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Original Article

Clinical Staging, Histopathological Features and Treatment Outcomes in Malignant Melanoma: A 10-Year Retrospective Single-Center Study

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ABSTRACT

Objectives: We aimed to retrospectively evaluate the clinical stage at diagnosis, histopathological features and treatment outcomes of adult patients with malignant melanoma over a 10-year period at Van YüzüncüYıl University Hospital. **Materials and Methods:** We reviewed 95 adult patients diagnosed between January 2010 and December 2019. Collected data included demographics, melanoma subtypes, tumor location, AJCC stage, treatment approaches and survival outcomes. **Results:** The cohort consisted of 52.6% males and 47.4% females, with a mean age of 56.9±16.4 years. Cutaneous melanoma was the most common subtype (81.1%), with nodular melanoma as the predominant histological type. Lesion location significantly affected survival (*p*<0.05). Stage IV was the most frequent at diagnosis (43.2%). Interferon and chemotherapy were common adjuvant therapies. All ocular melanoma cases underwent surgical enucleation. The median follow-up was 24.4 months. Median overall survival was 11.3 months; the 5-year survival rate was 63.6%. **Conclusion:** Our findings emphasize the prognostic impact of histological subtype, tumor site and disease stage at diagnosis. Expanded access to novel therapies may improve outcomes in this patient population.

Keywords: Malignant Melanoma, Clinical Staging, Histopathology, Treatment, Survival.

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INTRODUCTION

Malignant melanoma is an aggressive form of skin cancer that originates from the malignant transformation of melanocytes, the pigment-producing cells in the epidermis. Although its incidence is relatively low in Turkey, melanoma contributes substantially to skin cancer-related mortality due to its high metastatic potential and frequent late-stage diagnosis.[1] Early detection is crucial for improving prognosis, as patients diagnosed in primary care settings are more likely to present with early-stage disease and have better outcomes.[2] Prognosis is strongly influenced by clinical stage at diagnosis, anatomical location of the lesion and histopathological features such as Breslow thickness, Clark level, ulceration, mitotic index and growth pattern.[3] These parameters not only reflect tumor biology but also guide treatment strategies.

This study aimed to retrospectively assess the clinical staging, histopathological characteristics and treatment outcomes of patients diagnosed with malignant melanoma at Van YüzüncüYıl University Hospital over a 10-year period. By presenting single-center data from a low-incidence region, this study aims to contribute to the limited body of national data on melanoma in Turkey.

MATERIALS AND METHODS

This retrospective descriptive study included adult patients (≥18 years old) diagnosed with malignant melanoma at Van YüzüncüYıl University Hospital between January 2010 and December 2019. A total of 95 patients were identified through hospital medical records. Histopathological parameters such as Breslow thickness, Clark level, ulceration, mitotic index and growth pattern were evaluated when available. Tumor staging, including histopathological assessment, lymph node involvement and distant metastasis, was performed according to the AJCC T, N and M classifications (Tables 1-3).

Demographic and clinical data were collected, including age, sex, year of diagnosis, melanoma subtype, tumor location and clinical stage according to the 2017 American Joint Committee on Cancer (AJCC) staging system.[4] The distribution of clinical stages is summarized in Table 4. Treatment strategies and survival outcomes were documented for all patients. Surgical margin

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assessments were performed in accordance with World Health Organization (WHO) guidelines (Table 5). Treatment protocols administered to each patient subgroup are summarized in Table 6. Statistical analysis was conducted using IBM SPSS Statistics, version 25.0. A *p*-value <0.05 was considered statistically significant.

Statistical Analysis

All statistical analyses were performed using IBM SPSS Statistics, version 25.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were used to summarize the demographic and clinical data. Categorical variables were expressed as frequencies and percentages and continuous variables as mean±standard deviation. Kaplan-Meier survival analysis was used to estimate overall survival and differences between groups were compared using the log-rank test. A **p**-value <0.05 was considered statistically significant.

Table 1: Tumor (T) Staging in Cutaneous Melanoma-AJCC 2017.

