Survival rates for invasive cutaneous malignant melanoma in South Korea in accordance with the Eighth edition AJCC Cancer Staging Manual: A retrospective single center study

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Abstract

Background: Cutaneous malignant melanoma is known to have a poorer prognosis in Asian patients as compared to Caucasians. Few studies have analysed the overall survival rate (OS) and melanoma-specific survival rate (MSS) of patients with cutaneous malignant melanoma in South Korea.

Aim: This study aims to analyse the OS, MSS and prognostic factors of patients with invasive cutaneous malignant melanoma in South Korea.

Methods: The medical records of patients diagnosed with invasive cutaneous malignant melanoma from July 2006 to June 2016 at Kyungpook National University Hospital were reviewed retrospectively. The OS/MSS of these patients were calculated in accordance with the Eighth American Joint Committee on Center staging system and the prognostic factors affecting MSS were analysed.

Results: A total of 202 patients with a mean age of 61.5 years were included. The 5-year OS/MSS was 64.4%/70.7% in the patients. The 5-year OS/MSS was 94.7%/97.1% for stage I, 67.2%/76.3% for stage II, 54.4%/59.1% for stage III, and 0%/0% for stage IV. On univariate analysis, the age, sex, Breslow thickness, ulceration, microsatellites, satellites, locally recurrent or in-transit metastasis, tumour metastasis in sentinel lymph nodes and clinicopathological stage were all significantly associated with the MSS, but not with acral distribution or *BRAF* mutation status. However, on multivariate analysis only the Breslow thickness, ulceration and stage IV were significantly associated with the MSS.

Limitations: This study was conducted retrospectively in a relatively small number of patients at a single tertiary center in South Korea.

Conclusions: The OS/MSS of patients with invasive cutaneous malignant melanoma in South Korea was lower than those in Caucasians. In addition to the Breslow thickness and ulceration, the impact of tumour location and sentinel nodal metastasis on cutaneous malignant melanoma should be reevaluated to better understand the disease prognosis in these patients.

Key words: Epidemiology, Korea, malignant melanoma, prognostic factors, survival rate

How to cite this article: Lee SH, Ha GU, Lee HJ, Chung HY, Huh S, Ha D-L *et al*. Survival rates for invasive cutaneous malignant melanoma in South Korea in accordance with the Eighth edition AJCC Cancer Staging Manual: A retrospective single center study. Indian J Dermatol Venereol Leprol. 2024;90:163–9. doi: 10.25259/IJDVL_352_2022

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Received: April, 2022 **Accepted:** March, 2023 **EPub Ahead of Print:** May, 2023 **Published:** February, 2024

DOI: 10.25259/IJDVL_352_2022 **PMID:** 37317716

Plain Language Summary

This study investigates the survival of patients with invasive cutaneous malignant melanoma (a type of skin cancer) in South Korea. A review of the medical records of 202 patients with melanoma found that the survival rate was lower in South Korea compared to Caucasians. Factors influencing survival included the thickness of the cancer, the presence of ulceration and the stage of the melanoma. The authors suggest that more attention should be given to the depth of the cancer invasion and its condition (whether it had ulcerated or not), rather than where the cancer is located and whether it has spread to lymph nodes to better understand the prognosis of invasive cutaneous malignant melanoma in South Korea. However, this study only looked at a small number of patients in one hospital, so more research is needed.

Introduction

Cutaneous malignant melanoma is an uncommon, but lethal, form of skin cancer. Its incidence is steadily rising, resulting in a significant increase in disease burden. The age-standardised worldwide incidence rate of cutaneous malignant melanoma increased 13% between 2012 and 2020 (from 3.0 to 3.4/100,000/year).[1,2] In South Korea the incidence increased from 2.6 to 3.0/100,000/year between 2004 and 2017.[3]

Asian patients with cutaneous malignant melanoma typically exhibit a more prominent acral distribution, advanced disease at diagnosis, and poorer prognosis compared to Caucasians.[4] The poorer prognosis has been noted even in Asian–American patients living in the USA: among 49,772 patients with invasive cutaneous malignant melanoma in the US reported by Cormier *et al*., the 5-year overall survival rate (OS) was 80.2% in Asian-American patients compared to 89.6% in Caucasian patients.[5] This suggests that ethnic and genetic factors may be more important than environmental factors (geographical location, ultraviolet radiation exposure) in influencing the prognosis of cutaneous malignant melanoma.[4,5]

