

Disease Activity Only Moderately Correlates with Quality of Life Impairment in Patients with Chronic Spontaneous Urticaria

I. Koti^{a, f} K. Weller^f M. Makris^{a, f} E. Tiligada^{a, b} T. Psaltopoulou^c
C. Papageorgiou^d I. Baiardini^g D. Panagiotakos^e F. Braido^g M. Maurer^f

^aAllergy Unit 'D. Kalogeromitros', ^{2nd} Department of Dermatology and Venereology, Attikon University Hospital, ^bDepartment of Pharmacology, ^cDepartment of Hygiene, Epidemiology and Medical Statistics and ^dUniversity Mental Health Research Institute (UMHRI), Medical School, University of Athens, and ^eDepartment of Nutrition and Dietetics, Harokopio University, Athens, Greece; ^fDepartment of Dermatology and Allergy, Allergie-Centrum-Charité, Charité – Universitätsmedizin Berlin, Berlin, Germany; ^gAllergy & Respiratory Diseases Clinic, University of Genova, Genova, Italy

Key Words

Chronic spontaneous urticaria · Disease activity · Quality of life · Chronic Urticaria Quality of Life Questionnaire · Dermatology Life Quality Index · Urticaria Activity Score

Abstract

Background: The impact of chronic spontaneous urticaria (CSU) on health-related quality of life (HRQoL) is widely held to be mainly influenced by disease activity and comorbidities. **Objective:** To assess the correlation between disease activity and HRQoL impairment by using validated disease-specific instruments. **Methods:** The Chronic Urticaria Quality of Life Questionnaire (CU-Q_{2oL}) was translated into Greek and subsequently applied to 110 CSU patients along with the Dermatology Life Quality Index and the Urticaria Activity Score. After the validity and reliability of the Greek CU-Q_{2oL} had been determined, we assessed the relation between disease activity and HRQoL impairment by computing correlations as well as by performing multiple regression analysis. **Results:** Exploratory factor analysis revealed a six-scale structure of the Greek CU-Q_{2oL} that explained 67.9% of its to-

tal variance. The internal consistency was satisfactory with Cronbach's $\alpha > 0.7$. Disease activity was the only predictor of quality of life impairment, but it only moderately correlated with the CU-Q_{2oL} total score ($r = 0.40$, $p < 0.0001$). **Conclusion:** Our results suggest that there are additional factors to disease activity that are responsible for the pronounced reduction of HRQoL in CSU, and this supports the recommendation to assess and monitor both disease activity and quality of life in CSU patients.

© 2013 S. Karger AG, Basel

Introduction

Chronic spontaneous urticaria (CSU) is a frequent skin disease that affects all age groups in both sexes. It is estimated that 0.5–1% of the population is suffering from CSU at any given time [1, 2]. The unclear origin of the disease in addition to the chronicity and the difficulties in obtaining adequate symptom control can discourage patients and physicians and negatively affect their relationship [3–6]. Since the disease is often difficult to treat, the

treatment goals have to be well defined, which requires instruments to assess disease burden. The Urticaria Activity Score (UAS) is commonly used to assess disease activity, but it has limitations with regard to measuring disease burden. For this reason, the Chronic Urticaria Quality of Life Questionnaire (CU-Q₂oL) has been developed to measure disease-specific quality of life impairment, and various language versions have been used in different CSU populations.

According to the World Health Organization [7], cultural specificities and values perception are important determinants of health-related quality of life (HRQoL). Furthermore, subjectivity and multidimensionality could hinder its measurement. Therefore, the use of different language versions of HRQoL instruments in different populations requires a structural process of translation, cross-cultural adaptation and validation.

Focused measurements of the HRQoL of CSU patients have revealed a remarkable impact of the disease on different areas of patients' quality of life. The reason for this substantial HRQoL impairment is usually attributed to disease activity and comorbidities [8–10]. However, as of yet, there are only limited data to prove this. The existence of a disease-specific questionnaire like the CU-Q₂oL facilitates the investigation of the parameters that drive HRQoL impairment. The CU-Q₂oL is currently the only available CSU-specific quality of life instrument and is already available in several language versions [11–16]. The aim of this study was to develop a Greek version of the CU-Q₂oL and to assess the relation between disease activity and HRQoL impairment.

