The effect of honey-coated bandages compared with silver-coated bandages on treatment of malignant wounds—a randomized study

Betina Lund-Nielsen, MHS, RN[1]; Lis Adamsen, PhD, MScSoc[1]; Hans Jørn Kolmos, MD, DMSci[2]; Mikael Rørth, MD, DMSci[3]; Anders Tolver, PhD, MSc[4]; Finn Gottrup, MD, DMSci[5]

1. The University Hospitals Center for Nursing and Care Research, Copenhagen, Denmark
2. Department of Clinical Microbiology, Odense University Hospital, Odense, Denmark
3. Department of Oncology, Copenhagen University Hospital—Rigshospitalet, Copenhagen, Denmark
4. Department of Basic Sciences and Environment, Faculty of Life Sciences, University of Copenhagen, Copenhagen, Denmark
5. Department of Dermatology, Bispebjerg University Hospital, Copenhagen Wound Healing Center, Copenhagen, Denmark

Reprint requests:
Mrs. B. Lund-Nielsen, The University Hospitals Center for Nursing and Care Research (UCSF), Department 7331, Copenhagen University Hospital, 9 Blegdamsvej, DK-2100 Copenhagen.
Tel: +45 3545 7337/+45 3545 0894;
Fax: +45 3545 7399;
Email: betina.lund-nielsen@rh.regionh.dk

Manuscript received: February 1, 2011
Accepted in final form: August 15, 2011

DOI:10.1111/j.1524-475X.2011.00735.x

ABSTRACT

Malignant wounds (MWs) occur in 5–10% of all cancer patients. Malodor and exudation are the most common side effects. The aim was to determine the influence of honey-coated compared with silver-coated bandages on treatment of MWs. Patients were randomly selected to enter either group A (honey-coated bandages) or group B (silver-coated bandages). Parameters were the following: wound size, cleanliness, malodor, exudation, and wound pain. Digital photographs, visual analog scales (VAS), and wound morphology registration were used for measurement at baseline and following the 4-week intervention. Sixty-nine patients with MWs and advanced cancer, aged 47–90 (median 65.6), were included. No statistically significant difference was noted between the groups with respect to wound size, degree of cleanliness, exudation, malodor, and wound pain. There was a median decrease in wound size of 15 cm^2 and 8 cm^2 in group A and B, respectively ($p = 0.63$). Based on post-intervention pooled data from the groups, improvement was seen in 62% of the participants with respect to wound size and in 58% ($n = 69$) with respect to cleanliness. The VAS score for malodor ($p = 0.007$) and exudation ($p < 0.0001$) improved significantly post-intervention.

Patients with reduced wound size had a median survival time of 387 days compared with 134 days in patients with no wound reduction ($p = 0.003$). The use of honey-coated and silver-coated bandages improved the outcome of MWs. No differences were found between the two regimens. Both types of bandages are recommended for use by patients with MWs containing tumor debris and necrosis.

In the literature, malignant wounds (MWs) are described as chronic wounds that occur in 5–10% of all cancer patients.[1] MWs are most often seen in connection with breast cancer, head and neck cancer, and in advanced cancer cases.[2] These wounds occur when a tumor penetrates the skin or via metastases.[3] MWs are often located in a previously irradiated area and have a negative influence on wound healing.[4] An MW typically remains inflamed due to the presence of tumor tissue in the wound bed. Malodor and exudation are the most common and burdensome problems for patients with MWs.[5–7] Psychosocial problems are also evident such as changed body image, shame, depression, and social isolation.[8–10]

Guidelines for treating MWs are usually developed based on experience rather than on evidence from randomized clinical trials (RCTs).[1] Research is lacking on treatment strategies and wound care products that facilitate healing and that meet the patient's physical and psychosocial needs.[11]

The application of carbon–silver-coated bandages has shown increased tissue granulation and epithelialization in nine of 12 women with MWs and advanced breast cancer. The women's sense of well-being improved as did their self-confidence due to the psychosocial support offered to them in parallel with the wound care.[12,13] This regimen was "standard practice" for these patients; however, larger randomized studies are needed to confirm the effectiveness of this treatment compared with other regimens.

Silver-coated bandages have shown antiseptic, antimicrobial, and anti-inflammatory properties when applied to chronic non-MWs.[14–16] Furthermore, honey-coated bandages have also shown pain-relieving properties in non-MWs beyond their effectiveness in cleansing, antimicrobial, anti-odor, and anti-exudation.[17–20] To our knowledge, research on the use of honey-coated bandages for MWs has not been previously published.

