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Prognostic analysis of
malignant melanoma according to the
surgical protocols

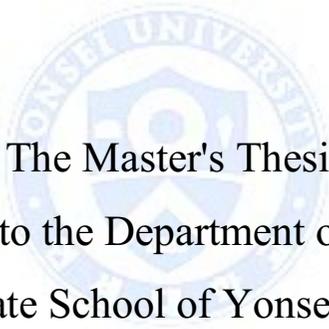


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Prognostic analysis of
malignant melanoma according to the
surgical protocols

Directed by Professor Kee Yang Chung

The logo of Yonsei University is a circular seal with a blue border containing the text 'YONSEI UNIVERSITY'. Inside the seal is a shield with a blue and white design, including a stylized figure and a book.

The Master's Thesis
submitted to the Department of Medicine,
the Graduate School of Yonsei University
in partial fulfillment of the requirements for the degree
of Master of Medical Science

Jimyung Seo

December 2015

This certifies that the Master's Thesis of
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ABSTRACT

Prognostic analysis of malignant melanoma according to the surgical protocols

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(Directed by Professor Kee Yang Chung)

Background: The importance of melanoma has recently been brought to light due to increasing incidence and the difficulty to treat in advanced stage of this disease. However, there is a paucity of reported data regarding melanoma behavior in Korea.

Methods: In a total of 423 melanoma patients, with 267 of them receiving a surgical treatment from 2005 to 2014 at Severance Hospital, the clinicopathologic characteristics of malignant melanoma and prognostic outcomes according to different surgical procedures were analyzed, retrospectively.

Results: When we compared the overall survival in four main types of cutaneous melanoma, nodular melanoma showed the worst prognosis, followed by acral lentiginous melanoma (ALM). Histologic subtype

significantly influenced overall survival ($p < 0.001$). Two hundred thirty patients with cutaneous melanoma were treated with conventional wide local excision, and 37 patients underwent slow Mohs procedures due to skin preservation, incompletely excised or recurred melanoma, difficult anatomical site, and unclear surgical margin. The follow-up analysis showed that slow Mohs surgery can be another efficacious for treating cutaneous melanomas, which have radial growth phase features and high-risk characteristics, with maximum conservation of surrounding tissue. In analysis of 62 patients with ALM of 1.01 to 2.0 mm thickness, wide excision with 1 versus 2 cm margins revealed no significant difference in the outcome analysis; no significant difference was observed in the frequency of total recurrence and death attributed to melanoma between the two groups ($p = 0.721$ and 0.623 , respectively).

Conclusion: The results of the present study will be an important contributor towards our understanding and treating the disease.

Key words : malignant melanoma; acral lentiginous melanoma; margin of excision; mohs micrographic surgery; wide local excision

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I. INTRODUCTION

Due to the increasing incidence, malignant melanoma has received considerable attention and has emerged as a leading cause of death among skin cancers.¹ Conventionally, cutaneous melanoma has been distinguished by four main types based on their morphology and histology; superficial spreading melanoma (SSM), lentigo maligna melanoma (LMM), nodular melanoma (NM), and acral lentiginous melanoma (ALM) by the World Health Organization (WHO) classification.^{2,3} Mucosal melanoma (MM) is another common variant other than cutaneous melanoma.³ Various clinicopathologic factors such as the proportion of melanoma subtypes and tumor behaviors are different in darker-pigmented individuals.^{3,4} In patients with skin of color, ALM might be particularly important because it represents a disproportionately high incidence and carries a worse prognosis than other subtypes.⁵

The primary treatment modality for cutaneous melanoma is surgical excision.⁶ There are an increasing number of patients who are diagnosed and surgically treated in early phase of the disease due to increased public awareness on the early detection of melanoma.^{4,7} However, there is a paucity of reported data on recurrence and survival outcomes after surgical treatment of melanoma in Korea.

In recent years, the utilizations of Mohs micrographic surgery (MMS) for the treatment of melanomas appear to be increasing.¹ MMS is a tissue-preserving surgical procedure that is widely used for recurrent and infiltrative nonmelanoma skin cancers.⁸ Even though wide local excision (WLE) is considered as a standard of therapy for primary cutaneous melanoma, MMS may have potential advantages for increasing cure rates in melanomas with features of radial growth phase. Therefore, more studies are needed to evaluate the effectiveness of MMS in the treatment of melanomas.

Furthermore, based on standard melanoma treatment guidelines, primary cutaneous melanomas of 1.01 to 2.0 mm thickness are widely excised with 1 to 2 cm margins.⁶ However, clear evidence is not available and most of the trials generally did not study melanoma of the digits or subungual (beneath fingernails or toenails) locations.^{6,9} ALM, which has a worse prognosis than other types of melanoma, might need wider excision to prevent recurrence. Current surgical margin recommendations for primary melanoma are uniform for all histosubtypes, and no study has explored whether 1 or 2 cm excision

margins for ALM of 1.01 to 2.0mm thickness would result in different outcomes.

