



ORIGINAL ARTICLE

Frequency of Trauma, Physical Stress, and Occupation in Acral Melanoma: Analysis of 313 Acral Melanoma Patients in Korea

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Background: Traumatic events are thought to be a cause of acral melanoma. However, little is known about the role of mechanical trauma or physical stress in the development of acral melanoma. **Objective:** In our study, we evaluated the frequency of trauma, physical stress, and occupation in patients with acral melanoma and aimed to identify any pathological correlates of these factors. **Methods:** We conducted a retrospective study of 313 acral melanoma patients from Chonnam National University Hospital. We mapped melanoma-developed anatomical sites of acral areas and assessed patients' history of trauma, physical stress, and occupation. **Results:** Among the 313 acral melanoma patients, many reported a traumatic event (84 of 313; 26.8%) or physical stress (91 of 313; 29.1%) before the melanoma developed. The most common anatomical sites in these patients were on the borders of the foot (136 of 313; 43.5%). Trauma was more commonly associated with the fingernails and toenails than other sites. The frequency of each type of physical stress depended on the site of the lesion. Farmer and fisherman were the most common occupations (130 of 313; 41.5%) of the ac-

ral melanoma patients. **Conclusion:** Our results demonstrate that traumatic events, physical stress, and certain occupations are common in acral melanomas. Further studies are needed to establish whether these are risk factors for acral melanomas. (*Ann Dermatol* 33(3) 228~236, 2021)

-Keywords-

Acral melanoma, Occupations, Physical stress, Site, Trauma

INTRODUCTION

There are racial differences in the prevalence of the subtypes of cutaneous melanoma, and acral melanoma is the most common subtype in Asian, Hispanic, and African populations¹. Acral melanoma occurs on the palms, soles of the feet, and nails. Unlike cutaneous melanomas in Caucasian populations, ultraviolet (UV) exposure is not a major etiological factor in acral melanoma². In addition, the number of melanocytic or dysplastic nevi is not a significant risk factor for acral melanoma³. A recent molecular classification of cutaneous melanoma found distinct subsets of genetic alterations in acral melanoma compared with other subtypes⁴⁻⁶. However, the pathogenesis of acral melanomas is still not clear. Recent Asian studies have shown that acral melanomas frequently occur on the heel and forefoot of the plantar surface, unlike benign acral melanocytic lesions such as acral nevi and lentiginos, suggesting a role of trauma or physical or mechanical stress in the development of acral melanomas⁷⁻⁹. Therefore, we conducted a retrospective study to investigate the frequency of trauma, physical stress, and occupation in patients with acral melanoma.

Received May 19, 2020, Revised October 1, 2020, Accepted for publication October 12, 2020

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MATERIALS AND METHODS

Patients with acral melanoma

The study enrolled 313 patients with acral melanoma seen at Chonnam National University Hospital and Chonnam National University Hwasun Hospital from 1992 to 2018. All patients were confirmed to have acral melanoma based on clinical and histopathological evaluations. This study was approved by the Institutional Review Boards of Chonnam National University Hwasun Hospital (IRB number: CNUHH-2018-165).

Anatomical mapping of the sites of acral melanoma

We mapped the sites of all 313 acral melanomas from the photographs of acral sites on the hands and feet. We included only non-glabrous volar surfaces of the acral skin and nail apparatus. For the analysis, we divided the sole into the forefoot, midfoot, and heel, and then subdivided each area into inner, central, and outer areas of the sole. We examined the border areas of the foot, which include the medial, lateral, and posterior parts of the sole and webspaces and the anterior parts of the toes. The border areas can be seen when patients stand, and are readily subject to physical stress while working. To mark the melanoma site, a small circle was placed on the foot where melanoma development began or where the deepest portion of the melanoma lesion was found.

Frequency of trauma, physical stress, and occupation

The present study defines trauma as an event that injures the skin, such as a contusion, laceration, or medical intervention. We excluded incidental and repeated minor traumas, but included traumas that were clearly remembered by patients. Medical interventions included actions with a secondary effect on pre-existing skin lesions, such as simple excision, nail extraction, and debridement. Physical stress refers to chronic stimulation or strong pressure on normal skin or existing benign acral lesions, such as abrading or rubbing calluses and keratoderma, application of chemical agents for folk remedies, and chronic friction or pressure caused by tight shoes or prolonged exposure to wet conditions. We obtained a history of trauma or physical stress in all patients and determined their occupations. We divided occupations into groups based on similarity of work environment. For example, in this southern part of Korea, many people work in agriculture and in the fisheries. Workers in these fields share an outdoor working environment and are vulnerable to similar traumas and physical stressors. Therefore, we placed these occupations in the same group. We used the same reasoning to group doctors, pharmacists, and office workers together.

