Effectiveness and Safety of Negative Pressure Wound Therapy on Melanoma-Resected Surgical Wounds

Jung Won Park

Department of Medicine

The Graduate School, Yonsei University

Effectiveness and Safety of Negative Pressure Wound Therapy on Melanoma-Resected Surgical Wounds

Directed by Professor Kee Yang Chung

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Jung Won Park is approved.

Thesis Supervisor : Kee Yang Chung

Thesis Committee Member#1 : Mi Ryung Roh

Thesis Committee Member#2 : Young Chul Suh

The Graduate School
Yonsei University

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ABSTRACT

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Jung Won Park

Department of Medicine
The Graduate School, Yonsei University

(Directed by Professor Kee Yang Chung)

Background Negative pressure wound therapy (NPWT), a wound dressing system that provides sub-atmospheric pressure throughout the wound site, promotes wound healing, and reduces surgical complications. Although it is contraindicated in malignant wound due to the potential risk of tumorigenesis, the evidence is limited.

Objectives To compare tumor recurrence and wound healing performance, and surgical complications to provide evidence for the use of NPWT on melanoma-resected wounds.

Methods We retrospectively reviewed the medical record of 232 patients who were histopathologically diagnosed with acral lentiginous melanoma without nodal and distant metastasis between Jan 2006-Feb 2020.One hundred and seventy-nine patients received NPWT, and 53 patients received conventional surgical dressing.

Results Fifty-one (28.5%) patients in the NPWT group had recurrence of which 18 (10.1%) were local recurrence, 17 (32.1%) patients who received conventional surgical dressing had recurrence of which 5 (9.4%) was local recurrence. There were no significant differences in recurrence free survival between both group (Log rank test, P=0.701). Patients who received NPWT with skin grafting showed significantly faster wound healing compared to those who received conventional surgical dressing alone, and NPWT without skin grafting ($P < 0.001$). Patients who received NPWT had lower surgical site infection rate than conventional surgical dressing (15.1% vs 28.3%, $P = 0.028$)

Conclusion NPWT does not significantly increase tumor recurrence in melanoma-resected wounds. Compared to conventional surgical dressing, NPWT offers several advantages in promoting wound healing and reducing surgical site infections.

Key words : Negative pressure wound therapy, melanoma-resected wound, melanoma, safety

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I. INTRODUCTION

Negative pressure wound therapy (NPWT) is a wound dressing system that provides sub-atmospheric pressure throughout the wound site. The system consists of a polyurethane foam sponge, a semi occlusive adhesive cover, a fluid collection system, and a suction pump. The foam contains pores ranging in size from 400 to 600 μm and can be trimmed to fit the size and geometry of any wound.[1] Approximately 100–125 mmHg of negative pressure is applied to the wound in continuous mode, with scheduled wound dressing changes every 5~7 days. NPWT promotes wound healing by facilitating wound contraction, removing extracellular fluid, and stabilizing the wound environment. These effects lead to reduced tissue edema, decreased bacterial colonization, increased blood flow and angiogenesis, formation of granulation tissue, and faster wound healing.[2] Furthermore, NPWT offers advantages such as reduced wound healing time, lower risk of surgical site infections, and decreased surgical complications like wound dehiscence, seroma, hematoma, and skin necrosis.[3] However, the use of NPWT is contraindicated in fragile skin, ischemic tissue, and the presence of malignancy. Considering the advantages of NPWT, it would seem logical to apply NPWT after malignancy resection. However, it is still contraindicated in malignancy resected wounds due to its potential risk of tumorigenesis and metastasis.[4] A mechanism that mechanical stress and stretch of cells imposed by

negative pressure promote the expression of genes that regulate cell proliferation has been suggested but there has been no literature that directly supports this hypothesis that NPWT modulates oncological progression.[5, 6] Some studies have reported that there was no significant difference in tumor recurrence when NPWT was compared with conventional surgical dressing.[3, 4, 7] But there has been no direct comparative study on tumor recurrence after NPWT application, and the evidence to support that oncological progression is caused by NPWT is still lacking. Nevertheless, NPWT is frequently used in the clinical setting as a postoperative therapy for malignancy-resected wounds based on the beneficial effects of NPWT on wound healing. Therefore, it is essential to provide evidence regarding the impact of NPWT on tumor recurrence and metastasis in malignancy-resected wounds, as well as its clinical significance. Among various malignancies, melanoma will be analyzed in this study because NPWT is most often applied after melanoma resection in our institution.

In this study, we aim to investigate whether the application of NPWT after melanoma resection affects tumor recurrence and metastasis. Additionally, we aim to compare wound healing times and wound complications between NPWT and conventional surgical dressing to present a rationale for using NPWT.

