

## INVESTIGATIVE REPORT

# Delay in Diagnosis and Treatment of Squamous Cell Carcinoma of the Skin

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**Advanced squamous cell carcinomas (SCC) of the skin can cause significant tissue destruction and may metastasize. Understanding the determinants of patient delay could help prevent advanced presentation. The purpose of the present study was to examine patient- and healthcare-related factors associated with delay before the detection and treatment of SCC. A sample of 308 patients with SCC treated at a dermatological referral centre in Italy were interviewed. Clinical data were obtained from the medical records. The highest quartile patients reported >9 months delay between noticing the lesion and the first medical visit (defined as long patient delay). Multivariate analysis showed that SCC arising on pre-existing chronic lesions were associated with long patient delay (odds ratio=3.17; 95% confidence interval 1.1–9.3). Controlling for confounders, the first physician's advice to remove the lesion immediately was associated with a shorter treatment delay ( $p<0.001$ ). In conclusion, our work emphasizes the importance of seeing a doctor about any change in a pre-existing lesion, particularly in light of the fact that SCC on chronic lesions are at greater risk of metastasis and recurrence. Key words: skin cancer; cutaneous; squamous cell carcinoma; delay.**

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The age-adjusted incidence of squamous cell carcinomas (SCCs) of the skin has increased by 50–200% over the past 10–30 years (1–3). Mortality is low; however, SCCs are associated with relevant morbidity and costs (4, 5). Advanced cases can result in significant tissue destruction, requiring major plastic surgery, with potentially serious psychological and functional consequences. Some higher risk cases can also metastasize. SCCs are among the most common malignancies capable of metastasis (6). Factors associated with a higher risk of metastasis and local recurrences include lesion diameter >2 cm, SCC arising on chronically diseased skin and immunosuppression (3, 6–8). SCC >2 cm in diameter have a metastatic rate of 30%, three times that of smaller lesions (8). We

have shown elsewhere (9) that long delay before surgical removal is significantly associated with invasive SCC >2 cm in diameter. Thus, understanding determinants of delay could help prevent advanced cases, with benefits for the individual and the healthcare system at large. Several studies have examined factors associated with diagnostic delay of melanoma (10–17). However, despite the increasing incidence and associated costs, very limited data are available on SCC (18). The objective of the present study was to evaluate patient- and healthcare-related factors associated with delay before detection and treatment of SCC.

## METHODS

This study is part of a wider project on the diagnostic and treatment patterns and delay times in SCC. As previously described (9, 19) we reviewed the pathology records of patients who had recently undergone surgical removal of SCC at IDI Hospital (Istituto Dermatologico dell'Immacolata), a dermatological referral centre for central and southern Italy. Patients meeting the study inclusion criteria were selected for a telephone survey. Of 2,179 SCC patients treated between 2004 and 2006, a total of 1,895 had the necessary baseline information and fulfilled the inclusion criteria: histologically confirmed cutaneous SCC within the last 24 months, age  $\geq 18$  years. Exclusion criteria were: genital and oral SCC, keratoacanthoma, organ transplant recipients, recurrent SCC, physical/cognitive impairment preventing the interview. Our sample did not include actinic keratoses and superficial low risk SCCs treated by cryotherapy, photodynamic therapy or other methods. Only SCC that were surgically removed and evaluated histologically were included.

The 1,895 patients fulfilling the inclusion criteria were stratified according to SCC size, into one group with SCC >2 cm in diameter and another group with SCC  $\leq 2$  cm in diameter. All 91 patients with SCC >2 cm in diameter were selected for telephone interviews. Oversampling of this subgroup aimed at ensuring inclusion of a sufficient number of higher-risk patients. Among them, 69 patients completed the interviews, while 22 (24.2%) could not be interviewed due to refusal, cognitive impairment or death. Concerning patients with lesions  $\leq 2$  cm in diameter, a sample of 287 patients was selected for the telephone interviews. During every interview session we interviewed consecutive patients operated on in a different month among the 21 months covered by the survey. This aimed at including patients treated during the whole 2-year study period. Among patients with lesions  $\leq 2$  cm in diameter, 246 patients completed the interviews, while 41 (14.3%) could not be interviewed due to refusal, physical/cognitive impairment, or failure to make contact. After the interviews, 7 of the 246 patients had to be excluded from the database because they did not fulfil some inclusion/exclusion criteria according to data

collected during the interviews. Thus, the analyses are based on a total of 308 patients, including 239 SCC  $\leq 2$  cm in diameter and 69 larger SCCs.

