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Clinical and epidemiological features of malignant melanoma: A 5-year single-center retrospective study

Mihaela Craescu [1], Ciprian Dinu [1], Iulia Chiscop [2], Elena Niculet [1,3]*, Alin Laurentiu Tatu [3,4,5], Caterina Dumitru [6], Mariana Lupoae [6], Bogdan Valentin Craescu [7]

[1] Department of Morphological and Functional Sciences, Faculty of Medicine and Pharmacy, "Dunarea de Jos" University, Galati, ROMANIA
[2] Department of Medical Surgical, Faculty of Medicine and Pharmacy, "Dunarea de Jos" University, Galati, ROMANIA
[3] Multidisciplinary Integrated Center of Dermatological Interface Research, "Dunarea de Jos" University of Galati, Galati, ROMANIA
[4] Department of Dermatology, "Saint Parascheva" Infectious Disease Clinical Hospital, Galati, ROMANIA
[5] Department of Clinical Medical, Faculty of Medicine and Pharmacy, "Dunarea de Jos" University of Galati, Galati, ROMANIA
[6] Department of Pharmaceutical Sciences, Faculty of Medicine and Pharmacy, "Dunarea de Jos" University, Galati, ROMANIA
[7] Faculty of Medicine and Pharmacy, "Dunarea de Jos" University, Galati, ROMANIA
***Corresponding Author:** helena_badiu@yahoo.com

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ABSTRACT

Skin cancer is one of the most common types of cancer found globally. Malignant melanoma (MM) (4-6%) is rare but very aggressive, accounting for about 75% of deaths from skin cancer. This is a retrospective study that aims to make an update on the information available, in the light of the latest developments in the literature, to retrospectively describe the demographics, clinical features, histopathology, and management of MM cases treated at a single oncology center. Sixteen patients were diagnosed with MM, accounting for 19.05% of the total number of hospitalized skin cancers. The patient group included 81.25% of patients over 55 years of age, 75% of those originating from the urban areas and 68.75% being females. Smoking and actinic keratosis were found in a percentage of 31.25% of patients. Axillary lymph node metastases were found in 31.25% of cases, while cerebral ones in 18.75%. The most common primary location was the extremities (50%). Sentinel lymph node biopsy was performed in 87.50% of patients. Palliative radiotherapy was done for all cases while chemotherapy was performed only in 18.75% patients, and immunotherapy in 37.50% of them. Although significant progress has been made in understanding both the biology and genetics of melanoma and its therapeutic approaches, this malignancy is still a major problem worldwide due to its high incidence and lack of curative treatment for advanced stages.

Keywords: malignant melanoma, multimodal management strategies, melanoma treatment, melanoma diagnosis

INTRODUCTION

Skin cancer is burdening health systems from all around the world due to its high morbidity and mortality rates, being associated with high medical services costs and constituting about 1/3 of diagnosed cancers, with involvement in autoimmune diseases such as systemic sclerosis or psoriasis, having the propensity to lead to functional deficiencies and tendinopathies, when there is important locoregional extension, or even (skin) metastases.

Basal cell carcinoma (BCC), squamous cell carcinoma (SCC), and malignant melanoma (MM) are the 3 major skin cancer types having different development, treatment and prognosis traits [1-10]. BCC, the most common one (80%), develops from epidermal basal cells, has a slow progression rate, high morbidity and rare metastatic capacity. Prolonged sun exposure and old age are the most important risk factors for its development. In general, it is successfully treated by surgical approach, with a favorable prognosis, but recurrences are frequent in more advanced cases or on intensely sun-exposed skin [11-15]. SCC is more aggressive, has metastatic potential, develops on ultraviolet (UV) light-exposed skin areas, and actinic keratosis is considered a risk factor for its development. Besides surgical excision, in advanced or metastatic cases, additional treatment options such as radiation therapy or immunotherapy may be necessary [2, 16, 17]. MM (4-6%) is a rare but very aggressive form of melanocytic skin cancer, responsible for 75% of skin cancer deaths. It has high metastatic and mortality rates, with risk factors such as excessive exposure to UV radiation, family history of melanoma, the presence of atypical nevi and certain genetic mutations. Currently, treatments for melanoma include surgery, immunotherapy, targeted therapies and radiotherapy, with a higher success rate if applied in the early stages. It most often occurs on the lower limbs (24-40%), followed by the head and neck region (22-38%), trunk (19-24%) and upper limbs (10%) [18-20].

