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Quality of life, treatment satisfaction, and adherence to treatment in patients with vesicular hand eczema: A cross-sectional study

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Abstract

Background: Recurrent vesicular hand eczema frequently has a chronic course and needs long-term treatment.

Objectives: To evaluate health-related quality of life (HRQoL), treatment satisfaction, and adherence in patients with vesicular hand eczema.

Methods: Patients using one main treatment for at least three months were included. Data on HRQoL (Quality of Life in Hand Eczema Questionnaire [QOLHEQ]), treatment satisfaction (Treatment Satisfaction Questionnaire for Medication, version II), and treatment adherence (4-item Morisky Medication Adherence Scale) were collected. Univariate and multivariate regression analysis were used to predict variables associated with HRQoL.

Results: HRQoL was moderately impaired, with the highest impact in the QOLHEQ subdomain symptoms. Female sex, more severe hand eczema, and lower treatment satisfaction were associated with more impairment in HRQoL. Patients with severe/very severe hand eczema had significant lower "global satisfaction" scores compared with the other severity groups. The "global satisfaction" and treatment adherence in patients using systemic treatment were significantly higher compared with those with only topical treatment.

Conclusions: In patients with vesicular hand eczema disease severity affects both HRQoL and treatment satisfaction. Systemic treatment of severe hand eczema could improve the severity and as a result also HRQoL, treatment satisfaction, and medication adherence.

KEYWORDS

health-related quality of life, patient-reported outcomes, recurrent vesicular hand eczema, treatment adherence, treatment satisfaction

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1 | INTRODUCTION

Hand eczema can be classified into different clinical subtypes. Recurrent vesicular hand eczema is a typical clinical subtype that is characterized by development of small (1-2 mm) vesicles most often interdigitally or on the palms. The patient experiences episodes of vesicles mostly at unpredictable intervals, which can result in a chronic course of recurrent vesicular hand eczema. In addition to a clinical diagnosis, it is important to classify hand eczema etiologically. The cause of hand eczema is often multifactorial. It can be classified into one or more of the following etiological diagnoses: allergic contact dermatitis, irritant contact dermatitis (ICD), protein contact dermatitis, and atopic hand eczema.[1]

The treatment of chronic hand eczema is often challenging and at times insufficient and unsatisfactory.[2,3] Studies on treatment effectiveness are mainly based on physician-reported outcomes. Fewer studies have actually evaluated treatment benefit in terms of patient-reported outcomes.[4,5] However, chronic hand eczema can have a remarkable impact on quality of life.[2,6]

To evaluate the impact of disease and treatment on physical, psychological, and social functioning, the Quality of Life in Hand Eczema Questionnaire (QOLHEQ) was recently developed. It measures overall health-related quality of life (HRQoL) impairment in four domains: "symptoms," "emotions," "functioning," and "treatment and prevention."[7,8] Other patient-reported outcomes are treatment satisfaction and treatment adherence.[9,10] Previous studies in several therapeutic areas demonstrated a positive association between treatment satisfaction and adherence to therapy.[11] In this study we aimed to examine HRQoL, treatment satisfaction, and treatment adherence in patients with recurrent vesicular hand eczema.

2 | METHODS

2.1 | Study design and participants

This cross-sectional study was conducted at the Dermatology Department of the University Medical Center Groningen (Groningen, The Netherlands), a tertiary referral center for hand eczema, between December 2016 and May 2019. Patients were recruited while they were on a routine visit at the outpatient clinic. Despite the fact that some patients had mild contributing atopic dermatitis, hand eczema was the main reason for consultation. Inclusion criteria were adult age (>18 years old), diagnosis of chronic (>3 months) vesicular hand eczema (classification of Menné et al[1]), and use of at least one main treatment for at least three months. Patients concomitantly treated with bursts of oral corticosteroids in the last 3 months were excluded. Included patients needed to be able to read and understand the Dutch language. Patients were interviewed according to a structured questionnaire. The study was reviewed and approved by the Medical Ethical Review Board of the University Medical Center Groningen (reference METc M17.207552).

2.2 | Clinical characteristics

Data collected were basic characteristics (age, sex, education [low/middle vs high]), employment status (low- vs high-risk occupation for hand eczema[12]), and elevated total and specific immunoglobulin E inhalant allergens. Etiological hand eczema diagnosis was based on fixed criteria (see Data S1).

Data on current (topical, UV, and systemic treatment) and previous (topical, UV, systemic treatment, and hospitalization) treatments for hand eczema were collected. All patients with vesicular hand eczema were treated according to the Dutch guidelines of hand eczema.[13,14] Previous treatment with oral corticosteroids for over 2 weeks was counted as a history of systemic treatment. The current treatment was based on the most potent medication (systemic treatment vs nonsystemic treatment). Patients with systemic treatment may have used concomitantly topical corticosteroids. Disease severity was assessed by the physician with the photographic guide of Coenraads et al.[15] For a complete overview of all variables, see the questionnaire in Data S1.

2.3 | Quality of life, treatment satisfaction, and adherence

To evaluate the HRQoL, the Dutch translation of the QOLHEQ was used, range 0-89. This disease-specific questionnaire consists of 30 questions covering four subdomains: "symptoms" (7 questions), "emotions" (8 questions), "functioning" (8 questions), and "treatment and prevention" (7 questions). Response categories are never, rarely, sometimes, often, and always.[7,8] For the recently validated Dutch language version, these are scored as 0, 1, 1, 2, and 3, respectively. The severity band for the QOLHEQ overall score for Dutch patients is as follows: not at all, 0-13; slightly, 14-28; moderately, 29-44; strongly, 45-64; and very strongly, ≥65.[16]

Satisfaction was assessed with the Dutch version of the Treatment Satisfaction Questionnaire for Medication, version II (TSQM-II), range 0-100.[9] The TSQM-II is an 11-item validated questionnaire comprising three domains: "effectiveness" (2 questions), "side effects" (4 questions), and "convenience" (3 questions). Moreover, "global satisfaction" (2 questions) was measured. Response categories are as follows: 1, extremely dissatisfied; 2, very dissatisfied; 3, dissatisfied; 4, somewhat satisfied; 5, satisfied; 6, very satisfied; and 7, extremely satisfied. The score per domain can be calculated with an algorithm ranging from 0 to 100, where higher scores equate to better outcomes.

