Received: 7 September 2020 | Revised: 8 October 2020 | Accepted: 18 October 2020

DOI: 10.1111/jjns.12394

ORIGINAL ARTICLE

JAPAN JOURNAL OF NURSING SCIENCE WILEY

Local wound management factors related to biofilm reduction in the pressure ulcer: A prospective observational study

Hiroe Koyanagi[1,2] | **Aya Kitamura**[3] | **Gojiro Nakagami**[3,4] | **Kosuke Kashiwabara**[5] | **Hiromi Sanada**[3,4] | **Junko Sugama**[6]

[1]Graduate Course of Nursing Sciences, Division of Health Sciences, Kanazawa University, Kanazawa, Japan

[2]Department of Nursing Administration and Advanced Clinical Nursing, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan

[3]Department of Gerontological Nursing/Wound Care Management, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan

[4]Division of Care Innovation, Global Nursing Research Center, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan

[5]Data Science Office, Clinical Research Promotion Center, The University of Tokyo Hospital, Tokyo, Japan

[6]Advanced Health Care Science Research Unit, Innovative Integrated Bio-Research Core, Institute for Frontier Science, Kanazawa, Japan

Correspondence
Junko Sugama, Advanced Health Care Science Research Unit, Innovative Integrated Bio-Research Core, Institute for Frontier Science, 5-11-80, Kodatsuno, Kanazawa, Ishikawa, 9200942, Japan.
Email: junkosgm@mhs.mp.kanazawa-u.ac.jp

Abstract

Aims: Critical colonization in pressure ulcers delays healing and has been studied. However, local wound management includes no clear strategy for preventing the development of biofilms. Therefore, this multicenter, prospective, observational study was conducted to examine the effect of local management on the biofilm area of pressure ulcers with critical colonization.

Methods: Participants were 34 patients with a pressure ulcer deeper than the dermis and in a state of critical colonization. The primary outcome was the change over a week in the proportion of the biofilm area in relation to that of the pressure ulcer area. We investigated the relationship between primary outcome and local wound management. The wound-blotting method was used for determining the biofilm area. To calculate the change in the biofilm area, baseline proportion was subtracted from proportion 1 week later.

Results: Six types of topical treatment were used in three facilities. The proportion of the biofilm area at 1 week follow-up was significantly smaller with iodine ointment than that without iodine ointment ($p = .02$). The standardized partial regression coefficient of iodine ointment adjusted by the type of medical facility was −0.26 ($p = .003$).

Conclusion: This study revealed that the use of iodine ointment reduced the proportion of the biofilm area in the pressure ulcer surface. To manage pressure ulcers in a state of critical colonization, these results suggest that local management include the use of iodine ointment.

KEYWORDS

biofilm, critical colonization, infection control, local wound management, pressure ulcer

1 | INTRODUCTION

The prevalence of pressure ulcers in hospitalized patients is still high. Reducing the prevalence is a primary responsibility of nursing. In 10 studies, the prevalence was found to range between 7.8% and 54%, according to the European Pressure Ulcer Advisory Panel methodology (Tubaishat, Papanikolaou, Anthony, & Habiballah, 2018). Until pressure ulcers heal, patients are forced to limit their daily activities in

 © 2020 Japan Academy of Nursing Science

order to remove external forces on the pressure ulcers; moreover, patients experience physical and mental discomfort from pressure ulcers. Thus pressure ulcers have varying effects on the quality of life of patients and caregivers. Therefore, nurses need to promote the healing of pressure ulcers.

In the wound management of pressure ulcers the ultimate goal is to close the ulcer wound. To promote wound healing, the state of the pressure ulcer must be assessed and management must be provided. Local wound management is based on the TIME concept wherein interventions for the following four conditions are involved: non-viable or deficient tissue (T), infection or inflammation (I), moisture imbalance (M), and edge of wound non-advancing or undermined epidermal margin (E) (Schultz et al., 2004). Physicians and nurses working toward local wound management for pressure ulcers use the TIME theory to guide their treatment plan.

