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Melanoma detection in Italian pigmented lesion clinics

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***Aim*. Accuracy in melanoma detection is important to recognize early curable melanomas and to minimize the unnecessary excision of benign lesions. The aim of this paper was to evaluate melanoma screening accuracy of Italian pigmented lesion clinics in terms of number needed to excise (NNE), melanoma thickness, and number of melanomas diagnosed during patient follow-up.**

***Methods*. Information on all skin tumors excised in 2011 were extracted from the databases of the participating centers. Information whether the lesion was excised at the baseline examination or during patient follow-up was recorded, as well as the overall number of patients examined in each center in 2011.**

***Results*. After e-mail solicitation, 22 of 40 centers agreed to**

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participate. A total of 8229 excised lesions were collected. The overall number of examined patients was 86.564, thus 9.5% of screened patients had a lesion removed. Of the excised lesions, 866 were diagnosed as melanoma (1% of examined patients) and 5311 (88.9%) were melanocytic nevi. Three NNE were calculated giving values of 7.9 excised lesions to find 1 melanoma, 7.1 melanocytic lesions to find 1 melanoma, and 3.7 lesions to find 1 skin malignancy. The median melanoma thickness was 0.6 mm, with only 15.1% of melanomas ≥1 mm of thickness. Melanomas detected over time were 96 (11.1%; mean thickness, 0.3 mm), with 15.6% of lesions excised after short-term follow-up and 84.4% after long-term follow-up.

***Conclusion*. The NNE values comparable to those achieved in specialized clinical settings and the high number of early melanomas diagnosed at the baseline examination or during patient follow-up indicate a high level of accuracy in melanoma screening achieved by Italian pigmented lesion clinics.**

KEY WORDS: Melanoma - Nevus, pigmented - Clinical laboratory techniques – Dermoscopy.

Accuracy in melanoma detection is important for two reasons: the first is related to the potential mortality of melanoma if early diagnosis is not carried out, and the second concerns the high incidence of its benign counterpart, the melanocytic nevus. The aim of a clinician is therefore to recognize every potential melanoma as soon as possible, but also to minimize the unnecessary excision of benign lesions, which is actually responsible of most of the costs and morbidity related to melanoma screening.[1]

Because of the increased public awareness on melanoma and the spreading use of dermoscopy in most of private and public pigmented lesion clinics, the number of excised early melanomas has increased dramatically in the last 20 years. Much attention is given today to the number needed to excise (NNE), a very useful way to measure the efficacy of melanoma screening, which is based on the number of benign lesions that are needed to be excised to find one melanoma. NNE values vary according to clinician expertise, with reported values ranging from 20 to 40 for general practitioners at non-specialized clinics, from 19 to 28 for general practitioners at skin cancer clinics, and from 4 to 18 for dermatologists at specialized clinics.[2, 3]

Thus, the less is the NNE value the better is supposed to be the screening performance. However, the NNE value cannot be used as a measure of the clinician accuracy in detecting early melanoma, which is better evaluated by taking into consideration the Breslow thickness, the number of excised in situ melanomas and the number and thickness of melanomas detected during patient follow-up. By analyzing the number and type of lesions excised during one year of routine activity in several Italian pigmented lesion clinics, the aim of this study was to evaluate the accuracy of melanoma screening in terms of NNE, melanoma thickness, and number of melanomas diagnosed during patient follow-up.

Materials and methods

Italian dermatology pigmented lesion clinics were invited to participate in the survey through e-mail solicitation to members of the Gruppo di Studio Diagnostica non Invasiva ed Epiluminescenza of the Società Italiana di Dermatologia medica, chirurgica, estetica e di Malattie Sessualmente Trasmesse (SIDeMaST). Recruitment was targeted to include cases from both public institutions and private practices.

