ORIGINAL CONTRIBUTION

Cutaneous Melanoma More Likely to Be Invasive in Fairer Skin Phototypes: A Retrospective Observational Study

Liam Mercieca, MD, MRCP (Edin);[1] Susan Aquilina, MD, FRCP (UK);[1] Neville Calleja, MD, PhD, FFPH;[2] Michael J. Boffa, MD, FRCP (Lond), MSc (Lond)[1]

ABSTRACT

Fitzpatrick skin phototype is one of the factors determining melanoma development, with fairer skin phototypes I and II known to be associated with a higher risk. This study aimed to identify any associations between skin phototype and the histologic subtype, Breslow's thickness, and the site of melanoma. Patients diagnosed with melanoma for over an 18-month period were included. Data were gathered from the Malta National Cancer Registry. There were 167 registered cutaneous melanoma patients, of which 135 were included in the study. Melanomas in patients with skin phototypes I and II were more likely to be invasive than *in situ* when compared to patients with skin phototypes III and IV ($P = 0.00027$). There was also an association between skin phototype and histologic type of melanoma ($P = 0.005$), with melanoma *in situ* being the most common subtype in patients with skin type III. This study confirms that fairer skin phototypes have an increased risk of melanoma. It also shows that in our population, melanoma in skin phototypes I and II is more likely to be invasive rather than *in situ* compared to melanoma in darker skin phototypes. Further studies are required to confirm these findings and identify possible reasons. (*SKINmed*. 2021;19:280–283)

Malta is located in the center of the Mediterranean with a high ultraviolet (UV) index lasting beyond the summer months. Melanoma incidence and mortality are on the increase in the Maltese population, a trend being observed in white populations worldwide.[1-3] The age standardized incidence for primary invasive cutaneous malignant melanoma in Malta increased from 3.7 per 100,000 population per year for male and 5.1 per 100,000 for female between 1993–1997 to 15.7 per 100,000 population per year for male and 13.5 per 100,000 for female in 2014.[3]

Numerous studies have identified various melanoma risk factors, including the Fitzpatrick skin phototype (SPT). This is based on a patient's reporting of acute skin response to sunlight and has been advocated as a means of determining an individual's relative risk of photo-aging and skin cancers. There is extensive evidence that fairer SPTs (I and II) are at a higher risk of cutaneous melanoma.[4-6]

From a previous study carried out in 2007, the most common SPT in the Maltese population is SPT III (52.4% of male, 43.8% of female) followed by SPT IV in male (30.4%) and SPT II in female (32.3%). Only 1.2% of the Maltese population is SPT I.[3] The aim of the present study was to determine whether SPT shows any association with histologic subtype of melanoma, Breslow's thickness, or site of melanoma. This information could be used to further educate the public during melanoma awareness campaigns.

METHODS

Patients who were diagnosed with histology-confirmed cutaneous melanoma over an 18-month period, between January 2012 and June 2014, were included in the study. Data were gathered from the Malta National Cancer Registry that includes all melanoma types diagnosed at public and private clinics on the Maltese islands. According to the latest census (held

From the Department of Dermatology, Sir Paul Boffa Hospital, Floriana, Malta[1] and the Department of Public Health, University of Malta, Msida, Malta[2]

Address for Correspondence: Liam Mercieca, MD, MRCP, Department of Dermatology, Sir Paul Boffa Hospital, Floriana, FRN 1941, Malta • E-mail: liam.mercieca@gov.mt

in 2011), the population of Malta is 416,055.[10] Only Maltese patients living in Malta for more than 5 years who were newly diagnosed with cutaneous malignant melanoma, both *in situ* and invasive, were included in the study. Foreign residents were excluded. Patients were contacted by phone and invited to participate, and a signed consent form was obtained. Their SPT was determined by a consultant dermatologist or a higher specialist trainee in dermatology via a doctor-led questionnaire and clinical examination. Training was provided by a single consultant dermatologist to standardize the results. Apart from SPT, further data gathered included gender, age at the time of diagnosis of melanoma, site, histologic subtype and Breslow's thickness of melanoma through electronic health records. The SPT of the Maltese general population (the control group) as determined in a 2007 study,[7] was compared with the SPT of our study population using Fisher's exact test. The association of SPT with histologic type, Breslow's thickness and site of the melanoma were analyzed using Fisher's exact test, Chi-squared test and Kruskal-Wallis statistical analysis. Ethical approval was obtained from the University of Malta research ethics committee.

