Scratching beneath the surface: innovative treatment modalities for burn patients

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Hand function recovers to near normal in patients with deep dermal hand burns treated with enzymatic debridement: a prospective cohort study

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Submitted

Abstract

Objective
To evaluate hand function in patients with hand burns treated with enzymatic debridement.

Methods
We prospectively evaluated patients with enzymatically treated deep dermal hand burns using an assessment scheme at discharge and 3, 6, and 12 months post-burn: hand function using Modified Kapandji Index scores, Composite Finger Flexion, Jebsen-Taylor Hand Function Test, strength (dynamometer), scar quality using the Patient and Observer Scar Assessment Scale, and quality of life using Quick Disability Arm Shoulder Hand Questionnaire, EuroQoL, Burn Specific Health Scare-Brief, and the Canadian Occupational Performance Measure.

Results
14 enzymatically treated hands in 10 patients were included. There was a significant improvement in hand function as measured by Kapandji scores ($p<0.0001$), Finger Flexion in all digits ($p<0.001$), and strength ($p<0.0001$). Scar quality improved in patient's overall opinion ($p=0.029$), observers' overall opinion ($p=0.030$), vascularity ($p=0.003$), and pliability ($p=0.012$). Quality of life improved using the Quick Disability Arm Shoulder Hand Questionnaire ($p<0.0001$), EuroQoL ($p=0.042$), Burn Specific Health Scare-Brief in the domains work ($p=0.003$), affect ($p=0.012$), and heat sensitivity ($p=0.025$), and by the Canadian Occupational Performance Measure ($p<0.0001$).

Conclusion
Hand function of patients with enzymatically treated hand burns returned to near normal 12 months post-burn. Scar quality and quality of life also improved.

Introduction

Deep dermal and full thickness burn wounds require surgical debridement and split skin grafting to minimize scar formation that can lead to poor functional and cosmetic outcomes.[1-4] There are several debridement techniques, and evidence in favor of any technique is lacking.[5] The most often used methods include debridement with surgical handheld knives, hydrosurgery, and enzymatic debridement.[5]

NexoBrid® (Mediwound Ltd. Yavne, Israel) is an enzymatic debriding agent consisting of proteolytic enzymes enriched in Bromelain which selectively debrides eschar in the early stage (<72 hours) while leaving vital tissue unharmed.[6] Studies showed that NexoBrid compared to standard of care (SOC), which usually consists of conventional tangential excision, leads to a shorter debridement time and reduction in surgical excision and skin grafting.[6-8] This is due to a more spontaneous wound healing.

The hands are a particular area of interest when it comes to burn wounds. The debridement of hand burns in the Netherlands is often delayed to await demarcation, which allows the burn surgeon to make a more adequate assessment of burn depth and need for excision.[9,10] However, this approach prolongs treatment, and has the risk of infection and delay of hand therapy. Therefore, early escharectomy can be desirable in the treatment of hand burns. The use of enzymatic debridement showed promising results in regard to the reduction in the need for surgery in burns of the hands[6, 8], but long-term results on hand function, scar quality and quality of life (QoL) are lacking.[11, 13-15]

In general, the evaluation of function and scar quality after hand burns is scarce[10], with most older studies describing hand function after hand burns in generic terms, without the use of validated instruments.[11-13] Moreover, hand function and scar quality are often not described over time. This is even more so for patients with hand burns specifically treated with enzymatic debridement.[11, 13-15]

Therefore, we performed a prospective cohort study to evaluate adults with deep dermal hand burns treated with enzymatic debridement using a standardized assessment scheme measuring hand function, scar quality, and quality of life over time.

Methods

Study design and participants

Our study was a single-center prospective cohort study performed between November 2016 and December 2019 in the Burn Center Beverwijk, the Netherlands. The study was conducted according to the principles of the Declaration of Helsinki (Ethics manual World Association revision 2013) and in accordance with the Medical Research Involving Human Subjects Act (WMO). The study was approved by the Medical Research Ethics Committee Noord-Holland (NL59342.094.16), and the institutional review board of the Red Cross Hospital, Beverwijk.

The inclusion criteria were: patients aged ≥18 years with deep dermal or mixed deep dermal and full thickness burns of one or both hands, which were treated with enzymatic debridement (NexoBrid®, Mediwound Ltd. Yavne, Israel). Burn wound depth was based on clinical assessment and, when available, with the use of a Laser Doppler Imaging to assess burn wound healing potential. Patients were ineligible if they had an insufficient knowledge of the Dutch language and/or if they were unlikely to comply with the requirements of the study protocol and follow-up. All patients or, in case the patient was temporary incompetent due to sedation and/or intubation, their legal representatives provided written informed consent.

Treatment protocol

Patients were treated with enzymatic debridement according to the regular treatment protocol[14] which consisted of a pre-soak phase of 2-24 hours with the application of gauzes drenched in antibacterial solution (Prontosan®, B. Braun Medical B.V. Oss, Nederland) to prepare the wound bed, the application of enzymatic debridement for four hours, and a post-soak phase of 2-24 hours with antibacterial solution to remove the remains of enzymes and eschar. Treatment after enzymatic debridement varied between patients, depending on the physician's preference and dermal preservation. In case of complete dermal preservation, e.g., no full thickness spots, Suprathel® (Polymedics Innovations GmbH, Denkendorf, Deutschland) was most often used. In case a few full thickness spots were present, donor skin was usually applied. Re-epithelialization was waited for approximately 4-5 weeks. In case re-epithelization stagnated, or in case of larger full thickness burn spots, split skin grafting was performed. Conservatively treated burns were treated until wound closure, using a combination of antibacterial solutions (e.g., Bactroban®, GlaxoSmithKline B.V. Amersfoort, The Netherlands or Fucidin®, LEO Laboratories Ltd. Dublin, Ireland), based on the patients' culture swabs.