From the databases of the participating centers we extracted information on all skin tumors that were excised in 2011 (during routine activity of melanoma screening) and diagnosed histopathologically. Lesions excised for cosmetic purposes were excluded. The data collected included the histopathologic diagnosis, the age and sex of the patient, and Breslow thickness in the case of melanoma. In addition, the information whether the lesion was excised at the baseline examination or during patient follow-up was recorded, as well as the overall number of patients examined in each of the participating centers in 2011. In all centers standard patient examination included clinical and dermoscopic assessment of the individual lesions.

Three NNE values were calculated: 1) melanoma *vs.* all benign lesions, by dividing the total number of excised benign lesions and melanomas by the number of melanomas; 2) melanoma vs nevi, by dividing the total number of excised melanocytic lesions by the number of melanomas; and 3) malignant vs all benign lesions, by dividing the total number of excised lesions by the number of malignant lesions.

Results

Twenty-two of 40 dermatologic centers that were solicited by e-mail agreed to participate in the survey. The participating clinics (18 public institutions

and 4 private units) contributed a total of 8229 histopathologically confirmed cases that were excised in 2011. In the same year, the overall number of examined patients was 86,564 (mean: 3934.7 patients per center); thus, 9.5% of patients seen at the participating centers had a lesion removed.

Patients with an excised lesion had mean age of 46.7 years (SD 17.2). Excision was performed in 103 (1.3%) patients aged <15 years, in 5011 (60.9%) patients aged 15-50 years, and in 2971 (36.1%) patients aged >50 years (age missing for 144 patients; Figure 1). Women had an excised lesion slightly more frequently than man (51.7% *vs.* 48.3%; gender missing for 183 patients).

Of the 8229 excised lesions, 866 were diagnosed histopathologically as melanoma, accounting for 1% of examined patients. A basal cell carcinoma was diagnosed in 1052 patients, whereas 305 lesions were squamous cell carcinomas (141 invasive e 164 in situ), and 30 lesions were classified as other malignancies (including 10 Kaposi sarcomas, 6 cutaneous lymphomas, 4 dermatofibrosarcoma protuberans, 4 adnexal carcinomas, 2 Merkel cell carcinomas, 2 skin metastases, 1 Paget's disease, and 1 atypical fibroxanthoma), for a total of 2253 excised malignant skin tumors.

Of the remaining 5976 excised lesions, 5311 (88.9%) were diagnosed histopathologically as melanocytic nevi (80.4% acquired/Clark nevi, 9.7% congenital nevi, 7.0% Spitz nevi, and 2.9% blue nevi). A seborrheic keratosis was diagnosed in 264 (4.4%) cases, a lentigo in 91 (1.5%) cases, dermatofibroma in 103 (1.7%) cases, angioma in 73 (1.2%) cases, and other benign skin tumors in 134 (2.2%) cases. Three NNE were then calculated giving values of 7.9 excised lesions to find 1 melanoma, 7.1 excised melanocytic lesions to find 1 melanoma, and 3.7 excised lesions to find 1 skin malignancy. The NNE to find a skin malignancy was also calculated subdividing patients in the 3 age groups previously mentioned, giving values of 103, 7.7 and 1.9 in patients aged <15 years, 15-50 years, and >50 years, respectively.

The mean age of patients with melanoma was 54.7 years (17 to 89 years; 52.4% females). Of the 866 excised melanomas, 333 (38.5%) were in situ, 377 (43.5%) had a Breslow thickness <1.0 mm, and 131 (15.1%) had thickness ≥1 mm (missing Breslow in 25 cases), with a median thickness of 0.6 mm (0.2 to 19 mm) for all invasive melanomas.

