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Original Article

# Factors affecting the healing of decubital lesions in patients wearing newly made dentures

Milica Jovanović <sup>a\*</sup>, Slobodan Janković <sup>b</sup>, Nemanja Okičić <sup>c</sup>,  
Andjela Milojević Šamanović <sup>a</sup>, Marko Milosavljević <sup>a</sup>

<sup>a</sup> Department of Dentistry, Faculty of Medical Sciences, University of Kragujevac, Kragujevac, Serbia

<sup>b</sup> Department of Pharmacy, Faculty of Medical Sciences, University of Kragujevac, Kragujevac, Serbia

<sup>c</sup> Department of Dental Prosthetics, Military Medical Academy, Belgrade, Serbia

Received 19 March 2023; Final revision received 27 March 2023

Available online 9 April 2023

## KEYWORDS

Dentures;  
Healing;  
Hyaluronic acid;  
Traumatic ulcer

**Abstract** *Background/purpose:* Decubital lesions or traumatic ulcers caused by dentures usually appear one or two day(s) after new dentures placement due to mismatch of the microrelief of the tissue and the microrelief of the gingival surface of the prosthesis. The study aimed to analyze factors that could influence the healing of ulcers during a one-week period after the placement of new partial and complete dentures.

*Materials and methods:* The prospective cohort study included 60 patients with new denture-induced traumatic ulcers. Traumatic ulcers were treated with denture adjustment, or combination of adjustment with 0.2% or 0.3% hyaluronic acid gels respectively for seven days. Healing of ulcers were observed through measurement of perimeter, area, maximum and minimum diameters on digital photographs. Multivariate logistic regression was used to predict other factors that could affect healing process.

*Results:* Perimeter, area, maximum and minimum diameters of denture-related ulcers were significant decreased after application of gels on the fifth and seventh day. The fifth day ulcers were not healed if dentures were only adjusted, while healed lesion was 40% for the other two groups. On the seventh day, the percent of healed lesion in the group with dentures adjustment was 20%, while it was increased to 75% healed lesions for combination of denture adjustment and hyaluronic acid gels. Anticoagulant/anti-aggregation drugs also had positive impact on ulcer healing; antihypertensives that included diuretics slowed ulcer healing, other monitored factors in the study did not show a significant impact.

*Conclusion:* Hyaluronic acid in combination with the dentures adjustment for seven days leads to higher healing rate, and reduction in size of ulcers that did not heal until this time point.

\* Corresponding author. Department of Dentistry, Faculty of Medical Sciences, University of Kragujevac, Svetozara Markovića Street, No. 69, Kragujevac, 34000, Serbia.

E-mail address: [micamonro@gmail.com](mailto:micamonro@gmail.com) (M. Jovanović).

## Introduction

Wearing removable dentures is associated with the presence of lesions on the oral mucosa, which can make it difficult for the patient to adapt to the dentures and reduce their quality of life.<sup>1,2</sup>

Oral lesions associated with wearing dentures make up 8.4% of all lesions occurring in the oral cavity.<sup>3</sup> Denture-related oral lesions can be caused by an acute or chronic reaction to the materials used to make the dentures, microbiological plaque on the dentures, or mechanical irritations from the prostheses. Denture-associated stomatitis, angular cheilitis, inflammatory fibrous hyperplasia, and traumatic ulcers are the most common oral lesions associated with dentures.<sup>4</sup> As the wearers of dental prostheses are mostly elderly people, the fact is that, with increasing age, the oral mucosa becomes more sensitive and less tolerant to damage and irritation than the skin. Systemic diseases, long-term use of concomitant medications, poor oral hygiene, and changes in saliva contribute to all of this.<sup>5</sup>

Traumatic ulcers on the oral mucosa most often appear one or two days after the placement of new dentures, but they can also occur later in the case of older or poorly fitting dentures.<sup>6</sup> Reasons that condition the irritation of the supporting tissue and the appearance of ulcers in the places with which the prosthesis is in direct contact are mismatch of the microrelief of the tissue and the microrelief of the gingival surface of the prosthesis.<sup>7</sup> Ulcers usually affect the epithelium and underlying connective tissue; they are covered by a fibrin slough and surrounded by erythema. The size and dimension of denture-related ulcers may vary from 1 to 8 mm in diameter, be oval or irregular in shape, or have hyperemic spots. The color of the ulceration can indicate the severity of the change; the moderate form is in the form of deep red, while the more severe forms are in the form of white ulceration surrounded by redness.<sup>8</sup>

The symptomatic appearance of a traumatic ulcer is most often accompanied by a feeling of pain at the site of the ulcer that can radiate to the surrounding tissue, as well as patient discomfort, which is why patients avoid wearing a prosthesis, which prolongs the adaptation period. The duration of traumatic ulcers in most cases is about 10–15 days.<sup>9,10</sup>

If the ulcerations are not treated and if they heal with difficulty, they can lead to hyperplasia of fibrous connective tissue and the development of inflammatory fibrous hyperplasia.<sup>11</sup> Any chronic mechanical irritation that is not treated is one of the risk factors for the development of oral malignancies.<sup>12</sup>

Therapy of traumatic ulcers includes adjustment of dentures, discontinuing the wearing of the dentures, as well as the application of systemic drugs and topical preparations that can accelerate healing, reduce

discomfort, and prevent the recurrence of oral ulcerations.<sup>13</sup> The use of ozone and low-power laser in the treatment of denture-related traumatic ulcers has been shown in studies to improve ulcer healing and reduce ulcer duration.<sup>6,10</sup> On the other hand, application of trister glycerol oxide gel in the treatment of denture-related traumatic ulcers is not effective.<sup>7</sup>

In the treatment of recurrent aphthous stomatitis, which is characterized by ulceration of the oral mucosa, studies have shown the effectiveness of topical application of hyaluronic acid.<sup>14,15</sup> Hyaluronic acid supports the healing process through the promotion of cell proliferation, migration, and angiogenesis, thus facilitating epithelization by the proliferation of basal keratinocytes and reducing the disposition of collagen.<sup>16</sup>

The purpose of this study was to analyze factors that could influence the healing of denture-related traumatic ulcers during a one-week period after the placement of new partial and complete dentures.

## Materials and methods

### Study design

A cohort-prospective design was used for this study. The study population consisted of 60 patients with newly made partial or complete dentures at the Department of Prosthodontics, from April 2021 to May 2022. The study was conducted in accordance with the Declaration of Helsinki (1975 as revised in 2013) regarding biomedical research in human subjects, and was approved by the Ethics Committee of Faculty of Medical Sciences, University of Kragujevac (approval No. 01-2780). Each participant signed an informed consent form for this study. The present study is reported according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement for cohort studies.

### Sample selection

After receiving their new dentures, the patients were coming the next day (after 24 h) to be examined. The patients who developed ulcers due to the misfit of their dentures were enrolled in the study, provided that the inclusion and exclusion criteria were met. The criteria for the inclusion of patients were: maxillary, mandibular, or both partial and complete dentures in which the principle of maximal extension of the denture base was observed during making dentures, the existence of at least one denture-related traumatic ulcer, and acceptance to come for a follow-up examination. Patients were excluded from the study if they didn't have denture ulcers at the baseline visit, if they had some form of parafunctional activity

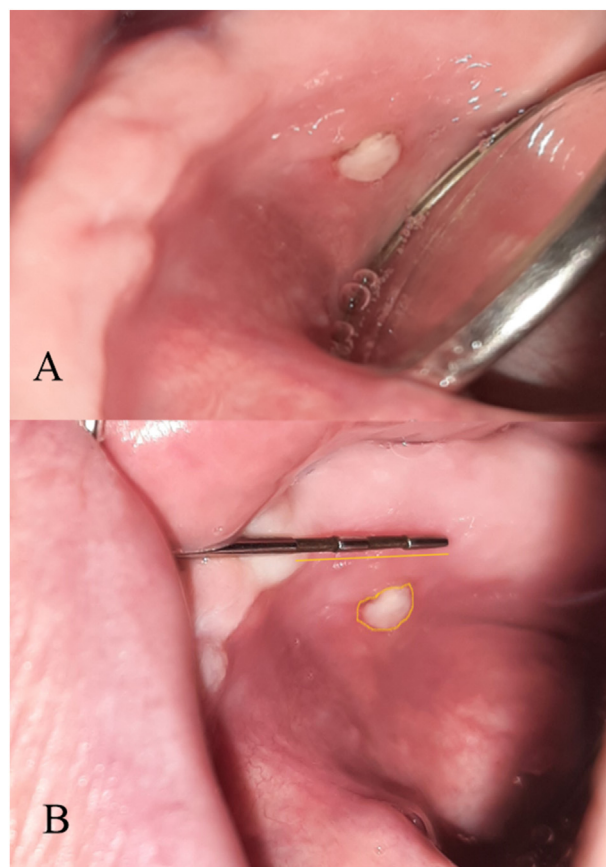
(grinding and clenching their teeth, biting a foreign body), or if they had some of the general diseases that make it difficult to heal wounds and that can increase the risk of damage in the oral cavity due to increased sensitivity of the oral mucosa (diabetes mellitus, neurologic or psychiatric disorders, autoimmune diseases, xerostomia or hypersalivation, abnormalities of bone or soft tissue). The sample used for the study was of convenient type, although consecutive, i.e., all patients who satisfied inclusion and without exclusion criteria within the study period were included. The screening failure rate was only 6.25%.