MM can present itself in various clinical forms (such as superficial spreading, nodular, acral), each with unique

Table 1. Epidemiological and clinical features of the 5-year study population

Variable		n	%
Patient group	Skin cancer cases	84	100
	Malignant melanoma	16	19.05
Year	2018	4	25.00
	2019	6	37.50
	2020	3	18.75
	2021	2	12.50
	2022	1	6.50
Age	40-55 years	3	18.75
	56-65 years	7	43.75
	66-75 years	6	37.50
Sex	male	5	31.25
	female	11	68.75
Environment of origin	urban	12	75.00
	rural	4	25.00

characteristics that can influence both diagnosis and treatment. Early detection and multidisciplinary approach are essential for proper management and improved patient prognosis [21].

Post-therapeutic monitoring with regular physical examinations, dermoscopic and imaging studies are recommended to assess the patient's condition and detect any new lesions. Establishing a diagnosis of MM is a multidisciplinary process involving careful clinical evaluation, histopathological confirmation, advanced imaging and molecular testing, counting on dermatologists, oncologists, radiation technicians, pathologists and imaging specialists to collaborate and devise a proper treatment plan.

The present paper aims to make an update on the information available, in the light of the latest developments in the literature, to retrospectively describe the demographics, clinical features, histopathology, and management of MM cases treated at a single oncology center.

MATERIALS AND METHODS

This retrospective study was carried out over a five-year period and included patients diagnosed with MM who were admitted to the department of radiotherapy and oncology of the "Sfântul Apostol Andrei" Emergency Clinical Hospital of Galați, Romania. The cases were diagnosed and treated between January 2018 and October 2022. Data were collected from patients' medical records, organized in a database, and subsequently analyzed statistically.

Patients were included in the study if they had a histopathologically confirmed diagnosis of MM, complete clinical documentation, and available follow-up data. Patients with other types of skin tumors, incomplete medical records, or without histopathological confirmation were excluded from the analysis. Due to the small cohort, the results and calculated percentages may not reflect broader population trends.

For each patient, the following information was recorded: age, sex, environment of origin, occupation, potential risk factors, symptoms at disease onset, location of the primary lesion, histopathological subtype, clinical status at admission, treatment received, and disease evolution over time. The extent of melanoma was evaluated at the time of diagnosis using clinical, imaging, and histopathological findings, and disease staging was established according to standard melanoma staging criteria. All patients provided informed consent, and the study was approved by the hospital's ethics committee (no. 5527/17.03.2025).

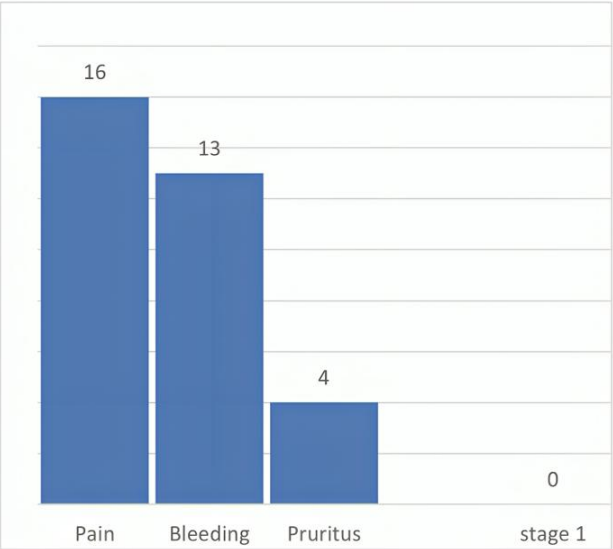

Figure 1. Main patient complaints (Source: Authors' own elaboration)