The aims of this study were to investigate the clinicopathologic characteristics of malignant melanoma in Korean patients and to analyze recurrence and survival outcomes according to different surgical procedures.



II. MATERIALS AND METHODS

1. Patient Group

A retrospective study was performed using the Clinical Data Retrieving System and melanoma registry (Yonsei University College of Medicine, Severance Hospital, Seoul, Korea), which contained a total of 423 melanoma patients diagnosed during January 2005 to December 2014. Clinical and demographic data, including age at first melanoma diagnosis, sex, anatomic site of melanoma, and American Joint Committee on Cancer (AJCC) stage at diagnosis, were recorded for each patient. All patients underwent a sentinel node biopsy if indicated by NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) for melanoma.¹⁰ This study demonstrated (1) clinicopathologic characteristics of malignant melanoma in Korean patients (n = 423), (2) outcome analysis of patients receiving surgical excision (MMS versus WLE) for the treatment of cutaneous melanoma (n = 267), and (3) comparison of 1 versus 2 cm excision margins for localized T2 ALM that was 1.01 to 2.0 mm thickness and node-negative (n = 62) (Fig. 1).

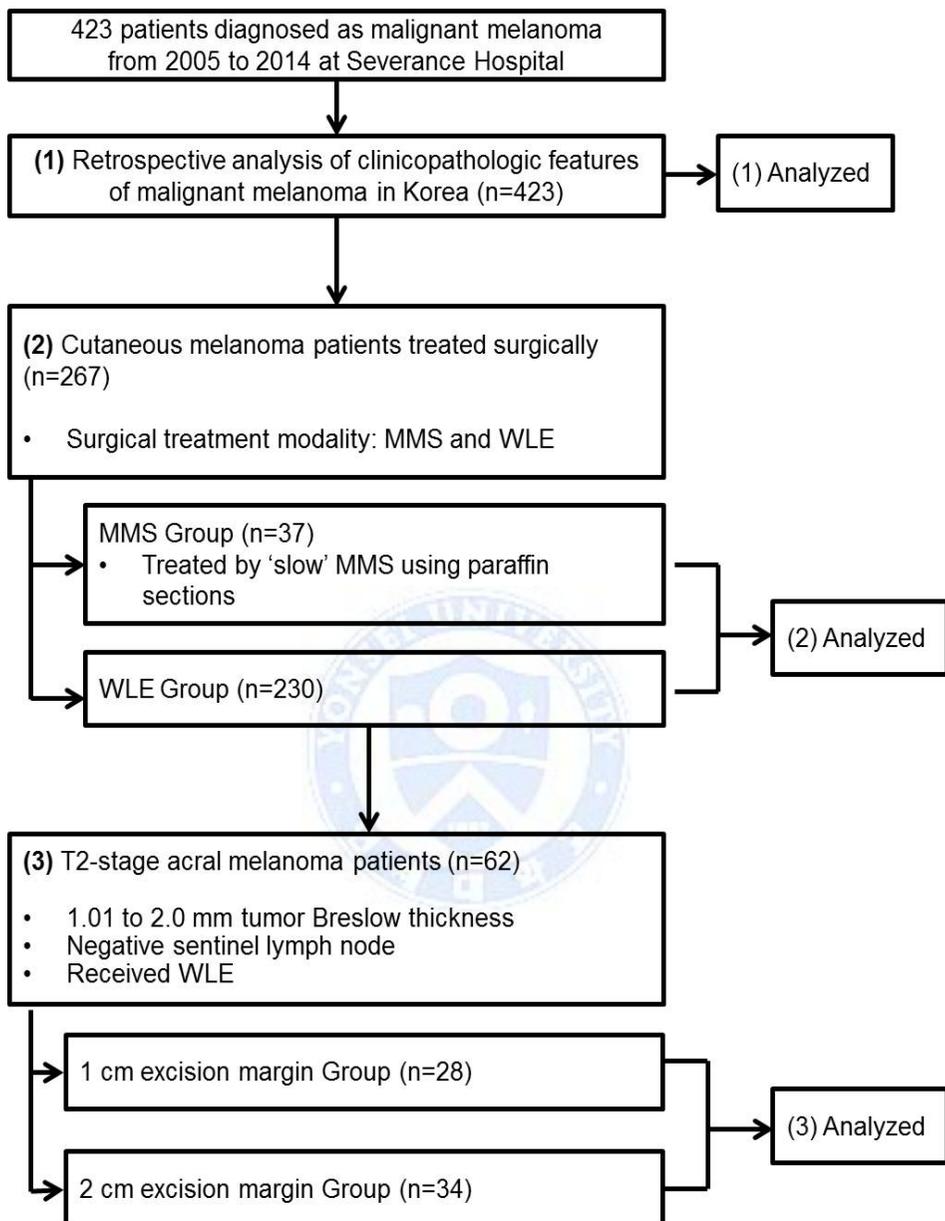


Figure 1. Study overview

2. WLE and MMS Methods

Wide excisions with 0.5 to 2.0 cm margins were performed, depending on the maximum Breslow thickness of the tumor. Based on available evidence and consensus opinion, specific surgical margin recommendations for primary invasive melanoma are shown in Table 1.^{6,9,11} For melanoma in situ, wide excision with 0.5 cm margin was performed. Melanomas \leq 1mm thick underwent tumor excision with 1 cm margin and melanomas $>$ 2mm thick underwent excision with 2 cm margin. For melanomas of 1.01 to 2.0 mm thickness, excision with 1.0 to 2.0 cm margin was performed.

