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Permanence of Modifications in Oral Microcirculation in Ex-Smokers

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Background: The aim of this study was to assess the long-term effects of smoking and to investigate the permanence of this damage to the oral microcirculation.

Material/Methods: We recruited 75 patients and divided them into 3 groups: group 1 was composed of 25 healthy non-smokers, group 2 was composed of 25 healthy current smokers, and group 3 was composed of 25 healthy ex-smokers. Video-capillaroscopic examination was performed on all patients.
The video-capillaroscopic investigation was performed on patients in sitting position, always with the same light source, at the same room temperature (23°C), in the morning, with the same operator (GAS), and was repeated many times for every area under investigation. An enlargement of 200× allowed us to explore point-by-point all the morpho-structural characteristics of the capillaroscopic field. For non-parametric data, we evaluated the visibility of the loops and their position in relation to the surface of the mucosa. The evaluated parametric data were length of capillary loop, diameter of the loop, capillary tortuosity, and capillary density.

Results: Our study clearly shows there was no remission of vascular damage, even 13 years after smoking cessation.

Conclusions: Our research shows that that the effects of smoking are still visible in ex-smokers, even at 13 years after cessation and also that ex-smokers are still subject to the risk of oral pathologies in the interval of time that we considered.

MeSH Keywords: Microcirculation • Smoking Cessation • Stomatitis

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Background

The effects of smoking, especially if prolonged over time, cause significant alterations in oral microcirculation [1–5]. In particular, the most significant alterations concern the morphological-structural elements and the density of capillaries per surface area [6–11]. Long-term smoking induces significant morphologic changes in the microcirculation of the human labial mucosa, and these changes can be easily and comfortably recorded with videocapillaroscopy [12].

The results of other studies indicate that smoking does not affect the vascular surface density, number of vessels, or fibronectin distribution in subepithelial gingival connective tissue [13]. Risk of periodontitis and teeth missing is increased significantly by long-term smoking, poor oral hygiene, and poor diet [14].

The destruction of periodontal tissue by smoking and the unfavorable clinical course of periodontal disease has been reported in cigarette-smoking patients [15]. Data from existing studies point to smoking and diabetes as biological associated factors for peri-implantitis [16]. In addition, smoking is a risk factor for persistent oral HPV infection, and oral HPV infection may be associated with increased concentrations of salivary IgG and lysozyme [17]. Smoking is also a risk factor in numerous pathologies of the oral mucosa [3,5].

The present study assessed the effect of smoking cigarettes on oral microcirculation by examining a group of healthy ex-smokers at an average of 13 years after they stopped smoking. Our aim was to assess the long-term effects of smoking and to investigate the reversibility of microvascular damage.

Material and Methods

We recruited 75 patients and divided them into 3 groups: group 1 consisted of 25 healthy non-smokers (never-smokers), group 2 consisted of 25 healthy smokers, and group 3 consisted of 25 healthy ex-smokers (Table 1). Subjects were included in the study after a thorough examination of their medical history, by means of which systemic or local diseases that might endanger the local microcirculation were excluded (e.g., connective tissue disease and diabetes), and by objective examination of the oral mucosa to exclude the presence of lesions or alterations in the oral cavity. In addition, none of the patients were found to have dentures. Oral melanosis and leukedema patients were excluded.

After giving their consent, all the patients underwent careful anamnesis to evaluate the state of their general health and to exclude the presence of any systemic pathology and/or any pharmacological therapy that could interfere with microcirculation.

An intra-oral evaluation was subsequently performed to evaluate oral health. Only patients without pathological alterations in oral mucosa or periodontal pathologies were included in the study. Plaque index, bleeding index, pocket depth, and loss of attachment were evaluated.

Group 1 consisted of volunteers who had never smoked and who had a negative anamnesis for known systemic illnesses; they were found to be in good health, both generally and orally. Group 2 consisted of healthy current smokers, with an estimated average of 23 cigarettes smoked per day (Table 2).

