ORIGINAL ARTICLE

Quality of life and disease severity in patients with atopic dermatitis

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Abstract

Background Atopic dermatitis (AD) affects quality of life (QoL) negatively in patients and their families. We examined the relationship between disease severity and QoL in patients with AD.

Methods Consecutive, newly referred outpatients with AD, 4 years of age or older, were assessed from January 2012 onwards by means of the dermatology life quality index (DLQI, range 0–30), the Scoring of AD (SCORAD) disease severity score (range 0–103), filaggrin gene (*FLG*) mutation status and paraclinical tests related to allergy.

Results A total of 250 patients with a mean age of 26.0 years were identified with complete data on DLQI; 148 (59.2%) females and 102 (40.8%) males. Of these 45.6% had asthma, 46.8% had hay fever, 22.7% had a loss-of-function mutation in *FLG*, and 61.9% had one or more inhalant allergic sensitizations. The correlation between SCORAD and DLQI was 0.42 ($P < 0.001$). After multivariate adjustment there was an increasing mean DLQI score with increasing disease severity measured by SCORAD (DLQI in mild = 5.30, moderate = 8.59 and severe = 11.94 AD), *P*-value for difference between groups <0.001; a higher mean DLQI among females than males (9.73 vs. 8.34), $P = 0.028$; and among patients reporting facial eczema (9.88 vs. 6.24), $P = 0.012$. No statistically significant influence on DLQI was found for hand or foot eczema, age, blood eosinophil count, allergic sensitization, asthma, hay fever, *FLG* mutation status and smoking. *FLG* null mutation status was not significantly associated with SCORAD.

Conclusion AD impacts negatively on the QoL, proportional to the severity of the disease. Furthermore, female sex and facial eczema are associated with low QoL. Positive *FLG* null mutation status is not associated with QoL or disease severity.

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Conflict of interest

None.

Funding sources

None.

Introduction

Atopic dermatitis (AD) is a common, chronic, inflammatory, pruritic and relapsing skin disease affecting 10–20% of children and 1–3% of adults.[1–3] Approximately 70% of all patients with AD have a family or personal history of allergic sensitization.[2] AD is part of the atopic triad, also including asthma and allergic rhino-conjunctivitis (hay fever).

AD can have a significantly negative impact on quality of life (QoL), which in some cases can lead to social isolation and psychological problems. Furthermore, itch which is a cardinal symptom in AD can lead to additional problems such as difficulties falling asleep, and subsequent daytime tiredness and irritability.[3,4] In more severe cases, AD poses challenges to the entire family,[5–7] which seems, however, to be changing for the better.[8] The amount of knowledge regarding AD and how disease severity is related to QoL and which factors determine QoL in patients with AD varies between cultures, despite its evident importance.[9,10] We examined QoL in a cohort of Danish outpatients with AD with respect to association with disease severity and paraclinical characteristics, particularly filaggrin gene (*FLG*) loss-of-function mutation status. Furthermore, we explored other factors associated with low QoL in these patients.

Methods

Patients

The patients were ascertained from the Danish Atopy Database,[11] which consecutively includes all newly referred, and

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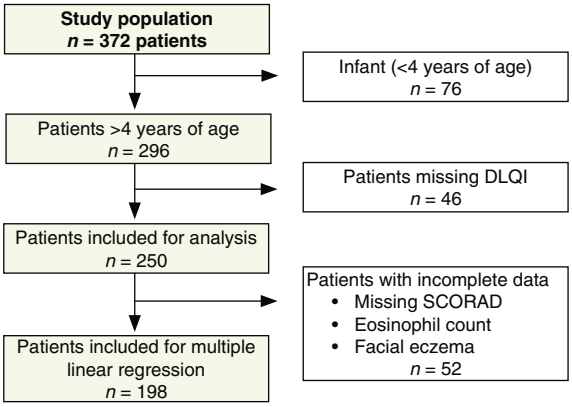

Figure 1 Study inclusion.

diagnosed outpatients with AD meeting the criteria defined by Hannifin and Rajka[12] at the Department of Dermatology, Bispebjerg Hospital, University of Copenhagen, Denmark from 2012 onwards. Assessments included all patients referred and diagnosed by a senior physician until July 2015 (Figure 1).