RESULTS

Between January 2018 and October 2022, a total of 84 oncology patients diagnosed with malignant skin tumors (BCC, SCC, and MM) were hospitalized and treated in the department of radiotherapy and oncology of the "Sfântul Apostol Andrei" County Emergency Clinical Hospital in Galati, out of a total of 2353 oncology patients with various neoplastic lesions and sites (**Table 1**). Malignant skin tumors account for 3.56% of the total number of oncological cases hospitalized during that period. Of the 84 cases of malignant skin tumors treated between 2018 and 2022, the histopathology of MM was found in 16 patients included in the study. The majority of MM cases were diagnosed in 2019, respectively 6 cases (37.50%), followed closely by 2018 with 4 cases (25%). The lowest number of diagnosed cases was in 2022, respectively 1 case (6.25%). The analysis according to age showed a minimum age of 42 years and a maximum age of 74 years, and most patients belonged to the age subgroup 56-65 years (43.75%), followed closely by those present in the age subgroup 66-74 years (37.50%). Based on age-group distribution, the estimated mean age of the study population was approximately 63 years. Regarding the sex differences among our patients, we observed a higher number of female patients (68.75%), with 75% of them from urban areas, regardless of gender. Among the known risk factors, sun exposure and fair skin were the most incriminated ones, being involved in all cases taken into consideration for the study, while smoking and solar keratosis were found in equal percentages among patients, respectively, 31.25%.

The most common patient complaints were pain (100% patients) and bleeding (81.25%) lesions. Only 25% of the patients analyzed presented with pruritus (**Figure 1**).

In our patients, the most frequently affected areas are the lower and upper limbs in 8 cases (50%), followed by the trunk area–6 cases (37.50%) (**Figure 2**).

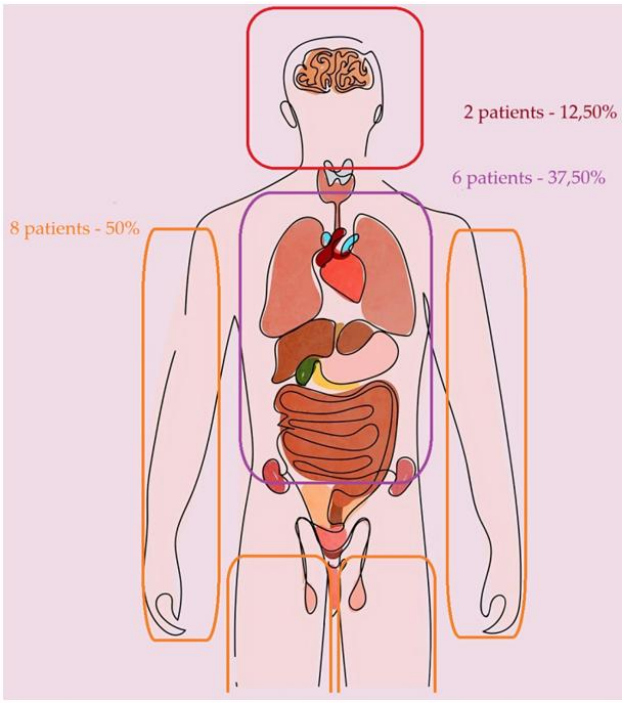

Figure 2. Frequent affected areas of the body (Source: Authors' own elaboration)

Table 2. Melanoma patient group by disease stage

Disease stage	Number of patients	Ratio (%)
I	0	0.00
II	2	12.50
III	1	6.25
IV	13	81.25

Table 3. Melanoma patient management options

Treatment options	Patient number	Ratio (%)
Surgical	84	100
Wide excision	69	82.14
Biopsy	64	76.19
External radiotherapy	84	100
Chemotherapy	6	7.14
Immune therapy	6	7.14

The areas most rarely affected (2 cases) are the head and neck, accounting for 12.50% of cases. The majority of cases in the studied group presented stage IV MM–81.25% (13 cases), while stage II was registered in only 2 patients (12.50%) (**Table 2**).

Stage I was not found in any of the analyzed cases. Sentinel lymph node biopsy was performed by 14 patients (87.50%), surgery was performed for 11 patients (68.75%), and reintervention was performed by 5 of them (31.25%) (**Table 3**).

