Topography of basal cell carcinoma and their correlations with gender, age and histologic pattern: a retrospective study of 1042 lesions

Topografia do carcinoma basocelular e suas correlações com o gênero, a idade e o padrão histológico: um estudo retrospectivo de 1.042 lesões

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Abstract: BACKGROUND: Basal cell carcinoma accounts for 75% of skin cancer. Sun exposure and genetics are related to its etiology. It's expected that biological and behavioral differences provide different patterns of involvement between sexes.
OBJECTIVES: To evaluate the topography of lesions and their correlations with gender, age and histological type.
METHODS: Retrospective study of basal cell carcinoma patients treated between 1999 and 2008 in the Skin Cancer Clinic of Santa Casa de Misericordia of Curitiba. We evaluated sex, age, location, histological type, margins commitment, sun exposure and family skin cancer history.
RESULTS: We found 1042 lesions in 545 patients (61% women), being more numerous in men ($p<0.01$). Their ages ranged between 27 and 95 years (median=65). Men had more sun exposure ($p<0.01$). The lesions were more frequent extra-cephalic recently ($p<0.01$). The margin involvement was higher in the head ($p<0.01$). The superficial type was less frequent on the head ($p<0.01$) and was associated with younger ages in women ($p<0.01$). The head housed 74% of lesions and the legs 2%. Women had a predilection for the legs, nose and upper lip and men to trunk, ears and scalp ($p <0.05$). The surgeries in the medial epicanthus and scalp occurred at younger ages ($p=0.01$).
CONCLUSIONS: We identified significant associations between the topography of lesions, gender, age and histological type, demonstrating the possible pathophysiological diversity and differential risk factors operation. In the period studied we found no trend of increase in the proportion of young or women among patients.
Keywords: Age distribution; Carcinoma, basal cell; Pathology; Sex distribution; Topography

Resumo: FUNDAMENTOS: O carcinoma basocelular corresponde a 75% dos tumores cutâneos. A exposição solar e a genética estão relacionadas à sua etiologia. Espera-se que diferenças comportamentais e biológicas proporcionem padrões diferenciados de acometimento entre os sexos.
OBJETIVOS: Avaliar a topografia das lesões e suas correlações com gênero, idade e tipo histológico.
MÉTODOS: Estudo retrospectivo de pacientes tratados por carcinoma basocelular entre 1999 e 2008 no ambulatório de câncer da pele da Santa Casa de Misericórdia de Curitiba. Avaliamos sexo, idade, localização, tipo histológico, situação das margens, histórico de fotoexposição e antecedentes familiares de câncer cutâneo.
RESULTADOS: Contabilizamos 1.042 lesões em 545 pacientes (61% mulheres), sendo mais numerosas nos homens ($p < 0,01$). As idades variaram entre 27 e 95 anos (mediana = 65). Os homens apresentavam mais fotoexposição ($p < 0,01$). As lesões extracefálicas foram mais frequentes recentemente ($p < 0,01$). O comprometimento de margens foi maior na cabeça ($p < 0,01$). O tipo superficial foi menos frequente na cabeça ($p < 0,01$) e se associou a idades menores nas mulheres ($p < 0,01$). A cabeça abrigou 74% das lesões, e as pernas, 2%. As mulheres apresentaram predileção para pernas, nariz e lábio superior e os homens para tronco, orelhas e couro cabeludo ($p < 0,05$). As cirurgias no epicanto medial e couro cabeludo ocorreram em idades menores ($p < 0,01$).
CONCLUSÕES: Identificamos associação significativa entre a topografia das lesões, o gênero, a idade e o tipo histológico, demonstrando a possível diversidade fisiopatológica e de atuação dos fatores de risco. No período estudado não verificamos tendência de aumento na proporção de jovens e mulheres entre os pacientes.
Palavras-chave: Carcinoma basocelular; Distribuição por idade; Distribuição por sexo; Patologia; Topografia

Received on 08.06.2010.
Approved by the Advisory Board and accepted for publication on 15.06.10.
* Study conducted at the Skin Cancer Outpatient Clinic, *Santa Casa de Misericórdia*, Curitiba, Paraná, Brazil.
Conflict of interest: None / *Conflito de interesse: Nenhum*
Financial funding: None / *Suporte financeiro: Nenhum*

