Electronic Journal of General Medicine
2025, 22(2), em634
e-ISSN: 2516-3507
https://www.ejgm.co.uk/

MODESTUM

Original Article

OPEN ACCESS

Clinical and therapeutic aspects in skin cancer: Clinical study in a tertiary center from Romania

Mihaela Craescu [1,2], Carmen Bobeica [3], Elena Niculet [1,2*], Carmina Musat [1], Raul Mihailov [4], Florin Ciprian Bujoreanu [2,3,5], Laura Bujoreanu-Bezman [1,2,5], Gabriel Murariu [6], Andreea-Georgiana Dobre [7], Alin Codrut Nicolescu [8], Alin Laurentiu Tatu [2,9,10]

[1] Department of Morphological and Functional Sciences, Faculty of Medicine and Pharmacy, "Dunărea de Jos" University, Galați, ROMANIA
[2] Multidisciplinary Integrated Center of Dermatological Interface Research (MICDIR), "Dunărea de Jos" University, Galați, ROMANIA
[3] Medical Department, Faculty of Medicine and Pharmacy, "Dunărea de Jos" University, Galați, ROMANIA
[4] Clinical Surgical Department, Faculty of Medicine and Pharmacy, "Dunărea de Jos" University, Galați, ROMANIA
[5] Biomedical Doctoral School, "Dunărea de Jos" University, Galați, ROMANIA
[6] Department of Chemistry, Physics and Environment, Faculty of Sciences and Environment, "Dunărea de Jos" University, Galați, ROMANIA
[7] Department of Individual Sports and Kinetotherapy, Faculty of Physical Education and Sport, "Dunărea de Jos" University, Galați, ROMANIA
[8] Emergency Clinical Hospital Agrippa Ionescu, Bucharest, ROMANIA
[9] Clinical Medical Department, Faculty of Medicine and Pharmacy, "Dunărea de Jos" University, Galați, ROMANIA
[10] Department of Dermatology, "Sf. Cuvioasa Parascheva" Clinical Hospital of Infectious Diseases, Galați, ROMANIA
***Corresponding Author:** helena_badiu@yahoo.com

Citation: Craescu M, Bobeica C, Niculet E, Musat, Mihailov R, Bujoreanu FC, Bujoreanu-Bezman L, Murariu G, Dobre A-G, Nicolescu AC, Tatu AL. Clinical and therapeutic aspects in skin cancer: Clinical study in a tertiary center from Romania. Electron J Gen Med. 2025;22(2):em634. https://doi.org/10.29333/ejgm/15994

ARTICLE INFO

Received: 22 Aug. 2024

Accepted: 15 Feb. 2025

ABSTRACT

Introduction: Skin cancer registers worldwide high morbidity and mortality rates, with costly medical services, its major histopathology subtypes being basal and squamous cell carcinoma, melanoma.

Materials and method: This 5-year retrospective study included 84 patients admitted to the "Sfântul Apostol Andrei" Emergency Clinical Hospital of Galați in the oncology and radiotherapy clinic during January 2018-October 2022.

Results: Skin malignancies represented 3.56% of the oncological cases admitted from January 2018 to October 2022. The most prevalent etiological factors were sun exposure and light-colored skin (84.52%). Most cases registered discomfort due to local and persistent itching (59.52%). Histopathologically, most cases were squamous cell carcinomas (51.19%). The most frequent treatment methods were surgical intervention (100%), radiotherapy (100%), chemotherapy (7.14%), immunotherapy (7.14%), with a 5-year survival rate of 95.23%.

Conclusions: The available screening programs help with skin cancer early diagnosis, leading to favorable outcomes and reducing complication risks.

Keywords: skin cancer, squamous cell carcinoma, basal cell carcinoma, melanoma, histopathology subtypes

INTRODUCTION

Skin cancer is one of the major pathologies that health systems around the world have to deal with, due to the high morbidity and mortality rates, and high costs. This type of cancer is 1/3 of the total oncological diagnoses made, being frequently found among the white population and with a 3 to 4 times higher incidence than in the last decades, with major involvement by autoimmune diseases such as systemic sclerosis, psoriasis, or sarcomas, which can lead to functional deficiencies when local extension or metastatic disease takes place [1-6].

The main histopathological subtypes of skin cancer are basal cell carcinoma, squamous cell carcinoma and melanoma. Basal cell carcinoma is the most frequent one (80%), followed by squamous cell carcinoma (20%) and melanoma (4-6%), which is responsible for 75% of deaths by skin cancer [7, 8].

Precise epidemiological data regarding skin cancer are not available in Europe or globally, cancer registries lacking or having incomplete data. Of all the countries in Europe, only 10 (including Romania) lack a functional national cancer registry (which maintains updated data of the epidemiology, clinical and pathological characteristics of skin cancers) [9]. Preliminary data and clinical experience suggest that in Romania skin cancer diagnosis is a late one and usually in advanced stages, having high morbidity and mortality rates [10].

The current work aims at updating the current literature and at establishing the frequency of skin cancer among our patients, the initial symptoms, prevalence of histopathology subtypes and the treatment used.