Guidelines are available for the treatment for pressure ulcers with signs of infection, which is a key cause of exacerbating these ulcers (Klein et al., 2013). In clinical practice, when the clear signs of infection are observed, redness, heat sensation, swelling, pain, pus, and smell, the use of povidone–iodine with sugar or cadexomer iodine, which are antiseptic ointments, is recommended by a clinical practice guideline for pressure ulcer management (Japanese Society of Pressure Ulcers, 2015a).

Beyond the existing guidelines for managing pressure ulcers with infection, recent research attention has been focused on pressure ulcers that have no obvious signs of infection but are in a state of critical colonization, in which healing does not progress. In pressure ulcers that have progressed to critical colonization state, the presence of biofilms has been confirmed (Beele, Meuleneire, Nahuys, & Percival, 2010). The term biofilm describes a layer of microbial cells and their secreted exopolysaccharides that cover various surfaces. This biofilm exhibits phagocytotic activity through neutrophils and macrophages and has a high resistance to antimicrobial therapy (Parsek & Singh, 2003).

Biofilms are estimated to be present in 60% of chronic wound infections (James et al., 2008). In chronic wounds, biofilms may prolong and prevent healing, thereby causing chronic inflammation and increasing the risk of infection (Percival, 2017). Furthermore, pressure ulcers without biofilms have been shown to have lesser slough formation than pressure ulcers with biofilms (Nakagami et al., 2017). In other words, the presence of biofilm is the cause of delayed wound healing.

Several important questions must be addressed in clinical practice for successful local management of pressure ulcers in a critical colonization state. The treatments that reduce the presence of biofilms are unclear, although studies have focused on chronic wounds with critical colonization. In one case study of pressure ulcers that did not exhibit clear signs of infection, exudate on the wound surface was reduced by the use of polyurethane/silicone foam dressing, with subsequent accelerated healing of the ulcer (Takahashi, 2015). Moreover, the use of silver-releasing dressings in the management of wounds at high risk of infection may have a clinically favorable influence on wound prognosis (Meaume, Vallet, Morere, & Téot, 2005). However, in these studies the relationship between the methods for local management and biofilm was unclear, and the authors could not definitively state which localized management method should be selected for pressure ulcers in a critical colonization state. Consequently, to date no clear guidelines are available for the local management of pressure ulcers in a critical colonization state. Therefore, this study aimed to explore the methods of local management that are effective in reducing biofilm areas of pressure ulcers in a critical colonization state, in addition to the methods for local management selected by the pressure ulcer team.

2 | METHODS

2.1 | Setting

2.1.1 | Participants and pressure ulcers at baseline

This multicenter study in Japan was conducted at a university hospital in metropolitan Tokyo, at a general hospital in the Kanagawa Prefecture, and at an inpatient ward of a long-term medical facility in the Ishikawa Prefecture. These facilities have medical teams who use the medical learning approach of “rounds” to collaborate in the management of pressure ulcers. These teams are involved in decision making for patients with pressure ulcers, and they include nurses who specialize in wound care, ostomy care, and continence care. In the three institutions, these nurse specialists can assess patients for the onset of pressure ulcers and can appropriately evaluate pressure ulcers. In addition, they can perform pressure ulcer prevention and treatment according to the patient's condition while maintaining certain quality and standards.

2.2 | Study design and participants

In this multicenter, prospective, observational study, the state of the pressure ulcer and infection were surveyed twice: at baseline and 1 week later. The study was conducted from November 2015 to April 2019. Study participants were patients with pressure ulcers in a critical colonization state who were enrolled based on these inclusion criteria: a biofilm detected on the pressure ulcer surface at the baseline; hospitalization for 2 weeks or longer; and provision of consent to this study. Exclusion criteria were poor general condition and a clearly local infection evaluated using the DESIGN-R, based on the six components of the tool: depth, exudate, size, inflammation/infection, granulation tissue, and necrotic tissue (Matsui et al., 2011). A higher DESIGN-R score indicates a more severe state of pressure ulcers.

