



## Burns

# Feasibility and safety of enzymatic debridement for the prevention of operative escharotomy in circumferential deep burns of the distal upper extremity<sup>☆</sup>



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## ABSTRACT

**Background:** Burn-induced compartment syndrome is a severe sequela after circumferential burns of the extremities and is avoidable by immediate release of the underlying pressure under the eschar. Although the current gold standard is operative escharotomy, this procedure carries considerable morbidity. Our study evaluates the safety and effectiveness of immediate enzymatic debridement to prevent the need for operative escharotomy because of burn-induced compartment syndrome in selected patients.

**Patients and Methods:** From 2015 to 2017, all patients suffering from deep circumferential burns of the upper extremities requiring operative escharotomy were potential candidates for the treatment algorithm evaluated by this study. Exclusion criteria involved burn trauma > 12 hours, clinically established burn-induced compartment syndrome, intolerance to the enzymatic debriding agent, dry burns requiring presoaking, as well as blast and electrical injuries requiring fasciotomy or carpal tunnel release. All patients with the inclusion criteria received enzymatic debridement with Nexobrid immediately after admission to our burn center. Enzymatic debridement was applied according to the manufacturer's recommendations. After enzymatic debridement, extremities were revisited every 2 hours for 24 hours to determine the need for conversion to conventional operative escharotomy. The indication for and time to skin grafting was reviewed, and functional outcomes assessed during follow-up examination.

**Results:** Included in this study were 13 patients with 20 burned upper extremities. Enzymatic debridement provided a sufficient eschar removal in all patients. Conversion to conventional operative escharotomy was thus not necessary in any patient. Secondary skin grafting was required in 9 patients. Functional outcomes were favorable 11.9 months after burn trauma.

**Conclusion:** If the specific contraindications are respected, enzymatic debridement is safe and effective for the prevention of burn-induced compartment syndrome after deep circumferential burns at the upper extremity, and thus making operative escharotomy unnecessary.

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## Introduction

Deep burns with associated burned tissue (ie, eschar) diminish skin elasticity and form a rigid envelope over underlying tissues

and organs, triggering secondary edema formation. Especially in circumferential burns, which compromise more than two thirds of the circumference of the limb or thorax/abdomen, this envelope and the concomitant burn edema can lead to compartment syndrome and thus endanger tissue viability or abdominal and respiratory function.<sup>1</sup> Therefore, immediate release of the pressure via an operative escharotomy is recommended to prevent burn-induced compartment syndrome (BICS), because this escharotomy is readily available and directly effective.<sup>2</sup> Operative escharotomy, however, may be delayed because of logistical deficiencies or even avoided because of its invasiveness, especially by inexperienced surgeons. Even if performed in time, incorrect localization or depth of the escharotomy can damage functional structures, such

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as vessels, nerves, or tendons or may not completely relieve the increasing compartment pressure, especially in the lower leg. Furthermore, the incision itself may increase the risk of bleeding or infection and can create soft tissue defects requiring complicated flap coverage and the associated convalescence.<sup>3,4</sup>

In 2004, Rosenberg et al<sup>5</sup> introduced the Bromelain-based enzymatic agent Nexobrid (NXB, MediWound, Rüsselsheim, Germany) for the enzymatic debridement (ED) of burns. ED was shown to be effective and safe when applied on deep, second-degree and third-degree burn wounds compared with operative excision as standard procedure.<sup>5</sup> Of note, the enzyme works rapidly within 4 hours after application, selectively debriding eschar and sparing unburned tissue and structures. In a further study conducted by Rosenberg et al,<sup>6</sup> selective ED resulted in a decreased need for and extent of operative intervention compared with traditional operative excision.

Theoretically, early and selective ED may decrease the mass of burned tissue, thereby decreasing the inflammatory response and tissue edema—two factors that contribute to the development of BICS. In this context, Krieger et al<sup>7</sup> showed in an animal model a significant decrease of tissue pressure within 30 minutes after ED was performed on circumferential, full-thickness burns. They found that ED was as effective as operative escharotomy.<sup>7</sup> Therefore, early enzymatic removal of the eschar might be a less invasive alternative to the traditional operative escharotomy. Of note, according to the European Consensus Guidelines, ED is already recommended for removal of the burn eschar in the hand and forearm, and several specialized centers already perform ED to prevent the need for operative escharotomy; nevertheless, further clinical evidence for this specific use is lacking.<sup>8</sup>

The aim of this study was to analyze the safety and feasibility of ED for appropriate circumferential burns of the distal extremities as an alternative to operative escharotomy in an emergency setting of burn care.

