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Unraveling the Obesity Paradox: Exploring the Impact of Body Weight on Cutaneous Melanoma Prognosis in Asian Population

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Background: Obesity has been identified as a significant risk factor for various diseases, including certain cancers; however, its association with melanoma remains a subject of debate. Despite the increasing incidence of cutaneous melanoma in Taiwan, there has been limited research on its correlation with obesity. This study aims to investigate the relationship between obesity and the prognosis of cutaneous melanoma in Taiwan.

Methods: Between January 1, 2000, and December 31, 2022, 201 patients were diagnosed with cutaneous melanoma at our hospital, with 61.69% of them diagnosed with acral melanoma. Data on body weight, height, tumor stages and prognosis were collected and analyzed.

Results: The result revealed that older age (≥ 65 years old), male, advanced Breslow thickness stage (T3 and T4) and tumor ulceration were identified as risk factors for worse overall survival in both cutaneous melanoma and acral melanoma. In the adjusted multivariable analysis, being overweight was considered a protective factor in both cutaneous and acral melanoma.

Conclusion: Contrary to expectations, it was observed that melanoma patients with obesity exhibited better survival rates compared to those with normal or underweight status. Additionally, no significant differences were found between acral melanoma and non-acral melanoma subtypes regarding the impact of body weight on overall survival.

Keywords: melanoma, neoplasms, obesity, obesity paradox, survival analysis

Introduction

Melanoma, malignantly transformed from the pigment-producing melanocyte, occurs most commonly in the cutaneous.[1,2] Melanoma primarily causes by genetic mutations and environmental factors like UV radiation. Four main histological subtypes of cutaneous melanoma (CM) are categorized: lentigo maligna(LM) melanoma, superficial spreading melanoma (SSM), acral lentiginous melanoma (ALM) or acral melanoma (AM), and nodular melanoma. Other locations such as the eyes, ears, gastrointestinal tract, genitalia, urinary system, and meninges can also be seen. Although CM is most seen in Caucasian population, a rising incidence of AM in Asians are noticed recently.[3] AM is the most predominant subtype of melanoma in Asians. According to the statistics of WHO in 2020, Taiwan ranks 2nd upon the incident rate of cutaneous melanoma in East Asia, at about 0.71 per 100,000 people.[4] There are more than 200 newly diagnosed cases annually in Taiwan.[5]

AM is a subtype which occurs over palms, soles, digits and nails. It accounts for 60% of cutaneous melanoma in Asia.[6] Unlike other forms of melanoma, AM is not strongly associated with UV exposure. The relationship between

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trauma, mechanical stress and AM has been a topic of interest, though the connection is not fully understood.[7–10] In molecular biology, common gene mutations including KIT, BRAF, NRAS, and NF1 were found in melanoma.[11] AM holds lower mutational burdens compared to non-acral melanomas. It is also more aggressive and has a poorer prognosis with the five- and ten-year melanoma-specific survival rates 80.3% and 67.5%, respectively, which were significantly lower than the overall rates for all cutaneous malignant melanoma, which were 91.3% and 87.5% ($p<0.001$).[12] Among acral melanoma cases, the highest five- and ten-year melanoma-specific survival rates were observed in Caucasian persons (82.6% and 69.4%), followed by Black persons (77.2% and 71.5%), while the lowest rates were found in Asian persons (70.2% and 54.1%).[13]

Obesity results from excessive accumulation of fat which is a common major risk factor for most cardiovascular disease, diabetes and musculoskeletal disorders.[14] Based on the statistics from the WHO, obese population has grown 3 times since 1975 in worldwide. In 2019, 39% and 13% of adults were overweight and obese, respectively, around the world. Obesity has also been the 5th leading risk factor got death globally since 2019. In Taiwan, a rising increase of obesity or being overweight in the past 20 years has been recorded with average body mass index (BMI) currently 24.5 (±0.12) in men and 23.8(±0.13) in women.[15]

The association between obesity and malignancy has been investigated in numerous studies since the early 2000s.[16–18] Evidence has shown that increase in adiposity elevates the incidence of and mortality from several common cancers, including endometrial, breast, ovarian, prostate, liver, gallbladder, kidney and colon cancer.[15] However, higher BMI has also been correlated with improved outcomes in some cancers, an effect referred to as the "obesity paradox". A 2015 study found that obesity is associated with increased Breslow thickness, indicating more aggressive melanoma, with some studies linking obesity to a higher melanoma risk in men but not women.[19–21] However, other research found better survival rates for overweight individuals with melanoma, while some studies show no correlation between obesity and melanoma.[22,23]

Based on the above literature, the correlation between melanoma and obesity is still controversial.[24] However, little research has been reported about this issue. Given the rising incidence of cutaneous melanoma in Taiwan, we aim to find out the relationship between obesity and prognosis of cutaneous melanoma and its AM subtype in Taiwan.