The American Cancer Society reported melanoma-specific survival rates (MSS) in accordance with the staging criteria of the 8th edition of the American Joint Committee on Center (AJCC) staging system in 2017. Among 43,792 patients from 10 institutions in the USA, Europe, and Australia from 1998, the 5-year MSS in patients with stages I, II and III of the diseases were 98%, 90%, and 77%, respectively.[6] However, a recent retrospective study in patients with melanoma from South Korea using a customised research database from the National Health Insurance Sharing Service in 2002–2017 reported a much lower 5- and 10-year OS of 62.3 and 48.8%, respectively .[7]

Although an accurate understanding of survival rates is important for patient counselling, only a few studies have analysed the OS and MSS of cutaneous malignant melanoma patients in South Korea. Thus, we aimed to analyse the OS, the MSS, and prognostic factors in patients with invasive cutaneous malignant melanoma in South Korea.

Methods

This study was conducted at Kyungpook National University Hospital, a tertiary centre in South Korea and was approved by the institutional review board (KNUH 2021-07-024). Medical records from the hospital database between July 2006 and June 2016 were retrospectively reviewed and a total of 301 patients histologically diagnosed with malignant melanoma were retrieved.

The study only included patients diagnosed with primary invasive cutaneous malignant melanoma. Patients whose medical records were insufficient for clinical or pathological staging, those with a histological diagnosis of cutaneous malignant melanoma in situ or atypical melanocytic proliferation and those who presented with mucosal malignant melanoma or metastatic melanoma with unknown primary were excluded.

Thus, only 202 patients with invasive cutaneous malignant melanoma were included in the final analysis. The stages of all invasive cutaneous malignant melanomas were revised according to the 8th edition of the AJCC staging system.

The following data were collected:

1. Clinical characteristics: age at diagnosis, gender, duration from disease onset to the first visit, and anatomic location
2. Histopathological characteristics: including Breslow thickness, ulceration, presence of microsatellites, satellites, locally recurrent or in-transit metastasis, presence of tumour in sentinel lymph node, *BRAF* mutation status and clinicopathological stage
3. Follow-up data: date of mortality, OS, MSS, and follow-up period

The date of mortality was identified by checking the date of expiration from the National Health Insurance Sharing Service. Although other potential prognostic factors, such as family or personal history of melanoma were noted, they were not included in this study owing to their rarity among the patient population. The data were analysed and 3- and 5-year OS/MSS were calculated.

The Kaplan–Meier method was used to draw survival curves to estimate the OS and MSS of invasive cutaneous malignant melanoma patients. The difference between survival curves was determined by a log-rank test calculating the corresponding p values. The Cox proportional hazard model was used for both univariate and multivariate analyses to estimate prognostic factors associated with MSS. The statistically significant factors in the univariate analysis were consecutively tested using multivariate analysis. All statistical analyses were performed using PASW Statistics 18 (Release Version

18.0.0, SPSS, Inc., 2009, Chicago, IL, www.spss.com) and $P < 0.05$ was considered significant.

Results

Clinicopathological characteristics

The clinicopathological details of the 202 patients in this study are summarised in Table 1. There were 104 males and 98 females and the male to female ratio was 1:0.94. The mean age was 61.5 years and the majority of patients (149; 73.8%) were aged between 51 and 80 years. The duration of the disease at presentation showed bimodal peaks at <1 year (47; 24.2%) and >10 years (50; 25.8%).