Materials and Methods

Cross-Cultural Adaptation of the CU-Q₂oL

In accordance with the guidelines on the cross-cultural adaptation of HRQoL questionnaires, the original Italian version of the CU-Q₂oL was translated into Greek by an official native Greek translator. Afterwards, the Greek version was reviewed by physicians specialized in allergology and CSU. This led to slight expressional modifications. The revised questionnaire was then back-translated to Italian by a native Italian with fluent knowledge of Greek. This back-translated Italian version was reviewed and approved by the original Italian authors and the Greek research team. The resulting final consensus version of the Greek CU-Q₂oL was then applied to patients without further modification.

CU-Q₂oL

The CU-Q₂oL consists of 23 questions (items) that are evaluated on a five-point Likert scale. These 23 questions are grouped in scales, which are different in the original Italian [11] or Spanish [12] version in comparison with the German [13], Polish [14] or

Brazilian [16] version. The different structure of these language versions is critical for the maintenance of the validity and internal consistency of the questionnaire. The published scales for the Italian version are: 'Pruritus' (2 items), 'Swelling' (2 items), 'Impact on life activities' (6 items), 'Sleep problems' (5 items), 'Limits' (3 items), 'Looks' (5 items) [11]. The score for each scale as well as the total score is calculated as a percentage of the maximum possible score.

Disease Activity

According to the EAACI/GA²LEN/EDF/WAO guidelines, disease activity was approached by using the UAS, which was calculated for 7 consecutive days (UAS7) [17]. The UAS sums up the number of wheals and the intensity of pruritus on a four-point scale with a minimum and maximum of 0 and 6 points per day, respectively.

Patient Selection

The study took place in the outpatient clinic of the Allergy Unit of the Department of Dermatology of Attikon University Hospital in Athens, Greece. All subjects were at least aged 18 years. The diagnosis was based on the EAACI/GA²LEN/EDF/WAO definition of CSU [17].

Data Collection and Measurements

The data collection period was from January 2010 to January 2011. All patients were asked to fill in two different HRQoL questionnaires, the CU-Q₂oL and the Dermatology Life Quality Index (DLQI). The DLQI is the most frequently used dermatology-specific HRQoL instrument, consisting of 10 questions concerning 'Symptoms and feelings', 'Daily activities', 'Leisure', 'Work and school', 'Personal relationships' and 'Treatment' [18].

Each individual included in the study was examined at two different visits. On the first visit (day 0) patients signed a written informed consent form and were given instructions on how to complete the UAS. One week later (on day 8) they revisited our outpatient clinic and filled in the CU-Q₂oL and the DLQI. The second visit was proposed in order to increase their cooperation, resulting in enhanced reliability and feedback.

The study was approved by the local ethics committee.

Statistical Analyses

Initially, the data of the Greek CU-Q₂oL were tested regarding whether they met the criteria for an exploratory factor analysis (EFA). Both Kaiser-Meyer-Olkin and Bartlett's test suggested that the data fit an EFA. During the subsequent principal component analysis with varimax rotation with Kaiser normalization, only factors with an eigenvalue >1 were retained. The factors' eligibility was further confirmed using a scree plot and Horn's parallel analysis. The internal consistency of the obtained factors was evaluated with Cronbach's α reliability coefficient, pertaining to Nunnally's criterion that this coefficient should be at least 0.7.

The results were also tested against the two models obtained with EFA for the German and Italian versions. The model fit for the two six-factor structures was tested with first-order confirmatory factor analysis (CFA), while the internal consistency of the factors was computed with Cronbach's α reliability coefficient.