Materials and Methods

This was a retrospective cohort study approved by the Institutional Review Board of Taipei Veterans General Hospital. The participants were 201 patients who were diagnosed with cutaneous melanoma between 2000 and 2022 at Taipei Veterans General Hospital, a tertiary medical center in Taiwan. Exclusion criteria were applied to ensure data completeness and follow-up availability. Patients with unknown primary melanoma, mucosal melanoma, or multiple primary melanomas were excluded from the analysis. Additionally, patients who were lost to follow-up were also excluded. Anti-tumor therapy was not considered as a criterion for exclusion, allowing for the inclusion of patients regardless of the type of treatment received. Body mass index (BMI) was used as the measure of obesity and was calculated by dividing the weight of the patient in kilograms by the square of their height in meters (kg/m^2). The included participants were classified into four groups based on their BMI, underweight (BMI:<18.5), normal weight (BMI:18.5–24.9), overweight (BMI:25–29.9) and obesity (BMI: ≥30). The primary objective of this study focused on examining the correlation between obesity and the prognosis of cutaneous melanoma. The secondary objective aimed to compare the findings between the AM and the non-AM group, thereby assessing any potential differences in the observed relationship.

Statistical Analysis

The Analysis of Variance (ANOVA) test was used to assess for differences in continuous variables among the four groups of BMI and Chi-square test for categorical variables. To identify prognostic factors, both univariate and multivariate logistic regression analyses were conducted. These analyses enabled the evaluation of the potential factors that could influence the prognosis of cutaneous melanoma. Furthermore, Kaplan-Meier (KM) survival analysis was performed to analyze the overall survival and disease-free survival outcomes. This analysis helped to determine the impact of different variables on the survival rates of patients. In all statistical analyses, a significance level of $P<0.05$ was considered, which was employed to estimate any substantial differences or associations between the variables.

Results

Basic Characteristics

A total of 201 patients diagnosed with cutaneous melanoma were enrolled in the study. The male to female sex ratio was 1.71. The mean age was 66.9 years. More than half of patients (101 people) were within normal weight (50.24%), 75 people were overweight (37.31%), 15 had obesity (7.46%) and 10 were underweight (4.98%). The mean BMI was 24.56. Melanomas were mainly acral melanoma subtypes (61.69%).

The mean Breslow thickness was 4.17 mm. Patients with higher Breslow thickness (above 2 mm) accounted for 45.27%. There was no difference in distribution of Breslow thickness in different BMI groups. 37.81% of the cases had tumor ulceration. Patients fell into the following cancer stages; stage 0 (7.46%), stage I (14.43%), stage II (34.32%), stage III (18.91%), stage IV (22.39%) respectively. Of all patients, the local recurrence rate was 8.46%, and 47.76% with distant metastasis. The five-year mortality rates were 49.25%. The mean survival was 56 months. The distribution of mean survival according to BMI categories was as follows: 51.9 months for underweight, 50.6 months for normal weight, 61.9 months for overweight, and 65.5 months for obesity. (Table 1)

The univariate analysis of overall survival between different variables and melanoma subtypes respectively was conducted. As shown in Table 2, older age (≥ 65 years old), male sex, advanced Breslow thickness stage (T3 and T4) and tumor ulceration were risk factors of worse overall survival rates in both cutaneous melanoma and AM. Alcohol consumption and tobacco use were not associated with impacting overall survival of melanoma. (Table 2)

In adjusted multivariable analysis of overall survival between different variables and melanoma subtypes, older age (≥ 65 years old) and male were risk factors of worse overall survival rates in both cutaneous melanoma and AM. Interestingly, overweight {CM (OR: 0.457 [0.253–0.829]); AM (OR: 0.432 [0.199–0.934])} showed a protective relationship with both cutaneous melanoma (CM) and AM (P value < 0.05). (Table 3)

