Research Article

An epidemiological study of malignant skin tumors at Casa de Saúde hospital

Viçosa SJ,[1] Girardon DT,[2] Pereira LF[3]

[1]Medical course academic, Franciscan University, Brazil
[2]Digestive System Surgeon, Professor of Medicine, Franciscan University, Brazil
[3]Oncological Surgeon, Professor of Medicine, Franciscan University, Brazil

Correspondence: Sthefani Jardim Viçosa, Medical course academic, Franciscan University, Santa Maria, Rio Grande do Sul, Brasil, Tel +5555999369109, Email jardimvicos@gmail.com

Received: February 03, 2023 | **Published:** February 17, 2023

Abstract

Malignant skin tumors are the most frequent in Brazil, corresponding to 30% of all cancers registered in the country, of which melanoma skin cancer represents 3% of skin neoplasms. The most frequent non-melanoma skin cancers are basal cell carcinoma, followed by squamous cell carcinoma. The main risk factor for skin cancers is chronic exposure to sunlight, in addition to fair-skinned individuals. The research has as variables to be analyzed: patient's age, gender, skin color, profession, previous comorbidities, anatomopathological diagnosis and affected site, so that prevention campaigns can be invested from the analyzed epidemiological data. It was an observational, retrospective and descriptive study, with analysis and records of outpatient care records of Casa de Saúde Hospital, in the period of January 2017 to March 2021. We analyzed the electronic medical records of 491 patients who underwent surgical procedures at the hospital. 46 patients obtained the anatomopathological diagnosis of skin cancer and participated in the research. The average age of patients with skin cancer was 64 years old, with the prevalence of males than females. The white color was affected in 97.8% of the analyzed patients, as well as the main origin was Santa Maria/RS. Regarding those who informed the professions, farmers, construction workers and "home workers" obtained the highest percentages. The main comorbidities described were systemic arterial hypertension, diabetes mellitus and smoking (65.8%, 23.7% and 23.7% respectively). The BCCs were linked like the predominant lesions in the study, affecting 30 patients (65.2%), 2 of which were ulcerated (6.7%). Furthermore, its main locations were head/face and anterior/posterior trunk. On the other hand, SCC's totaled 13 cases (28.3%), located in the head/face, anterior/posterior trunk and lower limbs. Melanomic skin tumors were present in 3 cases (6.5%), 2 of them in the lower limbs and the rest in the anterior/posterior trunk. The greatest number of skin cancers was analyzed in areas more exposed to the sun, confirming the importance of primary prevention and the use of high SPF, in addition to behavioral measures. The results obtained suggest further studies with larger population samples for a better assessment of risk factors related to this pathology.

Keywords: skin cancer, melanomics, basal cell carcinoma (BCC), squamous cell carcinoma (SCC), prevention

Introduction

Skin tumors, or skin cancer, are the most frequent in Brazil, corresponding to 30% of all malignant tumors registered in the country.[1] They can be subdivided into non-melanoma and melanoma.[2] The most common non-melanoma skin cancer is basal cell carcinoma, followed by squamous cell carcinoma.[1]

According to the National Cancer Institute, melanoma skin cancer is estimated at 8,450 new cases in Brazil in 2020, with 4,200 men and 4,250 women. However, it represents only 3% of skin neoplasms. Furthermore, it is considered the most serious type of malignant skin neoplasms, due to its high rate of dissemination to other organs. Non-melanoma skin tumors, basal cell carcinoma (BCC) and squamous cell or squamous cell carcinoma (SCC), have a high prevalence and incidence – 176,930 new cases, 83,770 men and 93,160 women. Although they have low mortality rates.[2]

The epidemiology of cutaneous melanoma becomes differentiated from other types of cancer, as it often affects younger individuals with an average age of 50 years old,[3] however the age range of non-melanomic tumors is described in different studies such as over 60 years old[2] associated with chronic exposure to sunlight, described as the main cause of SCC and BCC.[4]

Basal cell carcinoma (BCC) is located preferentially in the upper two thirds of the face and its most important risk factor is exposure to sunlight in individuals, predominantly, with fair skin, light eyes and blond or red hair. Like BCC, squamous cell carcinoma also affects fair-skinned individuals.[5] In this context, it becomes necessary to assess the local regional epidemiology, when analyzing variables such as: patient age, gender, skin color, profession, previous comorbidities, anatomopathological diagnosis, and affected site to identify the main risk factors and which the higher prevalence of both melanoma and non-melanomic skin cancers, compared to national data. And from this assessment, to develop possible preventive strategies in order to raise awareness and elucidate the population's causal problem of the disease.

