Postprint: Prognosis and Influencing Factors in Patients with Malignant Melanoma

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Abstract

Background Malignant melanoma (MM) arises from the malignant transformation of epidermal melanocytes, exhibits extremely high malignancy, and has an increasing incidence annually. Its prevention and treatment represent a key focus in the field of dermatology. Objective To investigate the prognosis and its influencing factors in patients with malignant melanoma. Methods A total of 205 patients with acral MM admitted to the First Hospital of Shanxi Medical University from January 2006 to December 2021 were selected as study subjects. Clinical data were obtained by reviewing patients' electronic medical records, and overall survival (OS) was determined through telephone follow-up. The Kaplan-Meier method was used to plot OS survival curves for MM patients. Log-rank test was employed for univariate analysis of OS influencing factors. Multivariate Cox proportional hazards regression model was used to analyze the influencing factors of OS in MM patients. Results As of the last follow-up (December 31, 2022), the 1-year, 3-year, and 5-year overall survival rates of MM patients were 94.6%, 81.9%, and 72.6%, respectively, with a mean OS of 71.77 months and a median survival of 66.83 months. Univariate analysis revealed statistically significant differences in 5-year overall survival rates among MM patients with different gender, age, tumor thickness, tumor ulceration, lymph node metastasis, and neutrophil-to-lymphocyte ratio (NLR) (P<0.05). Multivariate Cox proportional hazards regression analysis identified male gender [HR=1.644, 95%CI (1.148, 2.498)], tumor thickness >1.94 mm [HR=2.466, 95%CI (1.419, 4.284)], tumor ulceration [HR=1.821, 95%CI (1.225, 2.708)], lymph node metastasis [HR=1.999, 95%CI (1.305, 2.892)], and NLR$ 3[$HR = 1.873, 95 $3 are factors associated with poor prognosis in MM patients. Medical practitioners should focus on MM patients with these poor prognostic factors, intensify care to improve their survival rates, and thereby better guide clinical practice.

Full Text

Prognosis and Influencing Factors of Patients with Malignant Melanoma

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Abstract Background Malignant melanoma (MM) arises from the malignant transformation of epidermal melanocytes, exhibiting extremely high malignancy and increasing incidence annually, making its prevention and treatment a key focus in dermatology. **Objective** To investigate the prognosis of MM patients and its influencing factors. **Methods** A total of 205 patients with acral MM admitted to the First Affiliated Hospital of Shanxi Medical University from January 2006 to December 2021 were enrolled. Clinical data were obtained from electronic medical records, and overall survival (OS) was determined through telephone follow-up. Kaplan-Meier method was used to plot survival curves for OS. Univariate analysis of OS influencing factors was performed using Log-rank test. Multivariate Cox proportional hazard regression model was employed to analyze influencing factors of OS. **Results** As of the last follow-up (December 31, 2022), the 1-year, 3-year, and 5-year overall survival rates were 94.6%, 81.9%, and 72.6%, respectively, with a mean OS of 71.77 months and median OS of 66.83 months. Univariate analysis revealed statistically significant differences in 5-year overall survival rates among patients with different genders, ages, tumor thickness, tumor ulceration, lymph node metastasis, and neutrophil-to-lymphocyte ratio (NLR) ($P<0.05$). Multivariate Cox regression analysis identified male gender [HR=1.644, 95%CI (1.148, 2.498)], tumor thickness >1.94 mm [HR=2.466, 95%CI (1.419, 4.284)], tumor ulceration [HR=1.821, 95%CI (1.225, 2.708)], lymph node metastasis [HR=1.999, 95%CI (1.305, 2.892)], and NLR ≥ 3 [HR=1.873, 95%CI (1.108, 3.166)] as influencing factors of OS ($P<0.05$). **Conclusion** Male gender, tumor thickness >1.94 mm, tumor ulceration, lymph node metastasis, and NLR ≥ 3 are adverse prognostic factors for MM patients. Healthcare professionals should focus on MM patients with these adverse prognostic factors and intensify care to improve survival rates, thereby providing better clinical guidance.