Overall, 7127 (86.7%) lesions were excised at the baseline patient examination and 1102 (13.4%)

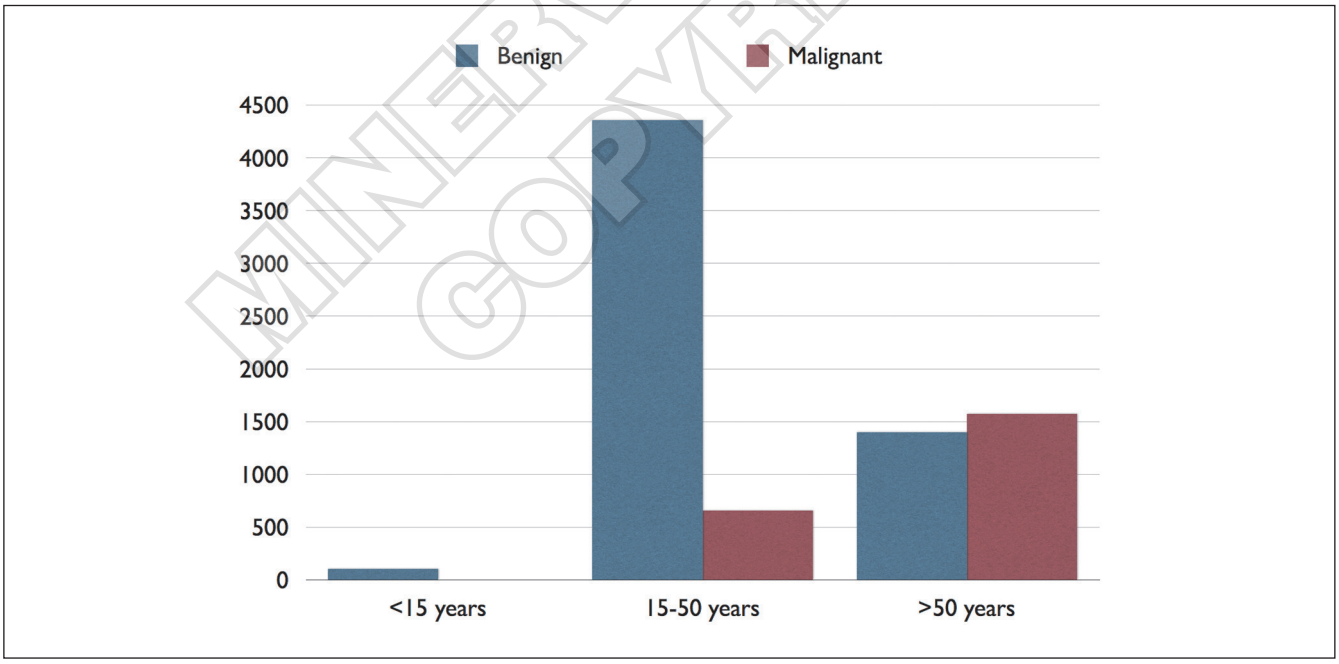

Figure 1.—Number of benign and malignant lesions excised in patients of different age groups.

lesions were excised during patient follow-up. Of those, 331 (30%) were excised after short-term follow-up (STFU, <6 months) and 771 (70%) after long-term follow-up (LTFU, 6 to 90 months). Melanomas detected during patient monitoring were 96 (11.1%), with 15 (15.6%) lesions excised after STFU and 81 (84.4%) melanomas diagnosed after LTFU (mean monitoring time of 15.4 months). Of the melanomas detected over time, 47 (49%) were situ, 42 (43.8%) had thickness <1.0 mm, and 7 (7.3%) had thickness ≥1 mm, with a mean thickness of 0.3 mm for all invasive melanomas excised during follow-up.

Discussion

Our analysis, conducted in 22 centers, provides various information concerning routine screening activity for skin cancer in Italy. About 10% of examined patients had a lesion removed and 1% was diagnosed with melanoma. In a previous study preformed in Australia,[4] about 9% of screened patients were referred to biopsy but only 0.2% were diagnosed with melanoma. The higher prevalence of melanomas in our population might be explained by the differences in the Italian and Australian health care systems. In Australia referrals are performed by general physicians, whereas in Italy patients are usually seen by the territorial dermatologist who will eventually better select suspicious lesions to be excised in the referral center.

