CLINICAL-PATHOLOGICAL CHARACTERISTICS OF CUTANEOUS MELANOMA IN THE EUROPEAN COUNTRY WITH THE HIGHEST INCIDENCE: A POPULATION-BASED STUDY, 1996-2011

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BACKGROUND

The incidence of cutaneous melanoma has increased worldwide over several decades, with the exception of Australia, where a recent decline has been observed. [1-2] Switzerland has the highest incidence rate of melanoma in Europe, even higher than those observed in other high-incidence countries such as Norway, Sweden, Denmark and the Netherlands. [1-3] Together with the increased incidence, a change in the mortality trend has not been reported in Europe yet. [1-2, 4] Early detection of melanoma is promoted in Switzerland through whole-body skin examinations by health professionals and through skin self-examinations. According to recent results from the Swiss Health Survey, the proportion of the population who had a skin examination by a health professional increased from 1997 onwards, reaching 35% in 2007. [5] The present study has two aims. First, to evaluate melanoma incidence and mortality trends over the past 15 years in Canton Ticino, the region with the highest European incidence rate. Second, to match melanoma incidence and mortality trends with clinical-pathological prognostic factors to gain insights into the effectiveness of the current spontaneous screening strategy and on the secondary prevention campaign organised during the last decade.

MATERIALS & METHODS

Case selection. All invasive and in-situ incident cases occurred in 1996-2011 were selected from the archives of the population-based Ticino Cancer Registry. Histological subtypes were defined as follows: superficial spreading melanoma (SSM; ICD-O-3: 8743), nodular melanoma (NM; ICD-O-3: 8721), lentigo maligna melanoma (LMM; ICD-O-3: 8742), melanoma not otherwise specified (MNOS; ICDO3: 8720) and other types (ICD-O-3: 8730, 8744, 8745, 8772). [6-7] Breslow thickness was classified as thin (≤ 1.00 mm), intermediate (1.01-2.00 mm) and thick (≥2.01 mm), as indicated by Balch *et al.* [8]

Statistical analysis. European age-standardized incidence and mortality rates were calculated per 100'000 person-years through the direct method. [9] Trends were measured as the annual percentage change (APC) and the corresponding confidence interval (95%CI), using the weighted least squared method (SEER*Stat 7.0.9 software, www.seer.cancer.gov/seerstat). In-depth trends analysis was performed by histological types and Breslow thickness.

RESULTS

Clinical-pathological characteristics data. A total of 1464 patients had a diagnosis of cutaneous melanoma, 1230 invasive and 234 in-situ. Table 1 summarises the main clinical-pathological characteristics of invasive melanomas according to the histological types, categorized as follows: SSM (55.7%), NM (10.0%), LMM (5.5%), MNOS (25.2%) and other-types (3.6%). The four histotypes differed significantly by mean age at diagnosis (*p<0.0001*), SSM being the youngest group. As expected, NM showed the highest mean Breslow thickness. Particularly, 77.1% of NM had a Breslow thickness higher than 2.00 mm, whereas SSM had a Breslow thickness ≤1.00 mm in 78.6% of cases (*p<0.0001*). NM also represents the histological type with the highest proportion of positive lymph node involvement (23.8%, *p<0.0001*). The highest prevalence of M1 cases was observed in MNOS (7.1%) and other types of melanoma (4.5%) (*p<0.0001*).

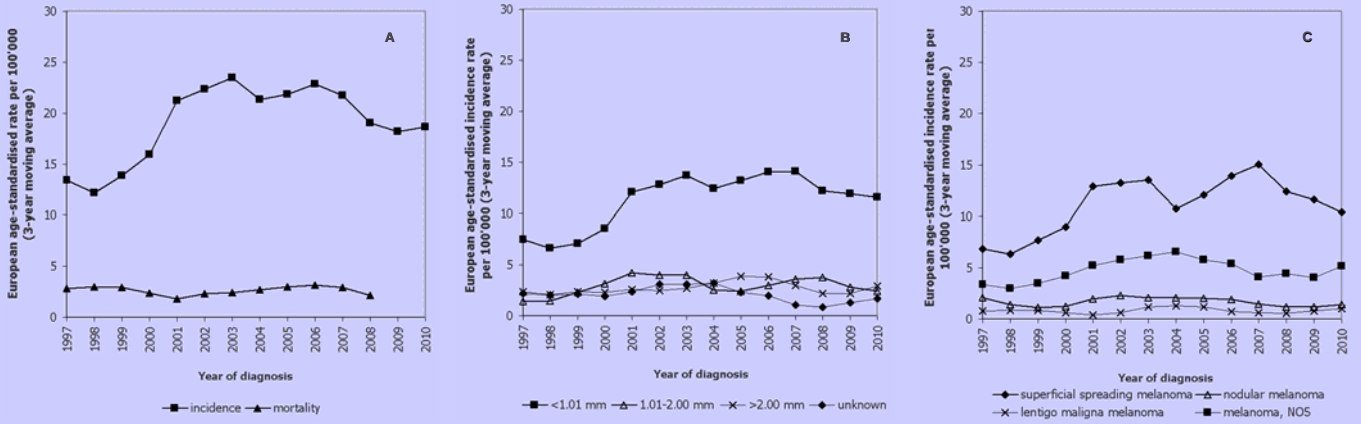
Table 1. Main clinical-pathological characteristics of invasive melanoma diagnosed in male and females, Canton Ticino, 1996-2011.