Clinical characteristics and outcomes

These include age, sex, cause of burn, Total Body Surface Area (TBSA) burned %, Body Surface Area (BSA) burned % of the hands, the need for echarotomy, surgical excision, autografting and percentage TBSA of autografting of their burned hands, the time to reach wound healing of their hands (defined as re-epithelialization >95%), bacterial colonization, the length of hospital stay (LOS), dominance of the hand, co-morbidities, smoking habits, return to work and the hand therapy. To assess edema of the hand we used the figure-of-eight method as described by Pellecchia et al.[15]

Study outcomes

Hand function

The hand function was measured at discharge and during the 3-, 6- and 12-months follow-up post-burn by the same occupational hand therapist, using a standardizes assessment scheme developed by specialists in the field of (hand) burn care in The Netherlands, including physicians, occupational hand therapists and researchers. The scheme consisted of the following assessments (Figure 1):

- *Modified Kapandji Index (MKI)*[16]: the MKI is a combined score of three tests (Figure 2); 1) thumb opposition test, by scoring 0 (impossible to do) to 10 (completely accomplished), and 2) finger flexion test, by scoring 0 (impossible to do) to 5 (completely accomplished), and 3) flat hand/extension fingers test, by scoring 0 (impossible to do) to 5 (completely accomplished). The maximum sum score is 35 points, indicating optimal function. This assessment was only performed if the patient was fully conscious.
- *Composite finger flexion (CFF)*: this assessment measures flexion in the joints of the fingers[17-20], by measuring the distance (cm) between the fingertips and the palmar crease. If complete flexion is possible and the fingertip reaches the palmar crease, then the score is 0 cm. This was assessed for each finger individually.
- *Strength*: the hand-grip dynamometer is used to assess grip strength of the hand expressed in kilograms. The references of strength vary between countries, and is influenced by age, gender, and dominance of the hand.
- *Jebsen-Taylor Hand Function test (JTHFT)*: the JTHFT is a standardized and objective test with 7 items representative of various hand activities, which include: 1) writing a short sentence, 2) turning over 3x5-inch index cards, 3) picking up small objects (paperclip, coin), 4) stacking checkers, 5) simulating eating, 6) picking up large light objects (empty cans), and 7) picking up large heavy objects (full cans). The activity is measured by the time it takes to complete the activity, and is either within normal range (1=yes) or not within normal range (0=no).

Assessments	Treatment phase (weekly)	Discharge	3 months	6 months	12 months
Hand function: edema, MKI, CFF	X	X	X	X	X
Hand function: strength, JTHF-test			X	X	X
POSAS			X	X	X
QoL: QDASH, EQ-5D		X (pre-burn)	X	X	X
QoL: BSHS-B, COPM			X	X	X
Return to work			X	X	X

Figure 1. outcome assessment scheme.
MKI=Modified Kapandji Index scores, CFF=Composite Finger Flexion, JTHT-test=Jebsen Taylor Hand Function-test, QoL=Quality of Life, QDASH= Quick (shortened) Disability Arm Shoulder Hand questionnaire, EQ-5D=Euro Quality of Life, BSHS-B=Burn Specific Health Scale-Brief, COPM=Canadian Occupational Performance Measure, POSAS=Patient and Observer Scar Assessment Scale.

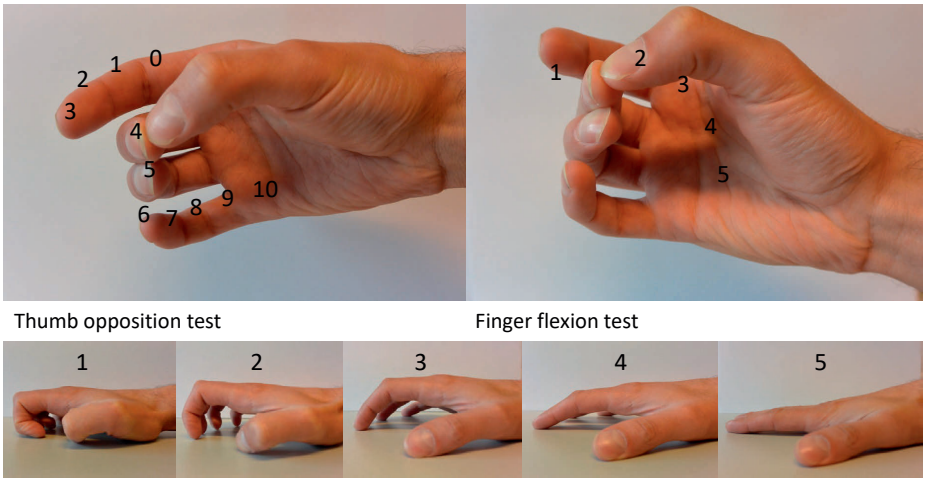

Figure 2. Modified Kapandji Index (MKI) scores

Scar quality

Scar quality was measured using the POSAS (Patient and Observer Scar Assessment Scale, version 2.0) at 3-, 6- and 12-months post-burn. The POSAS measures the quality of scar tissue and consists of a Patient and an Observer Scale. The patient scores: pain, pruritus, color, thickness, relief, pliability, and

overall opinion, on a scale ranging from 0 ("no, not at all") to 10 ("yes, very much"). The observer scores: vascularization, pigmentation, thickness, surface roughness, pliability, surface area, and overall opinion, on a scale ranging from 0 ("normal skin") to 10 ("worst scar imaginable"). Two different trained observers completed the Observer part of the POSAS, and the scoring of their items was averaged.[21]