Table 1: Clinicopathological characteristics of 202 patients with invasive cutaneous malignant melanoma

		202 invasive cutaneous malignant melanomas (%)*
Follow-up (months)		69.7 ± 41.7
Sex (male:female)		104:98
Age		61.5 ± 13.6
Age	**≤30**	3 (1.5)
	31–40	13 (6.4)
	41–50	26 (12.9)
	51–60	47 (23.3)
	61–70	59 (29.2)
	71–80	43 (21.3)
	>80	11 (5.4)
Duration from disease onset to the first visit (years)		
	***n* < 1**	47 (24.2)
	1≤ *n* <2	28 (14.4)
	2≤ *n* <3	22 (11.3)
	3≤ *n* <5	30 (15.5)
	5≤ *n* <10	17 (8.8)
	***n* > 10**	50 (25.8)
	N/A[a]	8
Primary sites		
	Head and neck	31 (15.3)
	Upper extremities	9 (4.5)
	Hands	26 (12.9)
	└ Fingernail	14 (6.9)
	└ Others	12 (5.9)
	Lower extremities	11 (5.4)
	Feet	100 (49.5)
	└ Toenail	16 (7.9)
	└ Others	84 (41.6)
	Trunk	25 (12.4)
Breslow thickness (mm)		
	<0.8	12 (6.0)
	0.8-1	19 (9.5)
	1.01–2	32 (16.0)
	2.01–4	43 (21.5)
	>4	94 (47.0)
	N/A[a]	2
Ulceration		
	Positive	122 (60.7)
	Negative	79 (39.3)
	N/A[a]	1
MSI		
	Positive	29 (14.4)
	Negative	172 (85.6)
	N/A[a]	1
Presence of tumour in sentinel lymph node		
	Positive	34 (26.0)
	Negative	97 (74.0)
	N/A[a]	71
***BRAF* mutation**		
	Positive	11 (11.7)
	Negative	83 (88.3)
	N/A[a]	108
Clinicopathological subtype		
	ALM	125 (64.4)
	Non-SUM	95 (49.0)
	SUM	30 (15.5)
	SSM	41 (21.1)
	NM	21 (10.8)
	LMM	7 (3.6)
	N/A[a]	8

*Values are presented as mean ± standard deviation or number (%).
MSI: microsatellites, satellites, locally recurrent, and in-transit metastasis; ALM: acral lentiginous melanoma; SUM: subungual melanoma; SSM: superficial spreading melanoma; NM: nodular melanoma; LMM: lentigo maligna melanoma.
[a]N/A: not available, excluded in the calculation of percentages.

The melanomas were located on the hands and feet in 126 (62.4%) patients, with the feet alone accounting for 100 patients (49%). The most common clinicopathological subtype was acral lentiginous melanoma (125; 64.4%) and this included subungual melanomas (30; 15.5%) [Table 1]. A Breslow thickness of >4 mm was seen in 94 (47.0%) patients and visible or microscopical ulceration was noted in 122 (60.7%) patients at presentation. Microsatellites, satellites, locally recurrent or in-transit metastasis were observed in 29 (14.4%) patients. Sentinel lymph node biopsies were performed in 131 (64.9%) patients and sentinel node involvement was noted in 34 (26.0%) patients. Only 11 (11.7%) of the 94 (46.5%) patients in whom *BRAF* mutation analysis was performed had mutations. The average follow-up period was 69.7 months.

Overall survival and melanoma-specific survival

The OS/MSS of patients in this study are summarised in Table 2. The 3- and 5-year OS/MSS were 72.3%/77.6% and 64.4%/70.7%, respectively. Of the patients, 40 (19.8%), 84 (41.6%), 66 (32.7%) and 12 (5.9%) were categorised as stages I, II, III and IV, respectively. For stages I–IV, the 5-year OS was 94.7%, 67.2%, 54.4% and 0.0% and the 5-year MSS was 97.1%, 76.3%, 59.1% and 0.0%, respectively [Table 2].

Table 2: The 3- and 5-year survival rates of 202 patients with invasive cutaneous malignant melanoma in South Korea for stages following the 8th edition of AJCC staging system

	Stage	*N*	Overall survival		Melanoma-specific survival	
			3 years (%)	5 years (%)	3 years (%)	5 years (%)
Total	-	202	72.3	64.4	77.6	70.7
8th AJCC Stages I–IV	I	40	97.5	94.7	100	97.1
	II	84	76.2	67.2	83.8	76.3
	III	66	63.6	54.4	67.3	59.1
	IV	12	8.3	0.0	11.1	0.0
8th AJCC Substages IA–IV	IA	22	95.5	95.5	100	100
	IB	18	100	92.9	100	92.9
	IIA	18	83.3	83.3	88.5	88.5
	IIB	35	77.1	64.9	85.0	74.3
	IIC	31	71.0	60.4	79.5	70.9
	IIIA	3	66.7	66.7	-[a]	-[a]
	IIIB	11	100	90.9	100	90.9
	IIIC	36	66.7	57.8	70.8	64.4
	IIID	16	31.3	18.8	31.3	18.8
	IV	12	8.3	0.0	11.1	0.0

AJCC: American Joint Committee on Center; N: number of patients.
[a]Not calculated because all cases are censored.

Table 3: Univariate analyses of prognostic factors for melanoma-specific survival rates in patients with invasive cutaneous malignant melanoma

	Score	Degree of freedom	*p* value	Exp(B)
Age at diagnosis	4.603	1	0.032*	
Sex	4.615	1	0.032*	
Duration from disease onset to the first visit	0.079	1	0.779	
Primary sites	7.474	5	0.188	
Acral/nonacral area	0.655	1	0.418	
Clinicopathological subtype	1.161	3	0.762	
Breslow thickness	37.819	1	<0.001*	
Ulceration	24.131	1	<0.001*	
MSI	4.786	1	0.029*	
Presence of tumour in sentinel lymph node	17.182	1	<0.001*	
***BRAF* mutation**	0.107	1	0.743	
Clinicopathological stage	105.806	3	<0.001*	
Stage II	1.068	1	0.051	2.909
Stage III	1.904	1	<0.001*	6.714
Stage IV	3.882	1	<0.001*	48.520

*$p < 0.05$, statistically significant.
Exp(B): exponentiated coefficient; MSI: microsatellites, satellites, locally recurrent, and in-transit metastasis.

The median survival time for stages II, III and IV were estimated as 10.42 (7.62–13.21 years), 5.42 (2.75–8.09 years) and 0.83 (0.27–1.40 years) years, respectively. The median survival time for stage I could not be estimated because of the small number of mortalities. The OS and MSS according to substages following the 8th edition of the AJCC staging system are shown in Table 2. A considerable decrease in the 5-year MSS was observed between stages IIA (88.5%) and IIB (74.3%) [Table 2].

Prognostic factors associated with melanoma survival

Potential MSS prognostic factors in patients identified by univariate analyses were age at diagnosis, sex, Breslow thickness, ulceration, microsatellites, satellites, locally recurrent, and in-transit metastasis, presence of tumour in sentinel lymph node and clinicopathological stage but not acral distribution or *BRAF* mutation status [Table 3].

However, on multivariate analysis only Breslow thickness, ulceration, the clinicopathological stages, were found to be statistically significant independent prognostic factors [Table 4]. Stages IV was found to be independent prognostic factors but on grouping the substages, the MSS between stages I–IIA and IIB–IV were not statistically significant despite the abrupt drop in survival rate from stage IIB.

Table 4: Multivariate analyses of prognostic factors for melanoma-specific survival rates in patients with invasive cutaneous malignant melanoma

	B	SD	*p* value	Exp(B)
Breslow thickness	0.082	0.042	0.050*	1.086
Ulceration	1.082	0.535	0.043*	2.950
Clinicopathological stage			0.001*	
Stage II	0.189	0.841	0.823	1.208
Stage III	1.267	1.066	0.235	3.549
Stage IV	4.754	1.408	0.001*	116.103

*$p < 0.05$, statistically significant.
B: regression coefficient; SD: standard deviation; Exp(B): exponentiated coefficient.

Discussion

Studies have shown that Asians with cutaneous malignant melanoma have a poorer prognosis as compared with Caucasians.[4,6,8–13] In 2017, the American Cancer Society reported the 5-year MSS for stages I–III based on the 8th edition of the AJCC staging system. The survival rates were 99% for stage IA, 97% for stage IB, 94% for stage IIA, 87% for stage IIB, 82% for stage IIC, 93% for stage IIIA, 83% for stage IIIB, 69% for stage IIIC, and 32% for stage IIID [Table 5].[6] According to the Cancer Statistics 2020 report, the 5-year relative survival rate for cutaneous malignant melanoma with distant metastasis (stage IV) was 25%.[8] Previous reports on survival rates of cutaneous malignant melanoma patients in Asian countries such as Japan, China, Singapore, and Taiwan have consistently shown lower rates compared to those in Western countries [Table 5].[6,9–13] Our study confirms the poorer prognosis of Asian patients with cutaneous malignant melanoma.

