Received: 22 March 2024 | Accepted: 8 July 2024

DOI: 10.1111/jdv.20351

JEADV JOURNAL OF THE EUROPEAN ACADEMY OF DERMATOLOGY & VENEREOLOGY

ORIGINAL ARTICLE

Long-term remission of Hailey–Hailey disease by Er:YAG ablative laser therapy

Marie-Eline P. H. Debeuf[1,2] | **Kèvin Knoops**[3] | **Carmen López-Iglesias**[3] | **Eline Lookermans**[1,2] | **Patty J. Nelemans**[4] | **Myrurgia Abdul Hamid**[5] | **Michel van Geel**[1,2,6] | **Antoni H. Gostynski**[1,2] | **Peter M. Steijlen**[1,2] | **Marieke C. Bolling**[7] | **Valerie L. R. M. Verstraeten**[1,2,8]

[1]Department of Dermatology, Centre of Expertise for Genodermatoses, Maastricht University Medical Centre+, Maastricht, The Netherlands

[2]GROW Research Institute for Oncology and Developmental Biology, Maastricht University, Maastricht, The Netherlands

[3]Microscopy CORE Lab, Faculty of Health, Medicine and Life Sciences, Maastricht University, Maastricht, The Netherlands

[4]Department of Epidemiology, Maastricht University, Maastricht, The Netherlands

[5]Department of Pathology, Maastricht University Medical Centre+, Maastricht, The Netherlands

[6]Department of Clinical Genetics, Maastricht University Medical Centre+, Maastricht, The Netherlands

[7]Department of Dermatology, University Medical Centre Groningen, UMCG Centre of Expertise for Genodermatoses and European Reference Network-Skin, University of Groningen, Groningen, The Netherlands

[8]Dermadok Huidkliniek, Antwerp, Belgium

Correspondence
Marie-Eline P. H. Debeuf, Department of Dermatology, Maastricht University Medical Centre+, P. Debyelaan 25, 6229 HX Maastricht, The Netherlands.
Email: marieeline.debeuf@mumc.nl

Abstract

Background: Hailey–Hailey disease (HHD) is a rare genetic therapy-resistant blistering disease with great disease burden. Treatment is currently focused on symptomatic relief. Er:YAG ablative laser therapy is a therapeutic modality with promising results, though evidence is currently scarce.

Objective: To analyse the effect of Er:YAG ablative laser therapy on clinical remission of erosive plaques in HHD and on patient's quality of life (QoL).

Methods: In this observational study eight patients were included and 77 erosive plaques were treated once only by Er:YAG laser and assessed for clinical remission. QoL was evaluated by obtaining Skindex-29 and DLQI questionnaires before laser therapy, 6 weeks and 3 years after laser therapy. Skin biopsies were taken to evaluate the depth of laser ablation. The intercellular distance between keratinocytes, the number of desmosomes and intermediate filament distribution were studied by electron microscopy before and after laser therapy and in clinically uninvolved skin and were compared to subjects without HHD.

Results: One single Er:YAG laser ablation to mid-dermis resulted in complete remission of 97.4% of HHD plaques (75/77) after median 38 months (range 7–63 months) and significantly improved QoL. Laser therapy restored the number of desmosomes, decreased intercellular distance and diminished perinuclear retraction of keratin filaments to a level comparable to the patient's clinically uninvolved skin. After laser ablation, the skin showed significantly fewer ultrastructural aberrations compared to the patient's clinically uninvolved skin and rather resembled the skin of healthy control individuals.

Conclusions: One single Er:YAG laser treatment resulted in long-term remission of HHD and significantly improved QoL. Our findings support a greater role for ablative laser surgery in the management of this recalcitrant disorder.

INTRODUCTION

Hailey–Hailey disease (HHD) is a rare autosomal dominant genodermatosis caused by pathogenic variants in the *ATP2C1* gene, encoding the Golgi-bound calcium pump hSPCA1 (Ca^{2+}/Mn^{2+}-ATPase1). These variants affect intracellular calcium homeostasis which is crucial for the processing and maturation of proteins that make up the desmosome. Weakened desmosomes

Linked article: D. Rogner. J Eur Acad Dermatol Venereol. 2025;39:895–896. https://doi.org/10.1111/jdv.20651.

