# CUTANEOUS MELANOMA IN OLDER AND ELDERLY PATIENTS

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## Background

In industrialised countries, the ageing population is steadily increasing. The incidence of cutaneous malignant melanoma (CMM) is higher in the elderly. This study aims to evaluate the clinic-pathological profile of CMM and diagnostic-therapeutic performance indicators in the elderly.

## Materials and Methods

This retrospective population cohort study included 1,368 incident CMMs registered in 2017 by the Veneto Regional Cancer Registry (north-eastern Italy). The very elderly were categorised as great elderly (≥ 80 years), elderly (65-79 years) and adult (<65 years). The strength of the association between pairs of variables was tested using the Cramér-V method. Using the age groups as dependent variable, an ordered logistic regression was applied using the variables of the clinical-pathological profile of CMM as covariate. In each of the three age groups, clinical performance indicators were calculated using the Clopper-Pearson exact method.

## Results

All the considered CMM clinicopathological variables differed significantly by patient age (Table 1). On comparing the three age-groups, significant differences emerged in CMM topography, prevalence of histotype and ulcer lesions, and CMM thickness. Moreover, the prevalence of high *versus* low mitotic count steadily increased by age (<65=21.8%; 65-79=32.8%; ≥80=50.3%) and very elderly patients showed a significantly higher prevalence of vertical growth pattern and the lowest prevalence of tumor infiltrating lymphocytes (TIL). At initial diagnosis, the prevalence of TNM stage I was lowest among very-elderly patients and steadily increased by age group (44.1% *versus* 60.4% *versus* 77.6%). Multivariable ordered logistic regression (Table 2) confirmed the associations between age groups and tumor site, prevalence of TILs and CMM stage at clinical presentation.
Table 3 focuses on the association between age groups and clinical performance indicators. The percentage of patients with 1-4 mm thick lesions admitted to sentinel lymph node biopsy (SLNB) decreased as age increased. Notably, fewer SLNB-positive patients underwent lymphadenectomy. The prevalence of TNM stage IB–III CMM patients treated with wide surgical excision who underwent nodal ultrasound within 12 months of CMM presentation was significantly lower in the ≥80s than in the other age groups.

| | CMM Patients by age groups | | | P value | | | |
|---|---|---|---|---|---|---|---|
| | <65 N = 779 (56.9%) | 65-79 N = 408 (29.8 %) | ≥80 N = 181 (13.2%) | All age groups | <65 vs. 65-79 | <65 vs. ≥80 | 65-79 vs. ≥80 |
| **Sex** | | | | | | | |
| Male | 371 (47.6) | 262 (64.2) | 93 (51.4) | **<0.001** | **<0.001** | 0.407 | **0.009** |
| Female | 408 (52.4) | 146 (35.8) | 88 (48.6) | | | | |
| **Primary CMM site** | | | | | | | |
| Lower limbs | 155 (20.4) | 62 (16.2) | 31 (18.1) | | | | |
| Upper limbs | 95 (12.5) | 46 (12.0) | 31 (18.1) | **<0.001** | **<0.001** | **<0.001** | **<0.001** |
| Head | 47 (6.2) | 68 (17.7) | 36 (21.1) | | | | |
| Hands/feet | 25 (3.3) | 19 (5.0) | 19 (11.1) | | | | |
| Trunk | 438 (57.6) | 188(49.1) | 54 (31.6) | | | | |
| **CMM histotype** | | | | | | | |
| Superficial spreading | 591 (75.9) | 269 (65.9) | 88 (48.6) | | | | |
| Nodular | 81 (10.4) | 72 (17.6%) | 53 (29.3) | | | | |
| Lentigo maligna | 8 (1.0) | 14 (3.4%) | 10 (5.5) | | | | |
| Acral-lentiginous | 11 (1.4) | 5 (1.2%) | 7 (3.9) | **<0.001** | **<0.001** | **<0.001** | **0.001** |
| Desmoplastic | 1 (0.1) | 3 (0.7) | 3 (1.7) | | | | |
| Spitzoid | 25 (3.2) | 5 (1.2) | 0 | | | | |
| CMM not otherwise specified | 62 (8.0) | 40 (9.8) | 20 (11.0) | | | | |
| **CMM thickness (Breslow)** | | | | | | | |
| ≤ 0.75 | 433 (58.4) | 171 (46.0) | 50 (29.9) | | | | |
| 0.76-1.50 | 174 (23.4) | 75 (20.2) | 29 (17.4) | **<0.001** | **<0.001** | **<0.001** | **<0.001** |
| 1.51-3.99 | 95 (12.8) | 73 (19.6) | 34 (20.4) | | | | |
| ≥ 4.00 | 40 (5.4) | 53 (14.2) | 54 (32.3) | | | | |
| **Clark's levels** | | | | | | | |
| I | 2 (0.3) | 1 (0.3) | 0 | | | | |
| II | 223 (33.1) | 77 (23.7) | 28 (19.2) | | | | |
| III | 283 (42.0) | 105 (32.3) | 39 (26.7) | **<0.001** | **<0.001** | **<0.001** | 0.096 |
| IV | 155 (23.0) | 122 (37.5) | 61 (41.8) | | | | |
| V | 11 (1.6) | 20 (6.2) | 18 (12.3) | | | | |
| **Growth pattern** | | | | | | | |
| Radial | 183 (28.8) | 69 (22.2) | 18 (14.1) | **<0.001** | 0.073 | **0.002** | 0.073 |
| Vertical | 452 (71.2) | 242 (77.8) | 110 (85.9) | | | | |
| **CMM Ulceration** | | | | | | | |
| Present | 94 (12.7) | 86 (23.1) | 71 (43.3) | **<0.001** | **<0.001** | **<0.001** | **<0.001** |
| Absent | 644 (87.3) | 286 (76.9) | 93 (56.7) | | | | |
| **Mitotic count per HPF** | | | | | | | |
| 0-2 | 546 (78.2) | 238 (67.2) | 76 (49.7) | **<0.001** | **<0.001** | **<0.001** | **<0.001** |
| >2 | 152 (21.8) | 116 (32.8) | 77 (50.3) | | | | |
| **TIL** | | | | | | | |
| Present | 520 (76.5) | 246 (70.7) | 96 (64.4) | 0.005 | 0.105 | 0.01 | 0.202 |
| Absent | 160 (23.5) | 102 (29.3) | 53 (35.6) | | | | |
| **TNM Stage** | | | | | | | |
| I | 588 (77.6) | 239 (60.4) | 78 (44.1) | | | | |
| II | 72 (9.5) | 80 (20.2) | 66 (37.3) | <0.001 | <0.001 | <0.001 | <0.001 |
| III | 72 (9.4) | 49 (12.4) | 20 (11.3) | | | | |
| IV | 26 (3.4) | 28 (7.1 | 13 (7.3) | | | | |