T Classification	Thickness	Ulceration
Tis	N/A	N/A
T1	≤1.0 mm	Uncertain or unknown
T1a	<0.8 mm	Ulceration absent
T1b	<0.8 mm	Ulceration present
T1b	0.8-1 mm	Ulceration present or absent
T2	1.0-2.0 mm	Uncertain or unknown
T2a	1.0-2.0 mm	Ulceration absent
T2b	1.0-2.0 mm	Ulceration present
T3	2.0-4.0 mm	Uncertain or unknown
T3a	2.0-4.0 mm	Ulceration absent
T3b	2.0-4.0 mm	Ulceration present
T4b	>4.0 mm	Uncertain or unknown
T4a	>4.0 mm	Ulceration absent
T4b	>4.0 mm	Ulceration present

RESULTS

Patient Characteristics

This study included 95 patients, comprising 50 males (52.6%) and 45 females (47.4%), with a mean age of 56.9±16.4 years (range: 24-90). Detailed demographic characteristics are presented in Table 7.

Melanoma Subtypes and Localization Cutaneous melanoma was the most common subtype (81.1%, *n*=73), followed by ocular (10.0%, *n*=9) and mucosal melanoma (8.9%, *n*=8). In five patients, the primary tumor site could not be identified. Nodular melanoma was the most prevalent histological subtype (46.7%, *n*=28), followed by lentigo maligna (21.7%, *n*=13), superficial spreading melanoma (13.3%, *n*=8) and acral lentiginous melanoma (13.3%, *n*=8). Information on histological subtype was missing in 35 cases. The extremities were the most frequent tumor location (33.7%, *n*=32), with the lower limbs accounting for 71.8% of these cases, followed by the head and neck region (22.1%) and the trunk (9.5%).

Table 2: Lymph Node (N) Staging in Cutaneous Melanoma-AJCC 2017.

N Classification	Number of Affected Lymph Nodes	Extent of Nodal Involvement
N0	No lymph node involvement	
N1	1 lymph node	
N1a		Micrometastasis
N1b		Macrometastasis
N1c		In-transit metastasis/satellites without metastatic nodule
N2	2-3 lymph nodes	
N2a		Micrometastasis
N2b		Macrometastasis
N2c		In-transit metastasis/satellites without metastatic nodule
N3	4 or more lymph nodes	
N3a		Micrometastasis
N3b		Macrometastasis
N3c		In-transit metastasis/satellites without metastatic nodule

Histopathological Findings

Breslow thickness was available in 43 patients: 24.5% had tumors ≤1 mm, 18.9% were 1.01-2.00 mm, 11.3% were 2.01-4.00 mm and 45.3% were >4 mm. Clark level was documented in 42 patients, with level IV being most common (54.7%). Ulceration was present in 39.7% of evaluable cases (*n*=27/68). Vertical growth was observed in 78.6% of cases (*n*=48/61). The mean mitotic index was 13.39±17.12. Pathological features are summarized in Table 8. Staging and Survival Outcomes Based on AJCC 2017 criteria, 43.2% of cutaneous melanoma patients were diagnosed at stage IV, 32.8% at stage II, 19.4% at stage I and 4.4% at stage III. The median follow-up period was 24.4 months (range: 0.1-222.8). During follow-up, 35.7% (*n*=34) of patients died. The median overall survival among deceased patients was 11.3 months, with a mean survival of 20.6 months. The Kaplan-Meier curve for overall survival is shown in Figure 1. The 5-year survival rate was 63.6%.

Prognostic Factors

Survival was significantly associated with melanoma subtype (**p**<0.001). Median survival was 24 months for cutaneous melanoma, 11 months for mucosal melanoma and not reached for ocular melanoma.[5] The distribution of clinical stages at initial diagnosis is illustrated in Figure 2. Among cutaneous subtypes, mean survival was 27.1 months (acral lentiginous), 26.7 months

Table 3: Distant Metastasis (M) Staging in Cutaneous Melanoma-AJCC 2017.