II. MATERIALS AND METHODS

1. Patient selection

A. Baseline characteristics

We retrospectively reviewed the medical record of 232 patients diagnosed histopathologically with acral lentiginous melanoma, from January 1, 2006, to February 28, 2020, in the Dermatology Department of Severance Hospital, Yonsei University Health system, Seoul, Korea. For staging, we used the 8th edition of the AJCC staging system. We excluded patients with nodal metastasis and distant metastasis. Patients who received

adjuvant radiotherapy at the primary tumor resection site were excluded. Only patients who visited the clinic for more than 3 years after removal of the primary melanoma were included. The patients' medical records were reviewed for age, sex, clinical photographs, tumor location, tumor stage, type of surgery, type of wound management, period and duration of dressing, type of graft for wound healing, time to complete re-epithelialization, and surgical complication.

B. Treatments

Primary melanoma was excised by slow Mohs micrographic surgery (slow MMS) or wide local excision (WLE) with 0.5-2.0 cm margins depending on the maximum Breslow thickness of tumor. The depth of resection was the mid-subcutaneous layer for melanoma in situ, and above the muscular fascia or bony layer for invasive melanoma. After complete removal of the tumor, high-dose adjuvant interferon-alpha (HD-IFNα) was administrated to patients with stage IIB and IIC diseases who could tolerate the treatment. Among 45 patients with stage IIB and IIC, 18 patients received HD-IFNα treatment.

C. Recurrence

Clinical types of recurrence were subclassified into local recurrence, regional metastasis including in-transit metastasis, nodal metastasis, and distant metastasis. Classification was performed according to the type identified at the first detection of recurrence event. We analyzed the time from tumor removal to the date of the last follow-up visit or detection of recurrence, and recurrence-free survival was calculated.

2. Dressing methods

Fifty-three patients received closed wound dressings on a regular basis (conventional surgical dressing group / CSD group) and 179 patients received NPWT after slow MMS or WLE. Closed wound dressing was applied at an interval of 3-7 days until the wound was completely healed. At every visit the wound was cleansed with 1% povidone iodine

solution. After cleansing, a nonadherent, porous silicone wound contact layer (Mepitel®; Mölnlycke Health Care, Gothenburg, Sweden) was applied directly to the wound, followed by nonadherent absorbent contact layer made from polyurethane foam (Mepilex®, Mölnlycke Health Care).

NPWT was applied using V.A.C device (Kinetic Concepts, Inc., San Antonio, TX, USA) or CuraVac (Daewoong Co, Ltd, Seoul, Korea), which is composed of an evacuation tube, a collecting canister, a vacuum pump, and a multiparous polyurethane sponge. After wound cleansing, a porous silicone wound contact layer (Mepitel®; Mölnlycke Health Care) and sponge were applied and then sealed with transparent cohesive film. A negative pressure of approximately 125mmHg was applied to the wound in continuous mode, with scheduled wound dressing changes every 5~7days. The NPWT device was applied when the size of the wound was large and there were large amount of edema or exudate, or to control local bacterial growth and promote granulation tissue formation.

3. Grafting methods

After confirming the complete removal of the melanoma through histopathological examination of surgical specimens, absence of wound infection by bacterial swab culture, and adequate granulation tissue growth, punch grafting or full thickness skin graft was performed. Punch grafting was performed as follows. We initially chose the inguinal area or lower abdomen to hide the donor site scars but now we use insole of the identical foot as the donor site. The donor site was anaesthetized with a field block by local injections of 1% lidocaine with 1:100,000 epinephrine (10mg/mL)/8.4% bicarbonate (1mL for 10mL of lidocaine) and the skin was harvested using a 3mm biopsy punch. The grafts were grasped with sterile forceps and cut at the dermal-subcutaneous fat junction level using sharp scissors. Punch grafts were then placed on a sterile 0.9% saline-moistened gauze, and laid down on the surgical defect, with the distance being 2-4 mm apart from each other. The skin defect containing the punch grafts was covered with a porous silicone wound contact layer (Mepitel®), and NPWT was applied in the same manner as above. The donor site was

closed using thin adhesive strips (Suture-strips®; Mediplast, Benelux), followed by the application of a foam dressing (Mepilex®). After 5-7 days, the defect was inspected, and dressing changes were performed every week. For the patients in the full-thickness skin graft group the grafts were obtained from the lower abdomen or buttocks and were secured to the margin of the defect with absorbable sutures. Bolster dressing was applied and removed 7 days after the operation.

