

# Clinical and prognostic factors in 98 patients with malignant melanoma in China

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## Abstract

**Objective:** To investigate clinical and prognostic factors in patients with malignant melanoma (MM) in China.

**Methods:** A total of 98 MM patients were enrolled in the study. Enumeration data were analyzed using Fisher's exact probability tests or  $\chi^2$  tests. Survival rates were calculated using log-rank tests. A Cox multivariate regression analysis was performed to determine independent prognostic factors.

**Results:** The male: female incidence ratio was 1.88:1. The highest incidence rate was seen in the 45–65 year age group. Primary lesion ulceration was seen in 60.2% of patients. The 1-year, 3-year and 5-year survival rates were 85.7%, 34.7% and 13.3%, respectively. In univariate analyses, the 5-year survival rate in patients was significantly associated with ulceration ( $P < 0.01$ ), clinical stage ( $P < 0.01$ ) and surgical excision of the tumor ( $P < 0.01$ ). Cox multivariate regression analysis confirmed that ulceration and clinical stage were independent prognostic factors.

**Conclusions:** Some clinical characteristics of MM patients in China are significantly different from those of patients in Western countries. Ulceration and clinical stage are independent risk factors for poor survival in MM patients.

## Keywords

Malignant melanoma, prognosis, survival analysis

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## Introduction

Malignant melanoma (MM) is one of the most common malignant tumors in Western countries and is known for its rapid progression, metastasis and poor prognosis.<sup>1</sup> It is relatively rare in Asian people. In recent years, MM has been one of the most rapidly increasing cancers in China.<sup>2</sup> It has been

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**Table 1.** Differences in clinical characteristics between Western and Chinese malignant melanoma patients.

Study	Characteristic	Highest incidence rate	
		Western	Chinese
Jemal et al. <sup>19</sup> , Boyle et al. <sup>20</sup> , Kachuri L et al. <sup>21</sup> , Melanoma Expert Committee of CSCO <sup>18</sup>	ethnic group	Caucasian (high)	Asian (low)
Chi et al. <sup>5</sup> , Luk et al. <sup>6</sup> , Bradford et al. <sup>7</sup> , Lasithiotakis et al. <sup>8</sup>	gender	female	male
Chi et al. <sup>5</sup> , Bradford et al. <sup>7</sup> , MacKie et al. <sup>15</sup> , Lasithiotakis et al. <sup>8</sup>	age (years)	mainly old	mainly 45–60
Balaban et al. <sup>9</sup> , Milo et al. <sup>22</sup> , Cress et al. <sup>23</sup> , Luk et al. <sup>6</sup>	tumor location	mainly torso	mainly limbs
Eggermont et al. <sup>10</sup> , Luk et al. <sup>6</sup> , Lasithiotakis et al. <sup>8</sup> , Chi et al. <sup>5</sup>	ulceration	relatively less	more common
Balaban et al. <sup>9</sup> , Milo et al. <sup>22</sup> , Cress et al. <sup>23</sup> , Chi et al. <sup>5</sup>	histological type	mainly SSM	mainly ALM

CSCO: Chinese Society of Clinical Oncology; SSM: superficial spreading melanoma; ALM: acral lentiginous melanoma.

reported that some clinical characteristics of MM patients are significantly different among different ethnic groups (Table 1).<sup>3</sup> However, extensive reports about MM mainly come from Western countries. **Relatively less is known about MM in Asian, and especially Chinese patients.** Therefore, we designed this study to investigate clinical and prognostic factors in MM patients in China, using both univariate and multivariate analyses.

## Material and methods

### Patients

A total of 98 consecutive MM patients at the Departments of Dermatology and Oncology, Jinan Central Hospital Affiliated to Shandong University were recruited from January 2001 to December 2010. Patients for whom the pathology confirmed MM following surgery or biopsy and patients who died of cancer were enrolled in the prognostic analysis. Seven patients were lost to follow up. Tumor–node–metastasis (TNM) staging according to the American Joint Committee on Cancer (AJCC) staging system (7th edition) was used for **clinical**

**staging** in 2010.<sup>4</sup> The study was approved by the Ethics Committee of Shandong University.

### Statistical analysis

Fisher's exact probability test or the  $\chi^2$  test was used to analyze enumeration data. Survival rates were analyzed using the log-rank test. Cox multivariate analysis was used to calculate independent prognostic factors. SPSS 13.0 software was used for statistical analysis, and P values of less than 0.05 were considered significant.