Although both the Western report[6] and our current study showed a decrease in 5-year MSS between stages IIA and IIB, from 94 to 87% and from 88.5 to 74.3%, the decrease (7% vs 14.2%) is much greater in our study [Table 5]. We

Table 5: Summary of recent survival analyses for cutaneous malignant melanoma patients in Western and Asian countries following the staging criteria of the American Joint Committee on Center

	Patients' ethnicity	Study period	Edition of AJCC stages	Stage	*N*	Overall survival 5-year (%)	Stage	*N*	Melanoma-specific survival 5-year (%)
AJCC (2017)	USA, Europe, Australia	Beginning 1998	8th	–	–	–	IA	5,225	99
				–	–	–	IB	5,749	97
				–	–	–	IIA	2,338	94
				–	–	–	IIB	1,688	87
				–	–	–	IIC	691	82
				–	–	–	IIIA	1,006	93
				–	–	–	IIIB	1,170	83
				–	–	–	IIIC	2,201	69
				–	–	–	IIID	205	32
JSCS (2019)	Japan	2005–2017	7th	–	–	–	IA	483	98.0
				–	–	–	IB	316	93.9
				–	–	–	IIA	238	94.8
				–	–	–	IIB	260	82.4
				–	–	–	IIC	182	71.8
				–	–	–	IIIA	181	75
				–	–	–	IIIB	309	61.3
				–	–	–	IIIC	278	41.7
				–	–	–	IV	198	17.7
Yeo *et al*. (2021)	Singapore	1996-2015	7th	I	19	100			
				II	25	45.7			
				III	15	43.1			
				IV	1	–			
Zhang *et al*. (2017)	China	2001-2010	7th	I	8	37.5			
				II	31	32.3			
				III	44	0.0			
				IV	15	0.0			
Chi *et al*. (2011)	China	2006–2010	6th	I	32	94.1	–	–	–
				II	292	44.0	–	–	–
				III	131	38.4	–	–	–
				IV	67	4.6	–	–	–
Chang *et al*. (2004)	Taiwan	1992–2001	5th	I	47	84.4	–	–	–
				II	23	56.0	–	–	–
				III	58	34.7	–	–	–
				IV	43	0.0	–	–	–
This study (2021)	Korea	2006–2016	8th	I	40	94.7	IA	22	100
							IB	18	92.9
				II	84	67.2	IIA	18	88.5
							IIB	35	74.3
							IIC	31	70.9
				III	66	54.4	IIIA	3	–
							IIIB	11	90.9
							IIIC	36	64.4
							IIID	16	18.8
				IV	12	0.0	IV	12	0.0

AJCC: American Joint Committee on Center; JSCS: Japanese Skin Cancer Society; N: number of patients.

feel that adjuvant cancer therapy should also be administered in Korean patients with stages IIB and IIC. Also, and careful monitoring of the prognosis of stages IIB and IIC patients is necessary.

Earlier studies have associated tumour thickness, ulceration and advanced stage as factors contributing to the poor prognosis in Asian cutaneous malignant melanoma patients.[6,14] and our study confirms these as independent prognostic factors.

The reasons why Asian patients tend to present with more advanced stages of the disease are a matter of controversy. Some reports emphasised the predominant acral distribution as a major difference in ethnicities and suggested that the acral melanoma itself carries a worse prognosis due to its natural aggressive histopathologic features.[15,16] However, a Japanese study reported no survival difference between acral and non-acral melanoma patients,[17] and a recent Korean study noted a better prognosis in patients with acral melanoma than non-acral melanoma located on the trunk.[18] The acral location was not a prognostic factor in our study and acral melanomas may have a similar prognosis to malignant melanomas at other cutaneous sites if properly treated.