M Classification	Anatomical Site	Serum LDH Level
M0	No distant metastasis	
M1	No distant metastasis	
M1a	Distant skin, subcutaneous or lymph node metastasis.	
M1a(0)		Normal
M1a(1)		Elevated
M1b	Lung metastasis	
M1b(0)		Normal
M1b(1)		Elevated
M1c	Visceral metastasis excluding CNS	
M1c(0)		Normal
M1c(1)		Elevated
M1d	Central nervous system metastasis	
M1d(0)		Normal
M1d(1)		Elevated

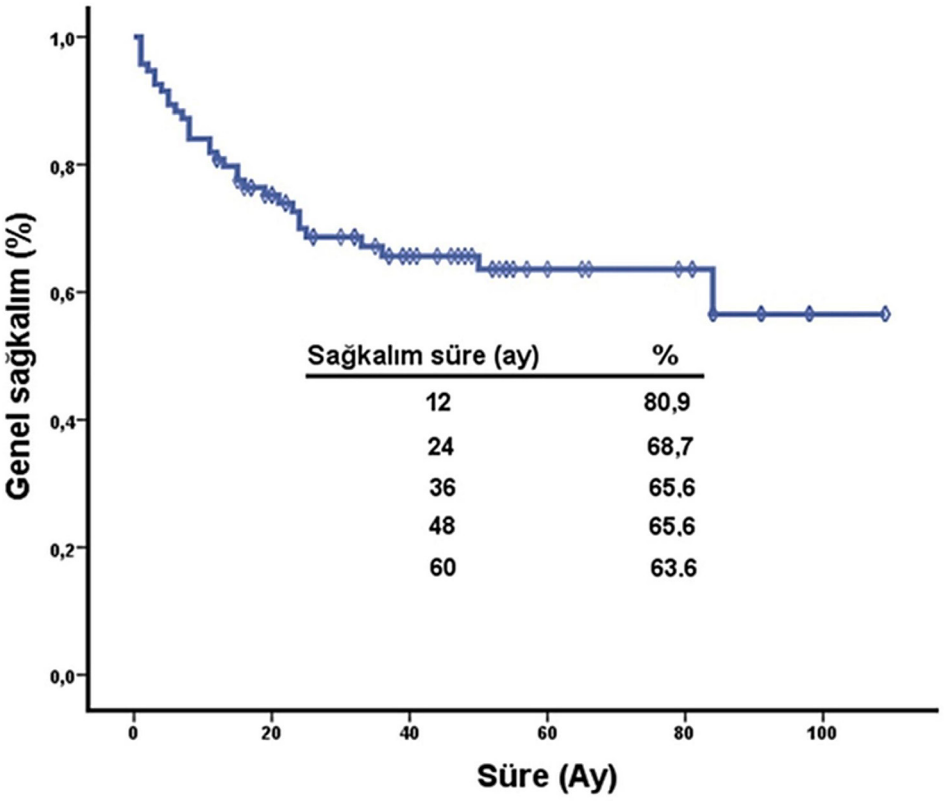

Figure 1: Kaplan-Meier overall survival curve for all patients with malignant melanoma (*n*=95). The median overall survival was 11.3 months (95% CI: 8.5-14.2). Censored data are indicated with vertical ticks.

Table 4: TNM Clinical and Pathological Staging in Cutaneous Melanoma - AJCC 2017.

T	N	M	Clinical Staging
Tis	N0	M0	0
T1a	N0	M0	IA
T1b	N0	M0	IB
T2a	N0	M0	IB
T2b	N0	M0	IIA
T3a	N0	M0	IIA
T3b	N0	M0	IIB
T4a	N0	M0	IIB
T4b	N0	M0	IIC
Any T, Tis	≥N1	M0	III
Any T	Any N	M1	IV
T	N	M	Pathological Staging
Tis	N0	M0	0
T1a	N0	M0	IA
T1b	N0	M0	IA
T2a	N0	M0	IB
T2b	N0	M0	IIA
T3a	N0	M0	IIA
T3b	N0	M0	IIB
T4a	N0	M0	IIB
T4b	N0	M0	IIC
T0	N1b, N1c	M0	IIIB
T0	N2b, N2c, N3b, or N3c	M0	IIIC
T1a/b-T2a	N1a or N2a	M0	IIIA
T1a/b-T2a	N1b/c or N2b	M0	IIIB
T2b/T3a	N1a-N2b	M0	IIIB
T1a-T3a	N2c or N3a/b/c	M0	IIIC
T3b/T4a	Any N ≥N1	M0	IIIC
T4b	N1a-N2c	M0	IIIC
T4b	N3a/b/c	M0	IIID
Any T, Tis	Any N	M1	IV