We found that when comparing overweight individuals to those with normal BMI or underweight respectively, the hazard ratio decreased. {Overweight-Normal BMI CM (HR: 0.472 [0.292–0.763]); AM (OR: 0.44 [0.271–0.712])}; {Overweight-Underweight CM (HR: 0.392 [0.169–0.912]); AM (OR: 0.336 [0.144–0.785])} This means that the risk of a negative outcome was lower for overweight individuals. The overall survival rates were also higher in the overweight individuals. This trend was observed both for cutaneous and AM outcomes. However, for underweight and obese individuals, while there were trends suggesting worse outcomes, we did not find statistically significant differences. (Table 4)

The overall survival rates of included cutaneous melanomas participants in different BMI groups are shown in Figure 1. The mean overall survival for the different BMI groups were: 108.6 months for normal weight, 64.7 months for underweight, 128.2 months for overweight and 82.1 months for obese. Only overweight individuals showed significant difference from normal weight individuals and its hazard ratio was 0.475 (CI: 0.309–0.728).

We re-categorized participants into 2 groups by non-excess body weight (BMI<25) and excess body weight (BMI≥25). As shown, individuals with non-excess body weight and excess body weight had mean overall survival of 107 and 114.8 respectively and a hazard ratio 0.563 (CI: 0.377–0.842), which indicated a better prognosis of cutaneous melanomas in individuals with excess body weight compared to individuals without non-excess body weight. (Figure 2)

We further divided these 201 patients into two groups, AM and non-AM, and conducted survival analysis based on whether they exceeded a BMI of 25 or not. Our findings revealed that there were no significant differences in overall survival. (Figure 3)

Discussion

The rising incidence of life-threatening acral melanoma in Asia demands investigation into its cause in order to prevent the disease.[10,25] The association between obesity and malignancy of many different organs has been reported previously, including for endometrial, breast, ovarian, prostate, liver, gallbladder, kidney and colon cancer.[26] Currently, the correlation between melanoma and obesity is inconclusive. Some studies have indeed pointed out that obese patients might have better survival rates after receiving melanoma treatment, a phenomenon known as the "obesity paradox." This refers to the situation where obesity appears to be associated with better outcomes in certain cancers or diseases, even though

Table 1 Clinical Characteristic

	Underweight (BMI:<18.5)	Normal weight (BMI: 18.5–25)	Overweight (BMI: 25–30)	Obesity (BMI: >30)	*p*-value
Patient, n (%)	10(5%)	101(50.2%)	75(37.3%)	15(7.5%)	
Age (SD)	66.7(17.4)	68.3(16.03)	66.8(14.6)	64.3(20.3)	0.802
Sex-Male (%)	6(60%)	65(64.3%)	45(60%)	11(73%)	0.778
Personal history					
Alcohol (g per day) Mean (SD)	0	1.113(9.62)	3.243(27.9)	0	0.840
Smoking (Pack-days) Mean (SD)	0.2(0.35)	0.175(0.427)	0.03(0.16)	0.2(0.41)	0.030
Subtype, n (%)					0.523
Superficial spreading melanoma	0	2(2%)	1(1.3%)	0	
Lentigo maligna melanoma	1(10%)	1(1%)	1(5%)	1(2.1%)	
Nodular melanoma	3(30%)	17(17%)	10(13.3%)	2(15.5%)	
Acral lentiginous melanoma	4(40%)	62(61.4%)	50(66.7%)	8(61.4%)	
Others	2(20%)	8(8%)	7(9%)	4(26.7%)	
Breslow thickness					0.847
T1(<1mm)	2(20%)	18(17.8%)	14(18.7%)	2(13.3%)	
T2(1–2mm)	2(20%)	17(16.8%)	16(21.3%)	2(13.3%)	
T3(2–4mm)	1(10%)	21(20.7%)	16(21.3%)	2(13.3%)	
T4(>4mm)	3(30%)	25(24.7%)	16(21.3%)	7(46.7%)	
Unknown	1(10%)	13(12.9%)	14(18.7%)	2(13.3%)	
Tumor ulceration	4(40%)	42(41.6%)	25(37.5%)	5(39%)	0.560
Anatomical site					0.007
Acral	3(30%)	70(69.3%)	56(74.7%)	9(60%)	
Head and neck	1(10%)	14(13.8%)	7(9.3%)	0	
Trunk	5(50%)	8(7.9%)	7(9.3%)	4(27%)	
Extremity	1(10%)	9(8.9%)	5(6.7%)	2(13.3%)	
Stage					0.233
0	0	6(6%)	8((10.7%)	1(6.7%)	
I	3(30%)	15(14.9%)	10(13.3%)	1(6.7%)	
II	2(20%)	32(31.7%)	27(36%)	8(53.3%)	
III	0	20(19.8%)	15(20%)	3(20%)	
IV	6(60%)	26(25.7%)	11(14.7%)	2(13.3%)	
Local recurrence	1(10%)	6(6%)	8(10.6%)	2(13.3%)	0.645
Distant metastasis	6(60%)	56(55.4%)	29(38.7%)	5(33.3%)	0.217
Mortality	7(70%)	57(56.4%)	25(33.3%)	10(66.7%)	0.004
Disease-free survival	37.3	39.5	43.3	57	0.660
Survival months	51.9(50.4)	50.6(56.4)	61.9(50.1)	65.5(47.9)	0.484