2.3 | Measurement

Data were collected for the following variables: participant characteristics, pressure ulcer characteristics, treatment of the pressure ulcers, and management of the pressure ulcer biofilm area. The survey items for participant and pressure ulcer characteristics, treatment of the pressure ulcer, the management of the pressure ulcer are noted in the *Prevention and Treatment of Pressure Ulcers/Injuries: Clinical Practice Guideline: The International Guideline*, 3rd edition, 2019 (EPUAP, NPUAP, and PANPACIFIC, 2019; pp 251-252). One wound, ostomy, and continence nurse conducted data collection and determined the pressure ulcer status.

2.3.1 | Participant and pressure ulcer characteristics

The researchers collected the data during medical rounds with the interdisciplinary pressure ulcer team. Patient demographic data included age, gender, type of medical facility, and Braden scale score. Pressure ulcer data included location, DESIGN-R score, and contamination by feces or urine. The DESIGN-R tool evaluates the following: depth, exudate, size, inflammation/infection, and pocket. The DESIGN-R scores were obtained by macroscopic assessment at the time of the survey and based on photographs taken using a digital camera. All scores were surveyed by one researcher who was certified in wound ostomy continence nursing.

2.3.2 | Treatment of pressure ulcer

The type of pressure ulcer dressing and ointment, presence or absence of systemic antimicrobials, and type of support surface were surveyed at the baseline.

2.3.3 | Biofilm area

To detect the distribution of the biofilm in pressure ulcers, biofilm components on the wound surface were sampled from the pressure ulcer surface using the wound-blotting method (Nakagami et al., 2017). The proportion of the biofilm area to the pressure ulcer area was measured using the following procedure. In this system, the biofilm on the surface of pressure ulcers is attracted by a nitrocellulose membrane, thereby enabling the biofilm components to be visualized, after which a simple staining procedure is performed. The portion with detected biofilm is stained (Figure 1).

The area of the pressure ulcer is determined by observation of the pressure ulcer on a photograph taken using a digital camera. The range of the biofilm is the portion that is stained in red; this stain color is because the ulcer constituents, exopolysaccharides, respond to ruthenium red stain. The biofilm area was determined by the one researcher certified in wound, ostomy, and continence together with a biofilm researcher who was trained to detect biofilm. The intraclass correlation coefficient was calculated for inter-rater reliability and determined to be 0.81. For each range, the pixels were measured using the image processing program ImageJ, version 5.1 (National Institutes of Health, Bethesda, ML, USA). The proportion of the biofilm area to the pressure ulcer area equal to the ruthenium red-positive area divided by the pressure ulcer area, which was measured twice, as shown in the following equation:

Proportion of the biofilm area to the pressure ulcer area = Biofilm area (pixels) / Pressure ulcer area (pixels).

2.4 | Procedure

Data collection was conducted during bedside visits by the pressure ulcer care team using the following steps: (a) the patient was positioned to be treated without pain; (b) the patient's hospital clothing was removed from the area of the pressure ulcer and wound dressing; (c) the patient was positioned to make the pressure ulcer accessible for treatment; (d) the wound dressing was removed; (e) the pressure ulcer surface was washed with sterile physiological saline; (f) wound blotting of the pressure ulcer surface was performed; (g) the pressure ulcer was

