Identifying High-Risk Features and Improving Follow-Up Strategies in Thin Melanoma: A Retrospective Cohort Study

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Objective

Importance: Understanding prognostic factors associated with thin cutaneous melanoma (TM) is crucial as it enables the identification of patients at a higher risk of recurrence.
Aim: This study aims to address the existing knowledge gap in prognostic factors in TM by examining demographic and prognostic aspects of patients with and without recurrence (NR and R, respectively). Current staging systems often fail to consider the possibility of tailored patient management in cases of specific high-risk subtypes among thin melanomas. Our study comes into play precisely in this scenario, where conventional methods might not provide comprehensive discrimination, aiming to shed light on prognostic determinants, their impact on prognosis, and their implications for patient care.
Design: A retrospective cohort study examined TM cases from 1998 to 2017 in two medical institutions.
Setting: Data were from the Veneto Oncology Institute and the University Hospital of Padua.
Participants: A cohort of 308 patients was divided into R (n = 53) and NR (n = 255) subgroups.
Intervention: The study focuses on the analysis of prognostic factors related to recurrence, without introducing new interventions.
Main results and measures: Items such as histologic subtype, Breslow thickness, ulceration, mitotic rate, lympho-vascular invasion, and treatments were evaluated in relation to recurrence. Survival rates and patterns of recurrence were also analyzed.

Materials and Methods

A retrospective cohort study was designed with the aim of investigating the association between prognostic factors and recurrence of thin cutaneous melanoma. Medical records of patients diagnosed and treated between 1998 and 2017 at the Veneto Oncological Institute (IOV) and at the Padua University Hospital (AOUP) were retrospectively analysed. Tumor stage was defined according to the eighth version of the American Joint Committee on Cancer (AJCC) staging system.
The study included all patients aged ≥18 years who received a diagnosis and/or treatment for thin cutaneous melanoma during the specified period. A dedicated local database was used to extract relevant data. Patients diagnosed with invasive cutaneous melanoma and Breslow thickness between 0.1 and 1 mm (thin melanoma) were included in the study. Data were collected on demographic characteristics, including age at diagnosis and sex. Tumor-related information such as Breslow thickness, TNM stage, site of presentation, mitotic count per mm2, Clark level, lympho-vascular invasion, and lymphocytic infiltrate (TIL) were also recorded. In addition, treatment details including wide excision, sentinel lymph node biopsy, complete lymph node dissection, and nonsurgical therapy were documented.
Patient follow-up data were extracted from electronic medical records. The standard follow-up protocol included visits every 6 months for the first 5 years and annual dermatologic checks thereafter. Overall survival was calculated from the date of diagnosis to the last visit or date of death. Melanoma specific survival usually begins at the time of diagnosis and ends at the time of death. Patients who died from causes other than melanoma are not counted in this measurement. Recurrences were classified as local, regional lymph node metastasis, in-transit or regional skin metastasis, or distant metastasis.

Key Points

Research Question: This study delves into the prognostic factors of thin cutaneous melanoma (TM) to facilitate enhanced management strategies.
Findings: Conducted as a retrospective cohort study involving 308 patients, the analysis revealed key determinants of TM prognosis. Ulceration, mitotic rate, and tumor thickness emerged as significant predictors of recurrence. Patients with nodular histology, higher mitotic count, and ulceration faced an elevated risk of recurrence. Conversely, an ultra-thin melanoma (Breslow ≤ 0.5 mm) proved protective against recurrence. The thickness of the tumor, especially beyond 0.5 mm, played a critical role in recurrence risk. Survival rates were notably lower in the recurrence group, underscoring the need for individualized follow-up strategies.

Results

Significant predictors of recurrence included ulceration, thickness and tumor mitotic rate. Nodular histology, the presence of ulceration and a high mitotic rate were correlated with an increased risk of recurrence. In contrast, ultrathin melanoma (Breslow ≤ 0.5 mm) was found to be a protective factor against recurrence. In contrast, tumors thicker than 0.5 mm were associated with an increased likelihood of recurrence. In addition, survival rates were significantly lower in the R group, highlighting the need for individualized follow-up strategies.