RESULTS

A total of 167 cutaneous melanoma patients were registered in Malta during the study period. Nine patients were foreigners and, hence, were excluded from this study. Six patients had since died and assessment of their SPT was not possible; four had died of metastatic cutaneous melanoma. Of the remaining 152 patients, 135 were contacted by phone and recruited in the study. Of the 135 recruited patients, 72 were female (53.3%) and 63 were male (46.7%), with an average age of 56.5 years (range 19–95 years) at the diagnosis of melanoma.

Table 1. Skin Phototypes of Patients with Melanoma and that of the General Maltese Population

Skin Prototype	Melanoma Patients in the Study Population	General Maltese Population (as Sampled in 2007)
I	16.3% ($n = 22$)	1.2% ($n = 9$)
II	60.7% ($n = 82$)	24.6% ($n = 186$)
III	21.5% ($n = 29$)	48% ($n = 363$)
IV	1.48% ($n = 2$)	26.2% ($n = 198$)

Skin Phototype and Risk of Melanoma

There were 22 patients (16.3%) with SPT I, 82 (60.7%) with SPT II, 29 (21.5%) with SPT III, and 2 (1.5%) with SPT IV (Table 1). Using Fisher's exact test, the association between melanoma and SPT was revealed to be statistically significant ($P < 0.001$). SPTs I and II were found to be more prevalent than SPTs III and IV in the melanoma population when compared with the general population.

Skin Phototype and Histologic Type of Melanoma

Invasive superficial spreading was the most common histologic type of melanoma (49.6%, $n = 67$) followed by the *in situ* type (29.6%, $n = 40$). These were followed by nodular melanoma SPTs (10.4%, $n = 14$), acral melanoma (4.4%, $n = 6$), lentigo maligna (3.7%, $n = 5$), lentigo maligna melanoma (0.7%, $n = 1$), desmoplastic melanoma (0.7%, $n = 1$), and Spitzoid melanoma (0.7%, $n = 1$). Table 2 illustrates the histologic types of melanoma and their percentages within each SPT.

Table 2. Melanoma Histologic Types within Each Skin Phototype

	Invasive Superficial Spreading	In Situ	Nodular	Acral	Lentigo Maligna	Lentigo Maligna Melanoma	Desmoplastic	Spitzoid
SPT I $n = 22$	13 (59.1%)	5 (22.7%)	3 (13.6%)	1 (4.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
SPT II $n = 82$	46 (56.1%)	21 (25.6%)	10 (12.2%)	3 (3.7%)	1 (1.2%)	0 (0.0%)	1 (1.2%)	0 (0.0%)
SPT III $n = 29$	7 (24.1%)	14 (48.3%)	1 (3.4%)	1 (3.4%)	4 (13.8%)	1 (3.4%)	0 (0.0%)	1 (3.4%)
SPT IV $n = 2$	1 (50.0%)	0 (0.0%)	0 (0.0%)	1 (50.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Abbreviation: SPT, skin phototype.

Table 3. Number of Melanoma Patients According to Breslow's Thickness for Different Skin Phototypes

	Breslow's Thickness					Mean Breslow (mm)
	0 mm (*in situ*)	<1 mm	1–2 mm	2.1–4 mm	>4 mm	
SPT I *n* = 22	5 (22.7%)	9 (40.9%)	5 (22.7%)	2 (9.1%)	1 (4.5%)	0.98
SPT II *n* = 82	21 (25.6%)	36 (43.9%)	10 (12.2%)	9 (11.0%)	6 (7.3%)	1.24
SPT III *n* = 29	19 (65.5%)	8 (27.6%)	1 (3.4%)	1 (3.4%)	0 (0.0%)	0.27
SPT IV *n* = 2	0 (0.0%)	1 (50.0%)	0 (0.0%)	1 (50.0%)	0 (0.0%)	1.31

Abbreviation: SPT, skin phototype.