Relationship between history of trauma or physical stress and melanoma duration

We aimed to evaluate the effects of trauma and physical stress on disease duration. We defined melanoma duration as the period of time taken to visit the hospital after the first detection of a lesion. We wanted to determine whether these durations were shorter for patients who had experienced trauma or physical stress compared with those who had not.

Table 1. Patient characteristics

Characteristic	Value
Sex	
Male	149 (47.6)
Female	164 (52.4)
Age (yr)	63.96 ± 13.06
20 ~ 29	1 (0.3)
30 ~ 39	16 (5.1)
40 ~ 49	27 (8.6)
50 ~ 59	60 (19.2)
60 ~ 69	88 (28.1)
70 ~ 79	89 (28.4)
80 ~ 89	29 (9.3)
≥ 90	3 (1.0)
Disease duration (mo)	46.61 ± 80.16
Site of lesion (right/left)	
Hand	15 (4.8) (6/9)
Palm	8 (53.3) (3/5)
Finger volar	7 (46.7) (3/4)
Foot	212 (67.7) (90/122)
Sole	191 (90.1) (81/110)
Forefoot	34 (17.8) (10/24)
Border*	16 (47.1) (6/10)
Non-border	18 (52.9) (4/14)
Midfoot	31 (16.2) (18/13)
Border*	19 (61.3) (9/10)
Non-border	12 (38.7) (9/3)
Heel	126 (66.0) (53/73)
Border*	82 (65.1) (35/47)
Non-border	44 (34.9) (18/26)
Toe	21 (9.9) (9/12)
Toe webspace	14 (66.7) (7/7)
Toe volar	7 (33.3) (2/5)
Border*	5 (71.4) (2/3)
Non-border	2 (28.6) (0/2)
Nail	86 (27.5) (44/42)
Finger nail	50 (58.1) (32/18)
Toe nail	36 (41.9) (12/24)

Values are presented as number (%) or mean ± standard deviation. Percentages have been rounded and may not total 100. *Border: areas that are frequently irritated by shoes, they include medial, lateral, posterior portion of sole, webspace and anterior portion of toe.

Statistical analysis

The data were evaluated using the statistical package IBM SPSS ver. 25.0 (IBM Corp., Armonk, NY, USA). To compare the baseline characteristics of the subgroups, Pearson's chi-square test or Fisher's exact test was used as appropriate for the categorical variables. A *p*-value less than 0.05 was deemed to indicate statistical significance.

RESULTS

Patient characteristics and sites of the acral melanomas

Of the 313 patients, 52.4% (n=164) were female and 47.6% (n=149) were male. The patients' mean age was 63.96 ± 13.06 years (range, 29~97 years), and 66.8% of the patients were over 60 years old. The mean duration of acral melanoma was 46.61 ± 80.16 months. The sites of the acral melanomas were divided into the hands, feet, and nails. In addition, the feet were divided into border and non-border areas (Table 1). Overall, 67.8% (n=212) were on the feet, 27.5% (n=86) in the nails, and 4.8% (n=15) on the hands. The incidence of acral melanoma was similar on the palms (53.3%, n=8) and fingers (46.7%, n=7), whereas the sole (90.1%, n=191) was involved ten times more often than the toes (9.9%, n=21). Regarding the nails, the fingernails (58.1%, n=50) were involved more often than the toenails (41.9%, n=36). The heel (66.0%, n=126) was the most common site on the sole, and toe web-spaces (66.7%, n=14) were involved two times more often than the volar toe (33.3%, n=7). Borders are areas that are frequently irritated when wearing shoes, and include the medial, lateral, and posterior portions of the sole, web-spaces, and anterior portions of the toes. Anatomical mapping revealed that acral melanomas mainly occurred at

the borders of the foot (Fig. 1). Of the 212 acral melanomas on the foot, border areas (64.2%, n=136) were involved about two times more frequently than other areas (35.8%, n=76).