The aim of this RCT study is to test the effect of honey-coated bandages vs. silver-coated bandages on wound size, cleanliness, malodor, exudation, and wound pain in patients with MWs and advanced stage cancer.

MATERIALS AND METHODS

Design

This prospective, open-labeled, RCT investigates a 4-week intervention using two forms of wound bandaging:

- Group A: *Manuka honey-coated bandages* (Algivon/Activon Tulle UMF 12+, AdvaNordic Medical Group A/S, Soroe, Denmark) and absorbent dressing (Sorbion/Drymax, Mediq Danmark A/S, Broendby, Denmark) as well as foam bandages (Allevyn Adhesive, Smith&Nephew A/S, Hoersholm, Denmark).
- Group B: *nanocrystalline silver-coated bandages* (Acticoat/Acticoat Absorbent, Smith&NephewA/S) and foam bandages (Allevyn Adhesive, Smith&NephewA/S)—in cancer patients with advanced stage cancer and MWs.

Approval was gained from the National Data Inspectorate (2006110013A). The study adheres to guidelines set by the Ethical Research Committee for Copenhagen and Frederiksberg municipalities ([KF] 01 2006-5491) and was registered under identifiers NCT00435474 at http://www.clinicaltrials.gov).

Outcomes

The primary outcome was a change in wound size. *Secondary outcome* was cleanliness of the MWs, degree of exudation, malodor, wound pain, and a correlation between survival time and healing.

Patients

Seventy-five patients with advanced stage cancer and MWs were consecutively recruited nationwide from oncology units of 10 hospitals in Denmark (see Table 1). Estimation of whether a wound could be characterized as malignant was established on the basis of history and clinical signs. No biopsies were taken. The clinical diagnosis was a nonhealing wound that developed due to the growth of a tumor through the skin or occurred in connection with metastases. Inclusion criteria were Danish-speaking cancer patients, aged 18+ years, with advanced stage cancer (metastases to the lungs, bone, liver, or locally advanced cancer), a minimum wound size of 1.5 cm^2, and a survival prognosis of at least 3 months. Exclusion criterion was received radiation therapy to the wound area over the past 3 months.

Randomization was done by the Clinical Research Unit at the Oncology Department of Copenhagen University Hospital (Rigshospitalet). The randomization process was computer-based and was stratified for gender, cancer diagnosis (±breast cancer) and treatment (±antineoplastic treatment).

A total of 75 patients were included consecutively in the study, six of whom were excluded for reasons shown in Figure 1.

This article describes the condition of MWs in the 69 included cancer patients prior to and after the intervention.

Evaluation parameters

Wound size was determined based on digital photos taken by the first author (B.L.N.). Prior to and on completion of the intervention, the photos were standardized for light, area to be photographed, and distance from the camera to the wound. The photographs were loaded to the software program "Quantify Image,"[21] and the images and sizes were recorded within 1 mm^2 precision.

Cleanliness of the MW was defined as the wound showing less necrosis and fibrin and increased vascularity and granulation tissue following the intervention. The degree of cleanliness of the wounds was estimated by four specialized wound care nurses based on the photographs taken over time. These four nurses were blinded to the type of treatment used. The nurses evaluated all the photos taken at baseline and after the intervention. The wounds were categorized as "cleaner," "less clean," or "unchanged cleanliness," compared with pre-intervention. Agreement was reached if three of the four or all four nurses scored the same. If two of the four nurses were not in agreement, the photographs were reevaluated. This occurred in four cases. Agreement between the four nurses was reached using Cohen's kappa score[22,23] after merging the group "unchanged cleanliness" with the "less clean" group.

Malodor was evaluated by the first author (B.L.N.) at baseline and following the intervention using the Haughton and Young 1995[24] four-step verbal rating scale (VRS), i.e., (1) no malodor, (2) slight malodor, (3) moderate malodor, and (4) strong malodor.

