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Published in:
Wound repair and regeneration

DOI:
10.1111/wrr.12438

Long-term scar quality in burns with three distinct healing potentials: A multicenter prospective cohort study

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Manuscript received: November 10, 2015
Accepted in final form: April 19, 2016

DOI:10.1111/wrr.12438

ABSTRACT

The laser Doppler imager is used in cases of indeterminate burn depth to accurately predict wound healing time at an early stage. The laser Doppler imager classifies burns into three estimated healing potentials as follows: high, <14 days; intermediate, 14–21 days; and low, >21 days. At this time, the relationship between these healing potentials and long-term scar quality is unknown. The objective of this study was to determine the long-term scar quality of burns with three distinct healing potentials. The secondary objectives were to compare treatment strategies in intermediate wounds, to study the effect of the timing of surgery on low healing potential wounds and to identify predictors of reduced scar quality. Hence, in a prospective cohort study, scar quality was determined in patients whose burns were assessed with laser Doppler imaging. Scar Quality was assessed with objective and subjective measurement tools, including overall scar quality (Patient and Observer Scar Assessment Scale) as a primary outcome and color and elasticity parameters. A total of 141 patients (>19 months postburn) with 216 scars were included. Wounds with high and intermediate healing potential did not significantly differ regarding scar quality. Wounds with a low healing potential had a significantly lower scar quality. Analysis of 76 surgically treated low healing potential wounds showed no significant differences in the primary outcome regarding the timing of surgery (≤14 days vs. >14). Predictors of reduced long-term scar quality were darker skin type and multiple surgeries. In conclusion, scar quality was strongly related to the healing potential category. Scar quality was very similar in high and intermediate healing potential wounds. No positive effects were found on scar quality or on healing time in surgically treated wounds with intermediate healing potential, advocating a conservative approach. Further studies should focus on the optimal timing of surgery in low healing potential wounds.

Quality of life (QOL) after burns is a multifactorial process and depends on functional, aesthetic, and psychological outcomes.[1–3] For favorable outcomes, good scar quality is crucial. Acute burn care has improved rapidly in recent decades, with better survival and improved clinical outcomes.[4] Hence, research priorities are shifting from research in the field of acute burn care to studies aiming to examine and improve QOL for severe burn survivors.[5] Scar quality, in particular, has become increasingly important; currently, many clinical (intervention) trials include scar quality as an important outcome of burn care.

Scar quality from a patient perspective depends on the presence or absence of several visual, tactile, and sensational features.[6] In daily practice, the patient opinion influences clinician treatment strategies. Therefore, patient reported outcome measurements are highly relevant. For research purposes, however, an ideal scar evaluation should include both subjective and objective measurements.[6] Several scar measurement scales and objective tools have been developed in recent years.[6–10] These scar assessment tools enable clinicians and researchers to

HP	Healing potential
HTS	Hypertrophic scar
LDI	Laser Doppler imaging
LOS	Length of stay
POSAS	Patient and Observer Scar Assessment Scale
QOL	Quality of life
TBSA	Total body surface area

systematically assess and measure different scar characteristics. Previously, poor scar quality was often defined as the presence of hypertrophy and contractures (pathological scarring). Currently, other clinically relevant scar characteristics, including color (vascularization and pigmentation), thickness, relief, pliability, pain and pruritus, can also be assessed. The patient observer scar assessment scale (POSAS), for example, consists of the following two six-item numeric scales: the Patient Scar Assessment Scale and the Observer Scar Assessment Scale. In contrast to another frequently used scale, the Vancouver Scare Scale, the POSAS also includes the patient assessment, which makes it a complete and reliable scale for scar evaluation after burns.[11–13]

The most widely used classification for (thermal) burn injuries divides burns into three categories of increasing depth as follows: superficial partial-thickness, deep partial-thickness, and full-thickness burns.[14] Superficial partial-thickness burns involve only the epidermal layer and the superficial part of the dermis. When healing occurs within two weeks, usually little or no scarring is noticed. In deep partial-thickness burns, the epidermis and the majority of the dermis are destroyed, with damage to deeper skin structures such as blood vessels, nerves, and hair follicles.[15] If reepithelialization does not occur within 14–21 days, then (hypertrophic) scarring may occur.[16,17] In full-thickness burns, all layers of the skin are destroyed, and there may also be damage to subdermal structures, such as muscle, cartilage, or bone. Because no viable epidermal appendages remain in the bottom of the wound, spontaneous healing will take place only from the wound margins. These wounds, whether they are treated conservatively or surgically, will always result in scarring, and often, in hypertrophic scarring (HTS).

