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ARTICLE

Enzymatic debridement of hands with deep burns: a single center experience in the treatment of 52 hands

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ABSTRACT

Background: Bromelain-based enzymatic debridement has been introduced as an alternative to surgical excision in deep partial thickness and full thickness burns. We aimed to analyze effectiveness and predictors of spontaneous epithelialization after enzymatic debridement of deep hand burns.

Methods: All patients who received enzymatic debridement for deep partial thickness or full thickness burns of the hands at our institution in the last 5 years were identified. Demographic, clinical and outcome data were collected and analyzed. For patients with deep partial thickness burns, Kaplan–Meier log-rank and subsequent multivariate Cox-regression analysis were performed to identify predictors of spontaneous epithelialization.

Results: 44 patients and 52 hands were treated in the observation period. Among these, 14 had full thickness burns and received split thickness skin grafts. In the 38 hands with deep partial thickness burns, predictors of 28-day epithelialization were total burn extent and mechanism of burn injury. During the first 3 years, 8 out of 13 treated deep partial thickness burns received split thickness skin grafts after a median of 3 days. The following 3 years, 5 out of 25 deep partial thickness burns received surgery after a median of 14 days.

Conclusions: Enzymatic debridement is a useful tool in the treatment of burned hands but the decision-making and correct timing of operative intervention in deep partial thickness burns after debridement requires experience. In our cohort, spontaneous healing of deep partial thickness burns was best in patients with contact burns and less than 15% burn TBSA.

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Introduction

Timely removal of eschar is considered one of the key factors in the treatment of burns [1]. Besides the traditional surgical excision with Weck knifes or hydrosurgery, enzymatic debridement of burn wounds has been studied with different reagents in the past leading to varying and unsatisfactory results [2].

Bromelain-based enzymatic debridement with the agent Nexobrid® (Mediwound GmbH, Germany), formerly named Debridase, has shown promising clinical results and could be established as an alternative to the surgical removal of eschar since its approval for the European market in 2012 [3]. Advantages of this method were confirmed in a first randomized controlled trial and showed selective debridement while sparing vital dermal tissue and led to less need for extensive surgery [4].

Burn injuries of the hand pose a clinical challenge due to the density of anatomic structures and functional relevance of the hand combined with limited soft tissue coverage, making selective debridement particularly valuable in this anatomical region. While a comparison of enzymatic debridement of the hands with standard operative debridement has been performed, both in retrospective cohort studies and prospective trials, no study has focused on analysis of predictive factors associated with spontaneous epithelialization time in this cohort of patients [4–7].

Thus, we aimed to perform a single institutional study on enzymatic debridement in deep partial thickness and full thickness burns of the hands to analyze effectiveness and predictors of spontaneous epithelialization.

Methods

All patients, who received enzymatic debridement of the hands with Nexobrid® for deep partial thickness or full thickness burns between April 2014 and April 2019 at our institution, were identified.

Retrospectively, demographics of the patients, clinical data, their course of treatment including complications and documented outcome were collected utilizing medical records.

Burn % of total body surface area (TBSA) was assessed using Lund–Browder charts and wound depth by clinical examination (blisters, capillary refill, color of wound bed, thrombosed veins, sensation) along with photo documentation upon admission. In awake patients without mechanical ventilation, regional plexus anesthesia was performed prior to enzymatic debridement with placement of a plexus catheter that was left in place for a minimum of 1 day post debridement depending on individual pain levels. In awake patients with both hands requiring enzymatic treatment, plexus catheters were placed bilaterally. The treatment protocol consisted of an initial mechanical removal of blisters and loose debris followed by a presoaking phase of 2 h with Serasept®, a polyhexanid containing agent [8]. After wound

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Table 1. Study population.

