

Original Article

Multivariate analysis and prediction model construction for distant metastasis of Acral Melanoma

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Abstract: Objective: To analyze the pathological characteristics of Acral Melanoma (AM) patients and identify the factors influencing distant metastasis, while constructing a predictive model for distant metastasis-free survival (DMFS). Methods: Conducted on 229 AM patients admitted to the Third People's Hospital of Bengbu and The First Affiliated Hospital of Anhui Medical University from January 1, 2012, to December 31, 2024. Data collected included gender, age, lesion location, initial diagnosis stage, trauma history, ulcer presence, Breslow thickness, mitotic rate, lactate dehydrogenase (LDH), albumin (Alb), and adjuvant therapy. DMFS was assessed through follow-up, with a deadline of March 31, 2025. Statistical analysis was performed to evaluate significant factors influencing distant metastasis. Results: The incidence of AM showed an increasing trend from 2012 to 2024. Of the 229 patients, 78 (34.06%) developed distant metastasis. The median follow-up period was 37 months, and 1-year, 3-year, and 5-year survival rates without distant metastasis were 93.45%, 74.24%, and 66.81%, respectively. Statistically significant factors affecting DMFS included initial diagnosis stage, ulcer presence, Breslow thickness, mitotic rate, LDH, and Alb levels (all $P < 0.05$). Risk factors for distant metastasis included stage III at diagnosis, ulcer presence, lack of adjuvant therapy, elevated LDH, and low Alb levels. Conclusions: The study identified key pathological factors influencing distant metastasis in AM patients. The constructed nomogram model demonstrated good predictive accuracy, with AUC values of 0.895 and 0.879 in the training and validation sets, respectively. This model can aid in the clinical screening of AM patients at risk for distant metastasis.

Keywords: Acral Melanoma, pathological features, distant metastasis, nomogram

Introduction

Melanoma is a malignant tumor originating from melanocytes and is highly metastatic, often spreading to other sites even in the early stages of the disease [1, 2]. The global incidence of melanoma has risen significantly, from 230,000 cases in 2012 to 325,000 in 2020, marking an increase of over 40% [3]. If this trend continues, by 2040, the number of new melanoma cases and deaths worldwide could reach 510,000 and 96,000, respectively [3]. Melanomas are classified by their primary site, including cutaneous, acral, mucosal, and uveal types [4]. Acral Melanoma (AM) arises from hairless areas such as the soles, subungual regions, and palms [5]. The incidence of AM varies by ethnicity and geography. While AM

accounts for only 2%-3% of melanomas in Western populations, it is the most common subtype in Asian, Spanish, and African populations, making up about 50% of all melanomas in Asians [6, 7].

Early manifestations of AM include deep pigmentation, plaques or irregular stripes, often with symptoms like itching, pain, or bleeding [8]. As the disease progresses, AM cells rapidly proliferate, forming ulcers or nodules, which invade surrounding tissues. Due to the unique anatomy of acral skin, AM cells are more likely to spread via lymphatic and blood vessels, leading to distant metastasis [9, 10]. Distant metastasis, a key feature of AM, significantly impairs patients' quality of life and survival. Symptoms differ based on the affected organ: pulmonary

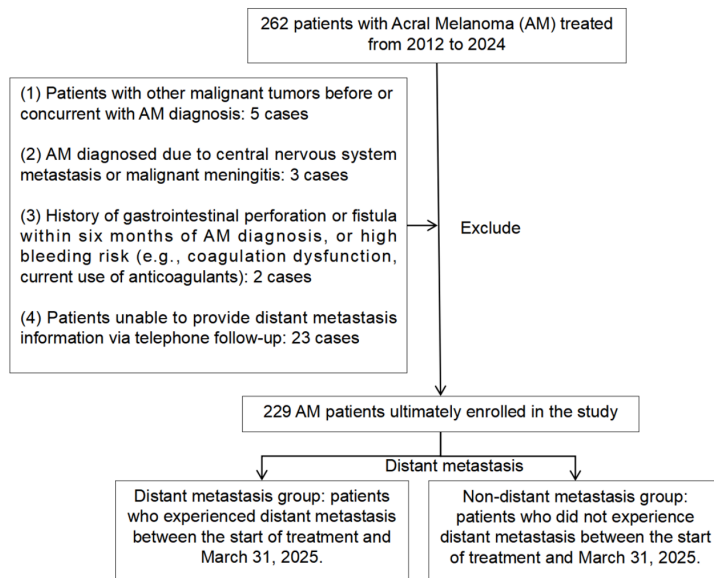


Figure 1. Process diagram for selecting research subjects.

metastasis can cause dyspnea, cough, and hemoptysis; liver metastasis may lead to abdominal pain, bloating, and jaundice; brain metastasis can result in headaches, seizures, and neurological dysfunction; and bone metastasis may cause severe pain and fractures [11-14]. These metastases cause substantial physical and emotional distress, often diminishing patients' ability to care for themselves, affecting daily life, and reducing survival [15]. Although there have been recent advances in clinical research on AM, understanding of its pathological characteristics and risk factors for distant metastasis remains inadequate, especially regarding the lack of models for predicting distant metastasis risk.