Early accurate diagnosis of burn depth is essential to enable the most appropriate treatment.[18,19] It is generally accepted that superficial dermal burns, with an expected wound healing of less than 14 days, require no surgical intervention (excision and grafting) and that deep partial-thickness and full-thickness burns, with an HP of more than 21 days, require surgical intervention. Hence, clinical decision-making for wounds with high and low HP is relatively easy. However, clinical decision making in burns of intermediate depth with an HP within 14–21 days is less straight forward.[16] Wounds of intermediate HP can heal with or without scarring. A surgical intervention in these wounds will always result in visible scars and possible morbidity at donor sites. In addition, burns are often of mixed depth, with both superficial and deep partial-thickness areas. In these wounds especially, the decision of whether or not to perform surgery at an early stage is difficult, as early excision can cause scarring in areas that would have been able to heal without scarring if treated conservatively. Conversely, postponing surgery too long could lead to a delay in healing time and, thus, an increased risk of HTS,[16] wound infection and prolonged hospitalization with subsequent increase in psychological stress and medical costs.

Hence, clinical decision making is unclear in wounds with an intermediate HP (14–21 days) as clinical assessments can be inaccurate. Evidence in patients with these wounds regarding the eventual outcome of scar quality is absent.

Regarding burn depth and wound healing time, demographic, and burn-related risk factors for scarring have been described and include female sex, young age,[20] skin type,[21] burn site(s) on the neck or upper limb, and type and number of surgeries.[20] Although, the literature is ambiguous, time to wound healing, representing burn depth, seems to be the most important factor.[17,22,23]

Currently, laser Doppler imaging (LDI) is the only technique that has been shown by significant evidence to accurately predict wound healing.[24] LDI combines the advantages of laser Doppler and scanning techniques in that the entire burn can be sampled, and no direct contact with the burn surface is necessary. As a result, LDI is able to classify wounds according to their estimated healing potential (low HP, >21 days; intermediate HP, 14–21 days; and high HP, <14 days).[25,26]

A few years ago, our team conducted a multicenter, randomized, controlled trial to determine the cost-effectiveness of LDI within the three Dutch burn centers.[27] Over 200 patients with wounds of indeterminate depth and a maximum TBSA burned of 20%, were scanned using LDI, and wound depth and wound healing time were documented. At the beginning of this study, all participants were at least 19 months postburn. Using this population, the primary objective of this current study was to determine long-term scar quality from burns with three distinct HPs. Our secondary objectives were to compare treatment strategies in intermediate wounds, to determine the influence of the timing of surgery on scar quality in wounds with low HP and to determine the effect of several patient and burn characteristics on scar quality.

METHODS

Participants and recruitment

All consecutive patients of any age with burns of indeterminate depth at the time of presentation in one of three Dutch burn centers who participated in the LDI trial[27] were eligible for the study and asked to participate in the follow-up study. The inclusion criteria were as follows: (1) complete LDI data on wound HP and wound healing time and (2) informed consent. The exclusion criteria for this follow-up study were as follows: (1) reconstructive surgery performed on all study wounds, (2) withdrawn informed consent or formally ended participation in the LDI study, or (3) missing contact details.

Approval from the Ethics Committee of the Maasstad Hospital Rotterdam under the registration number NL48539 was obtained to contact patients from the previously mentioned LDI trial.[27]

All eligible patients were sent an invitation letter to participate in the study. Patients gave consent to participate by returning the signed informed consent form. For patients <18 years old, written consent was given by at least one parent/caregiver, if possible. Children from age 12 up to and including age 17 were also asked to sign the informed consent. Patients who did not respond to the mailing were called to answer any questions and to discuss participation. Patients or parents/caregivers who agreed to participate were then called to make an appointment for a single outpatient visit to the burn center. If patients were willing to participate but unable to travel, they were visited at home by two members of the research team.

Laser Doppler imager

In the LDI study, a laser Doppler imager LDI2-B (Moor Instruments Ltd., Millwey, UK) was used. The accuracy of the LDI scan was verified, and the performance was good, with a sensitivity of 93.5% and a specificity of 88.6%.[27]

Study procedures and measurements

Before each study visit, patient study wounds were located using the LDI database. Wounds were categorized clinically by trained members of the research team, based on the dominant color of the LDI scan, into three different HP categories (<14 days [red], 14–21 days [yellow] and >21 days [blue]).[26] The dominant colors red, yellow, and blue corresponded to a healing potential color palette. If wounds were of mixed depth, the wound was categorized by the lowest HP (longest estimated healing time) that was present in the wound if this represented at least 10% of the surface area. If not, the dominant color present in the wound was chosen to determine the healing potential. For the exact location and extent of the acute burn wounds, the study LDI images were examined. Study wounds were then drawn on a chart (Lund and Browder) in the case record.

Scar quality was assessed using the POSAS, the Dermaspectrometer and the Cutometer. The primary outcome was the total score of the Observer scale of the POSAS.

Scar quality

Overall scar quality was assessed with the Patient and Observer Scar Assessment Scale (POSAS). This validated questionnaire[12,13] enables both the patient and two observers to assess the same scar on six different scar characteristics, with an overlap of roughly four characteristics (see Table 4). Both use a numerical 10-point scale, in which 1 represents a scar comparable with "normal skin," whereas 10 represents the "worst scar imaginable." Both the patient and observers independently assess the same scar.[13,28] The observer assessment was performed independently by two experienced and trained observers, a physician, a research nurse, or a researcher. In young children, the patient assessment was performed by or with the guidance of a parent.