The sentinel lymph node biopsy is a widely accepted diagnostic procedure to determine nodal staging for cutaneous malignant melanoma patients and presence of tumour in sentinel lymph nodes is one of the important predictors of relapse-free survival and OS.[19] However, several recent reports have demonstrated that the presence of tumour in sentinel lymph nodes is not an independent predictive factor of relapse or survival,[20] and this was confirmed in our study too.

BRAF and *NRAS* mutations are anticancer targets in melanoma and may have prognostic value. *BRAF* and *NRAS* mutations are present in 80% of all sporadic melanomas in Caucasians. However, *BRAF* mutations were present in only 30.4%–41.8% in Japan, 25.5% in China, 14.3% in Taiwan, respectively and in 11.9–19.4% in Korea, and *NRAS* mutations were present in 12.3% in Japan, 7.2% in China, 10.1% in Taiwan and 12.6%in Korea.[4,18,21] Similarly in our study, the frequency of *BRAF* mutation was 11.7%. The lower frequency of *BRAF* and *NRAS* mutation in Asian patients with cutaneous malignant melanoma may result in a lower utility of immune checkpoint inhibitors (ICIs; vemurafenib, dabrafenib, or trametinib).[4,18]

Mutations in *BRAF* genes did not influence the prognosis in our study and conflicting results have been reported in previous studies.[22] Further studies with large number of patients will be needed to determine whether the *BRAF* mutation status, with or without ICI and *BRAF*/*MEK* inhibitor therapy, plays a significant role in prognosis of invasive cutaneous malignant melanoma.

In addition, the difference in the timing of the introduction of ICIs by each country could also be the other contributing prognostic factor. ICIs had started to gain approval from the Food and Drug Administration for metastatic melanoma treatment beginning 2011, [23] but the aforementioned survival studies in China and Taiwan were conducted before 2011. In Japan, the Ministry of Health, Labour and Welfare has approved coverage for ICIs beginning 2014,[24] and ICIs had gained approval from the Ministry of Food and Drug Safety in Korea beginning 2014 and have been subject to insurance benefits from 2017.[7] In this study, most of the stage IV patients did not receive ICI treatment, and the 5-year OS/MSS of stage IV was low like 0%/0% and this could be a factor responsible for the lower survival rate [Table 5].

Our study has several limitations. As it was a retrospective analysis conducted at a single institution in South Korea and involved a relatively small number of patients, it was not possible to estimate survival rates for patients with stage IIIA melanoma. Furthermore, the study only compared melanoma survival rates reported by different countries and failed to take into consideration crucial factors such as governmental insurance support and timing of the study, which could potentially influence the results. Lastly, the study identified a perplexing paradox where the MSS for stage IIIB was higher than that of stage II, and a similar pattern was observed in data from the American Cancer Society for IIC and IIIA in 2017 [Table 5]. The reason behind this survival paradox is not apparent and requires further investigation through future studies to determine a more realistic survival rate according to the AJCC staging system.

Conclusion

This study presents 5-year OS and MSS as reference values for estimating survival rates of invasive cutaneous malignant melanoma patients in South Korea and showed that the prognosis was worse than that of Caucasians. In addition to already well-verified Breslow thickness and ulceration, the impact of tumour location and sentinel nodal metastasis on MSS should be reconsidered to better understand the prognosis of invasive cutaneous malignant melanoma patients in South Korea.

Declaration of patient consent

Institutional Review Board (IRB) permission obtained for the study.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. International Agency for Research on Cancer. Global Cancer Observatory. Globocan 2020. Melanoma of skin. Available from: https://gco.iarc.fr/today/fact-sheets-cancers.
2. Ferlay J, Soerjomataram I, Dikshit R, *et al*. Cancer incidence and mortality worldwide: Sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer 2015;136:e359–86.
3. TaeHo Kim, Siyeong Yoon, Dong-Eun Shin, *et al*. Incidence and survival rates of cutaneous melanoma in South Korea using national health insurance claims data. Cancer Res Treat 2021 Sep 30. doi: 10.4143/crt.2021.871. Epub ahead of print.
4. Chang JW, Guo J, Hung CY, *et al*. Sunrise in melanoma management: time to focus on melanoma burden in Asia. Asia-Pac J Clin Oncol 2017;13:423–7.
5. Cormier JN, Xing Y, Ding M, *et al*. Ethnic differences among patients with cutaneous melanoma. Arch Intern Med 2006;166:1907–14.
6. Gershenwald JE, Scolyer RA, Hess KR, *et al*. Melanoma staging: evidence-based changes in the American Joint Committee on Cancer eighth edition cancer staging manual. CA Cancer J Clin 2017;67:472–92.