Materials and methods

Research outline

An observational, retrospective and descriptive study was carried out, with an analysis of the medical records and outpatient care forms at Casa de Saúde Hospital, from January 2017 to March 2021. The outpatient care forms for minor procedures were reviewed later and the medical records of patients undergoing surgical procedures at Casa de Saúde Hospital, located in Santa Maria/RS.[6]

Sample and Inclusion/Exclusion Criteria

The sample included all patients who underwent excision of skin tumors, in which the procedure took place between January 2017 and

March 2021. A survey carried out in the Statistics sector of Casa de Saúde Hospital showed that in 2020, 156 excision of skin tumors. In this research, a total of 491 patients were analyzed over the course of 4 years, corresponding to the statistical data collected. Those tumors that after the anatomopathological analysis were not malignant were excluded, in addition to those for which the electronic medical records were completely lacking in data.

Data collection

Data were obtained by consulting the outpatient care records of Casa de Saúde Hospital. The following variables were analyzed: age, gender, skin color, profession, anatomopathological diagnosis, previous comorbidities and affected site of each of the patients included in the sample.

Data analysis

The collected data were initially tabulated in a database using Microsoft Excel 2016. 3.4, the data generated from the electronic medical records and stored in the researcher's spreadsheet were analyzed by comparing the variable age (quantitative, continuous), from according to sex, using the T-Student test (comparison of two means), and for the type of skin tumor (as there were 3 types) an Anova was used. When comparing categorical (qualitative) variables, according to sex (Fisher's Exact Test) and according to the type of tumor (Pearson's Chi-square Test).

Ethical procedures

Initially, the research project was sent to the COMIC of the Casa de Saúde Hospital, it was approved and sent for analysis and approval by the CEP of the UFN (registered through the Plataforma Brasil). The research only started after a favorable opinion to its realization.

It should be noted that, as this is a research carried out based on clinical records, that is, secondary data analysis, without any direct contact with the participants, there is no obligation to present and sign the Free and Informed Consent Form (TCLE), as well as risks are not foreseen, except for the possibility of breach of secrecy. For this reason, the responsible researcher undertakes to comply with this, by signing the Confidentiality Agreement, emphasizing that the information collected will be kept confidential and used, solely and exclusively, for the purposes of carrying out the research. It should be noted, however, that they may be disclosed completely anonymously in scientific papers, with the aim of contributing to greater knowledge of malignant skin lesions, benefiting the population in general. The data will be stored after completion of the research for a period of approximately five years and then destroyed.

As for the risks related to the research, it should be noted that, as it only involves collecting data from clinical records, without direct contact with the patients involved, risks are not foreseen. Regarding the benefits, evaluating the epidemiology of skin tumors at Casa de Saúde Hospital brings benefits to the local population, as through epidemiological analysis, projects for the prevention of skin tumors can be developed for a target audience, in addition to the interventions already performed.

Results

The electronic medical records of 491 patients who underwent surgical procedures at Casa de Saúde Hospital, under the responsibility of the small procedures outpatient clinic, from January 2017 to March 2021, were analyzed. These were excluded all the patients with the electronic medical records incomplete, beyond those who did not have malignant skin lesions after the anatomopathological diagnosis. In total, 46 patients obtained the anatomopathological diagnosis of malignant skin lesions and participated in the research, representing approximately 10% of patients undergoing surgical procedures, that is, for every 10 patients operated, one was diagnosed with skin cancer.