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INTRODUCTION

Basal cell carcinoma (BCC) is the most common form of skin cancer, corresponding to around 75% of malignant skin tumors. [1] Chronic sun exposure, which differs between men and women, is believed to be the principal cause of these lesions. [2] BCC is more common in individuals over 40 years of age with a history of chronic sun exposure and lesions are often located on the face. [1-3] According to some studies, as well as an increase in the incidence of this form of skin cancer, changes have also occurred in the form of presentation of BCC, including an increase in the number of lesions occurring in photo-protected areas of the body and a trend towards a greater occurrence in females; however, few studies have been carried out in Brazil to evaluate these trends. [4-16]

In addition to sun exposure, genetic susceptibility and exposure to other environmental carcinogens are factors that have been related to the etiology of these lesions. [1,2] Therefore, behavioral and biological differences between male and female patients would be expected to result in different patterns of behavior of BCC. [17-19]

The present study evaluated the anatomical site of the lesions, their histological type and their correlations with the gender and age of the patients in the study population.

METHODS

A retrospective analysis was conducted using the charts of patients treated for basal cell carcinoma in the skin cancer clinic of the *Santa Casa de Misericórdia* in Curitiba between 1999 and 2008. Data evaluated included: the patient's gender, age at the date of surgery, anatomical site of the lesions, histological type, status of the surgical margins, the patient's history of sun exposure and family history of skin cancer. The infiltrative, sclerosing and micronodular histological types were defined as aggressive. Proportions were described as percentages and compared using the chi-square test or Fisher's exact test. Continuous variables were shown as means and standard deviations or medians and interquartile deviations in accordance with the normality of the distributions calculated using the Lilliefors test and compared using Student's t-test for independent samples or the Mann-Whitney test. Correlations were evaluated using Pearson's correlation coefficient or Spearman's nonparametric test. The anatomical site of the lesions was then adjusted for age and compared between genders using multiple logistic regression. Two-tailed p-values < 0.05 were considered statistically significant.

RESULTS

A total of 1,042 lesions from 545 patients were evaluated in the study. Sixty-one percent of these patients were women. The number of lesions per patient ranged from 1 to 17, with a median of 1 and a mean of 1.9. Men had more lesions than women (2 ± 2 versus 1 ± 1; $p<0.01$; Mann-Whitney test). When only patients with extra-cephalic lesions were counted, the median number of lesions per patient was 2, with a mean of 2.8.

Age of the patients ranged from 27 to 95 years, with a median age at first surgery of 65 ± 20 years for female patients and 63 ± 16 years for males ($p = 0.68$, Mann-Whitney test) (Graph 1). Overall, 31.7% of the patients had a family history of skin cancer.

The male patients were significantly more likely to participate in outdoor activities compared to the women (36% versus 11%; $p < 0.01$; chi-square test).

No correlation was found between the age of the patients and the year in which they were first submitted to surgery within the study period (Rho Spearman = -0.007; $p = 0.87$).

There was a statistically significant trend towards an increase in the proportion of extra-cephalic lesions over time ($p = 0.02$; chi-square test for trend); however, this characteristic was almost exclusively associated with the sub-group of women ($p = 0.06$ versus $p = 0.72$; chi-square test for trend). Furthermore, when the last surgery performed on the patient consisted of the removal of an extra-cephalic lesion, this patient had already undergone a greater number of surgeries for the removal of lesions (2 ± 2 versus 1 ± 1; $p < 0.01$; Mann-Whitney test).