MMS was performed using paraffin-embedded sections. The tumor was removed with an average of 5 mm of clinically normal surrounding tissue as the first layer. Tissue was divided into multiple specimens that were mapped and color coded for precise anatomical orientation and sent for formalin-fixed, paraffin-embedded sections and stained with haematoxylin and eosin, i.e. slow Mohs.^{12,13} Staining with S-100 protein, HMB45, and Melan-A was performed, if needed.

Table 1. Surgical margin recommendations for primary cutaneous melanoma

Tumor thickness (mm)	Excision margin (cm)
In situ	0.5 cm
≤ 1.0 mm	1.0 cm
1.01 - 2.0 mm	1.0 - 2.0 cm
> 2.0 mm	2.0 cm



3. Prognosis evaluation

Local recurrence rates, locoregional and distant metastases, death attributed to melanoma, disease-free survival and overall survival were calculated. In the present study, local recurrence was defined as either persistent disease caused by inadequate excision or true recurrence adjacent to the scar after adequate prior excision. Locoregional recurrence represented recurrence at the site of primary lesion, regionally in the draining lymph node basin, or anywhere in between. Local recurrence cases were not included in locoregional recurrence cases. Spreading from the original tumor to distant organs or distant lymph nodes was considered as distant metastases.¹⁴⁻¹⁶

4. Statistical analysis

All the statistical analyses were performed using SPSS 19.0 software (SPSS, Chicago, IL). Categorical data are described using frequencies and percentages. Continuous data such as age are described using means \pm standard deviations or median (range) for normally distributed data. χ^2 test or Fisher's exact test was used to differentiate the rates of different groups, and differences in measurement data of two groups were evaluated by unpaired *t*-test. Survival curves were established using the Kaplan–Meier method and compared by the log rank test. Univariate analysis was performed using Cox proportional hazard model to identify prognostic factors for disease-free and overall survival. All statistical analyses were two-sided, and significance was set at $p < 0.05$.

III. RESULTS

1. Characteristics of the study population

The study population consisted of 423 patients diagnosed with malignant melanoma from 2005 to 2014 at Severance Hospital. The detailed demographic and clinicopathological characteristics of our patients are summarized in Table 2. The most common histopathological subtype was ALM (n = 193, 45.6%) followed by NM (n = 74, 17.5%), SSM (n = 70, 16.5%), MM (n = 39, 9.2%) and LMM (n = 14, 3.3%). Further, the feet and toes were the most frequent primary tumor location (n = 175, 41.4%). A statistically significant decrease in overall survival was seen according to melanoma subtypes, shown in Fig.2 ($p < 0.001$). NM showed the worst prognosis, followed by ALM. With respect to stage distribution pattern, 51 patients (12.1%) showed melanoma in situ. 207 patients (49.0%) had early stage melanomas (stages I and II) and 165 patients (38.9%) were in advanced stage (stages III and IV). 159 patients (37.6%) presented with positive sentinel lymph node biopsy specimens, and death was attributable to melanoma in 139 patients (32.7%). Median follow-up duration was 41.3 ± 28.1 months (range, 6-120).

Table 2. Clinicopathologic characteristics of 423 patients with melanoma

Factors	Melanoma patients (n = 423)
Age (years \pm SD)	58.3 \pm 13.9
Gender (no. (%) of patients)	
Male	200 (47.3)
Female	223 (52.7)
Primary site (no. (%) of patients)	
Head and neck	89 (21.0)
Upper extremities	19 (4.5)
Hands and fingers	46 (10.9)
Lower extremities	36 (8.5)
Feet and Toes	175 (41.4)
Trunk	58 (13.7)
Histopathological stages (no. (%) of patients)	
ALM	193 (45.6)
SSM	70 (16.5)
LMM	14 (3.3)
NM	74 (17.5)
MM	39 (9.2)
Unclassified	33 (7.8)
Stage	
Melanoma in situ	51 (12.1)
I	106 (25.1)
II	101 (23.9)
III	92 (21.7)
IV	73 (17.3)
Positive sentinel lymph node	
Yes	159 (37.6)
No	264 (62.4)
Median follow-up (months \pm SD)	41.3 \pm 28.1

ALM, acral lentiginous melanoma; SSM, superficial spreading melanoma; LMM, lentigo maligna melanoma; NM, nodular melanoma; MM, mucosal melanoma; SD, standard deviation.