MATERIALS AND METHOD

This is a 5 year-retrospective study done on a number of 84 patients diagnosed with these main skin cancer types–basal and squamous cell carcinomas and melanoma. The patients were admitted in the "Sfântul Apostol Andrei" Emergency Clinical Hospital of Galați in the department of radiotherapy and oncology from January 2018 to October 2022. The patient data were taken from their observation charts being centralized and statistically processed after the informed consent and ethical committee approval were obtained. A patient database was brought about in order to make the study analysis by taking into consideration the following aspects which we found to be relevant (respectively, the frequency distribution according to): time span/yearly distribution, age and sex classification, patients' origin environment and occupation, incriminating risk factors and initial disease symptoms, primary lesion location, histological subtype and degree of differentiation, disease progression and survival rate.

Precise inclusion criteria included: a histologically and clinically confirmed diagnosis of melanoma, basal cell carcinoma, squamous cell carcinoma; adults aged 18 years and older; patients with any stage of melanoma, BCC, or SCC; the ability to provide informed consent and comply with study protocols; residence in the study area or belonging to the population of interest, such as specific genetic or environmental risk factors.

Exclusion criteria included: a diagnosis of a cancer type outside the scope of melanoma, BCC, or SCC; presence of active infections that might interfere with treatment or assessment (such as untreated HIV, hepatitis B/C); history of severe autoimmune disorders that may worsen with study interventions (such as immunotherapy); exclude individuals with a history of malignancies other than melanoma, BCC, or SCC, unless in remission for a defined period (at least 5 years).

Regarding the statistical analysis, the current study uses a descriptive one, with the purpose of summarizing the baseline characteristics of the study population, taking into consideration continuous variables (including patient age) and categorical ones (patient gender or cancer type).

Table 1. Overview of cases included in the 5-year study

Variable	Patient number	Ratio (%)
Oncological cases		
Total	2,353	100
Skin cancer	84	3.56
Diagnostic year		
2018	21	25.00
2019	16	19.04
2020	13	15.47
2021	23	27.38
2022	11	13.10
Total number of skin cancer cases	84	100

Table 2. Patients' characteristics included in the study

Variable	Patient number	Ratio (%)
Age group		
< 35 years	1	1.19
36-64 years	22	26.19
> 65 years	61	72.62
Sex		
Male	45	53.57
Female	39	46.43
Employment status		
Retired	72	85.71
Employed	4	4.76
Unemployed	8	9.52
Risk factors		
Sun exposure and light skin	71	84.52
Patient age < 35 & > 65 years	62	73.80
Solar keratosis	35	41.66
Lymph node & distant metastasis	25	29.76
Origin environment		
Urban	60	71.42
Rural	24	28.57
Initial symptoms		
Local & persistent itching	50	59.52
Bleeding skin lesion	46	54.76
Pain	34	40.47

RESULTS

Patient Characteristics

From January 2018 to October 2022, a number of 84 patients were admitted to the "Sfântul Apostol Andrei" Emergency Clinical Hospital of Galați, Romania in the department of radiotherapy and oncology. These patients were diagnosed with various types of skin cancer (basal and squamous cell carcinomas, and melanoma), representing only a small percentage of the total number of 2,353 oncological patients that this department treated during that specific timeframe–3.56%.

Of the total number of 84 skin cancer cases treated from 2018 to 2022, most of them were diagnosed in 2021–respectively, 23 cases (27.38%), followed closely by 2018 with 21 cases (25%). The lowest number of diagnosed cases were registered in 2022–11 cases (13.09%) (**Table 1**).

Age group analysis revealed that only one patient was under 35 years of age (1.19%), while those found in the 36-64 years old group were 22 in total (26.19%), and those over 65 were 61 patients in total (72.61%) (**Table 2**).

Gender frequency distribution reveals a high number of skin cancers among male patients, with 45 cases (53.57%), as compared to female ones with 39 cases (46.42%). Most patients originated from the urban environment–71.42%, 60 cases, respectively, as compared to the rural environment with a ratio of 28.57% (24 cases). Most cases from the urban and rural environment were diagnosed in 2021 (16 cases and 7 cases, respectively) with ratios of 19.04% and 8.33%, respectively. From 2018 to 2020 a decrease in cases from both environments was registered, while in 2022 the number of cases were in almost equal numbers according to the original environment, with 5 urban cases (5.59%) and 6 rural ones (7.14%). Patient employment status revealed that out of the total number, 72 retired (85.71%), 4 were employed (4.76%) and 8 were unemployed (9.52%) (**Table 3**).

Of all of the risk factors for skin cancer development, the most frequently found among the group's patients were sunlight exposure and fair skin–in 71 cases–84.52%. As second place in frequency was the patient's age–lower than 35 and higher than 65–73.80% of patients. Third place was occupied by premalignant lesions–solar keratoses, which were found in 41.66% of patients, while as fourth placed risk factors were found lymph node and distant metastases–29.76% of patients. Smoking was a risk factor found in 12 cases (14.28%), and low

Table 3. Skin cancer subtype and its location and stage

Pathology subtype & location	Patient number	Ratio (%)
Squamous cell carcinoma	43	51.19
Head and neck	32	38.09
Extremities	10	11.90
Trunk	1	1.19
Basal cell carcinoma	25	29.76
Head and neck	22	26.19
Extremities	2	2.38
Trunk	1	1.19
Melanoma	16	19.04
Head and neck	2	2.38
Extremities	8	9.52
Trunk	6	7.14
Pathology and stage		
Stage I	0	0.00
Stage II	17	20.24
Stage III	21	25.00
Stage IV	5	5.95
Basal cell carcinoma		
Stage I	0	0.00
Stage II	15	17.86
Stage III	8	9.52
Stage IV	2	2.38
Melanoma		
Stage I	0	0.00
Stage II	2	2.38
Stage III	1	1.19
Stage IV	13	15.48

Table 4. Patient group risk factors

Risk factor	Ratio (%)
Sunlight exposure and fair skin	84.52%
Patient's age–Lower than 35 and higher than 65	73.80%
Premalignant lesions–Solar keratoses	41.66%
Lymph node and distant metastases	29.76%
Smoking	14.28%
Low immunity	2.38%
Prior local radiotherapy	2.38%

immunity and prior local radiotherapy were found in an equal number of cases–2.38%, respectively (**Table 4**).