Frequency of trauma, physical stress, and occupation

Of the 313 patients, 26.8% (n=84) had a history of trauma, of which contusion (36.9%, n=31) was the most common, followed by medical interventions, stabbing, burns, and frostbite (Table 2). Medical interventions included nail extraction, laser therapy, simple excision, debridement, and similar procedures. There was no significant difference in trauma between males and females (*p*=0.997). Patient 1 was a 78-year-old female with a sub-ungual melanoma. She had contused her left thumbnail after striking it with a hammer (Fig. 2A). Patient 2 was a 57-year-old male who had a melanoma on his heel; before his melanoma developed, he had injured this area by stepping on a stone (Fig. 2B).

Among the 313 patients, 29.1% (n=91) had a history of physical stress, of which abrading or rubbing were most common (44.0%, n=40), followed by chronic pressure, application of chemical agents, chronic friction, and chronic maceration. There was no significant difference between males and females in physical stress (*p*=0.359; Table 2). Patient 3 was a 69-year-old male with keratoderma and a callus on his heel; he had continuously scrubbed and abraded the keratoderma before the melanoma developed (Fig. 2C). Patient 4 was a 67-year-old female who had a melanoma on the volar surface of her right thumb. She was a farmer, and the site of the melanoma had been chronically irritated by a farming tool that she used in her work (Fig. 2D).

Analysis of the patients' occupational histories revealed that

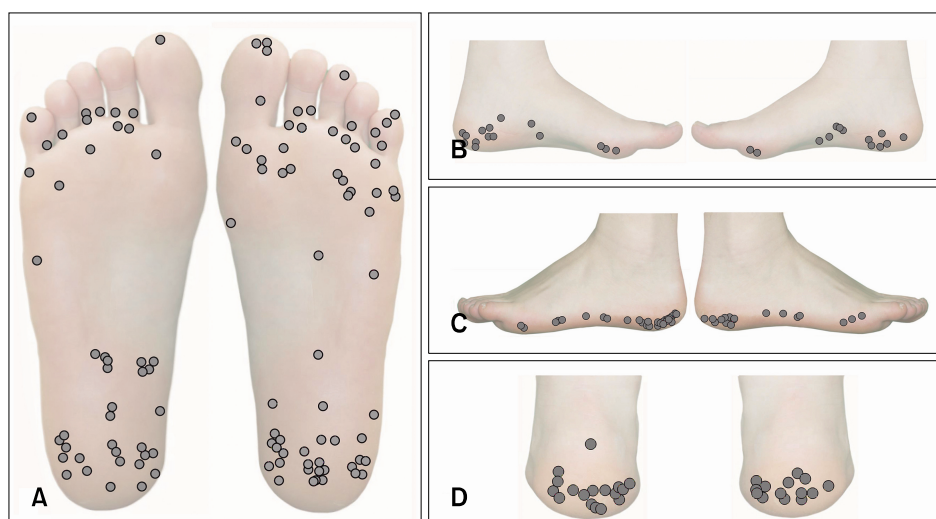


Fig. 1. Anatomical mapping of acral melanomas on the foot. Acral melanomas occur mostly on the foot, and most commonly in the weight-bearing portion of the sole (A) and in border areas (B~D).

Table 2. History of trauma and physical stress, and occupation according to sex and lesion site