## Results

As shown in Table 2, 64 (65.3%) patients were male and 34 (34.7%) were female (male: female ratio, 1.88:1). The ages of the 98 patients ranged from 36 to 96 years old. The tumors were located on the head and neck in 11 (11.2%) patients, on the trunk in 10 (10.2%), on the extremities in 71 (72.4%) and on the mucosa in 6 (6.2%). Fifty-nine (60.2%) patients had ulceration in their primary lesion. The pathological type of MM included nodular melanoma,

**Table 2.** Clinical characteristics and results of univariate survival analysis of malignant melanoma patients.

Clinical characteristic	No. patients enrolled	5-year survival		P value <sup>a</sup>
		No. patients surviving	Survival rate (%)	
All patients	98	13	13.3	
Gender				0.184
male	64	9	14.1	
female	34	4	11.8	
Age (years)				0.619
<45	6	1	16.7	
46–65	57	6	10.5	
>65	35	6	17.1	
Location				0.431
head and neck	11	1	9.1	
trunk	10	2	20.0	
extremities	71	10	14.1	
mucosal	6	0	0.0	
Ulceration				<0.01
yes	59	2	3.4	
no	39	11	28.2	
Histological type				0.725
NM	15	1	6.7	
SSM	18	3	16.7	
ALM	59	9	15.3	
mucosal	6	0	0.0	
Clinical stage				<0.01
I	8	3	37.5	
II	31	10	32.3	
III	44	0	0.0	
IV	15	0	0.0	
Operative type				<0.01
surgery	59	13	22.0	
biopsy	39	0	0.0	
Chemotherapy				0.250
yes	40	6	15.0	
no	58	7	12.1	
Radiotherapy				0.442
yes	27	4	14.8	
no	71	9	12.7	
Immunotherapy				0.678
yes	34	4	10.5	
no	51	9	15.0	

NM: nodular melanoma; SSM: superficial spreading melanoma; ALM: acral lentiginous melanoma.

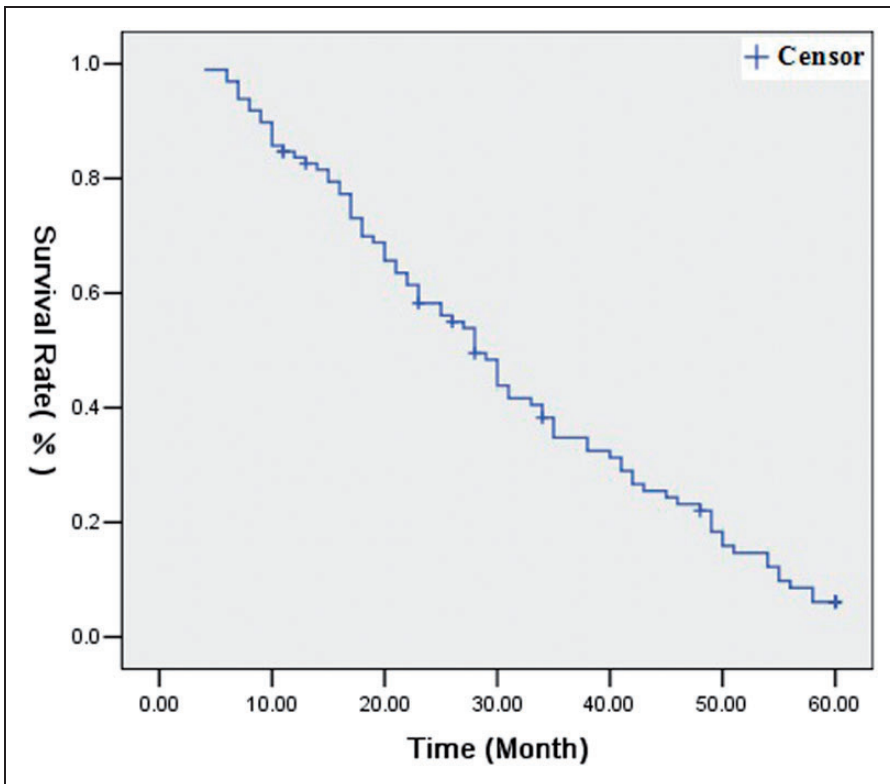
<sup>a</sup>P values were obtained with the log-rank test.

superficial spreading melanoma (SSM), acral lentiginous melanoma and mucosal melanoma. With respect to clinical stage, the incidence of localized disease (stages I–II) was 39 (39.8%), followed by node-involved (stage III) and metastatic disease (stage IV) with incidences of 44 (44.9%) and 15 (15.3%), respectively.