## Patients and methods

From 2015 to 2017, all patients encountered for deep partial-thickness or full-thickness burns covering more than two-thirds of the circumference of the distal upper extremities and burn trauma not older than 12 hours were included in this study. On admission to our burn center, all patients were awake and fully alert. Exclusion criteria involved known hypersensitivity to the Bromelain-based enzyme NXB, as well as pregnant or nursing women. Furthermore, dry burns attributable to a delay of transfer or the type of burn (eg, contact) had to be excluded from this study. The exclusion of these types of burn injuries was necessary, because the enzyme can only work in a moist environment. In such cases, burn wounds would usually undergo a moistening procedure, so called “presoaking”; however, recommendations for duration of “presoaking” are up to 12 hours, and thus, ED would be performed too late to prevent BICS.<sup>8</sup> An experienced burn surgeon decided, based on clinical experience, whether a patient’s burn wound was dry or moist at the time the patient was admitted to our burn center. In addition, high-voltage and blast injuries, demanding fasciotomy and carpal tunnel release, were excluded from this study (Figs 1 and 2). In addition, patients who already had symptoms of BICS, such as paresthesia, deep tissue pain, pulselessness, or compromised perfusion distally from the burn injury, underwent direct operative escharotomy and were not included in this study. The study was conducted in accordance with the local ethics committee and the Declaration of Helsinki.

### Enzymatic debridement

On admission to our burn center, patients with affected extremities that met the inclusion criteria were treated immediately



**Fig 1.** A burn wound after a high-voltage injury, which required fasciotomy and carpal tunnel release and thus was excluded from the study.



**Fig 2.** A deep, dry, full-thickness burn wound of the hand, which would have required a minimum of 2 hours of presoaking before enzymatic therapy and thus was excluded from the study.

with the enzymatic debriding agent NXB. Patients received regional anesthesia by brachial plexus catheter unless already under general anesthesia because of the severity of the burn trauma. We use anesthesia routinely, because mixed pattern burns with areas of superficial partial thickness and thus sensation are always possible.<sup>9</sup>

Upper extremities were first cleaned with an antiseptic agent containing 0.04% polyhexanide (Serasept, Serag-Wiessner, Naila, Germany) and covered subsequently with NXB (Fig 3, A). NXB powder was mixed with gel according to the manufacturer’s recommendation, and 2 g NXB were used for every 100 cm<sup>2</sup> of eschar. To keep the NXB gel in place and to provide hygienic conditions, the NXB-covered extremity was wrapped with a sleeve-shaped plastic foil (Suprasorb CNP EasyDress, Lohmann & Rauscher, Neuwied, Germany), which was sealed proximally with a circumferentially placed tape. If leakage was detected, an additional adaptive skin barrier paste (Comfeel Barrier Creme, Coloplast GmbH, Hamburg, Germany) was applied (Fig 3, B). After 4 hours, the plastic foil and the NXB gel were removed, and the burn wound was cleaned with Serasept (Fig 3, C). At this point, the extremity was re-evaluated for signs of compartment syndrome, and the indication for operative escharotomy was revisited. Of note, because patients received brachial plexus or general anesthesia, assessment of compartment syndrome was based on pulse, bleeding, temperature, and hardness of the underlying soft tissues. In addition, a detailed pattern of bleeding after ED was evaluated for the need for early skin grafting. Finally, treated extremities were wrapped in gauze soaked in polyhexanide solution (Serasept, Serag-Wiessner) for a



**Fig 3.** ED in patient 7. (A) Circumferential deep, partial-thickness burn of the right forearm and hand, which would otherwise need operative escharotomy. (B) After ED, the extremity is wrapped into a preformed plastic foil (Suprasorb CNP EasyDress, Lohmann-Rauscher, Neuwied, Germany), which is sealed proximal to the burn wound. (C) ED is verified (4 hours later) and the need for operative escharotomy is avoided. (D) and (E) The right hand at the 7-month follow-up.

minimum of 4 hours to remove remaining remnants of the eschar (the postsoaking phase). The need for operative escharotomy was evaluated again every 2 hours for 24 hours.

#### Follow-up examination

Medical records of all patients were reviewed, and each patient was scheduled routinely for follow-up examination at our burn facility. In addition to epidemiologic data, chart review involved the affected extremity, total burned body surface area (TBSA), time to ED, need for operative treatment, and number of operations. Routine examinations comprised time to follow-up, range of motion, and sensation. In addition, patients were asked to complete the disability of hand, arm, and shoulder questionnaire (DASH). Patient 7's progress is presented at the 7-month follow-up in Figs 3, D and E.