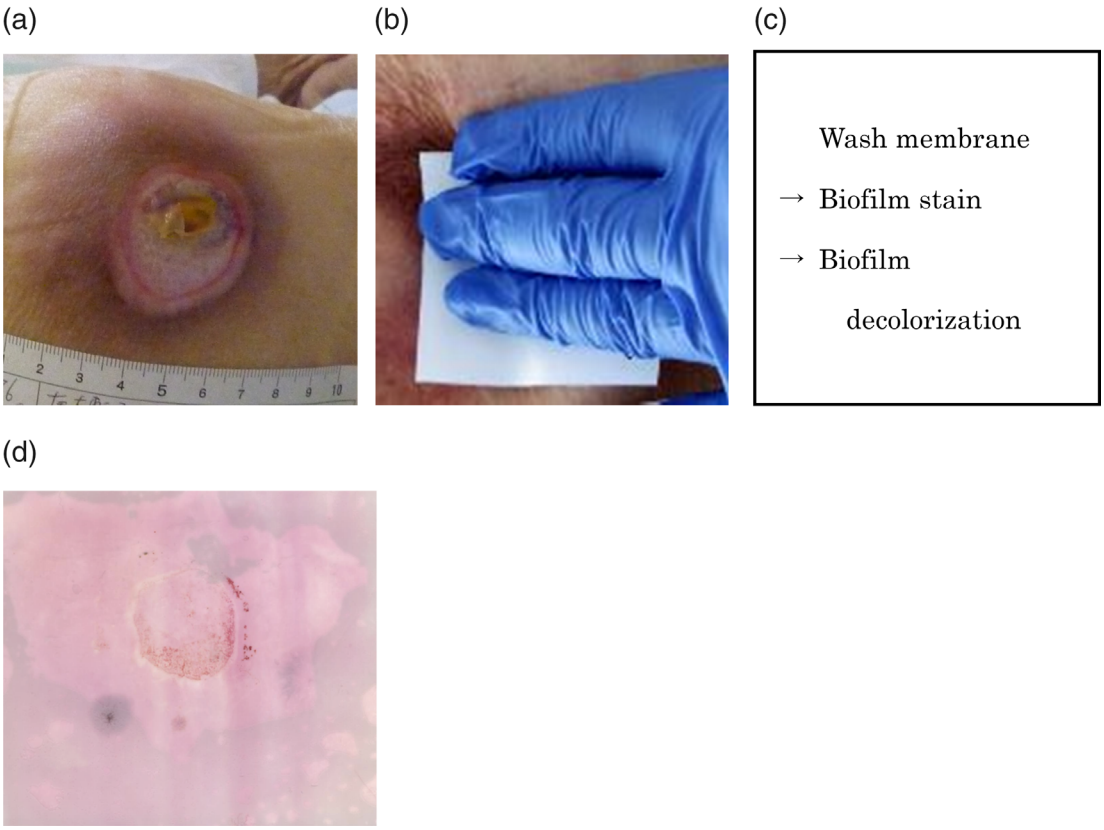

FIGURE 1 The wound-blotting method for detecting biofilm in the pressure ulcer surface. (Nakagami et al., 2017). Bedside images and processes. (a) Pressure ulcer surface was washed and the DESIGN-R score was determined. A photograph of the pressure ulcer was taken. (b) A nitrocellulose membrane was firmly pressed to the pressure ulcer surface for 10 seconds. Laboratory processes: (c) Wash membrane → Biofilm stain → Biofilm decolorization. (d) Ruthenium red stain was used to detect mucopolysaccharides in the biofilm. After 1 minute of staining, the membrane was washed by soaking in a 40% methanol/10% acetic acid solution for 30 minutes three times to decrease the amount of nonspecifically bound staining solution and thus facilitate clearer visualization

washed; (h) a photograph of the pressure ulcer was taken; (i) the DESIGN-R score was calculated; (j) local treatment was provided; and (k) the patient's position was adjusted, and a new hospital gown was provided, thus completing the procedure.

In laboratory, the following steps were taken: (a) the biofilm sample was processed with a protein staining kit and digital photographs were taken; (b) the ruthenium red stain was developed and digital photographs were taken; (c) the images were saved to a hard drive; (d) the images were measured using the ImageJ program for both the pressure ulcer area and the biofilm area; and (e) the size parameters determined the proportion of the biofilm area to the pressure ulcer area, which completed the procedure (Figure 1).

2.5 | Analysis method

The survey items were processed by descriptive statistics and presented using the number (%) or median (interquartile range). The dependent variable was the change in the proportion of the biofilm area (proportion at 1 week later minus the proportion at the baseline). A lower value indicates higher efficiency in biofilm reduction in a week. Independent variables were age, gender, support surfaces, contamination by feces and urine, use of systemic administration of antibiotics, Braden scale score, DESIGN-R score, and topical treatment. Spearman's rank correlation coefficient was used to analyze the relationship between the independent variables in the change in biofilm areas from baseline measurements to 1 week follow-up measurements. We used a linear mixed model in which type of medical facility was a random effect to assess the effect of the survey item on change in the proportion of the biofilm area. Statistical analyses were performed with the use of IBM SPSS Statistics for Windows, version 26.0 (IBM Corp., Armonk, NY, USA). A p value of 5% (two-tailed) was considered statistically significant.