Quality of Life

Quality of life was measured at 3-, 6- and 12-months post-burn by the following validated questionnaires:

- *Quick shortened Disability Arm Shoulder Hand questionnaire (QDASH)*: the QDASH is a shortened version of the DASH, which is a patient self-rated questionnaire that is specific of the function of the upper limb extremity (questions with regard to activities in household, sport, work, social), and has a scale from 1 ("no difficulty") to 5 ("impossible to carry out") which, by calculating using a formula, makes a minimal total score of 0 (best) to a maximum score of 100 (worst).[22] Patients also provided a QDASH questionnaire filled in as the situation was pre-burn.
- *EuroQol (EQ-5D-5L)*: the EQ-5D-5L is a short questionnaire that encompasses five questions covering five dimensions: mobility, self-care, usual activities, pain and anxiety/depression. The scale ranges from 1 ("no trouble/none") to 5 ("not capable/extreme problem").[23] Based on these dimensions, a single index score can be derived ranging from 0 ("death") to 1 ("full health"). Secondly, it asks the patient to rate their health on a scale from 0 (the worst health you can imagine) to 100 (the best health you can imagine). Patients also provided the EQ-5D-5L questionnaire filled in as the situation was pre-burn.
- *Burn Specific Health Scale Brief (BSHS-B)*: the BSHS-B is a validated scale consisting of 40 items which comprise different aspects of QoL divided in nine categories: simple abilities, hand function, heat sensitivity, treatment regimens, body image, affect, interpersonal relationships, sexuality and work. The questionnaire has a five-point scale, ranging from 0 (a lot) to 4 (not at all).[24] The scores were averaged within each of the nine categories.
- *Canadian Occupational Performance Measure (COPM)*: the COPM is a tool for occupational therapists to conduct a semi-structured interview in order to identify issues in areas of self-care, productivity, and leisure for individual patients. The patients themselves can choose problems they wish to focus on during occupational therapy. Each of these problems are rated on performance and satisfaction on a scale from 0 (worst) to 10 (best). Mean scores were calculated per patient, independent of the number of problems they reported.[25]

Statistical analysis

Continuous data was presented with their mean and standard deviation (SD, ±) in case of parametric data, and with the median and interquartile range (IQR) in case of non-parametric data. Friedman test (continuous data, categorical variables) and Cochran's Q test (dichotomous variables) was used to assess hand function, scar quality, and QoL over time. Both tests indicate whether there is a difference over time, without assessing between which time points and what the difference entails. In case of a statistically significant difference over time, post-hoc analysis with either the Wilcoxon (values in >2 scales) or McNemar test (dichotomous values) was conducted to evaluate the changes between the time-points.

The p-value of <0.05 was taken as a threshold for statistical significance. In case post-hoc analysis was conducted; a Bonferroni correction was applied (p=0.05 divided by the number of tests). The p-values provided in the Results section are the applied significance level corresponding to the test performed. Data were analyzed using the IBM Statistical Package for the Social Sciences (SPSS) version 24.

Results

Clinical characteristics

Of the 12 eligible patients, 10 patients were included between March 2017 and December 2018 (Figure 3). The patient group consisted of nine men and one woman, and they had a mean age of 56.3 ± 12.5 years (Table 1). Seven patients had both hands burned, of which in four patients both hands were treated with enzymatic debridement, leading to the inclusion of 14 enzymatically treated hands. In three patients the contralateral hand was treated with SOC. This was either because of previous escharotomy of the hand making enzymatic treatment hazardous due to the increased risk of bleeding in escharotomy wounds (n=1), or because of a more superficial burn depth in the contralateral hand (n=2). One of the included patients required an escharotomy of the hand, based on clinical assessment and the risk of burn-induced compartment syndrome, and was successfully treated with enzymatic debridement. Another included patient also required an escharotomy. Unfortunately, we were not able to perform enzymatic debridement in this patient due to the unavailability of trained personnel. This patient received a surgical escharotomy, and was treated with enzymatic debridement the next day.

All patients received hand therapy directly upon admission, and pressure garments as soon as re-epithelization was completed. The median duration of hand therapy was six months, with five patients still receiving therapy at 12 months post-burn. The duration of pressure garments had a median of eight months. Silicon therapy was administered in eight patients with a median of six months. None of the patients received corticosteroid treatment during their scar modulation phase up until 12 months post-burn. (Figure 4)