Scar color

Scar color was measured using the Dermaspectrometer (Cortex Technology ApS, Hadsund, Denmark), which was used to characterize vascularity (erythema) and pigmentation (melanin).[29] For the scar measurement, the spot that was most representative of the entire scar was chosen. To analyze the indices for erythema and melanin, the absolute values of the difference between the scar and the normal skin were used.

Scar elasticity

The Cutometer Skin Elasticity Meter 575 (Courage-Khazaka Electronic GmbH, Cologne, Germany) is a noninvasive suction device that has been applied for the objective and quantitative measurement of skin elasticity.[30] It measures the viscoelasticity of the skin by analyzing its vertical deformation in response to negative pressure.[9] Scars were measured following a standardized method, including five scar and two control measurements. Scars were divided by two imagined lines from the widest length and width through the center of the scar[30] (diamond shape). The 5 points were then chosen halfway between these lines and in the center. Elasticity was analyzed using the ratio of scarring to normal skin.

Control measurements

For both measurement tools, the first option for the control measurement was always the patient's contralateral site. In cases where the contralateral site was also affected, the most comparable and unaffected spot near the scar was used.

Other study parameters

For all patients included in the LDI trial, data were available regarding the following: demographics (age and sex), burn characteristics (% total burned body surface area burned [TBSA], % superficial partial-thickness, % deep partial-thickness, and % full-thickness burns as assessed clinically on admission, anatomical site(s) affected, etiology, and clinical characteristics (date of injury, date of first clinical assessment, date of LDI, wound HP, wound colonization, wound infection, date of adverse events, date of surgery, number, and characteristics of surgery [type of excision, use of mesh graft], date/time of wound healing). The time to wound healing was assessed by experienced burn specialists and defined as >95% reepithelialization, which is a reliable and valid method.[31]

During the follow-up visit, skin type was assessed with the Fitzpatrick skin type scale.[32] Patients were also asked whether reconstructive surgery had been performed on (parts of) the study wounds. If reconstructive surgery had indeed been performed, additional data on the date, indications, technique, and number of operations were collected from the Dutch Burn Repository (R3). Reconstructive surgery was defined by consensus to be any operation on a wound after initial wound closure.

Statistical analysis

A chi-square test for categorical data and the nonparametric Mann Whitney test for continuous data were used to perform a nonresponse analysis (per subgroup) by comparing patient, burn, and treatment characteristics (sex, age, % TBSA burned, etiology, burn depth and location, length of stay [LOS] and surgery and reconstructive procedures) of responders vs. nonresponders.

Differences in scar quality among groups with distinct HPs (<14, 14–21, and >21 days) were tested. As burn centers have different treatment strategies, and several patients had more than one wound, multilevel regression analyses were conducted to account for correlated samples. A variance components correlation structure was used to model the within-subjects correlation. On the basis of the likelihood ratio tests, a two-level regression model with random intercept and a variance components covariance structure for random effects was selected. The two levels were patients and burn wounds; the third level, burn centers, was excluded.

Differences in mean scar quality scores and specific scar dimensions among the three HP groups were assessed post hoc using the Sidak comparison of means with different

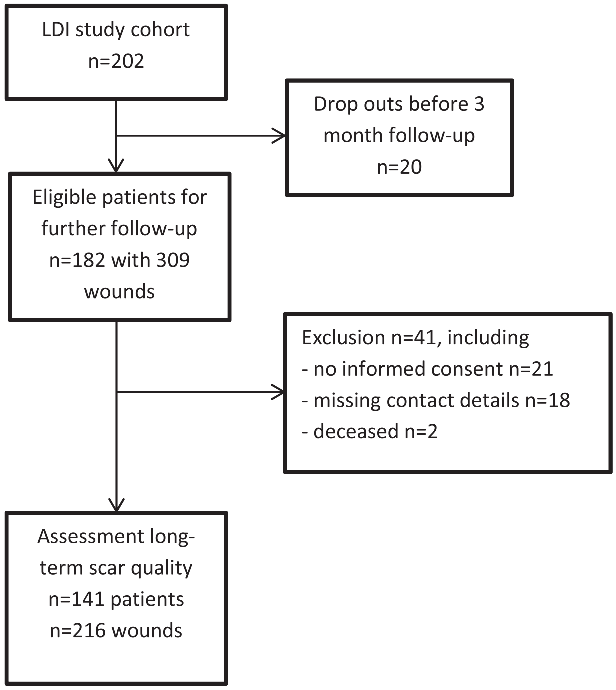

Figure 1. Eligibility and patient inclusion flow chart.

variances. In addition, to explore determinants of long-term scar quality, demographic and clinical characteristics, such as skin type, sex, influence of >1 surgery in the same area and wound healing time (<21 or >21 days), were included as independent variables in a multilevel regression analysis.

