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**Title page**

**Telangiectasia of the face: risk factors for reappearance in patients treated with dye laser.**

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## Abstract

**Background:** Lasers can be successfully used in the treatment of facial telangiectases. Nevertheless, reappearance of telangiectasias after successful laser treatment is a significant problem. Risk factors involved in the reappearance have not been previously investigated.

**Objective:** To evaluate whether personal, clinical and behavioural factors can influence the recurrence or new appearance of telangiectasias after treatment.

**Methods:** 415 women and 69 men obtaining complete clearance after laser treatment were included in the study and the role of different risk factors in the reappearance of telangiectasias was analyzed. Immunocompromised patients were excluded. A statistical analysis was then performed.

**Results:** 24% of women and 14,5% of men enrolled showed a persistent clearance after treatment. In women in which telangiectasias reappeared, logistic regression highlighted the importance of tanning addiction, aesthetic medicine and surgery procedures as risk factors while therapy for menopause was found to be a protective factor. Hypertension was found to be a risk factor in men.

**Conclusions:** The efficacy of laser for treatment of telangiectasias of the face has been previously proven. Nevertheless, this is the first study presenting an analysis of risk factors involved in the new appearance of telangiectasias after the clearance induced by therapy.

## Text

### Introduction

Telangiectasias are chronically dilated capillaries appearing as small, dull red or livid, linear, stellate or punctate markings. They usually represent dilatations (expansion, stretching) of pre-existing vessels.<sup>1</sup> In particular, facial telangiectasias can occur spontaneously or they can be

influenced by aging, excessive ultraviolet (UV) exposure, hormonal variations, smoking, alcohol ingestion, filler implants, topical and systemic corticosteroid administration or can be associated with collagen-vascular disease or rosacea.<sup>2-6</sup>

Laser treatment of cutaneous vascular lesions has progressed significantly over the past 30 years, based on the theory of selective photothermolysis.<sup>7</sup>

Unfortunately there is no treatment that can guarantee a permanent result. Therefore, we sought to identify possible risk factors involved in reappearance of telangiectasia of the face after successful laser treatment and to describe features found in people showing a persistent clearance.

## **Materials and methods**

### *Study population*

This is a retrospective study including, 415 consecutive women and 69 consecutive men with telangiectasias of the face, treated by FLPP (flashlamp-pumped pulsed) Dye laser devices manufactured by Candela Corporation (Boston, USA), between 2000 and 2014. Exclusion criteria were factors that could introduce a bias: autoimmune diseases, acquired immunodeficiency syndrome, diabetes or corticosteroids and the presence or history of recurrent flushing and/or follicular and nonfollicular papules and pustules and/or glandular hyperplasia, the presence of telangiectasias located on the ala nasi<sup>8</sup>.

These two latter characteristics were excluded since our preliminary investigation on these two groups revealed a 100% of reappearance in 1-12 months.

The complete clearance after treatment was clinically evaluated by two expert doctors; it was identified as the complete absence of telangiectasia (in a scoring system from 0 = no changes to 4=complete clearance, patient could be enrolled only when ranking 4).

The appearance of facial telangiectasia after complete clearance induced by laser treatment was investigated by two doctors and correlated with different data, as specified below, collected through a questionnaire and clinical information.

Standard follow up was scheduled at 1 month, 3 months, 6 months, 1 year after the treatment and every 6 months after one year. The follow up after the clearance of telangiectasias lasted 1-5 years, with 89% of subjects with a follow up of more than 2 years. Patients were instructed to carefully evaluate the treated area once per month and to come to our attention in case they noticed telangiectasias at any time.

The work described has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki).

*Information collected through questionnaire and clinical examination*

Age groups were divided in <44 years and  $\geq 44$  years; phototypes definition followed Fitzpatrick scale and were grouped in 1 and 2 versus 3 and 4. Menopause and drug intake for hypertension were considered. Hormonal treatment for menopause was also taken into account. Smoking habits included smokers and non-smokers. Ex-smokers were included in the non-smokers group when they stopped smoking at least 10 years before the enrollment otherwise they were put into the smoker group.

Alcohol consumption was divided into two categories: <30 g/day and  $\geq 30$  g/day<sup>9</sup> (corresponding to one superalcoholic glass or two glasses of wine or three small beers). Previous filler implants and aesthetic surgery procedures were evaluated. Exposure to sunlight or to artificial ultraviolet (UV) was investigated.<sup>10</sup> Subjects with a higher solar UV habits were identified by sunny holidays during >2 weeks/year or spending at least 1 year in countries with higher sun irradiance or avoiding sunscreens while more than 20 tanning sessions/year using sunbeds. Time intervals before new appearance were expressed in months.

