Epidemiological comparison of cases of malignant melanoma of the Hospital Universitario Austral (HUA) vs. Argentine Registry Cutaneous Melanoma (RAMC)

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ABSTRACT

We performed an epidemiological comparison between patients with malignant melanoma from the Hospital Universitario Austral (HUA) and patients with malignant melanoma from the records of the Argentine Cutaneous Melanoma Database (RAMC). The purpose of the study was to recognize the epidemiologycal profile of our patients and compare it with that of the patients enrolled within the RAMC; to identify the risk groups within the HUA; and to define if there are any differences in relation to the diagnosis taking as main indicators both the Breslow thickness index and tumor ulceration by the time of diagnosis.

Materials and methods: We registered 197 cases of malignant melanoma at AUH, while 3238 cases were recorded by RAMC, assuming the latter to be the domestic standard. We selected the following epidemiological data: 1) gender distribution, 2) age distribution, 3) Breslow thickness index, and 4) tumor ulceration. As descriptive statistical measures we performed: mean, standard deviation and proportions. To analyze numeric variables we used Student-t tests for two independent groups; and to analyze categorical or ordinal variables we conducted chi-square test. The p-value was established at 0.05.

Results: The results showed that overall sex and age distribution are similar in both groups. However, age-stratified distribution showed a higher percentage of both male and female younger patients at AUH in relation to RAMC. The time of diagnosis proved to be earlier at AUH than RAMC; and as for tumor ulceration, we did not find any differences.

Conclusion: We considered this comparison with the Argentine Cutaneous Melanoma Database highly important, since this enabled us to know our population, thus identifying their risk factors (Dermatol Argent 2010;16(1):34-38).

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Introduction

Malignant melanoma (MM) is a tumor originated in the melanocytes usually located in the epidermis, dermis or mucosal epithelium. It can develop from a precursor lesion, such as dysplastic nevi or giant congenital melanocytic nevus, or from healthy skin too. The common age of diagnosis is between 45 to 55 years old. Nowadays, melanoma is one of the cancers with the fastest growing incidence and the cause of most skin cancer deaths. The prognosis depends largely on the stage of development at the moment of diagnosis.[1] It is well known the causal association between sun exposure and skin cancer development for both melanoma and not melanoma.[2-9]

Any measure designed to reduce the risk factor will result in a direct decreased incidence of these tumors. Because the prognosis is closely related to the development stage in which it is diagnosed, there are two basic mechanisms to reduce its incidence and improve survival: the prevention and early detection and diagnosis. The latter is the most important method which can influence on the prognosis of melanoma.[10] The risk of regional lymph node involvement, which clouds the prognosis, clearly increases with increasing tumor thickness and the same is true with respect to distant metastasis. To achieve a detection on early stages, several factors must be taken into consideration: I) education of the population to examine themselves, II) of training of health professionals in order to be properly trained alert to detect suspicious skin lesions, iii) the encouragement of full skin examinations, regular and thorough, such as those proposed on educational and detection campaigns, and IV) the appropriate use of diagnostic tests: of these, the histopathologic study of skin is the most accurate.[11]

The primary criteria for T staging classification of localized melanoma on stages I and II are the thickness measured in millimeters (Breslow index) and the presence or absence of ulceration, determined histopathologically.[12-14] The Hospital Austral Universitario Austral (HUA) is a recent hospital opened on May 2000. It is located on a semirural area and therefore with a population with a higher potential of sun exposure. Over the last eight years (May 2000 to April 2008) we have registered 197 patients with malignant melanoma (MM).

Argentine Registry of cutaneous melanoma (ARCM) is a registration system for melanoma sponsored by the Dermatological Argentinean Society and the Argentinean Skin Cancer Foundation. This is also a new entity and it became operational on October 2003 and keeps records of patients with a melanoma from around the country since January 1, 2002 onwards.[15]

Due to the similarity on the onset of both registration systems, the particular characteristics from the population of the HUA (young population with high exposure to sunlight), and that the epidemiological profile of the ARCM is somehow the national standard for this disease, we found valuable and useful to compare epidemiological link between cases MM reported at the HUA and the ARCM.