Table 1. Demographic and clinical characteristics of patients entering the study

Variable	Group A Honey ($n = 34$)	Group B Silver ($n = 35$)	p-value
Sex			
Female	30	31	1.000
Male	4	4	
Age (years)			
Median	66.1	60.7	0.355
Range	50.9–86.8	47.4–89.6	
Cancer diagnosis			
Breast	27	28	0.619
Head/neck	5	3	
Others	2	4	
Antineoplastic treatment			
Yes	28	28	1.000
No	6	7	
Antibiotic treatment			
Yes	4	7	0.513
No	30	28	
Wound duration (months)			
Median	7.5	6.0	0.834
Range	1–86	1–48	
Wound size cm^2 (baseline)			
Median	137.76	128.95	0.448
Range	0.07–756.51	0.17–893.14	

The last column displays the p-value for testing for homogeneity before intervention.

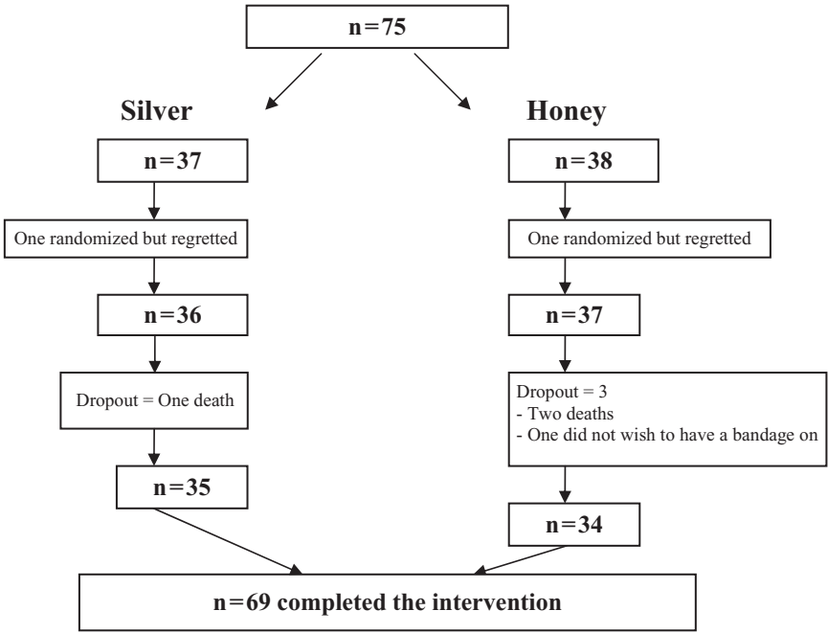

Figure 1. Patients' flow chart. Description of patients included in the study.

Exudation was evaluated (B.L.N.) prior to and following the intervention and was based on a four-step VRS: (1) dry (no dressing change in a week); (2) slight fluidity (dressing change frequency once a week); (3) moderate fluidity (dressing change frequency every 2–3 days); and (4) heavy fluidity (dressing changed daily or every second day).

Malodor and exudation were evaluated by the patients at baseline and following the intervention using a 100 mm graduated mechanical visual analog scale (VAS). *Wound pain* was measured using the same methodology.

Malodor, exudation, and wound pain data measurements were documented using a morphology registration sheet.

Intervention

See Table 2.

Statistical analyses

Our pilot study,[12,13] which captured data from 12 patients (18 wounds), showed a change in wound size of 8.0 ± 36.6 cm^2

Table 2. The intervention

Intervention	The intervention period (28 days)
1. Modern wound healing principles: • Cleansing with faucet water and liquid medicinal soap (pH factor 4.5) and continued with the aid of tweezers, Metzenbaum scissors, and nonwoven pads • Wound treatment with modern wound care products: *Group A: Manuka honey-coated bandages (Algivon/Activon Tulle UMF 12+), absorbent dressing (Sorbion/Drymax), and foam bandages (Allevyn Adhesive); or Group B: nanocrystalline silver-coated bandages (Acticoat/Acticoat Absorbent) and foam bandages (Allevyn Adhesive)* 2. Psychosocial support: dialogues about coping with the illness and particularly with a malignant wound 3. Relaxation training: prerecorded CDs with relaxation exercises	• Both wound treatments took place in the patient's homes, on average, every 2–3 days with approximately 1.5 hours per visit. Cleansing of the wounds was carried out in the same manner in both groups. • The primary author (B.L.N.) and the patient collaborated with the wound care nurse/district nurse to complete the procedure. Wound care was administered after training and guidelines were provided by the primary author. • Wound evaluation was carried out once weekly by the primary author. • The patients participated in 1-hour dialogues held weekly with the primary author, structured in accordance with the cognitive therapy model. • The patients underwent 20 minutes of progressive relaxation training at least once every other day.