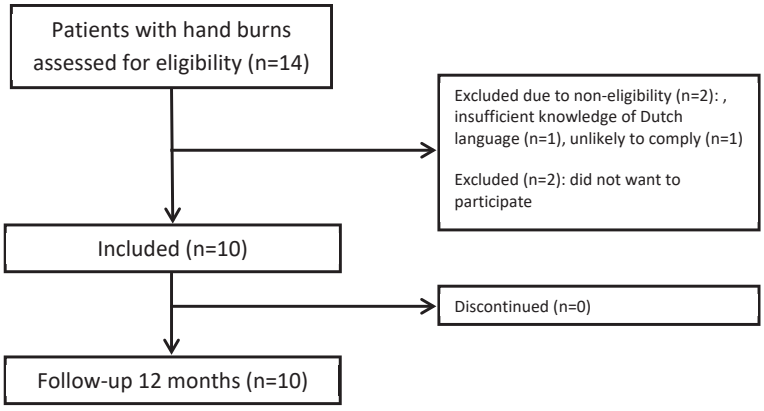

Figure 3. Flowchart

Table 1. Patient and clinical characteristics

Patient and clinical characteristics (n=10, 14 enzymatically treated hands)	
General	
Male (n)	9
Age (years)	56.3 ± 12.5
Smoking (yes, n)	3
Comorbidities (yes, n):	
Diabetes Mellitus	1
Cardiovascular disease	2
Cause of burn:	
Flame (n)	9
Scald (n)	1
Right hand dominance (n)	9
TBSA burned total (%)	11.0 ± 8.1
Time to wound healing (days)	35.1 ± 12.6
Length of hospital stay (days)	25.3 ± 15.6
Enzymatic treated hands (n=14)	
TBSA burned (%)	1.8, 1.5-2.5
TBSA burned 2nd degree (%)	1.5, 1.0-2.5
TBSA burned 3rd degree (%)	0, 0-1.0
TBSA excised (%)	0.3, 0-1.3
TBSA skin grafted (%)	1.0 ± 0.6
TBSA skin grafted in percentage of TBSA burned (%)	57.6 ± 31.7
Time to wound healing (days)	31.0, 24.0-39.0
Wound colonization pathogenic bacteria (n)	6

Values are presented as mean with standard deviation (±) in case of parametric data and in median with interquartile range in case of non-parametric data.

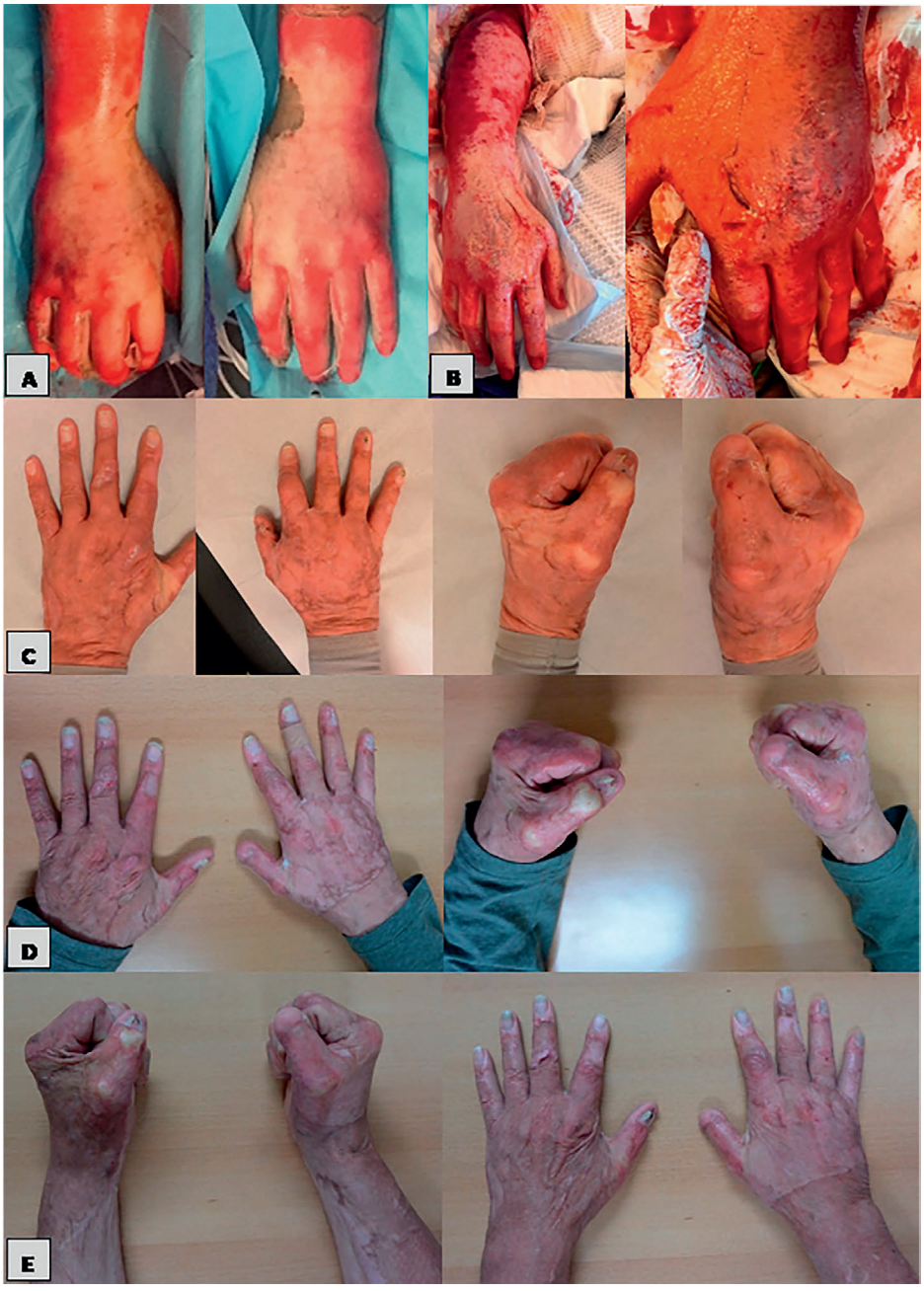

Figure 4. hand burn up to 12 months follow-up; A=flame burn; B=post enzymatic debridement; C=3 months post-burn; D=6 months post-burn; E=12 months post-burn

Clinical outcomes

In five patients, additional excision of 0.3 (IQR 0-1.3) % BSA burned of the hand was needed after the enzymatic debridement. In eight patients, additional skin grafting without excision was needed of 57.6 ± 31.7% of the enzymatic treated hand. The median time to wound healing of the enzymatic treated hands was 31.0 (IQR 24.0-39.0) days. There was reduction in edema over time (p=0.007), with a median of 51.0 cm (IQR 47.0-54.9) at baseline, reduced to a median of 48.5 cm (IQR 46.3-51.0) at 12 months post-burn. However, post-hoc analysis showed no statistically significant difference over time for this outcome between any of the time points.