### *Statistical analysis*

Median and percentage frequency were used to express characteristics of the population. The correlation between risk factors and the reappearance of telangiectasia was evaluated with Pearson  $\chi^2$  test and expressed as “p”, with a confidence interval of 95%, being therefore significant when  $<0,05$ .

Correlations among different variables were assessed with Spearman rank test. To test the effect of different variables on telangiectasia recurrence, logistic regression analysis was also carried out.

All analysis were performed with SPSS<sup>®</sup> statistical package (SPSS Inc., Chicago, IL, USA).

## **Results**

### **Women**

415 female patients were included in this study. The mean age was  $44,4\pm 8$  years, ranging between 29 and 64 years. 24% of women recruited showed a persistent clearance of telangiectasia after laser treatment while in 76% of reappearance occurred.

#### ***Group showing persistent clearance***

The mean age was  $41,3\pm 6,2$ . Characteristics of this group were reported in Table I. 93% of subjects enrolled were characterized by phototype 3 and 4. 15% of patients were post-menopausal women; of these, 73% followed hormonal therapy. Less than 10% were smokers, alcohol consumers, affected by hypertension, tan addicted, undergoing aesthetic procedures both medical and surgical.

#### ***Group showing recurrence***

The mean age was  $45,4\pm 8,3$ . Results obtained from the univariate analysis have been reported in Table II. All the factors taken into account were found to influence the recurrence of telangiectasia after clearance. Moreover, a correlation between factors has been explored. In detail, menopause ( $p<0,001$ ) was found to be significantly associated with hypertension ( $\rho=0.254$ ), previous surgical ( $\rho=0.469$ ) and medical aesthetic procedures ( $\rho=0.457$ ) as well as between smoking and alcohol consumption ( $\rho=0.295$ ) and between aesthetic surgery and medicine procedures ( $\rho=0.295$ ).

Therefore aging was also related to menopause ( $\rho=0.821$ ), hypertension ( $\rho=0.295$ ), aesthetic treatments both surgical ( $\rho=0.325$ ) and medical ( $\rho=0.342$ ).

Results of logistic regression showed that several conditions can be considered as risk factors: tanning addiction, fillers implants and aesthetic surgery procedures. Hormonal treatment for menopause was shown to be a protective factor (Table III).

Time intervals before the recurrence were also taken into account (Table IV). The longest time required for reappearance (14 months) was found in subjects avoiding UV exposure; following, about 13 months for subjects having less than 44 years, with phototype 1 and 2 and patients belonging to the non-menopause group; 10-11 months for persons without hypertension, non-smokers, teetolaters, not undergoing aesthetic surgery and medicine procedures. An earlier onset of recurrence (5-6 months) was observed in women in menopause, alcohol-consumers, with hypertension, with intense UV exposure, undergoing aesthetic surgery and medicine procedures.

### *Men*

69 men were enrolled in the same period.  $50,9\pm 6,8$  was the mean age. 14,5% showed a persistent clearance of telangiectasia (Table supplementary) while 85,5% were affected by reappearance with a mean time of  $7,3\pm 3$  months. The univariate analysis revealed the role of hypertension ( $p=0,022$ ).

### **Conclusions**

Vascular lesions of the face represent a source of cosmetic and psychological problems. The literature has highlighted different results of facial telangiectasias treatment exploiting photothermolysis principles. Studies of efficacy have shown clearance of telangiectasias ranging from 60% to 84% of cases in one session and an improvement of 80,8% after five sessions of laser treatment<sup>11-13</sup> while no data are available about characteristics of patients showing a persistent clearance after therapy and subjects with reappearance of telangiectasias.

This is the first study presenting a systematic analysis of factors involved in persistent clearance and reappearance of telangiectasias after successful laser therapy. In detail, subjects showing a persistent clearance (24%) were mainly represented by women in childbearing age and men older than 44 years, with phototype 3 and 4, non-smokers, non-alcohol abusers, avoiding aesthetic procedures and UV exposure. Results of multivariate analysis in women with reappearance of telangiectasias have highlighted the role of tanning addiction, fillers implants and aesthetic surgery procedures as risk factors while hormonal treatment for menopause was shown to be a protective factor for maintaining the clearance. UV exposure has been already identified as an important factor contributing to premature aging of skin (photo-aging)<sup>3</sup>, leading to a more visible vasculature under an atrophic epidermis, particularly in people with lighter phototype. Interestingly, a reduced collagen content was observed both in intrinsically aged and in photo-aged skin,<sup>4</sup> leading to the hypothesis that a reduced support of the stroma can induce vascular ectasia. Although patients undergoing aesthetic procedures are more likely to follow-up, thus to request new treatment's sessions, it is known that filler implants are involved in appearance of telangiectasias since they can induce-neoangiogenesis.<sup>5</sup> Similarly, previous data reported the association between facial surgery and local telangiectasia, related to an increased neoangiogenesis.<sup>14</sup> Proangiogenic activity has been related to by ischemic injury, inflammation occurring in tissue manipulation, shear stress caused by traction after wound edges are approximated, matrix effect exert by wound related to suture material and fibrin. Endocrinological changes, such as menopause, have been involved in amplifying collagen depletion.<sup>4</sup> Consequently, hormonal treatment for menopause can be considered as a protective factor to maintain clearance. Furthermore, the association between factors was explored. Intuitively, the correlation found between menopause, hypertension, previous surgical and medical aesthetic procedures can be easily explained because all these factors are more likely to occur together with increasing age. The association between smoking and alcohol intake and between aesthetic surgical and medical procedures can be justified respectively by behavioural attitudes and aesthetic concerns.