Shows the contents of the 28 days intervention period. CD, compact disc.

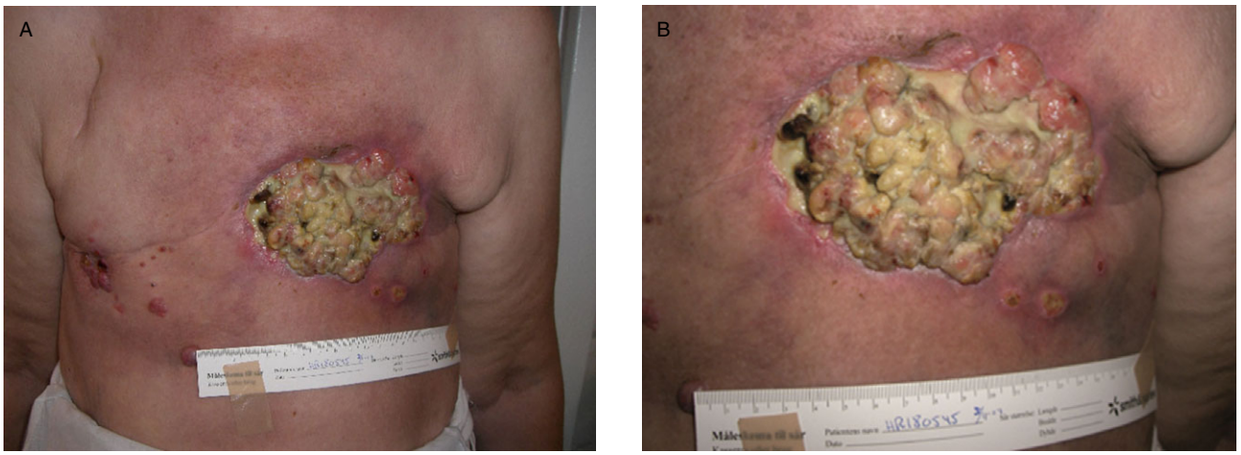

Figure 2. Photo samples: the wound size is measured by means of digital photography on the software program "Quantify Image Central." The resulting measurement reflects the "open" area of the wound. The area with complete skin coverage is not included in the measurement of the wound size. Photo: woman with breast cancer. Wound size: 75.65 cm^2.

(mean ± standard deviation) when "own" wound care was replaced by "professional" wound care using, among other products, silver bandages (before and after the intervention on the same patients). A standard deviation of 36.6 cm^2 for the change of wound size over the intervention period was used for power calculations in measuring the impact of the honey-coated and the silver-coated wound bandages. A sample size of 35 patients from each group was required to detect a difference of 24.8 cm^2 between the groups, with a power of 80% in a two-sided, unpaired *t*-test on a 5% significance level.

Mann–Whitney U-tests and Fisher's exact tests were used to compare the baseline characteristics of the treatment groups.

The change in wound size during the intervention period was analyzed using the Mann-Whitney U-test as well as linear regression. To meet the assumption of variance homogeneity, linear regression analysis was done on square root transformed data. The regression parameter described the size of the wound after the intervention, measured in percent of the wound size at baseline, and a test was performed for the hypothesis that this parameter equals 100%.

Cohen's kappa score was used to evaluate observer agreement between multiple inspections of wound cleanliness before and after the intervention.

Changes in subjective measures of malodor, exudation, and wound pain, measured on a VAS scale, were compared across treatment groups using a nonparametric Mann–Whitney U-test. Paired Wilcoxon tests were applied to detect changes over the intervention period. Due to the low number of patients in each response group for measures of malodor and exudation, categories "no" + "slight"—and "moderate" + "strong" were merged prior to statistical analysis. The resulting binary variables were analyzed using a logistic regression model, taking into account the correlation between variables analyzed using a logistic regression between observations on the same patients. Testing the effect of interaction between time and treatment as well as a marginal test for change over time is presented in the results.

The survival time for the patients following the intervention was described using Kaplan–Meier survival plotting, and log-rank testing was used to assess whether there was a longer survival period among patients experiencing a reduction in wound size during the intervention period. The survival rate was investigated in relation to change in wound size from baseline to post-intervention for all patients.