To evaluate treatment adherence four dichotomous questions (yes [1]/no [0]), the 4-item Morisky Medication Adherence Scale was used, range 0-4. A sum score of 0 represents a high patient adherence, a score of 1 or 2 represents a medium adherence, and a score of 3 or 4 represents a low adherence.[10]

2.4 | Statistical analyses

Data analyses were performed using IBM SPSS Statistics version 23.0 for Windows (SPSS/IBM, New York, New York). Descriptive statistics were presented as mean together with median and range for interval-scaled variables, and as relative frequency together with absolute numbers for categorical variables. The four QOLHEQ and TSQM subdomains were analyzed separately for the group of patients with nonsystemic therapy and for the group with systemic therapy. After controlling for normal distribution, the independent sample *t* test was used to analyze the differences in treatment satisfaction and HRQoL between both treatment groups. Fisher's exact test was used to test difference in nominal variables between the nonsystemic and systemic groups. Univariate regression analysis included as independent variables age, gender, level of education (high vs middle/low), duration of hand eczema (years), the current treatment (nonsystemic vs systemic treatment), hand eczema severity, treatment adherence, and "global satisfaction," which were suitable for inclusion ($P < .2$) into the multivariate regression model. Afterwards, multivariate linear regression was used including clinical characteristics associated with treatment satisfaction. *P*-values less than .05 were considered statistically significant in all analyses. Standardized β-coefficients were presented, with strong correlation defined as $\beta > 0.7$, moderate correlation as $0.7 > \beta > 0.4$, and weak correlation as $0.4 > \beta > 0.2$.[17] The interpretability of the Dutch and International QOLHEQ (subdomain and overall) scores was published by Oosterhaven et al.[8,16] See Data S3 for the Dutch (Table S3.3) and International (Table S3.4) single score bands. In this publication Dutch scores were presented; the International scores can be found in Data S3.

3 | RESULTS

In total, 168 (56.0% female) participants were included in this study. Sociodemographic and clinical characteristics are outlined in Table 1. The mean duration (median [range]) of a diagnosis of hand eczema

TABLE 1 Patient characteristics

Characteristics	All patients	Male	Female	Nonsystemic treatment[a]	Systemic treatment[b]
Number of patients, n (%)	168 (100)	74 (44.0)	94 (56.0)	112 (100)	56 (100)
Age (years), mean (SD)	43.1 (15.7)	44.4 (14.4)	42.0 (16.6)	67 (59.8)	27 (48.2)
High education, n (%)	35 (20.8)	15 (20.3)	20 (21.3)	40.0 (15.6)*	49.3 (14.1)*
High-risk occupation, n (%)	63 (37.5)	30 (40.5)	33 (35.1)	27 (24.1)*	8 (14.3)*
Duration of hand eczema (years), mean (SD)	9.2 (11.3)	10.1 (11.8)	8.5 (10.9)	48 (42.9)	17 (30.4)
Elevated total IgE level (>115 kU/L), n (%)	41 (37.6)[d]	21 (41.2)[e]	20 (34.5)[f]	7.5 (9.9)*	12.5 (13.3)*
Elevated serum-specific IgE inhaled allergens, n (%)	52 (50.0)[g]	30 (60.0)[h]	22 (40.7)[i]	27 (39.7)[j]	14 (34.1)[k]
Etiological diagnosis[c], n (%)					
Atopic hand eczema	91 (54.2)	38 (51.4)	53 (56.4)	56 (50.0)	35 (62.5)
Irritant contact dermatitis	81 (48.2)	36 (48.6)	45 (47.9)	57 (50.9)	24 (42.9)
Allergic contact dermatitis	61 (39.6)[d]	26 (35.1)[m]	35 (37.2)[n]	42 (42.0)[o]	19 (35.2)[p]
Protein contact dermatitis	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Etiologically unclassifiable hand eczema	20 (11.9)[q]	8 (10.8)[r]	12 (12.8)	16 (14.3)[s]	4 (7.1)
Current treatment, n (%)					
Only topical treatment[a]	111 (66.1)	45 (60.8)	66 (70.2)	111 (99.1)	–
Systemic treatment	56 (33.3)	29 (39.2)	27 (28.7)	–	56 (100)
Ciclosporin	25 (14.9)	11 (14.9)	14 (14.9)	–	25 (44.6)
Alitretinoin	12 (7.1)	7 (9.5)	5 (5.3)	–	12 (21.4)
Methotrexate	7 (4.2)	3 (4.1)	4 (4.3)	–	7 (12.5)
Dupilumab	7 (4.2)	4 (5.4)	3 (3.2)	–	7 (12.5)
Azathioprine	4 (2.4)	3 (4.1)	1 (1.1)	–	4 (7.1)
Tacrolimus	1 (0.6)	1 (1.4)	0 (0)	–	1 (1.8)
UV therapy	1 (0.6)	0 (0)	1 (1.1)	1 (0.9)	–
Previous treatment, n (%)					
Prior systemic treatment[b]	65 (38.7)	25 (33.8)	40 (42.5)	24 (21.4)*	41 (73.2)*
One prior systemic treatment	30 (17.9)	9 (12.2)	21 (22.3)	14 (12.5)*	16 (28.6)*

(Continues)

TABLE 1 (Continued)

Characteristics	All patients	Male	Female	Nonsystemic treatment[a]	Systemic treatment[b]
More than one prior systemic treatment	35 (20.8)	16 (21.6)	19 (20.2)	10 (8.9)*	25 (44.6)*
Oral corticosteroids (<2 weeks)	60 (35.5)	29 (39.2)	31 (33.0)	32 (28.6)*	28 (50.0)*
UV therapy	58 (34.3)	23 (31.1)	35 (37.2)	44 (39.3)	14 (25.0)
Previous hospitalization	8 (4.8)	3 (4.1)	5 (5.3)	1 (0.9)*	4 (7.1)*
Disease severity, n (%)					
Clear	6 (3.6)	2 (2.7)	4 (4.3)	3 (2.7)	3 (5.4)
Almost clear	74 (44.0)	26 (35.1)	48 (51.1)	45 (40.2)	29 (51.8)
Moderate	48 (28.6)	26 (35.1)	22 (23.4)	35 (31.3)	13 (23.2)
Severe	31 (18.5)	14 (18.9)	17 (18.1)	22 (19.6)	9 (16.1)
Very severe	9 (5.4)	6 (8.1)	3 (3.2)	7 (6.3)	2 (3.6)