There was a statistically significant association between SPT and histologic type of melanoma (Fisher's exact test, $P = 0.005$). SPT I and II population had a higher incidence of invasive superficial spreading melanoma, while SPT III had a higher incidence of the *in situ* type. Only two patients with SPT IV had melanoma developing in our study (acral and invasive superficial spreading).

Skin Phototype and Breslow's Thickness

Table 3 illustrates the number of melanomas according to Breslow's thickness for different SPTs. An independent samples Kruskal-Wallis test showed that the distribution of Breslow's thickness (mm) was statistically different across categories of SPT ($P = 0.0017$). Melanoma patients with SPT III had a less invasive Breslow's thickness than SPT I and II population and tended to be excised at the *in situ* stage. Melanoma in patients with SPT I and II was more likely to be invasive when compared with patients with SPT III and IV (Chi-square; $P = 0.00027$) (Table 4).

Skin Phototype and Melanoma Site

The most common recorded site of melanoma for SPT II was the back and that for SPT III, the arms, but these were not statistically significant (Chi-square, $P = 0.186$). Using Fisher's exact test, the distribution of melanoma by site was found to vary significantly by gender ($P = 0.002$).

DISCUSSION

The association of SPT and melanoma has been clearly documented in many studies.[6,7] Our retrospective study confirms

Table 4. Number of Invasive and *In Situ* Melanomas in Skin Phototypes I and II Compared with Skin Phototypes III and IV

	Skin Phototype	
	I & II	III & IV
Invasive melanoma *n* = 69	77 (74.0%)	12 (38.7%)
In situ melanoma *n* = 46	27 (26.0%)	19 (61.3%)
Total *N* = 135	104	31

that people with the fairer SPTs (I and II) are at an increased risk of developing cutaneous melanoma when compared with those having SPTs III and IV. It goes further by illustrating that Maltese people with SPTs I and II are significantly more likely to have an invasive rather than *in situ* melanoma compared with darker SPTs grouped together, while those with SPT III are more likely to have *in situ* melanoma. To our knowledge, this finding has not been reported previously. Only two patients with SPT IV were diagnosed with melanoma in our study, and no conclusions could be drawn in this subgroup.

We can suggest two explanations for the observed association. The first is that patients with fairer SPTs may have a decreased intrinsic ability to restrict not only new onset of a cutaneous melanoma but also its invasion. Studies have shown that cutaneous SPT is genetically determined by melanocortin 1 receptor (MC1R) polymorphisms which stimulate eumelanin synthesis amongst other genes. Recent studies have also associated MC1R signaling with

antioxidant activation, DNA repair, and survival pathways[11–13]; furthermore, fairer SPTs have an increased risk of mutations and genetic differences associated with melanoma development.[14] This could suggest an increased risk of invasion attributable to genetic differences in fairer SPTs. Another possible explanation for the higher frequency of *in situ* melanoma rather than invasive melanomas in darker Maltese patients with SPT III could be that such patients generally have fewer nevi and lentigines than those with SPTs I and II[15]; thus, new or changing skin lesions might be more easily observed, leading to diagnosis at an early *in situ* stage. It should be noted that in Malta there is a generally high awareness of skin cancer with frequent media sun awareness campaigns reminding people to take precautions when in the sun and to regularly check their moles.[16]

A limitation of our study is the relatively small number of patients involved, especially those with SPT IV, and it remains to be seen whether our results are confirmed in larger studies in other predominantly white populations. Risk factors, such as family history of melanoma and previous ultraviolet (UV) exposure, were not assessed and could be confounding variables. We strived to keep the assessment of SPTs as consistent as possible between the two study populations by using the same questionnaire and by having the same consultant dermatologist to train the investigators. Both studies excluded foreigners. A higher percentage of women was present in the current study as opposed to the general population study (53.8% vs. 50.8%), but this difference is not enough to explain the associations noted.

CONCLUSIONS

This study shows that Maltese people with SPTs I and II are not only at a higher risk of developing cutaneous melanoma than people with SPT III, but they are also at higher risk of their melanoma being invasive rather than *in situ*. Sun awareness campaigns should highlight these risks to encourage people with the fairer skin types to not only take extra precautions when out in the sun, but also to be extra vigilant with their skin, so as to present as soon as possible with any suspicious pigmented lesions. Further studies are required to confirm these findings and identify possible explanations.

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