Objectives

Determine the epidemiological profile of patients with MM registered in HUA and ARCM, compare the epidemiological characteristics among patients with MM from HUA and ARCM and data provided by, identify risk groups in our area and finally determine whether there are differences between HUA and ARCM patients regarding early diagnosis, taking as indicator Breslow index and the tumor's ulceration at diagnosis.

Materials and Methods

In this study, we carry out an epidemiological comparison between patients registered in the HUA and ARCM since May 30, 2000 and April 30, 2008 vs. those provided by the ARCM registered between 1 January 2002 and May 30, 2008, in which 3238 cases were recorded.

The epidemiological data used on this study, all considered at the time of diagnosis, has been chosen using the same classification criteria used by this ARCM,[15] the Argentinean Consensus for Cutaneous Melanoma of the Argentinean Dermatological Society[17] and the American Joint Committee on Cancer:[1] distribution of patients by sex and age, Breslow and ulceration index. We used the latter two because they are the two most powerful characteristics and independent predictors for tumors staging:

Thickness of Tumor or Breslow index: is the melanoma's thickness vertically measured by an ocular micrometer from the top of the granular layer (or from the base of the ulcer if the lesion is ulcerated) to the deepest neoplastic melanocyte on the dermis or subcutaneous tissue.

Ulceration: is the absence of intact epidermis overlying the most of the primary melanoma based on a microscopic examination of the histological sections.

Inclusion criteria. Any patient diagnosed with melanoma under the 172 code of ICD9 during the period comprehended between May 30th, 2000 and April 30th, 2008.

Exclusion criteria. Any patient who was diagnosed with cutaneous melanoma and has attended the Dermatological Department for a second opinion, without carrying out the corresponding treatment and posterior follow-up.

We have performed a retrospective study using the HUA and ARCM databases. The following have been used as descriptors: average, standard deviations and rates. A t test was used for the analysis of numerical variables performed over two independent groups. For the analysis of categorical or ordinal variables a χ^2 test was applied. The value of statistical significance alpha was set at 0.05.

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FIGURE 1. Age of women at the time of diagnosis for both records (Group 1: <40 years, Group 2: 40-54 years, Group 3: 55-69 years, Group 4:> 69 years).

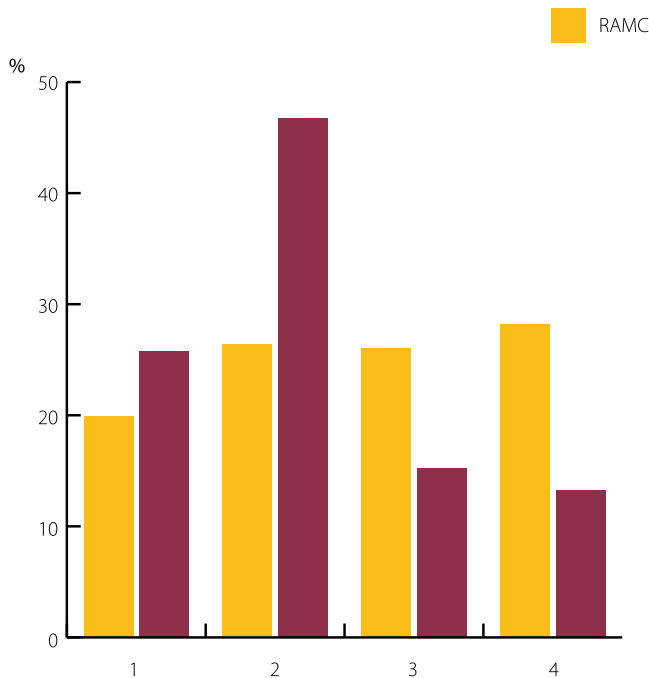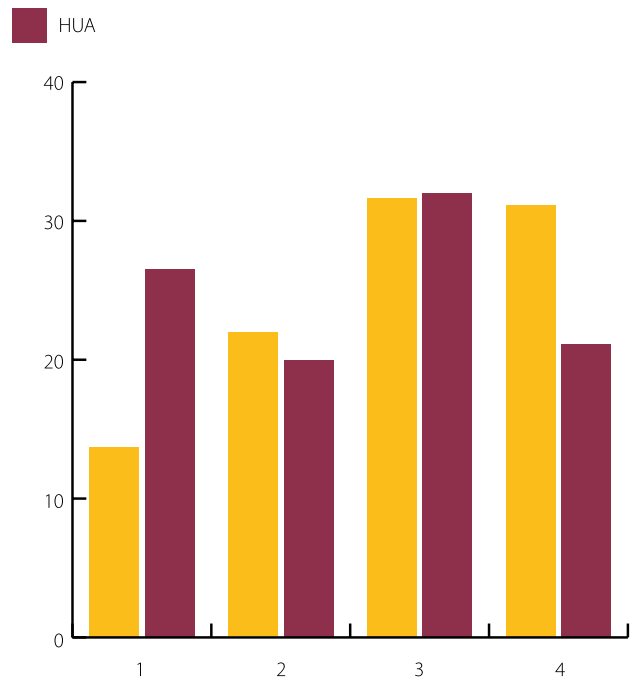**FIGURE 2. Age of males at diagnosis for both records (Group 1: <40 years, Group 2: 40-54 years, Group 3: 55-69 years, Group 4:> 69 years).**