The primary index used for model fit was the root mean square error of approximation (RMSEA), which is a measure of the mean

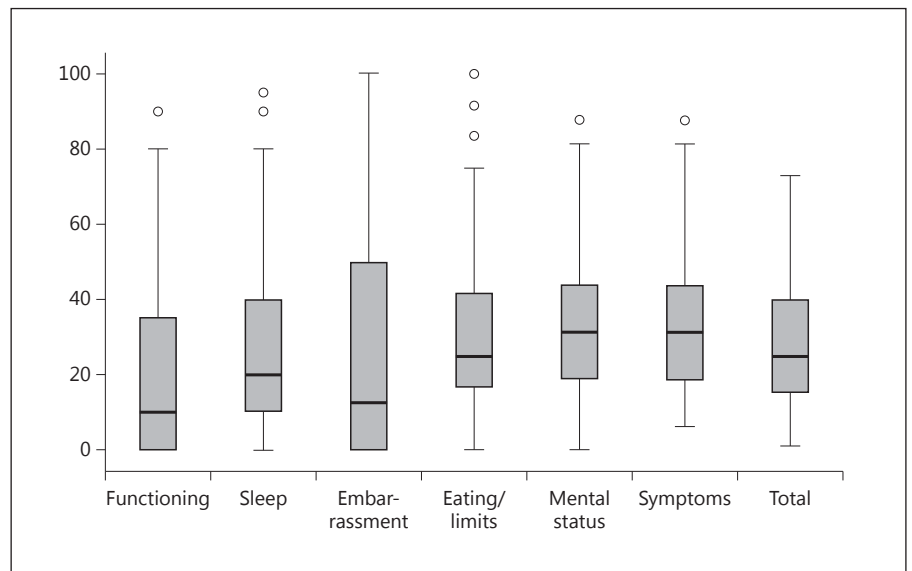


Fig. 1. Total and scale scores of the Greek version of the CU-Q₂oL.

discrepancy between the observed covariances and those implied by the model per degree of freedom. Values <0.05 are indicators of a good fit. Certain investigators consider 0.08 as an acceptable cut-off value, but certainly an RMSEA value >0.1 indicates a poor model fit.

Two additional incremental fit indices are reported: the Tucker-Lewis Index (TLI) and the Comparative Fit Index (CFI). The TLI, also known as ρ^2 , compares the discrepancy of the specified model in comparison to the baseline model. The typical range for the TLI lies between 0 and 1, but it is not limited to that range. TLI values close to 1 indicate a very good fit. As a rule of thumb a value of 0.9 is considered the cut-off value, above which there is an indication of a good model fit. The same is true for the CFI. In addition, the results of χ^2 analysis are reported. p values <0.05 reject the null hypothesis and indicate that the model fit is not satisfactory. Separate CFAs were performed for each factor, which were also tested for their internal consistency with Cronbach's α coefficients [19–22].

Finally, descriptive statistics were used to characterize the study sample and their HRQoL scores, and multiple linear regression analysis was used to assess significant predictors of the CU-Q₂oL scores.

Results

Sample Characteristics

110 patients (80 females, 30 males) with a mean age of 41.8 ± 12.8 years were included in the study. Mean UAS value was 19.1 ± 8.4 and mean disease duration was 3.5 ± 4.4 years. Less than 0.5% of the intended data entries were missing, which is relatively low.

Structure of the Questionnaire and Internal Consistency

EFA revealed a six-scale structure of the Greek CU-Q₂oL, which explained 67.9% of the variance of the 23 items (table 1). The six scales of the Greek CU-Q₂oL are: 'Functioning' (items 5, 6, 8, 9 and 22), 'Sleep' (items 7, 11, 12, 13 and 23), 'Embarrassment' (items 19 and 18), 'Eating/limits' (items 17, 10 and 21), 'Mental status' (items 14, 15, 16 and 20) and 'Symptoms' (items 1, 2, 3 and 4). Each item had a factor loading of at least 0.5, except for 'Medication side effects' (0.439) and 'Pruritus' (0.410). The symptom 'Pruritus' had a considerable loading also to scale I, II and III (0.301, 0.387 and 0.357, respectively), while 'Wheals' had a relatively high loading also to factor III (0.393). Internal consistency was satisfactory with Cronbach's $\alpha > 0.7$ for all six factors. Internal consistency for factors I–III was excellent (Cronbach's $\alpha > 0.8$).