Group 3 consisted of healthy ex-smokers, for whom the average duration of exposure to the risk factor was also evaluated, as well as the time passed since they stopped smoking. The average number of cigarettes smoked per day was estimated to be 23 (Table 3).

Table 1. The demographic data of the sample group.

	Non-smokers	Smokers	Ex-smokers
M/F ratio	12/13	13/12	11/14
Age (average)	57.04±3.4	52.31±4.5	58.44±3.6
Range	23–85	18–78	36–79

Table 2. Average duration of exposure and start (smokers).

Average duration of exposure to smoke	21.19 years
Average age for the start of exposure to smoke	19.8 years

Table 3. Average duration of exposure and time passed since giving up (ex-smokers).

Average duration of exposure to smoke	17.28 years
Average time passed since giving up smoking	13.28 years

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Each video-capillaroscopic examination took about 15 min. After having collected the administrative and clinical data, an intra-oral instrumental examination was performed with the subject in a sitting position, with the same light source (a 6500° K Medical neon light), at the same room temperature (23±1°C), in the morning, and by the same operator (GAS). The instrumental examination was repeated at least twice for each site analyzed [18–22].

The Videocap (Videocap 200-DS MEDIGROUP MILAN) is made up of:

1. A central body that includes a light source consisting of a cold halogen light emitted by a 100-W lamp fitted with an automatic control device to regulate luminosity.
2. A fiber optic probe made up of a flexible cable 2 meters in length that has a video-optic terminal, in turn constituted by a color high-definition micro-television camera and a support for holding the different lenses. The lenses were either contact or non-contact types with varying enlargements: 20×, 50×, 100×, 200×, 500×, 1000×.
3. A high-resolution color monitor.

An enlargement of 200× allowed us to explore, point-by-point, all the morpho-structural characteristics of the capillaroscopic field. For non-parametric data, we evaluated the visibility of the loops and their position in relation to the surface of the mucosa [21,22].

The visibility of the capillary loops was evaluated as follows:

- Score 1: simple to bring into focus (less than 30 s from the beginning of the examination);
- Score 2: mostly simple to bring into focus, between 30 s and 2 min from the beginning of the examination);
- Score 3: difficult to bring into focus (over 2 min from the beginning of the examination);
- Score 4: impossible to bring into focus.

The position of the loops in relation to the surface was also evaluated:

A. the loop is parallel to the surface;
B. the loop is perpendicular to the surface;
C. the loop is both parallel and perpendicular.

There followed an evaluation of the parametric data:

- Length of capillary loop
- Diameter of the loop
- Capillary tortuosity
- Capillary density

The evaluation of the tortuosity of the capillary loops was carried out by attributing points from 0 to 3, according to the number of crossings that they had:
Score 0: absence of crossing;
Score 1: a single crossing;
Score 2: more than 2 crossings;
Score 3: distorted loops.

It is important to emphasize that the parametric data originated from software related to video-capillaroscopy using a dedicated measuring instrument, with each optical magnification corresponding to an exact value of metric pixels in the scanned image.

The Bioethics Committee of the University of Palermo, Via Del Vespro, 129, 90127 Palermo, Italy examined and unanimously approved the protocol of the research (report No. 02/2010, session 03.02.2010).

Statistical analysis

The data gathered in underwent statistical analysis to discover any significant differences. The Mann-Whitney U test was used for non-parametric data; this test is found in Past ver.1.53 computer software and was developed by Ryan et al. in 1995. Being periodically updated, it represents one of the most efficient tests of its kind. Its precision is estimated to be around 95%. The level of statistical significance was set at $P<0.05$.

The results of the statistical analysis are reported below. An initial comparison was made between the smokers and ex-smokers, followed by another with the group of never-smokers, which is used as a constant reference for the state of oral health and for the absence of the risk factor.

Results

During the capillaroscopic examination, the visibility of the operating field was evaluated with a score equal to 1 (score=1) for the group of non-smokers, while it was equal to 2 (score=2) for the group of smokers. The third group, the ex-smokers, had values that were between 2 and 3 (score=2–3).