Clinicaltrials.gov number: NCT03849989.

cause suprabasal loosening of keratinocytes, that is, acantholysis, which is clinically reflected in symmetrical painful erythematous plaques with vesicles, bullae and erosions in skin folds of patients.[1] Early electron microscopy (EM) reports on HHD showed a reduced number of desmosomes, perinuclear clumping of keratin filaments, disorganized intracellular filamentous material and thickened bundles of tonofilaments, particularly in the stratum spinosum.[2–6]

Patients experience stinging and itch in the affected skin sites, which prohibits them from doing exercise and causes a lot of emotional distress, particularly when inguinal and genital skin sites are involved.[7,8] Unfortunately, treatment options are limited and long-term remission is rare.[9] Dermabrasion and surgical intervention, using wide excision with split-thickness grafting can provide long-term remission.[10,11] However, the cosmetic outcome is usually unsatisfying as dermabrasion and grafting are often associated with scarring, infections and impaired healing.[1,11] Laser therapy is less invasive and carries lower risk for complications. A variety of lasers have been used in an attempt to treat HHD.[1,9,12–16] Ablative laser therapy seems effective but there is currently little evidence.[9,16–18]

In this observational study, we evaluated the effect of Er:YAG laser therapy on the rate of long-term remission of 77 HHD plaques, quality of life and changes at the ultrastructural level as measured by electron microscopy.

Why was the study undertaken?

Hailey–Hailey disease (HHD) is a difficult to treat genodermatosis. Here, we evaluated the effect of one single Er:YAG ablative laser treatment on long-term remission of 77 HHD plaques across eight patients.

What does this study add?

In 75 out of 77 HHD plaques, complete long-term remission was achieved by one single Er:YAG laser ablation with median 38 months follow-up resulting in significant improvement in the patients' quality of life.

What are the implications of this study for disease understanding and/or clinical care?

While the use of ablative laser therapy in the management of Hailey–Hailey disease is currently limited, our results indicate that ablative laser therapy can be very valuable in the treatment of this devastating disorder.

MATERIALS AND METHODS

Study design

Eligible for participation were patients aged 18 years or older who had a clinical diagnosis of HHD which was confirmed by genetic analysis and/or histopathology. Patients treated with topical hormones, oral retinoids and tetracyclines in the 7 days prior to participation of the study were excluded. The primary outcome measure was clinical remission of the lesion. Secondary outcomes were quality of life (QoL) scores at 6 weeks and 3 years after laser therapy and ultrastructural effects of Er:YAG laser. Six-week endpoint was chosen to allow proper healing and 3-year endpoint to have a long-term follow-up. Depth of laser ablation was also evaluated. The inclusion of patients started in January 2019 and lesions that were treated by laser ablation after this date were evaluated prospectively on all endpoints. Part of the skin lesions that had already been treated by laser ablation before January 2019 were retrospectively evaluated for clinical remission based on the available photographic material before and after laser ablation. The study was performed at the Maastricht University Medical Centre+ (MUMC+) and approved by the Medical Ethical Committee Board and all participating patients had given informed consent.

Mode of treatment

The Er:YAG laser (Burane, BlooMedical, Benelux) was used at 10–15 Hz, spot size 2.5 mm and a fluence of 8–13 J/cm^2. Lidocaine 1% with adrenaline, buffered 1/10 with sodiumbicarbonate was used for local anaesthesia prior to performing Er:YAG laser ablation at a maximum dose of 7 mg/kg body weight with a maximum of 500 mg/day.[19]

Postoperative wound care consisted of application of fusidic acid ointment covered with non-adhesive gauze (Urgotul, URGO Medical) until the wound healed.

Quality of life

Validated questionnaires Skindex-29 and Dermatology Life Quality Index (DLQI) were used to assess QoL before laser therapy, and 6 weeks and 3 years after laser therapy. When completing the questionnaires, patients were asked to answer the questions with attention to one 'to-be-treated' skin site and not the whole body, in order to avoid bias. This approach has been taken before in investigating QoL in psoriasis.[20]

Histopathology

A 2-mm punch biopsy was taken immediately following laser therapy to verify the depth of laser ablation. The biopsy specimen was fixed in formaldehyde and processed for haematoxylin and eosin staining. Periodic acid–Schiff and Verhoeff's staining were performed.

Ultrastructural study by electron microscopy

In each patient, three 2-mm punch biopsies were obtained: one specimen of a Hailey–Hailey plaque before and 6 weeks

after laser therapy and one specimen of clinically uninvolved skin. A control skin sample was obtained from three unaffected individuals without HHD.

The specimens were fixed and prepared as described in the Appendix S1. For each sample, 10 randomly selected stratum spinosum keratinocytes showing a cross-section of the nucleus were evaluated for intercellular distance, number of desmosomes and distribution of keratofilaments. In total, 80 stratum spinosum keratinocytes were evaluated before laser treatment, 80 keratinocytes 6 weeks after treatment and 80 keratinocytes in clinically uninvolved skin. In skin of three unaffected individuals, 30 keratinocytes were evaluated.

Intercellular distance was defined as the distance between plasma membranes of neighbouring cells showing a cross-section of the nucleus. Acantholysis was defined as the loss of intercellular coherence due to the breakdown of intercellular connections (Appendix S1).[21]

Desmosomes were counted manually. Only evident electron dense intercellular junctions were counted. The keratin filament distribution was classified into three classes: 'no perinuclear retraction', 'perinuclear retraction' and 'clumping of keratofilaments'. Perinuclear retraction of the keratin network was defined as perinuclear aggregation of filaments (Figure 4c). A thick electron-dense packed perinuclear mass of filamentous structures was referred to as clumping (Figure 4d).