CU-Q₂oL Scores

The CU-Q₂oL scores of our study population based on the Greek version of the questionnaire are presented in figure 1. The scales 'Mental status' and 'Symptoms' showed the highest values while 'Functioning' was less affected. 'Sleep' and 'Eating/limits' also showed a meaningful impairment. The strongest variation of scores was seen in the 'Embarrassment' scale. The median scores were: 'Functioning' 10, 'Sleep' 20, 'Embarrassment' 12, 'Eating/limits' 25, 'Mental status' 31 and 'Symptoms' 31.

Table 1. Determination of the scale structure of the Greek version of the CU-Q₂oL

Items		Factor					
		I	II	III	IV	V	VI
6	Physical activities	0.829	0.100	0.057	0.180	0.142	0.186
8	Free time	0.781	0.272	0.218	0.064	−0.039	−0.005
9	Social relationships	0.735	0.078	0.311	0.090	0.151	0.140
5	Work	0.715	0.230	−0.022	0.185	0.147	0.166
22	Sport	0.563	0.251	0.286	0.343	0.078	0.210
12	Wake up	0.099	0.795	0.247	0.062	0.115	0.037
11	Fall asleep	0.126	0.750	0.199	0.221	0.140	0.078
13	Tired	0.101	0.722	0.160	0.123	0.366	0.064
7	Sleep	0.410	0.714	0.114	0.135	−0.116	0.185
23	Medication side effects	0.296	0.439	−0.205	0.061	0.248	0.241
19	Embarrassed in public	0.142	0.206	0.823	0.145	0.125	0.142
18	Bothered by signs	0.232	0.185	0.818	0.033	0.130	0.129
17	Limit food	0.098	0.163	0.037	0.852	0.057	0.040
10	Eating	0.279	0.241	0.012	0.818	0.013	0.009
21	Limit clothes	0.282	−0.154	0.231	0.500	0.364	0.002
16	Bad mood	0.221	0.439	0.079	0.036	0.714	0.024
20	Cosmetics	−0.172	−0.016	0.172	0.346	0.693	0.183
15	Nervousness	0.355	0.326	0.232	0.000	0.554	−0.050
14	Concentration	0.281	0.466	−0.044	−0.147	0.506	−0.024
4	Lips swell	0.008	0.008	0.060	0.025	−0.094	0.832
3	Eyes swell	0.267	0.088	0.063	0.073	0.171	0.743
2	Wheals	0.188	0.209	0.393	−0.059	0.069	0.542
1	Pruritus	0.301	0.387	0.357	0.067	0.123	0.410
Eigenvalue		3.679	3.526	2.193	2.108	2.093	2.011
Percentage of variance explained		16.0%	15.3%	9.5%	9.2%	9.1%	8.7%
Cronbach's α reliability coefficient		0.874	0.839	0.853	0.735	0.715	0.731

Table 2. Correlations between CU-Q₂oL and DLQI scores

	CU-Q ₂ oL Functioning	CU-Q ₂ oL Sleep	CU-Q ₂ oL Embarrassment	CU-Q ₂ oL Eating/limits	CU-Q ₂ oL Mental status	CU-Q ₂ oL Symptoms	CU-Q ₂ oL Total
DLQI	0.474	0.374	0.381	0.288	0.283	0.624	0.557
Symptoms and feelings	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*
DLQI	0.565	0.425	0.553	0.450	0.410	0.475	0.655
Daily activities	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*
DLQI	0.729	0.481	0.503	0.533	0.446	0.537	0.748
Leisure	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*
DLQI	0.500	0.259	0.259	0.408	0.253	0.331	0.467
Work and school	<0.001*	0.06 ^{ns}	0.06 ^{ns}	<0.001*	0.08 ^{ns}	<0.001*	<0.001*
DLQI	0.530	0.381	0.297	0.316	0.429	0.395	0.552
Social relationships	<0.001*	<0.001*	<0.001*	<0.01*	<0.001*	<0.001*	<0.001*
DLQI	0.456	0.401	0.305	0.407	0.482	0.320	0.550
Treatment	<0.001*	<0.001*	<0.01*	<0.001*	<0.001*	<0.01*	<0.001*
DLQI	0.691	0.492	0.501	0.501	0.478	0.580	0.749
Total	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*

* $p < 0.05$; ns = not significant.