Acquired/Clark nevi were the most frequently excised benign lesions and most of them were excised in patients aged 15 to 50 years (Figure 1). Similar findings were reported in a multicenter survey aimed to assess accuracy in melanoma detection based on NNE values over a 10-year period.[5] In this study, the highest overall number of excised nevi was from patients between 31 and 40 years of age, followed by the 21 to 30 years of age group and the 41 to 50 years of age group. These findings might be explained by the higher prevalence of patients with multiple atypical nevi in young age groups. Nevi that exhibit atypical clinical features require excision to rule out melanoma; consequently, much of the economic burden of melanoma screening results from excisions and biopsies of benign lesions, especially in young adults with multiple nevi.[1]

NNE values achieved in our study are similar to those obtained in specialized clinical settings.[5] In Italian pigmented lesions clinics, about 8 lesions were excised to find 1 melanoma, about 7 melanocytic lesions to find 1 melanoma, and about 4 lesions to find 1 skin malignancy. In the survey previously mentioned,[5] the overall NNE values (the number of excised melanocytic lesions to find 1 melanoma) achieved in specialized and non-specialized clinical settings in the 10-year period (between 1998 and 2007) were 8.7 and 29.4, respectively. The NNE improved over time in specialized centers (from 12.8 to 6.8), but appeared unchanged in non-specialized centers. The most plausible explanation for these data could be the expanding use of dermoscopy, especially in specialized settings.[6, 7] In an earlier study conducted in a specialized center over a 5-year period when dermoscopy was gradually introduced, the malignant/benign ratio improved from 1:18 to 1:4.3, but only for clinicians who used dermoscopy. No significant improvement was found for clinicians who did not use dermoscopy.[3] In Italy diagnosis occurs mainly in dermatology unit (91%) and clinical and dermoscopy examination is available at first consultation in more than 70% of the centers.[8]

A quite surprising result of our study is related to the proportion of thick melanomas found on routine patient examination in Italy. In our survey involving dermatologic centers, only 15% of melanomas were thicker than 1 mm, eventually reflecting a very high efficiency in detecting early melanoma. In 2 recent, large studies conducted in Australia and United States,[9, 10] the reported prevalence of melanomas thicker than 1 mm was about 30%, *i.e.* twice as many as is our study. Our data should, therefore, be interpreted cautiously. A previous study assessing time trends of melanoma in Queensland, Australia and Central Europe found that in Central Europe, the median tumor thickness decreased from 1.2 mm in 1986 to 0.8 mm in 1996, whereas it varied insignificantly between 0.5 mm and 0.6 mm in Queensland.[11] In our study, a median thickness of 0.6 mm was found, thus comparable to that reported in Central Europe and Queensland. However, the lower proportion of thick melanomas in our study can presumably be explained by a tendency of thicker melanomas to be excised in oncologic or plastic surgery settings rather than in dermatologic pigmented lesion clinics.

In all, about 13% of lesions were excised during patient follow-up and, of those, 70% after LTFU. About 11% of melanomas were detected during patient monitoring and the majority (84.4%) were

excised after LTFU (mean monitoring time, 15.4 months). It is a matter of fact that a certain proportion of melanomas are today discovered over time.[12] The strategy of monitoring patients has the 2-fold advantage to decrease the number of unnecessary excision of benign lesions while maximizing the early detection of inconspicuous melanomas that are not recognizable at the baseline examination. Two monitoring strategies are employed, one (STFU) designed for patients with individual slightly atypical lesions,[13] and the second (LTFU) used for patients with multiple nevi.[14, 15] The fact that most of the melanomas detected over time were excised after LTFU indicates that in our study the follow-up procedure was mainly used for patients with multiple nevi. In these patients most melanomas discovered on follow-up were slow-growing as demonstrated by the low mean thickness (0.3 mm) and by the high proportion of in situ and thin invasive melanomas excised over time (92.8%). Our study thus confirms the safety of this procedure, as previously reported in a study involving 103 melanomas excised after a median follow-up of 20 months.[16]

Conclusions

In conclusion, our study provides useful information on the screening activity performed in Italian pigmented lesion clinics. The NNE values comparable to those achieved in specialized clinical settings and the high number of early melanomas diagnosed at the baseline examination or during patient follow-up indicate a high level of accuracy in melanoma screening achieved by Italian clinicians devoted to the daily activity of melanoma screening.