Results

1. **Patient distribution by gender.** We observed no difference on gender distribution among patients of ARCM and of HUA (42.3% on women of ARCM vs. 43.65% on women of HUA and 57.7% on males of ARCM vs. 56, 35% on men of HUA, p = 0.129).

2. **Age at time of diagnosis.** We observed no statistically significant differences on mean age values at the moment of diagnosis (56.62 years on ARCM of vs. 54.43 years on HUA; confidence interval of 95%: -0.2714 to 4.651; t = 1.745 with 3228 degrees of freedom, p = 0.081).

3. **Age at time of diagnosis with gender discrimination.** The following age groups were studied: 1: <40, 2: 40-54, 3: 55-69, and 4: >69. We have observed significant differences on women, especially on the age group between 40 to 54 years old (46.51% on HUA vs. 26.29% on ARCM). This difference is larger on patients below 55 years old. On ARCM patients, 46.11% have less than 55 years old, while HUA patients of the same age group sum a total of 72.09% (p=0.000) **(Figure 1)**. We also find this difference on men. The most notorious one is observed on men under 40 years (26.61% en HUA patients vs. 13.87% on ARCM, p=0.001) **(Figure 2)**.

4. **Breslow Index.** When we classified the Breslow index as the following: 1: *in situ*, ≤1; 2; 1.01-2; 3; 2.01-4; 4; ≥4, we were able to observe significant differences at the time of diagnose between patients from ARCM and

HUA. *In situ* melanomas and up to 1 mm account for 74.11% on HUA and 56.23% on ARCM (p=0.000). This difference is evident between genders. On women, in situ melanomas and up to 1 mm represent 76.74% on HUA 26.36% on ARCM (p=0.000) **(Table 1)**. In the case of men, there is also such a difference, being *in situ* melanomas and up to 1 mm 66.67% on HUA 42.26% on ARCM (p=0.000) **(Table 1)**. Thicker melanomas (of more than 2 mm thick) correspond to 11.71% on HUA and 34.19% on ARCM (p=0.000) **(Table 2)**.

5. **Presence of Ulceration.** No significant differences were found between 2338 patients from ARCM and 137 patients from HUA on the presence of ulceration on melanomas, being 77.86% vs. 74.26% respectively (p=0.343).

6. **Correlation between Breslow index, gender and age.** On women, patients from HUA under 54 years old (72%) are predominant over those from ARCM (46%) (p=0.000). There are 25% less than 40 years in the HUA. And while 77% of patients in the HUA reach the diagnosis with melanoma *in situ* or with Breslow index of less than 1 mm (better prognosis) while on ARCM is 50%. This difference is significant (p = 0.000). In men there is a similar phenomenon but not as marked. The group under 54 years accounted for 47% in the HUA and 36% in the ARCM. In the group under 40 years, the HUA has a 27% significant difference in respect of the ARCM, who has a 14% (p = 0.001). Also men of HUA reach a

TABLE 1. Breslow thickness in women at the time of diagnosis. Breslow group in less than 1 included *in situ* cases.