[**Key words**] Malignant melanoma; Prognosis; Cox models; Nomograms; Over-

all survival; Root cause analysis; Shanxi province

Introduction

Malignant melanoma (MM) is a highly malignant tumor derived from epidermal melanocytes, which normally produce pigment in the basal layer of the epidermis [1-3]. In 2012, approximately 55,000 deaths worldwide were attributed to MM (accounting for 0.7% of total cancer mortality) [4]. Among known skin cancers, MM is the most aggressive form, characterized by high insidiousness, early distant metastasis, and high fatality rates [5]. Although MM represents only about 5% of all skin cancers, it causes 75% of skin cancer-related deaths [6]. Compared with Western countries, MM incidence is lower in Asia. However, despite its relatively low incidence in China, the absolute numbers of cases and deaths remain substantial due to the large population, with nearly 20,000 new cases of cutaneous MM diagnosed annually in recent years [7]. Melanoma is preventable and treatable, but lack of awareness results in many patients presenting with distant metastasis at admission and poor prognosis. Therefore, investigating the unique epidemiological characteristics and high-risk prognostic factors in our region is crucial for improving melanoma diagnosis and treatment.

1. Materials and Methods

1.1 Study Subjects

We selected 205 patients with acral MM admitted to the First Affiliated Hospital of Shanxi Medical University from January 2006 to December 2021 as study subjects. **Inclusion criteria:** (1) Complete clinical data (including admission records, progress notes, discharge records, surgical records, preoperative biochemical test reports, pathology reports, and follow-up contact information); (2) Pathologically confirmed MM through surgical resection or biopsy. **Exclusion criteria:** (1) Concurrent other skin malignancies; (2) Concurrent severe cardiovascular or cerebrovascular diseases; (3) Concurrent mucosal melanoma.

1.2 Research Methods

Clinical data were collected from electronic medical records, including gender, age, tumor thickness, tumor ulceration, treatment method, Karnofsky Performance Status (KPS) score, lymph node metastasis, BRAF V600E mutation, lactate dehydrogenase (LDH), and neutrophil-to-lymphocyte ratio (NLR). Treatment methods were categorized as immunotherapy or targeted drug therapy. Immunotherapy included interferon, interleukin monoclonal antibodies, small RNA interference technology, multivalent cell vaccines, peptide vaccines, and anti-P97 or anti-gp240 glycoprotein antibodies. Targeted drug therapy included vemurafenib and dabrafenib.

1.3 Follow-up

The study endpoint was overall survival (OS), determined through telephone follow-up. OS was defined as the time from diagnosis to death or last contact for lost-to-follow-up patients [8]. Follow-up continued until December 31, 2022.

1.4 Statistical Methods

Data analysis was performed using R software and SPSS 26.0. Categorical data were expressed as relative frequencies and compared using ^{2} test. Kaplan-Meier method was used to plot OS survival curves. Univariate analysis of OS influencing factors employed Log-rank test. Multivariate Cox proportional hazard regression model was used to analyze influencing factors of OS, with nomograms calculated for survival-related factors. P<0.05 was considered statistically significant.

2. Results

2.1 Clinical Characteristics of MM Patients

Among the 205 MM patients, 111 were male (54.1%) and 94 were female (45.9%). The median age was 54 years (range: 4-95 years), with 87 patients (42.4%) aged $ $50 years and 118 (57.6%) aged >50 years. The median tumor thickness was 1.94 mm (range: 0.10-17.42 mm), with 109 patients (53.2%) having tumor thickness $ $1.94 mm and 96 (46.8%) >1.94 mm. Tumor ulceration was present in 110 patients (53.7%) and absent in 95 (46.3%). Lymph node metastasis occurred in 112 patients (54.6%) and was absent in 93 (45.4%). NLR was <3 in 93 patients (45.4%) and $ $3 in 112 (54.6%) . As of the last follow-up, the 1-year, 3-year, and 5-year overall survival rates were 94.6%, 81.9%, and 72.6%, respectively, with a mortality rate of 34.6%. The mean OS was 71.77 months and median OS was 66.83 months [Figure 1: see original paper].

2.2 Univariate Analysis of OS Influencing Factors

Univariate analysis showed statistically significant differences in 5-year overall survival rates among MM patients with different genders, ages, tumor thickness, tumor ulceration, lymph node metastasis, and NLR (P<0.05). Specifically, female patients had higher 5-year overall survival than males; patients aged $ $50 years had higher rates than those >50 years; patients with tumor thickness $ $1.94 mm had higher rates than those > 1.94 mm; patients without tumor ulceration had higher rates than those with ulceration; patients without lymphno
3 had higher rates than those with NLR $ $3 (P<0.05) [TABLE:1, FIGURE:2-7].

2.3 Multivariate Analysis

Using MM patient OS outcome as the dependent variable, six statistically significant indicators from univariate analysis (gender, age, tumor thickness, tumor ulceration, lymph node metastasis, and NLR) were included as independent

variables in the Cox proportional hazard regression model (variable assignments shown in). Results showed that male gender, tumor thickness >1.94 mm, tumor ulceration, lymph node metastasis, and NLR$ $3 were influencing factors of OS in MM patients (P<0.05) .