Clinical Picture

The most frequent symptoms found in all three types of skin cancer were itching, pain, and bleeding lesion. Most cases (50 patients) reported discomfort due to local and persistent pruritus–59.52%, followed by the development of a bleeding skin lesion in 46 cases (54.76%). Pain is less frequent among skin cancer patients–it was reported in 34 cases–in 40.47% of all studied cases. Histopathologically, most skin cancers were squamous cell–43 cases, 51.19% of patients. As a second placed subtype, 25 cases were basal cell carcinoma–29.76%. Melanoma was the least diagnosed malignancy, being found in 16 cases–19.04%.

Histopathology Cancer Subtypes and Staging

Skin cancer patient classification according to pathology subtype and lesion location: for squamous cell carcinoma the elected locations were the head and neck regions (32 patients)–38.09%. A number of 10 patients (11.90%) had lesions located on the extremities and 1 case registered a truncal-located tumor (1.19%). Basal cell carcinoma preferential locations were the head and neck regions (22 patients–26.19%), while the least frequent ones were the extremities (2 cases) and trunk region (1 case) –2.38% of patients, and respectively 1.19%. Melanoma cases registered different preferential locations, most of them being found in the extremities–8 cases (9.52%), followed by trunk–6 cases (7.14%), while the lowest number of cases were located in the head and neck–2 cases, or 2.38%.

Table 5. Treatment options in skin cancer cases

Treatment options	Patient number	Ratio (%)
Surgical	84	100
Wide excision	69	82.14
Biopsy	64	76.19
External radiotherapy	84	100
Squamous cell carcinoma		
Palliative	10	11.90
Curative	33	39.29
Basal cell carcinoma		
Palliative	8	9.52
Curative	17	20.24
Melanoma		
Palliative	16	19.04
Curative	0	0.00
Chemotherapy	6	7.14
Immune therapy	6	7.14
5-year survival rates		
Survivors	80	95.23
Deceased	4	4.76

Most cases in the studied group were stage II–40.47% (34 cases), followed by stage III–35.71% (30 cases) and stage IV–23.80% (20 cases). There were no stage I cases. Stage II was most frequent in squamous cell carcinoma (17 cases), followed by basal cell carcinoma–15 cases and melanoma–2 cases. Stage III was found among 21 squamous cell carcinoma patients, 8 basal cell carcinoma patients and one case of melanoma. Stage IV was found in 13 cases of melanoma, 5 of squamous cell carcinoma and 2 cases of basal cell carcinoma.

Provided Treatment

Surgical treatment (biopsy and wide excision) and radiotherapy were the most frequent management options chosen for 100% of cases, while chemotherapy and immune therapy were used in 7.14% of cases, respectively (namely for 6 patients, each). From a surgical standpoint, 69 patients benefitted from wide excision–82.14% of the total number fo patients, while the second surgical method used was biopsy, in 64 patients (76.19%). All patients received external radiotherapy, most of them suffering from squamous cell carcinoma (33 patients) and receiving curative radiotherapy (60 Gy/30 fractions), while the rest of 10 patients received palliative radiotherapy (one patient receiving a single 8 Gy dose and 9 patients receiving 30 Gy/10 fractions). For basal cell carcinoma, palliative radiotherapy was administered to 8 patients, from which one patient received a single 8 Gy dose and 7 patients received 30 Gy/10 fractions dose. Most patients received curative radiotherapy–17 patients, with a dosage of 50 Gy/25 fractions in 7 patients and a dosage of 60 Gy/10 fractions in 10 patients. Melanoma patients benefited only from palliative radiotherapy, mostly using a dosage of 20 Gy/10 fractions in 10 patients, 30 Gy/10 fractions in 5 patients and a 40 Gy/20 fractions dosage in one patient (**Table 5**).

Chemotherapy was administered only in 6 cases–3 squamous cell carcinomas (6.97%) and 3 cases of melanoma (18.75% of all melanoma cases). No basal cell carcinoma case received chemotherapy. The most frequently used medication

was carboplatin and paclitaxel, administered both separately or combined. For 2 squamous cell carcinomas only carboplatin was used, while for the other case these two medications were combined. All three melanoma cases received the same medication–the two agents combined. From the total number of patients taken into consideration for the current study, 6 cases received immune therapy–melanoma cases, 37.50% of the total number of cases, treated with dabrafenib, trametinib, interferon, and nivolumab.

Patient Outcomes

The 5 year survival rate analysis revealed that 80 patients survived (95.23%); only 4 died (4.76%) and from these, one case was a squamous cell carcinoma (an 80 year-old female with 1 year survival rate) and 3 were melanoma–the first case was an 80 years-old female patient with one year survival rate, while the other 2 were female patients of 47 and 60 years of age, with 2-years survival rates. Most cases with favorable outcomes were basal cell carcinomas (60%–15 cases)., while only 53.48% (23 cases) were squamous cell carcinomas and 31.25% (5 cases), melanomas.