A 5% significance level was used throughout the study. The statistical analyses were made using "*R: A Language and Environment for Statistical Computing, version 2.10.1*."[25]

RESULTS

Baseline data

Demographic and clinical characteristics of the 69 patients are shown in Table 1. Groups A and B were comparable at baseline for age, gender, cancer diagnosis, duration of wound size. Similarly, subjective patient ratings for malodor, exudation, and wound pain using a VAS scale did not differ between the groups prior to the intervention.

Eighty-eight percent of the participants were women. Eighty percent had breast cancer, 12% had head and neck cancer, and 8% had other diagnoses. Eighty-one of the participants received antineoplastic treatment, and 16% were simultaneously undergoing antibiotic treatment. The median values were the following: age, 65.6 years; wound duration, 7 months; and wound size, 130.9 cm^2 (see photograph: example of MW, Figure 2).

Intervention data

No significant differences were found between the effects of the honey-coated and silver-coated bandages on wound size, degree of cleanliness, malodor, exudation, and wound pain. The two treatment groups A and B were therefore pooled in a subsequent analysis to investigate whether treatments from the pooled group showed any effect over time.

Table 3. *p*-Values for testing if the two treatments have the same effect over the intervention period

		p-values: test for effect of: treatment time		Intervention (A + B): mean ± standard deviation	
Variable	Scale	(A vs. B)	(A + B)	Before	After
Malodor	VRS	0.862*	0.036*		
Exudation	VRS	0.728*	0.926*		
Malodor	VAS 0–10	0.551	0.007	2.3 ± 3.0	1.4 ± 2.1
Exudation	VAS 0–10	0.730	<0.0001	3.5 ± 2.7	1.9 ± 2.2
Wound pain	VAS 0–10	0.733	0.202	2.1 ± 2.1	1.8 ± 2.4

The first column displays the *p*-values for testing for changing between treatment groups. The second column displays the *p*-values for testing if there is a change over the intervention period at all when data from the two treatment groups are pooled together. The last two columns show mean and standard deviation before and after intervention for the pooled data containing both treatment groups A and B. Due to the low number of patients in each category for the variables measured on a verbal rating scale (VRS), the *p*-values marked with a * were computed by merging the groups "no + slight" and "moderate + strong."

Wound size

The median decrease in wound size in Group A (honey-coated bandages) was 15 cm^2 compared with 8 cm^2 in Group B (silver-coated bandages). This difference was not statistically significant ($p = 0.563$). There was no significant reduction in wound size for all patients ($p = 0.388$) in spite of the fact that 62% of the patients experienced a decrease in wound size. Two wounds healed during the intervention period.

Wound cleanliness

The average kappa score of agreement by the observers (Light's kappa) was 0.52, indicating moderate strength of agreement.[23,26] The effect on cleanliness seems superior for the honey-coated bandages (23 of 34 improved) compared with the silver-coated bandages (17 of 35 improved). However, the proportion of wounds with improved cleanliness during the intervention did not differ *between* treatment groups ($p = 0.145$). This is calculated to be 58.0% (40 of 69 patients), with a 95% confidence interval (46.3%, 69.6%) for all patients.

Malodor and exudation

There was no significant difference between groups for the malodor variable when using a VRS ($p = 0.862$). However, a slightly significant reduction over time was detected for all patients ($p = 0.036$) (see Table 3).

There was no difference in exudation between the groups when using the VRS ($p = 0.728$) and no significant change over time ($p = 0.926$).

No significant differences *between* the treatment groups were found for malodor, exudation, and wound pain as reported by the patients when using a VAS scale of 0–10 (see Table 3, column 1).

A significant change during the intervention period was found in both treatment groups for malodor (p-value = 0.007) and exudation (p-value < 0.0001).

Wound size and survival time

A strong association during the intervention was seen between wound size change and patient survival time. Patients with reduced wound size had a median survival time of 387 days compared with 134 days for patients with no reduction in wound size. The survival curves differed significantly ($p = 0.003$, log-rank test) (see Figure 3).

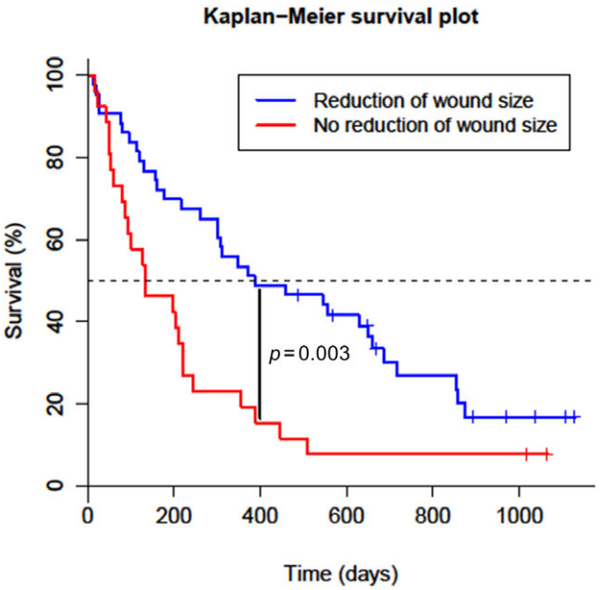

Figure 3. Kaplan–Meier survival plot. The figure shows the association between the change in wound size during the intervention period and survival time of the patients.

DISCUSSION

To our knowledge, the current RCT study is the first of its kind to describe the effects of using honey-coated bandages vs. silver-coated bandages on wound size, cleanliness, malodor, exudation, and wound pain in patients with MWs and advanced stage cancer.

The strength of this study is its randomization and representation of a national cohort in which patients with MWs and advanced stage cancer are included from oncology departments from around Denmark.

The same wound care products were used throughout the 2.5-year data collection period, and procedures were carried out in the same manner by B.L.N. and the trained nurses under her supervision.

The weakness of this study is the absence of a control group. Our previous research (the pilot study)[13] showed that women with MWs and breast cancer did not have professional help with their MWs but simply applied paper towels, handkerchiefs, sanitary napkins, and at best, gauze to their wounds. The 4-week wound care intervention for the pilot used carbon–silver dressings and was supplemented with psychosocial support. The pilot study therefore explored active treatment vs. "nonactive treatment." Following the intervention, nine wounds (75%) showed improvement with increased granulation and epithelialization and complete wound healing in one participant. Seepage was considerably reduced in 83% of cases, and there was an average 75% reduction in the number of bandage changes. As the results were promising, it was felt to be unethical to include a control group without active wound care/treatment in the current RCT study. In addition, developments since the pilot study led to the majority of the patients using modern bandaging (typically foam bandages, alginate, and gel) prior to joining the RCT study. It was therefore seen as irresponsible to allow a control group to be treated, e.g., with the use of paper towels or handkerchiefs.

Another drawback of the current study could be that the primary outcome was wound size. The scarcity of literature on healing MWs is probably due to the fact that healing MWs is an unrealistic goal due to the underlying cancer disease.[1] However, the most important issues for the patients with MWs include malodor, exudation, and cleanliness, and as such, we recommend that future research focus on these issues and not on wound size alone. These recommendations are in line with a recent publication on outcomes for wound healing and care.[27]

Because MWs contain tumor tissue in the wound bed it is expected that the wounds will remain chronic, nonhealing, and lifelong for the majority of the patients. This is reflected by the association between wound size and survival time. We found that patients with reduced wound size had a median survival time of 387 days compared with 134 days for patients with no reduction in wound size. This indicates that when the MW worsens, there is a parallel worsening effect on the patient's overall health and survival status. Saeed et al. in 2004[28] informs that out of 77 patients with MWs, 66% died within the first 6 months and 75% died within the first 12 months following the appearance of the wound. MWs are associated with poor prognosis.

In the present study, two MWs *did* heal during the intervention period. The characteristics of these wounds were that they were superficial and small (2.44 cm^2 and 1.98 cm^2). There was a larger amount of healthy tissue in the wounds, which allowed for administering concomitant antineoplastic therapy in combination with the optimal wound care procedure.

Despite the study's patient group members having advanced stage cancer, a wound size reduction for 62% of patients and improvement in wound cleanliness for 58% of patients were achieved when treated with honey-coated or silver-coated bandages. Cleanliness evaluation by all four observers may have influenced not achieving the same level of improvement (75%) in the wound healing process as was done in the pilot study.

In the current study, the wounds that showed increased granulation tissue and vascularity had less necrosis, reduced malodor, and exudation. This result was further confirmed by the fact that both malodor and exudation were statistically significantly less following the intervention than at baseline in both treatments rated by the patients' VAS scores.

Malodor and exudation are described in the literature as debilitating problems that have consequences for the patient's general well-being, causing anxiety, depression, shame, affected sexuality, and social isolation.[5,7] Because a positive result was achieved using honey-coated and silver-coated bandages, it can be expected that these treatments will increase patient well-being.