RESULTS

Patients

From July 1, 2014 until July 1, 2015, a total of 141 patients (77.5%) of the initial cohort of 182 eligible patients were included in the study (see Figure 1). The most frequent reasons for nonparticipation/exclusion were no informed consent ($n = 21$) and missing contact details ($n = 18$). Furthermore, two patients died (not burn-related) before the start of the study. The mean age of the participants was 31.9 years (0–87, ±23.5), and the majority were male (61.0%; Table 1). The most frequent causes of burn injury were flames (42.6%) and scalds (33.3%) which, together with other causes (24.1%), inflicted burns with a mean TBSA of 5.4% (0–20, ±4.2). A total of 60 patients (42.6%) underwent surgery for their burns (Table 1).

A nonresponse analysis on key patient, burn, and treatment characteristics showed an overrepresentation of males in the nonparticipants group (61.3 vs. 77.8%, $p < 0.05$) and more burns to the head, face and neck in the participant group (8.8 vs. 0.0%, $p < 0.05$). Furthermore, there was a trend toward an older age in the nonparticipant group (31.9 vs. 39.2 years, $p = 0.078$) due to decreased participation of patients in the oldest age category (>65 years; Table 1).

Scars

A total of 216 scars (1.53 scar per patient) were measured to determine long-term scar quality, of which 50.9% of scars had low HP, 22.2% an intermediate HP and 26.8% high HP. The mean time to 95% reepithelialization was significantly different among the three HPs ($p < 0.001$): wounds with high HP healed within 12.6 days (7–23, ±2.93), whereas wounds with an intermediate HP healed within 18.4 days (10–41, ±4.81), and wounds with low HP healed in 23.9 days (10–57, ±8.83). The mean time postburn at the time of the measurements was 28.2 months (19–36, ±3.05).

High vs. Intermediate vs. Low healing potential wounds

Primary outcome

Mean total POSAS observer scores were not significantly ($p = 0.142$) different between wounds with high or intermediate HP. Wounds with low HP had significantly higher mean total scores ($p < 0.001$), representing a poorer scar quality, than high and intermediate HP wounds (Figure 2; Appendix S1).

Secondary outcomes

Scar quality from the patient perspective, which was assessed with the patient part of the POSAS, showed no significant differences ($p = 0.975$) between wounds with high or intermediate HP. Again, wounds with low HP had a significantly ($p < 0.001$) higher mean total patient score, corresponding to a poorer self-reported scar quality (Figure 2; Appendix S1).

Scar color, which was represented as erythema and melanin indices, showed an increase in absolute differences from high to low HP on both indices, indicating worse scar quality. However, the only significant difference ($p = 0.022$) was the mean absolute difference in melanin between high and low HP wounds (Figure 3; Appendix S2).

The elasticity results showed a significantly ($p = 0.022$) lower maximal skin extension (Uf) between wounds with a high and low HP, indicating worse scar quality. No differences were shown between high and intermediate or intermediate and low HP. Other visco-elasticity parameters of the Cutometer showed similar results (Figure 4; Appendix S2).

Consistent with the mean total POSAS scores, the six specific dimension scores of both the observer and patient part also showed no significant differences between high and intermediate wounds and significantly ($p \leq 0.001$) higher scores for all dimensions in low HP wounds compared with high and intermediate HP wounds (see Appendixes S3 and S4). Furthermore, no pain was reported in high and intermediate wounds, and pruritus seemed to be a minor long-term problem (see Appendix S4).

Intermediate wounds

Forty-eight out of the 216 scars (22%) resulted from burn wounds with intermediate HP. Most of these wounds were treated conservatively ($n = 34$, 70.8%). In 29.2% of the wounds, the burn staff decided to perform surgery. Surgery had no significant effect on the mean total POSAS observer or patient scores, the absolute differences in

Table 1. Patient, burn, and treatment characteristics eligible patients and by response

	Eligible patients $n = 182$	Participants $n = 141$	Nonparticipants $n = 41$	p-Value
Sex: male (%)	119 (65.4)	86 (61.0)	33 (80.5)	0.025
Mean age (range, SD)	33.6 (0–89, 23.4)	31.9 (0–87, 23.5)	39.2 (0–89, 22.7)	0.078
Age category (%)				0.083
0–4	31 (17)	27 (19.1)	4 (9.8)	
5–17	21 (11.5)	18 (12.8)	3 (7.3)	
18–65	114 (62.6)	87 (61.7)	27(65.9)	
>65	16 (8.8)	9 (6.4)	7 (17.1)	
Etiology (%)				0.147
Scald	55 (30.2)	47 (33.3)	8 (19.5)	
Flame	84 (46.2)	60 (42.6)	24 (58.5)	
Other	43 (23.6)	34 (24.1)	9 (22.0)	
Mean TBSA burned (range, SD)	5.7 (0.3–20, 4.3)	5.4 (0.3–20, 4.2)	6.5 (0.3–16, 4.7)	0.155
Body regions affected* $n = 309$				0.011
Head/face/neck	12 (3.9)	12 (8.5)	0 (0.0)	
Trunk	47 (15.2)	40 (28.4)	7 (17.1)	
Arm	100 (32.4)	69 (48.9)	31 (75.6)	
Hand	71 (23)	51 (36.2)	20 (48.8)	
Legs	62 (20.1)	44 (31.2)	18 (43.9)	
Feet	17 (5.5)	16 (11.3)	1 (2.4)	
Healing potential wound†				0.114
HP 0–13 days	74	57	17	
HP 14–21 days	78	48	30	
HP >21 days	157	110	47	
LOS in days (range, SD)	10.1 (0–43, 10.1)	10.4(0–43, 10.5)	9.0 (0–38, 8.6)	0.419
Surgery (%)	78 (42.9)	60 (42.6)	18 (43.9)	0.655
Reconstructive surgery (%)		5 (3.5)	Unknown	

*Multiple locations per patient is possible.
†Multiple categories per patient is possible.

erythema and melanin indices (Table 2) or the elasticity ratios (data not shown). The surgically treated wounds did, however, show a trend toward a longer wound healing time than those that were treated conservatively (17.3 vs. 20.4, $p = 0.063$). TBSA burned was similar (5.3 vs. 6.0%, $p = 0.529$).

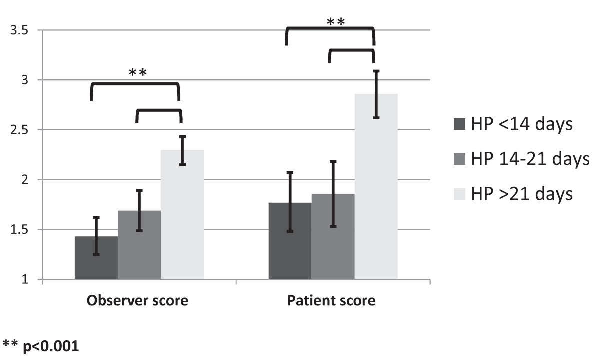

Figure 2. Scar quality per healing potential: mean total POSAS observer and patient score.

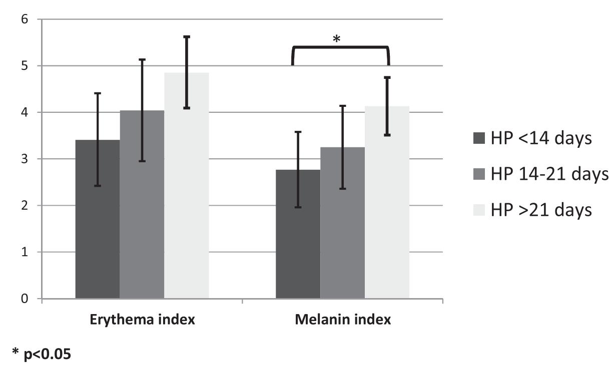

Figure 3. Scar colour per healing potential: absolute difference in erythema and melanin.

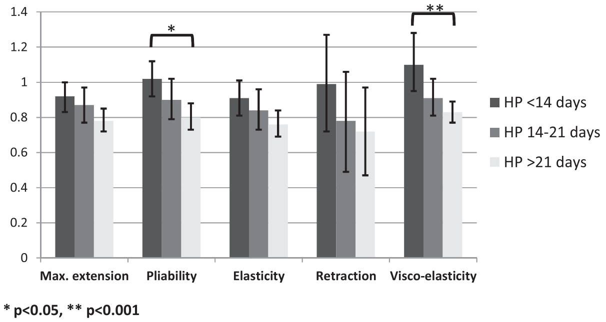

Figure 4. Scar elasticity per healing potential.

Timing of surgery in wounds with low healing potential

In this cohort, 76/110 (69.1%) low HP wounds were treated surgically. A comparison between wounds that were operated on within, vs. after, 14 days postburn suggested poorer scar quality in wounds that were operated on after 14 days (Table 3, data elasticity ratios not shown). However, the only significant difference was a higher melanin index, indicating poorer scar quality, in wounds operated on after 14 days (3.2 vs. 5.7, $p = 0.012$). Overall, wound healing time was not significantly different between the two categories, although the time to 95% reepithelialization from surgery onwards was significantly shorter in wounds that underwent surgery after 14 days (12.4 vs. 6.1, $p = 0.001$; Table 3).

A total of 34 (30.9%) low HP wounds were not treated surgically. These wounds had a significantly lower mean total POSAS observer score, indicating an improved scar quality, compared with wounds that underwent surgery after 14 days. Wound healing time, conversely, was significantly longer in these wounds than in low HP wounds that were operated on within 14 days (Table 3).