Statistical analysis

Continuous variables (such as QoL, intercellular distance and total number of desmosomes) were presented as median values with range. Differences between QoL scores before and after laser therapy were analysed using the non-parametric Wilcoxon signed-rank test. Ultrastructural differences on intercellular distance and number of desmosomes between baseline and 6-week follow-up, between baseline and uninvolved skin and between 6-week follow-up and uninvolved skin were analysed using the non-parametric Mann–Whitney *U*-test. The chi-squared test was used to evaluate the changes in keratin filament distribution. Statistical analysis was performed in the statistical software SPSS (version 26). A p-value less than 0.05 was considered to be statistically significant.

RESULTS

Patient characteristics

Eight patients, five women and three men were included in this observational study. A total of 77 skin sites were treated by Er:YAG laser (Table 1). Of the eight included patients, 47 skin sites had been treated after January 2019 and were evaluated prospectively; 30 lesions had been treated before January 2019 and were retrospectively evaluated for clinical remission (Figure S1). Mean age was 48.5 years and median patient follow-up was 38 months (range 38–39 months). Median lesion follow-up was 38 months (range 7–63 months).

Clinical remission

Before laser therapy, all patients showed erythematous plaques with fissures and erosions (Figure 1a). By Er:YAG ablation, the epidermis and upper part of the dermis were removed, creating a wound (Figure 1a). Complete remission was observed in 97.4% of lesions (75/77) after median 38 months (range 7–63 months) (Figure 1a, Figures S2 and S3).

In the prospective study, two minor recurrences (not proven by histopathology) were noted: one in the submammary fold 17 months post-treatment which disappeared permanently with short-term application of clobetasol ointment and another small recurrence in the inguinal fold 16 months after laser ablation which had not expanded at 3-year follow-up (Figure S4). As the recurrences in these areas remained minor, there was no reason for the patients to contact the outpatient clinic. Hence, no specimens were collected to confirm HHD and laser ablation was not repeated. Hypopigmentation could be observed in all treated skin sites at the last follow-up visit, enabling accurate follow-up for recurrence. Hypertrophic scarring occurred in one patient after treatment of HH plaques in the elbow folds. Retrospectively, none of the patients had experienced a flare in the laser-treated area that required medical need (Table 1).

Several patients experienced a temporary flare of disease at the borders of the laser-treated skin area immediately after laser therapy which resolved after application of clobetasol ointment. There was no need for topical steroids to maintain long-term remission of HH plaques after laser therapy. In some patients, new spots of HHD developed throughout the months/years after laser therapy, though always at the periphery of the laser-treated area or elsewhere on the body. The elasticity of the treated skin was comparable to that of the surrounding clinically uninvolved skin.

Quality of life

The total median scores of DLQI and Skindex-29 questionnaires decreased significantly from baseline to 6 weeks after treatment. Median scores of DLQI were 17.5 at baseline and 1.5 at 6 weeks post-treatment ($p = 0.008$). Median scores of Skindex-29 were 55.41 at baseline and 20 at 6 weeks post-treatment ($p = 0.016$), indicating significant improvement in QoL. Between 6 weeks and 3 years after laser therapy, QoL scores continued to decrease (Figure 1b,c). As shown in Table S1, the median scores on the subdomains 'symptoms' and 'social functioning' significantly improved from baseline to 6 weeks

TABLE 1 Patient characteristics.

Patient characteristics			Lesion characteristics		Follow-up prospective lesions		Follow-up retrospective lesions		
Patients	Gender	Age	Total lesions treated by laser (*n*)	Treated skin sites	Total lesions (*n*)	Median duration, months (range)	Total lesions (*n*)	Median duration, months (range)	Previous treatments
HH1	F	44	9	Axillary folds, submammary and inguinal fold left, labia majora left	6	16 (12–39)	3	63 (61–63)	• Topical steroids • Flucloxacillin • Fusidic acid cream
HH2	F	48	18	Neck dorsal and left side, inguinal, gluteal, elbow and axillary folds, submammary fold left, vulva, labia majora left, peri-anal area	8	15 (7–39)	10	52 (43–58)	• Topical steroids • Minocyclin
HH3	M	54	12	Axillary and submammary folds, scrotal area, peri-anal area	8	36 (31–39)	4	42 (40–44)	• Topical steroids • Topical antibiotics • Botulin toxin
HH4	F	43	5	Axillary folds	2	40 (40–40)	3	50 (47–51)	• Topical steroids • Cyclosporin
HH5	M	32	14	Inguinal folds, scrotum, peri-anal area, rima ani	7	14 (8–39)	7	46 (41–50)	• Topical steroids • Doxycyclin
HH6	F	47	6	Inguinal and axillary folds	5	37 (18–39)	1	47 (47)	• Tacrolimus 0.1% ointment • Topical steroids • Doxycyclin
HH7	F	57	7	Inguinal folds, labia majora left, chest, anal area	7	34 (34–39)	0	NA	• Topical steroids
HH8	M	63	6	Inguinal folds, scrotal and peri-anal area	4	37 (35–39)	2	40 (39–40)	• Topical steroids

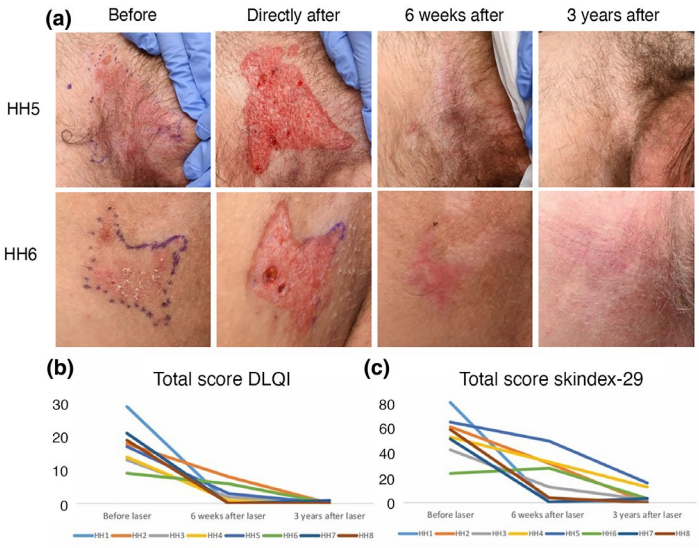

FIGURE 1 Hailey–Hailey (HH) lesions before, directly after, 6 weeks and 3 years after laser therapy with associated quality of life scores. (a) HH lesions of patients HH5 and HH6. (b) Total DLQI scores before laser therapy, 6 weeks after laser therapy and 3 years after laser therapy. (c) Total Skindex-29 scores before laser therapy, 6 weeks after laser therapy and 3 years after laser therapy.

post-treatment ($p = 0.016$; $p = 0.008$) while scores on the subdomain 'emotions' did not ($p = 0.109$). The latter did significantly decrease 3 years post-treatment ($p = 0.008$). All DLQI subdomain scores showed significant improvement 6 weeks and 3 years post-treatment except for the subdomain scores 'work' and 'treatment' (Table S2). Questions within these domains relate to impairment at work and the time-consuming burden of disease. There was no significant difference as patients already experienced little impact of their disease at work and did not find their treatment time-consuming or discomforting at home.

Depth of laser therapy

Out of eight biopsies taken immediately after laser ablation, six were analysed. Two specimens could not be processed due to the small biopsy size. Removal of close to all of the papillary dermis was noted in all six specimens (Figure 2a,b). Adnexal structures remained intact. Minimal fibrosis or inflammation was observed. In one out of six specimens, a few small islets of epidermal tissue remained after laser therapy as indicated by the presence of the basal membrane (Figure 2c).

Electron microscopy

Intercellular distance

Before laser therapy, the median intercellular distance was increased in all HH plaques (1066 nm) when compared to median values in non-affected individuals (350 nm) (Figure 3a). Six weeks after laser therapy, the median value decreased significantly to 575 nm ($p = 0.015$) (Figure 3b,d). The median intercellular distance in clinically uninvolved skin did not differ significantly from that in laser-treated skin (516 nm; $p = 0.382$) (Figure 3c). Focal acantholysis was observed in all HH plaques at baseline which restored after treatment. The degree of acantholysis observed by EM did not correspond to the clinical severity of the HH plaques. The stratum spinosum of non-affected control individuals showed neither acantholysis nor intercellular widening (Table S3).

Number of desmosomes

Before laser therapy, desmosomes were scarce to absent in all HH plaques (median 5 per cell) (Figure 3a'). Six weeks after laser therapy, the number of desmosomes restored to a median value of 20 per cell in a well-organized pattern ($p < 0.001$) (Figure 3b',e). The difference with the median number of desmosomes in clinically uninvolved skin (18 per cell) was not significant ($p = 0.397$), but desmosomes seemed more evenly distributed in laser-treated skin. In non-affected control individuals, the number of desmosomes (22 per cell) was similar to that of treated and clinically uninvolved skin in HH patients (Table S3).

Keratin filament distribution

The percentage of keratinocytes with perinuclear retraction changed from 40% before laser therapy to 29% after therapy ($p < 0.001$). The percentage of clumping decreased from 49% to 2% ($p < 0.001$). Most of the keratinocytes showed no perinuclear retraction or clumping (Figure 4a,b). Most interestingly, laser-treated skin showed significantly less perinuclear retraction and clumping of keratin filaments when compared to the patient's own clinically uninvolved skin ($p < 0.001$) (Figure 4a). In keratinocytes of healthy control individuals perinuclear retraction or clumping were totally absent (Figure 4a). There was no correlation between keratin filament distribution and disease severity.