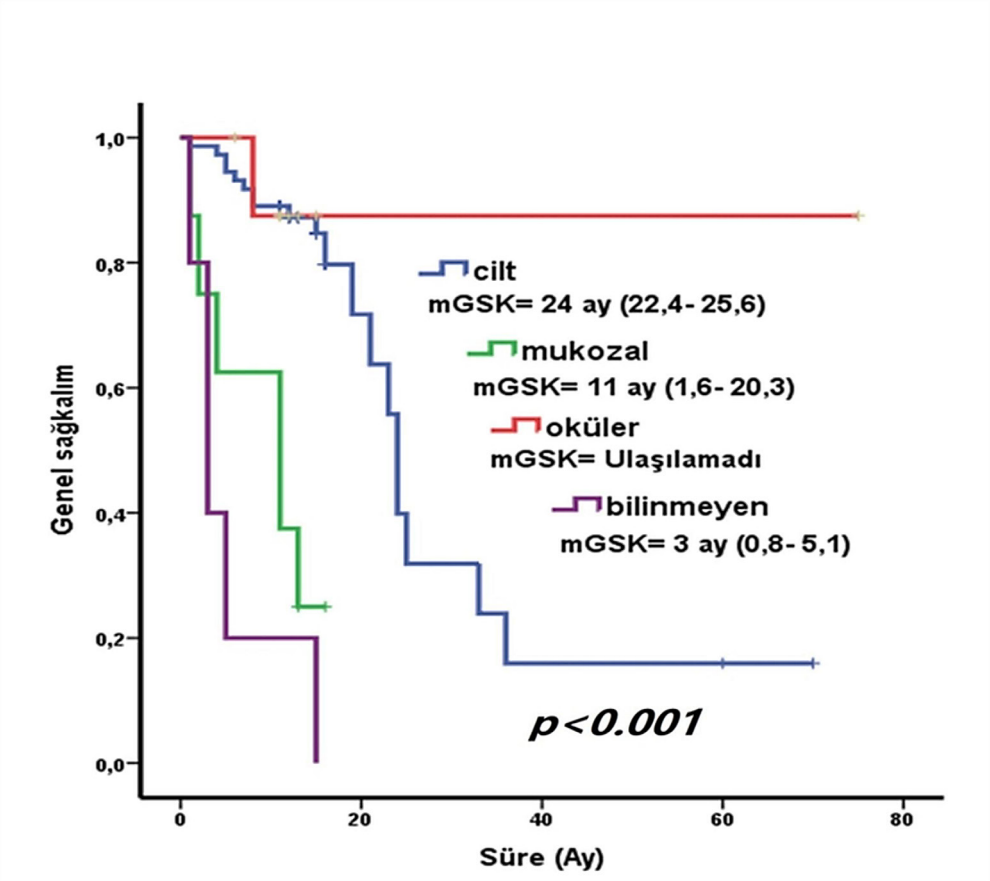

Figure 2: Distribution of patients by AJCC clinical stage at initial diagnosis. Stage IV was the most frequently observed (43.2%), followed by Stage III (25.3%). The percentage of patients in each stage is shown.

Table 5: WHO Recommendations for Surgical Margins in Cutaneous Melanoma.

Tumor Thickness	Surgical Margin
Melanoma *in situ*	0.5 cm
< 2 mm	1 cm
>2 mm	2 cm

(*lentigo maligna*), 24.4 months (superficial spreading) and 13.5 months (nodular). Lesion location (**p**<0.05), lymph node involvement (median survival 24.4 months vs. 6.27 months) and distant metastasis (**p**<0.05) were also significant prognostic factors.