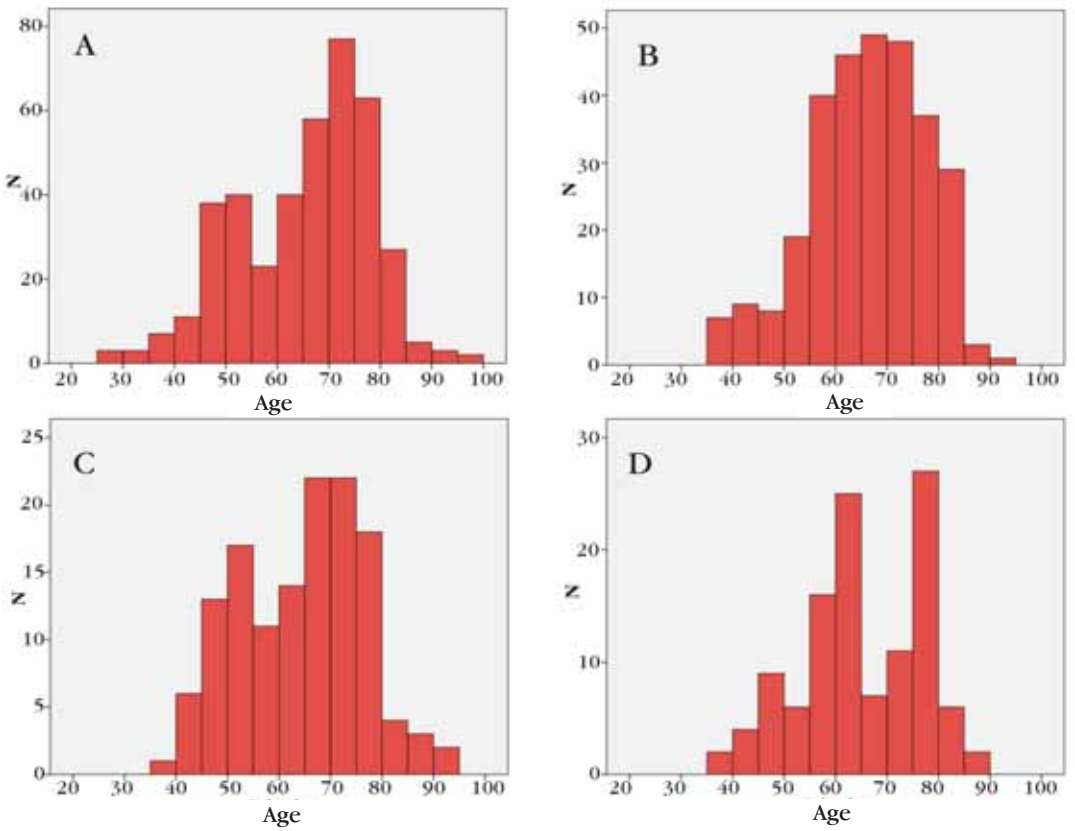
No trend was found towards an increase in the proportion of females among patients first presenting at this institute during the study period ($p = 0.27$; chi-square test for trend).

Regarding the type of lesion, 72% were solid, 16% were superficial and 12% consisted of one of the more aggressive types (infiltrative, micronodular or sclerosing).

A finding of positive margins was more common in lesions located on the head (7% versus 2%; $p < 0.01$; Fisher's exact test). Likewise, positive or close margins were more common in the more aggressive histological types (10% versus 4%; $p < 0.01$; chi-square test). Multiple logistic regression analysis showed that both the anatomical site of the lesion and more aggressive histological types were factors independently associated with a risk of positive margins ($p<0.05$).

The superficial histological type was significantly less common in lesions situated on the head (8% versus 37%; $p<0.01$; chi-square test). In addition, it was associated with younger ages in women (56 ± 17 versus 68 ± 19 years; $p<0.01$; Mann-Whitney test); however, not in men (69.5 ± 19 versus 66.5 ± 16 years; $p=0.28$; Mann-Whitney test).

Tables 1 and 2 show the distribution of the



Graph 1: Graphs of the patients' ages at the time of surgery according to the site of the lesion and patient's gender.
A: Cephalic lesions in women; **B:** Cephalic lesions in men; **C:** Extra-cephalic lesions in women; **D:** Extra-cephalic lesions in men.

Table 1: Bivariate comparison of the site of the lesions according to the patient's gender