4. Statistics

Discrete variables were presented as counts and percentages, and continuous variables were reported as median (range) or mean +/- standard deviation (SD). The Fisher's exact or Pearson chi-square test was used to assess associations between NPWT application and the baseline clinical features. We compared age, sex, tumor stage, Breslow thickness, follow-up duration, recurrence rate, surgical complication between the NPWT and CSD groups using Pearson chi-square tests or Fisher exact tests (when expected cell counts were less than 5) or unpaired, 2-tailed independent t-tests. Time to complete re-epithelialization were compared using the non-parametric Kruskal-Wallis test, with post hoc Dunn's test. Recurrence-free survival (RFS) rate was estimated using Kaplan-Meier graph. Log-rank test was used to evaluate the correlation of RFS with patient follow-up according to application of NPWT. Correlations between RFS and various patient and tumor factors were assessed using univariate and multivariate Cox proportional analysis. Factors significant in the univariate analysis ($P < .05$) and whether NPWT was applied, the duration of NPWT were included in the multivariate logistic regression models. Statistical tests were performed using IBM SPSS for Windows version 26 (IBM Corp, Released 2019, Armonk, NY). Differences were considered statistically significant at $P < 0.05$.

III. RESULTS

1. Demographics and clinical presentation

Demographics of a total of 232 patients with acral lentiginous melanoma, are summarized in Table 1. Mean age was 59.14 years (range 17-89 years) with 101 (43.5%) male patients and 131 female patients (56.5%). The most common anatomical site was the foot (66.8%), followed by fingernail (21.1%), toenail (8.6%), and hand (3.4%). One hundred fifty-three (65.9%) patients underwent slow MMS, and 79 patients (34.1%) underwent WLE for removal of the primary tumors. Among the patients with Stage I or II melanoma without nodal or distant metastasis, 77 (33.2%) patients were melanoma in situ, 24 (9.9%) patients were stage IA, 48 (20.7%) patients were stage IB, 34 (14.7%) patients were stage IIA, 34 (14.7%) patients were stage IIB, and 15 (6.5%) patients were stage IIC. When classified as T subcategory, it was as follows: melanoma in situ 77 (33.2%), T1a 23 (9.9%), T1b 14 (6.0%, T2a 35 (15.1%), T2b 13 (5.6%), T3a 21 (9.1%), T3b 21 (9.1%), T4a 13 (5.6%), and T4b 15 (6.5%). The mean invasion depth (±SD) measured by Breslow thickness was 1.70 (±1.92) mm for total cases, and 2.50 (±1.89) mm for patients with invasive melanoma. The mean follow-up period was 62.28 months. On the date of first detection of recurrence, local recurrence was detected in 23 (9.9%) patients, regional metastasis (which includes lymph node metastasis and in transit metastasis) in 32 (13.8%), and distant metastasis (which includes distant cutaneous metastasis and visceral organ metastasis) in 13 (5.6%). Forty-two (18.1%) patients had surgical site infection within the first month of surgery. Among a total of 232 patients, 179 patients received NPWT, and 53 patients received conventional surgical dressing. There were no significant differences in age, sex, and anatomical distributions. NPWT group had more patients who underwent slow MMS and CSD group had more patients who underwent WLE ($P < 0.001$). Also, CSD group had longer mean follow-up period, and higher rates of surgical site infection ($P < 0.001$, 0.028 respectively). Otherwise, both groups had no significant differences in the baseline characteristics including tumor stage, T subcategory, and tumor invasion depth.

Table 1. Demographics of the patients who received negative pressure wound therapy (NPWT) and conventional surgical dressing (CSD)

	Total n=232	NPWT n=179	CSD n=53	p value
Age				
Mean, y (range)	59.14 (17-89)	59.37 (17-89)	58.47 (31-85)	0.903
Sex (%)				
Male	101 (43.5)	76 (42.5)	25 (47.2)	0.543
Female	131 (56.5)	103 (57.5)	28 (52.8)	
Anatomical location (%)				
Foot	155 (66.8)	125 (69.8)	30(56.6)	0.341
Toenail	20 (8.6)	14 (7.8)	6(11.3)	
Hand	8 (3.4)	6 (3.4)	2 (3.8)	
Fingernail	49 (21.1)	34 (19.0)	15 (28.3)	
Type of surgery (%)				
Slow MMS	153 (65.9)	136 (76.0)	17 (32.1)	<0.001*
WLE	79 (34.1)	17 (50.0)	73 (55.3)	
Tumor stage (%)				
in situ	77 (33.2)	65 (36.3)	12 (22.6)	0.326
IA	24 (9.9)	17 (9.5)	7 (13.2)	
IB	48 (20.7)	33 (18.4)	15 (28.3)	
IIA	34 (14.7)	26 (14.5)	8 (15.1)	
IIB	34 (14.7)	25 (14.0)	9 (17.0)	
IIC	15 (6.5)	13 (7.3)	2 (3.8)	
T subcategory				
in situ	77 (33.2)	65 (36.3)	12 (22.6)	0.355
T1a	23 (9.9)	16 (8.9)	7 (13.2)	
T1b	14 (6.0)	9 (5.0)	5 (9.4)	
T2a	35 (15.1)	25 (14.0)	10 (18.9)	

T2b	13 (5.6)	8 (4.5)	5 (9.4)	
T3a	21 (9.1)	18 (10.1)	3 (5.7)	
T3b	21 (9.1)	15 (8.4)	6 (11.3)	
T4a	13 (5.6)	10 (5.6)	3 (5.7)	
T4b	15 (6.5)	13 (7.3)	2 (3.8)	
Invasion depth (mm) mean ± SD				
Total	1.70 ± 1.92	1.68 ± 1.90	1.76 ± 2.01	0.595
Invasive melanoma	2.50 ± 1.89	2.58 ± 1.85	2.28 ± 2.02	0.245
Mean follow-up period (months)	62.28	58.34	75.6	0.001*
Recurrence (%)				
Local recurrence	23 (9.9)	18 (10.1)	5 (9.4)	0.894
Regional metastasis	32 (13.8)	25 (14.0)	7 (13.2)	0.888
Distant metastasis	13 (5.6)	8 (4.5)	5 (9.4)	0.320
Total	68 (29.3)	51 (28.5)	17 (32.1)	0.615
Recurrence site (%)				
Primary site	23 (9.9)	18 (10.1)	5 (9.4)	
Lymph node	27 (11.6)	20 (11.2)	7 (13.2)	
In transit metastasis	5 (2.2)	5 (2.8)	0	
Distant cutaneous metastasis	1 (0.4)	1 (0.6)	0	
Visceral organ	12 (5.2)	7 (3.9)	5 (9.4)	
Surgical site infection (%)	42 (18.1)	27 (15.1)	15 (28.3)	0.028*

*p<0.05

Abbreviations; slow MMS, slow Mohs micrographic surgery; WLE, Wide local excision; NPWT, Negative pressure wound therapy; SD, Standard deviation *p ≤ 0.05.

2. Tumor recurrence

The total incidence of tumor recurrence in 232 patients was 68 (29.3%), with 23 (9.9%) being local recurrence, 32 (13.8%) being regional metastasis, and 13 (5.6%) being distant metastasis. In the NPWT group, 51 (28.5%) showed recurrence of which 18 (10.1%) were local recurrence, 25 (14.0%) were regional metastasis, and 8 (4.5%) were distant metastasis. In the CSD group, 17 (32.1%) showed recurrence of which 5 (9.4%) were local recurrence, 7 (13.2%) were regional metastasis, 5 (9.4%) were distant metastasis. Although the NPWT group showed lower total recurrence and distant metastasis, they showed higher rates of local recurrence and regional metastasis than the CSD group. However, there were no statistically significant differences in all types of recurrence. The life-table survival analysis found that 1, 2, 3, and 5-year recurrence-free survival rates for the NPWT and CSD groups to be as follows: 1-year: 95.0%, 94.3%; 2-year 84.2%, 86.7%; 3-year 79.0%, 80.9%, 5-year 71.1%, 74.1%, respectively. Also, local recurrence-free survival rates for the NPWT and CSD groups were as follows: 1-year: 98.9% vs 94.3%; 2-year 94.5% vs 95.9%; 3-year 92.6%, 95.9%, 5-year 89.4%, 93.2% respectively. When analyzing recurrence-free survival using the Kaplan-Meier graph (Figure 1), there was no significant difference in recurrence free survival between NPWT and CSD groups (Log rank test, $P = 0.701$) and the same result was obtained when recurrence free survival was compared only for local recurrence free survival (Figure 2, Log rank test, $P = 0.400$). In addition, according to the univariate Cox proportional analysis, age ≥ 60, higher tumor invasion depth, significantly raised hazard ratio (HR) for recurrence. Other factors including NPWT application, and NPWT duration had no significant correlation with tumor recurrence. When factors with statistical significance of p-value ≤ 0.05 in univariate analysis and whether or not to apply NPWT were included in the multiple Cox proportional model, only the adjusted HR of tumor invasion depth remained statistically significant (HR=3.530 for 2-4mm, 95% Confidence interval (CI)=1.991-6.256, $p < 0.001$, HR 5.347 for >4mm, 95% CI 2.895-9.876, $P < 0.001$) and application of NPWT was not statistically significant. Clinical features and their

relationship with recurrence are listed in Table 2.