### Management of denture-related ulcers

The day of enrollment was considered the baseline visit, when all ulcers caused by dentures were photographed and their perimeters, maximum and minimum diameters, and surface areas were measured and noted. On the third, fifth, and seventh days, the patients were examined again. In all patients, at each encounter, additional adjusting of the dentures (for occlusion and tissue adaptation) was made using a wolfram carbide bur, and the patients were released for home treatment. One group of 20 patients did not have specific treatment at home, while the second and third groups ( $n = 20$  each) were treating their ulcers by themselves with local administration of gel containing hyaluronic acid at 0.2% and 0.3%, respectively, and applying around 1 cm of the gel to each denture ulcer three times daily, after meals, for seven days. The gel with 0.2% hyaluronic acid (treatment I) was produced by Ricerfarma s.r.l., Milano, Italy, under the trade name GENGIGEL®, and the gel with 0.3% hyaluronic acid (treatment II) also contained taurine, a mixture of ginger and bisabolol, and mucosave (a mixture of olive leaf extract and prickly pear cactus) was produced by SUNSTAR Europe SA, Etoy, Switzerland, under the trade name GUM® AphtaClear Gel.

All procedures (steps in making dentures – using standard prosthetic protocols, including maximal extension of denture base, taking functional impression in individual trays and use of anatomically shaped artificial teeth, adjustment of dentures at encounter, suggested treatment for ulcers) were performed by the one experienced specialist in prosthodontics, who were not involved in research process.

Measurement of denture ulcer details was performed on digital photographs using the program ImageJ 1.53 (Image Processing and Analysis in Java, National Institutes of Health, Bethesda, MD, USA). The ulcers were photographed on each examined day (baseline, days 3, 5, and 7) using a smartphone camera of the Samsung S9 (Samsung Electronics, Seoul, South Korea) from the same distance. Using a visual estimate, an effort was made to hold the phone camera at the zenith above the denture ulcer and the lens parallel to the plane of the surface. The graduated periodontal probe was placed next to the ulcer in parallel with the healthy mucosa and included in the photographic frame to allow calculation of ulcer dimensions once uploaded to the computer. For each photographic image, measurements were calibrated using the periodontal probe, and the denture ulcer outline was defined from the photographic image using a digital pad (Fig. 1A and B). Following tracing, the



**Figure 1** Denture-related traumatic ulcer on the lingual surface of lower alveolar ridge. (A) Appearance of traumatic ulcer one day after insertion of new complete lower denture; (B) measurements of ulcer characteristics were calibrated using the periodontal probe, definition of traumatic ulcer outline in Image J software.

ImageJ software calculated the next dimensions of the denture ulcer: perimeter, maximum and minimum size, and surface area. If the patient had more than one denture-induced ulcer, the measured values of each variable were added, and the average was taken for further statistical processing.

### Study outcomes

The main study outcomes were the healing rate of denture-related traumatic ulcers and the total size of ulcers measured by their circumference, maximum and minimum diameters, and surface area. Possible confounders were extracted from the patient's anamnesis: demographic characteristics (age, sex), habits (smoking, coffee, tea, and alcohol consumption), Charlson's comorbidity index, and prescribed medication in last one year.

### Statistical analysis

All data were collected by one researcher who were not involved in manufacture, adjustment of dentures and suggestion of treatment. Collected data were first numerically

coded, tabulated, and checked for errors. The data were then described by measures of central tendency and variability (if continuous) or by frequencies, relative numbers, and percentages (if categorical). Mean and standard deviation were used as descriptors of normally distributed continuous data, while median and interquartile range described the data distributed in other ways. The effects of putative predictors and confounders on the study outcomes were analyzed by multivariate binary logistic regression. Before applying these multivariate techniques, their assumptions were checked to see if they were satisfied (binary outcome, independence of observations, no multicollinearity, no extreme outliers, and a sufficiently large sample for multivariate binary logistic regression). The quality of the regression models was checked by the Hosmer and Lemeshow test, the Cox & Snell R square, and the Nagelkerke R square. The results were considered statistically significant if the probability of the null hypothesis was 0.05 or below. All calculations were made by the Statistical Package for the Social Sciences (SPSS), version 25.0 (IBM SPSS Statistics for Windows, Armonk, NY, USA).

## Results

A total of 60 patients with oral ulcers caused by wearing partial or complete dentures participated in the study, of whom 26 (43.3%) were male and 34 (56.7%) were female. According to the treatment undertaken, the patients were divided into three groups of 20 each, one of which did not

receive any specific therapy (only denture adjustment were done), one in which the ulcers were treated with local application of 0.2% hyaluronic acid gel (treatment I), and one in which they were treated with local application of 0.3% hyaluronic acid gel (treatment II). In all of these patients, mechanical adjustment of the dentures and occlusal adaptation were carried out at each encounter day. Detailed characteristics of the groups at the beginning of the study are shown in Table 1.

Average sums of anatomical measures of all denture-related traumatic ulcers per patient (perimeter, maximum ulcer size (diameter), minimum ulcer size (diameter), and ulcer's area) at baseline and days 3, 5, and 7 of the treatment are shown in Table 2. Significant differences among the treatments are visible from day 5 and onwards. Post hoc analysis showed that there was a statistically significant difference between the groups with treatment and the group without specific therapy, while there was no difference between the treatments themselves. Denture-related ulcer and healing process on days 3, 5 and 7 are shown on Fig. 2A–D.