Currently, managing AM clinically depends largely on the initial diagnosis stage and pathological features, yet these factors are limited in predicting distant metastasis risk. Staging reveals tumor depth and extent but lacks comprehensive individualized risk assessment. Pathological features like ulceration, Breslow thickness, and mitotic rate correlate with distant metastasis but have limited predictive power individually [16]. Existing guidelines and treatment plans often inaccurately assess individual risk for AM patients due to limited data, potentially leading to under- or overestimation of distant metastasis risk, which affects treatment decisions and prognosis. Developing a

predictive model integrating multiple factors is essential for accurately assessing distant metastasis risk in AM patients. Such a model would provide clinicians with a comprehensive tool to develop more precise treatment plans and follow-up strategies, improving patient survival and quality of life. This study aims to construct a predictive model based on pathological characteristics to guide clinical practice in reducing metastasis risk.

Materials and methods

Patient selection

The data of 229 patients newly diagnosed with AM and admitted to the Third People's Hospital of Bengbu and The First Affiliated Hospital of Anhui Medical University between January 2012 and December 2024 were retrospectively collected.

Inclusion criteria: (1) Malignant melanoma confirmed by pathology; (2) Histological type of AM; (3) No distant metastasis at initial diagnosis; (4) Complete clinical and pathological data available.

Exclusion criteria: (1) Patients with other malignant tumors before or concurrent with AM diagnosis; (2) AM diagnosed due to central nervous system metastasis or malignant meningitis; (3) History of gastrointestinal perforation or fistula within six months of AM diagnosis, or high bleeding risk (e.g., coagulation dysfunction, current use of anticoagulants); (4) Patients unable to provide distant metastasis information via telephone follow-up. The study was approved by the Ethics Committee of The Third People's Hospital of Bengbu.

The research subjects were grouped according to the presence of distant metastasis. Among the 229 AM patients included, 78 patients with distant metastasis were categorized into the distant metastasis group, while 151 patients without distant metastasis were categorized into the non-distant metastasis group. The process and results of subject selection are shown in **Figure 1**.

Distant metastasis of AM

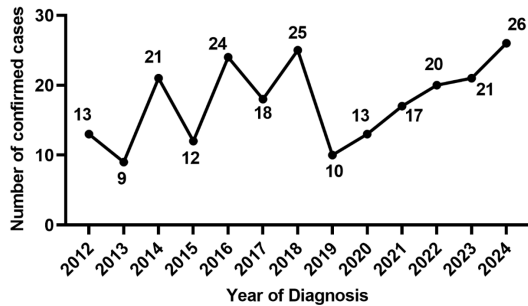


Figure 2. Changes in the incidence trend of AM, AM: Acral melanoma.

Data extraction

This was a retrospective analysis, with medical records of AM patients collected, including the first page of the medical records, admission records, first course, treatment records, examination reports, and pathological reports. The following factors were included: (1) Basic information: gender, age, primary tumor site, initial diagnosis stage [16], history of trauma or stimulation, distant metastasis, lactate dehydrogenase (LDH), and albumin (Alb) levels at initial treatment; (2) Pathological data: presence of ulcer, Breslow thickness, mitotic rate; (3) Treatment: whether postoperative adjuvant therapy was given. Patient survival information was obtained through telephone follow-up, with the follow-up deadline set for March 31, 2025. Distant metastasis-free survival (DMFS) was defined as the time from the start of treatment to distant metastasis or death [3].

Outcome measures

(1) Primary outcomes: Influencing factors of distant metastasis in AM patients and construction of the prediction model. Patients were divided into distant metastasis and non-distant metastasis groups based on the presence or absence of metastasis [1], and clinical data were compared. The 229 patients were split into a training set (160 cases) and a validation set (69 cases) in a 7:3 ratio using R software. In the training set, univariate and multivariate logistic regression were used to analyze factors affecting distant metastasis in AM patients. The specific influence of each factor was assessed by odds ratio (OR), and a nomogram model was created. (2) Secondary outcomes: Model validation. The receiver operating char-

acteristic (ROC) curve, calibration curve, and decision curve were used to evaluate the model's prediction efficiency.

Statistical analysis

SPSS 26.0 and R 4.2.2 software were used for statistical analysis. Quantitative data with a normal distribution were expressed as mean $\pm$ SD, while non-normally distributed data were expressed as median (P25, P75). For normally distributed measurement data, an independent sample t-test was used, and for non-normally distributed data, a rank-sum test was performed. Qualitative data were expressed as frequency (percentage) and analyzed using the chi-square test. Survival analysis was performed using the Kaplan-Meier method, and the Log-rank test was used to compare survival rates between different groups. A *P* value of less than 0.05 was considered statistically significant.

Results

Trends in the incidence of AM

As illustrated in **Figure 2**, a total of 229 AM patients admitted to the hospital from 2012 to 2024 were included. The number of confirmed cases showed an alternating upward trend from 2012 to 2018, followed by a steady increase from 2019 to 2024, peaking in 2024.

Clinical data and pathological characteristics of AM patients

The clinical data and pathological characteristics of the 229 AM patients are summarized in **Table 1**. Of these, 136 were male (59.39%) and 93 were female (40.61%). The average age was 62.88 ± 12.97 years. Among them, 185 patients (80.79%) had primary lesions on the foot; 56 patients (24.45%) were diagnosed with stage III at initial diagnosis; 141 patients (61.57%) had ulcers; 92 patients (40.17%) had Breslow thickness >4 mm; and 83 patients (36.24%) had a mitotic rate $>5/\text{mm}^2$.