The data generated from electronic medical records and stored in the researcher's spreadsheet were analyzed by comparing the variable age (quantitative, continuous), according to gender, using the T-Student test (comparison of two means), and for the type of skin tumor (as there were 3 types) an Anova was used. When comparing categorical (qualitative) variables, according to sex (Fisher's Exact Test) and according to the type of tumor (Pearson's Chi-square Test).

The general characteristics of the analyzed patients (Table 1) show us the analyzed variables and their prevalence in the studied population. The average age of patients with malignant skin tumors was 64 years old, with a prevalence, even if low, of males over females. The white color affected the majority (97.8%) of the analyzed patients, as well as the main origin was Santa Maria/RS. Regarding the professions of the patients, the majority had incomplete medical records, but of those who informed, farmers, construction workers and those who work in their own homes obtained the highest percentages. Only eight patients (17.4%) had no previous comorbidities out of a total of forty-six.

Table I General characteristics of studied patients

Variables	Average ± dp	% (N=46)
Age (years)	64 (±14,2)	
Genre		
Masculine		56.5 (26)
Female		43.5 (20)
Color		
White		97.8 (45)
Not white		2,2 (1)
Origin	-	
Santa Maria		84,6 (39)
Itaara		2,2 (1)
Agudo		2,2 (1)
São Pedro do Sul		2,2 (1)
Mata		4,4 (2)
Julio de Castilhos		4,4 (2)
Profession		
From home		17,4 (8)
Farmer/Applies pesticides to crops		13 (6)
Construction worker		8,8 (4)
Mechanic		4,4 (2)
Carpenter		2,2 (1)
Dressmaker		2,2 (1)
Civil Servant		2,2 (1)
Truck driver		2,2 (1)
Receptionist		2,2 (1)
Real estate agency		2,2 (1)
Uninformed		43,2 (19)
Presence of comorbidities		
One		43,5 (20)
Two or more		39,1 (18)
Absence of comorbidities		17,4 (8)

The main comorbidities described (Table 2) were: systemic arterial hypertension, diabetes mellitus and smoking (65.8%, 23.7% and 23.7% respectively), with thirty-eight patients having previous diseases, and of these, eighteen patients with more than two. When analyzing pathologies that affect the skin tissue, psoriasis was present

in one patient and other previous tumors, including: skin, breast and colon, accounted for a total of three patients.

Table 2 Main comorbidities in the patients studied

Comorbidities	% (N=38)
Systemic Arterial Hypertension	65,8 (25)
Diabetes Mellitus	23,7 (9)
Obesity	2,6 (1)
Smoking	23,7 (9)
Chronic obstructive pulmonary disease	5,3 (2)
Heart disease (valvular heart disease, arrhythmias)	5,3 (2)
Depression	10,5 (4)
Previous cancer (skin, breast, colon)	7,9 (3)
Psoriasis	2,6 (1)
Fibromyalgia	2,6 (1)
Hypothyroidism	2,6 (1)
GAD	2,6 (1)
Personality disorder	2,6 (1)

Note: 18 patients with more than two comorbidities.

The anatomopathological diagnosis (Table 3) of the patients studied was proportionally similar to most epidemiological studies on skin tumors. Basal cell carcinomas obtained, in this study, the predominance of lesions affecting 30 patients (65.2%), of which 2 were ulcerated (6.7%). Furthermore, their main locations were: head/face and anterior/posterior trunk (Table 4). Squamous cell carcinomas (SCC) were slightly above the national average (15%),[1] as they totaled 13 cases (28.3%), located in the head/face, anterior/posterior trunk and lower limbs, in the majority (Table 4). Melanoma skin tumors were present in 3 cases (6.5%), 2 of them in the lower limbs and the rest in the anterior/posterior trunk (Table 5).

Table 3 Anatomopathological diagnosis of skin lesions in the patients studied

Anatomopathological lesions	% (N=46)
Basal cell carcinoma	65,2 (30)
ulcerated basal cell carcinoma	6,7 (2)
squamous cell carcinoma	28,3 (13)
Melanoma	6,5 (3)

Table 4 Location of skin lesions in the patients studied

Location of lesions	% (N=46)
Head/Face	47,8 (22)
anterior/posterior trunk	39,1 (18)
Upper limbs	15,2 (7)
Lower limbs	13 (6)

Note: 7 patients with lesions in two or more sites.