The association of the study variables with the healing of the ulcers (a binary outcome: yes or no) was tested by univariate and multivariate binary logistic regressions. The multivariate models (one for day 5 and another for day 7 of the treatment) were built by the biological reasoning method starting with the most plausible predictors: treatment, anticoagulant or antiplatelet drugs, and therapy with diuretics. The assumptions of a binary outcome (ulcer healed or not), independence of observations, no

**Table 1** Characteristics of patients (average  $\pm$  standard deviation, range or frequency).

Characteristic	Denture adjustment (n = 20)	Treatment I (n = 20)	Treatment II (n = 20)	P- value
Age (years)	68.8 $\pm$ 10.3 [42–90]	67.2 $\pm$ 11.04 [38–90]	65.6 $\pm$ 8.2 [47–86]	0.417
Gender (m/f)	10/10 (50%/50%)	12/8 (60%/40%)	4/16 (20%/80%)	0.03*
Active smokers (yes/no)	7/13 (35%/65%)	6/14 (30%/70%)	10/10 (50%/50%)	0.502
Coffee consumption (yes/periodically/no)	17/1/2 (85%/5%/10%)	16/2/2	18/1/1 (90%/5%/5%)	0.936
Tea consumption (yes/periodically/no)	3/13/4 (15%/65%/20%)	7/10/3 (35%/50%/15%)	7/10/3 (35%/50%/15%)	0.62
Alcohol consumption (yes/periodically/no)	3/4/13 (15%/20%/65%)	3/7/10 (15%/35%/50%)	0/4/16 (0%/20%/80%)	0.198
Charlson Comorbidity Index	3 $\pm$ 2.15 [0–6]	2.7 $\pm$ 2.2 [0–7]	2.7 $\pm$ 1.4 [0–5]	0.643
Use of drugs – angiotensin-converting-enzyme inhibitors (yes/no)	8/12 (40%/60%)	10/10 (50%/50%)	12/8 (60%/40%)	0.502
Use of drugs – beta blockers (yes/no)	5/15 (25%/75%)	7/13 (35%/65%)	11/9 (55%/45%)	0.179
Use of drugs – diuretics (yes/no)	5/15 (25%/75%)	2/18 (10%/90%)	5/15 (25%/75%)	0.444
Use of drugs – calcium antagonists (yes/no)	4/16 (20%/80%)	2/18 (10%/90%)	6/14 (30%/70%)	0.346
Use of drugs – anticoagulants and antiplatelet agents (yes/no)	7/13 (35%/65%)	7/13 (35%/65%)	7/13 (35%/65%)	>0.99
Use of drugs – antilipemic (yes/no)	2/18 (10%/90%)	3/17 (15%/85%)	3/17 (15%/85%)	>0.99
Use of drugs – antidepressants (yes/no)	4/16 (20%/80%)	2/18 (10%/90%)	4/16 (20%/80%)	0.749
Use of drugs – thyroid drugs (yes/no)	4/16 (20%/80%)	1/19 (5%/95%)	1/19 (5%/95%)	0.344
Use of drugs – vitamin supplements (yes/no)	5/15 (25%/75%)	1/19 (5%/95%)	2/18 (10%/90%)	0.246
Use of drugs – antiarrhythmic, antirheumatic, steroids, antiasthmatic, analgesics etc. (yes/no)	6/14 (30%/70%)	6/14 (30%/70%)	4/16 (20%/80%)	0.813

\*significant difference  $P < 0.05$  (Fisher's exact test).

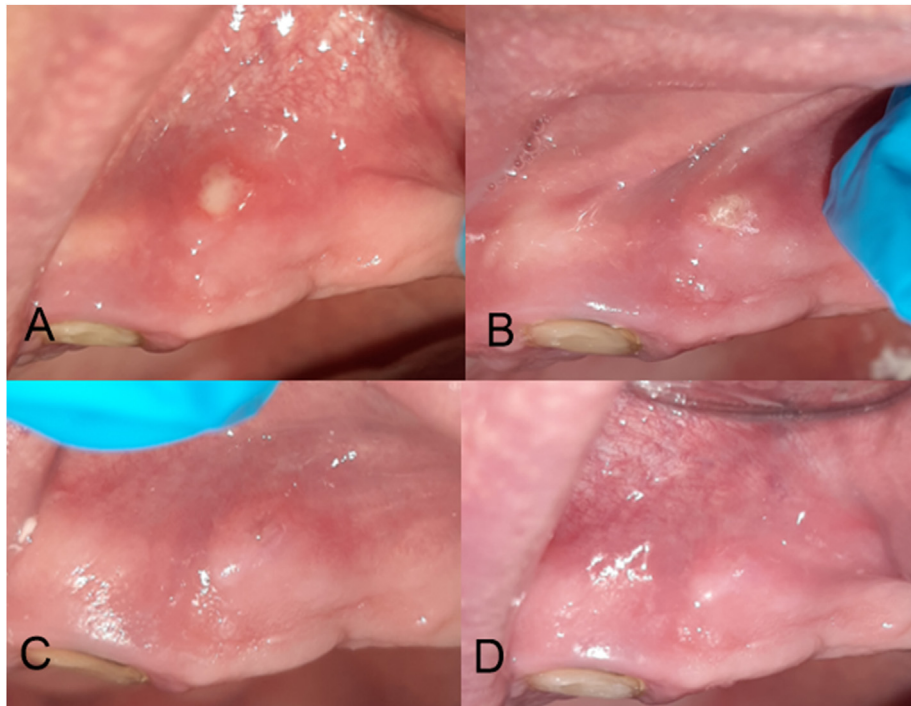
**Table 2** Healing of denture-related traumatic ulcers (average  $\pm$  standard deviation).