DISCUSSION

This study showed complete and long-term remission of 75/77 HH plaques upon one single Er:YAG ablative laser

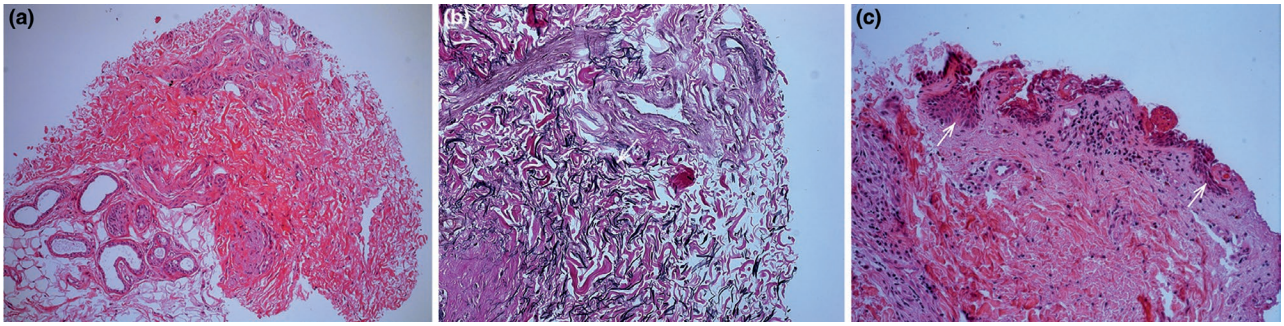

FIGURE 2 Histopathology of a biopsy specimen taken immediately after laser therapy. (a) Haematoxylin and eosin staining showing ablation to mid-dermis with normal eccrine glands at the dermal–subcutaneous junction. 100× magnification. (b) Verhoeff's staining showing ablation up to the reticular dermis characterized by densely packed elastin fibres (black lines – white arrow). 200× magnification. (c) In one patient (HH6), some small islets of epidermis remained after laser ablation (white arrows). 200× magnification.