Distant metastasis of AM patients

Of the 229 AM patients, 78 (34.06%) developed distant metastasis. A comparison of clinical data between the distant metastasis group and the non-distant metastasis group revealed

Table 1. Clinical data and pathological features of AM patients

Variable	n (%) / Mean $\pm$ SD	Variable	n (%) / Mean $\pm$ SD
Gender		No	208 (90.83)
Male	136 (59.39)	Alb (g/L)	39.86 $\pm$ 5.46
Female	93 (40.61)	Ulcer	
Age (years)	62.88 $\pm$ 12.97	Yes	141 (61.57)
Location of primary tumor		No	88 (38.43)
The-foot	185 (80.79)	Breslow thickness	
Non-foot	44 (19.21)	>4 mm	92 (40.17)
Staging at initial diagnosis		1-4 mm	126 (55.02)
Phase III	56 (24.45)	<1 mm	11 (4.80)
Phase II	114 (49.78)	Mitotic rate	
Phase I	59 (25.76)	>5/mm ²	83 (36.24)
History of traumatic irritation		1-5/mm ²	130 (56.77)
Yes	53 (23.14)	<1/mm ²	16 (6.99)
No	176 (76.86)	Adjuvant Therapy	
Elevated LDH		Yes	170 (74.24)
Yes	21 (9.17)	No	59 (5.76)

Note: LDH: lactate dehydrogenase; Alb: albumin.

significant differences in the initial diagnosis stage, LDH elevation, Alb levels, ulcer presence, Breslow thickness, mitotic rate, and adjuvant therapy (all $P < 0.05$). Detailed data are presented in **Table 2**.

DMFS in patients with different pathological characteristics

As of the follow-up deadline on March 31, 2025, all 229 patients were successfully followed up for survival. The overall survival analysis showed a median follow-up time of 37 months (range: 3-157 months). The DMFS rates at 1, 3, and 5 years were 93.45%, 74.24%, and 66.81%, respectively. The median DMFS was not reached (**Figure 3A**). Analysis of DMFS for patients with and without ulcers revealed that the median DMFS for patients without ulcers was not reached, while the median DMFS for patients with ulcers was 48 months, significantly lower than that of patients without ulcers (Log-Rank $\chi^2 = 15.790$, $P < 0.05$) (**Figure 3B**). For patients with Breslow thickness < 1 mm and 1-4 mm, the median DMFS was not reached, while the median DMFS for patients with Breslow thickness > 4 mm was 46 months (Log-Rank $\chi^2 = 16.055$, $P < 0.05$) (**Figure 3C**). For patients with a mitotic rate $< 1/\text{mm}^2$ and 1-5/ mm^2 , the median DMFS was not reached, while the median DMFS for patients with a mitotic

rate $> 5/\text{mm}^2$ was 45 months (Log-Rank $\chi^2 = 14.348$, $P < 0.05$) (**Figure 3D**).

Comparison of patients' data between the two datasets

As shown in **Table 3**, the clinical and pathological characteristics of patients in two sets were similar ($P > 0.05$), indicating that the two datasets are comparable.

Univariate analysis of factors affecting distant metastasis in AM patients

Logistic regression analyses were performed in the training set, with the assignment of each variable shown in **Table 4**. Both univariate and multivariate analyses identified the following factors as influencing distant metastasis in AM patients: initial diagnosis stage, ulcer, adjuvant therapy, LDH, and Alb levels (OR = 2.644, 5.658, 0.028, 10.792, and 0.771, respectively). Among these, stage III at initial diagnosis, ulcer presence, no adjuvant therapy, elevated LDH, and low Alb levels were found to be risk factors for distant metastasis in AM patients (**Table 5**).

Construction of nomogram model

The results of the multivariate logistic regression analysis were visualized to construct the

Distant metastasis of AM

Table 2. Comparison of data of patients with different metastatic conditions

Variable	Distant metastasis group (n = 78)	Non-distant metastasis group (n = 151)	χ^2/t	P
Gender			0.002	0.969
Male	45 (34.56)	89 (65.44)		
Female	31 (33.33)	62 (66.67)		
Age (years)	63.33±12.52	62.64±13.23	0.381	0.227
Location of primary tumor				
The-foot	61 (32.97)	124 (67.03)		
Non-foot	17 (38.64)	27 (61.36)		
Staging at initial diagnosis			11.946	0.001
Phase III	29 (51.79)	27 (48.21)		
Phase II	36 (31.58)	78 (68.42)		
Phase I	13 (22.03)	46 (77.97)		
History of traumatic irritation			1.703	0.192
Yes	22 (41.51)	31 (58.49)		
No	56 (31.82)	120 (68.18)		
Elevated LDH			14.374	<0.001
Yes	15 (71.43)	6 (28.57)		
No	63 (30.29)	145 (69.71)		
Alb (g/L)	35.98±4.00	41.86±5.02	8.989	<0.001
Ulcer			11.781	0.001
Yes	60 (42.55)	81 (57.45)		
No	18 (20.45)	70 (79.55)		
Breslow thickness			10.723	0.001
>4 mm	43 (46.74)	49 (53.26)		
1-4 mm	33 (26.19)	93 (73.81)		
<1 mm	2 (18.18)	9 (81.82)		
Mitotic rate			6.978	0.008
>5/mm ²	39 (46.99)	44 (53.01)		
1-5/mm ²	34 (26.15)	96 (73.85)		
<1/mm ²	5 (31.25)	11 (68.75)		
Adjuvant Therapy			6.351	0.012
Yes	50 (29.41)	120 (70.59)		
No	28 (47.46)	31 (52.54)		