Characteristic	Denture adjustment (n = 20)	Treatment I (n = 20)	Treatment II (n = 20)	P-value
Area – baseline	8.52 $\pm$ 5.28	8.93 $\pm$ 4.04	8.98 $\pm$ 5.84	0.934
Perimeter – baseline	13.09 $\pm$ 7.32	13.51 $\pm$ 5.39	14.51 $\pm$ 7.30	0.770
Major dimension – baseline	5.04 $\pm$ 2.99	4.75 $\pm$ 2.12	5.06 $\pm$ 2.59	0.982
Minor dimension – baseline	3.35 $\pm$ 2.49	3.11 $\pm$ 0.93	2.97 $\pm$ 1.56	0.383
Area – day 3	6.79 $\pm$ 4.38	4.76 $\pm$ 2.43	4.03 $\pm$ 3.06	0.103
Perimeter – day 3	11.62 $\pm$ 6.62	9.62 $\pm$ 4.06	9.27 $\pm$ 4.80	0.500
Major dimension – day 3	4.44 $\pm$ 2.69	3.35 $\pm$ 1.52	3.39 $\pm$ 1.76	0.416
Minor dimension – day 3	2.95 $\pm$ 2.44	2.11 $\pm$ 0.74	1.81 $\pm$ 0.88	0.188
Area – day 5	4.59 $\pm$ 3.23	1.82 $\pm$ 1.80	1.44 $\pm$ 1.90	0.001*
Perimeter – day 5	9.21 $\pm$ 5.38	4.34 $\pm$ 4.10	4.15 $\pm$ 4.58	0.002*
Major dimension – day 5	3.67 $\pm$ 2.47	1.49 $\pm$ 1.42	1.55 $\pm$ 1.65	0.003*
Minor dimension – day 5	2.39 $\pm$ 2.27	0.90 $\pm$ 0.85	0.68 $\pm$ 0.75	0.001*
Area – day 7	2.89 $\pm$ 2.60	0.52 $\pm$ 0.84	0.43 $\pm$ 0.91	<0.001*
Perimeter – day 7	6.60 $\pm$ 4.48	1.58 $\pm$ 2.28	1.41 $\pm$ 2.65	<0.001*
Major dimension – day 7	2.72 $\pm$ 2.42	0.55 $\pm$ 0.81	0.47 $\pm$ 0.86	<0.001*
Minor dimension – day 7	1.88 $\pm$ 2.31	0.31 $\pm$ 0.49	0.26 $\pm$ 0.47	<0.001*
Healed ulcers on day 3 (yes/no)	0/20 (0%/100%)	0/20 (0%/100%)	0/20 (0%/100%)	NA <sup>a</sup>
Healed ulcers on day 5 (yes/no)	0/20 (0%/100%)	8/12 (40%/60%)	8/12 (40%/60%)	0.001**
Healed ulcers on day 7 (yes/no)	4/16 (20%/80%)	13/7 (65%/35%)	15/5 (75%/25%)	0.001**

\*Significant difference (Kruskal–Wallis test)  $P < 0.05$ .

\*\*Significant difference (Fisher's exact test)  $P < 0.05$ .

<sup>a</sup> Not applicable.



**Figure 2** Healing process of denture-related traumatic ulcer treated with combination of denture adjustment and application of hyaluronic acid gel. (A) Ulcer one day after insertion of new complete upper denture; (B) third day of healing; (C) fifth day of healing; (D) seventh day of healing.

multicollinearity (the variance inflation factor – VIF was below 2 for all predictors), no extreme outliers, and a sufficiently large sample were all met in both methods. The linear relationship between explanatory variables and the

logit of the outcome was confirmed for all variables by the Box–Tidwell test. The final models of binary logistic regression included variables shown in Table 3 and were a satisfactory fit of the data (Cox&Snell R square = 0.269,

**Table 3** Logistic regressions for the healing of the oral ulcers on days 5 and 7.

Characteristic	OR (crude)	P-value	OR (adjusted)	P-value
Healing of oral ulcers on day 5				
Treatment	3.85 (1.213–9.447)	0.02*	3.177 (1.366–7.389)	0.007*
Anticoagulant and antiplatelet drugs	8.574 (1.200–61.284)	0.032*	1.667 (0.515–5.391)	0.394
Antihypertensive drugs – diuretics	0.409 (0.052–3.249)	0.398	0.897 (0.210–3.839)	0.884
Healing of oral ulcers on day 7				
Treatment	3.503 (1.522–8.061)	0.003*	3.471 (1.647–7.318)	0.001*
Anticoagulant and antiplatelet drugs	16.344 (1.468–181.934)	0.023*	1.711 (0.580–5.045)	0.331
Antihypertensive drugs – diuretics	0.074 (0.007–0.762)	0.029*	0.357 (0.094–1.351)	0.129

\*Significant difference  $P < 0.05$ .