Site	Total	Female	Male	Odds Ratio (95% CI)	p-value
Head*	715(74%)	404(75%)	311(72%)	1.19 (0.90 - 1.59)	0.23
Neck*	41(4%)	22(4%)	19(4%)	0.93 (0.50 - 1.74)	0.82
Trunk*	127(13%)	60(11%)	67(15%)	0.69 (0.47 - 0.99)	<0.05
Upper limbs*	70(7%)	36(7%)	34(8%)	0.84 (0.52 - 1.37)	0.49
Lower limbs**	19(2%)	16(3%)	3(1%)	4.40 (1.27 - 15.21)	0.01
	Comparison between sub-divisions of the head (n=704)				
Nose *	235(33.4%)	156(39.1%)	79(25.9%)	1.84 (1.33 - 2.54)	<0.01
Ears**	24(3.4%)	2(0.5%)	22(7.2%)	0.06 (0.02 - 0.28)	<0.01
Pre-auricular region*	24(3.4%)	10(2.5%)	14(4.6%)	0.53 (0.23 - 1.22)	0.13
Retro-auricular region**	12(1.7%)	4(1.0%)	8(2.6%)	0.38 (0.11 - 1.26)	0.14
Upper eyelid**	5(0.7%)	2(0.5%)	3(1.0%)	0.51 (0.08 - 3.05)	0.66
Lower eyelid*	43(6.1%)	23(5.8%)	20(6.6%)	0.87 (0.47 - 1.62)	0.66
Internal canthus**	24(3.4%)	15(3.8%)	9(3.0%)	1.28 (0.55 - 2.98)	0.68
Forehead*	79(11.2%)	48(12.0%)	31(10.2%)	1.21 (0.75 - 1.95)	0.44
Temple*	49(7.0%)	17(4.3%)	32(10.5%)	0.38 (0.21 - 0.70)	<0.01
Zygoma *	22(3.1%)	10(2.5%)	12(3.9%)	0.63 (0.27 - 1.47)	0.28
Upper lip**	41(5.8%)	33(8.3%)	8(2.6%)	3.35 (1.52 - 7.36)	<0.01
Lower lip**	5(0.7%)	4(1.0%)	1(0.3%)	3.09 (0.34 - 27.68)	0.40
Jaw angle**	16(2.3%)	5(1.3%)	11(3.6%)	0.34 (0.12 - 0.99)	0.04
Cheek*	100(14.2%)	57(14.3%)	43(14.1%)	1.02 (0.66 - 1.56)	0.94
Chin**	13(1.8%)	9(2.3%)	4(1.3%)	1.74 (0.53 - 5.69)	0.41
Scalp**	12(1.7%)	4(1.0%)	8(2.6%)	0.38 (0.11 - 1.26)	0.14

* Chi-square test; ** Fisher's exact test.

Table 2: Comparison made using multivariate logistic regression between the site of cephalic lesions and gender, adjusted according to age (n = 690)*

Variables	Odds Ratio	95% CI		p-value
Age	1.00	0.99	1.02	0.60
Nose	-	- -	<0.01	
Ears	0.05	0.01	0.20	<0.01
Pre-auricular region	0.37	0.16	0.89	0.03
Retro-auricular region	0.25	0.07	0.84	0.03
Upper eyelid	0.33	0.05	2.03	0.23
Lower eyelid	0.57	0.30	1.11	0.10
Internal canthus	0.84	0.35	2.02	0.70
Forehead	0.78	0.46	1.32	0.35
Temple	0.28	0.14	0.54	<0.01
Zygoma	0.50	0.20	1.25	0.14
Upper lip	2.04	0.90	4.64	0.09
Lower lip	1.95	0.21	17.73	0.56
Jaw angle	0.22	0.07	0.66	0.01
Cheek	0.72	0.44	1.18	0.20
Chin	1.10	0.33	3.69	0.88
Scalp	0.26	0.08	0.89	0.03
Constant	1.60	0.00	0.00	0.31

* p-value (of the model) < 0.001; Dependent variable: gender female

lesions according to gender, 74% of the lesions occurring on the head and only 2% on the lower limbs.

Compared to the other sites, the surgeries carried out on the trunk occurred at younger ages in women (66 ± 20 versus 67 ± 21 years; p=0.01; Mann-Whitney test); however, not in men (63 ± 18 versus 67 ± 16 years; p = 0.87; Mann-Whitney test).

Analysis of the distribution of the cephalic lesions showed that the surgeries performed on the ears, preauricular region and forehead occurred at older ages (74 ± 13 versus 67 ± 17 years; p<0.01 / 71 ± 14 versus 67 ± 17 years; p<0.05 / 71.5 ± 13 versus 67 ± 17 years; p<0.02; Mann-Whitney test). On the other hand, the surgeries performed on the medial canthus and on the scalp occurred at younger ages (55 ± 19 versus 68 ± 17 years; p = 0.01 / 61 ± 15 versus 68 ± 18 years; p = 0.01; Mann-Whitney test).

