Cutaneous melanoma epidemiology in Argentina: analysis from the Argentine Cutaneous Melanoma Registry

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ABSTRACT

Introduction: Argentina has scarce data on cutaneous melanoma (CM) incidence: The Argentine Skin Cancer Foundation and the Argentine Society of Dermatology developed a joint project, aimed at gathering information on the epidemiological aspects of CM in Argentina.

Objectives: to present the RAMC results from January 2003 till April 2009; to deliver useful information for CM control actions and to stimulate collaboration among professionals who diagnose and treat CM.

Methods and Design: the records are actively sought from diverse medical specialties sources. A database is constructed, controls are implemented and the analysis of the data is performed.

Results: 3.832 cases were analyzed. Median age: 55.1 years (females); 58.5 years (males) ($p<0.001$). The most frequent location in women were the lower limbs; in males the trunk ($p<0.001$). Superficial spreading melanoma was the most frequent clinical type (54%), followed by nodular melanoma (27%), lentigo maligna melanoma (8%) and acrolentiginous melanoma (6%). Fifty six percent of the lesions had Breslow thickness index <1mm. Among women, the Breslow thickness index changed with age. Among those younger than 40 years, 61.8% had tumors <1.01 mm. CM cases registered from public health institutions presented significantly higher Breslow thickness scores than those from the private sector. ($p<0.05$ for all age and sex groups, except those >70 years).

Conclusions: The Breslow thickness index findings from public institutions suggest the need for greater control measures in that sector. Greater participation is needed by all those involved in the care of CM patients to determine its true incidence in Argentina (Dermatol Argent 2010;16(1):39-45).

Keywords: *cutaneous melanoma, Argentina, tumor registry, epidemiology.*

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Introduction

The incidence rate, defined as the number of new cases that occur each year in a geographically defined population, is the best way to determine the occurrence of a tumor. This is achieved through the activity of cancer registries, which collect population-based cases information on geographically defined populations. The establishment of these population-based registries is so important, that the International Agency for Research on Cancer (IARC) has announced as primary objective of the Descriptive Epidemiology Group, to stimulate its creation, in particular in developing countries, among which are those of Latin America.[1]

Recently MacKie et al.,[2] in an update on the epidemiology of cutaneous melanoma (CM), pointed out

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that cancer registries are the main sources of information on the incidence of all tumors, including melanoma.
According to the latest data from the World Health Organization, of all Central and South American countried, only Costa Rica has incidence data of CM regarding the entire country. In the rest of the continent, there is data on CM only for a particular area and just in some countries.[3] Table 1 presents these data together with those reported by some records from other continents. In the United States in 2008, the number of estimated cases of CM was 62,480, representing the sixth and seventh most common cancer in men and women, respectively.[4]
In Argentina there is little data on the occurrence of CM. The mortality rate, adjusted for age, during the period 1997-2001 was 1.1 per 100,000 for males and 0.6 per 100,000 for women[5] with an increasing trend in rates during the period 1997-2004 (about 3% per year for both genders) (Loria, personal communication). In terms of incidence, nowadays, only two population-based registries, one in the Department of Concordia (Entre Rios) and the other in the south of Buenos Aires province, have released their results, but without providing data on the level of invasion or stage of the lesions, which are essential for the identification of risk groups.[6]
This lack of information regarding the CM is what has prompted the Argentinean Society of Dermatology (ASD) and the Skin Cancer Foundation, jointly, to the creation of the Argentine Registry of Cutaneous Melanoma (RAMC) as a tool to gather more information on the occurrence of this tumor in order to apply these results to disease control initiatives.
The present publication summarizes the activity of the RAMC, from its creation until April 2009. The results will allow anyone who works in the construction of this large database, see how the contribution of their cases are reflected in results such as frequency of occurrence, in a general sense and the various features of CM in our population, in particular.
Finally, the data presented provide useful information for the design of actions and measures aimed to the control of the disease.