	Breslow (mm)				
	1	2	3	4	Total
ARCM					
(N)	511	243	156	114	1.024
(%)	49,90	23,73	15,23	11,13	100,00
HUA					
(N)	66	15	3	2	86
(%)	76,74	17,44	3,49	2,33	100,00
Total					
(N)	577	258	159	116	1.110
(%)	51,98	23,24	14,32	10,45	100,00

Pearson $\chi2(3) = 25,8764$; p = 0,000
Likelihood-ratio $\chi2(3) = 30,3185$; p = 0,000
Cramer V = 0,1527
Gamma = -0,5301; ASE = 0,087
Tau-b de Kendall = -0,1418; ASE = 0,022
Note: missing data were excluded fromcomparisons.

TABLE 2. Breslow thickness in men at the time of diagnosis. Breslow group in less than 1 included *in situ* cases.

	Breslow (mm)				
	1	2	3	4	Total
ARCM					
(N)	465	253	212	161	1.091
(%)	42,62	23,19	19,43	14,76	100,00
HUA					
(N)	74	24	8	5	111
(%)	66,67	21,62	7,21	4,50	100,00
Total					
(N)	539	277	220	66	1.202
(%)	44,84	23,04	18,30	13,81	100,00

Pearson $\chi2(3) = 28,9922$; p = 0,000
Likelihood-ratio $\chi2(3) = 32,1828$; p = 0,000
Cramer V = 0,1553
Gamma = -0,4482; ASE = 0,073
Tau-b de Kendall = -0,1422; ASE = 0,023
Note: missing data were excluded from comparissons.

67% with melanoma *in situ* or less than 1 mm (better prognosis) while on ARCM is 43%. This is a significant difference (p = 0.000).

Discussion

Overall, we found no significant differences in gender distribution and average age on both groups. We could infer with these data that HUA risk groups are similar to those of the ARCM, assuming the ARCM as a national standard. But, if we stratify by age we see clearly that there is a greater percentage of young women at the time of diagnosis, since those under 54 years represent 72% in the HUA while in the ARCM are 46%. The same applies to men in the group under 40 years, being in the HUA 27% and 14% ARCM significant differences. On a study conducted in our country, with 26 patients diagnosed with melanoma, the average age was 70 years.[18] In the United Kingdom, the incidence of MM in children under 39 years is 20% .[19]

While the overall average age in both groups (HUA vs. ARCM) is similar, this may be due to extreme age data records (outliers). But by stratifying we observe that HUA has a higher percentage of young patients with melanoma.

Taking into account the Breslow index, we also observed significant differences: melanomas in the HUA (74%) are thinner (in situ or less than 1 mm) than in the ARCM (56%).[6] In women the difference is 77% in the HUA vs. 50% in the ARCM and in males is 67% in the HUA vs. 43% in the ARCM. These differences are significant.

As the HUA is a private hospital, this feature was noted by the ARCM when stratified melanomas reported by the private sector (thinner melanomas) and those reported by the public sector (thicker).[19] This significant difference in patients with MM under the Breslow index from HUA vs. ARCM could be explained by a stronger culture of preventive medicine or by having greater access to health resources in the private sector. This analysis may be valid for the HUA as for the ARCM. Regarding the ulceration, we found no significant diferencias.[9]

Now well, this analysis allow us to state that there is a higher proportion of young patients with melanoma in the HUA population that in the national standard and that they arrive before for medical consultations to show finer Breslow indexes. These epidemiological data of a greater proportion of MM in our younger population match a recent social phenomena of population growth in the area of Pilar.[16] One might also suspect that the higher sun exposure would have some impact on the greater amount of MM in these particular age groups, but this cannot be stated on this study. While every patient with MM requires very close monitoring, the age at which appear the melanomas in our young patients presents us with a risk population from the probability of occurrence of a second primary melanoma over their life. In addition, MM's onset impacts the lives of patients and the medical control of the immediate family, as the latter risk increases from 2 to 10 times.[19, 21]

Conclusions

We found that the gender distribution and the average global age is similar HUA and ARCM. Stratification by age distribution showed a higher percentage of young patients of

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both women and men in the HUA compared to the ARCM and the time of the diagnosis as measured by Breslow's index was earlier detected in the HUA that in the ARCM.