DISCUSSION

These data show that onset of the lesions generally occurred after the sixth decade of life, although there were cases of patients who were diagnosed prior to 30 years of age. There was no statistically significant difference in age at presentation between men and women, women forming the majority of patients. Although some older studies have reported that BCC is more common in men, several more recent studies have shown that women form the majority of patients. [1,9,15,16]

A considerable percentage of the patients had multiple lesions, principally the men, giving strength to the concept of the occurrence of new lesions in individuals with a previous diagnosis of BCC. [20,21]

This study found no evidence of any increase in the proportion of younger patients or in the proportion of female patients in recent years, contradicting observations made in some international studies. [5-14] Nevertheless, a greater proportion of extra-cephalic lesions was observed in recent years compared to previous years, principally among women. This finding, which has also been reported in other studies [9], may be due to an actual change occurring recently in the profile of patients as a result of behaviors associated with greater recreational exposure to solar radiation. However, this variable was not part of the scope of this study. It should be remembered, however, that, if lesions on the trunk and limbs are indeed more likely to be multiple and recurrent, as suggested by these data, the very fact that these patients are being followed-up may generate a bias resulting from the identification of a greater proportion of new lesions in these areas, thus indicating an actual change not only in the profile of these patients, but also in the profile of the lesions treated in this service over the years.

These data highlight the importance of defining the surgical margins in accordance with the different histological types of BCC, since these findings show that margins are more likely to be positive or close when the histological type of the tumor is more aggressive. Likewise, the margins were more likely to be positive in cases involving cephalic lesions, which may also be due to a lack of adjacent tissue or concerns regarding cosmetic appearance. [22,23] As expected, the most common histological type was the solid type, corresponding to 3/4 of the lesions, followed by the superficial type. This latter type was associated with lesions on the neck, trunk and limbs and with younger ages in women, which gives weight to earlier observations that this may be a type of lesion that is physiopathologically different from other types of BCC. [24,25]

The superficial histological type and lesions located on the trunk were more common at younger ages only in the group of female patients. This, associated with the trend described above of an increase in the proportion of extra-cephalic lesions in this subgroup, may indicate that the risk behavior for this type of lesion, such as greater recreational exposure to the sun, particularly when the lesion is situated on the trunk, represents a more recent type of behavior in women compared to men. This may also coincide with cultural changes brought about by social movements such as feminism or by an increase in the cosmetic value given to tanned or brown skin in recent times. These observations are in agreement with the findings of de Vries et al. [9], who conducted an extensive review on the incidence of BCC in the Dutch population between 1973 and 2000 and reported a progressive

increase in the general incidence of these lesions in the study period, this increase being more pronounced in young women and for lesions of the trunk and limbs.

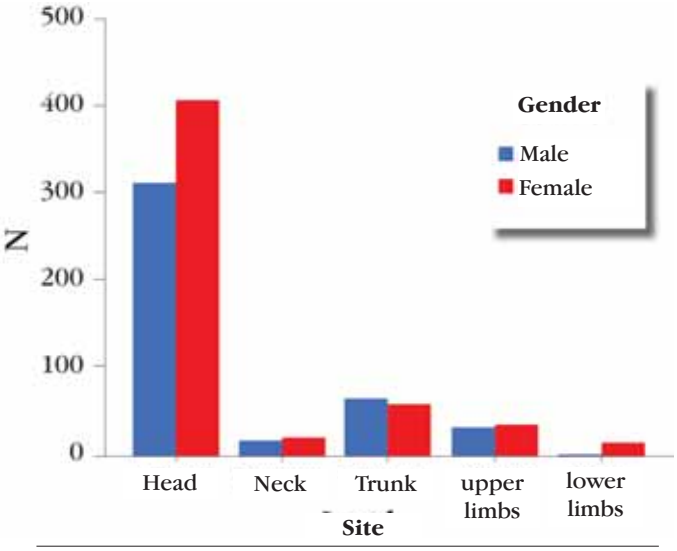
Both when the data were analyzed according to the anatomical site of the tumor and when analysis was conducted according to subdivisions of the head, the difference between men and women with respect to the anatomical site affected by BCC was evident. Many of the findings corroborate previous international studies that had already reported a predilection of BCC for the trunk in men and for the lower limbs in women (Graph 2). [18, 26-28] No other statistically significant trends were found with respect to any of the other body sites in either males or females. Regarding the face, there was an evident propensity for women to develop lesions on the nose and upper lip and for men to develop lesions on the sides of the face, ears and scalp (Graph 3). Explanations attribute these differences primarily to behavior such as longer hairstyles for women and a lesser likelihood for women to develop intense male-pattern baldness. These characteristics would lead to different patterns of exposure to ultraviolet (UV) radiation. However, there are other known risk factors such as genetic susceptibility and exposure to environmental carcinogens, including chemical products for personal care and hygiene, which cannot be ignored.