[a]Nonsystemic treatments included UV therapy, topical corticosteroids always combined with neutral emollients, occasionally with concomitant use of calcineurin inhibitors or tar preparations.
[b]Systemic treatment included alitretinoin, acitretin, azathioprine, ciclosporin, dupilumab, methotrexate, mycophenolic acid/mycophenolate mofetil, oral corticosteroids (>2 weeks), and tacrolimus.
[c]Patients can have one or more etiological hand eczema diagnoses.
[d]59 patients were not tested.
[e]23 patients were not tested.
[f]36 patients were not tested.
[g]64 patients were not tested.
[h]24 patients were not tested.
[i]40 patients were not tested.
[j]43 patients were not tested.
[k]33 patients were not tested.
[l]14 patients were not patch tested, necessary for allergic contact dermatitis classification.
[m]Nine patients were not patch tested, necessary for allergic contact dermatitis classification.
[n]Five patients were not patch tested, necessary for allergic contact dermatitis classification.
[o]12 patients were not patch tested, necessary for allergic contact dermatitis classification.
[p]Two patients were not patch tested, necessary for allergic contact dermatitis classification.
[q]Three patients were not patch tested, necessary for allergic contact dermatitis classification.
[r]Three patients were not patch tested, necessary for allergic contact dermatitis classification.
[s]Three patients were not patch tested, necessary for allergic contact dermatitis classification.
*P < .05, nonsystemic vs systemic treatment.
Abbreviations: IgE, immunoglobulin E; SD, standard deviation.

was 9.2 (11.3 [0.3-65]) years. The severity grades were pooled for the total group (n = 168) because of the small numbers, clear (n = 6) and almost clear (n = 74); severe (n = 31) and very severe (n = 9; Table 1). Female patients had more often clear/almost clear hand eczema compared with male patients, although this was only borderline significant (P = .06).

Patch tests were performed in most patients (91.9%, n = 154). Of the patch-tested patients 69.5% (n = 107) had at least one positive patch test reaction to an allergen from the European baseline series. Most patients were patch tested with additional series; 79.2% (n = 122) had at least one positive reaction to allergens from all series tested. Polysensitization was found in 24.0% (n = 37). Of all patients, 37.5% (n = 63) had a high-risk occupation for developing hand eczema. See Data S2 for the list of these occupations. The median (range) treatment duration for nonsystemic and systemic treatments was 0.5 (0.3-32) years and 0.8 (0.3-7) years, respectively.

3.1 | Health-related quality of life

The overall QOLHEQ scores indicated no impairment of HRQoL in 15.0% of patients (n = 25), slight impairment in 29.8% (n = 50), moderate impairment in 38.1% (n = 64), strong impairment in 12.5% (n = 21), and a very strong impairment in 4.2% (n = 7; Table 2). The mean overall QOLHEQ scores and the mean QOLHEQ subdomain scores are presented for the total group in Table 3, stratified by sex and type of treatment (systemic vs nonsystemic). The mean overall QOLHEQ score was 31.2, representing a moderately impaired HRQoL. The most affected subdomain was "symptoms"; the mean score was 9.1, representing a moderately impaired HRQoL. The other mean QOLHEQ subdomains scores represented slightly impaired HRQoL.

Differences in HRQoL impairment were evaluated for sex and treatment groups. The overall QOLHEQ score and subdomain "functioning" showed moderate impairment in females and slight

TABLE 2 Health-related quality of life impairment assessed with the Quality of Life in Hand Eczema Questionnaire (QOLHEQ) in patients with vesicular hand eczema: interpretation of the overall QOLHEQ score and the QOLHEQ subdomain scores

	Health-related quality of life impairment[a] (n = 167)				
	Not at all (n, %)	Slightly (n, %)	Moderately (n, %)	Strongly (n, %)	Very strongly (n, %)
QOLHEQ overall score	25 (15.0)	50 (29.9)	64 (38.3)	21 (12.6)	7 (4.2)
Symptoms	2 (1.2)	60 (35.9)	48 (28.7)	45 (26.9)	12 (7.2)
Emotions	67 (40.1)	59 (35.3)	30 (18.0)	4 (2.4)	7 (4.2)
Functioning	17 (10.2)	77 (46.1)	34 (20.4)	26 (15.6)	13 (7.8)
Treatment and prevention	60 (35.9)	48 (28.7)	39 (23.4)	8 (4.8)	12 (7.2)

[a]One patient missing.

TABLE 3 Means for health-related quality of life impairment (QOLHEQ), treatment satisfaction (TSQM), and treatment adherence (MMAS) for the total group and stratified by sex and type of treatment (systemic vs nonsystemic)

	All patients				
Characteristics	Male (n = 74)	Female (n = 94)	All (n = 168)	Nonsystemic treatment[a] (n = 112)	Systemic treatment[b] (n = 56)
HRQoL impairment (QOLHEQ Dutch subscales), mean (SD)[c]					
Overall score (0-89)	28.3 (14.4)**	33.6 (17.8)**	31.2 (16.5)	32.5 (16.0)	28.9 (17.4)
Symptoms (0-21)	8.4 (3.7)*	9.6 (4.4)*	9.1 (4.2)	9.8 (3.8)*	7.6 (4.5)*
Emotions (0-24)	6.9 (4.7)	7.8 (5.1)	7.4 (4.9)	7.7 (5.0)	6.9 (4.9)
Functioning (0-24)	6.5 (4.3)**	8.2 (5.6)**	7.4 (5.1)	7.6 (5.0)	7.1 (5.3)
Treatment and prevention (0-20)	7.3 (4.0)*	8.8 (4.7)*	8.1 (4.5)	8.3 (4.3)	7.8 (4.7)
Treatment satisfaction (TSQM subscale), mean (SD)					
Effectiveness (0-100)	57.2 (17.7)	60.0 (19.0)	58.7 (18.4)	55.9 (17.9)*	64.4 (18.4)*
Side effects (0-100)	87.0 (21.1)	88.9 (19.1)	88.1 (19.9)	89.3 (20.2)	85.7 (19.4)
Convenience (0-100)	64.3 (17.1)	66.7 (12.5)	65.6 (14.7)	64.4 (13.0)	68.1 (17.5)
Global satisfaction (0-100)	61.0 (18.0)	64.2 (16.2)	62.7 (17.1)	60.8 (14.7)*	66.8 (20.6)*
Treatment adherence (MMAS-4), n (%)					
High	18 (24.3)*	40 (42.6)*	58 (34.5)	31 (27.7)*	27 (48.2)*
Medium	41 (55.4)	43 (45.7)	84 (50.0)	58 (51.8)	26 (46.4)
Low	15 (20.3)	11 (11.7)	26 (15.5)	23 (20.5)	3 (5.4)

Abbreviations: HRQoL, health-related quality of life; MMAS-4, 4-item Morisky Medication Adherence Scale; QOLHEQ, Quality of Life in Hand Eczema Questionnaire; SD, standard deviation; TSQM, Treatment Satisfaction Questionnaire for Medication.

[a]Nonsystemic treatments included UV therapy, topical corticosteroids always combined with neutral emollients, occasionally with concomitant use of calcineurin inhibitors or tar preparations.

[b]Systemic treatment included alitretinoin, azathioprine, ciclosporin, dupilumab, methotrexate, and tacrolimus.