Results regarding time intervals before the new appearance of vessels showed the role of menopause, hypertension, alcohol, intense UV exposure, aesthetic surgery and medicine procedures in inducing an earlier recurrence.

A limitation of this study is the low number of men enrolled that did not allow a comparison with results obtained in women. Nevertheless, hypertension was found to be a significant risk factors in men. Another limitation is the evaluation of factors involved in the reappearance of telangiectasia of the nasal area, considering its high frequency, since their rate of recurrence is 100%.

In conclusion, this is the first study describing the influence of several factors in the appearance of telangiectasias after clearance in patients treated with laser. In particular, apart from individual characteristics that cannot be modified like skin phototype, age, menopause and hypertension, we identified some behavioural changes (hormonal treatment for menopause, aesthetic procedures , UV exposure) that can be considered as preventive measures in order to maintain a persistent clearance of telangiectasias after successful laser treatment in women.

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## Figure legend

### Figure 1

Graphic showing on the x-axis time intervals (in months) before the reappearance of telangiectasias after successful treatment in 315 women.

**Table I.** Characteristics of 100 patients with persistent clearance of telangiectasias.

<i>Essential telangiectasia</i>	
Age	
<44	65
≥44	45
Fitzpatrick's phototype	
1	0
2	7
3	53
4	40
Menopause	
No	85
Yes	15
Smoking	
No	95
Yes	5
Alcohol consumer	
No	99
Yes	1
Hypertension	
No	97
Yes	3
Filler implants	
No	95
Yes	5
Aesthetic surgery	
No	91
Yes	9
UV exposure	
No	93
Yes	7

**Table II.** Univariate analysis of factors predicting recurrence of telangiectasias of the face.

<b>Characteristic</b>	<b>No. of patients</b>	<b>Cumulative of patients showing recurrence, %</b>	<b>p-value</b>
Age, yo			
<44	197	132 (67,0)	<0,001
≥44	218	183 (83,9)	
Fitzpatrick's phototype			
1 and 2	162	155 (95,7)	<0,001
3 and 4	253	160 (63,2)	
Menopause			
No	261	175 (67,0)	<0,001
Yes	154	140 (90,9)	
Hypertension			
No	382	285 (74,6)	0,036
Yes	33	30 (90,9)	
Smoking			
No	367	272 (74,1)	0,018
Yes	48	43 (89,6)	
Alcohol consumption			
No	394	295 (74,9)	0,033
Yes	21	20 (95,2)	
Filler implants			
No	342	247 (72,2)	<0,001
Yes	73	68 (93,2)	
Aesthetic surgery			
No	340	249 (73,2)	0,007
Yes	75	66 (88,0)	
UV exposure			
No	248	155 (62,5)	<0,001
Yes	167	160 (95,8)	

**Table III.** Results of multivariate logistic regression performed with the stepwise forward method.

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 1(a)	UV exposure	20,035	4123,712	0	1	0,996	5,03E+08
	Constant	1,168	0,306	14,557	1	0	3,214
Step 2(b)	Menopause therapy	-2,2	0,73	9,091	1	0,003	0,111
	UV	20,741	3993,09	0	1	0,996	1,02E+09
	Constant	2,367	0,604	15,369	1	0	10,667
Step 3(c)	Menopause therapy	-2,878	0,839	11,78	1	0,001	0,056
	Fillers	1,907	0,871	4,794	1	0,029	6,731
	UV	21,177	3785,501	0	1	0,996	1,57E+09
	Constant	2,132	0,611	12,189	1	0	8,435
Step 4(d)	Menopause therapy	<b>-2,746</b>	0,871	9,935	1	0,002	0,064
	Aesthetic surgery	<b>1,831</b>	0,834	4,819	1	0,028	6,243
	Fillers	<b>2,26</b>	0,945	5,716	1	0,017	9,58
	UV	<b>21,59</b>	3719,036	0	1	0,995	2,38E+09
	Constant	1,031	0,748	1,9	1	0,168	2,803