**Table 1. Cutaneous malignant melanoma (CMM): pathology by age.**

| | ≥65 *versus* <65 | | ≥80 *versus* <80 | |
|---|---|---|---|---|
| | OR | p-value | OR | p-value |
| **Sex (reference: Female)** | | | | |
| Male | 1.66 | **<0.001** | 0.95 | 0.763 |
| **Tumor site (reference: Upper limbs)** | | | | |
| Lower limbs | 0.86 | 0.486 | 0.73 | 0.259 |
| Head | 2.72 | **<0.001** | 1.33 | 0.314 |
| Hands/feet | 2.10 | **0.019** | 2.17 | **0.030** |
| Trunk | 0.69 | **0.043** | 0.48 | **0.003** |
| Missing | 1.75 | 0.204 | 0.63 | 0.421 |
| **Histologic subtype (reference: Nodular melanoma)** | | | | |
| Superficial spreading | 1.06 | 0.768 | 0.83 | 0.472 |
| Other | 0.68 | 0.113 | 0.78 | 0.394 |
| **Growth type (reference: Radial)** | | | | |
| Vertical | 1.24 | 0.186 | 1.60 | 0.099 |
| Missing | 1.70 | 0.012 | 2.28 | 0.012 |
| **Mitotic count per high power microscopic field** | | | | |
| >2 | 1.18 | 0.374 | 1.55 | 0.076 |
| Missing | 1.08 | 0.770 | 1.29 | 0.460 |
| **Tumor infiltrating lymphocytes (reference: Present)** | | | | |
| Absent | 1.37 | **0.028** | 1.30 | 0.182 |
| Missing | 1.14 | 0.577 | 1.72 | 0.078 |
| **TNM Stage (reference: stage I)** | | | | |
| II | 2.66 | **<0.001** | 2.40 | **0.001** |
| III | 1.35 | 0.198 | 0.89 | 0.731 |
| IV | 1.81 | 0.114 | 1.08 | 0.875 |
| Missing | 1.18 | 0.697 | 0.49 | 0.244 |