Acknowledgements

References

1. Balch CM, Buzaid AC, Soong SJ. Final version of the American Joint Committee on Cancer staging system for cutaneous melanoma. J Clin Oncol 2001;19:3635-3648.

2. Elwood JM, Gallagher RP, Hill GB. Pigmentation and skin reaction to sun as risk factors for cutaneous melanoma: Western Canada Melanoma Study. BMJ 1984:288:99-102.

3. Elwood JM, Gallagher RP, Hill GB. Cutaneous melanoma in relation to intermittent and constant sun exposure. The Western Canada Melanoma Study. Int J Cancer 1985:35:427-433.

4. Stern RS, Weinstein MC, Baker SG. Risk reduction for nonmelanoma skin cancer with childhodd sunscreen use. Arch Dermatol 1986;122:537-545.

5. Weinstock MA, Colditz GA, Willett WC. Nonfamilial cutaneous melanoma incidence in women associated with sun exposure before 20 years of age. Pediatrics 1989;84:199-204.

6. Corona R, Dogiotti E, D'Errico M. Risk factors for basal cell carcinoma in Mediterranean population. Arch Dermatol 2001;137:1162-1168.

7. Van Dam RB, Huang Z, Rimm EB. Risk factors for basal cell carcinoma of the skin in men: results from the health professionals follow-up study. Am J Epidemiol 1999:150:459-468.

8. Kricker A, Armstrong BK, English DR. Pigmentary and cutaneous risk factors for non-melanocytic skin cancer. A case control study. Int J Cancer 1991;48:650-662.

9. Fitzpatrick TB, Pathak MA. Preventive Treatment of sunburn, dermatoheliosis, and skin cancer with sun-protective agents. En: Fitzpatrick TB, Eisen AZ, Wolff K, et. al. Dermatology in General Medicine, 4ta. edición, Estados Unidos: McGraw Hill; 1993. p. 1694.

10. Balch CM, Soong SJ, Gershenwald JE. Prognostic factors analysis of 17.600 melanoma patients: validation of the American Joint Committee on cancer melanoma staging system. J Clin Oncol 2001;19:3622-3634.

11. Sahin S, Rao B, Kopf AW, Lee E, et al. Predicting ten-year survival of patients with primary cutaneous melanoma. Corroboration of a prognostic model. Cancer 1997;80:1426-1431.

12. Karakousis CP, Emrich LJ, Rao U. Tumor thickness and prognosis in clinical stage I malignant melanoma. Cancer 1989;64:1432-1436.

13. Balch CM, Wilkerson JA, Murad TM. The prognostic signifi cance of ulceration of cutaneous melanoma. Cancer 1980;45:3012-3017.

14. Gershenwald JE, Thompson W, Mansfi eld PF. Multi-institutional melanoma lymphatic mapping experience: The prognostic value of sentinel lymph node status in 612 stage I or II melanoma patients. J Clin Concol 1999;17:976-983.

15. Registro Argentino de Melanoma Cutáneo (RAMC). Sociedad Argentina de Dermatología y Fundación del Cáncer de Piel. www.sad.org.ar

16. Fuente: INDEC, Censo Nacional 2001. República Argentina

17. Consenso sobre Melanoma Cutáneo. SAD. Pautas para la prevención, diagnóstico, tratamiento y seguimiento. 1998, actualización de 2003. www.sad.org.ar

18. Fontana MI, Barbarulo A, Gavazza S, Spelta MG y cols. Melanoma: incidencia y factores de riesgo en nuestra institución. Dermatol Argent 2007; 13:336-344.

19. Concise Guidance to Good Practice Nº 6. The prevention, diagnosis, referral and management of melanoma of the skin. Royal College of Physicians. Br A of Dermatology, Jul 2007.

20. Loria D, Latorre C, González A. Malignant Melanoma Occurrence in Argentina. Early results from the Argentine Cutaneus Melanoma Registry (RAMC) Poster. Congreso Mundial de Dermatología, octubre 2007. Buenos Aires, Argentina.

21. Garbe C, Hauschild A, Volkenandt M. Evidence and interdisciplinary consensebased German guidelines: diagnosis and surveillance of melanoma. Melanoma Research 2007;17:393.