Increasing difficulty in bringing the field under observation into focus is correlated to increase in the quota of keratinization, which characterizes the epithelium of the smokers, which has been subject to particular and continuous thermal and mechanical stimuli.

Table 4 shows the distribution of loop positions. Three images were used for each measurement. These were anatomically easy to see and record by the capillaroscope. The results are recorded in Tables 5–8.

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Table 4. Orientation of the loops in relation to the surface.

	Non-smokers	Smokers	Ex-smokers
Orientation of the loops in relation to the surface	A= 21	A=19	A=21
	B=2	B=6	B=3
	AB=2	AB=0	AB=1

Table 5. Summary of the values relative to average density and to the presence of microhaemorrhages and microaneurysms. The noting of aneurismatic and microhaemorrhagic areas represents a parameter which is purely occasional in a healthy subject but is often present in smokers.

	Contorl	Smokers	Ex-smokers
Density PER mm²	9.96±1,13	16.82±0.98	18.61±0,68
Microhaemorrhage	No	Yes 5 patients	Yes 7 patients
Microaneurism	No	No	Yes 5 patients

Table 6. Statistical comparison between non-smokers and smokers.

Parameter of interest	Non-smokers	Smokers	Significance
Loop length mean ±SD	0.10±0.0017	0.009±0.0012	NS
Loop diameter mean ±SD	0.029±0.007	0.013±0.007	S
Afferent loop diameter mean ±SD	0.080±0.009	0.086±0.008	NS
Efferent loop diameter mean ±SD	0.054±0.006	0.062±0.004	S
Density mean SD	9.96±1.13	16.82±0.98	S

Table 7. Statistical comparison between non-smokers and ex-smokers.

Parameter of interest	Non-smokers	Smokers	Significance
Loop length mean ±SD	0.10±0.0017	0.008±0.0012	S
Loop diameter mean ±SD	0.029±0.007	0.011±0.006	S
Afferent loop diameter mean ±SD	0.080±0.009	0.063±0.001	S
Efferent loop diameter mean ±SD	0.054±0.006	0.01±0.001	S
Density mean SD	9.96±1.13	18.61±0.685	S

Table 8. Statistical comparison between smokers and ex-smokers.

Parameter of interest	Non-smokers	Smokers	Significance
Loop length mean ±SD	0.009±0.0012	0.008±0.0012	NS
Loop diameter mean ±SD	0.013±0.007	0.011±0.006	S
Afferent loop diameter mean ±SD	0.086±0.008	0.063±0.001	NS
Efferent loop diameter mean ±SD	0.062±0.001	0.01±0.001	S
Density mean SD	16.82±0.983	18.61±0.685	NS

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Discussion

The results obtained in this study found clear signs of alteration in capillary circulation in subjects who continuously engage in active cigarette smoking.

The length of the capillary loops progressively decreased, but these differences were not found to be statistically significant between non-smokers and smokers. The data become significant when comparing non-smokers *vs.* ex-smokers. The data relative to the non-significance between the smokers and the ex-smokers is also interesting, suggesting that the parameter of the total length of the loop continues to be reduced. Another result that has to be interpreted is that, relative to the size of the total diameter of the loop, the tendency towards the lower values is progressive as we go from non-smokers to smokers to ex-smokers.

The vascular damage from inflammation progressively reduced the diameter of the loop due to reduced oxygen supply to the capillaries. The differentiated study of the afferent or arteriolar diameters and the efferent or venular ones need to be considered appropriately. The comparison of the data relative to these anatomical segments shows that the absolute values have a growing tendency to increase, also significantly. Statistical comparison, however, shows that for the afferent portion, there is non-significance only in the group of non-smokers and smokers. The comparisons in all the other cases appear to be highly significant. The analysis of the venous element also shows a high significance in all the comparisons made and keeps increasing steadily.

The density increased in the group of active smokers and that of the ex-smokers. This parameter can also be ascribed to a context of clear alteration of the vascular pattern. This is specifically due to the angiogenetic action of nicotine [23,24].