Table 5 Variables analyzed, according to the anatomopathological result of the skin lesions

Anatomopathology of skin lesions

Variables	CBC (N=30)	CEC (N=13)	Melanoma (N=3)	p
Age (years)	63 (±14,8)	68,4 (±11,6)	55,3 (±17,9)	0,02
Genre (%)				0,826
Masculine	61,5 (16)	30,8 (8)	7,7 (2)	
Female	70 (14)	25 (5)	5 (1)	
Color (%)				0,761
White	64,4 (29)	28,9 (13)	6,7 (3)	
Not white	100 (1)	-	-	
Origin (%)				0,745
Santa Maria	64,1 (25)	28,2 (11)	7,7 (3)	
Another city	71,4 (5)	28,6 (2)	-	

Table Continued...

Anatomopathology of skin lesions

Variables	CBC (N=30)	CEC (N=13)	Melanoma (N=3)	p
Profession (%)				0,342
Greater sun exposure	80 (8)	20 (2)	-	
Less sun exposure	70,6 (12)	17,6 (3)	11,8 (2)	
Uninformed	52,6 (10)	42,1 (8)	5,3 (1)	
Comorbidities (%)				0,066
Present	50 (4)	25 (2)	25 (2)	
Absent	68,4 (26)	28,9 (11)	2,7 (1)	
Lesion site (%)				0,056
Head/Face	78,9 (15)	21,1 (4)	-	
anterior/ posterior trunk	64,7 (11)	29,4 (5)	5,9 (1)	
Upper limbs	75 (3)	25 (1)	-	
Lower members	16,7 (1)	50 (3)	33,3 (2)	

Caption: BCC, basal cell carcinoma; SCC, squamous cell carcinoma

Profession:

1. Greater exposure: Construction worker/farmer/applicates pesticides in the field

2. Less exposure: the others

When analyzing the patients according to gender: the male had an average age of 67 years old while the female 59 years old. Practically all cases were white, with only one non-white male case. When the professions are informed, it can be concluded that males with the highest number of cases receive more sun exposure, while females receive less sun exposure. In addition, males had a greater absence of comorbidities compared to females. And, finally, males, compared to the three anatomopathological diagnoses analyzed, always had a higher number of cases than females (Table 6).

Table 6 Variables analyzed, according to the gender of the patients studied

Variables	Gender		p
	Male (N=26)	Female (N=20)	
Age (years)	67,4 (±13,2)	59,6 (±14,7)	0,033
Color (%)			0,56
White	55,6 (25)	44,4 (20)	
Not white	100 (1)	-	
Origin (%)			0,020
Santa Maria	64,1 (25)	35,9 (14)	
Another city	14,3 (1)	85,7 (6)	
Profession (%)			0,042
Greater sun exposure	90 (9)	10 (1)	
Less sun exposure	41,2 (7)	58,8 (10)	
Uninformed	52,6 (10)	47,4 (9)	
Comorbidities (%)			0,51
Absent	62,5 (5)	37,5 (3)	
Present	55,3 (21)	44,7 (17)	
Anatomopathological of the lesion (%)			0,89
Basal cell carcinoma	53,3 (16)	46,7 (14)	
Squamous cell carcinoma	61,5 (8)	38,5 (5)	
Melanoma	66,7 (2)	33,3 (1)	
Injury site			1,00
Head/Face	57,9 (11)	42,1 (8)	
Anterior/posterior trunk	58,8 (10)	41,2 (7)	
Upper limbs	50 (2)	50 (2)	
Lower limbs	50 (3)	50 (3)	

Discussion

The average age of the patients analyzed in the research was 64 years old, being 67 years old for males and 59 years old for females, considering the high prevalence of non-melanomic skin tumors, which, according to Simoneti et al.,[2] are aged over 60 years old, and not isolating the comparison in melanoma tumors, the results of this research corroborate with previous studies on this topic. In other words, the importance of a semiological investigation of skin tumors in patients over 60 years old is evident, since according to the data obtained in this research, 1 out of 10 patients operated one had a skin neoplasm.