Nagelkerke R square = 0.392, Hosmer and Lemeshow Test  $P = 0.736$  for the day 5 model, and Cox&Snell R square = 0.354, Nagelkerke R square = 0.473, Hosmer and Lemeshow Test  $P = 0.198$  for the day 7 model).

## Discussion

Our study showed that applied gels have the greatest impact on ulcer healing. It was shown that the use of anticoagulant/antiplatelet drugs could support the healing of ulcers on the 5th and 7th days. On the other hand, concomitant therapy with antihypertensives that include diuretics slows ulcer healing, which is visible only after 7 days of follow-up. Other monitored factors in the study did not show a significant impact.

Although we live in an era of the availability and successful application of dental implants to replace lost teeth, the use of conventional complete or partial acrylic dentures is still at a high level due to their cheap and simple fabrication. Prosthetic rehabilitation with such restorations requires compliance with the principle of maximum extension, which in some cases can lead to overextended edges of the denture, which can cause the appearance of ulcers already a day after the placement of the new denture. The appearance of ulcers is usually caused by mismatch of the microrelief of the tissue and the microrelief of the gingival surface of the prosthesis, as well as inadequate occlusal contacts.<sup>7</sup>

Age is a factor that can predispose to appearance and adversely affect healing of oral lesions, since it is usually associated with concomitant diseases and the chronic use of medication.<sup>13</sup> The senescence process is also directly associated with morphological changes in the oral cavity. The stratified squamous epithelium becomes thinner, loses elasticity, and atrophies with age.<sup>17</sup> These changes in the epithelium and reduced synthesis of collagen in the connective tissue reduce the regenerative abilities of the oral epithelium and make it more vulnerable to irritants.<sup>6,18</sup> In addition, the sensitivity of the epithelium to irritants in the elderly is enhanced by the presence of concomitant diseases, changes in the viscosity and amount of saliva, parafunctional activity, and poor oral hygiene.<sup>19</sup>

Ulcers that appear as a result of wearing dentures manifest as a whitish or yellowish surface surrounded by an erythematous halo and affect the epithelium and connective tissue. They can be different shapes and sizes. In this

study, at the baseline day, the maximum size (diameter) of the ulcers was between 4.75 mm and 5.06 mm, the minimal size was ranging from 2.97 mm to 3.35 mm, and the perimeter and area surface were, on average, 13.09 mm–14.51 mm for the perimeter and 8.52 mm<sup>2</sup> to 8.58 mm<sup>2</sup> for the area. Ulcer sizes in the study of Jivanescu et al. that examined effects on denture-related ulcers healing with a hydrogel patch were between 4.3 and 10.2 mm (mean 7.1 mm) in their greatest dimension, and the smaller lesions were initially 4 mm on average, ranging from 2.0 to 7.0 mm. In their study did not performed measurement of minimum and maximum size of ulcers, neither for perimeter and area.<sup>13</sup> On the other hand, Alzarea et al. examined the effect of ozon in the treatment of denture-related ulcers, and they found that the maximum ulcer size was about 8 mm, while the minimum ulcer size was about 3.5 mm.<sup>10</sup>

There have been no studies on the healing of denture-related ulcers using digital measurement of denture-related ulcer characteristics in digital photography. The measurement of wound area on leg ulcers by analyzing digital images in the study conducted by Aragón-Sánchez et al. provides excellent reliability for wound area estimation.<sup>20</sup> They also conclude that this method provides a free, rapid, and accurate way to measure wounds and could routinely be used to document wound healing in daily clinical practice.

Patients experience pain, discomfort, difficulty speaking, and difficulty eating as a result of ulcers appearing as a result of wearing prostheses, lowering the patient's quality of life. In order to prevent these consequences and enable faster healing of the ulcer, a treatment is needed that would be more effective than adjusting the prosthesis itself.

Hyaluronic acid is a linear polymer of glucuronic acid N-acetylglucosamine disaccharide and an essential extracellular component of the skin. Its activity is present during the entire wound healing process, since it is involved in proliferation, migration, and tissue remodeling.<sup>21</sup> Hyaluronic acid promotes the formation of a fibrin clot as well as the production and release of interleukins and proinflammatory cytokines. Apart from these biological effects, hyaluronic acid is also characterized by its hydrophilicity, biocompatibility, and ability to be chemically modified, widening its applicability to different areas.<sup>22</sup> The use of hyaluronic acid has been established in many medical disciplines, such as ophthalmology, dermatology, and

rheumatology.<sup>23</sup> In dentistry, positive effects of hyaluronic acid gel and mouth rinse were established for reducing the number, healing period, and pain of oral lesions in patients suffering from recurrent aphthous stomatitis.<sup>14</sup> Hyaluronic acid spray had positive effects on swelling and trismus in the immediate postoperative period after impacted third molar surgery.<sup>24</sup> Also, positive effects were found in the treatment of human infrabony defects.<sup>25</sup> In our study, lesion reduction was observed already on the third day after local administration of the gels, while a statistically significant difference in the perimeter, area surface, and diameter of the lesions between the treatment and non-treatment groups existed on the fifth and seventh days.