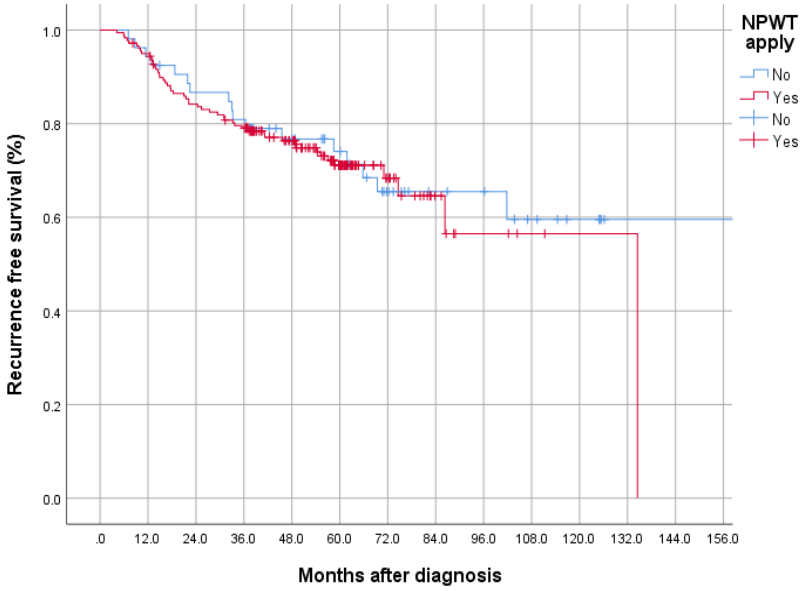

Figure 1. Comparison of recurrence-free survival in acral lentiginous melanoma patients who received NPWT or CSD after resection of the primary tumor (Kaplan-Meier graph, Log-rank test P = 0.701)

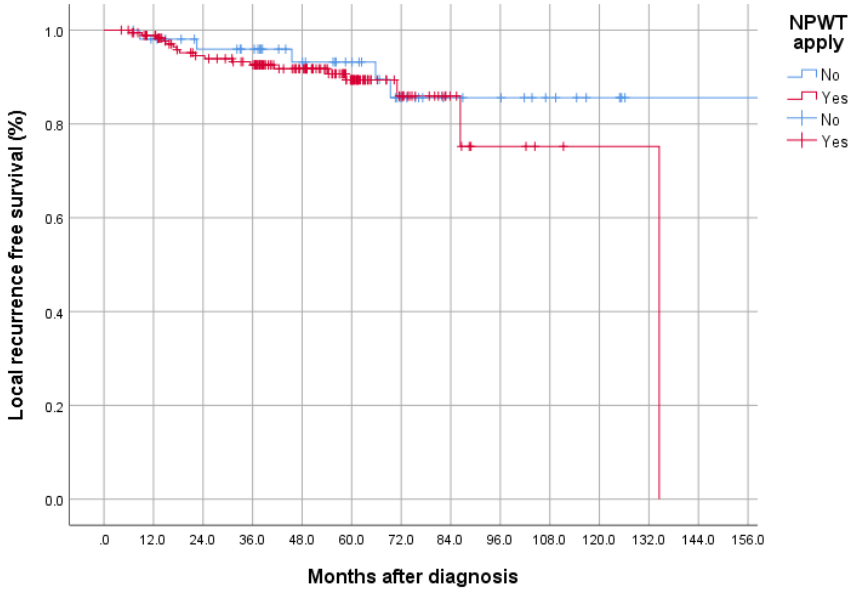

Figure 2. Comparison of the local recurrence-free survival in acral lentiginous melanoma patients who received NPWT or CSD after resection of the primary tumor (Kaplan-Meier graph, Log-rank test P = 0.400)

Table 2. Univariate and multivariate Cox proportional model for recurrence

	Univariate Cox proportional model		Multiple Cox proportional model	
	HR (95% CI)	**p value**	**Adjusted HR (95% CI)**	**p value**
Age				
<60				
≥60	1.714 (1.044-2.815)	0.031*	1.301 (0.782-2.164)	0.311
Sex				
Male	1.180 (0.733-1.901)	0.496		
Female				
Type of surgery				
Slow MMS	1.227 (0.730-2.063)	0.439		
WLE				
NPWT apply				
Yes	1.115 (0.636-1.957)	0.703	1.082 (0.619-1.892)	0.783
No				
NPWT apply duration (days)				
<30				
≥30	1.112 (0.624-19.82)	0.718		
Anatomical location				
Foot	1.833 (0.869-3.866)	0.111		
Hand				
Tumor invasion depth				
<2mm				
2-4mm	3.772 (2.156-6.601)	<0.001*	3.530 (1.991-6.256)	<0.001*
>4mm	5.582 (3.041-10.246)	<0.001*	5.347 (2.895-9.876)	<0.001*
Tumor stage				
In situ				
IA	0.342 (0.041-2.843)	0.321		
IB	3.855 (1.539-9.653)	0.004*		
IIA	6.457 (2.558-16.297)	<0.001*		
IIB	10.600 (4.369-25.714)	<0.001*		
IIC	10.364 (3.657-29.369)	<0.001*		

Postoperative HD-IFNα adjuvant therapy†		
Yes	1.827 (0.856-3.898)	0.119
No		

Abbreviations; HR, Hazard ratio; CI, Confidence interval; slow MMS, slow Mohs micrographic surgery; WLE, Wide local excision; NPWT, Negative pressure wound therapy; HD-IFNα, High dose interferon alpha; *$p \leq 0.05$.

† Among 45 stage IIB or IIC patients, the Hazard ratio of recurrence was calculated by comparing the 18 patients received adjuvant HD-IFNα treatment and 27 untreated patients.

3. Wound healing time

To compare the wound healing time between NPWT and CSD groups, patients with melanoma on the sole and heel were selected because those are the most frequent site and most suitable to evaluate the degree of wound healing. Since we only had data on the size of postoperative wound and not the volume of postoperative defect, we excluded patients with melanoma in situ to minimize confounding effects related to different wound depth because the depth of resection was mid-subcutaneous layer for melanoma in situ and above the muscular fascia or bone for invasive melanomas. We classified the patients into the following three groups. Twenty patients in CSD group who had not received NPWT, 19 patients in NPWT only group who received NPWT without skin graft, 63 patients in NPWT with skin graft group who received NPWT and delayed skin graft for faster wound healing. The demographics of these patients are summarized in Table 3. There were no significant differences in the sex, age, anatomical site, and the defect size among the three groups. However, the time to complete wound healing showed a significant difference among the three groups ($P < 0.001$). CSD group showed the slowest wound healing time with a mean of 110.32 days, followed by NPWT only group with 97.42 days and NPWT with skin graft group with 68.44 days (Figure 3). Post-hoc Dunn's test revealed that the NPWT with skin graft group showed significantly faster wound healing compared to the other groups ($p < 0.001$ for each comparison). NPWT only group showed faster wound healing than the CSD group, but the difference was not significant ($P = 0.433$).

Table 3. Clinical characteristics of patients in the CSD group, NPWT only group, and NPWT with skin graft group

	CSD (1)	NPWT only (2)	NPWT with skin graft (FTSG, Punch graft) (3)	p value†
Number of patients	20	19	64	NA
Age (Mean)	61.9	64.0	62.9	0.800
Sex, n (%)				
Male	9 (45.0)	8 (42.1)	31 (48.4)	0.877
Female	11 (55.0)	11 (57.9)	33 (51.6)	
Anatomical site, n (%)				
Sole	9 (45.0)	10 (52.6)	30 (46.9)	0.878
Heel	11 (55.0)	9 (47.4)	34 (53.1)	
Grafting method				
FTSG			9 (14.1)	
Punch grafting			55 (82.8)	
Complete wound healing time (days)				
Mean ± SD	110.32 ± 36.73 (43-180)	97.42 ± 32.98 (51-170)	68.44 ± 33.10 (34-153)	<0.001*††
Defect size				
Mean ± SD (Range)	29.05 ± 23.78	31.13 ± 24.67	26.40 ± 17.74	0.917

Abbreviations; FTSG, Full-thickness skin graft; SD, Standard deviations; *p ≤ 0.05. † Non-parametric Kruskal-Wallis test for age, complete wound healing time, and defect size, Chi-square test for sex and anatomical site. †† Post-hoc Dunn's test was performed to analyze intergroup differences. The post-hoc P-values of time to complete healing in (1) versus (2), (1) versus (3) and (2) versus (3) were 0.433, <0.001 and <0.001, respectively. SD, standard deviation.