DISCUSSION

The exact causes for basal cell carcinoma development are not fully understood, but its growth on the basis of basal cells–namely germinative cells, is well known [11].

Ultraviolet radiation are abnormally absorbed by DNA forming various bridges between adjacent bases, with final DNA endonuclease repair. Due to a lack or loss of endonuclease in patients suffering from xeroderma pigmentosum, one can explain the precocious deterioration of skin and rapid basal cell carcinoma development. Another factor which is in favor of basal cell carcinoma development is the CYP2D6 gene which encodes the P540 cytochrome, with major role in detox and photosynthesizing agent inactivation [12].

The process of squamous cell carcinoma development was investigated in 1963 by Winklemann through the use of the photo-cancerous studies on UV radiation on mice. Since then, mutations in the p53 gene (tumor suppression gene) were found to be involved in the development of such cancer. P53 mutations are found in more than 90% of tumors and in approximately 1/3 of Bowen's disease. The skin responds to UV-B radiation by regulating p53, leading to cell cycle suppression and/or deteriorated keratinocyte apoptosis. When p53 mutations take place, deteriorated keratinocytes proliferate instead of regress. Other genetic anomalies which are frequently observed in squamous cell carcinoma consist of p14, p16, Rb and CDH1(E-caderin) mutations [13].

Cutaneous melanoma is a proliferation affecting its melanocytic system and which develops at the level of a pre-existing pigmented lesion or in a lesion-free area [14].

Germline mutations affect chromosome p21, respectively the CDKN2A tumor suppressor, being responsible for approximately 40% of the hereditary melanoma incidence. This mutation is in favor of early melanoma development, as compared to the mean incidences of the population predisposed to the development of such malignancy. CDKN2A gene is responsible for p16 protein and p14ARF coding (alternate reading frame). p16 protein injury leads to the limitless multiplication of cells and thus to neoplasia development, while p14ARF, which acts with the help of the p16 protein, leads to cell division arrest or cell apoptosis [15].

According to our study carried out during January 2018-October 2022 on a number of 84 patients (of a total of 2,353 oncology patients admitted to the department of radiotherapy and oncology), the following was observed: the most frequent histological subtype of skin cancer found was squamous cell carcinoma (51.19%), followed by basal cell carcinoma (29.76%) and melanoma (19.04%).

Current literature studies highlight the fact that the most frequent histologic subtype reported is basal cell carcinoma, followed by squamous cell carcinoma [16-23]. This aspect can be explained by the fact that squamous cell carcinoma is frequently diagnosed in advanced stages, with relapses and metastases (unfavorable consequences of other frequent malignancies), needing multiple therapy options, as compared to basal cell carcinoma which in most cases needs only surgical intervention with clear surgical margins. The current study reveals a low ratio of melanoma cases, in accordance with the specialty literature [24, 25].

An objective observation resides in the fact that the incidences of the three histopathologic malignancies found are directly proportional with advancing age. Most patients were over 65 years of age (72.61%), followed by the 35-64 years category (26.19%). These results are confirmed by the majority of prior literature data which report as prevalent patient age of over 65 [26-29].

Male patients were prevalent among the group's patients, in comparison with females: 53.57% versus 46.42%. This particular aspect is confirmed by multiple other studies, the main risk factor residing in solar radiation exposure through professional and/or recreational exposure, with secondary involvement by smoking, ionizing radiation or chemical exposure, supporting skin cancer development [30-38].

Thus being said, there are few exceptions in some literature reports mentioning the increasing tendency of skin cancer development in females, as compared to male patients [39].

By analyzing the age and gender of the patient group, a higher incidence was found among both sexes of over 65 years of age (males 40.47%, respectively females 32.14%), in what concerns skin malignancy development–a fact which is in accordance with literature data [40].

This particular aspect is due to the risk factor stemming from prolonged sun exposure which alters the DNA and its regenerative capacity (a reality which is also reflected by the aging process) [41, 42].

Surprisingly, 71.42% of patients come from urban areas and only 28.57% of them come from the rural ones. According to the studies in [22, 43], individuals from the rural environment are more predisposed to skin cancer development, with more advanced disease stages, due to the specific characteristics of agricultural work and their lack of sun protection measures. Thus being said, one cannot exclude urban patients due to the fact that some workplaces involve chemical or even ultraviolet exposure, and urban hospitals are a bonus for such patients in the early detection and treatment of skin cancers [43]. During their medical check-up, most patients complained of such symptoms as: itching/pruritus (59.52%), skin bleeding lesions (54.76%) and pain (40.47%). In cases of squamous and basal cell carcinomas the most frequently found symptom was itching, while for melanoma, local pain.

Basal cell carcinoma location was most frequent at the head and neck level, and less frequent in the extremities and trunk, in accordance with the specialty literature [44].

The same applies in squamous cell carcinoma cases, where the preferential sites for development are the head and neck areas (as it is also reported by the literature data), followed by the extremities and trunk area [45].