2.6 | Ethical considerations

The objectives, methods, and safety of the study were explained in writing by the researchers to the study participants, and those who provided consent were included as participants. This study was approved by Kanazawa University Ethics Review Board (Examination number: 533-1).

3 | RESULTS

3.1 | Participant characteristics

In this study, 34 participants from three facilities were included. The median age of the participants was 80 years, and 61.8% of the participants were male. The participants received care in these types of facilities: 35.3% in a long-term setting, 4% in a general hospital, and 52.9% in a university hospital. The median Braden scale score was 13 points. The pressure ulcer locations were the trunk for 76.5% of participants and the limbs for 23.5%. The depth was small "d" (shallower than the dermis) in 52.9% of participants, large "D" (deeper than subcutaneous tissue) in 32.4%, and DU (defined as impossible to measure the depth) in 14.7%. The median DESIGN-R score total was 11.5 points (Table 1).

TABLE 1 Participant characteristics (N = 34)

Variable	Median/ n (%)	Interquartile range
Age	80	69–86
Gender, male	21 (61.8)	
Type of medical facility		
Long-term care hospital	12 (35.3)	
General hosepital	4 (11.8)	
University hospital	18 (52.9)	
Braden scale		
Sensory perception	3	2–4
Moisture	3	3–3
Mobility	1	1–2
Activity	2	1–3
Nutrition	2	2–3
Friction and shear	1.5	1–2
Total	13	10–16
Pressure ulcer		
Location		
Trunk[a]	26 (76.5)	
Limb	8 (23.5)	
DESIGN-R		
Depth		
d2	18 (52.9)	
D3	10 (29.4)	
D4	1 (2.9)	
DU	5 (14.7)	
Exudate	1	1–3
Size	6	2–6
Inflammation/infection	0	0–0
Granulation	3	0.25–1
Necrotic tissue	0	0–3
Pocket	0	0–0
Total	11.5	5.25–15.75
Contamination by feces and urine		
Yes	3 (8.8)	

Note: DESIGN-R score: Depth (d2: lesion extends into dermis, D3: lesion extends into the subcutaneous tissue, D4: lesion extends to muscle, tendon and bone, DU: it is impossible to measure the depth).
[a]Trunk: sacrum, buttocks, coccyx, ischium, ilium, back, shoulder; limb: heel, malleolus, greater trochanter, forearm.

3.2 | Treatment of pressure ulcer

Methods for the local management included iodine ointment in 29.4%, prostaglandin E1 ointment in 2.9%, sulfadiazine silver ointment in 20.4%, hydrocolloid dressing in 11.8%, polyurethane/silicone foam dressing in 2.6%, and gauze dressing in 8.8% of participants. Systemic antibiotics were administered in 26.5%. Pressure ulcers with contamination by feces and urine were observed in 8.8%. The types of support surfaces were foam mattresses for 20.5% and air mattresses for 79.4% (Table 2).

3.3 | Factors related to the change in the proportion of the biofilm area

The correlation coefficient of iodine ointment use for the change in the proportion of the biofilm area was −0.42 (Table 3). The change between the proportion of the biofilm area at the baseline and at 1 week follow-up in the group using iodine ointment was significantly lower than that in the group not using iodine ointment ($p = .02$) (Table 4). Multivariate analysis revealed that the use of iodine ointment was

negatively related to the change in the proportion of biofilm (β = −.26, 95% confidence intervals: −0.44 to −0.09; p = .003, Table 5).