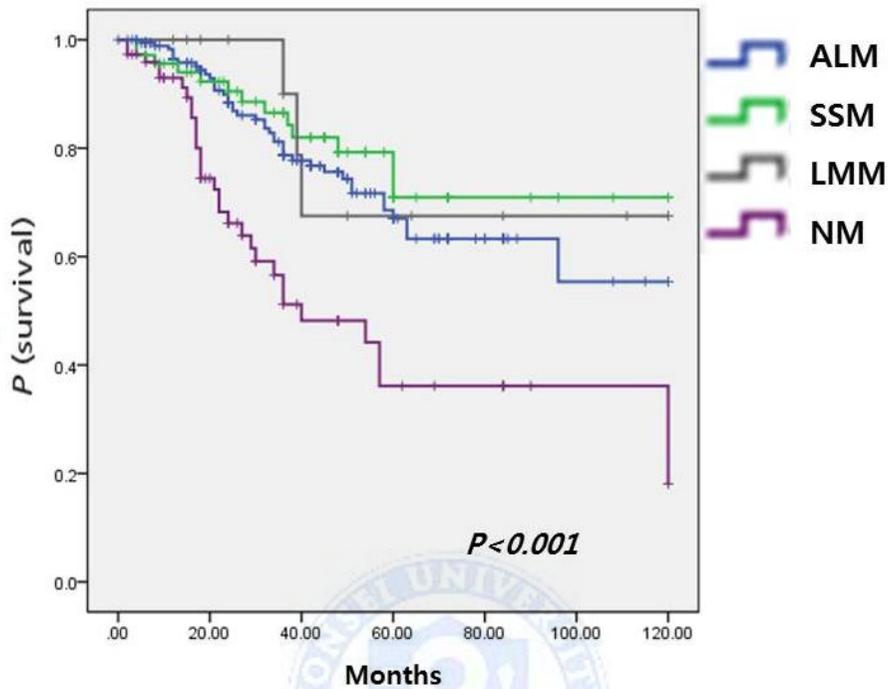


Figure 2. Overall survival of melanoma patients in relation to histologic subtype

2. MMS versus WLE

Of a total of 423 melanoma patients, 267 patients (115 male, 152 female) with cutaneous melanoma were treated surgically at our dermatology department between 2005 to 2014; 230 patients (86.1%) underwent wide excision and 37 patients (13.9%) were treated with slow Mohs surgery. Features of the 267 patients treated with WLE or MMS are summarized in Table 3. Mean number of stages of MMS for clearance was 1.8 (range; 1-4), whereas 19 patients (19/230, 8.2%) who underwent WLE with a positive histological margin had to undergo a second excision for complete removal. Median follow-up duration was 42.5 ± 27.8 months (range, 6-120).

Histopathological subtypes of melanomas treated with MMS are shown in Fig. 3. MMS was mainly used for treating cutaneous melanomas with radial growth phase features, especially ALM. Fig. 4 demonstrates the reasons for our Mohs surgery. Preservation of surrounding normal skin was the most common reason, representing 45.9% (n = 17) of the 37 patients treated with MMS. Of these 17 patients, 11 patients had melanoma involving palm and sole. The remaining six patients had subungual melanoma (n = 5) and melanoma located on the eyelid (n = 1). Other reasons for MMS included incomplete excision before referral to our clinic (n = 8, 21.6%), recurrence (n = 6, 16.2%), difficult anatomical sites such as finger, genitalia, eyebrow and scalp (n = 5, 13.5%), and unclear surgical margin due to infection and ulceration (n = 1, 2.7%).

Each treatment group showed no significant difference in stage distribution of primary melanoma ($p = 0.106$). When we compared recurrence and survival between the MMS group and the WLE group, more frequent recurrences of melanoma were observed in the WLE group (18.9% vs 26.5%). However, no significant differences were found in total recurrence ($p = 0.325$), local recurrence ($p = 0.870$), locoregional metastases ($p = 0.953$), and distant metastases ($p = 0.150$). In addition, there was no significant difference in death attributable to melanoma between the two group ($p = 0.228$) (Table 4). Furthermore, Kaplan-Meier methods for overall and disease-free survival according to surgical types did not find a significant difference between the two groups ($p = 0.620$ and $p = 0.430$, respectively), shown in Fig. 5. In Cox regression analysis of the patients treated with WLE versus MMS, the estimated hazard ratios for overall and disease-free survival were 0.846 (95% CI, 0.255-2.811) and 0.726 (95% CI, 0.328-1.604), shown in Table 5.

Table 3. Patient characteristics treated by Mohs micrographic surgery and wide local excision

Factors	Melanoma patients (n = 267)
Age (years \pm SD)	58.2 \pm 14.1
Gender (no. (%) of patients)	
Male	115 (43.1)
Female	152 (56.9)
Treatment (no. (%) of patients)	
MMS	37 (13.9)
WLE	230 (86.1)
Primary site (no. (%) of patients)	
Head and neck	23 (8.6)
Upper extremities	15 (5.6)
Hands and fingers	30 (11.2)
Lower extremities	26 (9.7)
Feet and Toes	143 (53.6)
Trunk	30 (11.2)
Histopathological stages (no. (%) of patients)	
ALM	146 (54.7)
SSM	57 (21.3)
LMM	10 (3.7)
NM	51 (19.1)
Other †	3 (1.1)
Stage (no. (%) of patients)	
Melanoma in situ	48 (18.0)
I	96 (36.0)
II	73 (27.3)
III	50 (18.7)
Positive sentinel lymph node (no. (%) of patients)	
Yes	50 (18.7)
No	217 (81.3)
Median follow-up (months \pm SD)	42.5 \pm 27.8
No. of Mohs stage (mean \pm SD, range)	1.8 \pm 0.9 (1-4)

ALM, acral lentiginous melanoma; SSM, superficial spreading melanoma; LMM, lentigo maligna melanoma; NM, nodular melanoma; SD, standard deviation

†Three patients with desmoplastic melanoma were included.