Predictors of reduced long-term scar quality

Several patient-, burn-, and treatment-related characteristics were found to affect long-term scar quality. Dark skin (Fitzpatrick type V–VI), wound healing time exceeding 21 days and more than one operation (in the acute phase) on the same wound area resulted in significantly higher POSAS observer and patient scores. Females had significantly higher mean score than males on the observer part of the POSAS, but not on the patient part. In multivariate analysis, however, only dark skin and more than one operation on the same wound area remained independent predictors of reduced long-term scar quality (Table 4).

DISCUSSION

This was the first prospective study that assessed long-term scar quality in relation to estimated HP using an LDI scan in a large cohort at the wound level. The available LDI data, in combination with the short prospective follow-up measurement, enabled us to draw meaningful conclusions on long-term scar quality of burns with three distinct HPs. This information may be helpful in the decision process for optimal treatment with regard to long-term scar quality, and it will also provide burn patients with an early and more accurate prognosis on long-term scar quality once an LDI scan is performed.

Scar quality in burn wounds with intermediate HP did not significantly differ from those with high HP. Wounds with low HP, conversely, scored significantly more poorly on the primary outcome (observer score of the POSAS) and most other measured outcomes. Except for the absolute difference in melanin index, there were no significant differences in long-term scar quality in low HP wounds regarding timing of surgery. Fitzpatrick skin type IV–V (dark skin) and more than one operation in the same area were identified as risk factors for reduced long-term scar quality. These risk factors are mostly consistent with those identified in previous studies,[16,20,21] except for (young) age, which was not identified as a risk factor for poor scar quality in this cohort or in other studies.[17,23] However, due to differences in the assessment of scars among studies, the effect on long-term scar quality in these studies could not be compared with our results.

In this study, special attention was paid to burns with an intermediate HP because, unlike wounds with high or low HP, there is no consensus on the optimal treatment of these wounds. The majority of the wounds with intermediate HP were treated conservatively (70.8%). Intermediate wounds healed with a mean healing time of 18.4 days and with very similar long-term scar quality as that of wounds with high HP. Healing time was comparable with that of a recent study of Kishikova et al., who found a wound healing time for intermediate wounds of 15.6 days in wounds with <4% TBSA burned and 20.4 days for wounds with

Table 2. Scar quality in wounds with an intermediate healing potential

	No surgery	Surgery	*p*-Values
Number of wounds (%)	34 (70.8%)	14 (29.2%)	
Mean POSAS observer score (95% CI)	1.59 (1.37–1.82)	1.82 (1.52-2.20)	0.244
Mean POSAS patient score (95% CI)	1.72 (1.39–2.05)	2.06 (1.61–2.51)	0.228
Mean difference in erythema index (95% CI)	4.47 (3.07–5.87)	3.55 (1.64–5.47)	0.439
Mean difference in melanin index (95% CI)	2.97 (2.08–3.85)	3.54 (2.35–4.74)	0.437
Mean time to wound healing *(95% CI)	17.3 (15.4–19.3)	20.4 (17.8–23.1)	0.063
Mean TBSA burned (95% CI)	5.3 (0.8–12.5, 3.3)	6.0 (1.2–18, 4.5)	0.529

*In days, defined as >95% reepithelialization.

Table 3. Effect of timing of surgery on wound healing and scar quality in low HP wounds

	Surgery within 14 days	Surgery after 14 days	No surgery	*p*-Values Within 14 – after 14 After 14 – no surgery Within 14 – no surgery
Number of wounds (%)	43 (39.1%)	33 (30.0%)	34 (30.9%)	
Mean POSAS observer score (95% CI)	2.37 (2.06–2.67)	2.56 (2.23–2.91)	1.96 (1.67–2.25)	0.712 0.016 0.129
Mean POSAS patient score (95% CI)	2.90 (2.35–3.46)	3.17 (2.54–3.80)	2.59 (2.11–3.07)	0.943 0.347 0.637
Mean difference in erythema index (95% CI)	4.52 (3.15–5.90)	6.11 (4.56–7.66)	4.36 (2.91–5.81)	0.428 0.316 0.994
Mean difference in melanin index (95% CI)	3.16 (1.92–4.40)	5.68 (4.29–7.08)	3.85 (2.63–5.06)	0.012 0.124 0.772
Mean time to wound healing (95% CI)*	21.9 (19.3–24.5)	23.4 (20.4–26.3)	27.1 (24.1–30.2)	0.859 0.253 0.036
Mean time to wound healing postoperative (95% CI)	12.4 (9.9–14.9)	6.1 (3.2–8.9)	n/a	0.001
Mean TBSA burned (95% CI)	6.67 (5.33–8.00)	8.14 (5.33–9.73)	5.73 (3.97–7.48)	0.428 0.990 0.756

*In days, defined as >95% reepithelialization.