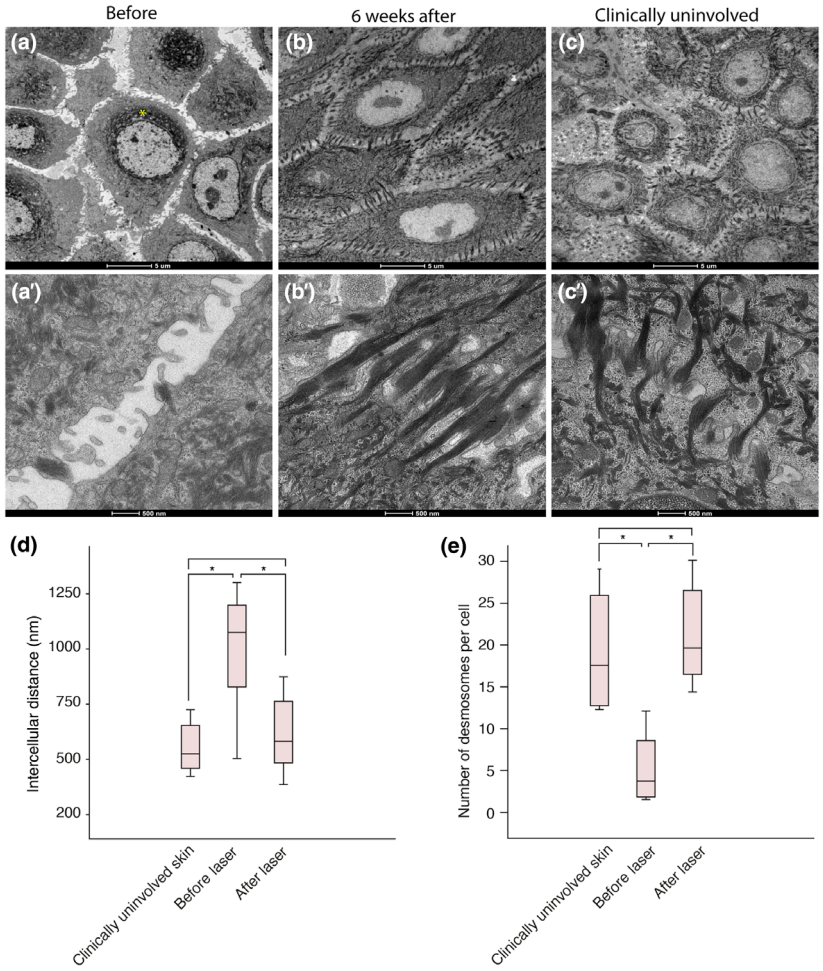

FIGURE 3 Intercellular distance between keratinocytes and number of desmosomes before and 6 weeks after laser therapy and in clinically uninvolved skin. (a) Widened intercellular space in the stratum spinosum before laser therapy, keratinocytes showing severe perinuclear clumping of keratin filaments (yellow asterisk). (b) Keratinocytes after laser therapy without perinuclear clumping or retraction of keratofilaments. The desmosomes are well organized and interconnect adjacent keratinocytes. (c) Clinically uninvolved skin with perinuclear retraction of keratofilaments. (a') Reduced amount of desmosomes in affected skin before laser therapy. (b') Restored and well-organized desmosomes after laser therapy. (c') Desmosomes in clinically uninvolved skin. (d) The intercellular distance (nm) between keratinocytes in the stratum spinosum of clinically uninvolved skin, before laser therapy (baseline) and 6 weeks after laser therapy. (e) Number of desmosomes per cell in clinically uninvolved skin, before laser therapy (baseline) and 6 weeks after laser therapy. * indicates p-value <0.05 determined by Mann–Whitney U-test. – indicates the median intercellular distance/number of desmosomes.

treatment. Regardless of the genetic defect in *ATP2C1*, the treated area remained free of disease at long-term follow-up.

The treated skin remained hypopigmented, which allowed for accurate follow-up over time. Quality of life improved significantly at 6 weeks after laser therapy and remained as such at 3-year follow-up. Patients were still anxious about disease recurrence at 6-week follow-up, a concern that completely faded at 3-year follow-up.

Ablation of both epidermis and papillary dermis induced long-term remission. This is consistent with previous case studies using dermabrasion and CO_2 laser.[17,22,23] Removal of both epidermis and papillary dermis over the full size of the treated area is crucial for long-term remission. In comparison to CO_2 laser, Er:YAG laser ablation is less prone to scarring due to its 10-fold higher absorption in water and therefore, speedy ablation and little thermal damage.[24,25] Dermabrasion has similar long-term results but more recurrences have been observed.[10,26] Er:YAG ablation induced complete remission in 97% of cases compared to 83% with dermabrasion.[10,26] Like dermabrasion, Er:YAG laser therapy is an elaborate procedure that requires accurate wound care upon treatment, and might therefore not be ideal for older patients with reduced mobility and a lot of comorbidities. In case of extensive skin-on-skin contact in the skin folds such as the submammary fold, laser treatment might not be ideal as wound healing is compromised. HHD involving large body surface area requires multiple laser treatments, which is a limitation of ablative laser therapy. Depending on the maximum lidocaine dose per body weight, approximately 64–80 square centimetres can be treated per single laser session. In this study, treatment was provided by one practitioner which may limit generalization.

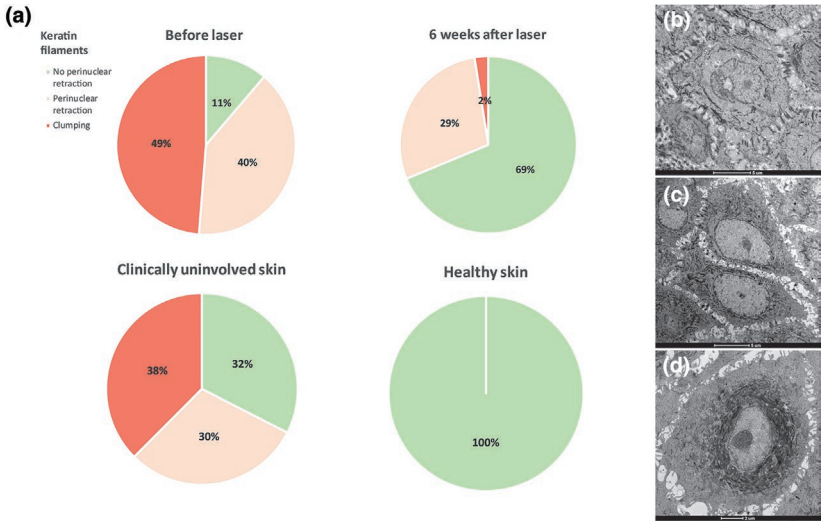

FIGURE 4 Keratin filament distribution. (a) Mean keratin filament distribution of 80 keratinocytes before laser therapy, 6 weeks after laser therapy, in clinically uninvolved skin and mean keratin filament distribution of 30 keratinocytes in skin of unaffected individuals. (b) No perinuclear retraction or clumping of keratin filaments. (c) Perinuclear retraction of keratin filaments. (d) Thick electron dense packed keratin filaments around the nucleus, that is, clumping.