Some authors suggest that sebum may act as a natural sunscreen and that patients with seborrheic or acne-prone skin would have a lower risk for BCC. [29] If this were true, it could be speculated that female skin, which is less oily compared to male skin, would be proportionally more susceptible to damage by solar radiation and to developing BCC, principally in photo-exposed areas and those parts of the body that are rich in androgen-sensitive sebaceous glands such as the nose, where the difference in sebum production between the genders would theoretically be greater.

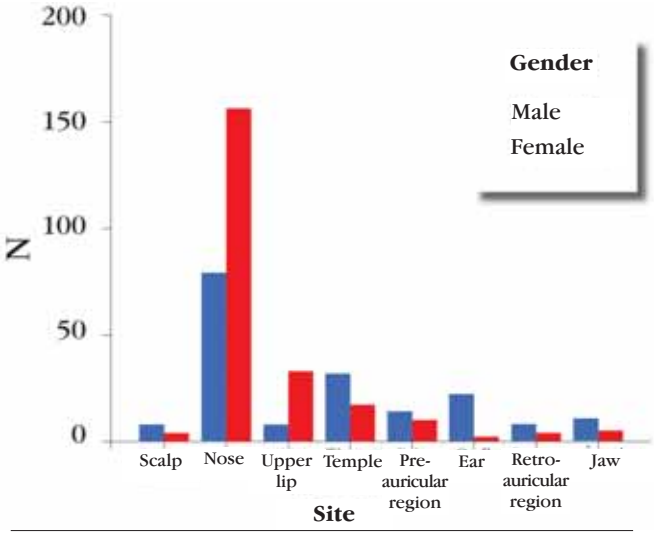
One intriguing question concerns the fact that lesions on the scalp and those in the internal canthus occur at younger ages, particularly in women. Since these are relatively photo-protected areas, the effect of radiation would be expected to occur later or at least not any earlier. This controversial finding suggests the participation of factors not directly related to UV radiation at these sites. [27] On the other hand, surgeries for the removal of these lesions from the ears occurred when patients were older, coinciding with the ages at which alopecia and baldness are more pronounced, consequently offering less protection to these areas. Nevertheless, the possibility cannot be ignored that diagnosis of these lesions may have been delayed as a result of them being less noticeable to the patient compared to lesions on the face.

The propensity of women to develop BCC on the legs has been reported in other studies, which some authors believe indicates similarities in the photocarcinogenesis of BCC and melanoma, the occurrence of which is also common on the legs in women, suggesting that in some cases, acute, intense exposure may be more prejudicial than prolonged exposure. [26] Likewise, the findings of the present study confirm the male propensity for lesions on the trunk, although the strength of this association was not as great as that of the lower limbs for women.

In conclusion, the present study showed statistically significant associations between the anatomical site of BCC lesions, gender, histological type and the patient's age, confirming results from other previous studies and offering new data for the prevention and understanding of this disease that is common in dermatology patients. [30] ❑



Graph 2: Distribution of the lesions according to body segment and gender



Graph 3: Distribuição das lesões da cabeça nas regiões de maior diferença de acometimento entre os gêneros

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How to cite this article/*Como citar este artigo*: Souza CFD, Thomé EP, Menegotto PF, Schmitt JV, Shibue JRT, Tarlé RG. Sites of basal cell carcinomas and correlations with gender, age and histological pattern: a retrospective study of 1042 lesions. An Bras Dermatol. 2011;86(2):272-7.