Assessments

Scoring of AD (SCORAD),[13] comprised of objective signs of disease (disease extent and intensity), and subjective short-term symptoms (pruritus and sleep loss),[14] is a commonly used severity index in AD (range: 0–103 points with a high score indicating severe disease).[15,16] SCORAD was assessed by a staff nurse. QoL was evaluated using translated Danish editions[17] of the dermatology life quality index (DLQI) for patients aged 16 years and above and the Children's dermatology life quality index (CDLQI)[18] for patients aged 4–15 years. DLQI/CDLQI scores ranged from 0 to 30 points with a high score indicating increased impairment in QoL. Furthermore, a questionnaire exploring disease characteristics, personal and family history, as well as previous treatments of each patient, was completed. This questionnaire included assessment of self-rated health on a 5-point scale with a high score indicating excellent self-rated health.[19] Infants (<4 years of age) did not report CDLQI and were therefore excluded from the analysis. Young children were allowed parental/guardian assistance for the CDLQI and questionnaire.

The allergic sensitization diagnosis was ascertained with a positive skin prick test and/or elevated serum IgE ($>0.35 \times 10^3$ IU/L) specific for at least one allergen of the standard inhalation panel [birch, grass, mugwort, horse, dog, cat, house dust mite (D. Pteronyssinus and D. Farinae) and moulds (Alternaria iridis and Cladosporium herbarum)]. Total serum IgE (considered elevated at $>150 \times 10^3$ IU/L) and blood eosinophil count (considered elevated at $>0.5 \times 10^9$ IU/L) were also assessed by blood samples. Genomic DNA from whole blood was genotyped for the three most common loss-of-function mutations in *FLG*: R2447X, R501X and 2282del4.

Statistical analysis

The patients were divided into age groups 4–15 years (children) and >15 years (adults). SCORAD was grouped after severity, with mild disease representing a score <15, moderate ranging 15–40 and severe being >40.[20] QoL was assessed using DLQI/CDLQI, comprising ten questions evaluating disease impact on key aspects of patients' lives. Descriptive statistics exploring the relationship between SCORAD and QoL, overall and between groups, were computed using IBM SPSS statistics 22 (SPSS, Inc., Chicago, IL, USA). Univariate linear regression analyses were performed with DLQI and CDLQI as response variable and with SCORAD, sex, age, asthma, hay fever, *FLG* mutation status, allergic sensitization, serum total IgE, blood eosinophil count, smoking and self-reported eczema distribution within the past month (facial, hands, feet and total number of anatomical sites with eczema) as explanatory variables. Multivariate linear regression analysis was carried out including the variables with a *P*-value <0.10 in the univariate analyses. Factors of which we lacked information in a greater number of participating subjects were excluded from the multivariate analysis. The self-reported total number of anatomical sites affected by eczema within the past month was also excluded from the multivariate model due to its co-linearity with SCORAD. As a consequence of this, the multivariate analysis included the following factors: age, sex, facial, hand and foot eczema, blood eosinophil count and SCORAD. QoL responses for children and adults (CDLQI and DLQI) were analysed together due to the fact that no statistically significant interactions were observed between age and any of the covariates in relation to DLQI/CDLQI. All comparisons were two-tailed using $P < 0.05$ as significance level.

Results

Of the population of 296 patients, 4 years of age or above, 250; 148 (59.2%) females and 102 (40.8%) males had complete data on CDLQI/DLQI. Mean age was 26.3 years for females and 25.7 years for males; age range 4–73 years. A total of 45.6% had asthma, 51.5% had hay fever, 22.7% had a *FLG* loss-of-function mutation and 61.9% had RAST- (radioallergosorbent test) or prick-test verified allergic sensitization tested against the standard panel. The fraction of patients with, respectively, mild, moderate and severe eczema according to SCORAD was 18.4%, 46.4% and 35.1% (Table 1).