Return to work

Seven out of ten patients were working at the time of their burns. At 3 months, four patients had returned to work, of which one returned to the same working hours as before their burns. At 12 months all patients returned to work, of which four had a reduction in the hours that they worked pre-burn. All patients kept the same profession, albeit in an adjusted setting.

Hand function

MKI

there was a statistically significant increase over time between baseline (median 19.5, IQR 10.5-28.5) and 6 months (median 30.0, IQR 29.0-33.0) (Z=-2.669, p=0.008), and between baseline and 12 months (median 32.0, IQR 30.5-33.0) (Z=-3.149, p=0.002) (Figure 5).

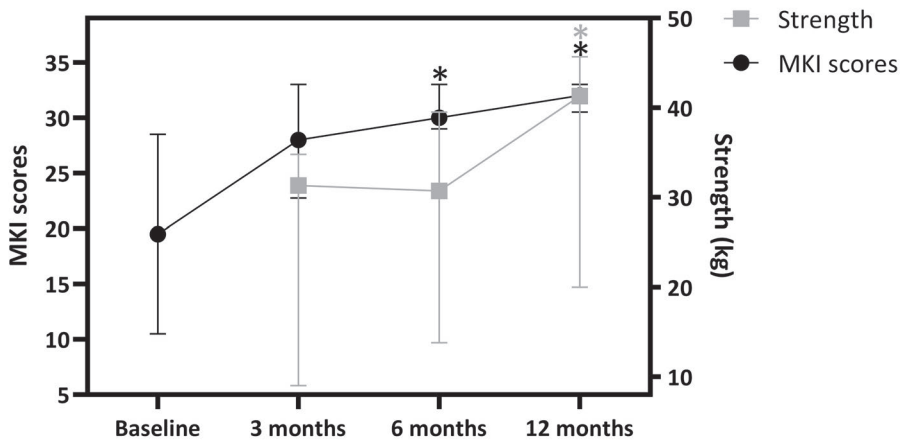

Figure 5. MKI scores and strength over time

CFF

there was a statistically significant decrease between baseline and 6 months (Z=-2.659, p=0.008) and between baseline and 12 months in CFF2 (CFF digit 2, Z=-2.937, p=0.003) (baseline median 5.0, IQR 0.8-6.6, 6 months median 0.0, IQR 0.0-2.1, 12 months median 0.0, IQR 0.0-0.0), CFF4 (baseline median 3.3, IQR 0.0-8.0, 6 months median 0.0, IQR 0.0-0.6, 12 months median 0.0, IQR 0.0-0.0) (respectively Z=-2.677, p=0.007; Z=-2.812, p=0.005) and CFF5 (baseline median 3.0, IQR 1.0-5.8, 6 months median 0.0, IQR 0.0-1.0, 12 months median 0.0, IQR 0.0-0.0) (respectively, Z=-2.670, p=0.008; Z=-2.805, p=0.005). There was a statistically significant decrease between baseline (median 4.5, IQR 0.0-7.5) and 12 months (median 0.0, IQR 0.0-0.0) in CFF3 (Z=-2.805, p=0.005), but not between baseline and 6 months (median 0.0, IQR 0.0-0.5). (Figure 6)

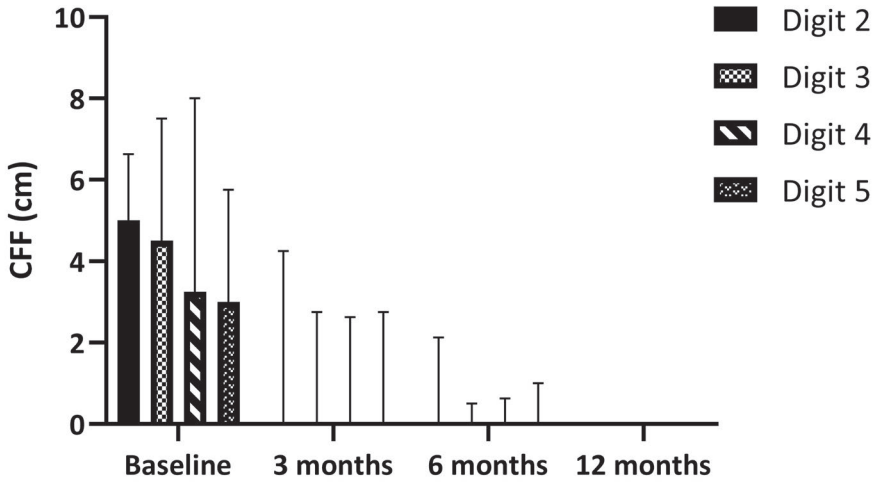

Figure 6. CFF scores over time

Strength

there was a statistically significant increase between 3 months (median 31.3, IQR 9.0-34.8) and 12 months (median 41.3, IQR 20.0-45.7) (Z=-3.297, p=0.001) and between 6 months (median 30.7, IQR 13.8-39.5) and 12 months (Z=-3.235, p=0.001) (Figure 5).

JTHFT

Cochran's Q test determined that there was a statistically significant difference in outcome of the test over time in picking up large light objects (n=14, X2(2) = 7.60, p=0.022), and picking up large heavy objects (n=14, X2(2) = 6.50, p=0.039), with both activities showing an increase in patients who completed the activity within

range at 12 months (light objects 8/14 hands; heavy objects 7/14 hands) compared to 3 months (light objects 3/14 hands; heavy objects 3/14 hands). However, post-hoc analysis revealed no statistically significant differences between the time points in picking up large light objects or picking up large heavy objects. There was no significant difference in the ability to write a short sentence (p=0.135), turning over 3x5-inch index cards (p=0.717), picking up small objects (p=0.074), stacking checkers (p=0.651), and simulating eating (p=0.549).