Clinical and pathology information and date of surgical removal of SCC were obtained from medical records. The remaining variables were obtained through patient interviews. The questionnaire was developed based on a literature review (11, 14, 17), and included sociodemographic information, skin cancer history and information on circumstances of diagnosis. For example, patients were asked: "Who noticed the lesion the first time? Answers: I noticed it myself; a relative or friend; a dermatologist; a general practitioner; another doctor; others (please specify...)", "When did you (or the person/doctor who first noticed the lesion) notice the lesion the first time? Approximate date..."; "When did you have the first medical visit for the lesion? Approximate date...".

The institutional ethics committee approved the study protocol. Patients' skin cancer related knowledge and behaviours after surgical removal have been reported elsewhere (19).

#### Statistical analysis and variable definitions

Three main time-intervals were calculated (Fig. 1): patient delay (from first noticing the lesion to the first medical visit); treatment delay (from first visit to surgical removal); total delay (from first noticing the lesion to surgical removal). Treatment delay included two minor time intervals: recommendation delay (from the first visit to when a doctor recommended removal) and removal delay (from when removal was recommended to surgery).

Patients with SCCs noticed first by a doctor during a medical visit ( $n=27$ ) were excluded from analyses regarding patient delay. Due to the non-normality of the distribution of delay times, delay variables were transformed in quartiles and dichotomized in long delay (upper quartile) vs. short delay.

Not easily visible anatomical sites included the neck, scalp and posterior trunk. A chronic lesion was defined as a pre-existing long-standing skin lesion, including scars, non-healing wounds, ulcers (3, 8). Actinic keratosis and Bowen's disease were not included. Individual observations were weighted by the reciprocal of the sampling probabilities to obtain prevalence and odds ratios (ORs), with their corresponding 95% confidence intervals (95% CI) from the original target population. The sampling weight is calculated as  $N/n$ , where  $N$ =the number of elements in the population and  $n$ = the number of elements in the sample. Stratified samples and weighted analyses are commonly used in order to ensure sufficient statistical stability for analyses on specific subgroups that might otherwise be too small (18, 20). In our study, stratification was based on SCC size, and this was taken into account in the analyses through the weighting process using the `svy`-command of the computer package STATA 9 (Stata Corp, College Station, TX, USA). All presented data are weighted. In addition, absolute numbers from the original sample are reported.  $\chi^2$  statistics was used for categorical variables. Multivariable logistic regression was used to examine factors potentially associated with delay. We used the dichotomous delay variables (long vs. short delay), examining patient, treatment and total delay as the outcome variables in three different models. Explanatory variables included variables associated with delay at univariate analyses at  $p < 0.1$ , in addition to age and gender. For all other analyses significance was set at  $p < 0.05$ . Invasive and *in situ* SCCs were examined as potential explanatory variables in the multivariable logistic regression analyses. In addition, subgroup analyses were also performed separately for invasive and *in situ* cases. *In situ* SCC was defined as intraepidermal "full-thickness" keratinocyte atypia, with loss of polarity, numerous mitotic figures, dyskeratotic cells, hyperchromasia, lack of maturation and nuclear

crowding. Invasive SCC consisted of malignant epidermal cells extending beyond the dermoepidermal junction into the dermis (21, 22).

