Feasibility of Pure Silk for the Treatment of Large Superficial Burn Wounds Covering Over 10% of the Total Body Surface

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Large, superficial burn wounds require many painful dressing changes and, thus, dressings that can stay on the wound and peel off during re-epithelization such as Biobrane® and Suprathel® are preferred, but they are costly. Natural silk has shown good outcomes with respect to wound healing, scarring, and patient satisfaction. This study aimed to evaluate the efficacy of natural silk compared with that of initially used dressings for the treatment of superficial burn wounds greater than 10% of the TBSA. Patients with superficial burns covering >10% of the TBSA were treated with pure silk for the first time (treatment group). Complications during wound healing with respect to the need for further surgery and scarring were compared with those of patients with similar burns of more than 10% TBSA and treated with nylon mesh and collagen instead of silk (treatment group). The treatment and control group comprised 25 and 13 patients, respectively. In total, 88% of patients in the treatment group did not require further treatment, while two patients with chemical burns needed further surgeries. Moreover, patients reported high satisfaction with respect to scarring and aesthetic outcome. Meanwhile, 85% of patients in the control group healed without further surgery and showed higher median hypopigmentation and hyperpigmentation after 12 months. Silk is an effective wound dressing for the treatment of large superficial burn wounds. It avoids painful dressing changes and yields satisfactory aesthetic outcomes. However, especially in large burns, careful initial wound depth assessment is crucial to prevent infection and reoperations.

The worldwide rate of burn injuries, including in Germany, is high. In particular, large and deep burn wounds can lead to infection because of the wound size, accompanying excessive edema and impaired blood circulation.² Burn wounds require distinct treatment because of their high secretion rate and the resulting adhesion of the dressing to the wounds, which can cause secondary trauma during the often multiple dressing changes in the course of wound healing.³ There are several available types of wound dressings that offer fast and sufficient wound healing as well as protection from microbial infections.^{4,5} In general, the optimal dressing material should have good biocompatibility, prevent dehydration, reduce the inflammatory reaction, and accelerate wound healing and epithelialization. Dressings like Biobrane® and Suprathel® stay on the wound and detach slowly during re-epithelization, ⁷⁻¹⁵ preventing painful and time-consuming dressing changes prevented. 7-15 However, these dressings are expensive and,

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thus, cheaper but equally effective dressings are needed.

Silk has been used medically as surgical suture and wound dressing material. 16,17 Silk protein membranes can promote skin recovery by improving fibroblast growth factor expression and secretion. 18 Recent animal studies with mice showed that silk dressings are effective burn wound dressings because they showed better healing compared with control groups without any dressing applications. Additionally, no microbial infections or secondary injuries were detected after silk dressings. 16,19 In one study, a 2- × 2-cm standard second-degree burn was produced on the back of 10 rats, and these wounds were randomly divided into four groups. The control group received no dressing, whereas the three experimental groups received one of the three types of silk dressing materials.¹⁹ The silk-treated burn wounds showed more re-epithelialization than the control group. Furthermore, the silk-treated groups developed smaller residual scars than the control group. 19 Similarly, Dressilk® showed good results as a dressing for skin graft donor sites. It allowed effective and safe healing, with overall low complication rates with respect to infection and exudation.²⁰

Biobrane® has been the standard material for wound care for superficial wounds in our clinic. However, the availability problems we encountered in 2014 and 2015 prompted us to search for a cheap and effective alternative to Biobrane®. Consequently, we conducted a prospective study aimed to compare between Biobrane® and Dressilk® intraindividually for the treatment of superficial partial-thickness burn wounds.¹⁴ We found no differences in re-epithelialization, pain, inflammation, acute bleeding, and long-term results for scarring. Hereby, the cost efficiency of Dressilk® compared

with Biobrane® was an interesting aspect. 14 Due to these positive results, we started to use Dressilk® as the routine treatment for all sizes of superficial burns.

However, there has been no report on the use of silk as dressing for large burn to date. Therefore, this study aimed to evaluate the efficacy of natural silk as treatment of superficial burn wounds covering greater than 10% of the TBSA and compare it with that of more conventional treatment such as Biobrane[®]. To the best of our knowledge, this is the first study to evaluate the efficacy of natural silk for the treatment of superficial burn wounds covering greater than 10% of the TBSA.