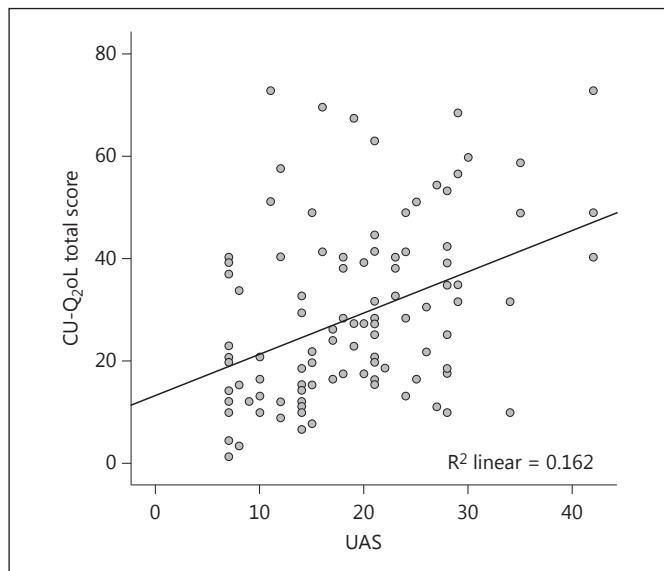


Fig. 2. Distribution of patients in relation with disease activity (UAS) and quality of life impairment (CU-Q₂oL).

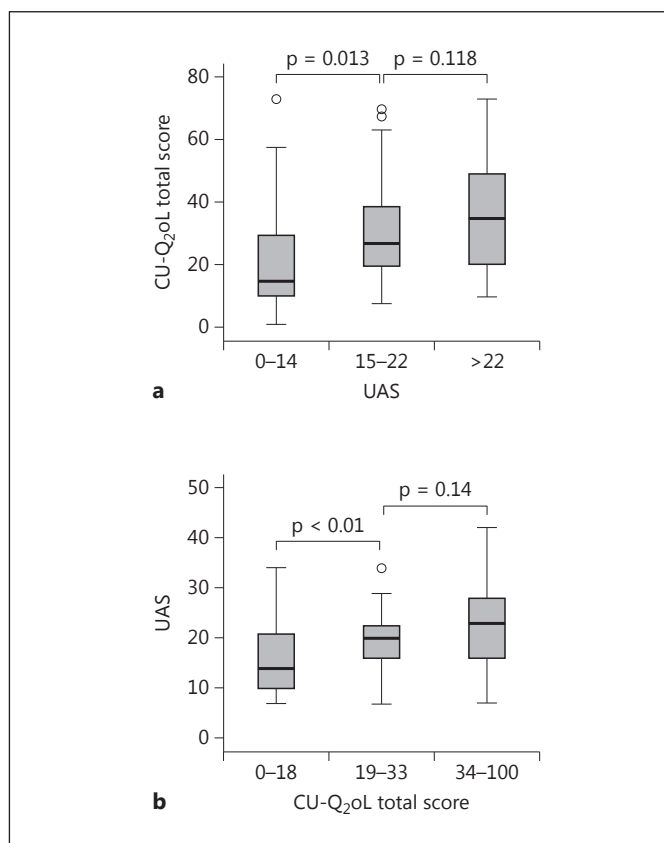


Fig. 3. a CU-Q₂oL total score for all UAS groups. **b** UAS score for all CU-Q₂oL total score groups.

Convergent Validity

We found a strong correlation between the total scores of the CU-Q₂oL and the DLQI ($r = 0.75$, $p < 0.0001$) and also between different scales of the Greek version of the CU-Q₂oL and DLQI subheadings (table 2). For example, the 'Functioning' scale of the Greek CU-Q₂oL correlated with all DLQI subheadings, but showed the strongest correlation with DLQI subheadings 'Leisure' ($r = 0.73$, $p < 0.0001$), 'