseline • Preoperativno | 2.66 (2.00-5.64) | 2.37 (2.00-5.24) | 0.15 |
| 3 years • 3 godine | 0.003 | 0.021 |
| Percentage of sites with PPD 4-6 mm (%) • Postotak mjesta s PPD-om 4 - 6 mm (%) | 26.88 (1.92-49.31) | 30.36 (8.67-45.65) | 0.92 |
| Baseline • Preoperativno | 4.92 (0-34.67) | 2.17 (0-27.38) | 0.84 |
| 3 years • 3 godine | <0.001 | 0.003 |
| p-value* • p-vrijednost* | | | |
| Percentage of sites with PPD ≥ 7mm (%) • Postotak mjesta s PPD-om ≥ 7mm (%) | 4.63 (0-23.81) | 1.45 (0-9.62) | 0.19 |
| Baseline • Preoperativno | 0 (0-8.64) | 0 (0-2.00) | 0.52 |
| 3 years • 3 godine | <0.001 | 0.017 |
| p-value* • p-vrijednost* | | | |
| Percentage of sites with CAL 4-6 mm (%) • Postotak mjesta s CAL-om 4 - 6 mm (%) | 29.15 (1.92-52.50) | 35.71 (10.0-46.38) | 0.79 |
| Baseline • Preoperativno | 8.33 (8.07-04) | 2.50 (78.21) | 0.35 |
| 3 years • 3 godine | 0.046 | 0.033 |
| p-value* • p-vrijednost* | | | |
| Percentage of sites with CAL ≥ 7 mm (%) • Postotak mjesta s CAL-om ≥ 7 mm (%) | 4.63 (0-25.00) | 1.67 (0-10.67) | 0.37 |
| Baseline • Preoperativno | 0.30 (0-24.07) | 0 (0-15.38) | 0.22 |
| 3 years • 3 godine | 0.003 | 0.097 |
| p-value* • p-vrijednost* | | | |

*Wilcoxon test: comparison between baseline and 3 years. • Wilcoxonov test: usporedba između polazne točke i kontrole nakon tri godine. **Mann-Whitney test: comparison between SCP and NSCP groups. • Mann-Whitneyev test: usporedba između SCP i NSCP skupina.

Abbreviations • Kratice:
- PPD: Probing pocket depth • dubina sondiranja;
- CAL: Clinical attachment loss • klinički gubitak gingivnog pričvrstka;
- BOP: Bleeding on probing • krvarenje poslije sondiranja;
- SCP: Susceptible • podložni;
- NSCP: Non-susceptible • neosjetljivi;
IL-6, IL-10 and Periodontal Treatment Outcome
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Clinical outcomes of periodontal treatment and IL-10 genotype

The clinical parameters of the IL-10 SCP and NSCP patients at baseline and 3 years following periodontal therapy are shown in Table 3. No significant differences between the SCP and NSCP groups were detected at baseline (p>0.05), while a significant clinical improvement was observed at 3 years (p<0.05) apart from the percentage of sites with CAL ≥ 7 mm in the NSCP group. Individuals SCP to chronic periodontitis exhibited statistically significant reductions in PPD, CAL, BOP, percentage of sites with PPD=4-6 mm, percentage of sites with CAL=4-6 mm, and percentage of sites with CAL≥7 mm at 3 years following the treatment (p=0.03). In comparisons between groups, neither SCP nor NSCP patients showed any significant difference with respect to the examined parameters (p>0.05).

A subgroup analysis was also performed to compare the clinical parameters at baseline and 3 years following a non-

Table 3. Clinical parameters of the IL-10 SCP and NSCP patients at baseline and 3 years following periodontal therapy