## Results

### Acute phase: ED to prevent the need for operative escharotomy

From 2015 to 2017, 24 patients with 35 burned extremities suffered from circumferential burns in the distal upper extremity principally requiring escharotomy. A total of 14 extremities revealed a dry burn injury, which would have required prolonged presoaking before ED treatment, and thus, these 14 extremities received immediate operative escharotomy. Another extremity was excluded because of an electrical burn injury demanding fasciotomy. The remaining 20 extremities underwent ED treatment in an attempt to prevent BICS and the need for operative escharotomy according to our protocol. Of note, mean TBSA was 21%, indicating massive burns with substantial risk to general edema and swelling and thus BICS. After ED, sufficient debridement defined by

**Table 1**  
Patient demographics.

Pt	Age (years)	Number of UE	UE Side	Burn depth	TBSA (%)	Need for skin graft	Total surgeries	Time to wound closure (days)	Time to follow-up (months)	ROM	Sensibility	DASH
1	43	1	rt FA	2a-b	7	n	0	13*	N/A	N/A	N/A	N/A
2	39	2	bil FAs	2b	30	y	1	11	N/A	N/A	N/A	N/A
3	53	2	bil hands	2b	23	y	2	11	5	imp	Norm	8.3
4	54	1	lt FA	2b-3	27	y	1	16	11	norm	imp	26.2
5	54	2	bil wrists	2b-3	29	y	2	14	20	Norm	Norm	3.3
6	63	2	bil FAs/hands	2b-3	40	y	2	21	N/A	N/A	N/A	N/A
7	26	1	rt FA/hand	2a-b	14	n	0	14*	7	imp	Norm	8.3
8	81	2	bil hands	2b	13	y	2	17	17	imp	Norm	42.5
9	50	1	lt hand	2b-3	7	y	1	6	7	norm	Norm	1.7
10	48	2	bil FAs	2a-b	26	n	0	27*	34	norm	Norm	18.3
11	80	1	rt FA	2b-3	25	y	1	13	N/A	N/A	N/A	N/A
12	43	1	rt hand	2b-3	7	y	1	10	3	norm	Norm	8.3
13	19	2	bil FAs	2a-b	25	n	0	16*	3	norm	norm	8.3
mean/total	50.2	n = 20	—	—	21	—	1.0	17.5*/13.2	11.9	3/9	1/9	13.9
SD	17.9	—	—	—	10.4	—	0.8	6.5*/4.4	10.2	—	—	13.1

Pt, patient; UE, upper extremity; rt, right; lt, left; bil, bilateral; FA, forearm; TBSA, total body surface area; ROM, range of motion; DASH, disability of arm and shoulder; norm, normal; imp, impaired; N/A, not available.

\* Mean time to wound closure of extremities that received ED only and did not require operative treatment.

bleeding pattern, viable tissue, and absence of burned tissue was evident in all cases, and operative escharotomy was not necessary in any patient. Occurrence of edema did not impair ED effectiveness. Subsequent operative treatment with skin grafting was necessary in 14 extremities. Autologous transplantation of split-thickness skin grafts was performed 9.9 days on average (range 3 to 27 days) after ED application. In 6 extremities, a second operative procedure, attributable to remaining defects and graft failure, was necessary. Complete wound healing was evident after a mean of 17.5 days in case of ED and spontaneous healing, or 13.2 days after split-thickness skin grafting subsequent to ED. Demographic data of all patients included in this study are presented in the Table 1.

#### Follow-up phase

A total of 9 patients with 14 treated extremities were available for follow-up. Mean follow-up was 11.9 months. Range of motion revealed no limitations in 9 extremities (6 of 9 patients). In the remaining 5 extremities (3 of 9 patients), finger flexion and extension were slightly diminished. In detail, mean fingertip-to-palm distance from digit 2 to 5 was 0.3/0.2/0.3/0.6 cm (SD: 0.7/0.7/0.7/1.1) on the right side and 0/0/0/0.1 cm (SD: 0/0/0/0.3) on the left side. Mean fingernail-table distance from digit 2 to 5 was 0.1/0.2/0.3/0.8 cm (SD: 0.2/0.4/0.7/1.6) on the right side and 0.2/0.1/0/0.4 cm (SD: 0.7/0.3/0/0.8) on the left side. Range of motion revealed a patient-reported trend toward full recovery in these patients. Sensibility in terms of impaired 2-point discrimination was affected in one extremity (1 of 9 patients) only but was also reported as gradually improving. Outcomes of questionnaires showed minimal disabilities in DASH scores. Outcomes of each patient are presented in the Table 1.