Almost all of this study involved white-skinned patients (97.8%), a fact that confirms the high incidence of skin tumors in light-skinned people.[5] Females resulted in less sun exposure, as greater sun exposure was considered for construction workers and farmers/applicates pesticides in crops, in which case 58.8% of patients with little sun exposure had skin cancer compared to males who obtained 41.2% of the cases with little exposure to the sun. Males obtained 90% of the highest sun exposure to females with 10%. It is worth noting that 43.2% of the total number of patients did not have their profession informed in an electronic medical record, thus not being subject to analysis. When considering this fact, it is clear that the greater number of skin tumors is not related to sun exposure in this study, as 15 patients with non-melanomic skin tumors were part of the group with less sun exposure, compared to 10 patients with greater sun exposure, therefore, does not confirm most previous studies, since according to Broetto et al.,[4] chronic exposure to sunlight was described as the main cause of SCC and BCC. The questions remain: the lack of information in the electronic medical records corroborated the change in these results; Or else, the group of housewives should be included in the greatest sun exposure; or even, the group selected as greater sun exposure had some type of protective factor for the skin.

According to Hoff et al.,[5] smoking increases the risk of late onset of BCC, as well as radiotherapy, phototherapy and chronic exposure to arsenic, however other chronic comorbidities are not described in their studies. Chronic ulcers and scarring are the most common appearance of SCC. In the research above, 43.5% of the patients analyzed had a previous chronic disease and 39.1% had two or more, considering that only 17.8% of the patients did not have any comorbidity, it was essential to analyze which are the main associated diseases, they were: Systemic arterial hypertension, Diabetes Mellitus and Smoking. Males resulted in 55.3% of presence of comorbidities while females 44.7%, in the comparison of absence of comorbidities, males represented 62.5% while females 37.5%. Systemic arterial hypertension affects a quarter of the adult Brazilian population,[7] thus, the study population being formed entirely by adults, corroborates with the national parameters of systemic arterial hypertension, even if this does not have associations with malignant skin tumors as a causal factor. The prevalence of Diabetes Mellitus in Brazil is 7.5%,[8] compared to the results of this study, which were 23.7%. However, in several epidemiological population studies, the high association of Systemic Arterial Hypertension with DM is described. On the other hand, the only comorbidity associated with BCC, previously described in studies of malignant skin tumors, is smoking, and thus, questions remain about SAH and DM, because due to the high prevalence in the Brazilian population, they could have some association with malignant skin tumors, or their high rates would only be associated with the age range in which this population is affected.

According to the National Cancer Institute (2020), melanoma corresponds to 3% of malignant skin neoplasms, in the patients of this research the results were higher, proportionally, since they were 6.5%, which corresponds to 3 patients of the total of 46 analyzed. Although the total number of patients is not relevant for further assertions, the percentage of melanoma in this study was twice the national average. Thus, it is important to promote studies with a larger population sample, so that the prevalence of melanoma skin tumors in the local population can be analyzed. The locations of the melanoma tumors in this study were 1 case in the anterior/posterior trunk and 2 cases in the lower limbs, thus inquiring the location of melanomas is also extremely relevant, the analysis of the body as a whole would be ideal for more results. However, the number of patients in this research cannot be compared with national INCA data, but it is known that the number of melanomas is increasing. Basal cell carcinoma is responsible for 70% of malignant cutaneous neoplasms, represented in this study by 32 patients (69.5%), results compatible with the national average.[1] There were a total of 13 cases of SCC (28.3%), slightly above the values described in previous articles, which corresponded to 15% of malignant skin tumors.[9]