Ulcer healing takes an average of 8–15 days. In a clinical study by Alzarea et al., they showed that ulcer healing in patients who did not wear prostheses took an average of 14 days. The same group of researchers showed that the application of ozone shortened the healing period to 8–11 days.<sup>10</sup> Positive effects on denture-related ulcer healing in treatment with the Er,Cr:YSGG laser are established in research conducted by Kurtulmus-Yilmaz et al., which showed reduction of lesions on the first day after laser treatment.<sup>6</sup> On the other hand, treatment of denture-related ulcers with triester glycerol oxide is no more effective than a placebo (corn oil).<sup>7</sup>

A clinical study that examined different gels and mouthwashes (triester glycerol oxide gel, D-panthenol gel, hyaluronic acid gel, D-panthenol mouthwash, and L-arginine mouthwash) for local treatment of denture-related traumatic ulcers found that there were no significant differences in healing periods and ulcer dimensions among treatments, except for L-arginine mouthwash on the third day.<sup>26</sup>

The role of anticoagulants and antiplatelet drugs in wound healing is controversial, because these drugs can inhibit the first phase of wound healing—more precisely, the coagulation process. That is why it is mentioned in the literature that these medications can potentially inhibit the early stages of wound healing.<sup>27</sup> Recent research on the effect of these drugs on the wound healing process after tooth extraction, on the other hand, has shown that patients seem to demonstrate that this therapy can positively influence the healing process after tooth extraction.<sup>28</sup> This could be attributed to the greater blood supply at the wound level and the longer bleeding time, with a consequent increase in the number of cells necessary for healing. To some extent, these data can explain the positive effect on the healing process of traumatic lesions on the oral mucosa, which in our research show statistical significance on the fifth day from the appearance of the lesion.

As for diuretics, it is known that their use can increase the prevalence of xerostomia, periodontitis, dental caries, and mucosal lesions.<sup>29</sup> This fact explains the possible influence of diuretics on the inhibition of the healing of traumatic lesions in the oral cavity, which in our study was statistically significant on the seventh day.

The limitation of this research is possible confounders that could affect the healing process of denture related traumatic ulcers independently from the treatment but were not included in study (e.g., eating habits, taking spicy foods or juices, etc.).

The results of this research indicate that hyaluronic acid in form of gel, both in concentration of 0.2% and 0.3%, may accelerate healing process of denture-related traumatic ulcers. Hyaluronic acid in combination with the adjustment of the dentures for seven days leads to higher healing rate, and reduction in size of ulcers that did not heal until this time point; its use has potential to shorten the period of adaptation of patients to new dentures. Anticoagulants/antiplatelet drugs can potentially accelerate wound healing, while diuretics can slow down the healing process. Therefore, the recommendation would be to conduct further research that would include a larger number of patients, with a focus on other systemic drugs (administration time and pharmaceutical doses) that could affect the healing process, patients with additional comorbidities and other adjuvant local drugs, which is our next goal.

## Declaration of competing interest

The authors have no conflicts of interest relevant to this article.

## Acknowledgments

This work was supported by the Internal Project of Faculty of Medical Sciences, University of Kragujevac (Project number 09/21).

## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jds.2023.03.019>.

## References

1. Adam RZ, Kimmie-Dhansay F. Prevalence of denture-related stomatitis in edentulous patients at a tertiary dental teaching hospital. *Front Oral Health* 2021;2:772679.
2. Perea C, Suárez-García MJ, Del Río J, Torres-Lagares D, Montero J, Castillo-Oyagüe R. Oral health-related quality of life in complete denture wearers depending on their socio-demographic background, prosthetic-related factors and clinical condition. *Med Oral Patol Oral Cir Bucal* 2013;18:371–80.
3. Shulman D, Beach MM, Rivera-Hidalgo F. The prevalence of oral mucosal lesions in U.S. adults: data from the Third National Health and Nutrition Examination Survey, 1988-1994. *J Am Dent Assoc* 2004;135:1279–86.
4. Brantes MF, Azevedo RS, Rozza-de-Menezes RE, et al. Analysis of risk factors for maxillary denture-related oral mucosal lesions: a cross-sectional study. *Med Oral Patol Oral Cir Bucal* 2019;24:305–13.
5. Jainkittiving A, Aneksuk V, Langlais RP. Oral mucosal lesions in denture wearers. *Gerodontology* 2010;27:26–32.
6. Kurtulmus-Yilmaz S, Yilmaz HG, Tumer H, Sadettinoglu K. Clinical evaluation of the Er,Cr:YSGG Laser therapy in the treatment of denture-related traumatic ulcerations: a randomized controlled clinical study. *Photomed Laser Surg* 2015; 33:224–9.
7. Geckili O, Bektas-Kayhan K, Eren P, Bilgin T, Unur M. The efficacy of a topical gel with triester glycerol oxide in denture-related mucosal injury. *Gerodontology* 2012;29:715–20.