Material and methods

The RAMC began in October 2003 recording CM cases, invasive or *in situ*, of known or unknown location and date of diagnosis from January 1 2002 onwards. The data collection methodology is called *mixed*, it involves an active data recollection, which means going to pick up cases from potential sources, and a passive one, receiving data spontaneously from professionals/institutions. Cases come from diverse specialties (dermatologists, oncologists, surgeons and pathologists, etc.), from different types of institutions (public, private) and from different provincial cancer registries. The data required for each CM case includes: personal information, family and personal history of CM, and topographic and histological data of the tumor. Trained staff manually enters the information previously registered on paper, in a specially designed digital database. For topographical and histological classification it is used the International Classification of Diseases for Oncology, Third Edition[7], and for staging, as recommended by the American Joint Committee on Cancer (AJCC).[8]
The RAMC is a tumor registry but not of patients, this means that if an individual has more than one CM will be included more than once in the database. Systematically, and before each new data analysis, we explore the base looking for incongruous, missing data, duplicates, inconsistencies and other errors, and carrying out the corrections and adjustments as appropriate seeking the cooperation of informants to complete properly the data.
For this study, primary tumor location was grouped into: head and neck, trunk, upper and lower limbs. The patient's age at the time of occurrence, was grouped in: <40 years, 40-54 years, 55-70 years and >70 years. Breslow thickness was analyzed as a categorical variable divided into: <1.01 mm, 1.01 to 2.00 mm, 2.01 to 4.00 mm, and >4.00 mm. for each case it was noted in the database if the information came from the private or public health care system.
The association between categorical variables were examined with chi-square test.
For statistical analysis, a p value <0.05 was considered as an indicator of significant difference. We used STATA statistical software version 10.0 (StataCorp LP, College Station, Texas, USA).

Results

A total of 3832 tumors were included up to April 2009. 49.4% occurred in women and 50.6% in men.
The average age of onset of tumors in women was 55.1 years with a range of 2-99 years (SD = 17.8) and 58.5 in men with a range of 3-100 years (SD = 16.7) (p <0.001). The location of tumors varied with gender: in woman the presentation in the lower limbs was more common where as in men it was in the trunk **(Figure 1)**. This difference was statistically significant (p <0.001). Missing data was reported in 533 cases (13.9%).
The clinical variety of all tumors was recorded, with missing data in 33% of cases. The most common type was the superficial spreading melanoma (54%) followed by nodular melanoma (27%), lentigo malignant melanoma (8%) and Acrolentiginous melanoma (6%). This distribution did not differ with patient's genders.
A total of 596 (15.6%) lesions corresponded to in situ melanoma. Among the invasive CM, 46% had a Breslow thickness lower than 1.01 mm. Among women, the Breslow thickness differed with age at diagnosis. In patients under 40 years of age, 61.8% of lesions had a Breslow <1 mm and

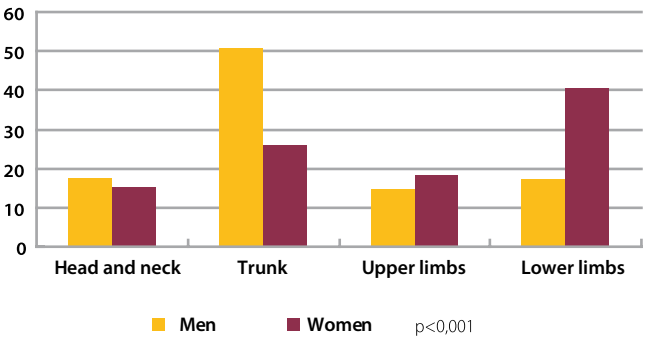
TABLE 1. Number of cases and incidence rates of cutaneous melanoma data by Gender According to the International Agency for Cancer Research.[3]

	Period	Women		Men	
		Cases	Incidences	Cases	Incidences
Argentina, Bahía Blanca	1998-02	29	2,9	27	3,3
Brazil, Brasilia	1998-01	122	4,2	102	4,2
Brazil, Goiania	1998-02	93	4,5	69	4,4
Brazil, São Paulo	1998-02	1.687	5,7	1.392	6,5
Chile, Valdivia	1998-02	32	3,5	16	1,8
Colombia, Cali	1998-02	135	2,9	124	3,5
Costa Rica	1998-02	173	2,1	188	2,4
Equator, Quito	1998-02	92	2,8	73	2,5
Peru, Trujillo	1998-02	23	2,1	16	1,8
Germany, Munich	1998-02	1.113	12,7	1.078	11,5
Italy, Torino	1998-02	399	10,7	4.256	11,4
Spain, Murcia	1997-01	239	6,5	276	7,0
Australia, Queesland	1998-02	6.504	55,8	4.821	41,4
USA***	1998-02	33.579	14,8	26.085	10,5

* Total number of tumors during the reporting period. ** Incidence rate expressed as an average of new cases per year per one million habitants of each gender in the specified area and period of time. *** Set of 14 cancer registries covering 26.1% of the country's population.