METHODS

Patients and Ethical Approval

This retrospective study evaluated patients with burn wounds covering more than 10% of their TBSA; the wounds were initially identified as superficial partial-thickness burns. The patients were treated between 2015 and 2016 with Dressilk® at the Department of Plastic Surgery, Hand Surgery, Burn Center, University of Witten/Herdecke at Cologne Merheim Medical Center, Germany (hereafter referred to as the treatment group).

Further, patients with similar burn wounds treated in the same time period with nylon mesh and collagen, which had been our previous standard of care, were enrolled into the control group. During the introduction of the new material, some patients were also treated with nylon mesh since we still had this in stock.

This study has been approved by the Ethical Review Committee of the University of Witten/Herdecke, Germany, and complied with the Declaration of Helsinki. Informed consent was obtained from all patients.

Therapy

Our standard of care for all burn wounds includes mechanical debriding and cleaning with Prontosan® Wound Irrigation Solution (B. Braun Medical Inc., 34212 Melsungen, Hessen, Germany) immediately after admission to the burn intensive care unit. Then, a photo documentation and wound depth evaluation was performed by the burn surgeon on duty (Figure 1a). In cases of acid burn, decontamination was performed by rinsing the wound with water.

After evaluating the burn wound as superficial partial-thickness wound, Dressilk® (PREVOR, Moulin de Verville, 95760 Valmondois Cedex, France) (Figure 1b) or Biobrane® (Smith & Nephew, London, UK) was applied because we still had this on stock and, therefore, decided to deplete it.

Dressilk® is made of 100% natural silk (Figure 1b). In addition to Dressilk® or Biobrane®, an external dressing was applied using Prontosan® moistened cotton gaze (Figure 1b). The external dressing was changed every 2 days until fluid secretion decreased. Then, the external dressing was removed (Figure 1c). As re-epithelization proceeded, Dressilk® and Biobrane® detached from the wound and were gradually cut back. In case of infection, the dressings were removed in the operation theater, the wounds cleaned, and, if necessary, debrided again (Figure 2b). Depending on the wound depth after debridement, either Suprathel® was applied or skin grafting was performed (Table 1). Patients received standard

pain medication with Ibuprofen® for 2 days with low-dose opioids, with the opioid dose tapered gradually as pain levels decreased. Patients were discharged when re-epithelization and wound healing proceeded and pain was sufficiently managed with Ibuprofen® or Novalminsulfon®. The dressings were left on the wounds until re-epithelization was complete.

Follow-up Follow-up comprised weekly visits in our outpatient care facility until wound closure and after approximately 12 months by the same treatment team. Patients who did not follow through with their schedule were contacted by telephone and mail.

During these visits, the scar was evaluated according to our standard of care using the Vancouver Scar Scale (VSS) (Tables 2 and 3), which is a commonly used scar-rating scale that evaluates pigmentation, pliability, vascularity, and height in a point system.^{21–25} Until 1994, pain and itch were also recorded but, due to problems with the reliable measurement of these parameters, they are no longer recorded.²¹ VSS was used during follow-up as it allows easy documentation.

RESULTS

Patients

Between 2015 and 2016, 38 patients were diagnosed with superficial partial-thickness burns wounds covering more than 10% of the TBSA. Patients treated with silk (n = 25) had a mean TBSA of 20.76 \pm 13.21% (range, 10–49% TBSA), while those treated with nylon mesh with collagen (n = 13) had a mean TBSA of 17.83 \pm 6.80% (range, 10.5–29.5% TBSA; Table 1).

The mean patient age in the treatment group was 46 ± 13.96 years (range, 22–82 years), and 73% (19/25) were men. Burns were caused by hot fluid, fire, and acid. Meanwhile, the mean patient age in the control group was 38 ± 11.41 years, and 92% (12/13) were men. Burns were caused by hot fluid and fire. Acid burns were not treated with nylon mesh.

