Prevalence of Actinic Keratoses and Associated Factors in a Representative Sample of the Italian Adult Population

Results From the Prevalence of Actinic Keratoses Italian Study, 2003-2004

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Objective: The Prevalence of Actinic Keratoses Italian Study (PraKtis) was designed to estimate the point prevalence of actinic keratoses (AKs) and associated factors in a representative sample of the Italian adult population.

Design: A representative sample of people 45 years or older was selected from the electoral rolls according to a stratified random sampling design.

Setting: A total of 180 specifically trained interviewers contacted the sampled subjects and conducted face-to-face, computer-assisted interviews and skin assessments.

Participants: A total of 12 483 subjects contacted and interviewed from March 1, 2003, through April 30, 2004.

Main Outcome Measures: History of AKs and evidence of AKs at the interview.

Results: Overall, an estimated 34% of the Italian population reported ever having undergone a dermatological examination. A history of AKs was reported by 0.3% of the total sample. Topical therapy was the most popular treatment according to 39% of subjects, whereas 25% re-

ported that they did not receive therapy. Based on the interviewer's judgment, the point prevalence of AKs was 1.4% (95% confidence interval, 1.2%-1.8%). Forty-two percent of people with AKs were unaware of their condition. The prevalence was higher among men than women and increased steadily with age. The prevalence increased with lighter phenotype and with more severe facial wrinkling. It also increased with the reported number of hours spent in the sun during the week and on holidays. No clear variation was observed according to the reported use of sunscreens. Lesions were usually multiple (median number, 4). There was a strong association between a history of nonmelanoma skin cancers and the presence of AKs (odds ratio, 4.5; 95% confidence interval, 1.8-11.0).

Conclusions: The prevalence of AKs in our study was remarkably lower than expected based on data from the United States and Australia; in Italy, AKs seem to be underdiagnosed and undertreated.

Arch Dermatol. 2006;142:722-726

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A CTINIC KERATOSES (AKs) ARE skin lesions, especially common in fair-complexioned people living in sunny climates, which have been strongly associated with the risk of both basal cell carcinoma and squamous cell carcinoma and are considered to be precursors (or even an early form) of invasive squamous cell carcinoma.[1-4] In spite of being common, only limited data on the epidemiology of AKs derived from country-based surveys are available. Moreover, most studies have been conducted in Australia or the United States, with scanty data from most European countries.[5-14] The Prevalence of Actinic Keratoses Italian Study (PraKtis) was designed to estimate the point prevalence of AKs in the Italian adult population; assess variations according to age, sex, sociodemographic variables and environmental exposures; and describe treatment modalities.[15]

METHODS

A representative sample of people 45 years or older was selected according to a stratified random sampling design. Subjects were subsequently visited at their homes, where a face-to-face, computer-assisted personal interview and skin examination were conducted.

SAMPLING PROCEDURE

The sampling procedure was envisaged in collaboration with Doxa, the Italian branch of the Gallup International Association. The universe, or statistical population, to which the survey refers to was made up of all Italian adults,

men and women 45 years or older. It was estimated that this universe was composed of about 24.8 million people (about 11.3 million men and 13.5 million women). The universe was subdivided into sections, or strata, according to 2 characteristics: region and size of community. The number of interviews to be carried out in each stratum was set in proportion to the distribution of the population of the strata in the area. Within each stratum the sampling units (communities, districts of communities, and individuals) were chosen in the following way:

Stage 1: The choice concerned the communities or municipalities (sampling points where the interviews were to be conducted).

Stage 2: In each municipality, an adequate number of electoral wards were extracted at random so that the various types of inhabited areas of the community were represented in the right proportions.

Stage 3: The names and addresses of the persons to be interviewed were extracted at random from the electoral lists of the wards selected in the second stage.

This method is known as a proportional stratified sample.[16] We adopted a sampling with replacement procedure.