Scar quality

Patient scores

There were no statistically significant differences over time in any of the items (n=10). The item overall opinion showed a decrease between 3 (median 6.5, IQR 3.8-7.0) and 12 months (median 3.5, IQR 2.0-6.0) (Figure 7). However, this did not reach statistical significance based on the corrected p-value (Z=-2.179, p=0.029; threshold p<0.017). (Figure 4)

Observer scores

Between 3 and 6 months, there were no statistically significant differences for any of the items. Between 3 and 12 months, there was a statistically significant decrease for the items vascularity (median 5.3, IQR 3.9-6.1 versus median 3.5, IQR 1.9-5.0; Z=-3.054, p=0.002), pliability (median 5.0, IQR 4.5-6.5 versus median 3.5, IQR 2.5-5.6; Z=-2.553, p=0.011), and for the overall opinion (median 5.0, IQR 3.9-5.1 versus median 3.8, IQR 3.0-5.0; Z=-2.549, p=0.011) (Figure 7). Between 6 and 12 months, there was a statistically significant decrease in the item vascularity (median 4.0, IQR 3.8-6.0 versus median 3.5, IQR 1.9-5.0; Z=-2.610, p=0.009). There were no statistical significance differences over time in the following items: pigmentation, thickness, relief and surface.

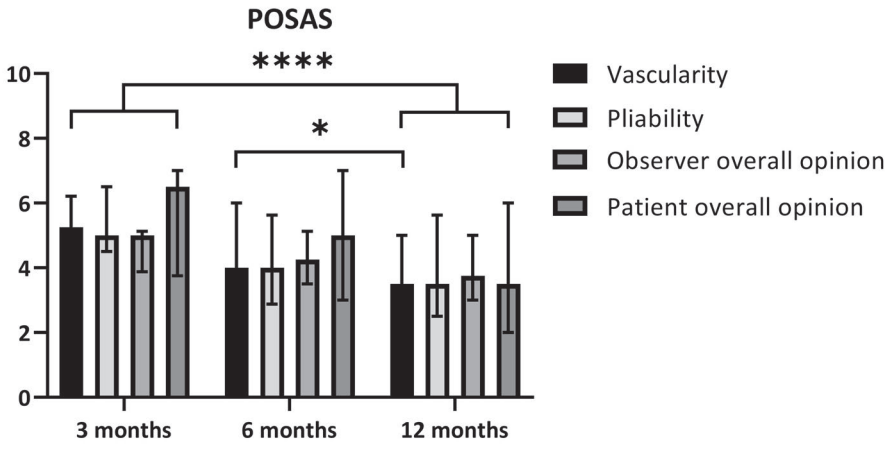

Figure 7. POSAS scores over time

Quality of Life

QDASH

There was a statistically significant increase (p=0.005) between pre-burn (median 0.0, IQR 0.0-2.8) and 3 months (median 39.1, IQR 18.6-58.4), and between 3 months and 12 months (median 12.3, IQR 5.8-36.1) (p=0.005) (Figure 8).

EQ-5D-5L

There was no statistically significant difference in the EQ-5D-5L score between any of the time points. There was no statistically significant difference in the score patients gave their health between any of the time points (p=0.604) (Figure 8).

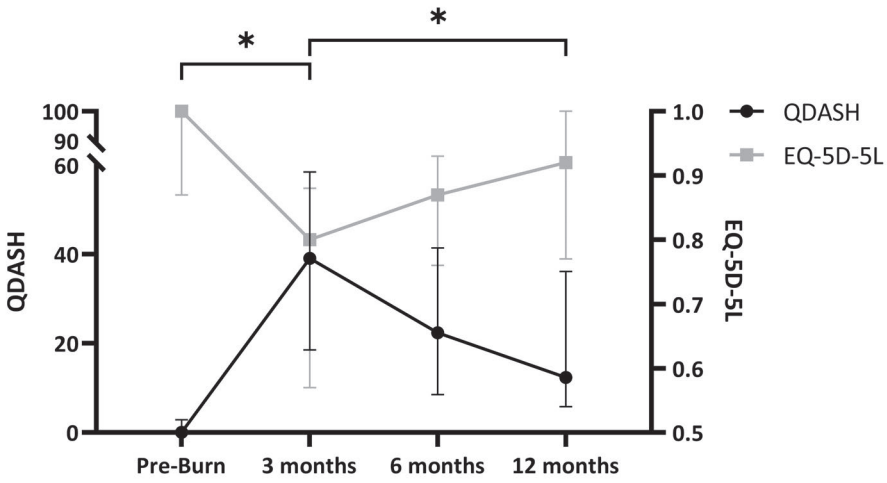

Figure 8. QDASH and EQ-5D-5L scores over time

BSHS-B

Between 3 and 6 months, there was a statistically significant increase for the domain work (median 2.8, IQR 0.0-3.1 versus median 3.1, IQR 1.2-3.6; Z=-2.609, p=0.009) (Figure 9). Between 3 and 12 months, there was a statistically significant increase for the domains work (median 2.8, IQR 0.0-3.1 versus median 3.3, IQR 2.8-4.0; Z=-2.524, p=0.012), and heat sensitivity (median 2.8, IQR 1.9-3.7 versus median 3.7, IQR 3.3-3.9; Z=-2.439, p=0.015). There was no statistically significant difference in any domain between 6 and 12 months.