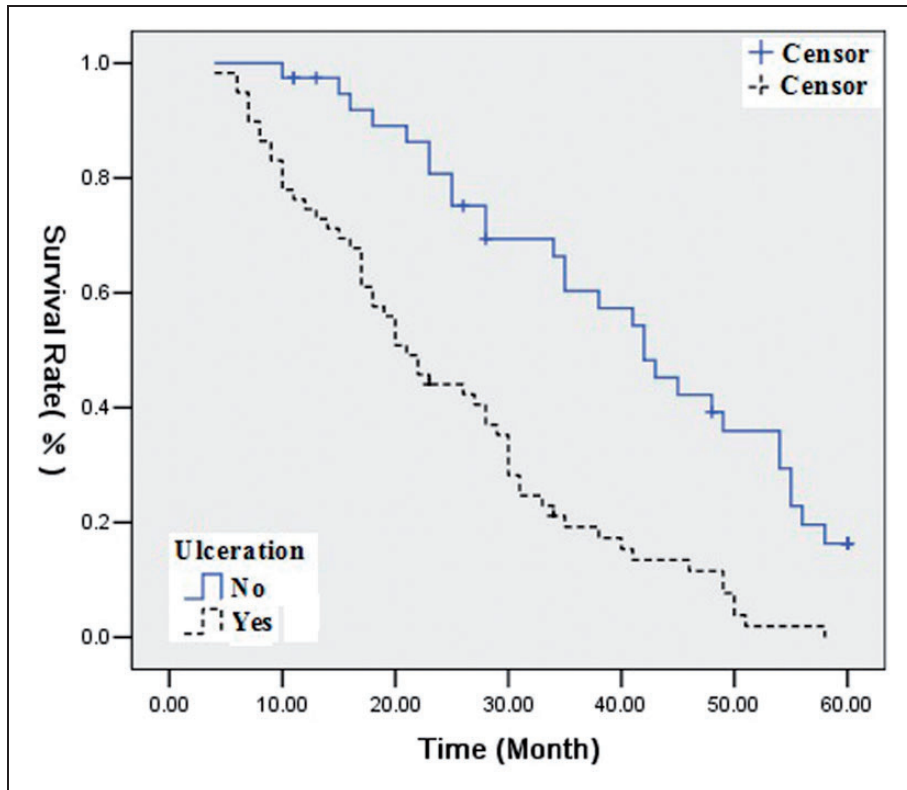
There were 59 patients who had undergone local excision, extended excision, or extended excision with regional nodal dissection of their tumors. Forty patients received adjuvant chemotherapy, 27 received adjuvant radiotherapy, and 34 received immunotherapy (interferon).

The 1-year, 3-year and 5-year survival rates of the 98 patients were 85.7%, 34.7% and 13.3%, respectively (Figure 1). In a

univariate analysis using the log-rank test, the 5-year survival rate of patients with ulceration was significantly lower than that of patients without ulceration ( $P < 0.01$ ) (Figure 2). The overall survival rates at 5 years, stratified by clinical stages at diagnosis, were 37.5%, 32.3%, 0.0% and 0.0% for stage I–IV disease, respectively ( $P < 0.01$ ) (Figure 3). The 5-year survival rate in patients was also significantly associated with surgical excision ( $P < 0.01$ ). There was no statistically significant effect of gender, age, tumor location, histological type, chemotherapy, radiotherapy or immunotherapy. We also performed a multivariate analysis to identify independent prognostic factors for survival in the 98 MM patients. The results of Cox multivariate regression



**Figure 1.** Kaplan–Meier analysis of overall survival rate in malignant melanoma patients.



**Figure 2.** Kaplan–Meier analysis of overall survival rate in patients with and without ulceration.

analysis confirmed that ulceration and clinical staging were relevant independent factors (Table 3).