## RESULTS

### *Sociodemographic and clinical characteristics of the study sample*

Patients' characteristics are shown in Table I. The sample included 55.9% men and had a mean age of 70.8 years (SD=9.2). As previously described (9, 19) the sample's age and sex distribution was similar to all SCC patients treated at our hospital during the study period (57.3% men; mean age 72.1 years, SD=11.5). Patient interviews were completed after a mean of 8 months (SD=5) from treatment. Among the first 47 recruited patients we compared the telephone interviews with data collected during the dermatological visit regarding the date of first noticing the lesion and of the first visit, finding very good agreement (91.2%;  $k=0.81$  and 85.1%;  $k=0.69$ , respectively). In addition to the index SCC, 30.0% of participants also reported a past skin cancer (basal cell carcinoma 15.2%; SCC 7.7%; melanoma 2.2%; not specified 4.9%). Patients

Table I. Sociodemographic and clinical characteristics of the study sample ( $n=308^a$ )

Characteristics	<i>n</i> (%) <sup>b</sup>
Sex	
Male	187 (55.9)
Female	121 (44.1)
Age groups	
<65 years	70 (24.3)
65–74 years	120 (41.0)
$\geq 75$ years	118 (34.7)
Education	
<6 years	136 (43.1)
6–13 years	119 (40.1)
>13 years	47 (16.8)
Cohabiting partner	
No	89 (28.3)
Yes	215 (71.7)
Anatomical site of squamous cell carcinoma	
Cheek/cheekbone	43 (15.9)
Nose	35 (13.9)
Ear	35 (11.2)
Forehead	31 (10.6)
Periorbital region	24 (10.2)
Lips	30 (7.0)
Scalp/neck	25 (6.4)
Lower limbs	32 (10.3)
Upper limbs	28 (7.3)
Anterior trunk	19 (5.3)
Posterior trunk	6 (1.9)
Histological subtype	
<i>In situ</i> squamous cell carcinoma	129 (57.8)
Invasive squamous cell carcinoma	168 (42.2)
Squamous cell carcinoma size	
Smaller lesion ( $\leq 2$ cm diameter)	239 (91.2)
Larger lesion ( $> 2$ cm diameter)	69 (8.8)

<sup>a</sup>Totals may vary because of missing values. <sup>b</sup>Weighted frequency.

with invasive SCC represented 42.2% of the sample; they were older than *in situ* cases (46.8% vs. 25.6% were  $\geq 75$  years;  $p < 0.001$ ), but they were similar regarding gender ( $p = 0.29$ ), anatomical SCC site ( $p = 0.08$ ), visible vs. not visible site ( $p = 0.82$ ), SCCs arising on a chronic lesion ( $p = 0.56$ ), prevalence of large lesions ( $p = 0.07$ ), prevalence of ulceration/bleeding on SCC ( $p = 0.62$ ), personal skin cancer history ( $p = 0.11$ ).

*Total delay, patient delay, treatment delay and the pattern of detection*

Time to diagnosis and surgical removal of the SCC are summarized in Fig. 1. The median total delay time was 6 months. The highest quartile patients reported >18 months between noticing the lesion and removal, defined as long total delay. The median patient delay was 2 months. The highest quartile patients reported >9 months between noticing the lesion and the first visit, defined as long patient delay. The median treatment delay was 2 months. The highest quartile patients reported >4 months treatment delay, defined as long treatment delay. The most frequently cited signs/symptoms were itching/discomfort (33.6%), increase in lesion size (27.5%), and bleeding (12.2%). The lesion was first noticed by the patient in 89.2% of cases, by a doctor in 6.1% of cases, and by others in 4.7% of cases. The first doctor seen for the lesion was a dermatologist (in 63.9% of cases), a general practitioner (GP) (in 33.2% of cases), and another specialist (in 2.9% of cases). If the first doctor was a dermatologist the initial advice was to remove the lesion (72.4%), wait (8.4%), see a plastic surgeon (5.3%), or some other advice (medical treatment, cryotherapy, biopsy) (14.3%). If the first doctor was a GP the initial advice was to remove the lesion (13.8%), wait (8.8%), see a dermatologist or plastic surgeon (66.6%), or some other advice (10.8%).