#### Discussion

In this study, we demonstrated that ED of deep circumferential burns in the distal upper extremities can prevent BICS, thus preventing the need for and morbidity of operative escharotomy. According to our treatment algorithm, safety and efficiency could be proven by the fact that none of the extremities required conversion to operative escharotomy. Successful treatment was substantiated during midterm follow-up, in which patients had already revealed a close to normal function and an extremity-related quality of life comparable to a healthy population. Of note, subsequent operative procedures could be performed, because ED

already led to proper eschar removal. Nevertheless, burns with a dry surface may still require operative escharotomy, because ED would require an individual, presoaking phase of unpredictable duration and thus potentially an unacceptable delay in releasing the increased tissue pressure. In addition, a combination of burn and mechanical or high-voltage trauma might require ED for the prevention of BICS combined with fasciotomy/neurolysis to immediately release both the muscle compartment and the nerve tunnel (eg, carpal tunnel) pressures.

Recommendations regarding escharotomy for the prevention of BICS vary considerably in the literature. Although some reports indicate the need for escharotomy for circumferential full-thickness burns only, others suggest the need for escharotomy also for burns of deep partial thickness.<sup>10–12</sup> Authors of the former claim that only full-thickness necrotic tissue prevents the skin from dilating; whereas burns of deep partial thickness still allow elasticity, making incision of the eschar unnecessary.<sup>13</sup> In contrast, Barros et al<sup>12</sup> and Kamolz et al<sup>14</sup> suggest including burns of deep partial thickness, because burn wounds are often of a mixed pattern and subsequent edema can increase tissue pressure substantially, even in partial-thickness burn wounds. Burd et al<sup>10</sup> underlined the importance of the presence of edema in the development of BICS and recommended escharotomy selectively even in nonburned limbs of patients suffering from severe generalized edema with symptoms of extensive burn trauma. In our experience, extensive edema, which is often seen after large-volume resuscitation, can dramatically change the compression ratio in soft-tissue compartments and lead to BICS even in noncircumferential and/or deep partial thickness burns. Increased permeability of the capillary wall, induced by inflammatory mediators, is anticipated to cause an extravascular volume shift and thus cause increased tissue pressure, further compromising the ischemic tissue. In this context, we believe that emergency ED is superior to operative escharotomy in the prevention of BICS, because debridement removes the eschar and inflammatory mediators and thereby decreases or even averts associated edema.

The use of ED, however, can only be safe and effective in the very early (emergency) phase after burn injury, making crucial the time at which ED is begun. According to Wong et al,<sup>15</sup> an imbalance between burned skin that cannot expand and the inflammation-associated formation of edema reaches its most critical point within 24 to 48 hours. Experimental data suggest that nerves and muscles undergo irreversible damage within 12 to 24 hours and 4 to 6 hours of ischemia, respectively.<sup>12</sup> Consequently, if clinical symptoms of BICS are present, immediate pressure release

by operative escharotomy is mandatory, because a period of 4 hours of effective ED duration cannot be justified.

In our study, one primary inclusion criterion for patients to receive ED was that the burn trauma occurred fewer than 12 hours earlier. This point was chosen, because in our clinical experience, maximum edema formation is usually evident 24 hours after burn trauma or even later, which is well in accordance with the findings of Wong et al.<sup>15</sup> Of note, clinically evident BICS, which we defined as exclusion criterion for ED, was not seen in any patient in this study. Instead, the reason for direct operative escharotomy and not ED was either the type of injury (eg, blast or high voltage), dryness of the burn wound, or late arrival at our center.

In this context, diagnosis of BICS on admission of the patient or during the monitoring of ED was based solely on clinical examination and judgment. We believe that no objective method currently available can supplant the use of clinical signs of BICS and, thus, we maintain that these direct methods have no any additional value in clinical decision making. This opinion is in accordance with that of Orgill and Piccolo,<sup>1</sup> who wrote

...decreased or absent oximetry (or loss of the) Doppler probe signal, increased compartment pressures, and sudden onset of neurologic symptoms are common reasons to perform an escharotomy. However, the long-term decision on whether to perform an escharotomy is ultimately based on experience and overall clinical judgment.

Kamolz et al<sup>14</sup> share an even more progressive opinion and recommend escharotomy depending on circumference and depth of the burn irrespective of the presence of any clinical signs. If the pulse of the radial or ulnar artery disappears in the clinical course after escharotomy, escharotomy needs to be extended immediately or probably “converted” to fasciotomy. Of note, escharotomy should be performed before the onset of clinical symptoms of BICS and immediately if clinical signs, such as when pulse and perfusion pattern do not clearly prove the absence of BICS.