Variable	Total	Sex		Hand	Site of lesion			
		Male	Female		Foot		Nail	
					Border*	Non-border	Fingernail	Toenail
Trauma history								
Contusion	31 (36.9)	14 (35.0)	17 (38.6)	0 (0)	12 (50.0)	2 (8.3)	11 (52.4)	6 (46.2)
Medical intervention [†]	23 (27.4)	6 (15.0)	17 (38.6)	1 (50.0)	4 (16.7)	11 (45.8)	6 (28.6)	1 (7.7)
Stabbing	18 (21.4)	11 (27.5)	7 (15.9)	0 (0)	7 (29.2)	6 (25.0)	3 (14.3)	2 (15.4)
Burn	3 (3.6)	3 (7.5)	0 (0)	0 (0)	1 (4.2)	2 (8.3)	0 (0)	0 (0)
Frostbite	2 (2.4)	1 (2.5)	1 (2.3)	1 (50.0)	0 (0)	1 (4.2)	0 (0)	0 (0)
Others	7 (8.3)	5 (12.5)	2 (4.5)	0 (0)	0 (0)	2 (8.3)	1 (4.8)	4 (30.8)
Total	84 (100)	40 (100)	44 (100)	2 (100)	24 (100)	24 (100)	21 (100)	13 (100)
Physical stress history								
Abrading or rubbing	40 (44.0)	24 (51.1)	16 (36.4)	1 (20.0)	19 (41.3)	12 (54.5)	6 (60.0)	2 (25.0)
Chronic pressure	21 (23.1)	9 (19.1)	12 (27.3)	1 (20.0)	13 (28.3)	3 (13.6)	1 (10.0)	3 (37.5)
Applying chemical agent	19 (20.9)	8 (17.0)	11 (25.0)	0 (0)	9 (19.6)	6 (27.3)	1 (10.0)	3 (37.5)
Chronic friction (irritation)	9 (9.9)	4 (8.5)	5 (11.4)	3 (60.0)	3 (6.5)	1 (4.5)	2 (20.0)	0 (0)
Chronic maceration	2 (2.2)	2 (4.3)	0 (0)	0 (0)	2 (4.3)	0 (0)	0 (0)	0 (0)
Total	91 (100)	47 (100)	44 (100)	5 (100)	46 (100)	22 (100)	10 (100)	8 (100)
Occupation history								
Agriculture or fishery industry	130 (41.5)	65 (43.6)	65 (39.6)	7 (46.7)	61 (44.9)	28 (36.8)	21 (42.0)	13 (36.1)
House wife	58 (18.5)	0 (0)	58 (35.4)	2 (13.3)	31 (22.8)	9 (11.8)	10 (20.0)	6 (16.7)
Commercial industry	26 (8.3)	10 (6.7)	16 (9.8)	3 (20.0)	8 (5.9)	12 (15.8)	3 (6.0)	0 (0)
Doctor, pharmacist, office job	24 (7.7)	18 (12.1)	6 (3.7)	2 (13.3)	12 (8.8)	8 (10.5)	1 (2.0)	1 (2.8)
Construction industry	16 (5.1)	15 (10.1)	1 (0.6)	1 (6.7)	6 (4.4)	2 (2.6)	4 (8.0)	3 (8.3)
Policeman, soldier	6 (1.9)	6 (4.0)	0 (0)	0 (0)	4 (2.9)	0 (0)	2 (4.0)	0 (0)
Transport business	6 (1.9)	6 (4.0)	0 (0)	0 (0)	0 (0)	4 (5.3)	1 (2.0)	1 (2.8)
Manufacturing industry	7 (2.2)	4 (2.7)	3 (1.8)	0 (0)	0 (0)	2 (2.6)	4 (8.0)	1 (2.8)
Sales man	4 (1.3)	2 (1.3)	2 (1.2)	0 (0)	2 (1.5)	1 (1.3)	0 (0)	1 (2.8)
Non-available [‡]	36 (11.5)	23 (15.4)	13 (7.9)	0 (0)	12 (8.8)	10 (13.2)	4 (8.0)	10 (27.8)
Total	313 (100)	149 (100)	164 (100)	15 (100)	136 (100)	76 (100)	50 (100)	36 (100)

Values are presented as number (%). Percentages have been rounded and may not total 100. Statistically significant at $p < 0.05$. *Border: areas that are frequently irritated by shoes, they include medial, lateral, posterior portion of sole, webspace and anterior portion of toe. [†]Medical intervention: including nail extraction, laser therapy, simple excision, skin biopsy, debridement, etc. [‡]Non-available: patients whose data is non-available.

farmers and fishermen were the most common occupations (41.5%, $n = 130$), followed by housewives, commercial industry, and office jobs. There was a significant difference in the proportions of border and non-border areas according to occupational history ($p = 0.021$). Patients with melanomas in border areas were mostly engaged in agriculture or fishing (44.9%, $n = 61$) (Table 2).

Correlation of trauma with the sites of acral melanomas

There was a significant difference in the presence of trauma among the lesion sites ($p = 0.002$). Acral melanomas on the nails were more strongly associated with trauma than melanomas on the volar areas. Fingernail melanomas (42.0%; 21 of 50) were most commonly associated with trauma, followed by toenail melanomas (36.1%; 13 of

36). There were 34 trauma-associated subungual melanomas, of which five were excluded because clinical photos were unavailable and the site could not be identified. Among the 29 subungual melanoma patients, melanomas with ulcerated or nodular lesions with nail dystrophy (75.9%; 22 of 29) were more commonly associated with a trauma history than melanonychia-associated melanoma (24.1%; 7 of 29). On the foot, border areas (17.6%; 24 of 136) were less closely related to trauma than non-border areas (31.6%; 24 of 76).