The impressive clinical remission following Er:YAG laser therapy was reflected in the significant improvement at the ultrastructural level. In accordance with previous EM studies, desmosomes were scarce or absent in HH plaques, an increased intercellular distance was noted and keratin filaments were retracted to the perinuclear area, in some cases leading to clumping.[2–6] Upon Er:YAG laser treatment, the skin showed significant increase in the number of desmosomes which became similar to the number in patient's clinically uninvolved skin. The newly formed epidermis showed reduced intercellular distance and limited clumping. Most interestingly, perinuclear retraction and clumping were more common in the patient's clinically uninvolved skin than in the treated skin. The newly formed skin rather resembled the skin of healthy control individuals. The previously observed lack of plakoglobin at the desmosomal junction, might contribute to the observed clumping of keratin filaments in clinically uninvolved skin of HHD patients.[27] Upon wounding, during re-epithelialization, epigenetic changes may occur that lead to an improved expression, processing and/or localization of desmosomal proteins in the newly formed epidermis. This may lead to stronger desmosomal junctions and proper keratin filament networks critical for cellular strength and a solid skin barrier, for many years.

Alternatively, as also suggested by an earlier study, the adhesion defect might not be present anymore in the re-epithelialized skin after treatment.[28] Er:YAG laser therapy ablates the epidermis and thereby, removes the epidermal stem cells. Regarding the depth of the hair follicle and the preserved hair growth after laser ablation, we assume the hair follicle bound stem cells remain intact. Hair follicle isthmus and bulge region stem cells have previously been shown to be essential for re-epithelialization upon wounding.[29,30] Importantly, a small fraction of the bulge cells transdifferentiate into long-lived epidermal stem cells.[31] Epigenetic changes that might have occurred during wound healing, a process largely unknown, could potentially be stably incorporated in the epidermal stem cells and contribute to long-term remission. Newly formed keratinocytes may therefore exhibit the necessary hSPCA1 expression and/or upregulate alternative calcium pumps to maintain intracellular calcium homeostasis.

In conclusion, our study shows high effectiveness of a single ablative laser treatment in the treatment of HHD, with significant improvement in QoL and recurrence-free long-term remission.

ACKNOWLEDGEMENTS

We would like to thank all Hailey–Hailey patients for their participation in this project. This project is part of the European Reference Network-SKIN (https://ern-skin.eu). We would like to thank Pauline Peeters for her wonderful help in designing the Graphical Abstract.

FUNDING INFORMATION

None.

CONFLICT OF INTEREST STATEMENT

The authors have no conflict of interest to declare.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICAL APPROVAL

This study was reviewed and approved by the Maastricht University Medical Centre+ Ethics Committee (METC 2018-0816 and METC 18-047).

ETHICS STATEMENT

The patients in this manuscript have given written informed consent to publication of their case details.

ORCID

Marie-Eline P. H. Debeuf https://orcid.org/0009-0003-2028-2973
Patty J. Nelemans https://orcid.org/0000-0002-9669-7353
Antoni H. Gostynski https://orcid.org/0000-0002-1091-2914