8. Kivovics P, Jáhn M, Borbély J, Márton K. Frequency and location of traumatic ulcerations following placement of complete dentures. *Int J Prosthodont (IJP)* 2007;20:397–401.
9. Mortazavi H, Safi Y, Baharvand M, Rahmani S. Diagnostic features of common oral ulcerative lesions: an updated decision tree. *Int J Dent* 2016;2016:7278925.
10. AlZarea BK. Management of denture-related traumatic ulcers using ozone. *J Prosthet Dent* 2019;121:76–82.
11. Coelho CM, Zucoloto S, Lopes RA. Denture-induced fibrous inflammatory hyperplasia: a retrospective study in a school of dentistry. *Int J Prosthodont (IJP)* 2000;13:148–51.
12. Piemonte ED, Lazos J. Evidence for chronic mechanical irritation as a causative factor in oral cancer: application of Bradford Hill criteria. *Transl Res Oral Oncol* 2018;3:1–10.
13. Jivanescu A, Borgnakke WS, Goguta L, Erimescu R, Shapira L, Bratu E. Effects of a hydrogel patch on denture-related traumatic ulcers; an exploratory study. *J Prosthodont* 2015;24:109–14.
14. Dalessandri D, Zotti F, Laffranchi L, et al. Treatment of recurrent aphthous stomatitis (RAS; aphthae; canker sores) with a barrier forming mouth rinse or topical gel formulation containing hyaluronic acid: a retrospective clinical study. *BMC Oral Health* 2019;19:153.
15. Lee JH, Jung JY, Bang D. The efficacy of topical 0.2% hyaluronic acid gel on recurrent oral ulcers: comparison between recurrent aphthous ulcers and the oral ulcers of Behçet's disease. *J Eur Acad Dermatol Venereol* 2008;22:590–5.
16. Chen J, Abatangelo G. Functions of hyaluronan in wound repair. *Wound Repair Regen* 1999;7:79–89.
17. Mckenna G, Burke FM. Age-related oral changes. *Dent Update* 2010;37:519–23.
18. Jainkittivong A, Aneksuk V, Langlais RP. Oral mucosal lesions in denture wearers. *Gerodontology* 2010;27:26–32.
19. Razak PA, Richard KM, Thankachan RP, Hafiz KA, Kumar KN, Sameer KM. Geriatric oral health: a review article. *J Int Oral Health* 2014;6:110–6.
20. Aragón-Sánchez J, Quintana-Marrero Y, Aragón-Hernández C, Hernández-Herero MJ. ImageJ: a free, easy, and reliable method to measure leg ulcers using digital pictures. *Int J Low Extrem Wounds* 2017;16:269–73.
21. Nyman E, Henricson J, Ghafouri B, Anderson CD, Kratz G. Hyaluronic acid accelerates re-epithelialization and alters protein expression in a human wound model. *Plast Reconstr Surg Glob Open* 2019;7:e2221.
22. Graça MFP, Miguel SP, Cabral CSD, Correia IJ. Hyaluronic acid-based wound dressings: a review. *Carbohydr Polym* 2020;241:116364.
23. Huynh A, Priefer R. Hyaluronic acid applications in ophthalmology, rheumatology, and dermatology. *Carbohydr Res* 2020;489:107950.
24. Koray M, Ofluoglu D, Onal EA, et al. Efficacy of hyaluronic acid spray on swelling, pain, and trismus after surgical extraction of impacted mandibular third molars. *Int J Oral Maxillofac Surg* 2014;43:1399–403.
25. Sehdev B, Bhongade ML, Ganji KK. Evaluation of effectiveness of hyaluronic acid in combination with bioresorbable membrane (poly lactic acid-poly glycolic acid) for the treatment of infrabony defects in humans: a clinical and radiographic study. *J Indian Soc Periodontol* 2016;20:50–6.
26. Bural C, Güven MÇ, Kayacıoğlu B, Ak G, Bayraktar G, Bilhan H. Effect of over-the-counter topical agents on denture-induced traumatic lesions: a clinical study. *Int J Prosthodont (IJP)* 2018;31:481–4.
27. Levine JM. The effect of oral medication on wound healing. *Adv Skin Wound Care* 2017;30:137–42.
28. Sammartino G, Gasparro R, Spagnuolo G, Miniello A, Blasi A, Marenzi G. Influence of the antithrombotic therapy in the healing of simple post-extraction sockets: a randomized clinical trial. *J Clin Med* 2022;11:3654.
29. Prasanthi B, Kannan N, Patil R. Effect of diuretics on salivary flow, composition and oral health status: a clinico-biochemical study. *Ann Med Health Sci Res* 2014;4:549–53.