Variable	All cases *N = 1230* (100%)	SSM *N = 685* (55.7%)	NM *N = 123* (10.0%)	LMM *N = 68* (5.5%)	MNOS *N = 310* (25.2%)	Other *N = 44* (3.6%)	*P*-value
Age (yrs) mean±SD median range	58.4±17.2 60 13-95	55.5±16.4 56 17-95	64.2±16.3 67 24-94	72.3±11.0 73.5 48-95	58.7±18.2 60 13-94	62.8±16.6 63.5 26-90	*<0.0001* *<0.0001*
Age-specific groups, n (%) <50 50-59 60-69 70-79 ≥80	398 (32.4%) 211 (17.1%) 250 (20.3%) 243 (19.8%) 128 (10.4%)	262 (38.3%) 133 (19.4%) 129 (18.8%) 116 (16.9%) 45 (6.6%)	28 (22.8%) 11 (8.9%) 27 (22.0%) 40 (32.5%) 17 (13.8%)	2 (2.9%) 8 (11.8%) 18 (26.5%) 24 (35.3%) 16 (23.5%)	96 (31.0%) 54 (17.4%) 63 (20.3%) 53 (17.1%) 44 (14.2%)	10 (22.7%) 5 (11.4%) 13 (29.6%) 10 (22.7%) 6 (13.6%)	*<0.0001*
Sex, n (%) women men	611 (49.7%) 619 (50.3%)	356 (52.0%) 329 (48.0%)	53 (43.1%) 70 (56.9%)	30 (44.1%) 38 (55.9%)	148 (47.7%) 162 (52.3%)	24 (54.5%) 20 (45.5%)	*0.2580*
Tumour localisation, n (%) head and neck trunk upper limb and shoulder lower limb and hip not otherwise specified	175 (14.2%) 436 (35.5%) 262 (21.3%) 309 (25.1%) 48 (3.9%)	43 (6.3%) 278 (40.6%) 170 (24.8%) 180 (26.3%) 14 (2.0%)	20 (16.3%) 53 (43.1%) 26 (21.1%) 21 (17.1%) 3 (2.4%)	55 (80.9%) 5 (7.3%) 4 (5.9%) 3 (4.4%) 1 (1.5%)	47 (15.2%) 96 (31.0%) 53 (17.1%) 86 (27.7%) 28 (9.0%)	10 (22.7%) 4 (9.1%) 9 (20.5%) 19 (43.2%) 2 (4.5%)	*<0.0001*
Breslow thickness (mm) mean±SD median range unknown (n)	1.57±2.56 0.72 0.09-36.00 143	0.94±1.46 0.60 0.09-25.00 23	4.40±3.19 3.33 0.60-18.00 5	0.68±0.72 0.45 0.10-5.00 6	2.07±3.70 1.05 0.11-36.00 97	2.57±2.74 1.7 0.30-10.00 12	*<0.0001* *<0.0001*
Breslow thickness categories, n (%) ≤1.00 mm 1.01-2.00 mm ≥2.01 mm unknown	698 (64.2%) 182 (16.7%) 207 (19.1%) 143	520 (78.6%) 91 (13.7%) 51 (7.7%) 23	9 (7.6%) 18 (15.3%) 91 (77.1%) 5	51 (82.3%) 9 (14.5%) 2 (3.2%) 6	106 (49.8%) 56 (26.3%) 51 (23.9%) 97	12 (37.5%) 8 (25.5%) 12 (37.5%) 12	*<0.0001*
Lymph nodes status N0 N+ Unknown	1019 (90.7%) 105 (9.3%) 106	631 (96.0%) 26 (4.0%) 28	93 (76.2%) 29 (23.8%) 1	59 (96.7%) 2 (3.3%) 7	208 (83.2%) 42 (16.8%) 60	28 (82.4%) 6 (17.6%) 10	*<0.0001*
Distant metastasis M0 M1	1200 (97.6%) 30 (2.4%)	683 (99.7%) 2 (0.3%)	119 (96.7%) 4 (3.3%)	68 (100%) 0 (0%)	288 (92.9%) 22 (7.1%)	42 (95.5%) 2 (4.5%)	*<0.0001*