**Table 2. Ordered logistic regression models**

| INDICATOR | TH (%) * | Age <64 years % (95% C.I.) | Age 65-79 years % (95% C.I.) | Age ≥80 years % (95% C.I.) | P-value All age groups | P-value <65 *vs* 65-79 | P-value <65 *vs* ≥80 | P-value 65-79 vs ≥80 | N | % |
|---|---|---|---|---|---|---|---|---|---|---|
| Percentage of new cases of invasive CMM assessed for neoplastic ulcer | ≥90 | 94.87 (93.07-96.31) | 91.42 (88.27-93.95) | 90.61 (85.39-94.43) | 0.024 | 0.085 | 0.089 | 0.870 | 1,368 | 100.00 |
| CMM-TNM stage I–IIA (%) undergoing head CT scans, chest CT/MRI scans, abdominal CT/MRI scans, or PET scans within 180 days after diagnosis | <10 | 3.03 (1.81-4.75) | 3.82 (1.85-6.91) | 3.45 (0.72-9.75) | 0.779 | - | - | - | 943 | 68.93 |
| Percentage of patients with 1-4-mm thick lesions undergoing sentinel lymph node biopsy (SLNB) | ≥90 | 94.16 (89.20-97.29) | 81.63 (72.53-88.74) | 60.00 (45.18-73.59) | <0.001 | 0.007 | <0.001 | 0.008 | 1,066 | 77.92 |
| Percentage of patients with lesions <0.8 mm in thickness and no reported ulceration or mitoses undergoing SLNB | <10 | 4.43 (2.44-7.32) | 3.76 (1.23-8.56) | 2.44 (0.06-12.86) | 1.000 | - | - | - | 490 | 35.82 |
| Percentage of patients with time elapsing between biopsy and complete excision <60 days | ≥90 | 62.27 (58.62-65.83) | 59.77 (54.45-64.93) | 58.47 (49.04-67.47) | 0.600 | - | - | - | 1,192 | 87.13 |
| Percentage of cases with pT1-T2 disease ≤2.0 mm in thickness and surgical margins <0.8 cm | <10 | 31.74 (27.99-35.68) | 26.07 (20.57-32.19) | 32.84 (21.85-45.40) | 0.251 | - | - | - | 887 | 66.59 |
| Percentage of cases with pT1, pT2 disease ≤ 2.0 mm in thickness and surgical margins > 1.2 cm | No-TH | 24.23 (20.81-27.91) | 30.34 (24.52-36.67) | 38.81 (27.13-51.50) | 0.015 | 0.173 | 0.044 | 0.247 | 887 | 66.59 |
| Percentage of cases with pT3, pT4 disease 2.0 mm in thickness and surgical margins <1.6 cm | <10 | 57.50 (45.94-69.78) | 59.30 (46.17-69.76) | 69.57 (54.25-82.26) | 0.381 | - | - | - | 212 | 15.69 |
| Percentage of cases with pT3, pT4 disease >2.0 mm in thickness and surgical margins >2.4 cm | No-TH | 3.75 (0.78-10.57) | 6.98 (2.60-14.57) | 4.35 (0.53-14.84) | 0.727 | - | - | - | 212 | 15.69 |
| Percentage of SLNB-positive patients | ≥15 | 18.01 (14.18-22.37) | 18.85 (13.56-25.13) | 16.36 (7.77-28.80) | 0.911 | - | - | - | 607 | 44.37 |
| Percentage of SLNB-positive patients undergoing lymphadenectomy | No-TH | 85.45 (73.34-93.50) | 84.38 (67.21-94.72) | 44.44 (13.70-78.80) | 0.024 | 1.000 | 0.039 | 0.051 | 96 | 7.02 |
| Percentage of patients undergoing SLNB in a regional reference center | ≥90 | 62.88 (57.67-67.88) | 59.38 (52.07-66.39) | 50.00 (35.81-64.19) | 0.187 | - | - | - | 605 | 44.23 |
| Percentage of TNM stage IB–III patients undergoing nodal US within 12 months of wide excision | ≥95 | 61.69 (56.41-66.77) | 62.38 (55.31-69.08) | 38.64 (28.44-49.62) | <0.001 | 0.945 | <0.001 | <0.001 | 645 | 48.24 |

* No-TH were established in the absence of supporting scientific evidence.
Acronyms: TH= thresholds; CMM: Cutaneous malignant melanoma; SLNB: sentinel lymph node biopsy

**Table 3. Clinical performance indicators by age groups**

## Conclusion

In very elderly patients, the clinicopathological presentation of CMM differs from that of general population. Compared to malignancies at a younger age, very elderly patients showed a higher prevalence of the head, hands, or feet as the primary site, a higher TNM stage at presentation, and a lower prevalence of tumor infiltrating lymphocytes.
Clinical management also differs, with less frequent SLNB biopsies and lymphadenectomy (in SLN-positive cases). In all cases, but particularly in very elderly frail patients, tele-dermatology could efficiently activate secondary prevention strategies

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