Literature data report that melanoma is located mostly in the trunk area, followed by the extremities and the head and neck area, but the current study reports a different preferential area, namely the extremities, followed by trunk and head and neck. In the studies in [46-48], which caried out during the COVID-19 pandemic (a limiting factor in patient numbers), it was found that the most frequent affected area by melanoma development was the head and neck, although SARS-COV-2 infection is currently linked to various forms of skin involvement.

In accordance with literature data, most cases benefitted from surgical intervention and radiotherapy. The most frequently used treatment options were surgical intervention (biopsy and wide excision) and radiotherapy–100% of patients, followed by chemotherapy and immune therapy–7.14%. Other unconventional treatment options with skin lesion healing properties (possibly having effect on not necessarily the tumor mass itself, but the associated inflammation, superimposed infection and skin destruction) could be phytopharmaceuticals, such as ointments with aloe or chamomile [49-51].

Incomplete excisions found among the patients in our group were relapse premises. Thus, patients with incomplete initial wide surgical excision needed a second or even third wide surgical intervention in order to reach the desired result. This fact is also confirmed by the studies in [17, 37] in which a second wide excision surgical intervention was necessary for complete resection. The histopathology subtype with the widest excision surgical interventions found in our study was squamous cell carcinoma–8.33% [17, 37].

In order to obtain a most favorable, radiotherapy was used in all of the current study's cases where surgical intervention was not a viable option due to tumor location or due to an unfavorable functional and cosmetic result, or even post-surgery, in order to prevent further tumor (re-)development (with total destruction), a management method also reported [23, 35, 47].

The survival rates among the patients enrolled in the current study is influenced by post-therapy complications, associated pathology, ulceration, tumor thickness of over 2 mm and age (early development or advanced age) [52].

In accordance with the study in [53], of all post-therapy complications, the most frequent ones were radiotherapy induced first degree dermatitis, infections, mucositis and bleeding. These lesions need treatment and in later years, besides the commonly used formulas, innovative natural extracts have been used (melatonin use could be an alternative due to its cytoprotective and anti-inflammatory properties) [54].

By analyzing the 5 years taken into consideration for this study, 2021 registered the most cases with skin cancer diagnosis–27.38%, a fact possibly due to the restrictions applied in 2020 during the COVID-19 pandemic state, limiting patient medical care. Once the restrictions were lifted, patients began re-addressing medical services regularly.

The 5-year survival rate was 95.23% among the patients in our study. Death was found in 4.76% of patients. The histopathology subtype with the highest death rates was melanoma (18.75%), followed by squamous cell carcinoma (2.32%), with a survival rate of 1-2 years following diagnosis. The only histopathology subtype with 100% survival rates was basal cell carcinoma.

The mortality rate of squamous cell carcinoma found in the studies in [36, 37] was 50%, squamous cell carcinoma having an advanced stage of disease.

Screening programs help in the early diagnosis of skin malignancies, leading to favorable results following treatment and to less complications. Likewise, patients who lack knowledge or health negligence are in most cases the leading causes for advanced stage disease diagnosis, confirmed by the studies in [19, 20, 55].

Patient education regarding healthcare and regular medical services addressing or when skin changes develop, along with cancer risk factor identification and protection, could lead to a reduction in skin cancer development.

CONCLUSIONS

Skin cancer registers a continuous rising incidence and newly diagnosed cases are much more frequently found as advanced stage disease. Patient education regarding self-health along with promoting regular medical services addressing or in cases of skin changes, are important tools for early skin cancer detection. Having general knowledge regarding cancer risk factors and possible day-to-day or workplace protective measures against such threats can lead to a reduction in the development of skin cancer.

Author contributions: MC, CB, EN, RM, FCB, LB-B, & ALT: data acquisition, analysis, and interpretation and conception and design of the work & **CM, GM, A-GD, & CAN:** supervision and revision. All authors have agreed with the results and conclusions.

Funding: This study was supported by "Dunarea de Jos" University, Galati, Romania through the Multidisciplinary Integrated Center of Dermatological Interface Research by the Grant RF 2484/31.05.2024.

Ethical statement: The authors stated that the study was approved by the Ethics Committee at Sfântul Apostol Andrei Emergency Clinical Hospital of Galaţi on 14 May 2024 with approval number 10534/14.05.2024. Written informed consents were obtained from the participants.

Declaration of interest: No conflict of interest is declared by the authors.

Data sharing statement: Data supporting the findings and conclusions are available upon request from the corresponding author.

REFERENCES

1. Alonso-Belmonte C, Montero-Vilchez T, Arias-Santiago S, Buendía-Eisman A. Current state of skin cancer prevention: A systematic review. Actas Dermosifiliogr. 2022;113(8):781-91. https://doi.org/10.1016/j.ad.2022.04.018 PMid: 35526566
2. Bobeica C, Niculet E, Craescu M, et al. Etiological factors of systemic sclerosis in the southeast region of Romania. Exp Ther Med. 2021;21(1):79. https://doi.org/10.3892/etm.2020.9511 PMid:33363590 PMCid:PMC7725016