Correlation between physical stress and site of acral melanoma

There was no significant difference in the presence of physical stress among the lesion sites ($p = 0.218$; Table 3).



Fig. 2. Clinical findings of acral melanoma according to a history of trauma, physical stress, and occupation in agriculture and the fishery industry. (A) A 78-year-old female hit her left thumbnail with a hammer. (B) A 57-year-old male stepped on a stone with his heel. (C) A 69-year-old male continuously scrubbed and abraded the keratoderma and callus on his heel. (D) A 67-year-old female was a farmer and the site of the melanoma had been chronically irritated by a farming tool while working. We received the patient’s consent form about publishing all photographic materials.

Table 3. Correlations between physical stress, and lesion site and impact on the disease progression

Variable	Trauma (+)	Trauma (-)	p-value	Physical stress (+)	Physical stress (-)	p-value
Site of lesion						
Volar (n=227)			0.002			0.218
Hand (n=15)	2 (13.3)	13 (86.7)		5 (33.3)	10 (66.7)	
Foot (n=212)						
Border (n=136)*	24 (17.6)	112 (82.4)		46 (33.8)	90 (66.2)	
Non-border (n=76)	24 (31.6)	52 (68.4)		22 (28.9)	54 (71.1)	
Nail (n=86)						
Fingernail (n=50)	21 (42.0)	29 (58.0)		10 (20.0)	40 (80.0)	
Toenail (n=36)	13 (36.1)	23 (63.9)		8 (22.2)	28 (77.8)	
Mean duration (mo)	26.9±42.6	53.9±89.2	<0.001	36.6±58.9	50.7±87.3	0.097

Values are presented as number (%) or mean±standard deviation. Percentages have been rounded and may not total 100. Statistically significant at $p < 0.05$. *Border: areas that are frequently irritated by shoes, they include medial, lateral, posterior portion of sole, webspace and anterior portion of toe.

However, the types of physical stress differed by anatomical site (Table 2). On the palm, chronic irritation from farming tools and chronic shear stress from repetitive counting of paper money were assumed to be relevant to melanoma development. On the foot, the types of physical stress on border and non-border areas differed. Border areas are exposed to the outside and in direct contact with

physical materials, and webspaces are easily irritated by direct contact with nearby skin. Tight shoes can cause chronic pressure or shear stress on the lateral and posterior side of the heel and the lateral side of the forefoot while walking. Chronic degeneration of the webspaces can result from working in wet conditions wearing boots. These injuries occur more often in the border areas (39.1%, 18

of 46). Injuries unrelated to the site of the lesion included abrasion or rubbing on calluses or keratodermas, chronic irritation caused by friction in areas used while working, and application of chemical agents to wounds or calluses. However, these injuries were associated with non-border areas more often than border areas. Chronic pressure from tight shoes and application of chemical agents was associated with toenail melanoma (75.0%), while abrasion and rubbing were associated with fingernail melanoma (60.0%).

Relationship between history of trauma or physical stress and melanoma duration

We examined the effects of trauma and physical stress on the melanoma disease duration. Patients with a history of trauma had a significantly ($p < 0.001$) shorter disease duration (26.9 ± 42.6 months) until the first hospital visit than the patients without trauma (53.9 ± 89.2 months). However, there was no significant difference in disease duration of acral melanoma according to the presence of physical stress ($p = 0.097$; Table 3).

DISCUSSION

We found that acral melanomas are common on the sole, especially the borders of the foot, and that more than half of patients have a history of trauma or physical stress. Farmers and fishermen were the occupations most commonly affected.

Acral melanoma occurs on acral sites, such as the hands, feet, and nails. Analysis of the site details revealed that only 15 of 313 (4.8%) patients had melanomas of the hands, whereas 212 patients (67.8%) had them on the feet and 86 patients (27.5%) on the nails. Therefore, acral melanomas occur predominantly on the feet, rather than the hands. Interestingly, we found that border areas of the feet (the medial, lateral, and posterior parts of the sole, the toe webspaces, and the anterior parts of the toes) are commonly involved. Previously, we reported that melanoma lesions on the soles were distributed mainly at the periphery⁷. There have also been reports of melanomas on the plantar surfaces of the forefoot and heels, suggesting that mechanical stresses such as plantar pressure and shear stress increase the formation of acral melanomas⁹. In the present study, the heel was the dominant site of plantar melanomas, and the edges of the foot were commonly involved; these areas are readily traumatized or irritated by chronic physical stresses.