ASSESSMENT AND DATA COLLECTION

Specifically trained interviewers contacted the sampled subjects and, after obtaining informed consent, conducted a face-to-face interview at the subject's house using a computer-assisted personal interviewing technique. The following set of information was collected: age; sex; occupation; smoking habits; skin, hair, and eye colors; degree of facial wrinkling; number and distribution of suspected AKs on the face and upper limbs; previous diagnoses and/or treatment for AKs (with number, location, and modality of treatment); and previous diagnoses of selected dermatological diseases. Skin color was evaluated using a 3-grade scale (light, medium, and dark) based on the examiner's judgment and comparison with representative sample photographs. Judgment on hair color was made on a 5-category scale, and judgment on eye color was made on a 6-category scale. A photonumeric scale was used to assess facial wrinkling, graded from 0 (none) to 8 (severe).[17-19] Actinic keratoses were evaluated with the help of a photographic atlas after appropriate training (described in the next subsection). Photographs of suspicious lesions were taken for further review by an expert panel. To improve compliance, educational materials on skin care were offered.

INTERVIEWERS' TRAINING SESSIONS

From February 1 through February 28, 2003, a total of 180 interviewers were trained. Training sessions were conducted in the 10 Italian dermatological (PraKtis) centers collaborating in the study. A detailed presentation of the clinical features of AKs and other common discrete skin lesions (eg, seborrheic keratoses and solar lentigo) were presented in a 2-hour teaching session. Using a specifically developed photographic atlas, interviewers also conducted practical exercises with a sample of subjects with and without selected skin lesions to improve the recognition of typical lesions and to assess skin phenotype and degree of facial wrinkling. In preliminary exercises, involving subjects with AKs and subjects without them, the interviewers' assessment of AKs had an average sensitivity of 63% and specificity of 79%. For the purpose of this study, we defined AKs as discrete lesions with ill-defined borders, dry surface, roughness on palpation, and color that varies from gray to red to reddish brown.

STUDY POWER

In the first Health and Nutrition Examination Survey (NHANES I)[5] conducted in the United States, the overall point prevalence increased from 15.9 per 1000 at ages 45 to 54 years to 65.1 per 1000 at ages 65 to 74 years. It was calculated that with a sample of about 12 000 subjects, estimates were sufficiently precise even for prevalence values as low as 1% (eg, expected prevalence, 1%; 95% confidence interval [CI], 0.7%-1.3%).

DATA ANALYSIS

We obtained weighted estimates of the frequencies of selected items, taking into account the distribution of the Italian population. Initially, we calculated the point prevalence estimate of AKs and the associated 95% CI in the whole sample and in strata of selected sociodemographic factors, phenotypic characteristics, and sun exposure habits. Then, for analytical purposes, we calculated odds ratios as estimates of the relative risks for AKs and their 95% CIs. Unconditional multiple logistic regression with maximum likelihood fitting models was applied to account for potential simultaneous effect of selected factors (ie, age, sex, area of residence, and phenotype).[20]

RESULTS

From March 1, 2003, though April 30, 2004, a total of 12 483 subjects were contacted and interviewed. Overall, a weighted estimate of 34% (29% of men and 38% of women) of the sample studied (n=4232) reported ever having undergone a dermatological examination. A history of AKs was reported by 0.3% of the total sample (n=40, of which 26 [65%] were also recognized as having had AKs by the interviewers). The most popular treatments for AKs in these subjects were, in order, pharmacological therapy (39%), treatment with liquid nitrogen (23%), and curettage (11%). Twenty-five percent of subjects reported that they had not received treatment.

Based on the interviewer's judgment, the point prevalence of AKs was 1.4% (95% CI, 1.2%-1.8%). Forty-two percent of patients with AKs, as classified by the interviewer, were unaware of their condition. The prevalence was higher among men (1.5%) than women (1.4%). It increased with age from about 0.6% (45-54 years) up to 3.0% (>74 years) (**Table 1**). Some variations were observed according to the geographic area, with lower prevalence rates in the center of Italy and higher rates in the islands of Sicily and Sardinia (2.9%; 95% CI, 1.8%-4.6%). The prevalence tended to be higher among people living in small centers (≤10 000 inhabitants) compared with larger ones (χ^2 trend,19.8; P=.001) and in people of the lower socioeconomic classes (χ^2 trend, 10.9; P=.001) (Table 1). The prevalence increased with lighter phenotype, and the highest prevalence rate for severe facial wrinkling (3.2%; 95% CI, 2.1%-5.0%) was observed in people with red or blond hair (**Table 2**). The combined effect of age and skin phenotype is shown in the **Figure**. The prevalence increased with the reported number of hours spent in the sun on weekdays (χ^2 trend, 14.0; P=.002) and during holidays (χ^2 trend, 8.6; P=.003). We did not observe a clear variation according to the reported use of sunscreens (**Table 3**). In subjects with AKs, usually more than 1 lesion was counted, with a mean value of 10.5 and a median value of