Treatment

After assessment of the burn depth and primary debridement, 25 received Dressilk® for wound treatment. The mean treated TBSA in the treatment group was 19.27 ± 13.21% TBSA (range, 10.0–49%). Of the 25 patients, 15 (64%) received Dressilk® treatment of the whole burned skin area. In 10 patients with mixed burn depth, only areas with grade 2a burns were treated with silk, while the other areas were skin grafted or treated with other substitutes (Table 1).

Meanwhile, the mean TBSA treated with nylon mesh in the control group (n = 13) was $14.73 \pm 5.43\%$ TBSA (range, 8.1-28.5%). In 7 of the 13 patients (54%), the complete burned area was treated with nylon mesh. The remaining six cases presented a mixed burn depth; grade 2a burn wounds were treated with nylon mesh, while the other areas were skin grafted or treated with other skin substitutes (Table 1). There were no differences in the application of the two dressings.

Wound Healing

In 23 of the 25 patients (92%) in the treatment group, the burn wounds healed with no further therapy or surgery (Figures 1

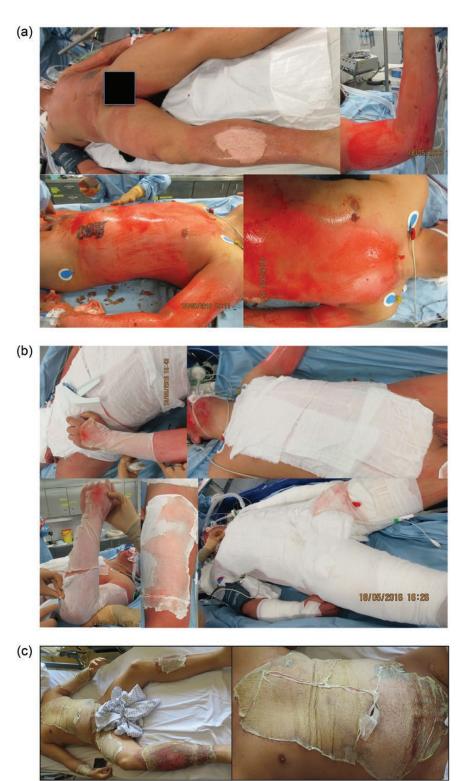


Figure 1. (a) Patient with a superficial burn of 32% TBSA. A before and B after wound debridement. (b) After wound debridement fixation of the silk with staplers and application of damp Prontosan-soaked cotton gauze. (c) Removal of external dressings 2 days after treatment and left open to dry. (d) A: Two weeks after treatment, re-epithelization is almost complete. B: Four weeks after treatment, uneventful healing without further surgery.

and 3). Meanwhile, the silk had to be partly removed in three cases because the burn was deeper than initially assessed and got superinfected.

In the first case, the injury was caused by acid, and 10% of the injury was treated with Dressilk® after decontamination. During the course of treatment, 1% of the injury developed



Figure 1. Contined

a smeary coating. When the wound dressing was removed, a deeper burn than initially assessed was found. The patient received an additional debridement and split skin grafting in this area. The remaining 9% of the initially burned surface area was already re-epithelized and could be left open.

In the second case, the patient suffered a burn injury of 49% TBSA caused by hot steam containing acid (Figure 2a–c). Unfortunately, at the time of treatment, it was unclear whether the hot liquid contains chemicals, and 20% of the injury developed a smeary coating. Therefore, Dressilk® in this area was removed and debrided surgically (Figure 2b). After debridement, these parts presented deeper burns than primarily assessed and a skin transplantation was performed.

The last case also developed a smeary coating on the back because silk could not dry in this region as the patient kept lying on his back. The wounds could be cleaned mechanically and were then treated with Suprathel®. All other nonchemical superficial burn injuries or large burns of the back healed uneventfully (Table 1).

After wound secretion decreased, the external dressings were removed during hospital stay. This is routinely performed between hospital day 2 and day 4. Afterwards, only the silk remained on the wound and was left to dry.

No cases of bleeding were detected. In cases with burns affecting the legs and the arms, particularly over big joints, patients were admitted until the pain was managed adequately. Generally, silk hardens as it dries and can be painful when removed from the joints. A previous intraindividual comparison of pain level during the treatment of Biobrane® and Dressilk® showed no significant difference. 14 Because pain is subjective and highly differs between individuals, we did not compare it in this study. Instead, the opioid dose was modified individually and gradually reduced. As soon as the pain declined and mobilization was possible, patients were discharged and were scheduled for weekly visits in our outpatient care facility (Figure 3). During the weekly visits, silk was cut back as re-epithelialization proceeded and the silk slowly peeled off. Re-epithelization was completed mostly after 14-18 days, with smaller wounds healing generally faster than the large ones. 14,20

Regarding the patients treated with the nylon mesh, two cases that sustained burns from fire and hot liquid showed local infection that required removal of the dressing. The wounds were also deeper than initially assessed, and they received skin transplantation. Apart from these two patients, all wounds healed uneventfully without bleeding or infection. Re-epithelization was also completed mostly after 14–18 days.

Scarring

Patients came to the outpatient care facility after approximately 12 months for follow-up examinations. During these visits, the scar was evaluated using the VSS. In total, 17 (68%) patients in the treatment group were evaluated. All patients reported high satisfaction regarding the aesthetic outcome (Table 2), including the two patients who underwent skin transplantation after silk application and who developed scars (Figure 2). The median VSS score in the treatment group, excluding the transplanted areas, was 0 for pigmentation, pliability, height, and vascularity of the burn scar. Solely four patients showed a hypopigmentation (Table 2). Further, visual differences monitored by the VSS did not appear.

In total, seven patients (53.84%) in whom large areas were treated with nylon mesh were evaluated after 12 months. Only one patient had a VSS of 0. The other 6 patients had documented differences between the burned and uninjured skin (Table 3).

DISCUSSION

This study evaluated the efficacy of silk as dressing for the treatment of large burn wounds over 10% of the TBSA and found that silk is an effective wound dressing for the treatment of these wounds. It allows fast re-epithelization, avoids painful dressing changes, and yields satisfactory aesthetic outcomes. To the best of our knowledge, this is the first report on this topic. Burn treatment is costly, thus the need for effective and affordable treatments. An intraindividual comparison of Dressilk® with Biobrane®14 showed encouraging results. Further, Dressilk® was found to be more cost effective than Biobrane® and Suprathel® and, thus, larger areas of superficial partial-thickness burns were treated with

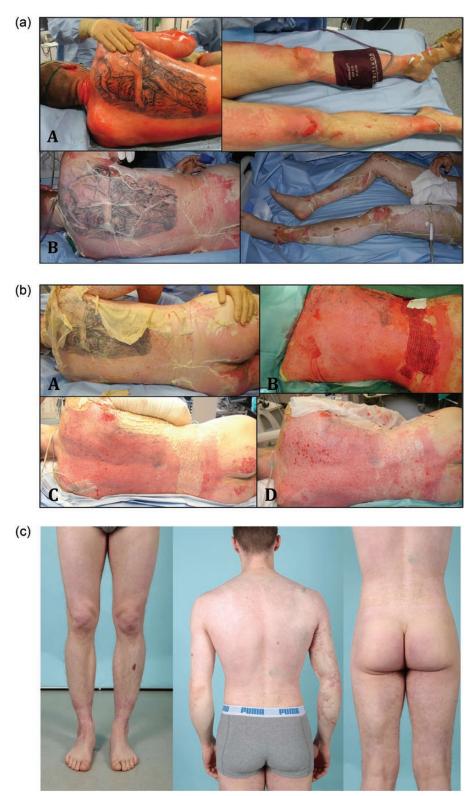


Figure 2. (a) A: Male patient with a superficial burn injury of 49% of the TBSA caused by hot steam containing chemicals after debridement. B: The silk on the back is very wet after 2 days. External dressings are applied here for further 2 days. (b) A: Smeary wound dressing after 5 days instead of dry silk as a sign for bad wound healing. B: Removal of silk and necrotomy. C: Ten days after skin transplantation. D: Satisfying wound healing. (c) Male patient with a superficial burn injury of 49% of the TBSA and following skin transplantation on the right arm and back. Outcome after 1 year.