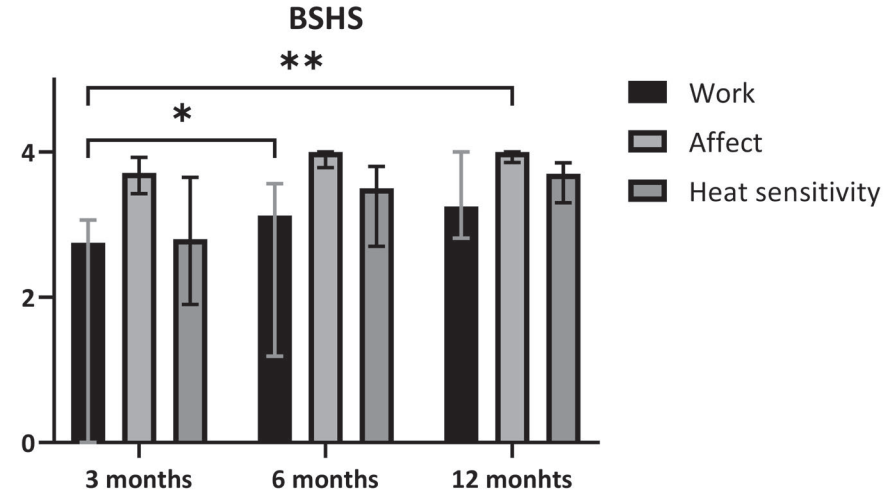

Figure 9. Domains of BSHS-B scores over time

COPM

The activities patients deemed most important varied greatly between patients, and included simple acts (turning a page, buttoning a shirt), daily activities (driving, walking the dog, cycling), and hobbies (playing tennis, crafts, fishing). There was a statistically significant increase (p=0.005) in performance scores between 3 months (median 6.1, IQR 3.8-7.4) and 12 months (median 8.8, IQR 7.9-9.8), and between 6 months (median 7.0, IQR 5.0-8.5) and 12 months (p=0.005), but not between 3 and 6 months (p=0.091) (Figure 10). There was a statistically significant increase (p=0.011) in satisfaction scores between 3 months (median 5.5, IQR 1.5-8.0) and 6 months (median 8.0, IQR 5.5-8.6), and between 3 and 12 months (median 8.3, IQR 7.6-9.9) (p=0.005), but not between 6 and 12 months (p=0.021).

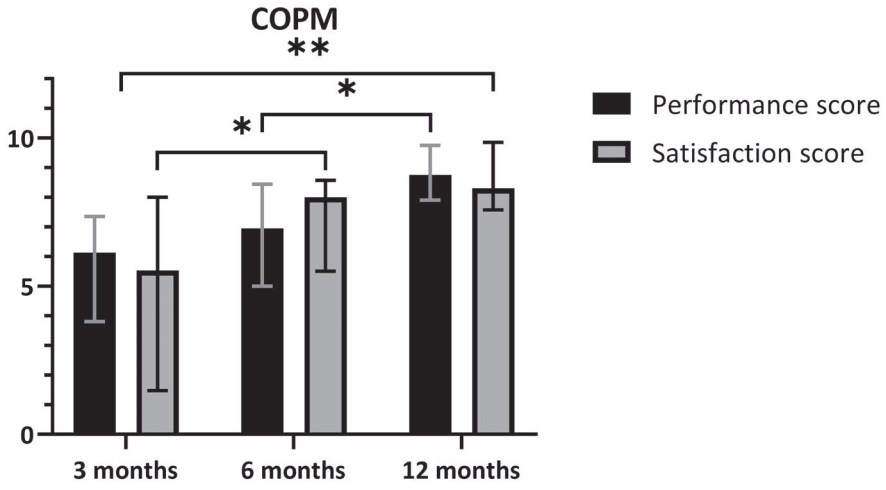

Figure 10. COPM performance and satisfaction scores over time

Discussion

This is the first study to evaluate the recovery pattern of hand function, scar quality and quality of life of patients after deep dermal hand burns treated with enzymatic debridement up to 12 months post-burn. Our overall results showed a near normal hand function at 12 months post-burn with an increase of scar quality and QoL over time.

Hand function improved over time, especially from 6 months post-burn onwards. This corresponds with the development of burns scars, which generally improve between 3-6 months but even more between 6-12 months.[26] The JTHFT showed no significant improvement over time. Despite this, patients reported a better functional outcome in their QoL assessment. The study by Holavanahalli 2007 et al[27] demonstrated that the JTHFT had a negative correlation with the Michigan Hand Questionnaire (MHQ), indicating that patients reported a better hand function than could be demonstrated by the JTHFT. Thus, the JTHFT might not be the right instrument to assess hand function in hand burn patients, which is supported by other authors.[28,29] Although grip strength varies between age and gender, our patients had a median of 41.33 kg grip strength, which is highly above the required 9 kg needed for functional hand use.[30]

Although the individual scar quality items, apart from the item vascularity in the observer scale, showed no change over time, the overall opinion on scar quality of both the patient and the observer improved over time. Although patients scores improve over time in burn patients with different etiologies and burn depths[26], to our knowledge, it is not known whether this is also applicable for specifically burns of the hands. We found an improvement in observer score vascularity over time. A high vascularity e.g., erythema, occurs in the first month's post-burn, so it is expected to decrease over time. A possible explanation as to why patients did not report a difference in color over time, could be due to the fact that while observers are asked to report specifically vascularity (=redness), patient are asked to assess the color of their scar. Deep burn scars often over time develop from red (due to increased vascularity) to hyper-, and/or hypo-pigmentation. Thus, patients possibly scored high on color due to their change in pigmentation over time.