SSM= superficial spreading melanoma; **NM**= nodular melanoma; **LMM**= lentigo maligna melanoma; **MNOS**= melanoma not otherwise specified

Incidence and Mortality data. Trends analyses are reported graphically in Figure 1. Incidence rate of invasive melanoma rose from 17.4 per 100'000 inhabitants in 1996-2003 to 20.6 in 2004-2011, with an overall APC of +2.1% (%95CI: -0.8/+5.1; *p=0.15*). The increasing incidence trend was particularly observed for SSM (APC= +2.9%; %95CI: -1.1/+7.0; *p=0.14*) and thin melanomas (i.e. ≤1.00mm) (APC= +3.4%; %95CI: +0.2/+6.7; *p=0.04*), whereas we detected a descriptive growing incidence for thick melanomas (APC= +2.1; %95CI: -1.4/+5.8; *p=0.22*). For the mortality data, age-standardised rates were substantially constant along the entire study period.

Figure 1. Trends of age-standardized rates (3-year moving average) for overall melanoma incidence and mortality (A), incidence by Breslow thickness (B) and histotypes (C), Canton Ticino, 1997-2010.



CONCLUSIONS

Some studies suggested that the increase of diagnosis of thin melanomas and superficial spreading melanomas can be attributable to early prevention campaigns. [10] Others have claimed that the increase in incidence of melanoma observed in many countries could be attributed to pathologists who more frequently diagnose melanoma instead of atypical or dysplastic melanocytic lesions. difficult to be demonstrated without a histological revision studies. [11] Our population-based study confirms that also in a country with the highest incidence of cutaneous melanomas, such as Switzerland, opportunistic screening strategy does not change the incidence of nodular and thick melanomas and does not reduce the overall mortality. If true control of melanoma mortality has been achieved during the past few years (maintaining a steady mortality despite increased incidence), it is probable that additional public health efforts could be proposed with the goal of a real mortality reduction.

REFERENCES

1. Curado MP, Edwards B, Shin HR, Storm H, Ferlay J, Heanue M, et al. *Cancer Incidence in Five Continents, Vol. IX. IARC Scientific Publications No. 160.* Lyon: IARC, 2007.
2. Ferlay J, Shin H, Bray F, Forman D, Mathers C, Parkin D. *GLOBOCAN 2008, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 10.* Lyon: International Agency for Research on Cancer, 2008.
3. Bordoni A, Spitale A, Peverelli S, Mazzola P. *Registro cantonale dei tumori.* http://www.ti.ch/cancer, 2011.
4. de Vries E, Coebergh JW. Cutaneous malignant melanoma in Europe. *Eur J Cancer* 2004;40(16):2355-66.
5. Wyss N, Roy E. *Epidemiology of Melanoma.* Federal Office of Statistics, Neuchatel 2012.
6. Fritz A, Percy C, Jack A, Shanmugaratnam K, Sobin L, Parkin DM, et al. *International Classification of Diseases for Oncology.* 3rd ed. Geneva: World Health Organization, 2000.
7. LeBoit PE, Burg G, Weedon D, Sarasin A. *Pathology and genetics of skin tumours.* Lyon: IARC*Press*; 2006.
8. Balch CM, Gershenwald JE, Soong SJ, Thompson JF, Atkins MB, Byrd DR, et al. Final version of 2009 AJCC melanoma staging and classification. *J Clin Oncol* 2009;27(36):6199-206.
9. Esteve J, Benhamou E, Raymond L. *Statistical methods in cancer research, vol. 4.* Lyon: IARC Scientific Publications, World Health Organisation, 1994.
10. Luke CG, Coventry BJ, Foster-Smith EJ, Roder DM. A critical analysis of reasons for improved survival from invasive cutaneous melanoma. *Cancer Causes Control* 2003;14(9):871-8.
11. Levell NJ, Beattie CC, Shuster S, Greenberg DC. Melanoma epidemic: a midsummer night's dream? *Br J Dermatol* 2009;161(3):630-4.