The role of trauma in melanoma development has long been controversial^{10,11}. In 1965, Lea¹⁰ performed a statistical analysis of the incidence of trauma in melanoma,

using basal cell carcinoma as a control. A history of trauma was present in 38% of 193 melanomas but in only 12% of 530 basal cell carcinomas, and the relationship between trauma and the development of melanoma was regarded as established beyond reasonable doubt. However, Briggs¹¹ could not find statistical evidence to support this relationship. The role of trauma is especially important in acral melanoma because acral sites are more exposed to traumatic events than other body sites. But a study conducted in Durban, South Africa found no evidence of traumatic acral melanoma in the deeply pigmented skin of Zulus¹². In Europe, single or recurrent traumatic events were more often associated with acral melanoma or melanoma located on the extremities than melanoma on other sites¹³. In China, a study of 685 cutaneous melanomas revealed a possible association between traumatic events and melanoma of the lower limbs¹⁴. In case-control studies, two major risk factors for hand and foot melanoma were previous trauma and nevi on the sole¹⁵.

In the present study, 26.8% of the patients recalled traumatic events. There was a significant difference in the frequency of trauma at the lesion sites ($p = 0.002$). Although melanoma development on burn scars has been reported, penetrating injuries and contusions are more common at acral sites¹⁶⁻¹⁹. There is a higher incidence of trauma in subungual melanoma compared with melanoma on the volar surfaces of hands and feet^{14,20}. Subungual melanoma was associated with a high incidence of traumatic events (40.5%, $n = 34$). The frequency of subungual melanomas located on the thumb and the nails of the big toe also suggests a role of trauma^{7,21}. In our study, fingernails (42.0%, 21 of 50) were the most frequently affected by trauma, followed by toenails (36.1%, 13 of 36). Trauma-associated subungual melanomas often presented with ulcerated or nodular lesions and nail dystrophy. Based on this finding, we postulate that patients with nail dystrophy, nodular lesions, or non-healing wounds after trauma to nails should watch for the development of acral melanoma. These patients should be followed up by a dermatologist and monitored for the development of skin cancer from chronic wounds or long-lasting ulcers. Border areas of the foot were less closely associated with trauma (17.6%, 24 of 136) than non-border areas (31.6%, 24 of 76). From this finding, we conclude that traumatic injuries can affect any part of the foot and not merely border areas.

Physical stress has not been well studied in melanoma. Anatomical mapping suggests that mechanical stress and chronic physical stress are associated with acral melanoma^{7,9}. However, the exact kind of physical stress is not known. In our study, physical stresses were found in 29.1% of acral melanoma patients, including abrading or

rubbing keratoderma or thick scales on the foot, maceration resulting from wet conditions, chronic friction caused by using farming tools, counting paper money with the fingers, and climbing mountains frequently wearing tight hiking boots. These physical stresses are not caused simply by body weight pressure.

One Japanese female developed a black patch on her thumb after working as a seamstress for more than ten years, and melanoma could not be excluded²². Such work-associated chronic physical stress might induce melanoma. Among our patients, melanoma developed on the left finger of a cashier who counted paper money continuously and in a farmer who handled tools for decades. A study conducted in 1941 found that trauma and chronic irritation were evident etiological factors in 25% of all cutaneous melanomas²³. The authors suggested that lack of information about melanoma delayed the diagnosis. In our study, about 56.0% of the acral melanoma patients had experienced trauma or physical stress. This high frequency might be explained by the fact that acral sites are more prone to trauma or physical stress and patients lack medical information about acral melanomas.

The mean duration of the acral melanomas before presentation in our study was 46.6 ± 80.2 months. Acral melanomas tend to be present for a long time before the first visit to the hospital. There are several reasons for this. First, acral lentiginous melanoma usually has a long radial growth phase and then subsequently invades. Another reason is the delay in diagnosing acral melanomas. Acral melanoma is less affected by genetics and UV exposure than other subtypes of melanoma; chronic stimulation is a more important factor in its development. Squamous cell carcinoma is known to arise in the setting of long-standing chronic inflammation, repeated injury, unrestrained fibroproliferative healing, and subsequent tissue stiffening. These alterations might change the biophysical performance of the mesenchyme and lead to carcinoma conversion of keratinocytes²⁴. We believe that acral melanoma, like squamous cell carcinoma, could develop gradually from chronic inflammation. Patients with a history of physical stress have experienced this stress over a long period of time, and may delay a visit to the hospital if they mistake melanoma lesions for calluses or benign lesions caused by chronic stimulation. Conversely, in our series, trauma led to a shorter disease duration and progression of the pre-existing acral melanoma. Trauma to a clinically apparent melanoma is a significant independent negative predictor of overall survival²⁵. Occupational risks for cutaneous melanoma have been reported. Cutaneous melanoma is more common in high socioeconomic groups than in low socioeconomic groups. However, low socioeconomic