[c]One patient missing.

*P < .05 (male vs female and systemic vs nonsystemic treatment), **P < .05 and different severity band.

impairment in males. The HRQoL impairment because of "symptoms" was significantly lower in the group with systemic treatment compared with the group with topical treatment. However, the mean scores in both treatment groups represented moderately impaired HRQoL.

The QOLHEQ overall scores were significantly different between each of the severity groups (P < .001). In the pooled group of patients with severe/very severe hand eczema (mean QOLHEQ overall score 41.1) and the group with moderate hand eczema (mean QOLHEQ overall score 33.3) a moderate impairment of HRQoL was found. The pooled group with clear/almost clear hand eczema (mean QOLHEQ overall score 25.3) showed a slight impairment (Table S3.1,S3.2).

3.2 | Treatment satisfaction

TSQM subdomain scores are presented in Table 3. Patients were most satisfied about the TSQM subdomain "side effects" and least satisfied about "effectiveness." Patients receiving systemic treatment had significantly higher TSQM treatment satisfaction scores for "effectiveness" and "global satisfaction" compared with patients receiving

nonsystemic treatment (Table 3). "Global satisfaction" scores for nonsystemic vs different individual systemic treatments are presented in Figure 1. Significantly higher "global satisfaction" scores were found for ciclosporin, alitretinoin, and dupilumab compared with nonsystemic treatment. Figure 2 shows the mean TSQM subdomain scores in different severity groups. Patients with severe/very severe hand eczema had significantly lower subdomain satisfaction scores in "effectiveness" (TSQM score: 47.3, standard deviation [SD]: 14.9) compared with patients with moderate (TSQM score: 55.4, SD: 15.0) or clear/almost clear hand eczema (TSQM score: 66.4, SD: 18.4), $P < .001$. Furthermore, TSQM subdomain scores of "global satisfaction" were significantly lower for severe/very severe hand eczema (TSQM score:

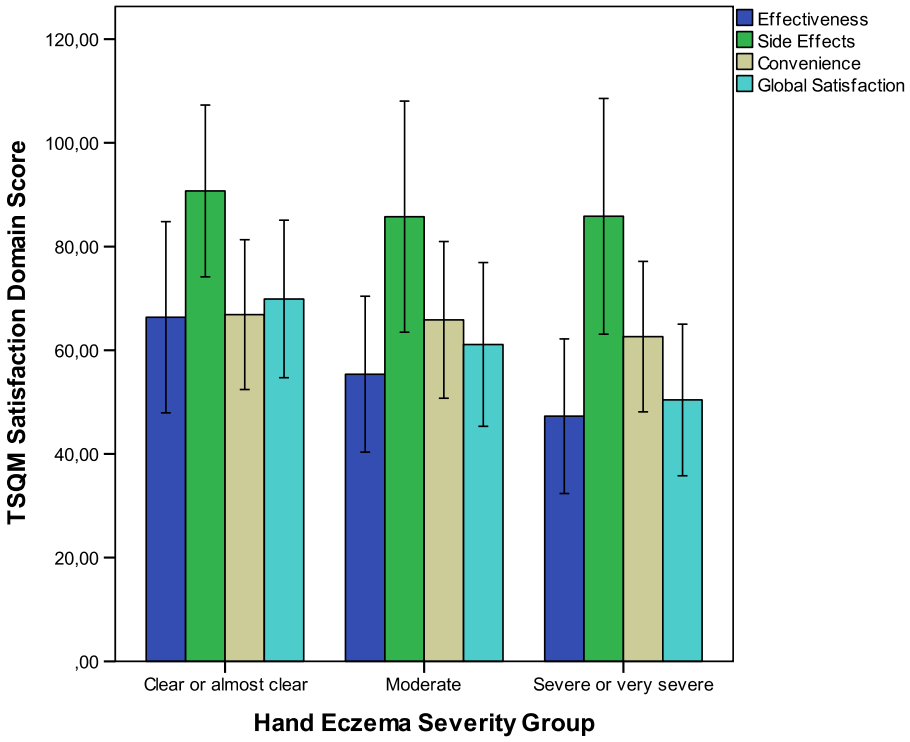

FIGURE 1 Treatment satisfaction scores (TSQM, range 0-100) for nonsystemic treatment vs different individual systemic treatments. A higher score of the TSQM subdomain "global satisfaction" indicates higher levels of treatment satisfaction. $P < .05$. Other treatments are azathioprine, tacrolimus, and UV therapy. TSQM, Treatment Satisfaction Questionnaire for Medication

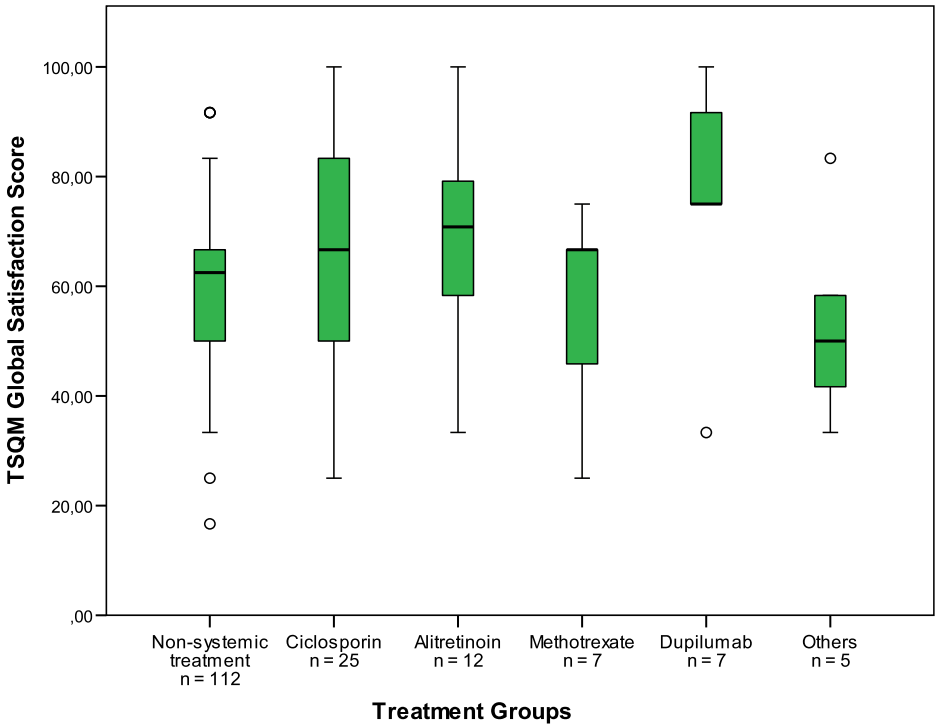

FIGURE 2 Treatment satisfaction domain scores (TSQM, range 0-100) in different hand eczema severity groups. Higher scores in the TSQM domains (bars) indicate higher levels of treatment satisfaction. Error bars represent standard deviation. $P < .05$ between groups. TSQM, Treatment Satisfaction Questionnaire for Medication

50.4, SD: 14.6) compared with patients with moderate (TSQM score: 61.1, SD: 15.8) or clear/almost clear hand eczema (TSQM score: 69.9, SD: 15.2), $P < .001$. No significant association between age, hand eczema duration, previous history of systemic treatment, and treatment satisfaction was found.

TABLE 4 Means of health-related quality of life (HRQoL) impairment and treatment satisfaction in different groups of treatment adherence

	Treatment adherence (MMAS-4)		
	Low (n = 26)	Medium (n = 84)	High (n = 58)
HRQoL impairment (QOLHEQ Dutch subdomains), mean (SD)[a]			
Symptoms (0-21)	10.0 (3.2)	9.5 (3.7)	8.0 (4.9)
Emotions (0-24)	7.5 (4.6)*	8.4 (4.8)*	5.9 (4.9)*
Functioning (0-24)	7.4 (4.9)	8.2 (4.9)	6.2 (5.4)
Treatment and prevention (0-20)	8.4 (4.1)	8.8 (4.1)	7.1 (5.0)
Overall score (0-89)	32.5 (15.1)*	34.2 (15.0)*	26.6 (18.4)*
Treatment satisfaction (TSQM subscale 0-100), mean (SD)			
Effectiveness	52.2 (17.2)*	57.7 (17.7)*	63.1 (19.1)*
Side effects	85.9 (24.6)	87.1 (21.1)	67.9 (13.7)
Convenience	61.3 (14.6)	65.3 (15.2)	67.9 (13.7)
Global satisfaction	56.1 (13.4)*	60.9 (16.8)*	68.5 (17.5)*

Abbreviations: MMAS-4, 4-item Morisky Medication Adherence Scale; QOLHEQ, Quality of Life in Hand Eczema Questionnaire; SD, standard deviation; TSQM, Treatment Satisfaction Questionnaire for Medication.
[a]One patient missing.
*$P < .05$.

3.3 | Adherence

About 50% of the patients had a medium treatment adherence. In the group of patients with high treatment adherence there were significantly more females than males and significantly more patients using systemic therapy compared with nonsystemic therapy (Table 3). The QOLHEQ and TSQM subdomains scores for different adherence groups are presented in Table 4. A high adherence was significantly associated with a lower QOLHEQ overall score and the QOLHEQ subdomain "emotions." Moreover, high adherence was associated with higher TSQM "global satisfaction" scores and a higher satisfaction about "effectiveness."

3.4 | Regression analysis

In the univariate analysis (see Data S4), taking the QOLHEQ domain score as the dependent variable, age, duration of hand eczema, education, and adherence were not associated with HRQoL. The multivariate regression model (Table 5) showed that female sex, more severe hand eczema, and lower treatment satisfaction were associated with more impairment of HRQoL (overall QOLHEQ score). This model explained 37% of the variance of the total HRQoL score (R^2). Severity was strongly associated with the QOLHEQ subdomain "symptoms." For the association of "global satisfaction," the standardized beta was similar for all QOLHEQ subdomains. Female sex was not associated with the QOLHEQ subdomain "emotions."

TABLE 5 Multivariate linear regression analysis assessing factors that would affect the health-related quality of life subdomain scores as the dependent variable

	Symptoms subdomain $R^2 = 0.41$		Emotions subdomain $R^2 = 0.26$		Functioning subdomain $R^2 = 0.33$		Treatment and prevention subdomain $R^2 = 0.25$		QOLHEQ overall score $R^2 = 0.37$	
Variable	Standardized β	*P*-value	Standardized β	*P*-value	Standardized β	*P*-value	Standardized β	*P*-value	Standardized β	*P*-value
Sex (female)	**0.23**	**<.001**	–	–	**0.23**	**.00**	**0.23**	**<.001**	**0.25**	**<.001**
High education	–	–	–0.06	.37	–	–	–	–	–0.25	.80
Current systemic treatment	–0.10	.11	–	–	–	–	–	–	0.05	.51
Severity	**0.33**	**<.001**	0.16	**.04**	0.19	**.01**	0.14	.08	**0.22**	**<.001**
Low adherence	0.05	.45	–0.03	.63	0.01	.88	0.05	.51	0.07	.31
Higher TSQM global satisfaction score	**–0.36**	**<.001**	**–0.41**	**<.001**	**–0.43**	**<.001**	**–0.40**	**<.001**	**–0.44**	**<.001**

Note: Numbers in bold represent $P < .05$ and standardized β coefficients >0.2.
Note: Variables with a indent (–) had a *P* value > .2 in the univariate regression analysis and were not suitable for inclusion in the concerning subdomain.
Abbreviations: QOLHEQ, Quality of Life in Hand Eczema Questionnaire; TSQM, Treatment Satisfaction Questionnaire for Medication.

4 | DISCUSSION

Overall, vesicular hand eczema patients showed a moderately impaired HRQoL, with the highest impairment noted in the QOLHEQ subdomain "symptoms." We demonstrated that more severe hand eczema was associated with more impairment in HRQoL. The association between severity and HRQoL is in line with previous studies that used the Dermatology Life Quality Index to assess HRQoL and included all types of hand eczema.[6,18] Female sex was associated with more impairment in HRQoL. Female sex is a well-known demographic factor affecting HRQoL. Other studies showed that female patients experienced more HRQoL impairment compared with male patients, or had similar impairment with less severe hand eczema.[2,6,7] In the current study "functioning" was particularly affected in females. Female patients probably had more distress related to limitations in work, leisure time, or domestic activities. Previous studies showed a considerable psychosocial burden of hand eczema and underline that anxiety and depression are more common in female patients.[2,19] In this study we did not find an association between female sex and impairment of HRQoL in the QOLHEQ subdomain "emotions." The regression analyses showed that lower "global satisfaction" was associated with more impairment of HRQoL; the standardized beta was −0.44, which indicates a moderate correlation. In previous studies in patients with gout and hypertension a correlation was also found between these outcomes.[20,21]

For the total group we have shown that patients were least satisfied with "effectiveness" of treatment. In patients with severe and very severe hand eczema significantly lower satisfaction scores were found for the TSQM subdomains "effectiveness" and "global satisfaction" compared with the other severity groups. Satisfaction about "side effects" and "convenience" were similar in the different severity groups. This implies that effectiveness of treatment is the major factor affecting "global satisfaction," which is supported by previous studies on, for example, patients with psoriasis and lichen sclerosis. These studies found that patients reported treatment effectiveness as the most important factor for overall treatment satisfaction.[2,22,23] The group using systemic treatment presented significantly higher satisfaction scores with regard to the "effectiveness," compared with the group without systemic treatment. The "global satisfaction" was significantly higher for alitretinoin, ciclosporin, and dupilumab compared with nonsystemic treatments. In patients with psoriasis data also showed lower "global satisfaction" scores for patients receiving nonsystemic treatment.[24,25] The use of biologicals for psoriasis resulted in substantially higher global patient satisfaction scores.[24,26] Recent observational studies showed promising results regarding the effectiveness of dupilumab in patients with hand eczema and might offer future perspectives for patients with difficult-to-treat vesicular hand eczema.[27,28]

Treatment adherence was significantly lower in patients receiving nonsystemic treatment compared with systemic treatment. The perception of the relative ineffectiveness and inconvenience of topical treatment and sometimes corticophobia are well known in dermatology. This may hinder adherence and treatment effectiveness.[29-31] Concerning adherence and QOLHEQ subdomains there was a significant association for the QOLHEQ overall and "emotional" subdomain scores, indicating that high adherence comes in line with less (emotional) HRQoL impairment (Table 4). However, a longitudinal study is needed to verify if less emotional impairment leads to higher adherence or if adherence leads to less emotional problems. A higher medication adherence was also significantly associated with a higher "global satisfaction," while this effect was not seen in the TSQM subdomains "side effects" and "effectiveness."

Some clinical and etiological characteristics need to be highlighted. Of note, half of the patients had ICD during treatment phase (>3 months) and even in the group treated with systemic therapy 40% had an ICD. In our department trained nurse practitioners provide one-to-one patient education for every patient with hand eczema. These are offered personalized glove advice to protect hands from irritant and allergic factors and improve topical treatment compliance. From the high proportion of ICD it can be deduced that despite all efforts it seems impossible for a large proportion of patients to avoid exposure to irritants.

Moreover, we found a high proportion of patients with allergic contact dermatitis (40%), compared with other studies.[32,33] A possible explanation is the fact that our center is a tertiary reference center for hand eczema. Finally, atopic dermatitis is a well-known risk factor for more severe and chronic hand eczema.[34] The number of patients with atopic hand eczema in this study was in line with previous studies (21.5%-57.5%).[32,33]

A limitation of our study is the monocentric design in a tertiary referral center. Presumably this patient cohort included more patients with a difficult-to-treat hand eczema in all groups. Nonsystemic treatment was compared with systemic treatment in terms of HRQoL and treatment satisfaction. Patients on systemic treatment are in general more difficult to treat and an effective treatment will influence their HRQoL and treatment satisfaction more strongly. Another limitation of our study is the smaller number of participants treated with systemic medication compared with nonsystemic medication and the small subgroups with individual systemic treatments. The majority of the patients reported relatively high satisfaction scores for systemic treatment. However, patients with higher levels of satisfaction were more likely to continue with treatment and therefore maybe overrepresented. Patients who discontinued treatment because of side effects or inefficacy within 3 months were not included because of our inclusion criteria of treatment longer than 3 months. This is probably one of the reasons for the favorable results for alitretinoin, which was previously demonstrated to be less successful in vesicular hand eczema.[35] If alitretinoin is effective, patients will continue treatment after 3 months.

In conclusion, our results indicate that disease severity affects both HRQoL and treatment satisfaction in patients with vesicular hand eczema. Patients only using topical treatment are less satisfied with their treatment and their treatment adherence is lower. Systemic treatment of severe hand eczema could improve the severity and as a result also HRQoL, treatment satisfaction, and medication adherence.

New systemic treatment options for patients with severe hand eczema, for example, biologicals or small molecules, could possibly contribute to this.

CONFLICTS OF INTEREST

There was no funding and the authors have no conflicts either actual or perceived.

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SUPPORTING INFORMATION

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

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Supplement 1

Quality of life, treatment satisfaction and adherence to treatment in patients with vesicular hand eczema – a cross sectional study

Klaziena Politiek, Robert F. Ofenloch, Maris Angelino, Ewoud van den Hoed, Marie L.A. Schuttelaar

Questionnaire used for the interview of the patients by the researcher supplemented with other collected data.

Definitions and categorization

Part 1 – based on medical file and interview			
Variable	**Question and response options**	**Categorization**	**Reference**
Socio-demographic factors			
1. Sex	• Male • Female		None
2. Age	Age?		None
3. Education	What is your highest level of completed education? • No degree (1) • Primary education, elementary school, special education (1) • Preparatory secondary vocational education (1) • Lower secondary general education (1) • Senior secondary vocational education (2) • Higher general secondary education (2) • Higher professional education (3) • Academic higher education (3)	1-2: Low/middle 3: High	None
4. High-risk occupation	What is your occupation? Open-ended question. High-risk occupation was defined as evident exposure to allergens and/or evident exposure to wet work/friction with a high probability of developing hand eczema	0: non-high-risk 1: high-risk	To determine high-risk occupations we used previous publications about high-risk occupations[1,2]
Clinical features			
5. Date of diagnosis hand eczema	When was your hand eczema diagnosed? Open-ended question.		None
6. Irritant contact dermatitis	To define an irritant contact dermatitis (ICD), we asked six questions: • On an average day, how many hours do your hands come into direct contact with water, fluids and/or moist products? Never (0)/less than 0.5 hours (1)/0.5 – 1 hour (2)/1 -2 hours (3)/more than 2 hours (4). • On an average day, how many hours do you wear gloves that are impermeable to fluids? Never (0)/less than 0.5 hours (1)/0.5 – 1 hour (2)/1 -2 hours (3)/more than 2 hours (4). • On an average day, how often do you wash your hands? Never (0)/less than 5 times (1)/5 – 10 times (2)/10 – 20 times (3)/more than 20 times (4).		Questions were based on the German "Technische Regeln für Gefahrstoffe" (TRGS) 401 criteria and studies by Oosterhaven and Uter et al.[1,3,4]

	• On an average day, how long do you skin demanding work? For example heavy lifting and/or towing or working with vibrating gear. Never (0)/less than 0.5 hours (1)/0.5 – 1 hour (2)/1 -2 hours (3)/more than 2 hours (4). • On an average day, how many hours do your hands come into contact with food? Never (0)/less than 0.5 hours (1)/0.5 – 1 hour (2)/1 -2 hours (3)/more than 2 hours (4). • On an average day, how long do your hands are expose to cold or very high heat? Never (0)/less than 0.5 hours (1)/0.5 – 1 hour (2)/1 -2 hours (3)/more than 2 hours (4).		
7. Diagnosis ICD	Irritant contact dermatitis was defined as minimally 2 or more from answer category 3, or 1 from answer category 4 (question 6)	0: No 1: Yes	
8. Allergic contact dermatitis	Were patch tests conducted? If yes: the data was extracted from the ESSCA database.		
9. Diagnosis allergic contact dermatitis	Allergic contact dermatitis (ACD) was defined as a final diagnosis of ACD localized at the hand. Data were based on our local European Surveillance System on Contact Allergies (ESSCA) database. Polysensitization was defined as being allergic to three or more unrelated allergens from the European baseline series.	0: No 1: Yes 2: Unknown	European Surveillance System on Contact Allergies[5–7]
10. History of atopic dermatitis	Did you have an itchy skin in childhood? Plus 3 or more of the following: 1 History of involvement of the skin creases such as folds of elbows, around the eyes, behind the knees, fronts of ankles or around the neck? 2 A personal history of asthma or hay fever? 3 A history of a general dry skin? 4 Visible flexural eczema? 5 Onset under the age of 2?	0: No 1: Yes 2: Unknown	UK criteria[8]
11. Current atopic dermatitis	Itch? Plus 3 or more of the following: 1 History of involvement of the skin creases such as folds of elbows, around the eyes, behind the knees, fronts of ankles or around the neck. 2 A personal history of asthma or hay fever. 3 A history of a general dry skin in the last year. 4 Visible flexural eczema. 5 Onset under the age of 2.	0: No 1: Yes	UK criteria[8]
12. Serum IgE	Increased total and serum specific IgE inhalant allergens	0: No 1: Yes 2: Not measured	
13. Protein contact dermatitis	Protein contact dermatitis was diagnosed if exposure to proteins (e.g. food proteins, latex) caused urticarial reactions and subsequent hand eczema and patients had a positive prick test or positive specific IgE.	0: No 1: Yes	
14. Etiological classification	• Irritant contact dermatitis (ICD) • Allergic contact dermatitis (ACD) • Atopic hand eczema (AHE) • Protein contact dermatitis (PCD) • Etiologic diagnosis could not established	Based on previous questions Q7 yes = ICD Q9 yes = ACD Q10 and/or 11 yes =	

	Patients could have one or more etiological diagnoses. In some patients no etiological diagnosis could be made.	AHE Q13 yes = PCD	
15. Mean hand eczema severity	Severity at the moment of inclusion (examination by researcher) • Clear (1) • Almost clear (2) • Moderate (3) • Severe (4) • Very severe (5)	1: Clear 2: Almost clear 3: Moderate 4: Severe 5: Very severe	Photographic guide by Coenraads et al.[9]
16. Treatment history	Which treatments did you use before • Emollientia • Topical corticosteroids • Tar • Calcineurin inhibitors • UV-therapy • Acitretin • Alitretinoin • Azathioprine • Ciclosporin • Dupilumab • Methotrexate • Mycophenolate mofetil and/or mycophenolic acid • Oral corticosteroids < 2 weeks • Oral corticosteroids > 2 weeks • Tacrolimus • Hospitalization • Other, ……	Possibility for more than one option	
17. Current treatment	Which treatment is your main treatment at the moment? • Emollientia (1) • Topical corticosteroids (1) • Tar (1) • Calcineurin inhibitors (1) • UV-therapy (1) • Acitretin (2) • Alitretinoin (2) • Azathioprine (2) • Ciclosporin (2) • Dupilumab (2) • Methotrexate (2) • Mycophenolate mofetil and mycophenolic acid (2) • Tacrolimus (2)	The order we used to conclude the main treatment: 1. Non – systemic treatment 2. Systemic treatment	None
18. Duration	When did you start your current treatment? Open-ended question.		None

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Supplement 2

Quality of life, treatment satisfaction and adherence to treatment in patients with vesicular hand eczema – a cross sectional study

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Table S2.1.
Occupations in the a vesicular hand eczema patient cohort stratified by high /non high risk, sorted descending.

High risk (n=63)	**n (%) N_{total} = 168**
Healthcare workers	13 (7.7)
Construction workers/carpenters	8 (4.8)
Housekeepers/cleaners	6 (3.6)
Plasterers/bricklayers	5 (3.0)
Cooks/kitchen workers	5 (3.0)
Metal worker/mechanics	5 (3.0)
Hairdressers	4 (2.4)
Beauty specialists/nail stylist	3 (1.8)
Car mechanics	3 (1.8)
Painters and varnishers	2 (1.2)
Postman	2 (1.2)
Laboratory worker	2 (1.2)
Agricultural workers/gardeners	1 (0.6)
Tile setters	1 (0.6)
Firefighter	1 (0.6)
Warehouseman freezer	1 (0.6)
Maternity assistant	1 (0.6)
Non high-risk (n=105)	**n (%)**
Not working	21 (12.5)
Retired	16 (9.5)
Student	14 (8.3)
Office worker	13 (7.7)
Shop assistant	7 (4.2)
Healthcare workers (without wet work)	6 (3.6)
Teacher	5 (3.0)
Driver	5 (3.0)
Engineer	4 (2.4)
Waitress/barkeeper	3 (1.8)
Consultant	3 (1.8)
ICT	2 (1.2)
Factory worker	2 (1.2)
Call centre	1 (0.6)
Concierge	1 (0.6)
Bridge keeper	1 (0.6)
Real estate broker	1 (0.6)

For every patient exposure at the workplace was evaluated. A high-risk occupation was defined as evident exposure to allergens and/or evident exposure to wet work/friction with a high probability of developing hand eczema.[1,2] If there was rarely exposure to irritants, for example nurses with mainly administrative task, this occupation was classified as non high-risk.

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Supplement 3

Quality of life, treatment satisfaction and adherence to treatment in patients with vesicular hand eczema – a cross sectional study

Klaziena Politiek, Robert F. Ofenloch, Maris Angelino, Ewoud van den Hoed, Marie L.A. Schuttelaar

Quality of Life in Hand Eczema Questionnaire scores

Table S3.1 Health related quality of life impairment assessed with the international Quality of Life in Hand Eczema Questionnaire (QOLHEQ) in vesicular hand eczema patients: interpretation of the overall QOLHEQ score and the QOLHEQ subdomain scores[1]

	Health related quality of life impairment[a] (n=167)				
	Not at all (n, %)	**Slightly (n, %)**	**Moderately (n, %)**	**Strongly (n, %)**	**Very strongly (n, %)**
Overall QOLHEQ score	14 (8.4)	54 (32.3)	56 (33.5)	31 (18.6)	12 (7.2)
Symptoms	2 (1.2)	45 (26.9)	63 (37.7)	46 (27.5)	11 (6.6)
Emotions	50 (29.9)	52 (31.1)	50 (29.9)	13 (7.8)	2 (1.2)
Functioning	25 (15.0)	51 (30.5)	45 (26.9)	34 (20.4)	12 (7.2)
Treatment and prevention	47 (28.1)	42 (25.1)	57 (34.1)	17 (10.2)	4 (2.4)

[a] 1 patients missing

Table S3.2 Means for health related quality of life impairment (international Quality of Life in Hand Eczema Questionnaire (QOLHEQ)) for the total group and stratified by sex and type of treatment (systemic vs non-systemic)

QOLHEQ subdomains, mean (SD)[c]	Male (n=74)	Female (n=94)	All patients (n= 168)	Non-systemic treatment[a] (n=112)	Systemic treatment[b] (n=56)
Symptoms (0-25)	10.7 (4.8)	12.0 (5.6)	11.4 (5.3)	12.2 (4.8)	9.7 (5.7)
Emotions (0-30)	9.8 (6.7)	11.4 (7.2)	10.7 (7.0)	11.2 (7.0)	9.8 (7.0)
Functioning (0-32)	9.6 (6.6)	12.1 (8.1)	11.0 (7.6)	11.4 (7.3)	10.2 (8.0)
Treatment and prevention (0-23)	8.1 (4.3)	9.8 (5.1)	9.0 (4.8)	9.2 (4.7)	8.7 (5.1)
Overall score (0-110)	42.3 (22.1)	50.1 (26.1)	46.7 (24.7)	48.8 (23.4)	42.4 (26.6)

[a] Non-systemic treatments included: UV-therapy, topical corticosteroids always combined with neutral emollients, occasionally with concomitant use of calcineurin inhibitors or tar preparations.

[b] Systemic treatment included: alitretinoin, azathioprine, ciclosporin, dupilumab, methotrexate and tacrolimus, [c] 1 patients missing.

Table S3.3 Dutch single score bands for health-related quality of life impairment expressed as single-scores on the Dutch Quality Of Life in Hand Eczema Questionnaire (QOLHEQ)

	Health related quality of life impairment				
	Not at all	**Slightly**	**Moderately**	**Strongly**	**Very strongly**
QOLHEQ overall	0 – 13	14 – 28	29 – 44	45 – 64	≥65
QOLHEQ overall (Males)	0 – 10	11 – 33	34 – 46	47 – 65	≥66
QOLHEQ overall (Females)	0 – 23	24 – 31	32 – 47	48 – 64	≥65
Symptoms	0	1 – 7	8 – 10	11 – 15	≥16
Emotions	0 – 5	6 – 10	11 – 15	16 – 17	≥18
Functioning	0 – 1	2 – 7	8 – 10	11 – 16	≥17
Treatment and Prevention	0 – 6	7 – 9	10 – 13	14 – 15	≥16

Adapted from the validation study of the Dutch Quality Of Life in Hand Eczema Questionnaire with permission of the author.

Table S3.4 International single score bands for health-related quality of life impairment expressed as single-scores on the Quality Of Life in Hand Eczema Questionnaire (QOLHEQ).

	Health related quality of life impairment				
	Not at all	**Slightly**	**Moderately**	**Strongly**	**Very strongly**
QOLHEQ overall	0 – 10	11 – 40	41 – 61	62 – 86	≥ 87
QOLHEQ overall (Males)	0 – 10	11 – 35	36 – 53	54 – 83	≥ 84
QOLHEQ overall (Females)	0 – 13	14 – 40	41 – 61	62 – 86	≥ 87
Symptoms	0	1 – 8	9 – 13	14 – 19	≥ 20
Emotions	0 – 6	7 – 12	13 – 20	21 – 26	≥ 27
Functioning	0 – 2	3 – 9	10 – 15	16 – 24	≥ 25
Treatment and Prevention	0 – 6	7 – 9	10 – 14	15 – 18	≥ 19

Adapted from the Interpretability of the International Quality Of Life in Hand Eczema Questionnaire with permission of the author.

REFERENCES:

1) Oosterhaven, Jart A.F. Ofenloch Robert. F., Schuttelaar M-LA. Interpretabity of the Quality Of Life in Hand Eczema Questionnaire. Accept J Investig Dermatology. 2019
2) Oosterhaven, Jart A.F. Ofenloch Robert. F., Schuttelaar M-LA. Validation of the Dutch Quality Of Life in Hand Eczema Questionnaire. Accept Br J Dermatology. 2019

Supplement 4

Quality of life, treatment satisfaction and adherence to treatment in patients with vesicular hand eczema – a cross sectional study

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Univariate regression analysis

Table S4.1 Correlations between patient characteristics and Quality of Life in Hand Eczema Questionnaire (QOLHEQ) domains – assessing factors that would affect the QOLHEQ domain score as the dependent variable.

Variable	Symptoms subscale		Emotions subscale		Functioning subscale		Treatment and prevention subscale		Overall QOLHEQ Score	
	Standardized β	P-value	Standardized β	P-value	Standardized β	P -value	Standardized β	P-value	Standardized β	P-value
Age	-0.06	0.40	-0.06	0.47	-0.01	0.92	-0.02	0.78	-0.04	0.62
Sex (female)	0.16	**0.04**	0.09	0.23	0.16	**0.04**	0.17	**0.03**	0.16	**0.04**
High education	-0.10	0.22	-0.14	**0.08**	-0.10	0.21	-0.09	0.24	-0.11	**0.14**
Duration of HE (years)	0.02	0.76	-0.03	0.75	0.08	0.28	0.08	0.33	0.06	0.43
Current systemic treatment	**-0.24**	**0.00**	-0.07	0.36	-0.04	0.59	-0.06	0.46	**-0.10**	**0.19**
Severity	**0.47**	**0.00**	**0.35**	**0.00**	**0.36**	**0.00**	**0.28**	**0.00**	**0.39**	**0.00**
Low adherence	0.18	**0.02**	0.17	**0.03**	0.12	**0.13**	0.13	**0.10**	0.16	**0.04**
Higher TSQM global satisfaction score	**-0.50**	**0.00**	**-0.49**	**0.00**	**-0.50**	**0.00**	**-0.44**	**0.00**	**-0.52**	**0.00**

Numbers in bold represent P values < 0.2 and Standardized β coefficients >0.2.
Univariate regression analysis was based on Dutch QOLHEQ scores.[1]

References:

1. Oosterhaven, Jart A.F. Ofenloch Robert. F., Schuttelaar, M.-L. A. (2019). Validation of the Dutch Quality Of Life in Hand Eczema Questionnaire. *Accepted in the British Journal of Dermatology*.