Table 1. Overview of patients treated with silk (n = 25) and nylon mesh (n = 13) with information regarding the etiology, infection, and secondary skin grafting

6 1 4 1	Sex TBSA silk/nylon mesh	Etiology Infection	grafting (%BSA)	after silk/nylon mesh (%BSA)
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0.00	6.80 5.43		0	2.08

Table 2. Vancouver Scar Scale of patients treated with silk after 12 months

Patient number	Pigmentation	Pliability	Height	Vascularity
1	0	0	0	0
2	0	0	0	0
3	0	0	0	0
4	1	0	0	0
5	0	0	0	0
6	0	0	0	0
7	0	0	0	0
8	0	0	0	0
9	0	0	0	0
10	1	0	0	0
11	0	0	0	0
12	_	_	_	_
13	0	0	0	0
14	_	_	_	_
15	_	_	_	_
16	_	_	_	_
17	_	-	_	_
18	1	0	0	0
19	1	0	0	0
20	0	0	0	0
21	_	_	_	_
22	_	_	-	_
23	0	0	0	0
24	0	0	0	0
25	0	0	0	0
Median	0	0	0	0
SD	0.42	0	0	0

Pigmentation (0-2): normal 0, hypopigmentation 1, hyperpigmentation 2; pliability (0-5): normal 0, supple 1, yielding 2, firm 3, banding 4, contracture 5; vascularity (0-3): normal 0, pink 1, red 2, purple 3; height (0-3): normal (flat) 0, 0-2 mm 1, 2-5 mm 2, >5 mm 3.

silkworm silk, which can be left on the wound and, therefore, prevent painful dressing changes similar to Suprathel® and Biobrane®.²⁶

This retrospective study found that Dressilk® can be applied on extensive superficial partial-thickness burn wounds. Almost all wounds healed adequately with a fast re-epithelization and did not need any further treatment or dressing changes. These results further support the findings by Baoyong et al who reported that silk membranes can promote skin recovery by improving fibroblast growth factor expression and secretion. ¹⁸ Furthermore, healing of large wound areas was also completed after 14 days, as described previously. ¹⁹ However, patients eligible for silk treatment need to be selected cautiously.

Although Dressilk® accelerates wound healing and protects against microbial infections as described in literature,⁴ three cases of superinfections occurred. These cases were evaluated further to evaluate the safety of silk in the treatment of large burn wounds. One of the patients had acid burns, and it is known that the depth of burn wounds caused by acids is difficult to assess particularly because these wounds may appear more superficial during the initial wound debridement and dressing application but can deepen after the initial trauma.²⁷ Therefore, large chemical burn wounds should not be covered

Table 3. Vancouver Scar Scale of patients treated with nylon mesh with collagen after 12 months

Patient number	Pigmentation	Pliability	Height	Vascularity
26	2*	1	0	1
27	2*	1	1	1
28	2*	0	0	0
29	_	_	_	_
30	_	_	_	_
31	_	_	_	_
32	_	_	_	_
33	_	-	_	_
34	1	0	0	0
35	2	2	2	2
36	2*	0	0	0
37	0	0	0	0
38	-	_	_	_
Median	2	0	0	0
SD	0.73	0.73	0.73	0.73

Vascularity marked with * showed hypopigmentation and hyperpigmentation. Pigmentation (0-2): normal 0, hypopigmentation 1, hyperpigmentation 2; pliability (0-5): normal 0, supple 1, yielding 2, firm 3, banding 4, contracture 5; vascularity (0-3): normal 0, pink 1, red 2, purple 3; height (0-3): normal (flat) 0, 0-2 mm 1, 2-5 mm 2, >5 mm 3.

with dressings that stay on the wound for a long time and do not allow a regular wound assessment immediately after the trauma. Instead, a second wound depth evaluation after a day or two might be helpful for a more accurate assessment before dressing application.

In our case, the patients with acid injury developed a smeary coating under the Dressilk® with signs of infection; as such, the dressing was removed and the wound was debrided in the operating theater. Consequently, almost the entire initial wound area showed complete re-epithelization, except for a small area of approximately 1% of the TBSA that had been assessed incorrectly or had deepened after the initial trauma; this area developed an infection and had to be skin grafted. Nevertheless, most wounds healed without skin grafting and the patient reported treatment satisfaction.