Treatment

Five patients received adjuvant interferon therapy. Among 17 patients with metastatic cutaneous melanoma, 11 were treated with temozolomide, 4 with nivolumab, 4 with ipilimumab and 2 with vemurafenib. All ocular melanoma cases underwent surgical enucleation. Treatment strategies are summarized in Table 9.

Table 6: Treatment Protocols and Dosing Schedules.

Treatment Protocol	Dose	Administration Schedule
Interferon alfa-2b	20 MU/m2	Days 1-5
		(during the first 4 weeks)
	10MU/m2	
		Days 1, 3 and 5
		(for 48 weeks)
		Once a week
Temozolomide	200 mg/m2	Days 1-5
		Every 28 days
Paclitaxel	80 mg/m2	Weekly
Paclitaxel-Carboplatin	80 mg/ m2- AUC=2	Weekly
İpilimumab	3 mg/kg/gün	Day 1
		Every 21 days
Nivolumab	1×240 mg	14 days/Every 21 days
Trametenib	1×2 mg	Continuous
Dabrafenib	2×150 mg	Continuous

Table 7: Patient and Clinical Characteristics.

	Characteristics	Number of Patients	Percentage (%)
Sex	Male	50	52.6
Sex	Female	45	47.4
Melanoma Type	Skin	73	76.8
Melanoma Type	Mucosal	8	8.4
Melanoma Type	Ocular	9	9.4
Melanoma Type	Unknown	5	5.2
Localization	Ocular	9	9.5
Localization	Skin	11	11.6
Localization	Head and Neck	21	22.1
Localization	Trunk	9	9.5
Localization	Lower Extremity	9	9.5
Localization	Upper Extremity	23	24.2
Localization	Mucosal	5	5.3
Localization	Oral Mucosa	1	1.1
Localization	Rectum	2	2.1
Localization	Unknown	5	5.3
Type of Surgery	Tumor Excision	58	86.6
Type of Surgery	Enucleation	9	13.4
Lymph Node Involvement	N0	47	78.3
Lymph Node Involvement	N1	2	3.3
Lymph Node Involvement	N2	2	3.3
Lymph Node Involvement	N3	9	15
Metastasis	Absent	50	79.4
Metastasis	Present	13	20.6
At Diagnosis Metastasis	Liver	12	34.2
At Diagnosis Metastasis	Brain	5	14.2
At Diagnosis Metastasis	Skin	2	5.7
At Diagnosis Metastasis	Lung	10	28.5
At Diagnosis Metastasis	Abdomen	6	17.1
During Follow-up Metastasis	Liver	4	12.9
During Follow-up Metastasis	Brain	7	22.6
During Follow-up Metastasis	Abdomen	14	45.2
During Follow-up Metastasis	Lung	6	19.4
MaleCOG	0	40	42.1
	1	36	37.9
	2	15	15.8
	3	4	4.2
Final Status	Malex	34	35.8
	Alive	61	64.2

Table 8: Pathological Characteristics and Frequencies.

	Characteristics	Number of Patients	Percentage (%)
Histology	Acral Lentiginous	8	13.3
Histology	Nodular	28	46.7
Histology	Lentigo Maligna	13	21.7
Histology	Superficial spreading	8	13.3
Histology	Ocular	3	5
Growth Phase	Absent	34	35.8
Growth Phase	Radial	13	13.7
Growth Phase	Vertical	48	50.5
Satellite Nodule	Absent	31	73.8
Satellite Nodule	Present	11	26.2
Ulceration	Absent	41	60.3
Ulceration	Present	27	39.7
LVI (Lymphovascular Invasion)	Absent	38	73.1
LVI (Lymphovascular Invasion)	Present	14	26.9
PNI (Perineural Invasion)	Absent	33	84.6
PNI (Perineural Invasion)	Present	6	15.4
Lymphocytic Infiltration	Absent	52	57.1
Lymphocytic Infiltration	Present	39	42.9
Surgical Margin	Absent	45	83.3
Surgical Margin	Present	9	16.7
Breslow Thickness (mm)	≤1 mm	13	24.5
Breslow Thickness (mm)	1.01-2.00 mm	10	18.9
Breslow Thickness (mm)	2.01-4.00 mm	6	11.3
Breslow Thickness (mm)	> 4 mm	24	45.3
Clark Level	Unspecified	43	50.6
Clark Level	Level 1	6	7.1
Clark Level	Level 2	4	4.7
Clark Level	Level 3	9	10.6
Clark Level	Level 4	23	27.1
BRAF Mutation	Absent	14	77.8
BRAF Mutation	Present	4	22.2