	$n = 44$ patients	$n = 52$ hands
Sex		
Male	35 (79.5)	
Female	9 (20.5)	
Age at operation		
≤30	8 (18.2)	
31–60	26 (59.1)	
>60	10 (22.7)	
Burn % TBSA		
<5	15 (34.1)	
5–10	13 (29.5)	
11–20	7 (15.9)	
>20	9 (20.5)	
Mechanical ventilation		
Yes	19 (43.2)	
No	25 (56.8)	
Treatment year		
2014–2016	16 (36.4)	20 (38.5)
2017–2019	28 (63.6)	32 (61.5)
Hand burn depth		
Deep partial thickness	33 (75)	38 (73.1)
Full thickness	11 (25)	14 (26.9)
Mechanism of injury		
Flame	19 (43.2)	21 (40.4)
Explosion	11 (25)	16 (30.8)
Contact	11 (25)	11 (21.2)
Electric	3 (6.8)	4 (7.7)
Timing of enzymatic debridement		
Day of injury	32 (72.7)	39 (75)
24–72h after injury	12 (27.3)	13 (25)
Wound coverage post debridement		
Standard antiseptic dressing	27 (42.6)	33 (63.5)
Foam dressing	7 (15.9)	8 (15.4)
Suprathel®	8 (18.2)	9 (17.3)
Other	2 (4.5)	2 (3.8)
Split thickness skin graft		
Yes	22 (50)	28 (53.8)
No	22 (50)	24 (46.2)

irrigation with saline, Nexobrid® was then applied according to the manufacturers instructions for 4 h followed by removal of eschar with a sterile spatula, wound irrigation with saline and reassessment of wound depth combined with photo documentation. Afterwards, standard antiseptic dressing including non-adherent gauze and polyhexanid gel were applied as post-soaking 12–24 h. Subsequently, definite wound coverage by standard antiseptic dressings, Polymem® foam dressing (mediset GmbH, Germany), Suprathel® (Polymedics GmbH, Germany) or split thickness skin graft in cases of full thickness burn wounds were applied. Dressing changes were performed as needed every 2–5 days. In full thickness wounds or deep partial thickness wounds that had no healing potential according to the assessment of a senior burn surgeon, split thickness skin grafting was performed after induction of pinpoint bleeding with a brush or weck blade during operation. Physiotherapy was initiated 5 days after skin grafting or one day after other wound coverage.

Timing of completed epithelialization was documented in progress notes of inpatient treatment in detail. All patients discharged without completed healing of the hand were seen in our outpatient clinic, where time of complete epithelialization was documented as well.

Statistics

Continuous variables are expressed as mean ± SD or median and range and categorical data as frequencies and percentages. Categorical variables were compared *via* Chi-Square test. For analysis of prognostic factors, Kaplan–Meier log-rank tests and multivariate Cox regression with backwards elimination of factors with $p < .01$ in log rank testing were performed. Here, full epithelialization without surgery represented the event and the time interval was counted in days with a maximum of 28. In patients receiving surgery, time was set at 28 days without occurrence of the event. Odds ratios were calculated for multivariate analysis and presented with 95% confidence interval in parenthesis. p-Value <.05 was considered statistically significant.

Results

A total of 44 patients could be included of which both hands were affected and treated in 8 patients resulting in a total of 52 treated hands. Patient characteristics are presented in Table 1. 35 patients (79.5%) were male and median age was 47 years (20–90 years). Median burned total body surface area (TBSA) was 9% (0.5–75) and 9 patients had more than 20% burned TBSA. Nineteen patients received mechanical ventilation. Of these, 10 had a burn TBSA of 20% or higher and six of them had inhalation injury. Out of the remaining nine patients, five had inhalation injury. A number of these patients were intubated by the emergency physician and reached our department ventilated but were extubated shortly after. We still regarded these patients as having received mechanical ventilation.

In 11 patients and 14 hands hand burns were full thickness and in the remaining 33 patients and 38 hands deep partial thickness. 19 patients (43.5%) suffered burns through direct flame contact, 11 patients (25%) suffered flame impact by explosion, 11 patients (25%) suffered contact burns and three patients (6.8%) electrical injury. No patient received enzymatic debridement for scald injury. In the majority of patients (72.7%) enzymatic debridement was initiated on the day of injury.

In 33 hands including 12 of the 14 full thickness burns, standard antiseptic dressings were continued after enzymatic debridement, foam dressings were applied in eight hands and in nine hands Suprathel® was applied to the wounds after debridement. All full thickness burn injuries (14 hands) received split thickness skin grafting with a median of 4 days (1–5) from enzymatic debridement until operation. In four of them surgical excision was performed prior to skin grafting. Out of the 14 hands with full thickness burns receiving split thickness skin grafting, four (28.6%) required a second skin grafting operation to cover residual defects. Among the 38 hands with deep partial thickness burns of the hands, 14 (36.8%) received split thickness skin grafts with a median of 8 days (4–28) from enzymatic debridement until operation. Of these, surgical excision prior to skin grafting was performed in eight hands.

The first 20 hands were treated 2014–2016 with 13 of them being deep partial thickness burn depth. Of these, 10 (69.2%) received operative intervention with skin transplantation after a median of 3 days post debridement. Of the 25 hands with deep partial thickness burns treated 2017–2019, only four (16%) received operative intervention after a median of 14 days post debridement. Overall, 21 out of 24 hands (87.5%) treated 2014–2016 but only 11 out of 28 hands (39.3%) treated 2017–2019 received surgery ($p = .001$). No escharotomy was needed in any of the treated hands.

Analysis of predictors for epithelialization in deep partial thickness burns

In patients without surgical intervention, epithelialization was completed after a median of 20 days (7–35). A case example is

Figure 1. (a–d) 42 year old male with deep partial thickness burn injury of the hand after an explosion. (a) Initial presentation after removal of blisters and presoaking, (b) occlusive dressing after application of Nexobrid®, (c) wound bed after enzymatic debridement, note the white appearance with single bleeding indicative of deep partial thickness burn depth, (d) appearance after 14 days with ongoing epithelialization. (e and f) Result after 4 weeks with fully epithelialized wounds and good functional outcome.

Table 2. Factors associated with spontaneous epithelialization after enzymatic debridement of deep partial thickness burns, uni- and multivariate analysis.

	n	Epithelialized without surgery within 28 days (%)	*p*-Value (log rank, univariate)	Odds ratio (Cox, multivariate)	*p*-Value (Cox, multivariate)
All hands with deep partial thickness burns	38	63.8 ± 7.8			
Sex			.743		
Male	33	63.6 ± 8.4			
Female	5	60 ± 21.9			
Age at operation			.193		
≤60	32	59.4 ± 8.7			
>60	6	83.3 ± 15.2			
Burn % TBSA			.006		
≤15	26	76.9 ± 8.3		Ref.	
>15	12	33.3 ± 13.6		0.28(0.08–1)	.05
Mechanism of injury			.025		
Flame/Explosion	26	61.5 ± 9.5		Ref.	
Contact	8	87.5 ± 11.7		3.37(1.2–9.44)	.021
Electric	4	25 ± 21.7		0.27(0.07–1.08)	.065
Mechanical ventilation			.062		
Yes	13	46.2 ± 13.8			
No	25	72 ± 9			
Timing of enzymatic debridement			.897		
Day of injury	30	63.3 ± 8.8			
24–72h after injury	8	62.5 ± 17.1			
Wound coverage post debridement			.008		
Standard antiseptic dressing	21	47.6 ± 10.9		Ref.	
Foam dressing	6	83.3 ± 15.2		1.2(0.26–5.57)	.812
Suprathel®	9	100		2.35(0.79–6.96)	.123
Other	2	–			
Treatment year			.005		
2014–2016	13	30.8 ± 12.8			
2017–2019	25	80 ± 8			