TABLE 2 Treatment of pressure ulcer (N = 34)

Variable	n (%)
Topical treatment	
Iodine ointment	10 (29.4)
Prostaglandin E1 ointment	1 (2.9)
Sulfadiazine silver ointment	7 (20.4)
Hydrocolloid dressing	4 (11.8)
Foam/slicone dressing	9 (264)
Gauze dressing	3 (8.8)
Systemic antimicrobials	
Yes	9 (26.5)
No	25 (73.5)
Support surface	
Foam mattresses	7 (20.6)
Air mattresses	27 (79.4)

TABLE 3 Correlation between the change in the proportion of the biofilm area and independent variables

Variable	ρ[a]
Age	.16
Gender	.01
Suport surfaces	−.28
Contamination	−.29
Systemic antibiotics	−.17
Braden scale score (baseline)	.00
Total DESIGN-R score (baseline)	.15
Biofilm area/pressure ulcer area (baseline)	−.59
Biofilm area/pressure ulcer area (1 week later)	.59
Iodine ointment	−.42

Note: The correlation coefficient of the management of pressure ulcers and propotion difference of pressure ulcer surface and biofilm area (1 week later and baseline); Area: Number of pixels.
[a]Spearman's correlation analysis.

4 | DISCUSSION

This study revealed that the use of iodine ointment reduced the biofilm in the pressure ulcer. During the 2018 autumn Symposium on Advanced Wound Care meeting in Las Vegas, an expert panel discussed these properties, with a focus on iodine and iodophors and their effects on biofilm prevention and treatment (Wolcott et al., 2020). The mechanisms underlying the effect of iodine ointment on the biofilm have been elucidated in basic research. An in vivo study reported that iodine inhibited the activity of enzymes involved in biofilm formation (Avshalom Tam, Shemesh, Wormser, Sintov, & Steinberg, 2006); however, to date no clinical studies have investigated the effects of iodine ointments on biofilms. This study suggests that iodine ointment may reduce the bioburden related to biofilm. With regard to the effect of iodine on tissues, a study showed that iodine is highly bactericidal (Nishioka, Seguchi, Yasuno, Yamamoto, & Tominaga, 2000). However, iodine has been reported to cause contact dermatitis. A more recent in vitro study showed that iodine has lower cytotoxicity than certain disinfectants containing chlorhexidine (Goswami et al., 2019).

Sulfadiazine silver ointment is an antibacterial ointment, and the effects of silver on biofilms are expected (Chaw, Manimaran, & Tay, 2005); however, the effects were unclear in this study. The non-iodine group showed a change of −0.02 in the change in the proportion of biofilm area from baseline to 1 week follow-up. The non-iodine group was treated with an ointment containing 29% silver or 71% polyurethane/silicone foam dressing, hydrocolloid dressings, gauze dressings, and other treatments containing oleaginous ointments. In other words, the non-iodine group contained not only silver-containing ointments but also other wound dressings and ointments.

This study emphasized that biofilm visualization at the bedside was important. Biofilms are present in pressure ulcers that are suspected of having a critical colonization state (James et al., 2008). Recently, a point-of-care method for detecting biofilm—which is one of the criteria for determining critical colonization—was established

TABLE 4 Proportion of biofilm according to the local treatment of pressure ulcers

	All (N = 34)	Others (N = 24)	Iodine ointmet (N = 10)	p value
Baseline	.50 (.29–.64)	.42 (.28–.60)	.62 (.49–.76)	.09
1 week later	.37 (.2–.5)	.40 (.27–.52)	.27 (.05–.57)	.23
1 week later-baseline	−0.09 (−.3 to −.08)	−.02 (−.20 to −.13)	−0.35 (−.7 to −.18)	.02

Note: Wilcoxon rank sum test.
Note: Median (interquartile range).

TABLE 5 Multivaraite analysis for the change in the proportion of the biofilm area

	Univariate analysis				Multivariate analysis			
	ß	95% CI		*p* value	ß	95% CI		*p* value
Iodine ointment	− .27	−0.45	− 0.09	.00	− .26	−0.44	−0.09	.00
Age	.00	0.00	0.01	.23	.00	0.00	0.01	.18
Antibiotics	− .11	−0.32	0.09	.28	− .16	−0.35	0.02	.08
Braden scale total	.00	−0.03	0.03	.96	.00	−0.02	0.03	.72

Note: Linear mixed model with facilities as random effects.
Abbreviation: CI, confidence interval; ß, standardized partial regression coefficient.