All of the patients analyzed underwent palliative radiotherapy. The common dose of radiotherapy was 20 Gy/10 fractions in 10 patients, followed by 30 Gy/10 fractions in 5 patients and 40 Gy/20 fractions in a single patient. Chemotherapy was performed in 3 of the patients (18.75%), and immunotherapy for only 6 patients (37.50%). The therapeutics administered in 6 cases of melanoma is represented by dabrafenib, trametinib, interferon, and nivolumab. By analyzing the outcomes at 5 years, we found that 3 patients died (18.75%). The first case of MM was an 80-year-old woman with a one-year survival rate. The other 2 cases of melanoma were also present in women, but this time they were 47 and 60 years old, respectively, with two-year survival rates (**Table 4**).

Table 4. Melanoma patient outcome

Patient outcome	Number of patients	Ratio (%)
Survivors	13	81.25
Deceased	3	18.75

DISCUSSION

Skin cancers are a heterogeneous group of tumors with a constantly increasing incidence. The worldwide incidence of cutaneous melanoma has increased annually at a faster rate compared to any other type of cancer and is associated with significant mortality due to its aggressiveness and tendency to metastasize [10, 22]. The current study revealed that MM diagnosis incidences decreased from the start of the COVID-19 pandemic. This particular finding which reveals lowered number of patients addressing medical services during the pandemic is a general one worldwide starting from 2019 and reported by multiple literature data; the reasons for such reduced patient medical care reachability are multiple, including patient fear and anxiety, government lockdowns or restrictions, lack of easy access to medical services, with increase in digital medical services addressability and an increase in mortality rates [23-25].

Cutaneous MM accounts for about 1-2% of all skin cancer cases, but it is responsible for about 75-80% of deaths, having a worse prognosis compared to other types of skin cancer. In the United States, the incidence of melanoma has increased by about 3-4% per year in recent decades, and in Europe and other parts of the world, this trend is also observable [26, 27]. Cutaneous MM is one of the most aggressive forms of skin cancer and one of the leading causes of cancer mortality due to its metastatic power [28].

An important factor in increasing the incidence of melanoma is exposure to UV radiation, both through direct exposure to the sun and through the use of tanning lamps. UV exposure plays a significant role in inducing genetic mutations that can lead to the development of melanoma, especially in young people who are heavily ex-posed to UV radiation. This trend is more evident among people with light skin phototypes, who are more susceptible to sunburn and long-term UV damage buildup, which is also present in our study, where we observed that all patients had this risk factor present [29]. UV light radiation from sunlight is the main environmental risk factor for developing melanoma skin cancer. The increased risk of melanoma due to sun exposure is directly associated with the UV level and especially the UV-B spectrum [30].

Host risk factors such as the number of congenital and acquired melanocyte nevi, genetic susceptibility, and family history play a central role in the development of melanoma [31]. About 25% of melanoma cases occur on a pre-existing nevus [32]. In this context, not only the total number of nevi, but also the size and type of nevi, are individually associated with an increased risk of melanoma [33].

In recent years, melanomas have also been found to occur in families that are generally prone to specific patterns of malignancies, such as familial atypical multiple-mole-melanoma syndrome and its variant, melanoma-astrocytoma

syndrome germline mutations of cyclin-dependent kinase inhibitor 2A (CDKN2A or p16) and, less commonly, mutations of cyclin-dependent kinase 4 (CDK4) are the most common genetic abnormalities identified in these families [34]. Other inherited conditions associated with an increased risk of developing melanoma are xeroderma pigmentosum, familial retinoblastoma, Lynch syndrome type II, and Li-Fraumeni cancer syndrome [35]. In our study, it seems that sun exposure was the primary factor in the development of the disease, and the presence of solar keratosis and smoking were 31.25% responsible for the occurrence of the disease. Regarding age, the study in [36] specifies that melanoma mainly affects young and middle-aged people (the average age at diagnosis, being 57 years). The incidence in-creases linearly after the age of 25 to the age of 50, and then decreases, especially in females. When analyzing incidence data in relation to sex, women are more common in younger age groups, while males predominate from the age of 55 [36, 37]. These aspects are also evident in our study, women being diagnosed more frequently compared to men (68.75%), and the most common age of diagnosis was between 56-65 years.