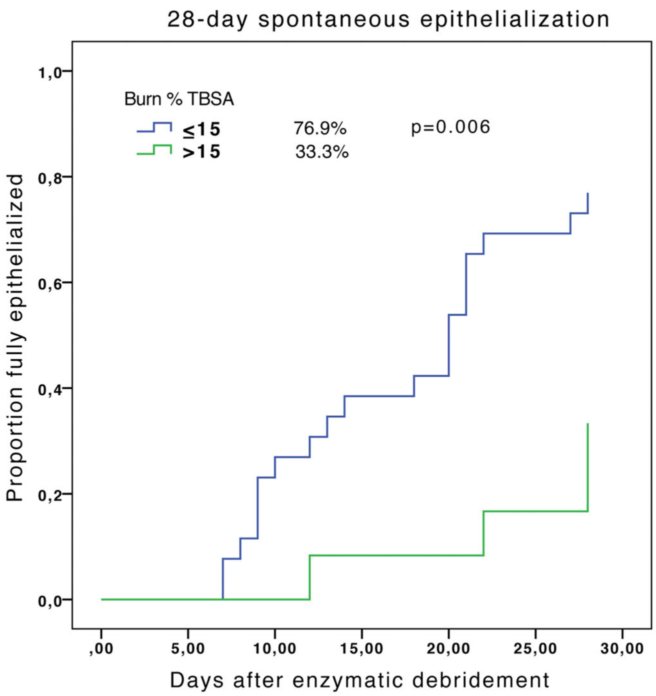

Figure 2. 28-day spontaneous epithelialization stratified by burn extent.

presented in Figure 1. Results of log-rank univariate and Cox-regression multivariate analysis are presented in Table 2.

Neither sex nor age was predictive of 28-days spontaneous complete epithelialization after enzymatic debridement in our collective. Application of Nexobrid on the day of injury or between 24–72 h after injury did not have an impact on epithelialization. Burn TBSA >15% and mechanical ventilation were significantly associated with worse spontaneous epithelialization. Burn TBSA > 15% was confirmed as negative predictive factor for epithelialization with an odds ratio of 0.28(0.08–1), $p = .05$. A Kaplan–Meier curve for 28-days epithelialization stratified by burn extent is presented in Figure 2.

Mechanism of injury was a predictor of spontaneous epithelialization in uni- and multivariate analysis with best outcome for thermal contact injury and worst for electrical injury. The odds ratio for contact injury compared to the average was 3.37(1.2–9.44) with $p = .021$ and for electrical injury was 0.27(0.07–1.08) with $p = .065$.

All nine hands, that received Suprathel dressings and five out of six hands (83%), that received foam dressings, epithelialized within 28 days without need for surgery. This was true only for 47.6% of hands with regular antiseptic dressings. This association was significant in univariate but did not reach significance in multivariate analysis given that all patients, who received either Suprathel or foam dressing had less than 15% burn TBSA.

Hands treated in the years 2014–2016 had significant lower rates of spontaneous 28-days epithelialization as compared to hands treated in 2017–2019 due to the high rate of operations in the first years as stated before. This factor was not included in multivariate analysis.

No relevant esthetic or functional impairments after spontaneous epithelialization were documented for the treated patients.

Discussion

While hands are a common location for burn injury, treatment is challenging due to the close proximity of anatomical structures and limited soft tissue coverage yet high functional demand in terms of outcome. In deep partial thickness burns and full thickness burns removal of eschar is needed for reduction of morbidity and optimization of healing potential. Previous studies have shown surgical excision to remove vital tissue as well [9], which, particularly in hands, is not ideal.

Bromelain-based enzymatic debridement has been shown to selectively remove non-vital tissue, both in animal models and human application [10–12].

Several studies have studied benefits of bromelain-based enzymatic debridement of burnt hands in comparison to standard operative excision. The first retrospective cohort study over a time span of 15 years by Krieger *et al.* analyzed 69 enzymatically debrided hands that were initially assessed as deep partial thickness or full thickness burn and found both number of patients needing operative measures and area needing skin grafting to be significantly lower than initially expected [7].

In subsequent prospective studies, a reduction of the need for operative excision or skin grafting for enzymatic debridement versus standard operative care and a comparable or better outcome in terms of time until epithelialization and Modified Vancouver Scar Scale was found while no functional disadvantages were observed [4,6].

Accordingly, although not assessed prospectively in this study, we did not observe esthetic or functional impairment as the result of enzymatic debridement and spontaneous epithelialization.

We did not find an impact of the timing of Nexobrid application within the recommended 72 h timeframe. Here, sufficient soaking and achieval of a moist wound bed are fundamental for the success of enzymatic debridemend as has been described in the European consensus paper [8]. Analogously to the finding of Schulz *et al.* in the description of their learning curve, we estimated exudation immediately after enzymatic debridement or after 2 h soaking too excessive for definite wound coverage [5]. Therefore we initiated antiseptic dressings with polyhexanide gel at least over night before definite wound coverage with Suprathel, foam dressings or skin grafts was performed. This is in accordance with the European consensus on Nexobrid treatment, where skin grafting is recommended not earlier than 2 days after debridement [8]. 4 out of 14 full thickness burns and 8 out of 38 deep partial thickness burn wounds received complementary surgical excision after the enzymatic process prior to skin grafting. The need for surgical excision was determined by the senior surgeon and it's hardly possible to discuss it in retrospective. However, if split thickness skin grafting was planned, the threshold to perform additional surgical excision was low to avoid graft loss and further healing delay.

We were able to show an association of a burn TBSA of >15% with worse spontaneous 28-day epithelialization. This may be caused by deeper burns in patients with larger burn TBSA but also systemic effects of larger burn wounds in the patients with severe burn injury, expanding the organism's resources for spontaneous wound healing. The mechanism of burn injury represented an independent prognostic factor of spontaneous 28-day-epithelialization in our collective of patients. Here, hands with electrical burns, an off label use of the product, showed the worst spontaneous healing while hands with contact burns showed the best spontaneous healing capacity.

Although an independent prognostic value of wound coverage was not found in multivariate analysis due to both Suprathel® and foam dressings being applied in patients with less than 15% TBSA burn only, all hands treated with Suprathel® healed spontaneously within 28 days. Here, a selection bias is possible, as the choice of wound coverage depended on individual experience of the burn surgeon in charge. In a non-inferiority comparative study of Suprathel versus skin transplantation in deep dermal wounds, it was demonstrated that Suprathel required longer time to heal but resulted in similar scar quality [13]. Therefore, the use of enzymatic debridement with subsequent Suprathel coverage combines two tissue preserving methods that aim to maximize self-healing potential of the wound. Analogously to the experience of Schulz et al., we have established Suprathel as the standard wound coverage of deep partial thickness burns after enzymatic debridement [5]. Prospective studies are needed to compare different wound coverage materials after enzymatic debridement in terms of surgical and functional outcome.

The comparison of the time periods 2014–2016 and 2017–2019 reveals a learning curve in the correct assessment of need for operative intervention. The debrided wound bed after enzymatic debridement is heterogenous and requires experience to adequately evaluate depth and healing capacity, which determines the further treatment algorithm. While the decision to initiate operative excision and/or skin transplantation remains case-by-case, we have learned to be more patient and conservative. However, in our experience and following the European consensus, the decision should be made not later than 21 days after debridement [8].

There are several limitations to this study. Although standard operative procedures (SOPs) exist for all procedures described at our center, homogeneity and quality of data is limited by the retrospective nature of the study. The decision to operate on patients due to missing progress in wound healing was made at the discretion of the senior burn surgeon in charge and had an impact on the further analysis of spontaneous 28-days epithelialization. In these patients, the course of wound healing without operative intervention is unclear but was expected to be unfavorable. As we have experienced a learning curve in the assessment of need for operative intervention demonstrated in this study, a bias by incorrect assessment needs to be considered.

Enzymatic debridement is a useful tool in the treatment of burned hands but the decision-making and correct timing of operative intervention in deep partial thickness burns after enzymatic debridement requires experience. Spontaneous healing of deep partial thickness burns was best in patients with contact burns and less than 15% burn TBSA.

Ethics approval

The responsible ethics committee waived the need for ethics approval due to the retrospective nature of the study.

Disclosure statement

MD and CW have acted as invited speaker for MediWound GmbH.

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