3. Bujoreanu FC, Bezman L, Radaschin DS, et al. Nevi, biologics for psoriasis and the risk for skin cancer: A real concern? (case presentation and short review). Exp Ther Med. 2021;22(6):1354. https://doi.org/10.3892/etm.2021.10789 PMid:34659500 PMCid:PMC8515562
4. Mihailov R, Tatu AL, Niculet E, et al. A narrative review of cutaneous manifestations and imaging landmarks of breast cancer. Electron J Gen Med. 2024;21(1):em566. https://doi.org/10.29333/ejgm/14117
5. Branisteanu DE, Georgescu S, Serban IL, et al. Management of psoriasis in children (review). Exp Ther Med. 2021;22(6):1429. https://doi.org/10.3892/etm.2021.10864 PMid:34707710 PMCid:PMC8543441
6. Niculet E, Bobeica C, Craescu M, et al. Multimodal considerations concerning basal cell carcinoma clefting–Profile of structural and aggressive traits–Perspectives. Clin Cosmet Investig Dermatol. 2022;15:2087-95. https://doi.org/10.2147/CCID.S385213 PMid:36199384 PMCid:PMC9529228
7. Dummer R, Green A, Pittelkow MR, Iwatsuki K, Elwan NM, Zipser MC. Skin cancer–A world-wide perspective. Heidelberg: Springer; 2011. https://doi.org/10.1007/978-3-642-05072-5
8. Nwabudike LC, Tatu AL. Reply to Gambichler T et al. altered epigenetic pathways and cell cycle dysregulation in healthy appearing skin of patients with koebnerized squamous cell carcinomas following skin surgery. J Eur Acad Dermatol Venereol. 2019;33(1):e3-4. https://doi.org/10.1111/jdv.15084
9. Geller AC, Annas GD. Epidemiology of melanoma and nonmelanoma skin cancer. Semin Oncol Nurs. 2003;19(1):2-11. https://doi.org/10.1053/sonu.2003.50000 PMid:12638376
10. Neagu A. Rata de supraviețuire a pacienților cu melanom rămâne sub 60% în Europa de Est, în timp ce în ţările occidentale depăşeşte 90% [The survival rate of melanoma patients remains below 60% in Eastern Europe, while in Western countries it exceeds 90%]. Available at: https://hotnews.ro/rata-de-supravietuire-a-pacientilor-cu-melanom-ramne-sub-60-n-europa-de-est-n-timp-ce-n-tarile-occidentale-depaseste-90-59458 (Accessed: 13 August 2024).
11. Sehmults DC. High-risk cutaneous squamous cell carcinoma: A practical guide patient management. Heidelberg: Spring; 2016. https://doi.org/10.1007/978-3-662-47081-7
12. NCCN. NCCN guidelines for patients: Basal cell skin cancer. Available at: https://www.nccn.org/patients/guidelines/content/PDF/basal-cell-patient-guideline.pdf (Accessed: 13 August 2024).
13. NCCN. NCCN guidelines for patients: Melanoma. Available at: https://www.nccn.org/patients/guidelines/content/PDF/melanoma-patient.pdf (Accessed: 13 August 2024).
14. Campbell C, Quinn AG, Ro YS, Angus B, Rees JL. p53 mutations are common and early events that precede tumor invasion in squamous cell neoplasia of the skin. J Invest Dermatol. 1993;100(6):746-8. https://doi.org/10.1111/1523-1747.ep12475717 PMid:8496613
15. Miller DL, Weinstock MA. Nonmelanoma skin cancer in the United States: Incidence. J Am Acad Dermatol. 1994;30(5 Pt 1):774-8. https://doi.org/10.1016/S0190-9622(08)81509-5 PMid:8176018
16. Neale RE, Davis M, Pandeya N, Whiteman DC, Green AC. Basal cell carcinoma on the trunk is associated with excessive sun exposure. J Am Acad Dermatol. 2007;56(3):380-6. https://doi.org/10.1016/j.jaad.2006.08.039 PMid:17097387
17. Fidelis MC, Stelini RF, Staffa LP, Moraes AM, Magalhães RF. Basal cell carcinoma with compromised margins: Retrospective study of management, evolution, and prognosis. An Bras Dermatol. 2021;96(1):17-26. https://doi.org/10.1016/j.abd.2020.11.001 PMid:33288370 PMCid:PMC7838108
18. Kappelin J, Green AC, Ingvar Å, Ahnlide I, Nielsen K. Incidence and trends of basal cell carcinoma in Sweden: A population-based registry study. Br J Dermatol. 2022;186(6):963-9. https://doi.org/10.1111/bjd.20964 PMid:34939666
19. Tiyawatanaroj A, Sudtikoonaseth P, Chayangsu O. Basal cell carcinoma trends in Thailand: A 10-year retrospective study of demographic, clinical and histopathological features. Dermatol Reports. 2021;14(1):9413. https://doi.org/10.4081/dr.2022.9413 PMid:35371421 PMCid:PMC8969878
20. El-Khalawany M, Hassab-El-Naby HMM, Mousa AM, et al. Epidemiological and clinicopathological analysis of basal cell carcinoma in Egyptian population: A 5-year retrospective multicenter study. J Cancer Res Clin Oncol. 2023;149(7):3121-9. https://doi.org/10.1007/s00432-022-04207-7 PMid:35870014 PMCid:PMC10314874
21. Ozbey R. Basal cell skin cancers: Retrospective analysis of 67 cases. J Cosmet Dermatol. 2022;21(12):7007-12. https://doi.org/10.1111/jocd.15441 PMid:36208006
22. Fahy EJ, Sugrue CM, Jones D, et al. A retrospective cohort study of cutaneous squamous cell carcinoma of the scalp: Features of disease and influence of sociodemographic factors on outcomes. Ir J Med Sci. 2022;191(3):1217-22. https://doi.org/10.1007/s11845-021-02699-9 PMid:34189657
23. Bortoluzzi P, Brambilla R, Berti E, Marzano AV, Piccinno R. The role of radiotherapy in the management of cutaneous squamous cell carcinoma: A retrospective study on 92 cases. Ital J Dermatol Venerol. 2022;157(4):363-7. https://doi.org/10.23736/S2784-8671.22.07286-3 PMid:35274884
24. Supekar BB, Tomar SS, Wankhade VH, Bhushan R, Singh RP, Bhat DM. Clinical spectrum of cutaneous malignancies in Central India: A retrospective study. Indian J Dermatol. 2021;66(3):284-90. https://doi.org/10.4103/ijd.IJD_543_19 PMid:34446952 PMCid:PMC8375545
25. Constantin GB, Firescu D, Voicu D, et al. The importance of systemic inflammation markers in the survival of patients with complicated colorectal cancer, operated in emergency. Chirurgia (Bucur). 2020;115(1):39-49. https://doi.org/10.21614/chirurgia.115.1.39 PMid:32155398
26. Jain C, Garg N, Singh S, Chattopadhyay S. Basal cell carcinoma-clinico-pathological study in Eastern India in correlation with different risk factors. Indian J Pathol Microbiol. 2022;65(4):869-72. https://doi.org/10.4103/ijpm.ijpm_180_21 PMid:36308196