Abbreviation: SD, standard deviation.

Table 2 Univariate Analysis with Respect to Overall Survival of Melanoma in CM and ALM Subtype

Characteristic	CM		ALM	
	OR (95% CI)	*p*	OR (95% CI)	*p*
Age				
< 65	1		1	
≥ 65	2.339(1.537 to 3.560)	<0.001	3.129(1.798 to 5.446)	<0.001
Gender				
Female	1		1	
Male	2.644 (1.673–4.179)	<0.001	3.610 (1.977 to 6.590)	<0.001

(*Continued*)

Table 2 (Continued).

Characteristic	CM		ALM	
	OR (95% CI)	*p*	OR (95% CI)	*p*
BMI				
Non-overweight	1		1	
Overweight	0.490 (0.279–0.862)	0.012	1.461 (0.813–2.625)	0.201
Alcohol (g per day) SD	0.975(0.913–1.040)	0.126	0.986(0.946–1.030)	0.316
Smoking (Pack-days) SD	1.388(0.641–3.006)	0.399	1.571(0.609–4.053)	0.340
Breslow thickness				
T1	1		1	
T2	4.074(1.517 to 10.938)	0.005	2.167(0.744–6.307)	0.156
T3	3.929(1.467 to 10.520)	0.007	4.857(1.634–14.435)	0.005
T4	10(3.806 to 26.271)	<0.001	8.571(3.019–24.330)	<0.001
Tumor ulceration				
Negative	1		1	
Positive	5.393(2.974–9.778)	<0.001	5.363(2.647–10.865)	<0.001
Tumor site				
ALM	1			
SSM	0.156(0.018–1.321)	0.088		
Nodular	1.329(0.690–2.560)	0.395		
LM	1.247(0.271–5.733)	0.778		

Abbreviations: OR, odds ratio; CI, confidence interval; CM, cutaneous melanoma; ALM, acral lentiginous melanoma; SSM, Superficial spreading melanoma; LM, lentigo maligna(LM) melanoma.

Table 3 Multivariate Analysis with Respect to Overall Survival of Melanoma in CM and ALM Subtype

Characteristic	CM		ALM	
	OR (95% CI)	*p*	OR (95% CI)	*p*
Age				
< 65	1		1	
≥ 65	2.114 (1.155 to 3.868)	0.015	2.560 (1.146–5.716)	0.022
Gender				
Female	1		1	
Male	2.868 (1.537–5.351)	0.001	4.710 (1.998–11.104)	<0.001
BMI				
Non-overweight	1		1	
Overweight	0.457 (0.252–0.829)	0.010	0.432 (0.199–0.934)	0.033

Notes: Adjusting for age, sex, T2DM, obesity, alcohol intake and smoking habits.
Abbreviations: OR, odds ratio; CI, confidence interval; CM, cutaneous melanoma; ALM, acral lentiginous melanoma.

obesity is generally considered a negative health factor.[21,27] This study aims to understand the association between obesity and melanoma while highlighting its primary outcome (The overall survival).