*Factors associated with delay*

The reasons for waiting among participants with long patient delay (>9 months) were that they did not think the skin problem was urgent/dangerous (97.7%) and

lack of time (1.8%). At univariate analysis longer patient delay was associated with age group 65–74 years, SCC arising on a pre-existing chronic lesion and *in situ* SCC (Table II). The most frequent pre-existing chronic lesions were non-healing wounds/ulcers (40.3%), scars (27.2%) and burns (7.7%). At multivariable analysis, presence of signs/symptoms noticed by patients were significantly associated with a lower likelihood of long patient delay, while SCCs arising on a chronic lesion were associated with a higher likelihood of long patient delay (OR = 3.17; 95% CI 1.1–9.3).

Treatment delay was associated at univariate analysis with not easily visible site, histological subtype, larger SCC size, and with the first physician’s advice (Table III). At multivariable analysis female gender and invasive SCC were associated with a lower likelihood of long treatment delay, while physicians’ advice to wait or undergo treatments other than removal (e.g. medical therapy, cryotherapy) were associated with longer delay (OR = 15.6; 95% CI 5.2–46.7 and OR = 9.51; 95% CI 3.7–24.2), vs. having been immediately advised to remove the lesion (Table IV).

Long total delay (>18 months between noticing the lesion and removal) was associated at univariate analysis with age group 65–74 years, no skin cancer history, SCC on a chronic lesion, larger lesion size, and *in situ* SCC. At multivariable analysis the likelihood of long total delay was lower for patients with skin cancer history (OR = 0.31; 95% CI 0.1–0.7;  $p = 0.003$ ) and invasive SCC (OR = 0.30; 95% CI 0.2–0.6;  $p < 0.001$ ), while it was higher for larger SCC (OR = 2.27; 95% CI 1.0–5.4;  $p = 0.06$ ) and SCCs on a chronic lesion (OR = 2.14; 95% CI 0.7–6.5;  $p = 0.18$ ), the latter not at statistically significant levels.

We repeated the above analyses separately for the subgroups with larger and smaller lesion size and *in situ* and invasive SCC. Results were similar to those of the total study sample. However, only a few associations reached statistically significant values, probably due to the small sample size of subgroups. In particular, the likelihood of long patient delay was higher for SCCs on chronic lesions among the subgroups with *in situ* SCC (OR = 4.95; 95% CI 0.9–28.4), invasive SCC

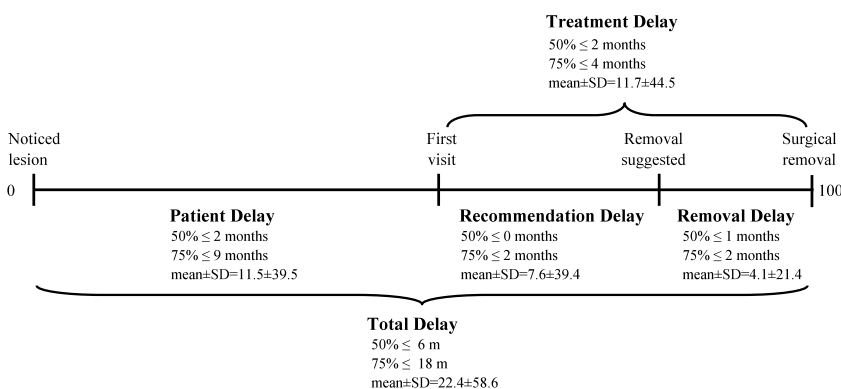


Fig. 1. Summary of delay intervals from the time of first noticing the lesion to surgical removal including patient delay, recommendation delay, treatment delay, total delay. Median (50%), mean ± standard deviation (SD) and upper quartile (75%) are reported.

Table II. Factors potentially associated with patient delay in squamous cell carcinoma (SCC) diagnosis. Univariate analysis and multiple logistic regression odds ratios (OR) and 95% confidence intervals (95% CI).