Note: LDH: lactate dehydrogenase; Alb: albumin.

nomogram model, as shown in **Figure 4**. The nomogram includes each influencing factor and its corresponding line segment of a specific length. Researchers can determine the score for each factor based on the subject's specific conditions, and the total score is obtained by summing the scores of all factors. A vertical line drawn downward on the total score axis provides the predicted risk of distant metastasis for that AM patient.

Validation of the nomogram model

The ROC curve was used to assess the model's discrimination in both the training and valida-

tion sets. As shown in **Figure 5A** and **5B**, the AUC of the model in the training set was 0.895 (95% CI: 0.846-0.944), and in the validation set, it was 0.879 (95% CI: 0.794-0.964), both values exceeding 0.7. The calibration curves (**Figure 6A** and **6B**) demonstrated that the model's prediction accuracy in both sets aligned well with the corrected prediction accuracy. According to the decision curve analysis shown in **Figure 7A** and **7B**, with a distant metastasis incidence of 34.06%, the benefit rate of the model was higher than the "all" and "none" curves within the threshold probability range of 6%-88% in

Distant metastasis of AM

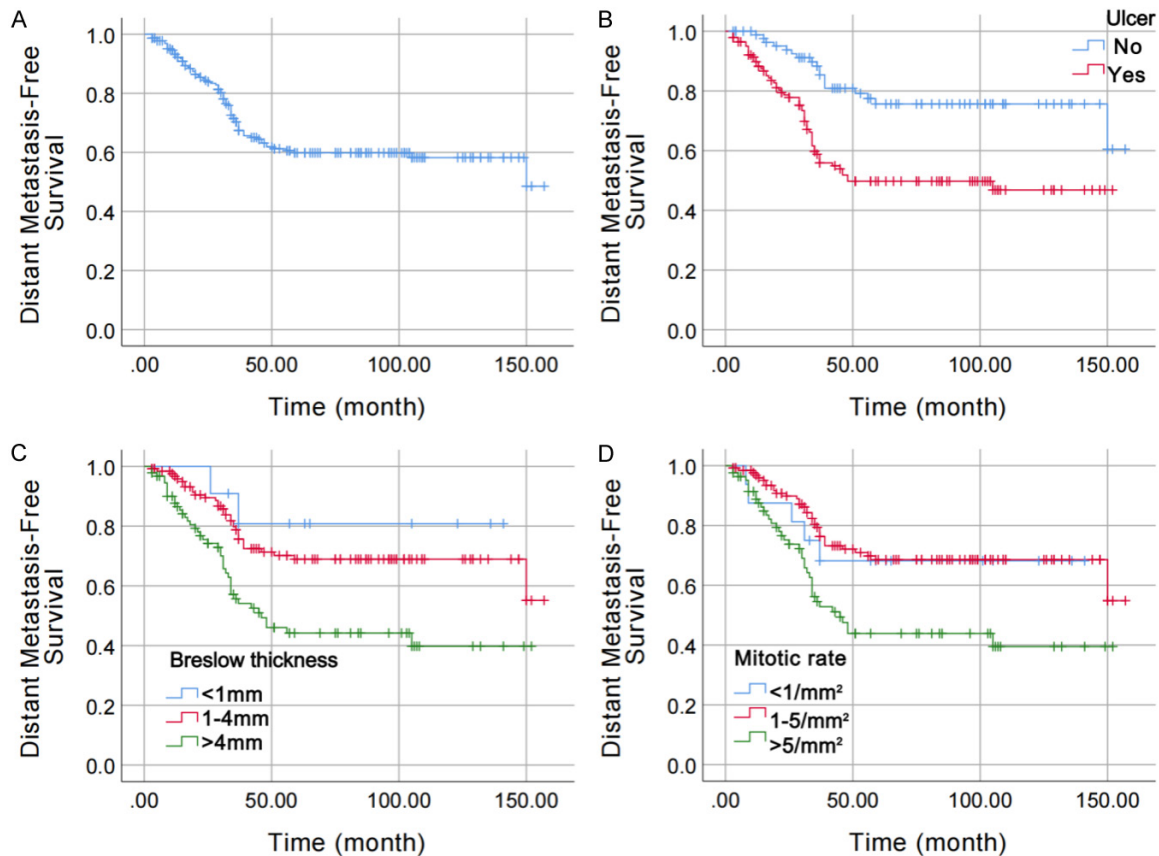


Figure 3. Distant metastasis-free survival in patients with AM, (A) All patients, (B) Ulceration, (C) Breslow thickness, and (D) mitosis rate.

the training set, and 6%-100% in the validation set.

Nomogram model and ROC comparison of various factors

The DeLong test results indicated that the ROC of the nomogram model was significantly higher than that for the initial diagnosis stage, ulcer, adjuvant therapy, LDH, and Alb levels ($z = 6.224, 7.388, 7.501, 11.197, 2.791$, all $P < 0.05$). Detailed results are presented in **Figure 8** and **Table 6**.

Discussion

This study analyzed the incidence trend of 229 AM patients admitted from January 2012 to December 2024 and observed changes in the incidence of AM during this period. From 2012 to 2018, the number of confirmed AM cases showed an alternating upward trend, which may be linked to both the natural growth trend

of melanoma and advancements in medical diagnostic techniques. With increased awareness of melanoma and continuous improvements in dermopathological diagnostic methods, more potential AM cases have been identified. The incidence of diagnosed AM increased from 2022 to 2024, a trend seen in many regions [17-20]. This rise is likely due to factors such as population aging, improved diagnostic technology, heightened public health awareness, and environmental changes [21-28]. Future studies should investigate the mechanisms behind these changes in AM incidence trends to inform public health policy and clinical interventions.

AM exhibits distinct biological behaviors, including a high incidence of distant metastasis and poor prognosis, which are closely related to the primary site, pathological features, and tumor microenvironment [29, 30]. In this study, we analyzed the clinical and pathological characteristics of 229 AM patients to

Distant metastasis of AM

Table 3. Comparison of patients' data between the two datasets

Variable	Training set (n = 160)	Validation set (n = 69)	χ^2/t	P
Distant metastasis			0.208	0.648
Yes	56 (71.79)	22 (28.21)		
No	104 (68.87)	47 (31.13)		
Gender			0.785	0.376
Male	92 (67.65)	44 (32.35)		
Female	68 (73.12)	25 (26.88)		
Age (years)	63.48±13.09	61.49±12.68	1.062	0.290
Location of primary tumor			0.009	0.925
The-foot	129 (69.73)	56 (30.27)		
Non-foot	31 (70.45)	13 (29.55)		
Staging at initial diagnosis			0.690	0.406
Phase III	40 (71.43)	16 (28.57)		
Phase II	82 (71.93)	32 (28.07)		
Phase I	38 (64.41)	21 (35.59)		
History of traumatic irritation			1.028	0.311
Yes	40 (75.47)	13 (24.53)		
No	120 (68.18)	56 (26.92)		
Elevated LDH			0.697	0.404
Yes	13 (61.90)	8 (38.10)		
No	147 (70.67)	61 (29.33)		
Alb (g/L)	39.78±5.69	40.03±4.92	0.319	0.750
Ulcer			1.065	0.302
Yes	102 (72.34)	39 (27.66)		
No	58 (65.91)	30 (34.09)		
Breslow thickness			0.738	0.390
>4 mm	70 (76.09)	22 (23.91)		
1-4 mm	80 (63.49)	46 (36.51)		
<1 mm	10 (90.91)	1 (9.09)		
Mitotic rate			0.084	0.772
>5/mm ²	62 (74.70)	21 (25.30)		
1-5/mm ²	84 (64.62)	46 (35.38)		
<1/mm ²	14 (87.50)	2 (12.50)		
Adjuvant Therapy			0.066	0.798
Yes	118 (69.41)	52 (30.59)		
No	42 (71.19)	17 (28.81)		

Note: LDH: lactate dehydrogenase; Alb: albumin.

explore the relationship between distant metastasis and pathological features. AM typically occurs in hairless areas such as the soles, palms, and subungual regions, where the skin structure is distinct and lymphatic and blood vessels are abundant. This increases the likelihood of tumor cells spreading to distant organs via these pathways [31, 32]. Previous studies [33, 34] have indicated a high rate of distant metastasis in AM, with

common metastatic sites including the lungs, liver, brain, and bones, which significantly affect patients' quality of life and prognosis. In our study, 34.06% of AM patients developed distant metastasis, which is slightly lower than the rates reported in previous studies [33, 34]. This discrepancy may be due to differences in the study populations but still underscores the high metastatic potential of AM.

Distant metastasis of AM

Table 4. Variable assignment

Variables	Assignment
Dependent variable	
Distant metastasis	0 = No, 1 = Yes
Independent variable	
Staging at initial diagnosis	0 = "Phase I", 1 = "Phase II", 1 = "Phase III"
Ulcer	0 = "No", 1 = "Yes"
Breslow thickness	0 = "<1 mm", 1 = "1-4 mm", 2 = ">4 mm"
Mitotic rate	0 = "<1/mm ² ", 1 = "1-5/mm ² ", 2 = ">5/mm ² "
Adjuvant Therapy	0 = "No", 1 = "Yes"
LDH	0 = "Normal or reduced", 1 = "Elevated"
Alb	Enter actual values

Note: LDH: lactate dehydrogenase; Alb: albumin.