2.4 Cox Proportional Hazard Regression Model Nomogram

Data from the Cox proportional hazard regression model were analyzed using R software survival and rms packages to generate a nomogram [Figure 8: see original paper]. This nomogram helps clinicians visually screen and predict survival time in MM patients, enabling early intervention. Points on the chart represent scoring criteria or scales. For each indicator, a vertical line drawn at the point intersects the axis to represent the score below the variable value, allowing calculation of each patient' s total score and corresponding survival probability (1-year, 5-year, or 10-year OS).

3. Discussion

Univariate analysis revealed that female MM patients had higher 5-year overall survival rates than males, while multivariate analysis identified male gender as an influencing factor of OS. This suggests that earlier and more successful treatment selection may occur before cancer progression. Men are less likely to perform self-examinations for MM or seek medical evaluation, potentially leading to later detection. Another consideration is inherent differences in skin anatomy and physiology between sexes [8-13]. Male skin is thicker with more abundant collagen and elastic fibers [14], contains less subcutaneous fat, and has different hair patterns due to androgen stimulation and estrogen inhibition [15]. These biological differences lead to varied responses to environmental stressors such as ultraviolet (UV) exposure, with male skin appearing more sensitive [16]. Recognizing these behavioral and biological differences between men and women [17] helps explain improved OS in women, indicating that female gender is an independent favorable prognostic factor for MM survival.

Univariate analysis showed statistically significant differences in 5-year overall survival rates between different age groups, but age was not identified as an influencing factor in multivariate analysis. Patients aged >50 years had lower 5-year overall survival (65.3%) than those $ $50 years (82.4%) (P<0.05), suggesting poorer prognosis in older patients. Elderly patients typically have higher ulceration rates and greater tumor thickness [18], and age as a risk factor may be incompletely represented, particularly since some elderly patients present at advanced stages with delayed diagnosis. Multicenter studies have confirmed [19] that older patients often have poorer prognosis, possibly because MM incidence increases with age and age-related risk factors such as cumulative sun exposure become more significant [20]. Although MM visibility (anatomical distribution) does not change with age, older individuals may observe or notice pigmented skin lesions less frequently and may be less concerned about appearance, potentially contributing to delayed detection [21].

Univariate analysis showed that patients with tumor thickness >1.94 mm had lower 5-year overall survival (55.0%) than those with thickness $ $1.94 mm (88.4%) (P<0.05), indicating poorer prognosis with greater tumor thickness. Multivariate analysis also identified tumor thickness as an influencing factor of OS. Thin melanomas generally have better prognosis, with increased tumor thickness associated with decreased OS, consistent with domestic and international literature [22-24]. Univariate analysis showed that MM patients with tumor ulceration had lower 5-year overall survival (56.1%) than those without ulceration (90.2%) (P<0.05), demonstrating that ulceration is significantly associated with poorer prognosis. Multivariate analysis identified tumor ulceration as an influencing factor of OS, consistent with studies by TURK et al. [25] and CALLENDER et al. [26]. Therefore, MM patients with tumor ulceration require better and more aggressive treatment.

Univariate analysis showed that lymph node metastasis was closely related to MM patient prognosis, and multivariate Cox regression analysis identified lymph node metastasis as an influencing factor of OS. Once lymph node metastasis is detected, timely lymph node dissection or metastatic lymph node excision should be performed [27]. Univariate analysis showed that elevated inflammatory marker NLR was associated with poorer prognosis in MM patients, and multivariate Cox regression analysis identified NLR$ $3 as an influencing factor of OS, consistent with previous research [28]. Thus, the inflammatory marker NLR is suitable for clinical use in patients requiring adjuvant therapy or unsuitable for surgical treatment.

4. Conclusion

This study demonstrates that male gender, tumor ulceration, tumor thickness >1.94 mm, NLR$ $3, and lymph node metastasis are independent adverse prognostic factors for malignant melanoma. Healthcare professionals can use these findings to intensify care for patients with adverse prognostic factors and improve survival rates. Since this study included only acral MM patients, the results apply specifically to acral MM; subsequent studies on MM at other sites will provide additional data support for clinical practice.

Author Contributions: WU Shuqin proposed the main research objectives, designed the study, implemented the research, and wrote the manuscript. WANG Yuanhan drafted and revised the final version of the manuscript. YU Hongmei provided guidance on statistical methods. WANG Yuanhan, ZHENG Kaiyuan, and HAN Hongjuan collected data and prepared figures and tables. KANG Jinxiu and YU Hongmei were responsible for quality control and review of the article and supervised the overall project.

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