References

1. Baade PD, Youl PH, Janda M, Whiteman DC, Del Mar CB, Aitken JF. Factors associated with the number of lesions excised for each skin cancer: a study of primary care physicians in Queensland, Australia. Arch Dermatol 2008;144:1468-76.
2. Hansen C, Wilkinson D, Hansen M, Argenziano G. How good are skin cancer clinics at melanoma detection? Number needed to treat variability across a national clinic group in Australia. J Am Acad Dermatol 2009;61:599-604.
3. Carli P, De Giorgi V, Crocetti E, Mannone F, Massi D, Chiarugi A *et al.* Improvement of malignant/benign ratio in excised melanocytic lesions in the "dermoscopy era": a retrospective study 1997-2001. Br J Dermatol 2004;150:687-92.
4. Aitken JF, Janda M, Elwood M, Youl PH, Ring IT, Lowe JB. Clinical outcomes from skin screening clinics within a community-based melanoma screening program. J Am Acad Dermatol 2006;54:105-14.
5. Argenziano G, Cerroni L, Zalaudek I, Staibano S, Hofmann-Wellenhof R, Arpaia N *et al.* Accuracy in melanoma detection: a 10-year multicenter survey. J Am Acad Dermatol 2012;67:54-59.
6. Rose SE, Argenziano G, Marghoob AA. Melanomas difficult to diagnose via dermoscopy. G Ital Dermatol Venereol 2010;145:111-26.
7. Roldán-Marín R, Puig S, Malvehy J. Dermoscopic criteria and melanocytic lesions. G Ital Dermatol Venereol 2012;147:149-59.
8. Stanganelli I, Ascierto P, Bono R, De Giorgi V, Pimpinelli N, Chiarion-Sileni V *et al.* Diagnostic Services for Melanoma in Italy. Dermatology 2013;226:3-6.
9. Baade P, Meng X, Youlden D, Aitken J, Youl P. Time trends and latitudinal differences in melanoma thickness distribution in Australia, 1990-2006. Int J Cancer 2012;130:170-8.
10. Criscione VD, Weinstock MA. Melanoma thickness trends in the United States, 1988-2006. J Invest Dermatol 2010;130:793-7.
11. Garbe C, McLeod GR, Buettner PG. Time trends of cutaneous melanoma in Queensland, Australia and Central Europe. Cancer 2000;89:1269-78.
12. Kittler H, Guitera P, Riedl E, Avramidis M, Teban L, Fiebiger M *et al.* Identification of clinically featureless incipient melanoma using sequential dermoscopy imaging. Arch Dermatol 2006;142:1113-9.
13. Menzies SW, Gutenev A, Avramidis M, Batrac A, McCarthy WH. Short-term digital surface microscopic monitoring of atypical or changing melanocytic lesions. Arch Dermatol 2001;137:1583-9.
14. Salerni G, Carrera C, Lovatto L, Martí-Laborda RM, Isern G, Palou J *et al.* Characterization of 1152 lesions excised over 10 years using total-body photography and digital dermatoscopy in the surveillance of patients at high risk for melanoma. J Am Acad Dermatol 2012;67:836-45.
15. Salerni G, Terán T, Puig S, Malvehy J, Zalaudek I, Argenziano G *et al.* Meta-analysis of digital dermoscopy follow-up of melanocytic skin lesions: a study on behalf of the International Dermoscopy Society. J Eur Acad Dermatol Venereol 2013;27:805-14.
16. Argenziano G, Kittler H, Ferrara G, Rubegni P, Malvehy J, Puig S *et al.* Slow-growing melanoma: a dermoscopy follow-up study. Br J Dermatol 2010;162:267-73.

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