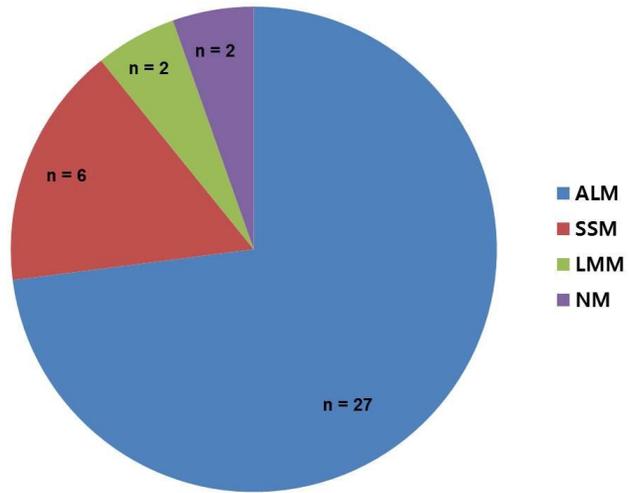


Figure 3. Histopathological subtype of melanomas treated with Mohs surgery

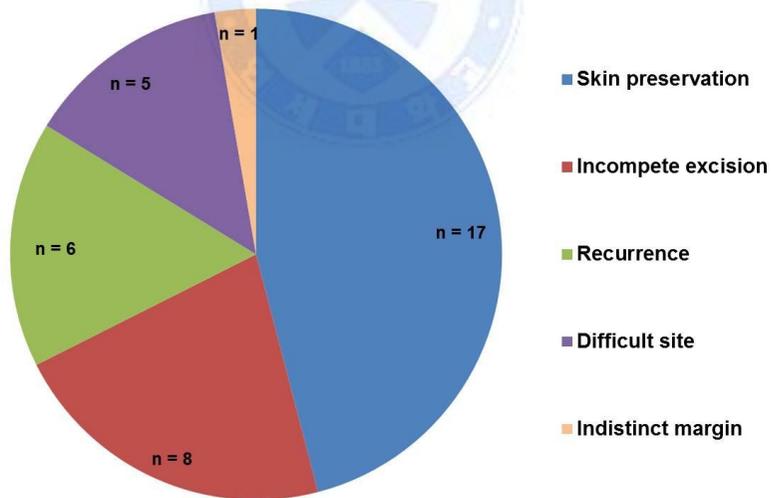


Figure 4. Reason for Mohs surgery

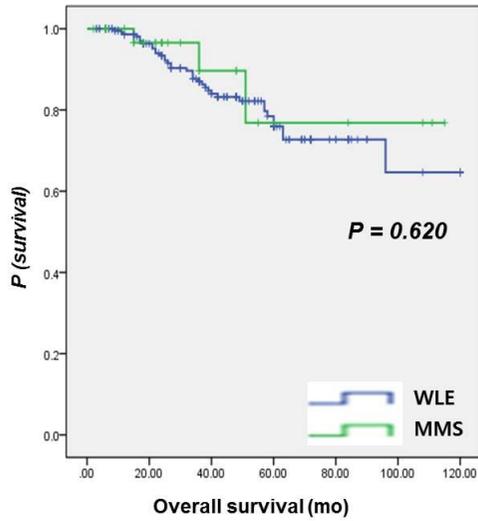
Table 4. Recurrence and survival data according to surgical types

Characteristics, no. (%)	Type of surgery		<i>P</i> -value ^a
	MMS (n = 37)	WLE (n = 230)	
Recurrence	7 (18.9)	61 (26.5)	0.325
Local recurrence	2 (5.4)	11 (4.8)	0.870
Locoregional metastases	3 (8.1)	18 (7.8)	0.953
Distant metastases	2 (5.4)	32 (13.9)	0.150
Death attributed to melanoma	3 (8.1)	36 (15.7)	0.228
Stage distribution pattern			
Tis	12 (32.4)	36 (15.7)	
I	11 (29.7)	85 (37.0)	
II	8 (21.6)	65 (28.3)	0.106
III	6 (16.2)	44 (19.1)	

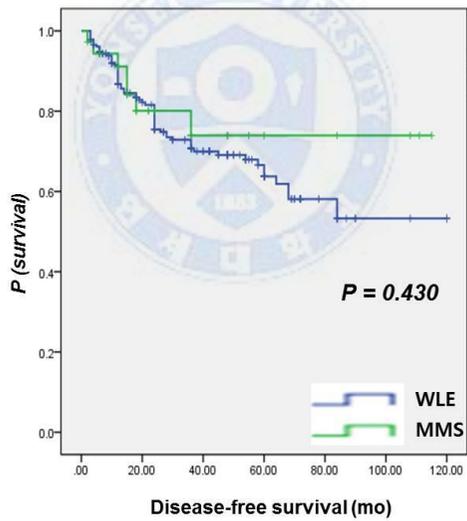
MMS, Mohs micrographic surgery; WLE, wide local excision

*Differences were considered statistically significant at $p < 0.05$.