Quality of life improved over time as measured by the QDASH, BSHS-B, and COPM, but not as measured by the EQ-5D-5L. The EQ-5D-5L is a more generic questionnaire which also includes mobility, while a lot of our patients solely had hand burns. The other questionnaires are specifically focused on burns of the upper extremity. Moreover, our patients overall scored fairly high on the EQ-5D-5L pre- and post-burn. An improvement in time, as measured by the BSHS-B, is in correspondence with literature.[31] The item work in the BSHS-B could be explained by the fact that a large part of the patients was not able to work the same hours as they did pre-burn, until 12 months post-burn. Assessment by COPM focused

on the activities important to the individual patient, and showed that there was improvement over time with fairly high performance and satisfaction scores. Thus, indicating that patients were very pleased with their results.

The need for skin grafting in our patient group was in correspondence with a recent study by Dardas et al[32] in which 53.8% of hand burn patients treated with enzymatic debridement received additional grafting. Their time to wound healing differed from ours with a median of 20 days (IQR 7-35, n=52) compared to our 35 (± 12.6) days, which was also longer compared to the study by Schulz et al[33] with a mean of 24.3 (± 6.5) days (n=20), and of Krieger et al, respectively, 23 (± 15.8) days[8] in spontaneous healed enzymatically treated hand burns (n=44) and 17 (± 13.1) days[34] in hand requiring additional surgery (n=25); and 25 (± 12.5) days (n=31). While nowadays we tend to perform a skin graft earlier after enzymatically treated burns, i.e., after approximately 21 days[34], in the earlier phase of implementation of enzymatic debridement the trend was to await spontaneous re-epithelialization for a longer period of time. The need for additional excisional surgery is not uncommon after enzymatic debridement. Two studies described the need for additional excision in 6 out of 16 patients with deep upper extremities burns[35] and in 4 out of 31 patients with deep hand burns[34], after enzymatic debridement.

There are few studies on the evaluation of hand function, scar quality and QoL after hand burns in general, e.g., not specifically enzymatically treated hand burns. Most studies date from before 1985 and are either focused mostly on clinical parameters[11] and/or use non-validated methods.[12, 13] Moreover, they did not assess hand function over time. A more recent randomized clinical trial by Omar et al[10] assessed hand function in patients with hand burns and observed better hand function in the early versus late excision group. While they used validated methods, including total active motion and the JTHFT, they assessed hand function up to 2 months post-burn only.[10] With regard to enzymatically debridement, only four studies have been looking solely at hand burns.[8, 33, 34, 36] Two of these studies made no assessments on long term hand function, cosmetic outcome or QoL.[8, 36] The two other studies only assessed scar quality at one time-point in the study, at three months[33], and 2-4 years post-burn[34], using the Modified Vancouver Scar Scale.

Our study has several strengths. The debridement of deep dermal burns has so far mainly been focused on clinical outcome parameters, e.g., time to wound healing and time to debridement, and little is known about long term scar quality as an outcome of debridement technique, specifically enzymatic debridement.[5] This is the first prospective longitudinal cohort study on the enzymatic debridement of hand burns that looked at the recovery pattern with regard to function, scar quality and QoL using a standardized and assessment scheme containing validated measurement instruments. The definition of a good hand function does not solely entail adequate range of motion, which is

a limited measurement, because it is not a reflection of functional ability.[18, 37] We chose to assess several domains of hand function, scar quality and QoL by multiple validated instruments, as to provide a complete overview of the recovery and long-term outcomes after deep dermal hand burns treated with enzymatic debridement. Moreover, hand function was measured by the same occupational hand therapist, trained and specialized in the treatment of burn patients and hand burns, at all-time points in all the patients. Lastly, we chose a prospective design with a long-term follow-up up to 12 months post-burn, thereby providing the development over time with a complete follow-up of all patients.

Our study has some limitations. We were not able to perform a comparative study in which we compared the results with patients who were treated with standard of care. For this, we had several reasons. First, we did not want to withhold patients with deep hand burns the treatment of enzymatic debridement as in our center this is the preferred choice of treatment for deep dermal hand burns. Secondly, patients with deep dermal hand burns are scarce. An alternative for this single-center study is the participation of more burn centers in a randomized trial. Another alternative for a classical randomized controlled trial is longitudinal systematical assessment of the outcomes of all patients with hand burns with the possibility to randomize within a cohort. Another limitation of our study is that we did not take into account other patient factors, e.g., burns other than the hands, that might be on influence on the outcome of QoL. Lastly, our test battery of the assessment of hand function was quite comprehensive, but is not practical to apply in daily clinical practice. Thus, a more confined assessment scheme (i.e., core outcome set) for patients with hand burns that includes relevant patient reported outcomes and objective parameters should be developed and implemented.

In conclusion, hand function, scar quality and QoL in patients with deep dermal hand burns treated with enzymatic debridement improves significantly over time. Patients had a near normal hand function at 12 months post-burn, and all employed patients returned to their old profession.

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Conflict of interest disclosure statement

Roelf S. Breederveld is the principal investigator of the local site (Red Cross Hospital, Beverwijk) that participated in the CIDS study (MW 2012-01-01) which is a multicenter, multinational, randomized, controlled, open label study, performed in children with thermal burns to evaluate the efficacy and safety of NexoBrid compared to standard of care treatment. The CIDS study is initiated and funded by Mediwound (Yavne, Israel), which is the manufacturer of NexoBrid. Kelly A.A. Kwa is a PhD-candidate not paid from the finances/grant received by Mediwound, but worked as the (local) researcher on the CIDS study. Paul P.M. van Zuijlen is the developer of the Patient and Observer Scar Assessment Scale.

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