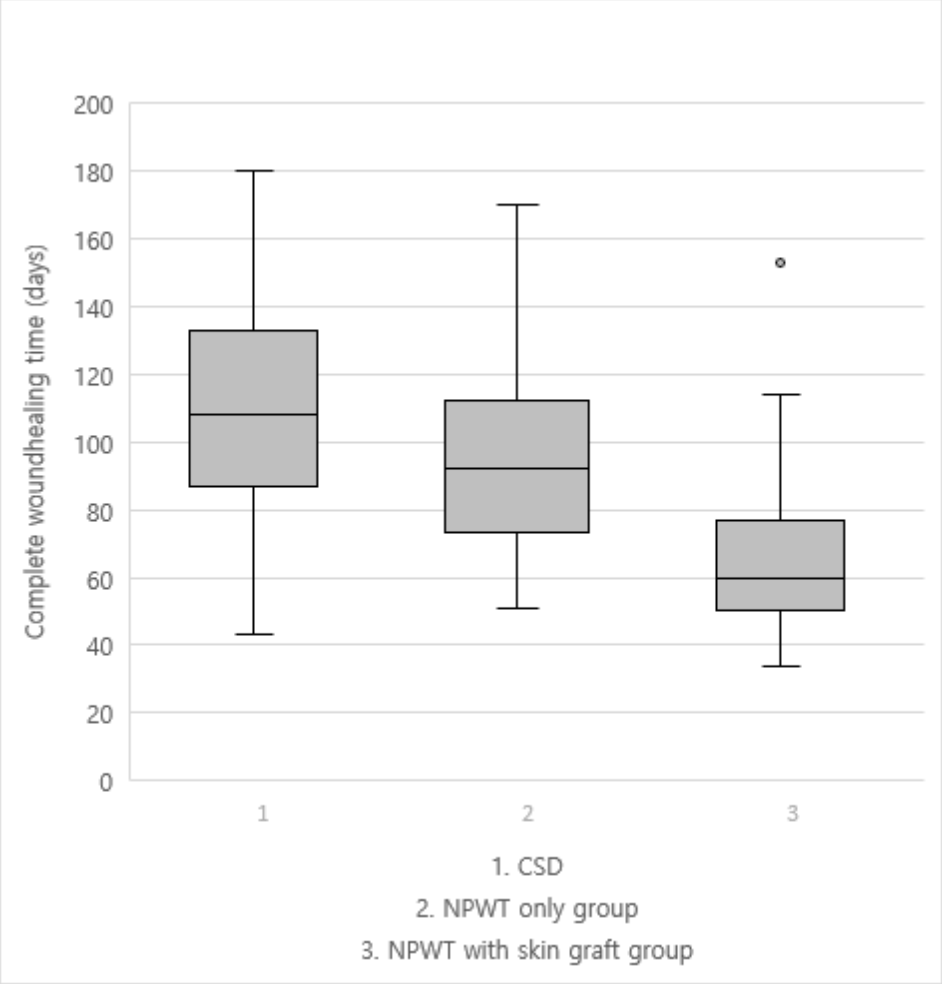

Figure 3. Time to complete wound healing in the CSD group, NPWT only group, and NPWT with skin graft group

IV. DISCUSSION

NPWT has increasingly been used for postoperative wound dressing because of its advantages by reducing tissue edema, improving angiogenesis, promoting granulation tissue formation in a variety of settings.[8] Defects in the acral areas including hands, fingers, feet, toes are difficult to reconstruct by simple closure due to the insufficient local skin pool and lack of mobility of the skin in the area. Reconstruction of these defects was mainly accomplished through secondary intention healing or skin graft, but NPWT has recently been suggested as an excellent therapeutic option for wounds on these areas.[9] But according to some authors, the use of NPWT is considered inappropriate for malignant wounds because when a mechanical stretch affects the cells, it can leads to increased cellular proliferation.[10] The mechanical stress imposed by negative pressure generates mechano-transduction signals and promotes the genes that regulate cell proliferation.[5, 11] Based on these theories, NPWT is even contraindicated in malignancy-resected wounds due to the potential risk of tumorigenesis and metastasis. However, these theories are not only extrapolated from studies on healthy tissues and difficult to be applied to malignant wounds, but also there are no literature that supports the evidence that NPWT promotes local malignant growth or neoplastic migration.[6] Recently, many studies showed that no significant difference in the recurrence rate exists between NPWT and conventional surgical dressing in oncological surgical wounds without residual malignancy but rather beneficial effects of NPWT can be observed in the risk of surgical complications such as surgical site infections, seroma, hematoma, and wound dehiscence.[3, 7] Nevertheless, there are still no studies which directly compared tumor recurrence in melanoma patients between NPWT and conventional surgical dressing groups.

Our study revealed that there were no significant differences in recurrence between NPWT and CSD groups. Also, Kaplan-Meier graph did not show significant differences

between both groups. Theoretically the negative pressure on the defect would induce mechanical stretching and cellular proliferation to affect local recurrence, but there was no significant difference in local recurrence between the two groups, which was also shown in the Kaplan-Meier graph. In addition to local recurrence, other types of recurrences including regional metastasis and distant metastasis also showed no significant differences. Cox proportional analysis with the factors affecting recurrence showed that age over 60 years and tumor invasion depth were significant in univariate analysis. However, in multivariate analysis, only tumor invasion depth remained significant. Whether NPWT was applied or not and the duration of NPWT application did not show a significant difference in recurrence. Taken together, NPWT does not significantly increase any type of tumor recurrence in melanoma-resected wounds.

The results of complete wound healing time showed significant differences in favor of NPWT with skin grafts over CSD group and NPWT only group without skin graft. Among these groups 55 patients (82.8%) underwent punch graft for wound healing. Punch skin grafts cover the defect with epithelium and also supply dermis. They increase the circumference of wound edges from which keratinocytes can migrate and deliver cytokines and growth factors for wound healing.[12, 13] Since the punch skin graft is just put on the wound base without any form of fixing, it is difficult to perform in areas with movement or weight-bearing. When NPWT is applied together with punch skin graft, NPWT helps graft fixation and accelerate the prolonged period of wound healing.[14-17] Other nine patients (14.1%) underwent full-thickness skin graft for wound healing and it also promotes faster wound healing than when NPWT used alone.[18] Although there was no statistically significant difference between the CSD and NPWT only groups, NPWT only group showed faster wound healing time. Also, previous studies showed benefits of NPWT over CSD not only in the wound healing time, also the cosmetic and functional outcome.[9, 19] In addition, NPWT significantly reduced the rate of surgical site infection in our study which is consistent with the result of several previous reviews in other surgical wounds[3, 20]. NPWT

is suggested to reduce the infection through reduced frequency of the dressing so the wound site is less exposed. Also, the increased blood supply to the wound bed delivers oxygen and leukocytes to reduce bacterial colonization and more effectively combat bacterial infection.[1] Although other complications, such as seroma and hematoma were not compared in this paper, NPWT is known to significantly lower these complications by reducing the tissue edema in previous studies.[21, 22] Overall, the NPWT groups showed a significant improvement in wound healing time and decreased the surgical complications rate over conventional surgical dressing.