A large-scale study on more than 90,000 adults conducted in the United States in 2003 found that higher BMI levels did not increase the mortality rate from melanoma in males or females.[28] Among 340 Italian melanoma patients with an average Breslow thickness of 0.4 mm, the prognosis was found to be similar between normal weight patients and those who are overweight or obese.[29] Hardie CM et al reported a recent analysis of the Leeds Melanoma Cohort, with a median follow-up of 6.7 years, found that BMI was not linked to overall survival or melanoma-specific survival.[30] Additionally,

Table 4 HR for the Association of BMI and Overall Survival

	HR with 95% CI	*p*-value	Adjusted HR with 95% CI	*p*-value
Normal Overweight	1 0.472(0.292–0.763)	0.002	1 0.440(0.271–0.712)	0.001
Normal Underweight	1 1.204(0.547–2.649)	0.645	1 1.307(0.592–2.887)	0.507
Normal Obesity	1 0.912(0.464–1.793)	0.789,	1 0.808(0.410–1.593)	0.539
Underweight Overweight	1 0.392(0.169–0.912)	0.030	1 0.336(0.144–0.785)	0.012
Underweight Obesity	1 0.758(0.288–1.993)	0.574	0.618(0.234–1.631)	0.331
Overweight Obesity	1 1.822(0.881–3.765)	0.106	1.862(0.884–3.923)	0.102

Notes: (Adjusted for Gender, Age, Alcohol (g per day) and Smoking (Pack-days).
Abbreviations: HR, Hazard ratio; CI, confidence interval; BMI, Body mass index.

a study of the Leeds Melanoma Cohort, comprising 2,182 melanoma patients, from the United Kingdom in 2015 revealed that overweight individuals exhibited better prognoses than normal weight individuals after adjustment for age and sex, and after further adjustment for site and Breslow thickness.[31] Contrarily, a multicenter study in Korea suggested that a BMI greater than 23 may be associated with disease metastasis and shorter overall survival (OR=2.10 [CI 1.2–3.6], P value=0.033).[32] Besides overall survival, obesity appeared to be a clinical independent risk factor of thicker cutaneous melanoma, which increased severity of cutaneous melanomas.[19] A possible explanation put forth was the "Obesity Paradox". Wang Z et al[33] shows that obesity accelerates immune aging, encourages tumor growth, and causes T cell dysfunction via the PD-1 pathway, partially influenced by leptin. Surprisingly, despite these negative effects, obesity improves the effectiveness of PD-1/PD-L1 blockade, suggesting that it could serve as a potential biomarker for specific cancer immunotherapies.[34] The authors also highlighted a paradoxical relationship where obesity worsens immune dysfunction and tumor progression but enhances anti-tumor responses and survival through checkpoint blockade.[29,35]

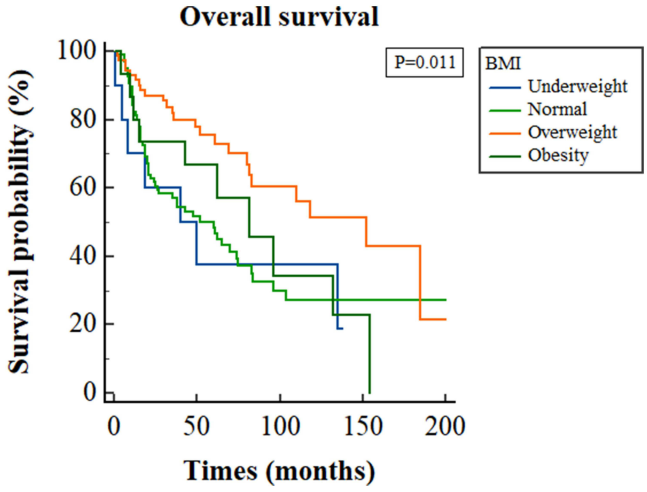

Figure 1 Estimated overall survival of patients with cutaneous melanoma based on BMI category.