Non-melanomic skin tumors are responsible for affecting areas of exposure to ultraviolet radiation,[5] the results of this study showed that 18 patients (39.1%) had involvement of the trunk, an area which have less sun exposure. The remaining 28 patients had involvement in the head/face and upper and lower limbs. It is also worth mentioning that 7 patients had malignant lesions in more than one body region. Thus, the greatest number of skin cancers are found in body areas with greater sun exposure, a fact that confirms the studies and publications cited above. For this reason, primary prevention becomes essential, such as the use of high SPF and behavioral measures: wearing long-sleeved shirts when exposed to the sun, wearing caps, hats, umbrellas; if possible, use sunglasses and avoid maximum intense sun exposure between 10 am and 4 pm, due to the high incidence of ultraviolet rays at these times.[10] In this study, specific skin locations were not obtained, due to the great topographic variability of this pathology, thus opting to perform the location by segments: face, trunk, limb.[11]

Melanoma skin tumors equally affect females and males, whereas non-melanomic skin tumors affect females more.[1] Males were more affected by cutaneous malignant tumors with 26 cases, while females with a total of 20 patients. Even if few cases of melanomas, the largest number (2 patients) are male and the rest (1 patient) female. Regarding non-melanomic tumors, 16 cases of basal cell carcinomas (53.3%) were described in men and 14 cases in women (46.7%), whereas squamous cell carcinomas resulted in 8 cases for males (61.5%) and 5 cases for females (38.5%).

Finally, although the municipality of Santa Maria has a coverage of 32 municipalities, which comprises the 4th Regional Health Coordination, only 5 other municipalities referred their patients for excision of skin tumors at Casa de Saúde Hospital, they are: Itaara (1 case), Agudo (1 case), Júlio de Castilhos (2 cases), São Pedro do sul (1 case) and Mata (2 cases). The other 39 remaining patients are residents of the municipality of Santa Maria. The questions cover contexts related to public health, as this study cannot assess the prevalence in other cities due to the low number of patients analyzed. Consultations and referrals would be being dissipated to other local hospitals, the number of cases of skin tumors in other cities is reduced, or perhaps Santa Maria receives a high rate of ultraviolet radiation; or even, the lack of diagnosis and follow-ups would be underestimating the number of cases in other cities.[12-18]

Conclusion

With the results of this research, it can be concluded that the age group of the analyzed patients is in agreement with the national

results and previous researches**.** In addition to the concordance of the age group, the white skin color, which was practically all cases, also confirms the bibliographic review of the study. It is also important to emphasize the higher prevalence of cases in the population over 60 years old, therefore, the cutaneous semiological investigation in these patients becomes essential, when considering the results of this research that for every 10 patients operated on, 1 obtained the anatomopathological diagnosis of skin cancer skin.

Although 43.2% of the patients did not have their profession informed, the greater number of skin tumors was not related to greater sun exposure, a result that did not show agreement with previous studies, even though the group chosen for high sun exposure had been construction workers, farmers and professionals who apply pesticides to crops.

The association of previous chronic comorbidities and skin cancer was strongly associated with smoking in previous studies. The results of this study showed other associated diseases such as Systemic Arterial Hypertension and Diabetes Mellitus, in addition to smoking, which was represented by a total of 9 cases out of the 46 analyzed.

The anatomopathological diagnosis showed the prevalence of basal cell carcinomas compared to squamous cell carcinomas and melanomas. The results of the BCC corresponded to the national values, since in this study there were a total of 32 cases (69.5%), with a national average of 70% (INCA, 2020). While squamous cell carcinomas resulted in values above those cited in previous articles, these being approximately 15% of malignant skin tumors, in the above study 28.3% of cases were obtained. On the other hand, melanomas are described as 3% of malignant skin neoplasms, in this study they resulted in 6.5% (with an n=3), corresponding to twice the national average, emphasizing the importance of studies with a larger number of patients so that these data are reliably compared to the national average.

When analyzing the locations of skin tumors, the highest number of skin cancers were analyzed in areas more exposed to the sun, a fact that confirms the importance of primary prevention and the use of high SPF in addition to behavioral measures. It can also be concluded that in this study the male sex was more affected by malignant cutaneous tumors, unlike the national results that highlighted the female sex as the most affected in non- melanomic tumors, and in melanoma the equality of involvement between the sexes.