7.1% a Breslow> 4.0 mm; whereas among patients older than 70 years old, 40.5% had a Breslow <1 mm and 18.4% of cases the thickness exceeded 4 mm **(Figure 2)**. In men, no significant association was found between Breslow and age.
Data on the presence or absence of ulceration was obtained in 2,752 cases (71.8%). Of these, only 688 presented ulceration (18%) and 2,064 tumors had no ulceration (53.9%). We analyzed the Breslow thickness according to age, type of melanoma and health care system. It was found that the average Breslow index was lower in those patients coming from the private sector, regardless of age or type of melanoma. In contrast, CM from the public system had the highest diagnostic level of invasion; this difference was statistically significant for all age groups and both genders. This difference disappeared at age 70 years **(Figure 3)**.

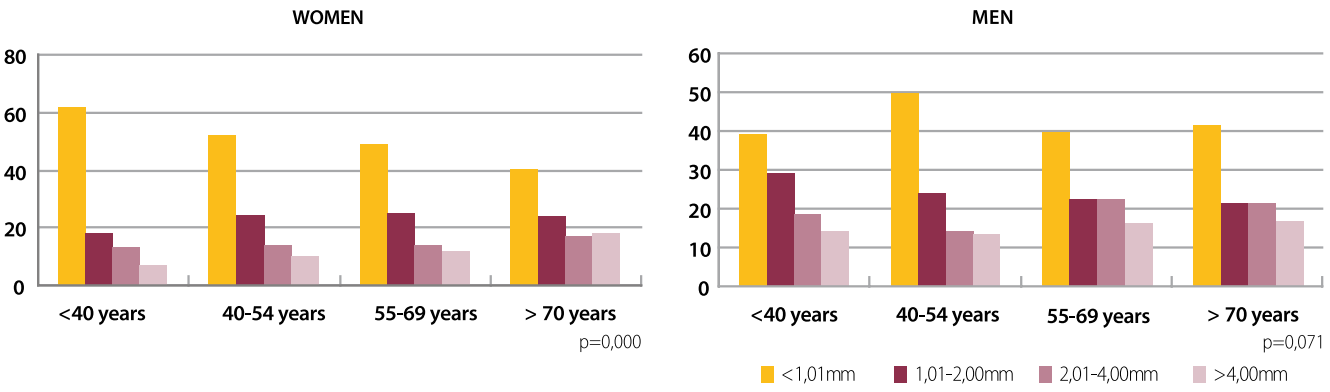
FIGURE 1. Distribution (%) of 3,299 of MC RAMC by localization and gender. [Men, Women; Head and Neck, Trunk, Upper Limbs, Lower Limbs]



Discussion

The 3832 registered CM cases in Argentinean residents, as from 2002, are the result of a search conducted by the RAMC on sources of various kinds. It is known that a quality criterion for a cancer registry database is to collect data of the same tumor from different independent sources because this increases the entirety of registration.[9] In Quebec it was detected a loss on reported cases in a registry as a result of using only hospital data sources.[10] Also, Brochez et al. described in detail the difficulties encountered by physicians and surgeons to include cases in a tumor registry where they found themselves overloaded with forms to complete, having little incentive to register their cases.[11]
Pathologists play a key role in cancer registries. However, the reported cases from pathology laboratories lack certain patient identification data (eg., age, residence, etc.).
Primary tumors location in our series of cases followed the profile of predominantly Caucasian populations, with predominance of lesions on the trunk in men and legs in women. It is described that in black populations, lesions predominate in feet soles.[12] The incidence and anatomical distribution of

FIGURE 2. Percent distribution of 2,457 cases of the RAMC by Breslows' thickness, according to the age group and sex. [Women, Men; años = years]



CM in the U.S. hispanic population shown to be intermediate between Caucasians and blacks.[13] Data from a hospital in Peru, where the ethnic composition of the population has similarities with that of the north-west region of our country, show a distribution of the CM localization similar to that described for blacks, with a predominance of ilesions in feet.[14] It also draws attention the anatomical distribution of CM found in a study of pathology reports of 5 hospitals in Santiago de Chile, with 22.8% of cases located in the feet of men and only 14.4% in the trunk.[15]

Argentina's population has a significant proportion of individuals descending from Europeans and Native Americans. According to the supplementary survey of indigenous peoples in 2001, it is estimated that the Native Americans population was consisted of 600,329 people distributed unevenly in the various provinces, were the regions of north-east, north-west and Patagonia (south) were those where the concentration of certain indigenous groups was higher.[16] In the future, the RAMC, while not specifically collecting information about the ancestors, pretends to analyze cases according to regions, in order to see if there are differences in the various epidemiological characteristics of CM.