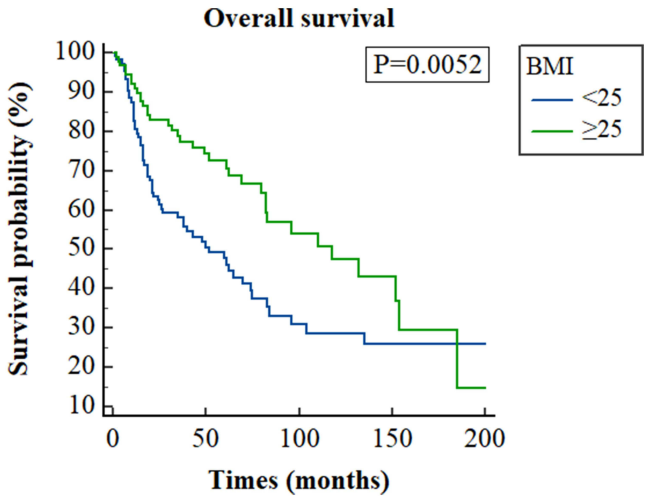

Figure 2 Estimated overall survival of patients with cutaneous melanoma based on whether BMI ≥25 (overweight and obesity).

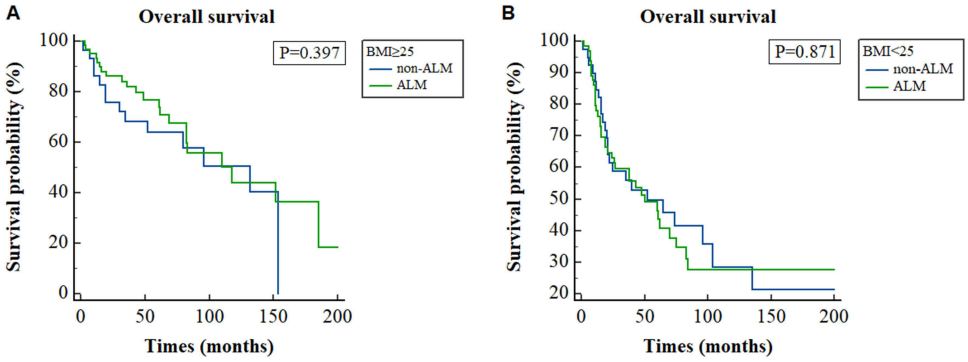

Figure 3 Estimated overall survival of patients according to ALM and non-ALM group based on BMI≥25 (**A**) and BMI<25 (**B**).
Abbreviation: ALM = acral lentiginous melanoma.

In our study, overweight was observed to be an independent protective factor for both cutaneous and AM {CM (OR: 0.457 [0.252–0.829]); AM (OR: 0.432 [0.199–0.934])} and have better outcomes in overall survival rates. The mean overall survival of overweight individuals was 128.2 months (108.6, 64.7 and 82.1 months in normal, underweight and obesity individuals) and had 0.475 in hazard ratio (CI: 0.309–0.728). Interestingly, we found no significant differences between obesity and Breslow thickness, a well-established prognostic factor of melanoma, which was contrary to previous study from Korea.[32]

Possible explanations for our findings include that research have found that obese melanoma patients may have higher survival rates after receiving certain immunotherapies, such as PD-1 inhibitors.[27,36] Several mechanisms could potentially elucidate this phenomenon. Firstly, obesity has been associated with alterations in immune system functionality, which may modify the patient's response to immunotherapy.[34] Secondly, individuals with higher adiposity may possess greater energy reserves, potentially ameliorating the adverse effects of treatment-related anorexia or cachexia.[37] Additionally, adipose tissue secretes various adipokines and cytokines, which could play a role in modulating inflammatory responses and, by extension, influence the efficacy of immunotherapeutic agents.[38] Moreover, the pharmacokinetics of drugs can vary with body composition; the increased adipose tissue in obese patients might affect the distribution and metabolism of administered immunotherapies, thereby impacting therapeutic outcomes.[38] Finally, it is also plausible that the chronic low-grade inflammation observed in obesity could interact synergistically with the

mechanisms of action of PD-1 inhibitors, enhancing their anti-tumor activity.[34] Further studies are warranted to explore these hypotheses and fully understand the relationship between obesity and melanoma patient outcomes in the context of immunotherapy. However, these findings do not mean that obesity is a protective factor. Obesity is still associated with numerous health issues, including other types of cancer and metabolic diseases. The impact of obesity on melanoma treatment requires further research to understand its underlying biological mechanisms.