^a χ^2 test for total recurrence, death attributed to melanoma, and stage distribution pattern; Fisher's exact test for local recurrence, locoregional metastases, and distant metastases.



(a) Overall survival according to surgical types



(b) Disease-free survival according to surgical types

Figure 5. Kaplan-Meier curves for disease-free and overall survival according to surgical types

Table 5. Univariate analysis of factors in patients with cutaneous melanoma who underwent surgical excision

Factor	Overall survival		Disease-free survival	
	HR (95% CI)	P-value	HR (95% CI)	P-value
Age (years)	1.024 (0.997-1.051)	0.077	0.998 (0.980-1.015)	0.778
Sex (male vs female)	0.426 (0.217-0.836)	0.013*	0.618 (0.381-1.001)	0.050
Primary site (hand and foot vs others)	0.497 (0.202-1.225)	0.129	0.619 (0.322-1.191)	0.151
Histopathological subtype (ALM vs others)	1.229 (0.577-2.617)	0.593	1.417 (0.796-2.525)	0.236
Stage (Tis/I/II vs III/IV)	5.441 (2.696-10.979)	<0.001*	3.170 (1.861-5.400)	<0.001*
Surgical type (WLE vs MMS)	0.846 (0.255-2.811)	0.785	0.726 (0.328-1.604)	0.428

ALM, acral lentiginous melanoma; MMS, Mohs micrographic surgery; WLE, wide local excision

*Differences were considered statistically significant at $p < 0.05$.

3. 1 versus 2 cm excision margins in T2 ALM patients

Of all 423 patients with malignant melanoma who visited our dermatology clinic, 62 patients (27 male, 35 female) with ALM of 1.01 to 2.0 mm thickness fulfilled the inclusion criteria. Mean patient age was 60.0 ± 14.9 years (range, 17-89 years). All patients presented with negative sentinel lymph node biopsy specimens, and were included in acral melanoma stage IB ($n = 38, 61.3\%$) and IIA ($n = 24, 38.7\%$) depending on the presence of ulceration. Fifteen cases (24.1%) in this series were located on the hands and fingers, whereas 47 cases (75.8%) were located on the feet and toes. Median follow-up duration was 41.2 ± 24.8 months (range, 6-120).

Of a total of 62 patients, 28 patients underwent tumor excision with a 1 cm skin margin and the tumors of the other 34 patients were excised with a 2 cm margin. The margins were decided according to the anatomical feasibility and the patients' general condition. Ulceration and mean Breslow thickness of the tumor were not significantly different between the two groups.

Recurrence and metastases occurred in 13 patients (20.9%). Even though recurrence was observed more frequently in the 1 cm group, there were no significant differences in the frequency of total recurrence ($p = 0.479$), local recurrence ($p = 0.890$), locoregional metastases ($p = 0.890$), and distant metastases ($p = 0.501$) during the follow-up period. In addition, with respect to death attributable to melanoma, no significant difference was observed between the two groups (10.7% vs 11.8%, $p = 0.897$), shown in Table 6. Kaplan-Meier

curve for disease-free survival according to tumor excision margin also failed to show a significant difference between the 1 and 2 cm groups ($p = 0.379$), shown in Fig. 6.

Furthermore, we performed additional analysis to identify how the patients including positive sentinel lymph node relate to treatment outcomes. Four patients treated with 1 cm excision margin and another four patients treated with 2 cm excision margin had ALM of 1.01 to 2.0 mm thickness with presence of tumor cells in sentinel lymph node, and were added to the original 62 patients with T2-stage ALM. Re-analysis was performed in 70 patients. The results of our further analysis also showed that there was no significant difference in both total recurrence and death attributed melanoma between the 1cm and 2cm margin groups ($p = 0.721$ and $p = 0.623$, respectively) (data not shown).

Table 6. Follow-up characteristics of patients with localized T2-stage acral lentiginous melanoma

Characteristics, no. (%)	Margin of surgery		P-value ^a
	1 cm (n = 28)	2 cm (n = 34)	
Recurrence	7 (25.0)	6 (17.6)	0.479
Local recurrence	1 (3.6)	1 (2.9)	0.890
Locoregional metastases	1 (3.6)	1 (2.9)	0.890
Distant metastases	5 (17.8)	4 (11.8)	0.501
Death attributed to melanoma	3 (10.7)	4 (11.8)	0.897
Mean Breslow thickness	1.38 ± 0.27	1.56 ± 0.29	0.907
Ulceration	13 (46.4)	11 (32.4)	0.257

^a χ^2 test for recurrence and ulceration; Fisher's exact test for local recurrence, locoregional metastases, distant metastases, and death attributed to melanoma; unpaired t-test for mean Breslow thickness.