This study has several limitations. Firstly, since only patients with acral melanoma were included, additional studies are needed for other subtypes of melanoma, and other malignancies. Secondly, there is a possibility of bias because the indication of NPWT and conventional surgical dressing has not been clearly established. Thirdly, we had data of the wound defect size, but the wound volume could not be measured. To correct for this bias, we included only invasive melanoma cases that were resected with a standardized surgical depth, but additional studies need to compare the effect of NPWT at similar wound volumes. Fourthly, patients who received adjuvant HD-IFNα treatment were included; however, the effect of IFNα on the recurrence free survival was not statistically significant in the Cox proportional analysis. Lastly, patients who visited our department recently are more likely to have undergone slow MMS and received NPWT, so there is significant difference in surgical methods between NPWT and CSD groups. However, in the Cox analysis, slow MMS showed no statistically significant difference in recurrence free survival compared to wide excision.

V. CONCLUSION

NPWT does not significantly increase all type of tumor recurrences in melanoma resected wounds. In addition, NPWT offers several advantages in promoting wound healing and reducing surgical complications compared to conventional surgical dressing.

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ABSTRACT(IN KOREAN)

악성 흑색종 절제 후 상처에 적용한 음압상처 치료의 효과와 예후 분석

<지도교수 정 기 양>

연세대학교 대학원 의학과

박 중 원

음압상처치료 (Negative pressure wound therapy, NPWT)는 상처 부위 전체에 대기압 이하의 압력을 제공하는 드레싱 방법으로, 상처 치유를 촉진하며 수술 합병증을 줄이는 드레싱 방법이다. 음압 환경이 종양 형성 및 전이 유발의 잠재적인 위험이 있어 악성 상처에서는 금기이지만 이에 대한 증거는 제한 적이다.

이에 본 연구에서는 흑색종 절제 후 수술상처에서 음압상처치료를 적용하였을 때 종양의 재발률을 비교하고, 상처 회복에 대한 효과와 수술 후 합병증 발생 여부를 비교하여 흑색종 절제 후 수술 상처에서 음압상처치료를 적용하는 근거를 제시하고자 하였다.

말단흑색점 흑색종으로 진단받은 232명의 환자의 의료 기록을 후향적으로 검토하였으며, 음압상처치료를 받은 군과 표준 수술 드레싱을 시행 받은 환자의 재발율을 확인하고자 하였다.

결과적으로 음압상처치료 환자군에서 총 51명의 환자에서 (51/173, 28.5%) 재발이 있었으며 이 중 18명(10.1%)의 환자는 국소 재발이 있었다. 표준 수술 드레싱을 받은 환자군에서는 총 17명 (17/53, 32.1%)의 환자에서 재발이 있었으며 이 중 5명(9.4%)는 국소 재발이 있었다. 음압상처치료 환자군과 표준 수술 드레싱 환자군 간 무재발생존기간에는 통계적으로 유의한 차이가 없었다. (p = 0.701). 232명의 환자에서 재발의 예후 인자를 분석 한 결과, 종양의 침윤 깊이 만이 단일 및 다중 Cox 비례

위험 모델 모두에서 위험비율 (Hazard ratio, HR)을 증가시켰으며 음압상처치료의 적용 여부와 기간은 위험비율을 증가시키지 않았다. 피부이식과 함께 음압상처를 받은 환자는 표준 수술 드레싱만 받은 환자와 피부이식없이 음압상처치료를 받은 환자에 비하여 빠른 상처치유를 보였다. ($p < 0.001$). 음압상처치료를 받은 환자는 표준 수술 드레싱을 받은 환자보다 수술부위 감염률이 낮았다. (15.1% vs 28.3%, $p = 0.028$)

본 연구를 토대로 음압상처치료는 흑색종 절제 후 수술 상처에서 종양재발을 유의하게 증가시키지 않는 것을 확인하였으며, 표준 수술 드레싱과 비교하여 상처 치유를 촉진하고 수술 부위 감염을 줄이는 장점이 있는 것을 확인하였다. 이를 고려하여 흑색종 절제 후 음압상처치료의 사용을 적극적으로 사용하는 것이 상처치유에 도움이 될 것이다.

핵심되는 말 : 음압상처치료, 흑색종 절제 후 상처, 흑색종, 안전성