The mean (SD) CDLQI was 7.15 (4.6), with a median of 6, and the mean DLQI was 9.79 (6.2) with a median of 9. The overall mean total CDLQI/DLQI was 9.16 (5.9). The three variables of the CDLQI/DLQI questionnaire with the highest mean scores (mean ± SD) were 'itch' (1.6 ± 0.8), 'sleep' (1.1 ± 1.0) and 'treatment' (1.1 ± 1.0) among children and 'itch' (1.8 ± 0.8), 'embarrassment' (1.3 ± 1.0) and 'clothes' (1.3 ± 1.1) among

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Table 1 Population characteristics

Variables	Females (n = 148)	Males (n = 102)	P-value*	Children (n = 59)	Adults (n = 191)	P-value†	Total (n = 250)
Age	26.27 (14.1)	25.65 (14.6)	0.737	8.84 (3.1)	31.32 (12.0)	<0.001	26.01 (14.3)
High IgE	55 (52.9)	34 (60.7)	0.342	18 (66.7)	71 (53.4)	0.205	89 (55.6)
Asthma	53 (39.0)	51 (55.4)	0.014	26 (50)	78 (44.3)	0.470	104 (45.6)
Hay fever	64 (47.4)	53 (57.6)	0.131	20 (38.5)	97 (55.4)	0.032	117 (51.5)
Allergic sensitization	66 (56.9)	54 (69.2)	0.083	34 (70.8)	86 (58.9)	0.140	120 (61.9)
FLG mutation	23 (22.3)	18 (23.1)	0.905	12 (29.3)	29 (20.7)	0.250	41 (22.7)
Food allergy	71 (48.0)	39 (38.2)	0.311	16 (27.1)	94 (49.2)	0.011	110 (48.9)
Eczema debut (months)	4.23 (9.2)	4.31 (8.3)	0.943	1.44 (2.8)	2.60 (9.2)	<0.001	4.26 (8.3)
Eczema							
Facial	115 (83.9)	72 (78.3)	0.276	36 (69.2)	151 (85.3)	0.008	187 (81.7)
Hand	93 (68.4)	63 (68.5)	0.988	31 (59.6)	125 (71.0)	0.120	156 (68.4)
Foot	36 (26.3)	36 (39.1)	0.040	18 (34.6)	54 (30.5)	0.575	72 (31.4)
Total sites	8.30 (3.7)	8.66 (3.8)	0.473	7.42 (4.2)	8.73 (3.5)	0.048	8.44 (3.7)
SCORAD (mean)	30.14 (17.0)	35.41 (18.2)	0.023	29.38 (14.0)	33.21 (18.6)	0.100	32.30 (17.7)
Mild	28 (19.9)	16 (16.3)		11 (19.3)	33 (18.1)		44 (18.4)
Moderate	72 (51.1)	39 (39.8)		30 (52.6)	81 (44.5)		111 (46.4)
Severe	41 (29.1)	43 (43.9)		16 (28.1)	68 (37.4)		84 (35.1)
Ezcema area	20.98 (22.8)	25.60 (22.5)	0.123	15.97 (16.4)	25.04 (24.0)	0.002	22.87 (22.7)
Eczema intensity	4.99 (3.2)	6.26 (3.5)	0.004	5.28 (3.0)	5.58 (3.5)	0.568	5.51 (3.4)
Itch (VAS)	5.23 (2.6)	5.16 (3.1)	0.866	4.91 (2.8)	5.29 (2.9)	0.379	5.20 (2.8)
Sleep (VAS)	3.32 (3.3)	3.27 (3.3)	0.902	2.84 (2.9)	3.44 (3.4)	0.230	3.30 (3.3)
Self-rated health	2.42 (0.95)	2.44 (0.9)	0.841	2.88 (0.9)	2.30 (0.9)	<0.001	2.40 (1.0)
CDLQI/DLQI	9.73 (5.9)	8.34 (5.9)	0.069	7.15 (4.6)	9.79 (6.2)	0.003	9.16 (5.9)

*P-value for difference between males and females.
†P-value for difference between children and adults.
All analyses were based on the available data for each variable.
All values are means (SD) except high IgE, asthma, hay fever, allergic sensitization, *FLG* mutation, food allergy, eczema (facial, hand, foot) and SCORAD categories (number, %).
SCORAD, Scoring of Atopic Dermatitis; CDLQI, Children's dermatology life quality index; DLQI, Dermatology life quality index; VAS, Visual analogue scale; IgE, Immunoglobulin E.

adults. The lowest scores for children were observed for 'friendship' (0.3 ± 0.6) and 'school/holiday' (0.3 ± 0.6), while 'sexual difficulties' (0.5 ± 0.9) was the least affected in adults (Table 2).