Variable		Recurrence		p-value
		No (N = 255)	Yes (N = 53)	
Sex	Female	130 (50.98%)	30 (56.60%)	0.552
	Male	125 (49.02%)	23 (43.40%)	
Histology subtype	Acral Lentiginous	5 (1.96%)	0 (0%)	0.016
	Lentigo Maligna	6 (2.35%)	1 (1.89%)	
	Nevoid	1 (0.39%)	1 (1.89%)	
	Nodular	8 (3.14%)	7 (13.21%)	
	Spitzoid	1 (0.39%)	1 (1.89%)	
	Superficial Spreading	234 (91.76%)	43 (81.13%)	
Breslow thickness (mm)	Min / Max	0.1 / 1.0	0.2 / 1.0	<0.001
	Med [IQR]	0.4 [0.3;0.6]	0.8 [0.6;0.9]	
	Mean (std)	0.5 (0.2)	0.8 (0.2)	
Ultra Thin Melanoma (Breslow ≤ 0.5 mm)	No	100 (39.22%)	48 (90.57%)	<0.001
	Yes	155 (60.78%)	5 (9.43%)	
Breslow ≤ 0.75 mm	No	31 (12.16%)	31 (58.49%)	<0.001
	Yes	224 (87.84%)	22 (41.51%)	
Breslow ≤ 0.80 mm	No	20 (7.84%)	28 (52.83%)	<0.001
	Yes	235 (92.16%)	25 (47.17%)	
T Stage	T1a	223 (87.45%)	21 (39.62%)	<0.001
	T1b	33 (12. 55%)	32 (60.38%)	
Ulceration	Absent	244 (95.69%)	44 (83.02%)	<0.001
	Present	7 (2.75%)	9 (16.98%)	
	Unknown	4 (1.57%)	0 (0%)	
Mitoses per mm²	Min / Max	0 / 5.0	0 / 9.0	<0.001
	Med [IQR]	0 [0;1.0]	2.0 [1.0;2.0]	
	Mean (std)	0.6 (0.9)	2.1 (2.0)	
Lymphovascular invasion	Absent	254 (99.61%)	49 (92.45%)	0.003
	Present	1 (0.39%)	2 (3.77%)	
	Unknown	0 (0%)	2 (3.77%)	

Table 1. Demographics clinicopathological and tumor characteristics differences in thin melanoma recurrence and non recurrence groups

Conclusion

The study highlights the necessity of adopting a patient-focused approach in managing TM. When interpreting Breslow values, it's crucial to account for additional prognostic factors like histotype, ulceration, and mitotic rate. The observed differences in survival rates between T1a and T1b melanomas underscore the importance of tailoring post-treatment surveillance and support to each patient's specific risk profile. In consideration of the worse prognosis for thin melanomas > 0.5 mm, it should be decided to perform the SLNB, to "intensify" follow up (in terms of duration, frequency and type of radiological investigations), for this last point it could be useful to describe when these recurrences occur: if they are "late" (more than 5 years) it is necessary to change the follow up duration currently recommended by the guidelines for thin melanomas (5 years) at the same time thin < 0.5 mm melanomas could do less intensive follow up.

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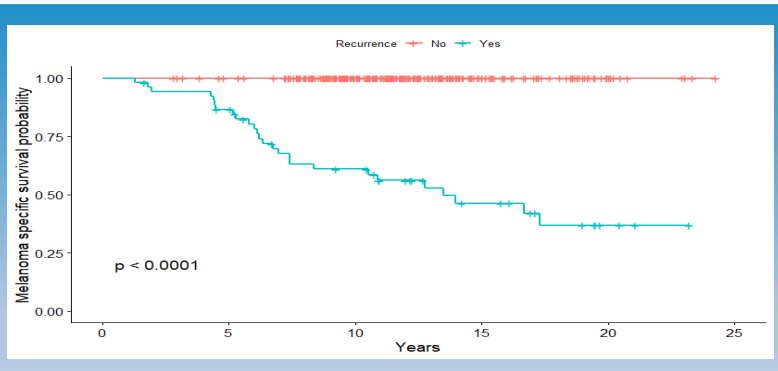

Figure 2. Melanoma specific survival probability for all thin melanomas with recurrence and without recurrence.