REFERENCES

1. Arora H, Bray FN, Cervantes J, Aizpurua LA. Management of familial benign chronic pemphigus. Clin Cosmet Investig Dermatol. 2016;9:281–90.
2. Gottlieb SK, Lutzner MA. Hailey-Hailey disease—an electron microscopic study. J Invest Dermatol. 1970;54(5):368–76.
3. Metze D, Hamm H, Schorat A, Luger T. Involvement of the adherens junction–actin filament system in acantholytic dyskeratosis of Hailey-Hailey disease: a histological, ultrastructural, and histochemical study of lesional and non-lesional skin. J Cutan Pathol. 1996;23(3):211–22.
4. Wilgram GF, Caulfield JB, Lever WF. An electronmicroscopic study of acantholysis and dyskeratosis in Hailey and Hailey's disease. J Invest Dermatol. 1962;39(5):373–81.
5. O'keefe EJ, Briggaman RA, Herman B. Calcium-induced assembly of adherens junctions in keratinocytes. J Cell Biol. 1987;105(2):807–17.
6. Ishibashi Y, Kajiwara Y, Andoh I, Inoue Y, Kukita A. The nature and pathogenesis of dyskeratosis in Hailey-Hailey's disease and Darier's disease. J Dermatol. 1984;11(4):335–53.
7. Harris A, Burge S, Dykes P, Finlay AY. Handicap in Darier's disease and Hailey-Hailey disease. Br J Dermatol. 1996;135(6):959–63.
8. Rogner D, Heimerl L, Heyer S, Biedermann T, Sattler E, Zink A. Patients' perspective, quality of life and treatment goals in Hailey–Hailey disease: lessons learned from the German National Registry. J Eur Acad Dermatol Venereol. 2023;38:419–29.
9. Lagha IB, Ashack K, Khachemoune A. Hailey–Hailey disease: an update review with a focus on treatment data. Am J Clin Dermatol. 2020;21(1):49–68.
10. Hamm H, Metze D, Bröcker EB. Hailey-Hailey disease: eradication by dermabrasion. Arch Dermatol. 1994;130(9):1143–9.
11. Ortiz AE, Zachary CB. Laser therapy for Hailey-Hailey disease: review of the literature and a case report. Dermatol Rep. 2011;3(2):e28.
12. Gabdrafike Z, Blazeviciute M, Janonyte U, Makstiene J, Valiukeviciene S. A case report of Hailey-Hailey disease treated with fractional carbon dioxide laser. Dermatol Rep. 2023;15(3):9658.
13. Duarte-Summers A, Ramani L, Yang S. Utility of pulsed-dye laser in the treatment of recalcitrant Hailey-Hailey disease. J Drugs Dermatol. 2023;22(11):e1–e3.
14. Dulmage BO, Ghareeb ER, Vargo JA, Patton TJ, Quinn AE, Flickinger JC. Severe refractory Hailey-Hailey disease treated with electron beam radiotherapy and low-level laser therapy. Cutis. 2021;107(1):E27–E30.
15. Garcia-Zamora E, Lopez-Estebaranz JL, Dradi GG, Alvarez-Fernandez JG. Carbon dioxide laser treatment in Hailey-Hailey disease. Dermatol Surg. 2022;48(1):146–8.
16. Wollina U, Hansel G, Lotti T, Vojvodic A. Successful treatment of a widespread pemphigus Chronicus Familiaris (Hailey-Hailey) by erbium-YAG-laser. Open Access Maced J Med Sci. 2019;7(18):3070–2.
17. Beier C, Kaufmann R. Efficacy of erbium: YAG laser ablation in Darier disease and Hailey-Hailey disease. Arch Dermatol. 1999;135(4):423–7.
18. Konrad H, Karamfilov T, Wollina U. Intracutaneous botulinum toxin a versus ablative therapy of Hailey-Hailey disease – a case report. J Cutan Laser Ther. 2001;3(4):181–4.
19. Alam M, Ricci D, Havey J, Rademaker A, Witherspoon J, West DP. Safety of peak serum lidocaine concentration after Mohs micrographic surgery: a prospective cohort study. J Am Acad Dermatol. 2010;63(1):87–92.
20. Ortonne J, Ganslandt C, Tan J, Nordin P, Kragballe K, Segaert S. Quality of life in patients with scalp psoriasis treated with calcipotriol/betamethasone dipropionate scalp formulation: a randomized controlled trial. J Eur Acad Dermatol Venereol. 2009;23(8):919–26.
21. Seshadri D, Kumaran M, Kanwar A. Acantholysis revisited: back to basics. Indian J Dermatol Venereol Leprol. 2013;79(1):120.
22. McElroy JA, Mehregan DA, Roenigk RK. Carbon dioxide laser vaporization of recalcitrant symptomatic plaques of Hailey-Hailey disease and Darier's disease. J Am Acad Dermatol. 1990;23(5):893–7.
23. Don PC, Carney PS, Lynch WS, Zaim MT, Hassan MO. Carbon dioxide laser abrasion: a new approach to Management of Familial Benign Chronic Pemphigus (Hailey-Hailey disease). J Dermatol Surg Oncol. 1987;13(11):1187–98.
24. Caniglia RJ. Erbium: YAG laser skin resurfacing. Facial Plast Surg Clin North Am. 2004;12(3):373–7.
25. Jasin ME. Achieving superior resurfacing results with the erbium: YAG laser. Arch Facial Plast Surg. 2002;4(4):262–6.
26. Farahnik B, Blattner CM, Mortazie MB, Perry BM, Lear W, Elston DM. Interventional treatments for Hailey–Hailey disease. J Am Acad Dermatol. 2017;76(3):551–8.e3.
27. Tada J, Hashimoto K. Ultrastructural localization of cell junctional components (desmoglein, plakoglobin, E-cadherin, and β-catenin) in Hailey-Hailey disease, Darier's disease, and pemphigus vulgaris. J Cutan Pathol. 1998;25(2):106–15.
28. Kirtschig G, Gieler U, Happle R. Treatment of Hailey-Hailey disease by dermabrasion. J Am Acad Dermatol. 1993;28(5):784–6.
29. Blanpain C. Skin regeneration and repair. Nature. 2010;464(7289):686–7.
30. Plikus MV, Gay DL, Treffeisen E, Wang A, Supapannachart RJ, Cotsarelis G. Epithelial stem cells and implications for wound repair. Semin Cell Dev Biol. 2012;23(9):946–53.
31. Brownell I, Guevara E, Bai CB, Loomis CA, Joyner AL. Nerve-derived sonic hedgehog defines a niche for hair follicle stem cells capable of becoming epidermal stem cells. Cell Stem Cell. 2011;8(5):552–65.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Debeuf M-E, Knoops K, López-Iglesias C, Lookermans E, Nelemans PJ, Abdul Hamid M, et al. Long-term remission of Hailey–Hailey disease by Er:YAG ablative laser therapy. J Eur Acad Dermatol Venereol. 2025;39:1038–1045. https://doi.org/10.1111/jdv.20351