| Clinical parameters • Klinički parametri IL-10 SCP i NSCP ispitanika preoperativno i tri godine nakon parodontološke terapije | SCP (n=26) | NSCP (n=11) | p-value** |
|---------------------------------------------------------------|----------|-------------|-----------|
| Full-mouth PPD (mm) • Sveobuhvatno sondiranje PPD-a (mm) |          |             |           |
| Baseline • Preoperativno | 3.18 (2.66-4.98) | 3.55 (2.21-4.44) | 0.35      |
| 3 years • 3 godine | 2.31 (2.00-3.71) | 2.50 (2.00-3.23) | <0.001    |
| p-value* • p-vrijednost* | >0.001   | >0.001      |           |
| Full-mouth BOP (%) • Sveobuhvatno BOP (%) |          |             |           |
| Baseline • Preoperativno | 100.00 (10.87-100.00) | 100.00 (35.26-100.00) | 0.48      |
| 3 years • 3 godine | 7.50 (0.100-0.00) | 11.26 (0-62.50) | <0.001    |
| p-value* • p-vrijednost* | 0.002    | <0.001      |           |
| Full-mouth CAL (mm) • Sveobuhvatno CAL (mm) |          |             |           |
| Baseline • Preoperativno | 3.55 (2.84-5.18) | 3.58 (2.21-5.02) | 0.63      |
| 3 years • 3 godine | 2.38 (2.00-4.54) | 2.66 (2.00-5.64) | 0.023     |
| p-value* • p-vrijednost* | 0.002    | <0.001      |           |
| Percentage of sites with PPD ≥ 4-6 mm (%) • Postotak mjesta s PPD-om 4 - 6 mm (%) |          |             |           |
| Baseline • Preoperativno | 23.81 (8.67-47.44) | 29.77 (1.92-49.31) | 0.25      |
| 3 years • 3 godine | 4.76 (1.28-34.67) | 3.21 (0-27.38) | <0.001    |
| p-value* • p-vrijednost* | <0.001   | <0.001      |           |
| Percentage of sites with PPD ≥ 7 mm (%) • Postotak mjesta s PPD-om ≥ 7 mm (%) |          |             |           |
| Baseline • Preoperativno | 2.56 (0-23.81) | 3.13 (0-18.75) | 0.66      |
| 3 years • 3 godine | 0 (0-3.33) | 0 (0-8.64) | 0.70      |
| p-value* • p-vrijednost* | 0.001    | 0.003       |           |
| Percentage of sites with CAL ≥ 4-6 mm (%) • Postotak mjesta s CAL-om 4 - 6 mm (%) |          |             |           |
| Baseline • Preoperativno | 29.17 (9.88-49.36) | 33.65 (1.92-52.50) | 0.77      |
| 3 years • 3 godine | 23.81 (8.67-47.44) | 5.06 (0-78.21) | 0.057     |
| p-value* • p-vrijednost* | 0.028    | <0.001      |           |
| Percentage of sites with CAL ≥ 7 mm (%) • Postotak mjesta s CAL-om ≥ 7 mm (%) |          |             |           |
| Baseline • Preoperativno | 4.76 (1.28-34.67) | 4.46 (0-22.22) | 0.50      |
| 3 years • 3 godine | 4.49 (0-25.00) | 4.46 (0-22.22) | 0.001     |
| p-value* • p-vrijednost* | 0.001    | 0.167       |           |

*Wilcoxon test: comparison between baseline and 3 years. * Wilcoxonov test: usporedba između polazne točke i kontrole nakon tri godine
**Mann-Whitney test: comparison between SCP and NSCP groups. • Mann-Whitneyev test: usporedba između SCP i NSCP skupina

Klinički ishodi parodontološkog liječenja i genotipa IL-10

Klinički parametri IL-10 pacijenata s SCP-om i NSCP-om na početku i i tri godine poslije parodontološke terapije prikazani su u tablici 3. Nisu ustanovljene značajne razlike između SCP i NSCP skupina (p > 0.05), a znatno kliničko boljšanje uočeno je nakon 3 godine (p < 0.05), osim postotka mjesta s CAL-om od 4 do 6 mm (p = 0.057) i postotka mjesta s CAL-om ≥ 7 mm (p = 0.167) u NSCP skupini. Pojedinci iz SCP skupine s kroničnim parodontitisom postigli su nakon trogodišnjeg tretmana (p < 0.03) statistički značajna smanjenja PPD-a, CAL-a, BOP-a, postotak mjesta s PPD-om = 4 do 6 mm, postotak mjesta s PPD-om ≥ 7 mm, postotak mjesta s CAL-om = 4 - 6 mm i postotak mjesta s CAL-om ≥ 7 mm. U usporedbi skupina ni pacijenti s SCP-om, ni oni s NSCP-om nisu pokazali značajnu razliku u odnosu prema ispitivanim parametrima (p > 0.05).

Obavljena je također analiza podskupine radi usporedbi kliničkih parametara preoperativno i tri godine poslije ne-

Abbreviations • Kratice:

PPD: Probing pocket depth • dubina sondiranja; CAL: Clinical attachment loss • klinički gubitak gingivnog pričvrstka; BOP: Bleeding on probing • krvarenje poslije sondiranja; SCP: Susceptible • podložni; NSCP: Non-susceptible • neosjedljivi
surgical periodontal therapy between individuals susceptible (n=13) to chronic periodontitis carrying both the susceptible genotypes for IL-6 (IL-6 GG) and IL-10 (IL-10 CA or IL-10 AA) with those non-susceptible (n=24) carrying one or all three non-susceptible genotypes IL-6 GC, IL-6 CC, IL-10 CC. Both subgroups showed similar age (p=0.50) and gender (p=0.25) distribution. Following the treatment, significant reductions were observed for the susceptible group in regards to BOP (p=0.001), PPD (p=0.001), CAL (p=0.013), PPD=4-6 mm (p=0.001), PPD≥7 mm (p=0.001) and CAL≥7 mm (p=0.01). Sites with CAL=4-6 mm demonstrated no significant differences between baseline and 3 years in the combined IL-6 and IL-10 susceptible subgroup (p=0.13). In the IL-6 and IL-10 non-susceptible combined subgroup, all examined clinical parameters showed significant reduc-

**Table 4**

Multiple logistic regression analysis for the association between the IL-6 -572 G/C and IL-10 -592 C/A genotypes and the demographic and clinical variables at baseline and 3 years.

| Parameters • Parametri | OR  | 95%CI | p-value* • p-vrijednost* | Adjusted p-value (Bonferroni correction) • Prilagođena p-vrijednost (Bonferronijeva korekcija) |
|------------------------|-----|-------|--------------------------|---------------------------------------------------------------------------------|
| **IL-6 Baseline • Preoperativno** |     |       |                          |                                                                                  |
| Age • Dob              | 1.12| 0.97-1.29 | 0.12                  | 0.99                                                                                  |
| Gender • Spol          | 52.09 | 2.41-1125.37 | 0.01      | 0.10                                                                                  |
| Smoking • Pušenje      | 1.09 | 0.09-13.01 | 0.95              | 7.56                                                                                  |
| Alcohol consumption • Konzumacija alkohola | 0.42 | 0.04-4.78 | 0.49 | 3.86                                                                                  |
| Number of teeth • Broj zuba | 1.79 | 1.00-3.22 | **0.05** | 0.41                                                                                  |
| Full-mouth BOP • Punjubi niz BOP | 0.97 | 0.93-1.02 | 0.21 | 1.66                                                                                  |
| Full-mouth PPD • Punjubi niz PPD | 0.10 | 0.01-104.32 | 0.52 | 4.17                                                                                  |
| Full-mouth CAL • Punjubi niz CAL | 35.69 | 0.07-18052.25 | 0.26 | 2.08                                                                                  |
| **3 years • 3 godine** |     |       |                          |                                                                                  |
| Age • Dob              | 1.09 | 0.96-1.25 | 0.19                | 1.56                                                                                  |
| Gender • Spol          | 26.86 | 2.00-360.16 | **0.01** | 0.10                                                                                  |
| Smoking • Pušenje      | 1.39 | 0.18-10.96 | 0.76               | 6.04                                                                                  |
| Alcohol consumption • Konzumacija alkohola | 0.35 | 0.05-2.38 | 0.29 | 2.28                                                                                  |
| Number of teeth • Broj zuba | 1.32 | 0.82-2.11 | 0.26              | 2.06                                                                                  |
| Full-mouth BOP • Punjubi niz BOP | 0.99 | 0.95-1.03 | 0.63 | 5.04                                                                                  |
| Full-mouth PPD • Punjubi niz PPD | 0.28 | 0.01-6.11 | 0.42 | 3.34                                                                                  |
| Full-mouth CAL • Punjubi niz CAL | 1.94 | 0.59-6.38 | 0.28 | 2.22                                                                                  |
| **IL-10 Baseline • Preoperativno** |     |       |                          |                                                                                  |
| Age • Dob              | 1.05 | 0.95-1.15 | 0.33              | 2.63                                                                                  |
| Gender • Spol          | 1.07 | 0.20-5.78 | 0.94              | 7.49                                                                                  |
| Smoking • Pušenje      | 0.18 | 0.03-0.93 | **0.04** | 0.33                                                                                  |
| Alcohol consumption • Konzumacija alkohola | 2.07 | 0.36-11.89 | 0.42 | 3.33                                                                                  |
| Number of teeth • Broj zuba | 1.08 | 0.73-1.59 | 0.70              | 5.58                                                                                  |
| Full-mouth BOP • Punjubi niz BOP | 0.98 | 0.95-1.01 | 0.16 | 1.30                                                                                  |
| Full-mouth PPD • Punjubi niz PPD | 0.46 | 0.01-109.19 | 0.78 | 6.25                                                                                  |
| Full-mouth CAL • Punjubi niz CAL | 3.37 | 0.02-541.77 | 0.64 | 5.11                                                                                  |
| **3 years • 3 godine** |     |       |                          |                                                                                  |
| Age • Dob              | 1.05 | 0.95-1.15 | 0.34              | 2.75                                                                                  |
| Gender • Spol          | 0.61 | 0.11-3.50 | 0.57              | 4.59                                                                                  |
| Smoking • Pušenje      | 0.18 | 0.30-0.05 | 0.06              | 0.45                                                                                  |
| Alcohol consumption • Konzumacija alkohola | 2.1 | 0.42-10.64 | 0.37 | 2.95                                                                                  |
| Number of teeth • Broj zuba | 0.80 | 0.51-1.26 | 0.34              | 2.68                                                                                  |
| Full-mouth BOP • Punjubi niz BOP | 1.01 | 0.98-1.05 | 0.48 | 3.82                                                                                  |
| Full-mouth PPD • Punjubi niz PPD | 1.58 | 0.13-19.75 | 0.72 | 5.78                                                                                  |
| Full-mouth CAL • Punjubi niz CAL | 0.63 | 0.25-1.60 | 0.33 | 2.62                                                                                  |