Regarding clinical and pathological varieties, in our records the superficial spreading melanoma type was the predominant followed by the nodular. A similar distribution, with a predominance of superficial spreading (61.6%), followed by nodular (25.9%) was found in a study of 229 tumors from a pathology laboratory in a Passo Fundo hospital, in southern Brazil.[17] It is interesting to note that this profile of the histological types of CM may not be uniform in Latin American populations. A study in Peru showed the prevalence of the Acrolentiginous type.[14]

Not always population-based cancer registries, have complete data on the histology of the CM. For example, the population registry of Goiania (Brazil) recorded 290 cases of CM from 1988 to 2000 and on 81% of the cases the detail histology was unknown.[18] This is why it is of importance the role of specific records for each type of tumor, as the RAMC, so as to obtain more detailed information about the characteristics of CM.

In our series, Breslow thickness varied according to age at diagnosis for CM in women. In the younger group, (less than 40 years of age) 61.8% had in situ CM or a Breslow thickness lower than 1.01 mm.

Coincidentally, in the previously mentioned Brazilian study there was a predominance of thin lesions in women. However, probably due to fewer number of cases, the difference was not statistically significant.[18]

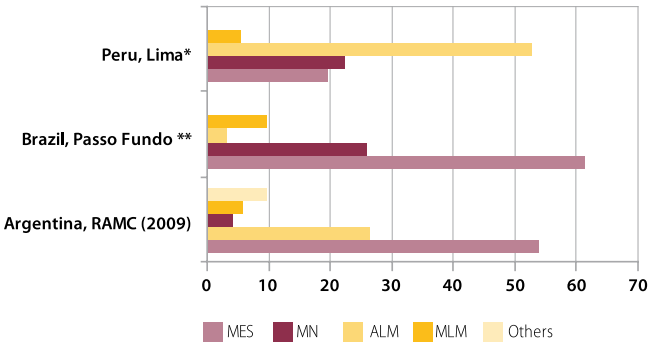
Breslow thickness is a leading independent predictive factor. It is therefore important to try to recognize factors that may be associated with a greater depth of invasion in order to be able to define risk groups.

Among these factors, it may be mentioned the patient's educational level, the preparation and dedication of physicians to detect lesions, the complexity of health systems to which the patient attends to, and the existence of family previously diagnosed with CM. A German study specially designed to determine the factors associated with thicker melanomas, showed that low educational level is an important risk factor.[19] In Italy it was also found that less educated individuals were more likely to have an advanced stage of CM at diagnosis.[20] The RAMC does not collect specific information about educational level, but the primary type of health care system used, either public or private, could be an indirect indicator of the socioeconomic status and/or cultural identity of individuals. The finding of tumors with greater Breslow thickness in patients with melanoma coming from the public domain in our study could be an indicator of the influence of socio-cultural level, and access to health care facilities linked to it, regarding the thickness of the tumor at diagnosis of the cases included in the RAMC database.

The RAMC does not collect information on the ethnic origins of patients, however, it is likely that there are regional variations in terms of frequency within ethnic

FIGURE 3. Percent of cutaneous melanoma by Breslows' thickness, according to gender and type of health care system. [Women, Private, Public; Men, Private, Public; years]

FIGURE 4. Distribution (%) of different histological types in Latin-american populations. [14.18]



MES: Extensive superficial melanoma. MN: Nodular melanoma. ALM: Acrolentiginous melanoma. MLM: Lentigo maligna melanoma.

groups since it is known, for example, that the general population frequency is higher in Native Americans in the northeast than in the center of our country. In addition, there could be a geographic association between the proportion of indigenous and the percentage of illiteracy.[21] A higher prevalence of indigenous would be associated with a higher illiteracy and this would make them not only to present in the area profiles of tumor localization and histological type different from those of predominantly white populations, but it could be presented tumors with higher Breslow index given the association of tumor thickness with the educational level.

Primary prevention activities for CM, mainly associated with a decreased exposure to ultraviolet radiation have shown diverse results.[22] In our country, various actions have been developed in recent years to increase awareness of population about the importance of self-protection and risk factors. An important example of these is the anually Skin Cancer Prevention campaign organized by the Argentinean Society of Dermatology. Not only it helps on primary prevention, rather more, one of the aims of education of the population is to increase early detection of CM (secondary prevention), key to reducing mortality rates.

One of the objectives of the RAMC is to point out groups of people who for some reason are at a higher risk of having CM or reach diagnosis with advanced lesions. In this sense, the data obtained on the more advanced lesions among the cases from the public health-care system in some way quantifies existing perception among health professionals and thus provides a tool set to be used in future preventive actions, for example, targeting prevention campaigns especially to identified high risk groups. Although the RAMC has reached a fairly large series of cases, it still requires the participation of more professionals and institutions to make coverage complete enough to produce good incidence data across the country in order to deepen on the description of cases.