groups were diagnosed at more advanced stages and had lower survival rates²⁶. In regard to UV exposure as a causal factor, male workers in Sweden who were exposed to artificial UV sources developed melanomas on the trunk, and females exposed to arsenic/mercury had increased risk^{27,28}. In Asia, acral melanoma is the most common form of melanoma and exposure to sunlight is not a risk factor²⁹. Therefore, the type of occupation and degree of exposure to UV differ in between Asian and Caucasian populations. In China, a higher risk of trauma-associated melanomas on the feet was observed in those living in the south of China, who preferred to walk bare-footed more often than those living in the north, who always wore shoes. Barefoot persons have higher risks of both localized trauma and melanoma on their lower extremities, indicating that the relationship between trauma and acral melanoma was significant in this population¹⁴. In our study, agriculture and fishery industry workers were the most common occupation with acral melanoma. Although these individuals are exposed to UV while working, the acral sites are not directly exposed to the sun. Instead, the patients might be subjected to trauma while working bare-footed or to physical stress from work shoes. People in these occupations had more melanomas at border sites and were subjected to significantly more physical stress.

The mechanism of the trauma- or physical stress-induced pathogenesis of melanoma is unknown. Chronic wounds and trauma induce local inflammation, which alters the microenvironment of immune cells. The inflammasomes involved in tissue damage provoke the development of melanoma^{30,31}. In addition, trauma and cellular damage might activate the cell cycle. Recurrent activation could contribute to cells experiencing critical telomere shortening at an earlier stage and provoking tumor growth via increased TERT expression³². Therefore, trauma or physical stress might induce melanoma-associated genetic changes. In our previous study, *BRAF* mutations were infrequent in acral melanomas³³, and there were no differences in anatomical site when analyzing melanomas by common mutation type³⁴. However, further studies of the pathogenic roles of trauma and physical stress-induced genetic alterations are warranted.

This study had several limitations. First, detailed trauma and physical stress histories were not available in 30% of the patients. This is a retrospective study, and accurate medical records were not available for former patients. Therefore, it was difficult to obtain precise histories for some patients. Second, the anatomical sites were not determined exactly at locations where border and non-border areas overlap for large lesions on the sole. To reduce this error, we used the location where patients reported

the acral melanoma first developed or the deepest area of the lesion. Third, our findings may not be generalizable to all Korean occupations because jobs differ in different areas. Our study was conducted in the southern part of Korea, where there are many farmers and fishermen. Fourth, the frequency of trauma and physical stress in our study should be compared to the frequency in patients without acral melanoma, or to the frequency in acral areas on patients' non-melanoma sides. However, even this approach could be subject to recall bias. Patients may preferentially remember injuries at sites that later develop melanoma.

Our study is the first to report a high frequency of history of trauma, physical stress, and certain occupations in patients with acral melanoma. Acral melanomas occurred primarily in the border areas of the foot and were associated with traumatic events or physical stress in more than half of the patients. Farmers and fishermen tend to develop melanomas more often than other occupation groups because of their working environment. However, further studies are needed to determine whether trauma, physical stress, and occupation are causal factors or risk factors for acral melanoma. These studies should compare the frequency of trauma, physical stress, and occupation of patients with acral melanoma and a matched control group. Studies of the molecular mechanism of the trauma- or physical-stress-induced pathogenesis of melanoma development are also needed.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

FUNDING SOURCE

This research was supported by Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education (NRF-2019R1D1A3A03103808), a grant (HCRI19029) from Institute for Biomedical Science Chonnam National University Hwasun Hospital, and the Bio & Medical Technology Development Program of the National Research Foundation (NRF) funded by the Korean government (MSIT) (No. NRF-2020M3A9G3080281).

DATA SHARING STATEMENT

Research data are not shared.

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