Bivariate correlation calculations were performed between CDLQI/DLQI and SCORAD (r = 0.42, P < 0.001), CDLQI/DLQI and total number of eczema sites (r = 0.43, P < 0.001) (Fig. 2), CDLQI/DLQI and self-rated health (r = −0.37, P < 0.001), and SCORAD and total number of eczema sites (r = 0.46, P < 0.001). Sensitivity analyses were performed between SCORAD and CDLQI/DLQI in *FLG* mutation carriers and non-carriers, respectively (r = 0.501 and r = 0.414), P-value for difference between correlations = 0.738; between total sites and CDLQI/DLQI in *FLG* mutation carriers and non-carriers, respectively (r = 0.436 and r = 0.412), P-value for difference between correlations = 0.641; and between self-rated health and CDLQI/DLQI in *FLG* mutation carriers and non-carriers, respectively (r = −0.408 and r = −0.412), P-value for difference between correlations = 0.958. We also performed these analyses stratified for age group (children vs. adults), but found no statistically significant interactions.

A significant relationship with CDLQI/DLQI in the univariate analyses was seen for age, sex, facial, hand and foot eczema, self-reported total number of anatomical sites affected by eczema within the past month, blood eosinophil count, SCORAD, high serum total IgE level and self-rated health, but not for asthma, hay fever, allergic sensitization, *FLG* mutation status and smoking. After multivariate adjustment, there was an increasing mean CDLQI/DLQI score with increasing SCORAD (CDLQI/DLQI in mild = 5.30, moderate = 8.59, and severe = 11.94 AD), P-value for difference between groups <0.001; an increasing mean CDLQI/DLQI with worse self-rated health (excellent = 6.56, very good = 7.44, good = 10.36 and bad = 12.88), P-value for difference between groups <0.001; a higher mean CDLQI/DLQI among females than males (9.73 vs. 8.34), P = 0.028; and among patients reporting facial eczema (9.88 vs. 6.24), P = 0.012 (Table 3).

No sex (P = 0.813) or age (P = 0.102) differences were found between the 198 identified patients with complete data, and the 98 patients without complete data on DLQI and covariates included in the final regression model (figure 1).

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Table 2 Mean ± standard deviation of each component of quality of life scores (CDLQI, DLQI) and SCORAD

CDLQI scores		DLQI scores				SCORAD				
Item	Mean (SD)	Item	Mean (SD)	Mean difference (CI)	*P*-value	Item	Children Mean (SD)	Adults Mean (SD)	Mean difference (CI)	*P*-value
Itch*	1.6 (0.8)	Itch*	1.8 (0.8)	0.20 (−0.039–0.43)	0.102	Area	16.0 (16.4)	25.0 (24.0)	9.1 (3.5–14.6)	0.002
Embarrassment	0.8 (0.8)	Embarrassment*	1.3 (1.0)	0.51 (0.26–0.76)	0.000	Redness	1.1 (0.8)	1.3 (1.0)	0.24 (0.015–0.50)	0.064
Friendships	0.3 (0.6)	Shopping/home/garden	0.9 (0.9)	0.62 (0.41–0.82)	0.000	Swelling	0.30 (0.5)	0.56 (0.7)	0.26 (0.095–0.43)	0.002
Clothes/shoes	0.7 (1.0)	Clothes*	1.3 (1.1)	0.56 (0.25–0.87)	0.000	Oozing/crusting	0.60 (0.8)	0.53 (0.8)	0.069 (−0.16–0.30)	0.556
Leisure/hobbies	0.4 (0.7)	Social/leisure	1.0 (1.0)	0.56 (0.34–0.79)	0.000	Scratch marks	0.98 (0.9)	1.0 (1.0)	0.045 (−0.24–0.33)	0.756
Swimming/sports	0.6 (1.0)	Sports	0.9 (1.0)	0.29 (0.018–0.60)	0.065	Lichenification	0.91 (1.0)	0.99 (1.0)	0.077 (−0.21–0.36)	0.597
School/holidays	0.3 (0.6)	Work/study	0.7 (0.9)	0.34 (0.14–0.54)	0.001	Dryness	1.4 (1.1)	1.2 (1.0)	0.26 (−0.049–0.57)	0.099
Teasing/bullying	0.1 (0.4)	Partner/close friend/relatives	0.7 (0.9)	0.61 (0.44–0.78	0.000	Intensity	5.3 (3.0)	5.6 (3.5)	0.30 (−0.72–1.32)	0.586
Sleep*	1.1 (1.0)	Sexual difficulties	0.5 (0.9)	0.62 (0.36–0.88)	0.000	Itch (VAS)	4.9 (2.8)	5.3 (2.9)	0.38 (−0.47–1.23)	0.379
Treatment*	1.1 (1.0)	Treatment	0.7 (0.8)	0.43 (0.18–0.68)	0.001	Sleeplessness (VAS)	2.8 (2.9)	3.4 (3.4)	0.29 (−0.018–0.60)	0.065
Total score	7.2 (4.6)	Total score	9.8 (6.2)	2.6 (0.92–4.35)	0.003	Total score	29.4 (14.0)	33.2 (18.6)	3.84 (−0.74–8.41)	0.100