Table 5. Univariate and multivariate analysis

Variables	Univariate analysis			Multivariate analysis		
	β	P	OR (95% CI)	β	P	OR (95% CI)
Staging	0.684	0.001	1.981 (1.318-2.978)	0.972	0.009	2.644 (1.272-5.495)
Ulcer	1.058	0.001	2.881 (1.555-5.335)	1.733	0.006	5.658 (1.631-19.623)
Breslowthickness	0.844	0.001	2.325 (1.394-3.879)	0.818	0.233	2.266 (0.590-8.702)
Mitotic rate	0.650	0.009	1.915 (1.177-3.114)	-0.164	0.735	0.849 (0.329-2.190)
Adjuvant Therapy	-0.744	0.013	0.461 (0.251-0.848)	-3.562	<0.001	0.028 (0.007-0.118)
Elevated LDH	1.750	0.001	5.754 (2.134-15.514)	2.379	0.002	10.792 (2.361-49.325)
Alb	-0.270	<0.001	0.764 (0.706-0.826)	-0.260	<0.001	0.771 (0.705-0.844)
Constant	-	-	-	8.671	-	-

Note: LDH: lactate dehydrogenase; Alb: albumin; OR: odds ratio.

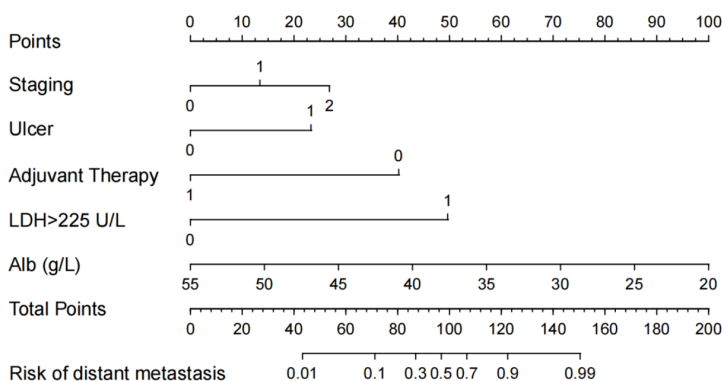


Figure 4. Nomogram prediction model for distant metastasis in AM patients, LDH: lactate dehydrogenase; Alb: albumin.

Regarding pathological features, the core characteristics of AM include ulcer formation, Breslow thickness, and mitotic rate. These features not only reflect tumor biology but are also closely related to distant metastasis. Our study found significant differences in DMFS among

AM patients with or without ulcers, varying Breslow thickness, and different mitotic rates. Ulceration suggests more aggressive tumor cells that can break through the skin barrier and spread to distant organs via lymphatic and blood vessels [35-37]. Breslow thickness, a critical measure of tumor invasion depth, shows that patients with a Breslow thickness greater than 4 mm have a significantly higher risk of distant metastasis and a much lower median distant metastasis-free survival compared to those with

thinner tumors. Greater Breslow thickness indicates deeper tumor cell penetration through the basement membrane, bringing the tumor closer to lymphatic and blood vessels and increasing the risk of distant metastasis [38, 39]. Mitotic rate is another key pathological

Distant metastasis of AM

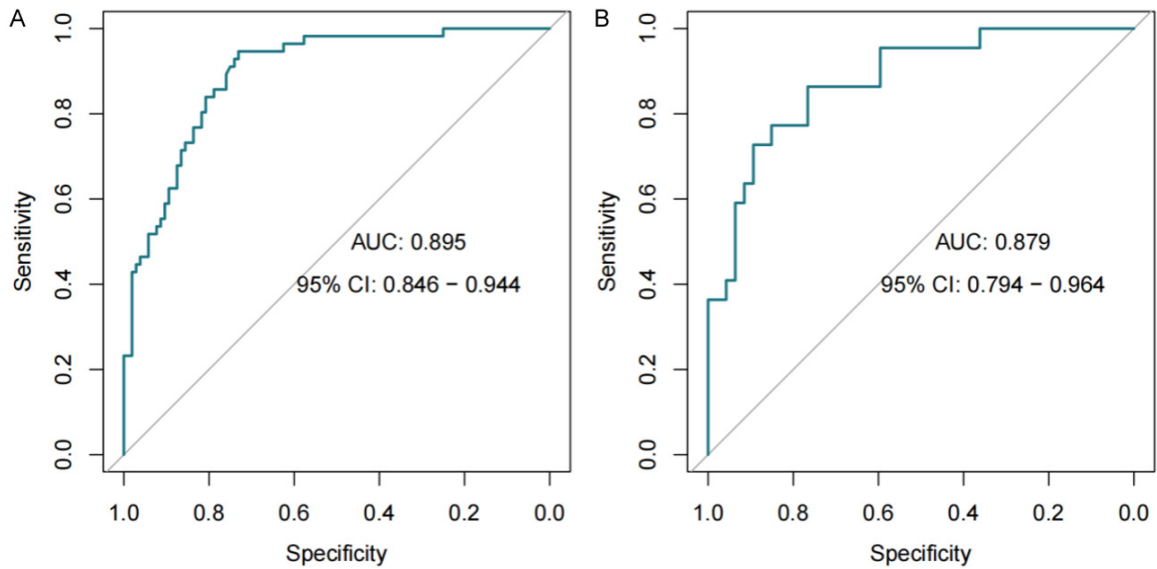


Figure 5. ROC curve, (A) training set, (B) validation set, AUC: Area under the curve.

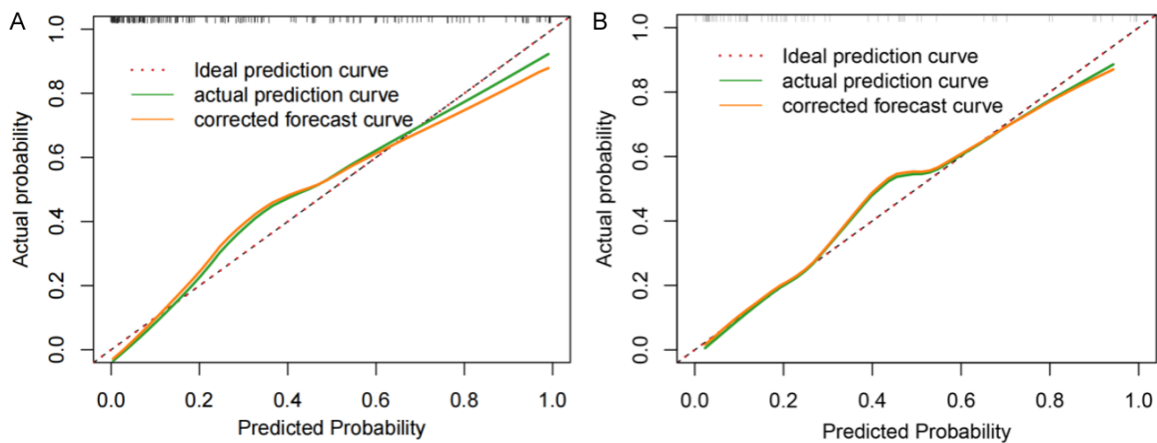


Figure 6. Calibration curve, (A) training set, (B) validation set.

feature influencing distant metastasis. In this study, patients with a mitotic rate greater than 5 per square millimeter had a significantly higher risk of distant metastasis than those with lower rates. A high mitotic rate means a higher proliferation rate of tumor cells, allowing tumors to grow faster, break through local tissue barriers, and facilitate distant metastasis [40, 41].

The results of Multivariate analyses showed that the initial diagnosis stage, ulcer presence, adjuvant therapy, LDH levels, and Alb levels were important factors influencing distant metastasis in AM. In this study, patients with stage III at initial diagnosis had a significantly higher risk of distant metastasis than those

with stage I and II. This is closely linked to the biological behavior of melanoma: as the tumor stage increases, so does the tumor's invasive and metastatic potential [42, 43]. Stage III patients often already have regional lymph node metastasis, and tumor cells are more likely to enter the bloodstream via the lymphatic system, thereby leading to distant metastasis [44, 45]. Therefore, stage III at initial diagnosis is an independent risk factor for distant metastasis in AM.

In our study, patients with ulcers had a significantly higher risk of distant metastasis than those without ulcers. Ulcers typically indicate that tumor cells have penetrated the skin's

Distant metastasis of AM

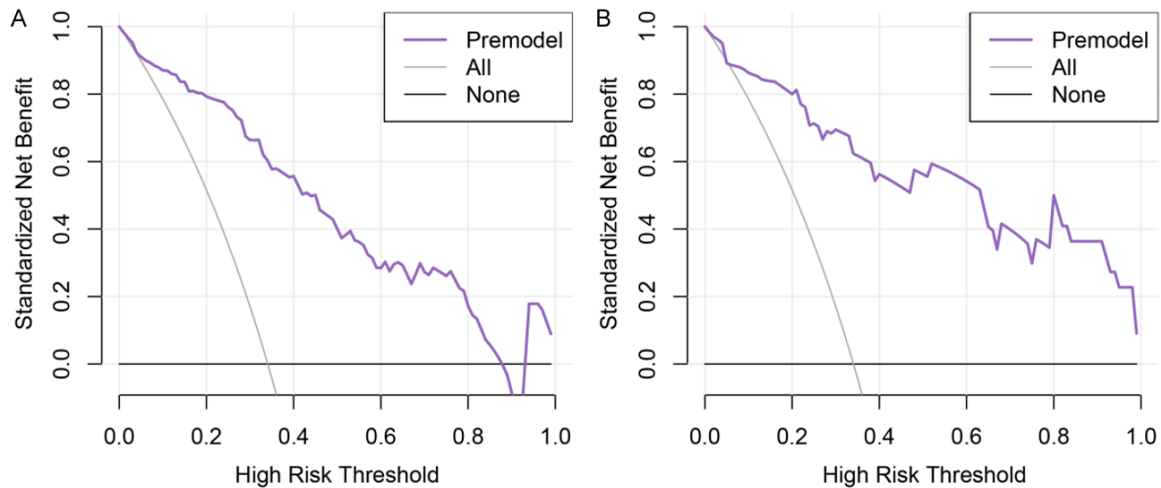


Figure 7. Decision curve, (A) training set, (B) validation set.