The second patient who needed further treatment suffered a burn injury of 49% of the TBSA caused by hot steam combined with chemical residues. In cases of burn injuries with hot fluids or steam, the initial depth evaluation is also difficult because these wounds can appear more superficial than they are.²⁸ Because the burn injury was caused by a combination of acid and steam, this wound was initially assessed incorrectly. Furthermore, there was no patient in 2015 and 2016 with large acid burns that had been treated with Biobrane®, which leads to a certain bias. An intraindividual study directly comparing silk and Biobrane® has already been performed previously to eliminate bias through different patient ages, individual wound healing differences, pre-existing illnesses, different burn etiology and different burn wound sizes.²⁹ Every study comparing two groups instead of choosing an intraindividual study design is confronted with certain bias, which can be minimalized through raising the number of patients. Since this is the first study focusing on the feasibility



Figure 3. A: Patient with a superficial burn of 44.5% TBSA. B: Treatment of the complete area with silk. Removal of external dressing after 2 days. C: Patient before hospital discharge. The silk is completely dry, clothes can be worn on top, and silk is cut back as re-epithelization proceeds.

of pure silk for the treatment of large superficial burn wounds covering over 10% of the total body surface, we decided to keep the patient group size small. Nevertheless, in future, this study should be repeated with larger patient groups to eliminate the mentioned bias.

In cases of burns with excessive edema, disturbed blood circulation, massive fluid loss caused by the capillary leakage, and high intravascular volume after the abatement of the edematous period, one could observe a loss of Dressilk®. Capillary leakage is induced by different mediators and by loss

of oncotic proteins such as albumin. These mechanisms lead to generalized edema. Capillary leakage is crucial in the first 24-36 hours. In burns, fluid management is important but also difficult. On the one hand, excessive fluid therapy can lead to pulmonary edema or to deepening of the burn wound because of decreasing perfusion. On the other hand, deficient fluid therapy may cause organ failure. In addition, severe skin scalding is difficult to assess and is often underestimated. Therefore, acid burn patients whose wounds are treated with Dressilk® should be monitored regularly. Furthermore, a correct primary assessment of the depth of the tissue damage is crucial.²⁸ Dressilk® treatment appears to be only suitable for superficial partial-thickness burns. Nevertheless, wounds should be able to dry under the silk. For instance, increasing moisture by lying on the back would hinder healing under the silk. In these cases, using other dressings such as Suprathel® should be considered. However, if used correctly, silk allows safe healing.

Interestingly, we found hypopigmentation in 22.22% of patients in the treatment group on follow-up. By contrast, Schiefer et al²⁹ reported no difference in pigmentation after 12 months in patients in whom smaller areas were treated (hands and faces). A slight hypopigmentation is often observed in deeper burns, and parts of the treated larger burns were probably deeper than the burns treated by Schiefer et al.^{29,30}

In 2018, Schmidt et al reviewed the management of scars following burn injuries and reported that hypopigmentation is a common finding after partial-thickness burns healing by secondary intent. This underlines our assumption that large superficial burns may have smaller, deeper areas that heal by secondary intent. In our experience with enzymatic debridement, we have often seen burns with a mixed depth.³⁰ Nevertheless, all patients including the ones with a slight hypopigmentation stated satisfaction regarding the aesthetic outcome.^{29,31–34}

Interestingly, hypopigmentation and hyperpigmentation was more frequent in the control group than that in the treatment group, which is also a novel finding that was not previously observed after the treatment of smaller burned areas. ^{29,33,35,36} The reason for this is unclear. Either the burns treated with Biobrane® had deeper areas than the wounds treated with silk or there might have been minor infections, which is often seen during treatment with Biobrane®, that might have led to a deepening of the burn in some areas and to more scarring. ¹⁴

CONCLUSION

This is the first report on the use of pure silk for the treatment of large superficial burn wounds up to 49% TBSA. The results showed that silk is an effective wound dressing for the treatment of superficial burn wounds. It allows fast re-epithelization, avoids painful dressing changes, and yields satisfactory aesthetic outcomes. Attentive initial assessment of the wound depth is crucial to prevent infection and reoperations.

All authors have made substantial contributions to all of the following: 1) the conception and design of the study, or acquisition of data, or analysis and interpretation of data; 2) drafting the article or revising it critically for important intellectual content; and 3) approving the final version to be submitted.

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