$\geq$4% TBSA.[19] Additionally, in the above study, different treatment strategies were applied for intermediate wounds, conservative treatment (different forms) vs. surgical treatment. Although the exact data were not provided, the treatment also seemed to be predominately conservative for intermediate wounds. In our study, 29.2% of the intermediate HP wounds was treated surgically and this decision was predominately based on lack of clinical signs of healing at wound inspection at day 12–16 postburn. No significant differences were found in long-term scar quality between conservatively or surgically treated intermediate wounds. Nevertheless, a trend toward faster wound healing was observed in conservatively treated wounds (17.3 vs. 20.4 days, $p = 0.063$). These results may suggest that a conservative approach for burns with intermediate HP is justified. Furthermore, it seems that long-term scar quality is primarily determined by the remaining viable dermal tissue in the wound, rather than the applied treatment, which

Table 4. Risk factors for reduced long-term scar quality assessed with POSAS (multivariable multilevel regression analysis)

	Number of wounds	Mean total observer score (95% CI)	Mean total patient score (95% CI)
Fitzpatrick skin type			
I–II	79	2.50 (2.16–2.84)	2.80 (2.24–3.35)
III–IV	100	2.30 (2.04–2.56)	2.84 (2.43–3.26)
V–VI	10	3.66 (3.06–4.27)**	3.99 (2.99–5.00)*
Number of operations			
1	84	2.48 (2.22–2.73)	2.85 (2.42–3.27)
More than 1	19	3.16 (2.75–3.58)**	3.58 (2.91–4.24)*

*< 0.05, **<0.01.

in cases of intermediate wounds, seems to be sufficient for satisfactory outcomes with respect to long-term scar quality. This is generally supported by the findings of Cubison et al. In their study, intermediate wounds were treated conservatively in one hospital and surgically in another hospital. The HTS rate was similar for both treatment strategies, with 20% in conservatively treated and 19% in surgically treated wounds.[16]

To our knowledge, no other studies have examined the long-term (mean time postburn >2 years) scar quality of wounds with distinct HPs, which is assessed using LDI. Thus, a comparison of our results with those of previous literature is not possible. However, over the past few years, the relationship between healing time/burn depth and scar quality has been studied more frequently. The available studies,[16,17,19,23] unfortunately, all have some methodological limitations, including a limited definition of scar quality[16,17,19] (confined to the presence of hypertrophy), a retrospective study design,[16,19] or a short follow-up period.[16] To our knowledge, Deitch et al. was one of the first to identify wound healing time as the most important indicator for the development of HTS. This prospective follow-up study included only conservatively treated patients with large mean TBSA burned (children 14% and adults 21%), which could have biased the effect of wound depth on healing time as larger wounds are associated with longer healing times.[19] The study by Cubison et al. found a strong link between healing time and the development of HTS, but this retrospective study was predominantly based on clinical notes in medical records, was limited to children, and also had a relatively short follow-up period in most patients. Van der Wal et al. assessed scar quality at 3, 6, and 12 months postburn.[23] This study retrospectively divided burns into either partial thickness or full-thickness burn categories and found that full-thickness wounds resulted in significantly higher POSAS scores (poorer scar quality). These findings are in line with our results as in our study, low HP wounds, as well as a wound healing time exceeding 21 days, were both associated with reduced scar quality.

The effect of the timing of surgery on scar quality has been examined before in a recent Cochrane review of Hoogewerf et al.[15] This review included only two studies that reported on scar quality. In agreement with our findings, no conclusive evidence in favor of early or delayed surgery was found on scar quality. It must be mentioned, however, that at present, a uniform definition of early and delayed surgery is lacking. In our study, a cutoff point of 14 days was chosen because in Dutch burn care, there is a reluctance toward surgery within the first 14 days postburn. Usually, the decision for surgery is postponed until there is clear demarcation of the wound to avoid unnecessary surgery in wounds or wound areas that are able to reepithelialize spontaneously and thus with little scarring. Therefore, in our population, surgery prior to 14 days postburn is considered early. Next to timing of surgery, the type of meshed grafts influences scar quality. We use meshed grafts with a ratio of 1 : 1 to 1 : 1.5 for burns on functional or esthetic important body regions and meshed grafts with a ratio of 1 : 3 for larger burns.

The strength of this study was its design, in which detailed information on individual burns in the acute phase, such as burn depth and wound healing time (both estimated as observed), was combined with a single scar measurement with both subjective and objective tools. Furthermore, the LDI study included burns of indeterminate depth, which resulted in the inclusion of burns from the entire spectrum of depths. Along with the inclusion of patients of all ages, the study cohort was representative of a Dutch burn center population. Additionally, our response rate was high (77.5%), especially given the long period until the follow-up measurement. The option of a home visit for those who were unable to come to the burn center contributed 6.4% to the overall response rate but was time consuming. To conclude, the high response rate, the minor differences in the nonresponse analysis and the representative cohort all contributed to a representative study sample of a Dutch specialized burn population.