*The three variables in CDLQI and DLQI with the highest scores (mean ± SD).
SCORAD, scoring of atopic dermatitis; CDLQI, Children's dermatology life quality index; DLQI, dermatology life quality index; VAS, visual analogue scale.

Discussion

Three main findings in our clinical study of AD patients, 4–73 years of age, from a dermatological university department, should be highlighted. First, increasing AD severity is associated with increased impairment in QoL independently of age and sex. Second, female sex and facial eczema are independently associated with low QoL in patients with AD. Third, having a *FLG* loss-of-function mutation appears to have no significant impact on QoL and is also not related to disease severity in patients with AD above 4 years of age.

In addition, paraclinical traits and comorbidities related to AD such as, serum IgE, eosinophil count, asthma and hay fever seem not to affect QoL significantly in patients with AD.

DLQI has been widely used to measure subjective impairment in several dermatologic conditions,[21] especially AD.[22] In a review performed by Rehal *et al.*,[15] DLQI was found to be the third most used tool for measuring QoL. However, DLQI along with other QoL instruments, show certain limitations, considering the same group of physicians developed the top four QoL tools used. This is considered to explain their increasing use, but also question the diversity of their scale and variety of characteristics. Yet, DLQI is an internationally and repeatedly validated QoL instrument[21–23] which reasons our choice of this tool in our patient assessment.

In general, AD patients experience lower QoL compared to healthy controls.[24,25] We observed a mean total CDLQI of 7.15 (median 6) and a DLQI of 9.79 (median 9) in this study. These values are slightly higher compared to Holm *et al.*[25] who in another study of 101 Danish AD patients attending Roskilde Hosptial, Denmark (35 children and 66 adults), observed a median CDLQI of 8 and a median DLQI of 5. In contrast, Kim *et al.*[6] found a mean CDLQI of 6.6 among 197 children and a mean DLQI of 10.7 among 147 adults, all assessed at university teaching hospitals affiliated with the Korean AD Association.

We observed that patients with severe AD also had a lower QoL compared to patients with milder AD with a statistically significant positive correlation between DLQI and SCORAD ($r = 0.42$). Several other studies have reported similar results.[6,24–29] Notably, Linnet *et al.*[24] showed a significant positive correlation ($r = 0.54$) between SCORAD and DLQI in a study of 32 Danish adults, whereas Kim *et al.*[6] found positive correlations between CDLQI/DLQI and SCORAD ($r = 0.36$ and 0.43, respectively) and between CDLQI/DLQI and severity of AD judged by the Rajka and Langeland criteria[14]($r = 0.30$ and 0.26 respectively) in 415 Korean patients. Furthermore, our results showed a significant correlation ($r = 0.43$) between the self-reported number of anatomical sites affected by eczema within the past month and QoL on the same magnitude as the correlation between CDLQI/DLQI and SCORAD. Accordingly, Haeck *et al.*[30] reported correlations between DLQI and disease activity assessed by the 'rule of nines' and SCORAD in 49 Dutch