*p-values in bold denote statistical significance (p<0.05). • p-vrijednosti u krvi podebljane označavaju statističku značajnost (p < 0.05)

Abbreviations • Kratice:
- PPD: Probing pocket depth • sondiranje parodontnih džepova;
- CAL: Clinical attachment loss • klinički gubitak gingivnog pričvrstva;
- BOP: Bleeding on probing • krvenanje poslije sondiranja
tions (p<0.04). SCP and NSCP subgroups showed similar clinical variables at baseline and 3 years (p>0.05).

Multiple logistic regression analysis

Multiple logistic regression analysis for the association between the IL-6 -572 G/C and IL-10 -592 C/A genotypes and the demographic and clinical variables at baseline and 3 years is shown in Table 4. At baseline, IL-6 genotype was significantly associated with gender (p=0.01) and the number of missing teeth (p=0.05), while IL-10 genotype and smoking status showed a significant association (p=0.04). In addition, there was a significant association between susceptibility to chronic periodontitis (as determined by the presence of the IL-6 -572GG genotype) with gender at 3 years (p=0.01). However, after the Bonferroni adjustment for multiple comparisons, these findings lost statistical significance (p>0.05).

After 3 years of periodontal treatment, there was no association between any of the variables tested (p>0.05).

Discussion

Current evidence suggests that the treatment outcome following non-surgical periodontal treatment may vary between patients, teeth as well as treated sites within individuals (18,19). Each individual's genetic background may explain the variation in treatment response. Since IL-6 -572 and IL-10 -592 gene polymorphisms have been significantly associated with chronic periodontitis (10-13) and since gene variant carriage could possibly affect the response to periodontal therapy (23), we investigated, in this study, the influence of genetic susceptibility to chronic periodontitis on periodontal treatment outcome over a three-year period of time.

In contrast with our hypothesis that patients susceptible to chronic periodontitis as determined by the presence of the IL-6 -572GG genotype or the IL-10 -592A allele would have significantly worse response to non-surgical periodontal treatment than non-susceptible individuals, a similar treatment outcome was observed for both included groups. More specifically, susceptible and non-susceptible to chronic periodontitis patients showed a statistically significant improvement in the examined clinical parameters at 45 days (as shown in our previous publication, 24) which has been maintained up to 3 years following the initial treatment (as shown in the present investigation). However, this significant clinical periodontal improvement was irrespective of a patient's genetic background.

To the best of our knowledge, this is the first study that evaluated the association between gene polymorphisms and non-surgical periodontal treatment over a long term period. Previous investigations included individuals that were followed-up for a period of time between 45 days to 6 months following a non-surgical periodontal therapy (23). Our findings may differ with previous studies due to the longer period of observation. Long-term monitoring and supportive periodontal treatment are of paramount importance to achieve long-term success of periodontal treatment and to minimize the risk of tooth loss (26). In addition, long-term studies can confirm or reject an association that has been shown in related studies.

Rametri pokazali su značajno smanjenje (p < 0.04). Za SCP i NSCP podgrupe zabilježene su slike kliničke varijable na početku i poslije tri godine (p > 0.05).

Multipla logistička regresijska analiza

Analiza multiplje logističke regresije za povezanost između genotipova IL-6 -572 G/C i IL-10 -592 C/A te demografskih i kliničkih varijabli inicijalno i nakon tri godine prikazana je u tablici 4. Na početku je genotip IL-6 bio značajno povezan sa spolom (p = 0,01) i brojem zuba koji nedostaju (p = 0,05), a genotip IL-10 i pušački status pokazali su značajnu povezanost (p = 0,04). Postojala je i značajna povezanost između podložnosti za pojavu kroničnog parodontitisa (što je određeno prisutnošću genotipa IL-6 -572GG sa spolom i dobi nakon tri godine (p = 0,01). No poslije Bonferroni jeve prilagodbe za višestruke usporede ti su nalazi izgubili statističku značajnost (p > 0,05).

Rasprava

Sadašnji dokazi upućuju na to da ishod liječenja nakon nekirurškog parodontološkog liječenja može varirati među pacijentima između zuba i liječenih mjesta (18, 19). Svaka genetska pozadina može objasniti varijacije u odgovoru na liječenje. Budući da su polimorfizmi gena IL-6 -572 i IL-10 -592 bili značajno povezani s kroničnim parodontitom (10 – 13) i zato što bi prijenos genske varijante mogao utjecati na odgovor na parodontološku terapiju (23), u ovom istraživanju analizirali smo utjecaj genetske osjetljivosti na kronični parodontitis i na ishod parodontološkog liječenja tijekom trogodišnjeg razdoblja.

Za razliku od naše hipoteze da bi pacijenti osjetljivi na kronični parodontitis utvrdili prisutnošću genotipa IL-6-572GG ili alela IL-10-592A imali značajno lošiji odgovor na nekirurško parodontološko liječenje u odnosu prema osobama koje nisu osjetljive, rezultati upućuju na sličan ishod liječenja u obje uključene skupine. Konkretnije, podložni i otporni na kronični parodontitis pokazali su statistički značajno poboljšanje ispitivanih kliničkih parametara u roku od 45 dana (kao što je predstavljeno u našoj publikaciji, 24) koje se zadržalo do tri godine nakon početnog liječenja (kao što je opisano u ovom tekstu). No to znatno kliničko poboljšanje parodonta nije bilo ovisno o pacijentovu genetskom po-drijetlu.

Prema našim spoznajama, ovo je prvo istraživanje u kojem je procijenjena dugoročna povezanost polimorfizama gena i nekirurškog parodontološkog liječenja. U dosadašnjim ispitivanjima bile su uključene osobe koje se pratilo od 45 dana do 6 mjeseci nakon nekirurške parodontološke terapije (23). Naši se nalazi mogu razlikovati od ostalih studija zbog du-ljeg razdoblja promatranja. Dugotrajno praćenje i podupiruće parodontološko liječenje iznimno su važni za postizanje dugoročnog uspjeha parodontološkog liječenja i minimiziranje rizika od gubitka zuba (26). U to, dugoročnim se istraživanjima može potvrditi ili isključiti povezanost koja se pokazala u razmjeru kratkoročnim istraživanjima. No tijekom longitudinalnih ispitivanja nije uvijek moguće održati po-
IL-6, IL-10 and periodontal therapy

IL-6 is a pleotropic cytokine that promotes the evolution of chronic inflammation and bone resorption through cytokine-IL-10 and the result of periodontal therapy. Chatzopoulos and co-authors discussed the role of cytokines such as IL-6 and IL-10 in periodontal disease. They highlighted that the treatment outcome following non-surgical periodontal therapy may be influenced by genetic and environmental factors. Specifically, smoking habits (light, moderate, heavy smoking) and genetic factors such as the IL-6 -572GG genotype and the IL-10 -592A allele were associated with the treatment outcome. Additionally, systemic medical conditions such as diabetes mellitus might affect periodontal healing and tissue homeostasis following periodontal therapy. In order to minimize the potential confounding factors, systematically healthy patients were only recruited. Moreover, the lack of association between smoking status and susceptibility to chronic periodontitis after adjusting for multiple comparisons may be due to different smoking habits (light, moderate, heavy smoking) of the included population.

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complex interactions (31). Since IL-6 polymorphisms are associated with an increased inflammatory response primarily in the presence of periodontal pathogens, IL-6 gene may play an important role in the pathogenesis of periodontitis (6, 7). IL-10 is considered an anti-inflammatory cytokine that suppresses immune and inflammatory responses which can protect against bone resorption (32). Polymorphisms in the IL-10 promoter -592 region are associated with a decrease in IL-10 production, which may result in the development of periodontal diseases (9). Although both polymorphisms are associated with an increased inflammatory response and therefore play an important role in disease onset and progression, their effect may not influence the healing process after periodontal treatment. IL-6 and IL-10, as shown in this study, may have no effect on the resolution of periodontal inflammation.

Future studies encompassing larger samples with different characteristics including smoking habits, various bacterial strains and systemic conditions from different populations and ethnicities are required to further examine the possible effect of gene polymorphisms on periodontal treatment outcome over a long period of time. In addition, further studies should include a greater number of patients with a generalized form of chronic periodontitis (>30% of sites) to determine whether the patients with a greater extent of periodontitis demonstrate significant differences with respect to treatment outcome. Due to the inclusion criteria of this study (interproximal CAL ≥ 3 mm, PPD ≥ 5 mm and BOP in two or more non-adjacent sites), the individuals with localized and generalized periodontitis were included in the analysis.

Conflict of interest

The authors declare that there is no potential conflict of interest regarding this article.

Contribution to the paper

G.S.C. concept and design, analysis and interpretation of data, drafting the article, revising it critically, final approval of the version to be published, agreement for publication; A.E.D. concept and design, acquisition of data, analysis and interpretation of data, revising it critically, final approval of the version to be published, agreement for publication; S.F. analysis and interpretation of data, revising it critically, final approval of the version to be published, agreement for publication; M.A. analysis and interpretation of data, revising it critically, final approval of the version to be published, agreement for publication; A.K. concept and design, acquisition of data, analysis and interpretation of data, revising it critically, final approval of the version to be published, agreement for publication.

Sukob interesa

Autori izjavljuju da nisu u sukobu interesa.

Doprinosi članku

G. S. C. – koncept i nacrta, analiza i interpretacija podataka, nacrta članka, kritičko pregledavanje teksata, odobravanje krajnje verzije za objavljivanje, suglasnost za objavljivanje; A. E. D. – koncept i nacrta, prikupljanje podataka, analiza i interpretacija podataka, kritičko pregledavanje članka, odobravanje krajnje verzije za objavljivanje, suglasnost za objavljivanje; S. F. – analiza i interpretacija podataka, kritičko pregledavanje članka, odobravanje krajnje verzije za objavljivanje, suglasnost za objavljivanje; M. A. – analiza i interpretacija podataka, kritičko pregledavanje članka, odobravanje krajnje verzije za objavljivanje, suglasnost za objavljivanje; A. K. – koncept i nacrta, prikupljanje podataka, analiza i interpretacija podataka, kritičko pregledavanje članka, odobravanje krajnje verzije za objavljivanje, suglasnost za objavljivanje.
Zaključak
Utvrđeni ugovorni, ovi genetski manifestaciji parodontološke terapije, nisu uvek svojstveni za sve posljednje tretmanu.
Svi su primili NSPT-a od jednog specijalista parodontologije koji nije
Zaključak
Ututar ogrenišćeg vodećiho kontaktu studije u kojoj su sudjelovali bijnici s
sličnim kliničkim parametrom se to prvi godine.

Ključne riječi
parodontološki postoperacijski dijagnozirani kroničnim parodontitom, pojedincima podložnim parodontitusu, kako je određeno prisutnom genotipu IL-6-572GG ili allele alela IL-10-592A (IL-10 SNP).

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