(Nakagami et al., 2017). Biofilm-based wound care guided by wound blotting is a promising measure to help clinicians eliminate bacterial bioburden more effectively and promote wound healing (Mori et al., 2019; Nakagami et al., 2020). If the biofilm was not visualized, then in clinical practice the pressure ulcers in a critical colonization state are defined as those with delayed healing for 2 weeks and those that respond to the use of antimicrobials to promote healing. Both sets of participants in that study were similar with the following characteristics: age 75–84 years; pressure ulcers defined based on the 2015 Japan Society of Pressure Ulcer Survey; and gender distribution was 50% male (Japanese Society of Pressure Ulcers, 2015b). In this current study, the median age of the participants was 80 years, and the gender distribution was 61.8% male. The results of this study indicated suggestions for timely interventions for pressure ulcers in a critical colonization state. These results are expected to promote healing of pressure ulcers and might prevent varying effects on the quality of life of patients and care givers.

The main limitations of this study were the unknown number of causalities and the large number of elderly people.

As this study was a prospective observational study, causal relationship between iodine ointment use and reduced biofilm proportion has not been established. However, it is plausible that antiseptic iodine ointment had a positive effect in reducing biofilm on the wound bed. Future interventional studies are needed to verify if the use of iodine ointment for pressure ulcers with critical colonization promotes wound healing.

5 | CONCLUSIONS

This multicenter, prospective, observational study examined the effect of local management of pressure ulcers with a critical colonization state on biofilm reduction. Results showed that the use of iodine ointment was related to the reduction in the proportion of biofilm area and the pressure ulcer area in 1 week. Therefore, based on bedside biofilm visualization, if the pressure ulcer is biofilm positive, the authors suggest the selection of local management using iodine ointment to facilitate wound healing through the reduction of biofilm-related bioburden.

ACKNOWLEDGMENTS

The authors would like to express their appreciation to all those who participated in this study.

CONFLICT OF INTEREST

There is no conflict of interests for this study.

AUTHOR CONTRIBUTIONS

All authors contributed to the conception and design of the study. K. H., K. A., and N. G. performed data collection. N. G., and K. K. made substantial contributions to analysis and interpretation of data. K. H. drafted the manuscript. S. J., and S. H critically reviewed the manuscript and supervised the whole study process. All authors read and approved the final version of the manuscript.

REFERENCES

Avshalom Tam, A., Shemesh, M., Wormser, U., Sintov, A., & Steinberg, D. (2006). Effect of different iodine formulations on the expression and activity of Streptococcus mutans glucosyltransferase and fructosyltransferase in biofilm and planktonic environments. *Journal of Antimicrobial Chemotherapy.*, *57*(5), 865–871.

Beele, H., Meuleneire, F., Nahuys, M., & Percival, S. L. (2010). A prospective randomised open label study to evaluate the potential of a new silver alginate/carboxymethylcellulose antimicrobial wound dressing to promote wound healing. *International Wound Journal.*, *7*(4), 262–270.

Chaw, K. C., Manimaran, M., & Tay, F. E. (2005). Role of silver ions in destabilization of intermolecular adhesion forces measured by atomic force microscopy in *Staphylococcus epidermidis* biofilms. *Antimicrobial Agents and Chemotherapy.*, *49*(12), 4853–4859.

Goswami, K., Cho, J., Foltz, C., Manrique, J., Tan, T. L., Fillingham, Y., ... Parvizi, J. (2019). Polymyxin and bacitracin in the irrigation solution provide no benefit for bacterial killing in vitro. *Journal of Bone and Joint Surgery. American*, *101*(18), 1689–1697.

James, G. A., Swogger, E., Wolcott, R., Pulcini, E., Secor, P., Sestrich, J., ... Stewart, P. S. (2008). Biofilms in chronic wounds. *Wound Repair and Regeneration.*, *16*(1), 37–44.

Klein, S., Stephan, S., Juergen, D., Gehmert, S., Niederbichler, A., Landthaler, M., & Lukas, P. (2013). Evidence-based topical management of chronic wounds according to the T.I.M.E. principle. *Journal Der Deutschen Dermatologischen Gesellschaft.*, *11*(9), 819–829.