Honey-coated and silver-coated bandages used in chronic non-MWs have proven to be effective in combating malodor, exudation, and pain.[29] The current study confirms these findings with the exception of wound pain. Our study's less favorable results with wound pain can be explained by the fact that not only were the skin, tissue, and nerve paths affected (as is the case in nonmalignant chronic wounds), but the growing tumor tissue in MWs also affected the underlying tissue and organs. Furthermore, MWs are typically larger, deeper, and localized within a substantially larger diameter than other types of chronic wounds, which can add to increased pain burden. Furthermore, it can be difficult for patients to distinguish wound pain from other types of pain.

In this study, we could not show statistically significant differences in effect on the MW between use of honey-coated and silver-coated bandages. These bandage types were used following recommendations made by product companies. Honey-coated wound dressings, changed on a daily basis instead of every 2–3 days, should be tested for increased impact on MWs.

As honey-coated and silver-coated bandages showed effect on malodor and exudation, both treatments can be recommended in the care of MWs. The cost of using honey-coated or silver-coated bandages is comparable in Denmark. Silver-coated bandages are generally easy to handle, although they can cause discoloring due to the silver content and are difficult to rinse off. Honey-coated bandages smell of honey and are sticky to the touch. Patients and personnel should be prepared for these inconveniences. Honey-coated and silver-coated bandages can cause a slight stabbing pain for a 20- to 30-minute period following their application and primarily during the wound's stage of inflammation (the stage at which MWs seem to remain). Pain is triggered by the release of silver ions to the tissue when using silver-coated bandages. In the case of honey-coated bandages, pain is triggered by the acid content in the honey, which stimulates the nociceptors to pain response.[30,31]

A drawback when using silver-coated bandages is that bacteria, e.g., *Enterobacter cloacae*,[32] can become resistant, which has not been the case to date when using honey-coated bandages.[33] However, to ensure a low risk of resistant bacteria, it is recommended that the bandages are used only when MWs are at the stage of inflammation.

In conclusion, no difference was seen in the effect of using honey-coated and silver-coated bandages on MWs. In the current study, both treatments led to a reduction in wound size

in 62% of the patients and improved wound cleanliness in 58% of the patients. The study results should be seen as positive efforts to improve the cancer patient's well-being and quality of life. Honey-coated and silver-coated bandages are therefore recommended for use in the treatment of patients with MWs.

ACKNOWLEDGMENTS

Particular thanks are extended to the participants of this study and to the following companies—Smith+Nephew A/S, AdvaNordic Medical Group, and Mediq Danmark A/S—for sponsoring the products.

The study was funded by the Danish Council of Nurses, The Novo Nordisk Foundation, The Lundbeck Foundation, The University Hospital of Copenhagen, the Danish Cancer Research Foundation, The Danish Wound Society, Einar Willumsen's Foundation, Bøghs Foundation, Wedell-Wedellsborg's Foundation, Hede Nielsen Foundation, and Inge and Jørgen Larsen's Memorial Award.

The products were sponsored by Smith+Nephew A/S, AdvaNordic Medical Group, and Mediq Danmark A/S. The authors have no financial relationship with these companies.