Table 1. Characteristics of Patients With Actinic Keratoses

Characteristic	Cases, No.	Prevalence, % (95% CI)	OR (95% CI)*
Total	180	1.4 (1.2-1.8)	
Sex			
Men	88	1.5 (1.2-1.8)	1.00
Women	92	1.4 (1.1-1.7)	0.69 (0.51-0.93)
Age, y†			
45-54	21	0.6 (0.3-0.8)	1.00
55-64	33	1.0 (0.6-1.3)	1.70 (0.98-2.95)
65-74	79	2.2 (1.7-2.7)	4.07 (2.51-6.60)
>74	46	3.0 (2.1-3.9)	5.26 (3.13-8.85)
Education, y			
Secondary school and university (>8)	32	0.9 (0.6-1.2)	1.00
Intermediate school (6-8)	53	1.3 (0.9-1.6)	1.29 (0.82-2.02)
Primary school (≤5)	95	1.9 (1.5-2.3)	1.23 (0.80-1.91)
Area of residence in Italy			
Northwest	36	1.0 (0.7-1.3)	1.00
Northeast	45	1.9 (1.3-2.4)	1.88 (1.20-2.93)
Center	28	1.1 (0.7-1.5)	0.97 (0.59-1.61)
South	33	1.2 (0.8-1.6)	1.32 (0.82-2.14)
Islands (Sicily and Sardinia)	37	2.9 (2.0-3.8)	2.94 (1.84-4.69)
No. of inhabitants in town of residence‡			
≤10 000	74	1.9 (1.5-2.3)	1.00
10 001-100 000	90	1.7 (1.3-2.0)	0.92 (0.67-1.26)
>100 000	16	0.5 (0.2-0.7)	0.28 (0.16-0.48)
Socioeconomic class§			
High	3	1.7 (0.0-3.6)	1.00
Middle	161	1.4 (1.2-1.6)	0.67 (0.21-2.12)
Low	16	3.9 (2.0-5.8)	1.48 (0.41-5.31)
Smoking habits			
Nonsmoker	102	1.5 (1.2-1.8)	1.00
Smoker	27	0.9 (0.6-1.2)	0.83 (0.53-1.32)
Former smoker	51	1.7 (1.2-2.2)	0.93 (0.64-1.35)

Abbreviations: CI, confidence interval; OR, odds ratio.
*Estimates from multiple logistic regression including, when appropriate, terms for sex, age, area of residence, and skin phenotype.
†χ^2 Trend, 56.7; P = .001.
‡χ^2 Trend, 19.8; P = .001.
§χ^2 Trend, 10.9; P = .001.

Table 2. Skin and Eye Characteristics of Patients With Actinic Keratoses (AKs)

Characteristic	No. of AK Cases	AK Prevalence, % (95% CI)	OR (95% CI)*
Skin color†			
Fair or pale	89	2.1 (1.7-2.5)	1.00
Medium	75	1.2 (0.9-1.5)	0.53 (0.39-0.73)
Dark or olive	16	0.7 (0.3-1.0)	0.32 (0.19-0.55)
Not evaluable	0		
Eyes color‡			
Black or brown	65	1.1 (0.8-1.4)	1.00
Light brown or green-brown	54	1.5 (1.1-1.9)	1.26 (0.88-1.82)
Gray, green, or blue	60	2.0 (1.5-2.5)	1.62 (1.14-2.32)
Not evaluable	1		
Hair color§			
Black or brown	74	0.9 (0.7-1.1)	1.00
Light brown/red brown	76	2.1 (1.6-2.6)	2.44 (1.76-3.39)
Blond or red	30	2.9 (1.9-3.9)	3.23 (2.09-5.00)
Not evaluable	0		
Facial wrinkling score‖			
<2	3	0.6 (0.0-1.3)	0.50 (0.15-1.67)
2-5	77	1.1 (0.8-1.3)	0.91 (0.64-1.30)
≥6	100	2.1 (1.7-2.5)	1.00