Table 9: Summary of All Treatments Administered.

	Treatment Type / Line	Number of Patients	Percentage (%)
Surgical	Tumor Excision	57	60
Surgical	Enucleation	9	9.4
Radiotherapy	Adjuvant	2	2.1
Radiotherapy	Palliative	2	2.1
Adjuvant interferon therapy		5	5.2
First-line palliative chemotherapy	Temozolomide	9	56.2
First-line palliative chemotherapy	Temozolomide+Cis	2	12.5
First-line palliative chemotherapy	Trametinib	1	6.25
First-line palliative chemotherapy	Dabrafenib+Trametinib	1	6.25
First-line palliative chemotherapy	Nivolumab	1	6.25
First-line palliative chemotherapy	Paclitaxel-Carboplatin	1	6.25
First-line palliative chemotherapy	Thalidomide	1	6.25
Second-line palliative chemotherapy	Temozolomide	1	12.5
Second-line palliative chemotherapy	Ipilimumab	2	25
Second-line palliative chemotherapy	Vemurafenib	2	25
Second-line palliative chemotherapy	Paclitaxel	1	12.5
Second-line palliative chemotherapy	Nivolumab	2	25
Third-line palliative chemotherapy	Ipilimumab	2	50
Third-line palliative chemotherapy	Nivolumab	1	25
Third-line palliative chemotherapy	Temozolomide	1	25

DISCUSSION

A notable limitation of our study was the incomplete documentation of histopathological data, such as missing values for Breslow thickness and histological subtype in a significant proportion of patients. Additionally, as a retrospective study conducted at a single tertiary center, selection and information bias may have influenced the results. Lack of access to novel therapies and variability in treatment protocols over the 10-year study period may also limit the generalizability of our findings. Recent clinical trials have demonstrated improved survival with immunotherapy and targeted therapies such as nivolumab, ipilimumab, and vemurafenib in advanced melanoma cases. [6–10]

CONCLUSION

This study provides a comprehensive overview of malignant melanoma cases diagnosed over a decade at a tertiary center in Eastern Turkey. Nodular melanoma emerged as the most prevalent histological subtype, with a substantial proportion of patients presenting at advanced clinical stages. Tumor localization and disease stage were identified as key prognostic factors influencing survival outcomes.

These findings underscore the critical importance of early detection, standardized histopathological evaluation and equitable access to contemporary systemic therapies. Public health strategies aimed at enhancing awareness and facilitating timely dermatological consultations, along with national policies to improve the availability of targeted and immunotherapeutic agents, are essential for optimizing outcomes in similarly low-incidence regions.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

FUNDING

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ETHICAL APPROVAL

The study was approved by the Ethics Committee of Van YüzüncüYıl University (Approval date: April 12, 2019; Protocol number: 2019/07-02). All procedures were carried out in accordance with the Declaration of Helsinki.

AUTHOR CONTRIBUTIONS

Zarife Türkoğlu contributed to study conception, data collection, statistical analysis and manuscript writing. Ramazan Esen supervised the study, contributed to interpretation of results and critically revised the manuscript. All authors contributed to the study's design, data collection, analysis and manuscript preparation. All authors approved the final version.

ABBREVIATIONS

AJCC: American Joint Committee on Cancer; **WHO:** World Health Organization; **mOS:** Median Overall Survival; **CI:** Confidence Interval; **MM:** Malignant Melanoma.

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