No statistically significant difference was observed between the two groups.

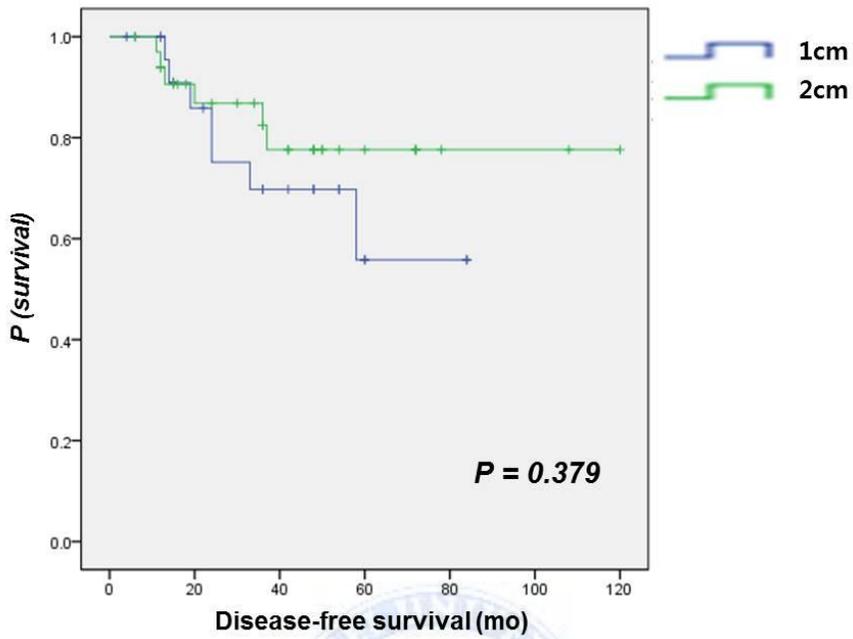


Figure 6. Kaplan-Meier curve for disease-free survival in localized T2 acral lentiginous melanoma

IV. DISCUSSION

The importance of melanoma has recently been brought to light due to increasing incidence and the difficulty to treat in advanced stage of this disease.^{3,17,18} However, there is a paucity of reported data regarding melanoma behavior in Korea. To the best of our knowledge, this is the largest study with melanoma cases treated at a single institution and the first study analyzing prognostic differences according to surgical modality in Korea. This study showed (1) clinicopathologic features of patients with melanoma, (2) a follow-up result of cutaneous melanoma patients after MMS and WLE, and (3) a comparison of important outcome parameters according to 1 versus 2 cm excision margin in T2 ALM patients.

In this study, ALM (45.6%) represented the most common subtype in Korean melanoma patients, followed by NM (17.5%), SSM (16.5%), MM (9.2%) and LMM (3.3%). The incidence of ALM was slightly lower than that of previous reports.^{19,20} This is because the study population in our study included melanomas occurring from the mucosa and unclassified melanoma cases such as desmoplastic melanoma and melanoma of unknown primary origin. Anatomical sites involved were similar to those in previous Korean studies: the feet and hands (52.3%) were the most commonly involved sites. When we compared the overall survival in four main types of cutaneous melanoma, NM showed the worst prognosis, followed by ALM. In addition, in terms of overall

survival, histologic subtypes significantly influenced follow-up result ($p < 0.001$).

Recent studies have shown that use of MMS for melanoma appears to be increasing.^{1,21} However, MMS for the treatment of melanoma still remains controversial because of the challenge of assessing melanocyte atypia in frozen sections.^{22,23} Despite the development of novel and highly specific stains or the use of immunohistochemical staining in frozen sections,^{1,22} there are a number of concerns of MMS for melanoma treatment. In our facility, we use the paraffin-embedded technique rather than frozen sections. MMS using paraffin-embedded sections (slow MMS) is a more time consuming process but is able to improve assessment of tumor clearance. Even though the results in our study showed no statistically significant difference in outcome parameters such as recurrence and death attributed to melanoma between the MMS group and WLE group, there was a lower risk of recurrence in patients treated by MMS. Furthermore, it is important to recognize that the MMS-treated melanomas were tumors with higher-risk characteristics, and the anatomic sites were considered more challenging. Therefore, both MMS and WLE can be an efficacious treatment option for treating cutaneous melanoma and factors such as tumor characteristics, tumor location, tumor size and closure options should be considered before choosing a surgical modality.

As mentioned above, the main drawback of MMS using paraffin sections is time. Another potential limitation is the discomfort from open wounds until the

tumor is completely cleared. However, as the most common subtype of melanoma in our facility is ALM which usually occurs on the difficult site for reconstruction and therefore we prefer secondary intention healing to restore surgical defects,⁴ MMS has provided a valuable contribution in that it ensures completeness of tumor excision with the smallest skin defect. As the present analysis has limitations in the selection of patients from a single institution and being a retrospective design, large prospective studies in the future might lead to qualify treatment outcomes of MMS for cutaneous melanomas.