Other studies from the global medical literature, such as the one from [38], which included a number of 399 patients aged 18-44 years with melanoma, over a 30-year period, specifically focusing on young adults/adolescents; they reported, similar to our findings, that even within a young adult group, the age at diagnosis increased over time (from 34.3 to 36.7 years). Another recent literature study reported by [39] included a large population-based cohort of 1,279 melanoma patients from the veneto cancer registry covering an entire region and used registry data to assess incidence, clinicopathological features, survival, and costs. They reported significant sex-related differences in cutaneous melanoma and found that while incidence was higher in women at younger ages, men had higher incidence among older adults, and tumor site and clinicopathological features differed by sex. In contrast, the current study, with a smaller, single-institution cohort, observed a higher proportion of female patients overall, likely reflecting local referral patterns and not a true population trend. A more regional-located cohort study done in [40] reported similar results to the current study, showing that melanoma predominantly affects middle-aged and older adults, aligning with general melanoma epidemiology, but also a similar female-patient predilection.

Global data on the incidence of skin cancer estimates that the incidence of melanoma is significantly higher in regions with intensive sun exposure, in the United States, the incidence is about 22 cases per 100,000 inhabitants, and in Europe, it varies between 5 and 20 cases per 100,000, depending on the region. A 2020 global study estimated that there are approximately 300,000 new cases of melanoma annually worldwide and more than 57,000 deaths associated with it [29, 41]. Research also shows an upward trend in melanoma incidence among young populations, which un-derscores the importance of public education and early prevention. In the study carried out at our center, most cases diagnosed were in 2019 (37.50%). Advances in melanoma treatments, particularly immunotherapy and targeted therapies, have significantly improved the prognosis of patients with advanced melanoma. Drugs such as nivolumab, pembrolizumab, and BRAF inhibitors have shown significant improvements in survival in patients with metastatic melanoma. However, melanoma remains a major cause of mortality among young people and those with metastatic forms [17, 42]. A ratio of 37.50% of the patients analyzed underwent immunotherapy, and 18.75 underwent chemotherapy, in our study due to the impaired prognostic index that did not allow the initiation of immunotherapy to a larger number of patients. At the end of the 5 years, 81.25% were survivors.

Most patients with newly diagnosed melanoma have early-stage disease. For these patients, surgical excision is the treatment of choice and is curative in most cases, an aspect also encountered in our study [43]. However, some patients will later relapse with disseminated disease, while about 10% of melanoma cases are diagnosed at an advanced stage and are unresectable or already metastatic. Of stage IV tumors, about one-third have visceral and cerebral involvement in diagnosis, with a severe prognosis and lower likelihood of having a sustained response to treatment [44]. In our study, 31.25% of the operated patients also had recurrence and needed reintervention. Some studies suggest that skin cancer might benefit from statin use, as preclinical studies revealed anti-proliferative and apoptotic effects, but this contradicts other findings which incriminate statins (and other therapeutic agents, such as dimethylfumarate) for skin cancer development [45, 46]. Further studies need to be done in order to reach a consensus on the matter of therapeutic agents for comorbidity and their link to skin cancer development, and more specifically, MM.

CONCLUSIONS

Skin cancer is a major public health problem globally, with an ever-increasing incidence. MM is an aggressive form of skin cancer, and its treatment involves complex and multidisciplinary management. Due to its potential for rapid metastasis and the increased risk of recurrence, addressing this type of cancer requires the involvement of several medical specialties, such as dermatology, oncology, surgery, radiology, immunology, pharmacology, but also genetic counseling. In this sense, each specialist plays a key role in the diagnosis, treatment and monitoring of patients. Multidisciplinary management of MM is essential to achieve the best therapeutic re-sults and to improve the patient's quality of life. This process involves collaboration between dermatologists, oncologists, surgeons, radiologists, pharmacologists, geneticists and psychologists, thus ensuring an integrated, personalized treatment with an optimal response. Recent advances in immunotherapy and targeted therapies offer new therapeutic options, but genetic counseling and careful monitoring of patients are essential for the long-term success of MM treatment.

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