Finally, although Santa Maria receives patients from 32 municipalities, only 5 cities participated in the study, with 7 cases of skin neoplasms out of a total of 46 analyzed.

Based on the results obtained, further studies with larger population samples are suggested for a better assessment of the risk factors related to this pathology, in view of findings such as the high incidence of melanoma compared to national averages.

Acknowledgments

Conflicts of interest

Authors declare that there is no conflict of interest.

References

1. Instituto Nacional do Câncer. *Tipos de câncer: Câncer de pele não melanoma*. Rio de Janeiro: INCA; 2020.

2. Simoneti F, Cunha LO. Epidemiological profile of patients with malignant skin tumors treated at a secondary service plastic surgery outpatient clinic in the interior of São Paulo. *Revista da Faculdade de Ciências médicas de Sorocaba*. 2016;18(2):98–102.

3. Ferrari NM, Muller H, Ribeiro M, et al. Cutaneous melanoma: descriptive epidemiological study. *São Paulo Med J*. 2008;126(1):41–47.

4. Broetto J, Freitas JG, Sperli AE, et al. Tratamento cirúrgico dos carcinomas basocelular e espinocelular: experiência dos Serviços de Cirurgia Plástica do Hospital Ipiranga. *Rev Bras Cir Plást*. 2012;27(4):527–530.

5. Hoff PMG, et al. *Manual de condutas em oncologia*. 3rd ed. [S.l.]: Editora Atheneu; 2018.

6. Fontelles MJ, Simoes MG, Farias SH, et al. Metodologia da pesquisa científica: diretrizes para a elaboração de um protocolo de pesquisa. *Revista Paraense de Medicina*. 2009;23(3):1–8.

7. Malta DC, Gonçalves RPF, Machado IE, et al. Prevalência da hipertensão arterial segundo diferentes critérios diagnósticos, Pesquisa Nacional de Saúde. *Rev Bras Epidemiol*. 2018;21(suppl 1).

8. Flor LS, Campos MR. Prevalência de diabetes mellitus e fatores associados na população adulta brasileira: evidências de um inquérito de base populacional. *Rev Bras Epidemiol*. 2017;20(1):16–29.

9. Prati WJ, Silva FCD. Demographic and epidemiological survey of skin cancer in the state of rondônia. *Brazilian Journal of Surgery and Clinical Research*. 2018;24(1):13–16.

10. Costa CS. Epidemiologia do câncer de pele no Brasil e evidências sobre sua prevenção. *Diagn Tratamento*. 2012;17(4):206–208.

11. Rivitti EA. *Manual de dermatologia clínica de Sampaio e Rivitti*. 1st ed. São Paulo: Editora Artes Médicas Ltda; 2014. 525–530 p.

12. Barreto EMT. Acontecimentos que fizeram a história da oncologia no Brasil: Instituto Nacional de Câncer (INCA). *Revista Brasileira de Cancerologia*. 2005;51(3):267–275.

13. Gershenwald JE, Scoyler RA, Hess KR, et al. *AJCC Cancer Staging Manual*. 8th Edition; 2016.

14. Hoff PMG. *Tratado de oncologia*. Editora Atheneu; 2013.

15. Rouquayrol MZ, Gurgel M. *Rouquayrol - Epidemiologia e saúde*. 8th ed. [S.l.]: MedBook; 2018.

16. Schachter J, Ribas A, Long GV, et al. Pembrolizumab versus ipilimumab for advanced melanoma: final overall surviver results of a multicentre, randomised, open-label phase 3 study (KEYNOTE-006). *Lancet*. 2017;390(10105):1853–1862.

17. Vilanova CMA, Lages RB, Ribeiro SM, et al. Epidemiological and histopathological profile of cutaneous melanoma at a center in northeastern Brazil from 2000 to 2010. *An Bras Dermatol*. 2013;88(4):545–553.

18. Wainstein AJA, Belfort FA. Management of cutaneous melanoma. *Rev Col Bras Cir*. 2004;31(3):204–214.