REFERENCES

1. Alexander S. Malignant fungating wounds: epidemiology, aetiology, presentation and assessment. *J Wound Care* 2009; 18: 273–4, 276–8, 280.
2. Langemo DK, Anderson J, Hanson D, Hunter S, Thompson P. Managing fungating wounds. *Adv Skin Wound Care* 2007; 20: 312–4.
3. Grocott P. Care of patients with fungating malignant wounds. *Nurs Stand* 2007; 21: 57–8, 60, 62, 64, 66.
4. Dormand EL, Banwell PE, Goodacre TE. Radiotherapy and wound healing. *Int Wound J* 2005; 2: 112–27.
5. Selby T. Managing exudate in malignant fungating wounds and solving problems for patients. *Nurs Times* 2009; 105: 14–7.
6. Hampton S. Malodorous fungating wounds: how dressings alleviate symptoms. *Br J Community Nurs* 2008; 13: S31–2, S34, S36, S38.
7. Alexander S. Malignant fungating wounds: managing malodour and exudate. *J Wound Care* 2009; 18: 374–82.
8. Lo SF, Hu WY, Hayter M, Chang SC, Hsu MY, Wu LY. Experiences of living with a malignant fungating wound: a qualitative study. *J Clin Nurs* 2008; 17: 2699–708.
9. Piggin C, Jones V. Malignant fungating wounds: an analysis of the lived experience. *J Wound Care* 2009; 18: 57–8, 60–4.
10. Alexander S. Malignant fungating wounds: key symptoms and psychosocial. *J Wound Care* 2009; 18: 325–9.
11. Adderley U, Smith R. Topical agents and dressings for fungating wounds. *Cochrane Database Syst Rev* 2007; (18): CD003948.
12. Lund-Nielsen B, Müller K, Adamsen L. Malignant wounds in women with breast cancer: feminine and sexual perspectives. *J Clin Nurs* 2005; 14: 56–64.
13. Lund-Nielsen B, Müller K, Adamsen L. Qualitative and quantitative evaluation of a new regimen for malignant wounds in women with advanced breast cancer. *J Wound Care* 2005; 14: 69–73.
14. Fong J, Wood F. Nanocrystalline silver dressings in wound management: a review. *Int J Nanomedicine* 2006; 1: 441–9.
15. Jørgensen B, Bech-Thomsen B, Grenov B, Gottrup F. Effects of a new silver dressing on chronic venous leg ulcers with signs of critical colonization. *J Wound Care* 2006; 15: 97–100.
16. Palfreyman SJ, Nelson EA, Lochiel R, Michaels JA. Dressings for healing venous leg ulcers. *Cochrane Database Syst Rev* 2006; (3): CD001103.
17. Jull A, Walker N, Parag V, Molan P, Rodgers A. Randomized clinical trial of honey-impregnated dressings for venous leg ulcers. *Br J Surg* 2008; 95: 175–82.
18. Molan PC. Debridement of wound with honey. *J Wound Technol* 2009; 5: 12–7.
19. van der Weyden EA. Treatment of a venous leg ulcer with a honey alginate dressing. *Br J Community Nurs* 2005; 10 (Suppl.): S21, S24, S26–7.
20. White R, Cooper R, Molan P, editors. *Honey: a modern wound management product*. Aberdeen: Wounds UK, 2005.
21. K:L:O:N:K. *Quantify image*. Sorø, Denmark. Available at http://www.quantifyimage.com (accessed September 19, 2011).
22. Cohen J. A coefficient of agreement for nominal scales. *Educ Psychol Meas* 1960; 20: 37–46.
23. Landis JR, Koch GG. The measurement of observer agreement for categorical data. *Biometrics* 1977; 33: 159–74.
24. Haughton W, Young T. Common problems in wound care: malodorous wounds. *Br J Nurs* 1995; 4: 959–63.
25. R Development Core Team. *R: a language and environment for statistical computing*. Vienna: R Foundation for Statistical Computing, 2009: Available at: http://cran.r-project.org/doc/manuals/refman.pdf (accessed September 19, 2011).
26. Lorentzen HF, Gottrup F. Interobservatørvariation ved sårbeskrivelser (interobserver variation in wound assessments). *Ugeskr Laeger* 1998; 160: 3215–8.
27. Gottrup F, Apelqvist J, Price P. Outcomes in controlled and comparative studies on non-healing wounds: recommendations to improve the quality of evidence in wound management. *J Wound Care* 2010; 19: 237–68.
28. Saeed S, Kaehn CA, Morgan MB. Cutaneous metastasis: a clinical, pathological, and immunohistochemical appraisal. *J Cutan Pathol* 2004; 31: 419–30.
29. Gethin G, Cowman S. Manuka honey vs. hydrogel: a prospective, open label, multicentre, randomized controlled trial to compare desloughing efficacy and healing outcome in venous ulcers. *J Clin Nurs* 2008; 18: 466–78.
30. Molan P, Betts J. Using honey dressings: the practical considerations. *Nurs Times* 2000; 96: 36–7.
31. Molan PC. The evidence supporting the use of honey as a wound dressing. *Int J Low Extrem Wounds* 2006; 5: 40–54.
32. Lansdown AB, Williams A. Bacterial resistance to silver in wound care and medical devices. *J Wound Care* 2007; 16: 15–9.
33. Cooper RA, Jenkins L, Henriques AF, Duggan RS, Burton NF. Absense of bacterial resistance to medical-grade Manuka honey. *Eur J Clin Microbiol Infect Dis* 2010; 29: 1237–41.