Biological and genetic mechanisms play significant roles in understanding the impact of obesity on various diseases. Adipose tissue, in particular, has been identified as a key player in altering both systemic and microenvironmental factors through the endocrine or paracrine pathways.[39] Several studies have shown, to better understand the development of melanoma in relation to obesity, it is crucial to investigate the role of the activated PI3K/Akt and the MAPK pathway, which can be activated by mutations in BRAF.[39,40] Additionally, specific genetic factors have been found to be associated with the severity of certain diseases. Research has shown a strong correlation between the frequency of the IGF-1$(CA)_{19}$ repeat and the severity of melanoma, as measured by the Breslow index.[41,42] Furthermore, the presence of the C allele in the rs17782313 single nucleotide polymorphism (SNP) within the melanocortin-4 receptor has been linked to increased body mass index and poorer overall survival.[33] These findings highlight the intricate relationship between biological and genetic factors and their impact on disease outcomes, providing valuable insights into potential avenues for further research and therapeutic interventions. By analyzing the biological and genetic aspects, we can examine the repeatability of IGF-1 and the SNPs of obesity-related genes. Such analyses can offer us valuable insights into the transformation of obesity's impact on diseases, enabling us to develop tools for treatment and prevention.

Obesity is influenced by numerous complex factors, many of which were not fully accounted for in this retrospective nature and association study. Additionally, the limited number of cases and the incomplete availability of data from a single center may not accurately represent the entire Asian population. Further, BMI, a widely-used tool since it was first introduced in the 19th century, did not differentiate between muscle and fat tissue or provide information about the distribution of fat tissue, whether it is central, peripheral, or around target organs.[43] Its accuracy is also limited for older adults and postmenopausal women.[44] However, currently, BMI can still serve as a marker that partially reflects biological genetic mechanisms, as well as lifestyle and external environmental factors. Other feasible measurement methods for assessing fat distribution include hip circumference, waist circumference, waist-to-height ratio, and waist-to-hip ratio. These alternative measures provide additional insights into the distribution of fat tissue and can be utilized alongside BMI to obtain a more comprehensive understanding of an individual's body composition. In order to enhance the evaluation of obesity, it is advisable to explore more suitable assessment methods such as bioelectrical impedance analysis (BIA), air displacement plethysmography (ADP), and dual-energy x-ray absorptiometry (DXA). Furthermore, it is important to investigate the molecular analysis of the relationship between obesity and melanoma. Such analysis can provide valuable insights into the intricate interplay between obesity and melanoma, potentially uncovering novel therapeutic targets and strategies for managing and preventing both conditions.

Future studies that consider a more comprehensive range of factors and involve diverse populations are required to provide a more robust understanding of the relationship between obesity and cutaneous melanomas.

Conclusion

In our study, we observed that melanoma patients with excess body weight had better survival outcomes compared to those with normal or underweight status. Additionally, no significant differences were found between AM and non-AM subtypes in relation to body weight impacting overall survival. Further investigation is needed to better understand the relationship between obesity and melanoma, including taking into account various factors such as genetic predisposition, tumor biology, and treatment responses. Such research endeavors will contribute to a more comprehensive understanding of the impact of obesity on melanoma prognosis and guide future therapeutic strategies.

Abbreviations

CM, Cutaneous melanoma; AM, Acral melanoma; ALM, Acral lentiginous melanoma; LM, lentigo maligna; melanoma; SSM, superficial spreading melanoma; BMI, Body mass index; ANOVA, Analysis of Variance; KM, Kaplan-Meier; survival analysis; OR, Odds ratio; CI, Confidence interval; HR, Hazard ratio; SNPs, Single nucleotide polymorphisms; BIA, Bioelectrical impedance analysis; ADP, Air displacement plethysmography; DXA, Dual-energy x-ray absorptiometry; SD, standard deviation.

Data Sharing Statement

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate

The Ethics Committee of Taipei Veterans General Hospital approved the present study (approval no. IRB-2021-05-002AC; IRB-2024-07-001BC). This study only collected clinical medical records of patients without gathering any personal identifying information, and all data were anonymized. Approval for a waiver of informed consent was obtained from the ethics committee, as the waiver did not negatively impact the rights or welfare of the research subjects. The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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