Matsui, Y., Furue, M., Sanada, H., Tachibana, T., Takao, T., Nakayama, T., ... Miyachi, Y. (2011). Development of the DESIGN-R with an observational study: An absolute evaluation tool for monitoring pressure ulcer wound healing. *Wound Repair and Regeneration.*, *19*(3), 309–315.

Meaume, S., Vallet, D., Morere, M. N., & Téot, L. (2005). Evaluation of a silver-releasing hydroalginate dressing in chronic wounds with signs of local infection. *Journal of Wound Care.*, *14*(9), 411–419.

Mori, Y., Nakagami, G., Kitamura, A., Minematsu, T., Kinoshita, M., Suga, H., ... Sanada, H. (2019). Effectiveness of biofilm-based wound care system on wound healing in chronic wounds. *Wound Repair and Regeneration*, *27*(5), 540–547.

Nakagami, G., Schultz, G., Gibson, D. J., Phillips, P., Kitamura, A., Minematsu, T., ... Sanada, H. (2017). Biofilm detection by wound blotting can predict slough development in pressure ulcers: A prospective observational study. *Wound Repair and Regeneration.*, *25*(1), 131–138.

Nakagami, G., Schultz, G., Kitamura, A., Minematsu, T., Akamata, K., Suga, H., ... Sanada, H. (2020). Rapid detection of biofilm by wound blotting following sharp debridement of chronic pressure ulcers predicts wound healing: A preliminary study. *International Wound Journal.*, *17*(1), 191–196.

Nishioka, K., Seguchi, T., Yasuno, H., Yamamoto, T., & Tominaga, K. (2000). The results of ingredient patch testing in contact dermatitis elicited by povidone-iodine preparations. *Contact Dermatitis*, *42*, 90–94.

Parsek, M. R., & Singh, P. K. (2003). Bacterial biofilms: An emerging link to disease pathogenesis. *Annual Review of Microbiology.*, *57*, 677–701.

Percival, S. L. (2017). Importance of biofilm formation in surgical infection. *The British Journal of Surgery.*, *104*(2), 85–94.

Schultz, G. S., Barillo, D. J., Mozingo, D. W., Chin, G. A., & Wound Bed Advisory Board Members. (2004). Wound bed preparation and a brief history of TIME. *International Wound Journal.*, *1*(1), 19–32.

Takahashi, M. (2015). Successful treatment of intractable wounds with heavy exudate using a new polyurethane foam/soft silicone dressing: A report on two cases. *Journal of Japanese Society of Wound, Ostomy, and Continence Management.*, *19*(1), 46–49. (in Japanese).

The Japanese Society of Pressure Ulcers. (2015a). Characteristics, care and local management of patients with pressure ulcer by facility. Investigation Committee. *Japan Journal of Pressure Ulcer.*, *17*(2), 127–140 (in Japanese).

The Japanese Society of Pressure Ulcers. (2015b). Prevention of pressure ulcer/management guideline (4th edition). Revision Committee. Academic Board of Education. *Japan Journal of Pressure Ulcer.*, *17*(4), 487–567.

Tubaishat, A., Papanikolaou, P., Anthony, D., & Habiballah, L. (2018). Prevalence of pressure ulcers in the acute care setting: A systematic review, 2000-2015. *Clinical Nursing Research.*, *27*(6), 643–659.

Wolcott, R., Cook, R., Johnson, E., Jones, C., Kennedy, J., Simman, R., ... Hermans, M. (2020). A review of iodine-based compounds, with a focus on biofilms: Results of an expert panel. *Journal of Wound Care.*, *29*(7), 38–43. https://doi.org/10.12968/jowc.2020.29.Sup7.S38

How to cite this article: Koyanagi H, Kitamura A, Nakagami G, Kashiwabara K, Sanada H, Sugama J. Local wound management factors related to biofilm reduction in the pressure ulcer: A prospective observational study. *Jpn J Nurs Sci*. 2020;e12394. https://doi.org/10.1111/jjns.12394