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Table 3 Univariate and multivariate relationships between different factors and CDLQI/DLQI

Variable	DLQI (mean, SD)	Mean diff 95% CI	Crude *P*-value	Adjusted *P*-value*
Age			0.003	0.459
4–15	7.15 (4.6)			
16+	9.79 (6.2)	2.64 (0.92–4.35)		
Sex			0.069	0.028
Men	8.34 (5.9)			
Women	9.73 (5.9)	1.39 (−0.11–2.88)		
Allergic sensitization (std. panel)			0.559	
Positive	9.51 (6.2)			
Negative	9.00 (5.4)	0.51 (−1.20–2.22)		
Filaggrin mutation			0.888	
Yes	9.24 (5.4)			
No	9.39 (6.1)	0.15 (−1.94–2.24)		
Eczema debut			0.968	
≤2 years	9.35 (5.8)			
>2 years	9.32 (6.4)			
Eczema distribution		0.03 (−1.60–1.66)		
Facial			<0.001	0.012
Yes	10.02 (5.9)			
No	6.24 (5.6)	3.78 (1.81–5.75)		
Hand			<0.001	0.207
Yes	10.29 (6.3)			
No	7.18 (4.7)	3.11 (1.47–4.76)		
Foot			0.004	0.645
Yes	10.99 (6.4)			
No	8.56 (5.7)	2.43 (0.76–4.09)		
Asthma			0.720	
Yes	9.49 (5.6)			
No	9.20 (6.4)	0.29 (−1.30–1.87)		
Hay fever			0.616	
Yes	9.51 (6.1)			
No	9.11 (6.0)	0.40 (−1.18–1.99)		
Eosinophil count			0.017	0.754
0.5	8.76 (6.1)			
≥0.5	10.80 (5.8)	2.04 (0.37–3.71)		
Smoking (active)			0.399	
Yes	10.52 (6.2)			
No	9.61 (6.2)	0.91 (−1.22–3.05)		
SCORAD			<0.001	<0.001
Mild	5.30 (5.1)			
Moderate	8.59 (5.2)	3.29 (1.50–5.11)		
Severe	11.94 (6.1)	3.35 (1.75–4.94)		
High IgE (≥150)†			0.008	
Yes	10.20 (6.7)			
No	7.77 (4.7)	2.43 (0.37–3.71)		
Food allergy			0.125	
Yes	9.83 (5.9)			
No	8.60 (6.1)	1.23 (0.34–2.80)		
Total eczema sites			<0.001	
≤5	5.52 (3.6)			
6 ≤ 10	9.43 (5.9)	3.91 (2.16–5.67)		
>10	12.20 (6.2)	2.77 (0.93–4.60)		

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Table 3 *Continued*

Variable	DLQI (mean, SD)	Mean diff 95% CI	Crude *P*-value	Adjusted *P*-value*
Self-rated health			<0.001	<0.001
Bad	12.88 (6.9)			
Good	10.36 (5.4)	2.52 (0.22–4.82)		
Very good	7.44 (5.4)	2.92 (1.22–4.63)		
Excellent	6.56 (4.0)	0.88 (−1.36–3.12)		

SCORAD, scoring of atopic dermatitis; CDLQI, Children's dermatology life quality index; DLQI, dermatology life quality index; IgE, immunoglobulin E.
*Statiscally significant ($P < 0.10$) variables from the univariate analysis were included in the multivariate analysis (linear regression).
†High IgE was not included in the multivariate analysis, due to insufficient number of patients with complete data.