In addition to the indications for and time point of escharotomy, the current literature also discusses “who” should perform this invasive and important procedure. Saffle et al<sup>2</sup> stipulate that operative escharotomy should only be performed by experienced professionals, because both the indications for and the method of operative escharotomy are crucial to assure a low morbidity and even in some cases even to prevent mortality. Furthermore, escharotomy can cause substantial bleeding, requiring appropriate hemostasis or cardiopulmonary stabilization. In contrast, Barros et al<sup>12</sup> stated that “any” physician, irrespective of clinicians or surgeons can perform escharotomy, or in case of absence of a physician, even paramedics should be able to undertake this urgent and lifesaving procedure. In our opinion, operative escharotomy is not a trivial procedure, demanding knowledge of the appropriate anatomic landmarks and muscular compartments, especially in the lower leg and belonging to a specialized burn care physician. In countries such as Germany, where a burn center is always nearby, operative escharotomy should wait within reason until an experienced burn surgeon is available—except an emergency escharotomy of the trunk in a case of ventilator restriction. The risk for complications is high, and an insufficient escharotomy attributable to a lack of experience can leave the surgeon with a false sense of security and the patient with permanent sequelae. All these aspects, however, can be avoided if ED is used in appropriate cases to prevent BICS. The major benefit of ED is that unburned tissues are preserved, and morbidity is limited because the affected tissues are debrided and ideally no eschar is left untreated. In addition, for patients in whom operative intervention was required after treatment of the deep burn with ED, the extent of operative debridement was decreased and only skin grafting was necessary, underlining the effectiveness of ED. In this context, we underwent

a learning curve during this study regarding the appropriate time point for skin grafting after ED.<sup>16</sup> Although at the beginning of the study we initially overdelayed skin grafting, we have since implemented a protocol according to the detailed pattern of bleeding after ED. If the pattern of bleeding after ED showed pinpoint capillary bleeding, currently we wait about 3 weeks before any further operative intervention, because spontaneous healing is probable. In contrast, if the bleeding pattern shows larger diameter vessels and exposed subdermal fat layers, immediate skin grafting surgery is initiated.

Although we demonstrated that ED prevented the need for escharotomy in a primary setting, it is very important to emphasize that electrical burns, blast injuries, dry burns that would require presoaking, as well as patients with clinical signs of BICS should receive operative escharotomy immediately by an experienced burn surgeon in a specialized burn center. Of the contraindications of ED, dry burns were the most common, involving almost 50% of cases in our study. Unfortunately, dry burns are more difficult to identify, and there is currently no easy objective method to establish the moisture content and therefore the difference of an appropriate burn for ED and that of a dry burn necessitating operative escharotomy. Therefore, ED should only be applied by physicians experienced in burn care and handling of ED. Future studies on objective and reproducible methods for moisture assessment are necessary to predict the need for and potential duration of the presoaking procedure and thus the possibility of treating dry burns in a certain timeframe.

A further limitation of ED is the additional acquisition costs, for which few nations reimburse health care centers. Although delivery and storage at 2°C to 8°C (35°C to 46°F) of the powder does not involve a great increase in economic burden, the purchase price of the enzymatic agent for treatment of a 1% TBSA burn (2 g of Nexobrid) is about 400 euros (approximately 420 US dollars [USD]). A study by Kern et al,<sup>17</sup> addressing the German health care system revealed that using enzymatic debridement leads to cost savings that are inversely related to the treated total burned surface area. If ED completely substitutes for the standard of care, the total cost per patient can be decreased by about 30% for a 5% TBSA burn. This calculation was based on operative excision and autografting as the standard of care (2,622 and 2,484 euros, respectively, irrespective of TBSA; approximately USD 2,700 and USD 2,500), with the assumption that ED saves operating room (OR) time, OR capacity, and staff needed for the debridement. Nevertheless, in the case of ED and the subsequent need for autografting, both costs and reimbursements increase in a certain ratio. Therefore, the technical advantages and the advantages to the patient versus the drawbacks, such as costs, must be weighed within the health care system.

In conclusion, if appropriate exclusion criteria are respected, early ED is capable of a safe and effective removal of the eschar, thus preventing BICS and the need for operative escharotomy on patients with deep-burn wound injuries of the upper extremities. Secondary conversion to operative escharotomy was not necessary in patients in this, study underlining the reliability of this procedure. If burns are not associated with high-voltage or blast injuries and there are no clinical signs of BICS, and if the eschar is not too dry, ED is a valuable alternative to operative escharotomy of the upper extremities.

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