Our investigation also addressed the outcome of patients with ALM of 1.01 to 2.0 mm thickness after treatment using 1 versus 2 cm excision margins. Selection of an adequate excision margin is very important for managing primary cutaneous melanoma. However, current guidelines for surgical treatment of melanoma are uniform for all histosubtypes, and no study to date has directly compared 1 versus 2 cm margins in melanoma with 1.01 to 2.0 mm thickness.^{14,24} Because ALM is well known to have a worse prognosis than other types of melanoma, we wanted to evaluate whether 1 or 2 cm excision margins for ALM (1.01 – 2.0 mm) would result in different outcomes. To minimize the effect of other variables, patients with positive sentinel lymph node biopsy specimens were excluded in this comparison first. Evaluation of important outcome parameters revealed that there was no significant difference in the frequency of locoregional and distant metastasis and disease-free survival between the two groups. Our ancillary analysis also failed to find significant

differences in total recurrence and death attributed melanoma, although we were able to add a limited number of patients for whom ALM with 1.01 to 2.0mm thickness was diagnosed with positive sentinel lymph node. This suggests that excision of T2 stage ALM with 1 cm excision margin may be safe and result in a comparable outcome to 2 cm excision margin. However, as there was a higher risk of recurrence in the patients with 1 cm excision margins, a prospective, randomized, longitudinal study is necessary to overcome this issue.



V. CONCLUSION

In conclusion, this study demonstrated the clinicopathologic characteristics of melanomas and long-term follow-up results of patients who underwent surgical excision. Acral melanoma was the most common subtype and histologic subtypes significantly influenced follow-up result. Regarding surgical treatment, slow MMS seems to be an efficacious option for treating cutaneous melanomas with radial growth phase features. In addition, ALM patients who underwent WLE with 1 or 2 cm margins revealed no significant difference in the outcome analysis. Because there is a lack of information regarding clinicopathologic behavior of melanomas of acral subtype, the results of the present study will be an important contributor towards our understanding and treating the disease.

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ABSTRACT (IN KOREAN)

악성 흑색종의 수술 방법에 따른 예후 분석

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서 지 명

배경 : 최근 흑색종의 발생 빈도 증가와 함께 조기에 수술적 치료를 받는 환자들이 증가하고 있다. 하지만 임상조직학적 특성 및 예후와 관련된 국내 자료가 부족한 상황이며 서구의 연구 결과를 우리나라에 적용하기에는 인종적 차이로 한계가 있다. 본 연구에서는 한국인의 악성 흑색종에서 임상적, 조직학적 특성을 확인하고, 수술적 치료법에 따른 예후의 차이를 분석하고자 하였다.

방법 : 2005년부터 2014년까지 연세의료원을 방문하여 악성 흑색종으로 진단된 환자 423명을 대상으로 임상적, 조직학적 특성을 분석하였으며, 이 중 수술적 절제를 받은 환자 267명을 대상으로 광범위 절제술과 모즈수술 치료 후 예후를 분석하였다. 또한 Breslow 두께 1.01~2.0mm 선단흑색점흑색종 환자 62명에서 1cm 와 2cm 절제 범위에 따른 예후의 차이에 대한 분석을 시행하였다.

결과 : 생존 곡선에서 임상조직학적 유형에 따른 뚜렷한 차이가 관찰되었으며 ($p < 0.001$), 결절성 흑색종이 가장 나쁜 예후를 보였고 선단흑색점흑색종이 그 뒤를 이었다. 피부에 발생한 흑색종으로 모즈수술을 받은 환자군 ($n = 37$) 과 광범위 외과적 절제술을 받은 환자군 ($n = 230$) 의 예후를 비교 분석한 결과, 모즈수술은 재발율을 낮추며 (18.9% vs 26.5%), 광범위 절제술에 뒤지지 않는 재발 및 생존율을 보였다. Breslow 두께 1.01~2.0mm의 선단흑색점흑색종의 경우 1cm ($n = 28$) 와 2cm ($n = 34$) 경계의 광범위 절제술을 시행한 환자에서 추적관찰기간 동안 재발 및 생존에 유의한 차이는 관찰되지 않았다.

결론 : 결과적으로 한국인의 악성 흑색종 환자는 임상조직학적 아형의 분포에 있어 서양환자들과 분명한 차이를 보이며, 아형에 따른 생존율의 차이 또한 보였다. 모즈수술은 정상조직을 최대한 보존하는 장점과 함께 재발이나 불완전 절제와 같은 위험요소를 갖는 흑색종의 치료에 효과적일 수 있다. Breslow 1.01~2.0mm 두께의 선단흑색점흑색종의 경우 1cm에서 2cm의 경계가 모두 적합하다고 생각된다.

핵심되는 말 : 광범위 절제술, 모즈미세도식술, 선단흑색점흑색종,

악성 흑색종, 절제 범위