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References

1. http://www.iarc.fr/en/research-groups/DEP/index.php (consulted: 30th August 2009).
2. MacKie RM, Hauschild A, Eggermont AMM. Epidemiology of invasive cutaneous melanoma. Annals of Oncology 20 (Supplement 6): vi1-vi7, 2009.
3. Curado MP, Edwards B, Shin HR, Storm H, et al. (eds). Cancer incidence in fi ve continents, Vol. IX. Lyon (France): IARC Scientific Publications 2007;160.
4. American Cancer Society: Facts and figures. http://www.cancer.org/docroot/STT/stt_0_2008.asp?sitearea=STT&level=1 (Consulted 30th August 2009).
5. Matos E, Loria D, Zengarini N, Fernández M y cols. Atlas de mortalidad por cáncer. Argentina 1997-2001, 2003. http://www.asarca.org.ar (Consulted 30th August 2009).
6. Parkin DM, Whelan SL, Ferlay J, Teppo L, et al. (eds). Cancer incidence in fi ve continents, Vol. VIII. Lyon (France): IARC Scientific Publications; 2002;155.
7. Clasificación Internacional de Enfermedades para Oncología. 3ª edición. Washington DC: Organización Panamericana de Salud. Publicación Científi ca y Técnica; 2003;586.
8. Balch CM, Buzaid AC, Soong SJ, Atkins MB, et al. Final version of the American Joint Committee on Cancer staging system for cutaneous melanoma. J Natl Compr Canc Netw 2006;4:666-684.

9. Exhaustividad. En: Parkin DM, Chen VW, Ferlay J, GalceranJ y cols. Comparabilidad y Control de Calidad en los Registros de Cáncer. Informe Técnico Nº 19. Lyon (Francia): Ed. Agencia Internacional de Investigación sobre Cáncer, IARC; 1995:21-48.
10. Gaudette LA, Gao RN. Changing trends in melanoma incidence and mortality. Health Reports 1998;10:30-41.
11. Brochez L, Verhaeghe E, Bleyen L, De Backer G, et al. Cancer registration in Belgium: experience from a melanoma registration program in the province of East-Flanders. Arch Public Health 2000;58:263-279.
12. Armstrong BK, English DR. Cutaneous malignant melanoma. En: Schottenfeld D, Fraumeni JF (eds). Cancer Epidemiology and prevention. Oxford; 1996:1282-1312.
13. Bergfelt L, Newell GR, Sider JG, Kripke ML. Incidence and anatomic distribution of cutaneous melanoma among United States Hispanics. J Surg Oncol 1989;40:222-226.
14. Zegarra del Carpio R. Situación del melanoma maligno cutáneo en el Hospital Militar Central de Lima 1985-2007. Dermatol Perú 2008;18(3):267-283.
15. Zemelman V, Roa J, Ruiz Tagle S, Valenzuela C. Malignant melanoma in Chile: an unusual distribution of primary sites in men from low socioeconomic strata. Clin and Exp Dermatol 2006;31:335-338.
16. http://www.indec.gov.ar/webcenso/ECPI/index_ecpi.asp. (consulted: 30th August 2009).
17. Zago Borges S, Bakos L, Cartel Al, Wagner M, et al. Distribution of clinical-pathological types of cutaneous melanomas and mortality rate in the region of Passo Fundo, RS, Brazil. Int J Dermatol 2007;46:679-686.
18. Sortino-Rachou AM, Curado MP, Dias de Oliveira Latorre M. Cutaneous melanoma: population-based study in Goiania, Brazil, from 1988 to 2000. An Bras Dermatol 2006;81(5):449-455.
19. Baumert J, Plewig G, Volkenandt M, Schmid-Wendtner M. Factors associated with a high tumour thickness in patients with melanoma. Br J Dermatol 2007;156:938-944.
20. Montella M, Crispo A, Grimaldi M, De Marco M, et al. An assessment of factors related to tumor thickness and delay in diagnosis of melanoma in southern Italy. Preventive Medicine 2002;35:271-277.
21. http://www.deis.gov.ar/indicadores.htm. (consulted: 30th 30th August) 22 Sancho-Garnier H, Defez C, Stoebner-Delbarre A, Loria D y cols. Radiaciones ultravioleta en prevención del cáncer: Estrategias basadas en la evidencia. Una guía de la UICC para América Latina. Uruguay: Ed. Unión Internacional Contra el Cáncer;2007:185-203.