Abbreviations: CI, confidence interval; OR, odds ratio.
*Estimates from multiple logistic regression including terms for sex, age, and area of residence (for the facial wrinkling score, skin phenotype was also included).
†χ^2 Trend, 24.4; P = .001.
‡χ^2 Trend, 7.4; P = .007.
§χ^2 Trend, 27.4; P = .001.
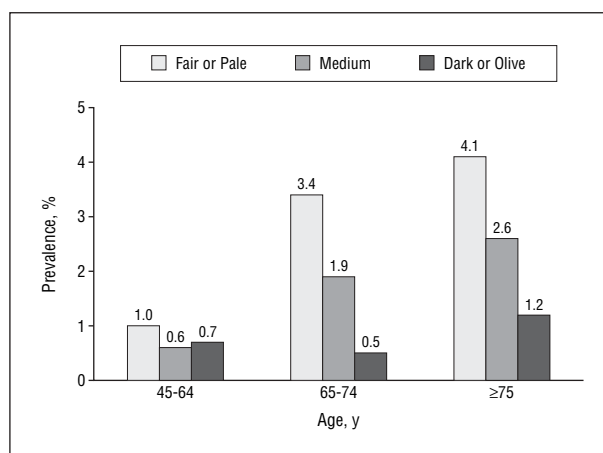‖χ^2 Trend, 10.8; P = .001.

Figure. Distribution of actinic keratoses (AKs) by age and skin type. The bars show the prevalence of AKs in the Italian population by skin type (fair or pale, medium, and dark or olive) in 3 different age groups (45-64, 65-74, and ≥75 years). Prevalence values (per 100 people) are indicated above the corresponding bars.

4. A history of nonmelanoma skin cancers was reported by 0.6% of the whole sample. There was a strong association between such a history and the presence of AKs as judged by the interviewer; the age- and sex-adjusted odds ratio was 4.5 (95% CI, 1.8-11.0).

COMMENT

Our study provides information about the prevalence of AKs in Italy. The study involved a complex proportional stratified sampling design, and our estimates are deemed to be representative of the whole Italian adult population (≥45 years). The prevalence in our study was remarkably lower than estimates obtained in other countries, such as the United States and Australia.[5-14] It should be noted that most of the available studies covered limited areas. The only study that was countrywide and relied on a sampling design similar to ours is the NHANES I study[5] conducted in the United States. The point

prevalence for AKs in that study ranged from 15.9 per 1000 at ages 45 to 54 years to 65.1 per 1000 at ages 65 to 74 years.[5] These figures are roughly 3 time higher than ours. To the best of our knowledge, only 3 studies provide estimates from European countries. In a study[12] conducted in south Wales, involving 1034 subjects 60 years or older, the prevalence of AKs was 23% (95% CI, 19.5%-26.5%). In a study[13] conducted in the Mersey region in northwest England of people older than 40 years (531 men and 437

Table 3. Sun Exposure and Sunscreen Use by Patients With Actinic Keratoses (AKs)