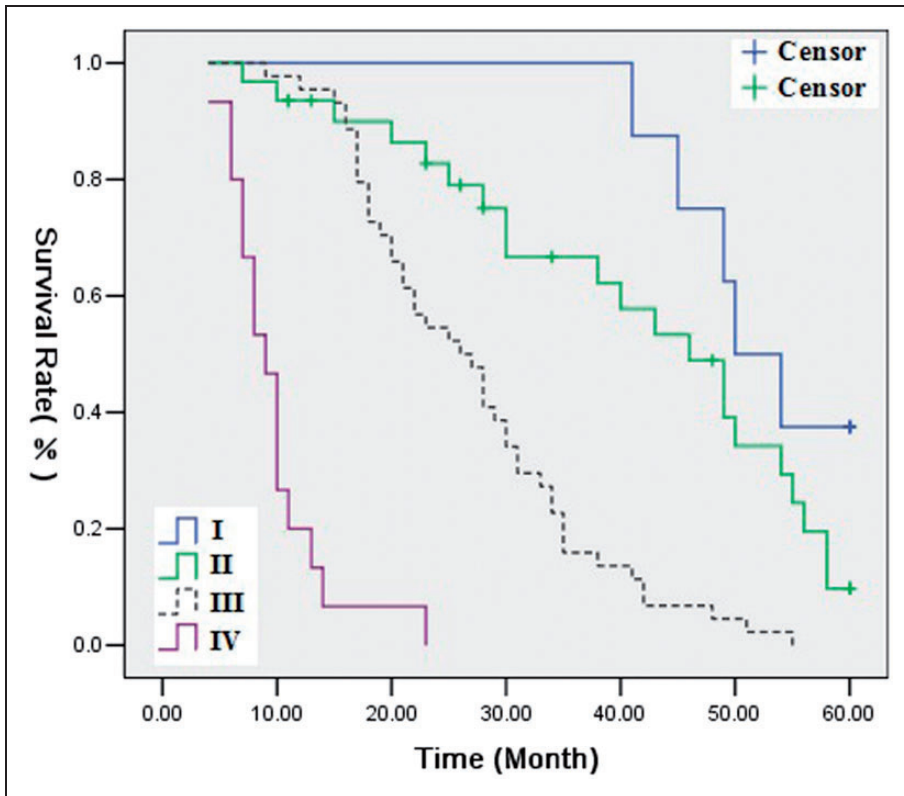
## Discussion

Recent reports have shown that the morbidity of MM in Asians has improved, but it has one of the more rapidly increasing incidence rates of malignant tumors in China.<sup>5</sup> Therefore, it is important to understand the clinical characteristics and prognostic risk factors of Chinese MM patients.

In our study, the incidence rate of males was higher than that of females, with a male:female incidence ratio of 1.88:1. Similar results were described in reports from other Chinese centers in Beijing and Hong Kong.<sup>5,6</sup> In contrast, it has been reported

that the incidence rate of males is lower than that of females for Caucasians in Western countries.<sup>7,8</sup> The incidence rate of MM in Caucasians increases with increasing age.<sup>7,8</sup> Our study showed that the highest incidence rate was seen in patients from 45–65 years old. The incidence rate declined in patients over 65 years old. This result was also similar to that reported by Chi et al. in Beijing, China.<sup>5</sup>

We found that the locations and histological subtypes of melanoma diagnosed in our patients differed substantially from those reported in Western populations. Melanoma originates from melanocytes, which in most cases are located in the skin. Melanoma can also arise at a variety of non-cutaneous sites. In Caucasians, the most common location is the torso, and the



**Figure 3.** Kaplan–Meier analysis of overall survival rate in patients with different clinical stages.

**Table 3.** Results of multivariate Cox regression analysis of survival.

	B	SE	Wald	P	HR	95% CI for HR
Gender	-0.364	0.286	1.615	0.204	0.695	0.396–1.218
Age	0.157	0.215	0.536	0.464	1.170	0.768–1.782
Location	-0.288	0.185	2.426	0.119	0.750	0.522–1.077
Ulceration	0.666	0.302	4.862	0.027	1.946	1.077–3.518
Histological type	0.153	0.165	0.857	0.355	1.165	0.843–1.610
Clinical stage	1.245	0.231	28.989	0.000	3.475	2.208–5.468
Operative type	-0.517	0.276	3.527	0.060	0.596	0.347–1.023
Chemotherapy	-0.159	0.256	0.387	0.534	0.853	0.517–1.408
Radiotherapy	-0.561	0.298	3.556	0.059	0.570	0.318–1.022
Immunotherapy	0.107	0.272	0.156	0.693	1.113	0.653–1.897