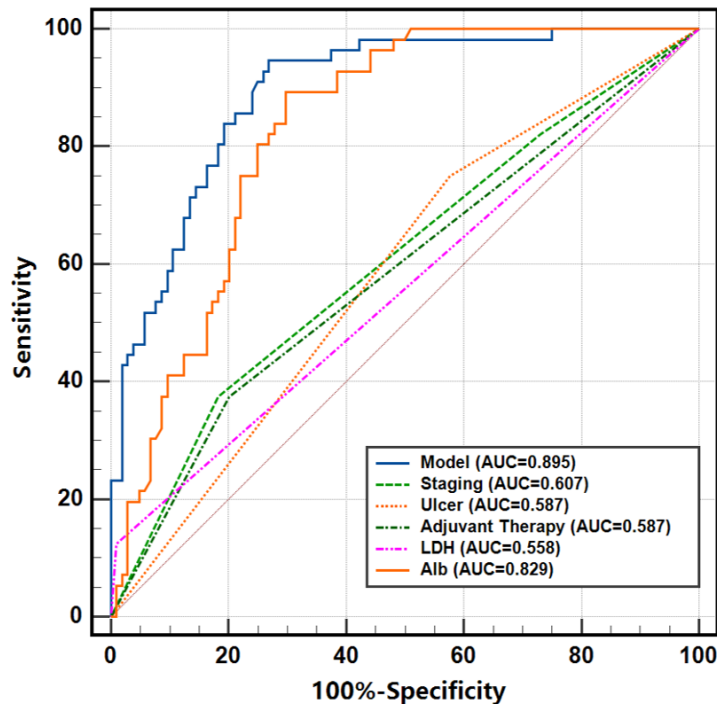


Figure 8. Nomogram model and ROC comparison of various factors, LDH: lactate dehydrogenase; Alb: albumin; AUC: Area under the curve.

basement membrane, invaded surrounding tissues, and caused local destruction and inflammation [46]. This local aggressiveness makes it more likely for tumor cells to enter lymphatic and blood vessels, promoting distant metastasis [47]. Ulcers may also correlate with tumor behaviors such as proliferation, invasiveness, and immune evasion [48, 49]. LDH is a marker

of inflammation and tissue damage, and higher levels may indicate tumor cells' strong ability to invade and destroy tissue [50-52]. Elevated LDH levels may also reflect inflammatory responses in the tumor microenvironment, which can further facilitate tumor metastasis [53, 54]. This study's results suggest that increased LDH levels are closely linked to melanoma's aggressiveness, metastatic potential, and poor prognosis.

Treatments like immunotherapy, targeted therapy, and chemotherapy can remove potential micro-metastases after surgery and reduce recurrence and distant metastasis risks [55-57]. Advances in immunotherapy, especially immune checkpoint inhibitors such as PD-1 and CTLA-4 inhibitors, have improved DMFS and overall survival in melanoma patients [58]. In this study, lower Alb levels

were identified as a risk factor for distant metastasis in AM. Alb is a key protein for nutrition and immune modulation, and its reduction may indicate poor nutritional status and weakened immune function, which can lower the body's ability to control tumor cells and increase distant metastasis risk [59, 60]. Reduced Alb levels may also be related to the tumor's

Table 6. Nomogram model and ROC comparison of various factors

Indicators	AUC	Cut-off values	SE	95% CI	Z	P
Model	0.895	≥0.249	0.025	0.836-0.938	-	-
Staging	0.607	≥1	0.044	0.527-0.683	6.224	<0.001
Ulcer	0.587	≥1	0.038	0.506-0.664	7.388	<0.001
Adjuvant Therapy	0.587	≥1	0.038	0.506-0.664	7.501	<0.001
LDH	0.558	≥1	0.023	0.477-0.636	11.197	<0.001
Alb	0.829	≥39.23 (g/L)	0.031	0.762-0.884	2.791	0.005

consumptive metabolism, affecting patient prognosis [61-63].

The performance of the nomogram model was satisfactory in both the training and validation sets, demonstrating high discrimination and calibration abilities. This model can assist clinicians in identifying high-risk AM patients at an early stage, enabling timely targeted interventions such as enhanced follow-up and early adjuvant treatment, ultimately reducing the incidence of distant metastasis and improving patient prognosis. Compared to previous studies, this study benefits from a longer follow-up period and provides representative data. We identified that the initial diagnosis stage, ulcer presence, adjuvant therapy, LDH levels, and Alb levels are independent factors influencing distant metastasis, potentially through their effects on tumor invasiveness and immune function. While some results align with previous research, there are differences. For example, the incidence of distant metastasis in this study was 34.06%, slightly lower than in some previous studies [33, 34], which may be related to differences in the populations included. Additionally, this study provides a more comprehensive evaluation of the interaction effects of multiple factors, offering a more accurate risk assessment tool for clinical practice. However, there are limitations in the study design. As a retrospective study, it has limitations in the data that can be collected. There may be additional risk factors for distant metastasis in AM patients, particularly gene-related factors, that were not included. Furthermore, due to the broad time range (2012-2024), collecting data for external validation would have required an extended period, so we did not perform external validation of the model. Future prospective studies should incorporate more factors and conduct external validation to explore the mechanisms of distant metastasis in AM, thereby providing a more comprehensive

theoretical basis for precise treatment and personalized management.

In conclusion, this study analyzed the clinical data and pathological characteristics of 229 AM patients to elucidate the relationship between pathological features and long-term metastasis and survival. It identified key factors influencing distant metastasis in AM, including initial diagnosis stage, ulcer presence, adjuvant therapy, LDH levels, and Alb levels. Based on these factors, a nomogram prediction model for distant metastasis was constructed. The model's performance was satisfactory in both the training and validation sets, with ROC values of 0.895 and 0.879, significantly higher than those predicted by each factor alone.

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Disclosure of conflict of interest

None.

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