The tortuosity of the loops was not significantly different between smokers and ex-smokers, but only between the non-smokers and all the others. The morphological comparison between the capillary loops of a subject who is a non-smoker and one who is a smoker shows macroscopic evidence of damage from hypo-oxygenation [24] and the total length is reduced. The total diameter is uniformly reduced while the efferent diameter appears increased in dimension, which reveals that there is difficulty also in the venous drainage of the mucosa.

In order to balance the reduced circulatory "efficiency" in some way, the number of loops increases significantly. To the best of our knowledge, this is the first such study to evaluate ex-smokers.

Other studies confirm that smoking is associated with cutaneous microvascular dysfunction and shows that the severity of this impairment is independently related to the duration and intensity of smoking [25].

Age and smoking are associated with approximately one-third of the variance in the endothelium-associated microvascular vasomotor activity in habitual smokers [26]. Our study shows with particular clarity that even after 13 years without the presence of the smoke, there was no remission of vascular damage. Instead, the pattern remains compromised and indeed worsens with regard to certain parameters. In particular, the comparison with smokers shows that the loops have shortened; with a reduced total diameter and with the efferent portion even more congested and dilated. The density per field appears to increase even more. This is probably a mechanism of compensation for assuring enough perfusion. It may be that this damage is permanent, but it is possible that 13 years is too brief a time for such an evaluation.

It is clear that altered vascular circulation in the mucosa is a predisposing factor for all the numerous pathologies that have an inflammatory etiology [27,28]. The natural defence mechanisms, properties of cell-mediated immunity, like those of the complement system, are notably less effective, also because of the reduced cellularity linked to the reduction in perfusion and thus to the reduced partial tension of the oxygen present [7–11].

Recent studies have shown that the nicotine emitted by the combustion of cigarettes does not have a direct action on the modification of the capillary microanatomy, but acts indirectly through other substances [1,3,4] such as noradrenaline, acetylcholine, and adenosine-phosphate. The action of these substances, which increase in subjects who smoke, alters the prodromal phase of the inflammatory mechanism, or rather the vasodilatation and the subsequent vasopermeability necessary for providing competent cells to the site in question [2]. The stomatognathic apparatus appears to be highly involved in these smoke-correlated processes. The effects can be divided into reversible and irreversible.

Firstly, it is common knowledge that subjects who smoke have unpleasant halitosis with a nicotinic smell. The teeth tend to become yellow and there is a tendency to accumulate deposits of tartar and plaque. The palate can sometimes undergo alteration with a tendency towards hyperkeratosis (smoker's palate), but it is reversible given that it is prevalently inflammatory, as are alterations to the tongue, such as the benign form of black hairy tongue [1,6,7,27].

The peripheral vasoconstriction due to the presence of carbon monoxide from burning reduces blood circulation by 40% in 1 hour and is a decisive factor in the failure of implants, as well as in the regeneration of the mucosa [24].

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All the oral pathologies that have an inflammatory etiopathogenesis are more common in subjects who smoke [6,23]. Smokers have a higher rate of oral carcinoma compared to those who do not smoke and this appears to be correlated to the carcinogenetic activity of nicotinic derivatives, as well as being due to the induced vascular changes [1,8–11]. Finally, the effects produced by the heat and by the continuous trauma that specific sectors of the lips undergo must not be underestimated [27].

The reduction of tension in the oxygen being transported due to the presence of carbon monoxide caused by combustion activates the numerous growth factors present, among which is VEGF (vascular endothelial growth factor), which in turn promotes neoangiogenesis, with the growth of new capillary loops. This is only one of the alterations in oral microcirculation present in subjects who smoke [20,21].

In fact, as our research has demonstrated, there are multiple microcirculatory alterations, and it is clear that an extreme attempt is made by the body to compensate for such degenerative variations by increasing the number of capillary loops. This is an extreme attempt to overcome the reduced functionality of each loop, morphologically shown by the altered diameters and the numerous crossings present.

Conclusions

We found that the effects of smoking are still visible in ex-smokers 13 years after they stopped smoking, and that ex-smokers are still subject to the risk of oral pathologies in the interval of time that we considered.

Conflict of interests

None.

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