27. Rodriguez M, Beal BT, Manmohan M, et al. Risk factors and timing of subsequent cutaneous squamous cell carcinoma in patients with cutaneous squamous cell carcinoma: A retrospective cohort study. J Am Acad Dermatol. 2022; 84(3):719-24. https://doi.org/10.1016/j.jaad.2020.08.083 PMid:32861709
28. Buja A, Rugge M, Damiani G, et al. Sex differences in cutaneous melanoma: Incidence, clinicopathological profile, survival, and costs. J Womens Health (Larchmt). 2022;31(7):1012-9. https://doi.org/10.1089/jwh.2021.0223 PMid:35076310 PMCid:PMC9299528
29. Karagas MR, Greenberg ER, Spencer SK, Stukel TA, Mott LA. Increase in incidence rates of basal cell and squamous cell skin cancer in New Hampshire, USA. New Hampshire Skin Cancer Study Group. Int J Cancer. 1999;81(4):555-9. https://doi.org/10.1002/(SICI)1097-0215(19990517)81:4<555::AID-IJC9>3.0.CO;2-R
30. Hakverdi S, Balci DD, Dogramaci CA, Toprak S, Yaldiz M. Retrospective analysis of basal cell carcinoma. Indian J Dermatol Venereol Leprol. 2011;77(2):251. https://doi.org/10.4103/0378-6323.77483 PMid:21393972
31. Lotfinejad S, Rashidi T, Eshghi MJ. Prevalence of malignant skin tumors among patients referring to URMI health centers, 1991-2001. J Ardabil Univ Med Scien. 2004;3:33-8.
32. Revenga Arranz F, Paricio Rubio JF, Mar Vázquez Salvado M, del Villar Sordo V. Descriptive epidemiology of basal cell carcinoma and cutaneous squamous cell carcinoma in Soria (north-eastern Spain) 1998-2000: A hospital-based survey. J Eur Acad Dermatol Venereol. 2004;18(2):137-41. https://doi.org/10.1111/j.1468-3083.2004.00829.x PMid:15009289
33. Hakami N. The study of main factors of effective epidemiologic & etiologic on divulging basal cell carcinoma of head &neck in hospitalized patients with the same diagnosis in Shahid Beheshti Hospitalin Zanjan City from 1993 to 2000. J Zanjan Univ Med Sci Health Serv. 2000;8:21-8.
34. Raasch BA, Buettner PG, Garbe C. Basal cell carcinoma: Histological classification and body-site distribution. Br J Dermatol. 2006;155(2):401-7. https://doi.org/10.1111/j.1365-2133.2006.07234.x PMid:16882181
35. Soydemir GP, Kandaz M, Melikoğlu M. The results of radiotherapy for squamous cell carcinomas of the skin. Dermatol Ther. 2019;32(5):e13058. https://doi.org/10.1111/dth.13058 PMid:31394022
36. Feinstein S, Higgins S, Ahadiat O, Wysong A. A retrospective cohort study of cutaneous squamous cell carcinoma with lymph node metastasis: Risk factors and clinical course. Dermatol Surg. 2019;45(6):772-81. https://doi.org/10.1097/DSS.0000000000001828 PMid:30789511
37. Tuominen S, Ukkola-Vuoti L, Riihilä P, et al. Retrospective, registry-based, cohort investigation of clinical outcomes in patients with cutaneous squamous cell carcinoma and basal cell carcinoma in Finland. Acta Derm Venereol. 2022; 102:adv00693. https://doi.org/10.2340/actadv.v102.2073 PMid:35356995 PMCid:PMC9574685
38. Stang A, Ziegler S, Büchner U, Ziegler B, Jöckel KH, Ziegler V. Malignant melanoma and nonmelanoma skin cancers in Northrhine-Westphalia, Germany: A patient- vs. diagnosis-based incidence approach. Int J Dermatol. 2007;46(6):564-70. https://doi.org/10.1111/j.1365-4632.2006.03056.x PMid:17550552
39. Muntyanu A, Savin E, Ghazawi FM, Alakel A, Zubarev A, Litvinov IV. Geographic variations in cutaneous melanoma distribution in the Russian Federation. Dermatology. 2020;236(6):500-7. https://doi.org/10.1159/000507617 PMid:32506063
40. Wainstein AJA, Duprat Neto JP, Enokihara MY, et al. Demographic, clinical, and pathologic features of patients with cutaneous melanoma: Final analysis of the Brazilian melanoma group database. JCO Glob Oncol. 2020;6:575-82. https://doi.org/10.1200/JGO.20.00005 PMid:32293941 PMCid:PMC7193775
41. Task Force on Community Preventive Services. Recommendations to prevent skin cancer by reducing exposure to ultraviolet radiation. Am J Prev Med. 2004;27(5):467-70. https://doi.org/10.1016/S0749-3797(04)00199-0 PMid:15556745
42. Bariani RL, Nahas FX, Barbosa MV, Farah AB, Ferreira LM. Basal cell carcinoma: An updated epidemiological and therapeutically profile of an urban population. Acta Cirurgica Brasileira. 2006;21(2):66-73. https://doi.org/10.1590/S0102-86502006000200003 PMid:16583057
43. Gilli IO, Zanoni AC, Andrade DP, Andrade DAS. Cutaneous melanoma diagnosis delay: Socioeconomic and demographic factors influence. Rev Assoc Med Bras (1992). 2022;68(10):1405-9. https://doi.org/10.1590/1806-9282.20220369 PMid:36417644 PMCid:PMC9683926
44. Backman E, Oxelblom M, Gillstedt M, Dahlén Gyllencreutz J, Paoli J. Basal cell carcinoma: Epidemiological impact of clinical versus histopathological diagnosis. J Eur Acad Dermatol Venereol. 2023;37(3):521-7. https://doi.org/10.1111/jdv.18774 PMid:36433707
45. Tripathi R, Knusel KD, Ezaldein HH, Bordeaux JS, Scott JF. Characteristics of patients hospitalized for cutaneous squamous cell carcinoma. Dermatol Surg. 2020;46(6):742-6. https://doi.org/10.1097/DSS.0000000000002117 PMid:31490307
46. Klepfisch L, Carbonnelle-Puscian A, Faisant M, et al. Impact of the COVID-19 lockdown on the severity of newly-diagnosed primary cutaneous melanoma: A retrospective regional study in France. Ann Dermatol Venereol. 2023; 150(1):49-51. https://doi.org/10.1016/j.annder.2022.09.002 PMid:36424300 PMCid:PMC9527197
47. Dumitru M, Rebegea LF, Anghel R, Bacinschi X, Firescu D, Nechita A. Radiotherapy delivering in COVID-19 pandemic context. Galati Radiotherapy Center's experience and recommendations of professional societies. Med Mod. 2020;27:97-101. https://doi.org/10.31689/rmm.2020.27.2.97
48. Tocu G, Mihailov R, Serban C, Stefanescu BI, Tutunaru D, Firescu D. The contribution of procalcitonin, C-reactive protein and interleukin-6 in the diagnosis and prognosis of surgical sepsis: An observational and statistical study. J Multidiscip Healthc. 2023;16:2351-9. https://doi.org/10.2147/JMDH.S422359 PMid:37601324 PMCid:PMC10439796
49. Marsidi N, Ottevanger R, Bouwes Bavinck JN, Krekel-Taminiau NMA, Goeman JJ, Genders RE. Risk factors for incomplete excision of cutaneous squamous cell carcinoma: A large cohort study. J Eur Acad Dermatol Venereol. 2022;36(8):1229-34. https://doi.org/10.1111/jdv.18101 PMid:35342992 PMCid:PMC9545629