	Patient delay			p-value <sup>c</sup>	OR (95% CI) <sup>d</sup>	p-value
	≤9 months (n=201) <sup>a</sup> n	>9 months (n=80) <sup>a</sup> n (%) <sup>b</sup>	Total (n=281) <sup>a</sup> n			
Sex						
Male	117	49 (26.4)	166		1.0 (ref)	
Female	84	31 (26.0)	115	0.95	0.91 (0.5–1.6)	0.75
Age group						
<65 years	48	17 (23.9)	65		1.0 (ref)	
65–74 years	74	39 (34.8)	113		1.88 (0.9–3.9)	0.09
≥75 years	79	24 (16.8)	103	0.02	0.70 (0.3–1.6)	0.41
Education						
≤13 years	166	71 (27.9)	237		–	
>13 years	31	9 (19.3)	40	0.26	–	
Cohabiting partner						
No	58	17 (21.1)	75		–	
Yes	141	63 (28.2)	204	0.26	–	
Skin examination practice						
No	131	59 (27.2)	190		–	
Yes	70	21 (24.4)	91	0.63	–	
Personal history of skin cancer						
No	141	65 (29.4)	206		1.0 (ref)	
Yes	60	15 (17.9)	75	0.06	0.53 (0.3–1.1)	0.07
Family history of skin cancer						
No	169	70 (27.9)	239		–	
Yes	22	8 (20.3)	30	0.40	–	
Comorbidity						
No	155	64 (27.7)	219		–	
Yes	46	16 (19.8)	62	0.25	–	
Presence of symptoms						
No	64	28 (32.5)	92		1.0 (ref)	
Yes	137	52 (22.5)	189	0.08	0.52 (0.3–1.0)	0.04
SCC on chronic lesion						
No	186	64 (24.6)	250		1.0 (ref)	
Yes	14	16 (47.9)	30	0.03	3.17 (1.1–9.3)	0.04
Anatomical site						
Head/neck	143	61 (27.3)	204		–	
Trunk	18	4 (15.9)	22		–	
Limb	40	15 (25.4)	55	0.58	–	
Visible site						
Easily visible	184	75 (27.1)	259		–	
Not easily visible	17	5 (12.1)	22	0.15	–	
Histological subtype						
<i>In situ</i> SCC	82	38 (31.7)	120		1.0 (ref)	
Invasive SCC	116	39 (18.9)	155	0.02	0.57 (0.3–1.1)	0.07
SCC size						
Smaller lesion (≤2 cm diameter)	162	58 (26.0)	220		–	
Larger lesion (>2 cm diameter)	38	22 (29.8)	60	0.65	–	

<sup>a</sup>Totals may vary because of missing values. <sup>b</sup>Weighted frequency. <sup>c</sup>Pearson's  $\chi^2$  test. <sup>d</sup>Odds ratio adjusted for sex, age, personal history of skin cancer, presence of symptoms, SCC arising on chronic lesion and histological subtype.

(OR=1.46; 95% CI 0.4–5.1), small SCC (OR=3.62; 95% CI 1.1–12.1) and large SCC (OR=4.16; 95% CI 0.7–23.6), while it was decreased by the presence of symptoms for all subgroups, except for large SCCs (data not shown).

We also examined separately some specific anatomical locations. The results are similar to those reported for the total study sample. For example, SCC of the lips were not significantly different from other locations regarding patient delay, treatment delay and total delay ( $p=0.14$ ,  $p=0.66$  and  $p=0.21$ , respectively).

However, subgroup analyses are limited due to the excessively sparse data if specific anatomical locations are analysed.

## DISCUSSION

Despite the increasing incidence of SCC of the skin and the associated morbidity and costs, only one previous study, including 48 SCC cases (18), examined diagnostic and treatment delay. As far as we are aware, ours is the first study based on a relatively large sample

Table III. Factors potentially associated with treatment delay in squamous cell carcinoma (SCC). Univariate analysis and multiple logistic regression odds ratios (OR) and 95% confidence intervals (95% CI).