Characteristic	Cases, No.	AK Prevalence, % (95% CI)	OR (95% CI)*
Sun exposure during weekdays, h†			
<2	23	1.1 (0.6-1.5)	1.00
2	18	0.7 (0.4-1.0)	0.83 (0.44-1.54)
3-4	48	1.5 (1.1-1.9)	1.91 (1.13-3.21)
≥5	62	1.8 (1.3-2.2)	2.17 (1.29-3.65)
Days of sun exposure during holidays‡			
<8	27	1.0 (0.6-1.4)	1.00
8-19	23	1.0 (0.6-1.4)	1.43 (0.81-2.54)
20-39	22	0.9 (0.5-1.3)	1.30 (0.73-2.32)
≥40	51	1.9 (1.4-2.4)	2.12 (1.31-3.45)
Use of sunscreens			
Usually	42	1.1 (0.8-1.4)	1.00
Sometimes	21	1.0 (0.6-1.4)	0.88 (0.52-1.51)
Occasionally or never	116	1.8 (1.5-2.1)	1.12 (0.77-1.65)

Abbreviations: CI, confidence interval; OR, odds ratio.
*Estimates from multiple logistic regression including terms for sex, age, area of residence, and phenotype score.
†χ^2 Trend, 14.0; P = .002.
‡χ^2 Trend, 8.6; P = .003.

women) treated at outpatient (nondermatology) clinics, the prevalence of AKs was 15.4% in men and 5.9% in women. In another study,[14] conducted in the community of Freixo de Espada à Cinta in northeast Portugal, AKs were identified in 9.6% of subjects, and no relation was documented between skin phenotype and AKs. Interestingly, AKs were diagnosed in 3.6% of 190 adults treated at a cancer prevention program in Rome.[21] There are many reasons for the discrepancies between our data and those obtained in other studies. The method used to collect information in our survey may be of concern because we relied on evaluations by interviewers who, even though they had been trained, may have missed or misclassified cases. However, in preliminary exercises, the performance of interviewers in correctly classifying cases of AKs was judged to be satisfactory. In addition, we were unable to document large discrepancies between interviewers in case identification.

As expected,[6,7,12,13] the prevalence of AKs was higher in men than women. It increased significantly with age, with increased number of hours spent in the sun during weekdays and on holidays, and with more severe signs of purported skin photodamage (ie, facial wrinkles); and it was higher in people with a lighter skin phenotype. Actually, differences in prevalent skin phenotype, latitude, and sun exposure habits may explain, at least partly, the differences in prevalence between our study and similar surveys in other countries. Interestingly, the prevalence of AKs in Japan is considerably lower than the one we reported, ranging from 0.2% to 0.7%.[8-10]

In agreement with other surveys in Europe and the United States,[22,23] the level of awareness about AKs in the general population of Italy was rather low; 42% of subjects with AKs were unaware of their skin lesions. Only about 25% of all the subjects with AKs interviewed reported ever receiving a diagnosis of the condition, and as many as 25% of people with a history of AKs did not undergo any therapeutic procedure for the disease. In the United States, it was documented that only 40% of physicians who were aware of AKs treated the condition.[24]

The need to treat AKs is debatable, and a lively debate exists about whether AKs should be actually considered and treated as early squamous cell carcinoma.[25,26] From an epidemiological point of view, it has been estimated that the transformation rate of individual lesions is less than 1 in 1000 per year[27] and that the lifetime risk of invasive squamous cell carcinoma developing in an individual with AKs is 6% to 10%.[12,28] In addition, a remarkable turnover rate of these lesions in the general population has been documented with high incidence and spontaneous regression rates.[29] Actinic keratoses appear more frequently as multiple lesions and are associated with a higher risk of developing nonmelanoma skin cancers as indicated by our survey. Preventive treatment of cancer-prone areas with sun protection[30] and topical agents seems to represent a more reasonable option than destructive procedures performed on individual lesions. In our study, we were unable to document a protective effect from the use of sunscreens, but the percentage of people using sunscreens in the whole population was notably low (about 30%).

In conclusion, the prevalence of AKs in Italy was considerably lower than the prevalence in the United States and Australia. Age, skin phenotype, and sun exposure were strongly associated with the prevalence of these lesions; they seem to be underdiagnosed and undertreated in our population.

MD); Ospedale Principale Militare, Taranto (V. Cantoro, MD, and V. Ingordo, MD); Clinica Dermatologica, Università Verona (A. Barba, MD, and G. Tessari, MD); and Clinica Dermatologica S. Lazzaro, Università Torino (M. Pippione, MD, and D. Albertazzi, MD).

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