50. Spurny-Dworak J, Steiner A, Breier F, Stella A, Feldmann R. Effects of the COVID-19 pandemic on the diagnosis of malignant melanoma: A retrospective study. Eur J Dermatol. 2022;32(5):615-7. https://doi.org/10.1684/ejd.2022.4340 PMid:36468738 PMCid:PMC10111314
51. Buzia OD, Con M, Tatu AL, et al. Stability and microbiological analysis of aloe barbadensis and chamomilla matricaria pharmaceutical forms. Rom J Oral Rehabil. 2022;14(1):216-28.
52. Cazzaniga S, Zahn CA, Seyed Jafari SM, Hunger RE. Melanoma prognosis and associated risk factors: A retrospective cohort study using semantic map analysis. Acta Derm Venereol. 2023;103:adv9591. https://doi.org/10.2340/actadv.v103.9591 PMid:37246807 PMCid: PMC10241251
53. Cordel N, Bonnecarrère L, Tressières B. Squamous cell carcinoma in the Afro-Caribbean community: An 11-year retrospective study. J Eur Acad Dermatol Venereol. 2017;31(9):1462-7. https://doi.org/10.1111/jdv.14348 PMid: 28543620
54. Anghel L, Baroiu L, Popazu CR, et al. Benefits and adverse events of melatonin use in the elderly (review). Exp Ther Med. 2022;23(3):219. https://doi.org/10.3892/etm.2022.11142 PMid:35126722 PMCid:PMC8796282
55. Mahon SM. Skin cancer prevention: Education and public health issues. Semin Oncol Nurs. 2003;19(1):52-61. https://doi.org/10.1053/sonu.2003.50005 PMid:12638381