	Treatment delay			p-value <sup>c</sup>	OR (95% CI) <sup>d</sup>	p-value
	≤4 months (n=209) <sup>a</sup> n	>4 months (n=98) <sup>a</sup> n (%) <sup>b</sup>	Total (n=307) <sup>a</sup> n			
Sex						
Male	121	65 (30.1)	186		1.0 (ref)	
Female	88	33 (24.2)	121	0.28	0.48 (0.2–0.9)	0.03
Age groups						
<65 years	47	23 (32.2)	70		1.0 (ref)	
65–74 years	86	33 (21.6)	119		0.84 (0.4–2.0)	0.69
≥75 years	76	42 (31.1)	118	0.19	1.75 (0.8–3.9)	0.18
Education						
≤13 years	177	78 (27.0)	255		–	
>13 years	28	18 (30.2)	46	0.66	–	
Personal history of skin cancer						
No	145	74 (30.6)	219		1.0 (ref)	
Yes	64	24 (20.1)	88	0.08	0.62 (0.3–1.3)	0.19
Presence of symptoms						
No	74	24 (24.9)	98		–	
Yes	135	74 (29.0)	209	0.47	–	
SCC on chronic lesion						
No	192	82 (26.7)	274		–	
Yes	17	14 (32.5)	31	0.56	–	
Anatomical site						
Head/neck	155	68 (26.5)	223		–	
Trunk	17	7 (22.9)	24		–	
Limb	37	23 (33.5)	60	0.55	–	
Visible site						
Easily visible	197	84 (26.1)	281		1.0 (ref)	
Not easily visible	12	14 (47.8)	26	0.04	1.94 (0.6–6.3)	0.27
Histological subtype						
<i>In situ</i> SCC	84	44 (34.4)	128		1.0 (ref)	
Invasive SCC	121	47 (18.2)	168	0.002	0.39 (0.2–0.7)	0.003
SCC size						
Smaller lesion (≤2 cm diameter)	170	67 (25.9)	237		1.0 (ref)	
Larger lesion (>2 cm diameter)	38	31 (45.6)	69	0.02	1.52 (0.6–3.7)	0.35
First physician's specialization						
Dermatology	119	50 (27.3)	169		–	
General practitioner	67	29 (26.2)	96	0.85	–	
First physician's advice						
To remove	124	23 (14.5)	147		1.0 (ref)	
To see a specialist	61	23 (23.2)	84		1.59 (0.8–3.3)	0.21
To wait	10	23 (68.7)	33		15.6 (5.2–46.7)	<0.001
Other (medical treatment, cryotherapy, etc.)	14	29 (61.4)	43	<0.001	9.51 (3.7–24.2)	<0.001

<sup>a</sup>Totals may vary because of missing values. <sup>b</sup>Weighted frequency. <sup>c</sup>Pearson's  $\chi^2$  test. <sup>d</sup>Odds ratio adjusted for sex, age, personal history of skin cancer, visible site, histological subtype, lesion size and first physician's advice.

of people with SCC. We have shown that SCCs arising on chronic lesions were associated with longer patient delay. An explanation might be that patients interpret these tumours as harmless changes in a lesion they have had for a long time. This highlights that more efforts are

needed to inform patients of the importance of seeing a doctor, not only for new skin lesions but also for any change in the colour, size, texture or appearance of pre-existing chronic lesions. This is especially important considering that SCCs on chronic lesions are at higher

Table IV. Summary of the main factors associated with delay in diagnosis and treatment at multivariable analysis

Main outcome variables	Factors significantly associated with delay in diagnosis and treatment
Patient delay before seeing a doctor	SCCs arising on pre-existing chronic lesions were associated with patient delay >9 months before seeing a doctor. Presence of signs/symptoms (itching, discomfort, bleeding) significantly decreased the likelihood of patients waiting >9 months before seeing a doctor.
Treatment delay before surgical SCC removal	The physician's advice to immediately remove the lesion, female gender and having an invasive SCC were associated with a treatment delay ≤4 months before surgical SCC removal.

SCC: squamous cell carcinoma.

risk of local and distant recurrences (3, 7, 23). Developing educational interventions, particularly for higher risk groups, and evaluating their cost-effectiveness are important areas for future research.