Notwithstanding the above, this study also had some limitations. Most importantly, the categorization of the LDI scans into three distinct HPs was not applicable to all wounds in this study as the depths of some burns were heterogeneous. To overcome this issue, we categorized these heterogeneous wounds into the lowest HP category (high, intermediate or low) present for at least 10% of the total surface area in that wound. This was decided because we assumed that the area with the lowest HP (the longest estimated healing time) within a burn is decisive for over 95% wound healing and the final scar quality. An alternative approach was to calculate the mean perfusion units (PU) of each LDI scan and use the threshold values provided by Pape et al. and Monstrey et al.[25,26] to categorize the wounds into three healing potentials. We did not choose this option because burn physicians in daily practice clinically assess LDI scans rather than work with PUs, and we intended to write this article from a clinical perspective. As a consequence of our categorization, 30.9% of all low HP burns were not treated surgically. These burns most likely had a relatively small wound area with low HP and were, therefore, given the time to heal from the wound margins. Low HP wounds without surgery had better scar quality, as indicated by the lower mean total POSAS observer score compared with those that were operated on within 14 days. However, this was also probably the result of a smaller wound size rather than result of the treatment strategy itself. Of all low HP wounds, wound healing time was the longest in the group without surgery (27.1 days), which confirms that these wounds were categorized correctly into the low HP category. An explanation for delayed surgery in 30% of the low HP wounds is probably the result of randomization in the LDI-study, because of this therapeutic decisions in our cohort were only partially based on the LDI-results, i.e., in about half of the cases.

This study cohort consisted of burns from a broad spectrum of depths. As a downside, a relatively small proportion of intermediate HP burns were included and analyzed to compare conservative vs. surgical treatment in these wounds. The trend toward reduced scar quality outcomes in surgically treated wounds was subtle and consistent but was statistically nonsignificant. A larger number of intermediate wounds would possibly have resulted in a significant effect.

Furthermore, our results with regard to scar quality apply to relatively small burns in patients with a maximum TBSA burned of 20% and thus a limited systemic inflammatory response. It has yet to be determined whether scar quality outcomes are similar in patients with larger TBSAs burned.

Finally, it is unclear to what extent the results of the Dermaspectrometer and Cutometer are representative of the entire scar, particularly in large scars with substantial heterogeneity within the scar. Despite multiple and standardized measurements in these scars, only a relatively small area of the scar is measured due to the small aperture size of both tools (resp. 2 and 7 mm). With the POSAS, conversely, the total scar is assessed as observers and patients come to a weighted average on each dimension while observing the entire scar. Unfortunately, data on the minimally clinically important difference of the POSAS are lacking. Therefore, is it difficult to interpret the statistically significant differences found in this study and translate these differences into clinically important and relevant differences for patients. Future studies should address this problem as this interpretation is necessary for clinical trials with scar quality as a primary outcome.

In conclusion, long-term scar quality is strongly related to estimated HP using LDI scans. Although the three healing potentials are distinctive for healing time, this does not apply for long-term scar quality in high and intermediate HP wounds, which exhibit very similar and acceptable scarring. Burn wounds with low HP have poorer scar quality, regardless of the timing of surgery. Recently, the value of the LDI scan in predicting the necessity of surgery was confirmed by Stetinsky et al.[33] Further research should focus on the optimal timing of surgery regarding scar quality in wounds with a low healing potential, ideally in a randomized controlled trial. This study, in turn, may contribute to a therapeutic approach in which the LDI scan plays a key role in the decision of whether or not to perform surgery and, moreover, which specific areas of the burn wound require excision and skin grafting with regard to optimal outcomes in long-term scar quality. This approach may result in decreased surgeries for wounds that are able to reepithelialize spontaneously (high and intermediate HPs) without time loss due to lengthy demarcation periods in low HP wounds.

ACKNOWLEDGMENTS

First, we would like to thank all of the participants, partners, and parents who, despite long travel distances, were very willing to participate in this follow-up study. Next, the authors would like to thank N. Trommel, registered clinical research nurse, Burn Center of the Maasstad Hospital Rotterdam, for her participation in the scar measurements, the critical review of the study procedures and the data collection; J. Hiddingh, Msc, registered clinical research nurse, Burn Centre of the Martini Hospital Groningen, for the scar measurements of patients treated in the Burn Center of the Martini Hospital; B.F.M. Wijnen, PhD-candidate, Department of Health Services Research Maastricht University, for his contribution to the writing of the research protocol; and, finally, E. de Graaf and O. Gostelie, medical students, for their assistance with the scar measurements.

Source of Funding: This study was supported by a grant from the Coolsingel Foundation (number 382). This research was financially supported by the Dutch Burns Foundation.

Conflict of Interest: None of the authors have a conflict of interest.

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Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher's web-site:

Appendix S1. Scar quality per healing potential: mean total POSAS Observer and Patient score.

Appendix S2. Scar color and elasticity per healing potential.

Appendix S3. Scar quality POSAS observer mean dimension scores per healing potential. $*p < 0.05$, $**p < 0.001$.

Appendix S4. Scar quality POSAS patient mean dimension scores per healing potential. $*p < 0.05$, $**p < 0.001$.