B, regression coefficient; SE, standard error; Wald, Wald value; HR, hazard ratio; CI, confidence interval.

superficial diffuse pathological type is the most common.<sup>9</sup> In our group, the most common location was the limbs, and the acral lentiginous pathological type was the most common.

Our study found that 60.2% of patients showed ulceration of their tumor at the time of initial diagnosis. Compared with other ethnic groups, the primary tumor of Asians is more likely to be ulcerated at initial diagnosis.<sup>10</sup> Ulceration has previously been shown in a multivariate analysis to be an independent prognostic indicator of disease-free survival in melanoma patients.<sup>11</sup> However, in a study by van Akkoi et al., it did not remain an independent prognostic factor for overall survival after multivariate analysis.<sup>12</sup> In a study of 309 melanoma patients, Roka et al.<sup>13</sup> reported that sentinel node status, Breslow's thickness and ulceration were all independent prognostic factors for disease-free survival, whereas Breslow's thickness proved to be the only significant factor with respect to overall survival upon multivariate analysis. In our study, the 5-year survival rate of patients with ulceration was significantly lower than that of patients without ulceration. To eliminate the impact on statistical analysis of mixed factors correlated with the results, Cox multivariate regression analysis was performed to determine the relevant independent factors, and the result showed that ulceration was an independent factor for poor prognosis.

Clinical stage has been repeatedly confirmed to be one of the most important prognostic indicators for MM.<sup>14-16</sup> However, most evidence presented in the literature originates in Western countries, and the most commonly diagnosed subtype of malignant melanoma is SSM. Because of the high prevalence of the disease in these countries, knowledge about diagnosis and screening is readily available and diagnoses are usually made at relatively earlier stages. Cascinelli reported that the 5-year survival

rates of patients was 80.8% among Caucasians in Western countries.<sup>17</sup> Our study found 39.8% of patients with stage I-II, and 60.2% of patients with stage III-IV disease. The 1-year, 3-year and 5-year survival rates of the 98 patients were 85.7%, 34.7% and 13.3%, respectively. The 5-year survival rate was significantly associated with clinical stage in both univariate and multivariate analyses. The lack of knowledge about the disease in Asian patients clearly hampers clinical understanding; thus, the development of proper treatment strategies for this particular group of patients is warranted, as well as further research into more effective diagnosis and treatment. We therefore consider our findings important, as the results confirmed the applicability of the updated AJCC staging system to Asian patients with different subtypes of MM.

Surgical excision is the standard treatment for localized MM. There is no standard therapy for advanced-stage melanoma. In China, the indications for treatment not only depend on "Chinese Guidelines for the diagnosis and treatment of melanoma"<sup>18</sup> but also on patients' willingness and economic status. In our study, 60.2% of patients with early and medium stage disease underwent surgery. The 5-year survival rate of patients undergoing surgery was significantly higher than that of patients without an operation. However, Cox multivariate analysis showed that this was not an independent prognostic factor.

The present study had several limitations. First, in China, the indications for treatment not only depend on doctors' preferences but also on patients' willingness and economic status. These factors may have influenced the relatively poor survival rate that was observed. Second, it has been reported that the thickness of the primary lesion, Clark grading and TNM stage are associated with prognosis. However, in our study, close to 60% of all patients had stage III or IV



disease, and Breslow thicknesses were recorded in less than 40% of patients with stage I and II disease; therefore TNM staging was not established in our database. Finally, this was a single-center retrospective study and the sample was relatively small. A multi-center study with a large series of cases is required to confirm the present findings.

In conclusion, some clinical characteristics of MM patients in China are significantly different from Western countries. Ulceration and clinical staging are independent risk factors for poor survival rate in Chinese MM patients.

### Declaration of conflicting interest

The authors declare that there are no conflicts of interest.

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