Despite the inherent differences regarding the presentation and progression of melanoma and SCC, a comparison concerning some aspects of delay can be interesting. In our sample, 64% of patients first showed the lesion to a dermatologist and 33% to a GP, which is similar to melanoma studies conducted in France (55% and 33%) (11), Germany (63% and 23%) (14) and the USA (50% and 20%) (10). Italy provides universal health coverage and like other European countries, access to a GP is rapid and free; access to a specialist either follows a GP referral or, without referral, involves a relatively high fee. In our study no patient reported out-of-pocket costs as a reason for delay. Similarly to the German study (14) we found no significant differences in the diagnostic and treatment practices of GPs and dermatologists. As expected, more GPs recommended a visit to a specialist, but this was not significantly associated with treatment delay. Other melanoma studies showed a more appropriate attitude and shorter medical delay when the first physician was a dermatologist (12). An American study (24) showed a shorter delay for dermatologists, due to a lower threshold for performing biopsy, but with no effect on stage at diagnosis.

Treatment delay is in part due to the patient (due to time waited from when removal was recommended to when the patient made an appointment for surgery) and in part to the healthcare system (due to long waiting lists and physicians' recommendations/actions). We found longer treatment delay to be associated at multivariable analysis with male gender and the first physician's advice. Lesion size might confound this association, with some larger lesions requiring more complex procedures (18). However, even controlling for size, the advice to immediately remove the lesion was associated with shorter treatment delay. Invasive SCC had shorter treatment delay, perhaps because lesions clinically considered at high risk have a greater treatment priority. However, in our study invasive and *in situ* SCCs were not significantly different regarding clinical characteristics and personal skin cancer history. The association between delay times and invasive vs. *in situ* SCC is difficult to interpret, and larger studies specifically examining these issues are needed. The purpose of the present study was to examine patient- and healthcare-related factors potentially influencing delay *before* depth of invasion was known. Depth of invasion could be regarded as a potential outcome of delay, if we consider that *in situ* and invasive SCC represent subsequent stages of the same disease (25, 26). However, our study showed a higher frequency of long patient and total delay for *in situ* SCC. As reported elsewhere (9), one hypothesis could

be that *in situ* SCCs can be divided into two groups: a more frequent type with slow vertical growth (and possibly superficial spread) and a less frequent type with rapid progression to invasive SCC. It should also be noted that, in some cases, the distinction between *in situ* and invasive lesions is controversial (22, 25, 26). Larger studies are necessary to examine additional factors related to histological subtype and time needed to evolve from *in situ* to invasive SCC. Furthermore, studies including sufficiently large numbers of SCCs of specific anatomical sites would be necessary in order to perform in depth analyses on specific high-risk sites.

Examining factors associated with delay is complex because many are inter-related. The cross-sectional design limits the possibility of making causal inferences. Moreover, studies in this field rely mainly on patient reports, for example regarding the date of noticing the lesion (11, 14, 17, 18). The results may be affected by recall bias or social desirability. To reduce recall bias we interviewed the majority of patients within 12 months of treatment and integrated interviews with hospital records. We also compared telephone interviews with clinical records, finding very good agreement in line with studies showing high validity of self-reported skin cancer information (27, 28). Patients with SCC  $\leq 2$  cm in diameter included in our study were selected using a systematic sampling procedure. Due to administrative issues a random sample could not be drawn. However, our sample provides a good representation of the reference population, as shown by the comparison with the total patient population treated at our hospital. Caution is needed in generalizing the findings, because the study is based on a single centre; however, it is among the largest dermatological hospitals in Italy, with 130,000 dermatological visits per year. A strength of the study is that it highlights specific patient- and healthcare-related factors that potentially can be modified to prevent delay and possibly advanced SCCs. We have shown elsewhere that long delay increased the likelihood of invasive SCCs  $> 2$  cm in diameter (9), which have a higher risk of local recurrences and metastasis.

### Conclusion

Considering the increasing incidence of SCC, with its associated morbidity and costs, greater efforts are warranted for improving prevention, early detection and treatment. SCCs on chronic lesions were associated with longer patient delay. This is especially noteworthy as SCCs on chronic lesions are at higher risk of local and distant recurrences. More efforts are needed to inform patients of the importance of seeking medical advice about any change in a pre-existing chronic skin lesion. The initial medical advice can have an important impact on shortening treatment delay.

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