7. Yang H-J, Park H-Y, Jeon SM, Kwon J-W. Survival and economic burden of melanoma: a retrospective cohort analysis in South Korea. Yakhak Hoeji 2020;64:257–64.
8. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2020. CA Cancer J Clin 2020;70:7–30.
9. Fujisawa Y, Yoshikawa S, Minagawa A, *et al*. Clinical and histopathological characteristics and survival analysis of 4594 Japanese patients with melanoma. Cancer Medicine 2019;8:2146–56.
10. Yeo PM, Lim ZV, Tan WD, *et al*. Melanoma in Singapore: a 20-year review of disease and treatment outcomes. Ann Acad Med Singap 2021;50:456–66.
11. Zhang M, Zhang N. Clinical and prognostic factors in 98 patients with malignant melanoma in China. J Int Med Res 2017;45:1369–77.
12. Chi Z, Li S, Sheng X, *et al*. Clinical presentation, histology, and prognoses of malignant melanoma in ethnic Chinese: a study of 522 consecutive cases. BMC Cancer 2011;11:85.
13. Chang JW, Yeh KY, Wang CH, *et al*. Malignant melanoma in Taiwan: a prognostic study of 181 cases. Melanoma Res 2004;14:537–41.
14. Balch CM, Soong SJ, Gershenwald JE, *et al*. Prognostic factors analysis of 17,600 melanoma patients: validation of the American Joint Committee on Cancer melanoma staging system. J Clin Oncol 2001;19:3622–34.
15. Bello DM, Chou JF, Panageas KS, *et al*. Prognosis of acral melanoma: a series of 281 patients. Ann Surg Oncol 2013;20:3618–25.
16. Bradford PT, Goldstein AM, McMaster ML, Tucker MA. Acral lentiginous melanoma: incidence and survival patterns in the United States, 1986-2005. Arch Dermatol 2009;145;427–34.
17. Wada M, Ito T, Tsuji G, *et al*. Acral lentiginous melanoma versus other melanoma: a single-center analysis in Japan. J Dermatol 2017;44:932–8.
18. Lim Y, Lee J, Lee D-Y. Is the survival rate for acral melanoma actually worse than other cutaneous melanomas? J Dermatol 2020;47:251–6.
19. Chen J, Xu Y, Zhou Y, Wang Y, Zhu H, Shi Y. Prognostic role of sentinel lymph node biopsy for patients with cutaneous melanoma: a retrospective study of surveillance, epidemiology, and end-result population-based data. Oncotarget 2016;7:45671–7
20. Portinari M, Baldini G, Guidoboni M, *et al*. The long-term prognostic impact of sentinel lymph node biopsy in patients with primary cutaneous melanoma: a prospective study with 10-year follow-up. Ann Surg Treat Res 2018;95:286–96.
21 Uhara H, Ashida A, Koga H, *et al*. *NRAS* mutations in primary and metastatic melanomas of Japanese patients. Int J Clin Oncol 2013;19:544–8.
22. Choi DY, Lee SP, Park S. Prevalence of *BRAF* and *NRAS* mutations and a comparative analysis in primary and metastatic melanoma of Korea patients. Ewha Med J 2014;37:30–5.
23. Fujisawa Y, Ito T, Kato H, *et al*. Outcome of combination therapy using *BRAF* and MEK inhibitors among Asian patients with advanced melanoma: an analysis of 112 cases. Eur J Cancer 2021;145:210–20.
24. Namikawa K, Yamazaki N. Targeted therapy and immunotherapy for melanoma in Japan. Curr Treat Options Oncol 2019;20:7.