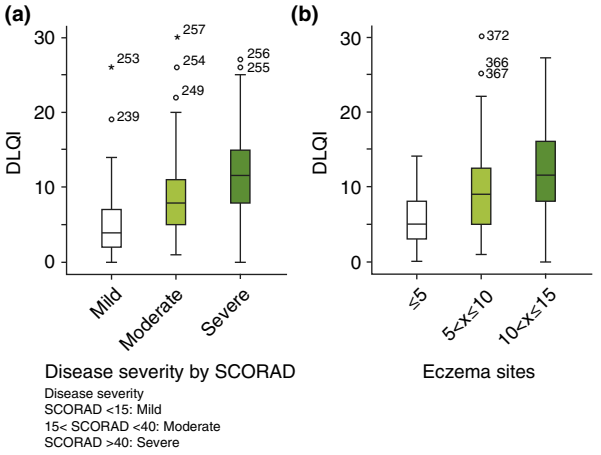

Figure 2 Boxplots on disease severity (a), total eczema sites (b) and quality of life.

adult patients before ($r = 0.25$ and $r = 0.17$) and after ($r = 0.49$ and $r = 0.34$) 6 weeks of treatment with cyclosporine. This agrees also with Taïeb *et al.*[31] who proposed a new self-assessment tool, evaluating the burden of AD before and after treatment, which showed promise by being correlated with disease severity. The similar correlations between self-reported and healthcare professional-assessed measures of disease activity found in our study supports the suggestion by Oosterhout *et al.*[32] comparing SCORAD to PO-SCORAD, reporting a positive correlation ($r = 0.63$, $P < 0.001$), as well as Baron *et al.*[33] who showed a reduction in DLQI and a significant correlation with decrease in SCORAD, between visits, when AD patients were referred to secondary care. Although DLQI supplies subjective information[6] that cannot been assessed by the physician, good doctor–patient contact improves QoL and should be prioritized.

Facial eczema is a major symptom in AD, and unfortunately not always easy to treat. Our results showed that facial eczema had a significantly negative impact on CDLQI/DLQI, thus confirming the considerable influence of visible AD on patients' QoL. Our data underlines the importance of clinicians' focus on facial eczema, and on finding a treatment that meets the expectations of the patients. In addition, our finding substantiates Linnet *et al.*[24] who showed a higher level of anxiety in AD patients compared to controls, and a positive correlation between anxiety and DLQI.[24] This was also the case in our patients with facial eczema, who showed significantly higher impact on the DLQI aspects related to anxiety (embarrassment and bullying; $P = 0.001$ and $P = 0.021$ respectively). Also, Holm *et al.*[25] compared 101 patients with AD with 30 controls and found that the psychological aspects of life were affected, rather than the physical aspects, in patients with AD. Disease impact on work productivity and activity impairment,[34] family life,[35] sleep quality[4,36] and sex life[37] has been emphasized in other studies.

Our results showed that positive *FLG* null mutation status does not predict greater impact on DLQI or SCORAD compared to non-mutation carriers in patients with AD older than 4 years of age. Ballardini *et al.*[38] found similar results with regards to disease severity, while our results contradict previous results published, predicting a biologically more severe disease with positive *FLG* mutation status,[39] as well as other studies exploring this relationship.[40–43] Conversely, the literature lacks information on the impact of *FLG* mutation status on QoL in AD patients. However, our results, along with Ballardini *et al.*,[38] suggest that patients, regardless of *FLG* mutation status, should expect roughly the same disease progress regarding severity and QoL. On this account, *FLG* mutation screening could be considered less valuable in clinical practice. However, more studies evaluating this should be conducted prior to any conclusion.

Strength of this study is the prospective inclusion of consecutive outpatients with clinically diagnosed AD from a tertiary dermatological referral centre with pre-determined guidelines for evaluation and diagnostics. We included self-reported as well as healthcare professional-assessed severity measures of disease on a large number of patients. A weakness of the study is that data was lacking on the outcome measures or on key explanatory variables for some patients, leaving the final analytical sample of

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two-thirds of the originally included patients. Still, the age and sex distribution were similar among drop-outs and the effective sample, which ensures the representativeness of the study.

The results add to an increasing amount of literature on how AD impacts negatively on the QoL proportional to the severity of the disease. Future studies are needed to update and expand our knowledge about AD, in order to grasp the full content of the disease, ensuring correct and effective treatment. Furthermore, the observed impact on QoL in patients with facial eczema indicates that the clinician should take great effort in obtaining a satisfying treatment of facial eczema. The lack of significance between positive *FLG* null mutation and QoL or disease severity suggests how disease mechanisms need yet further investigation.

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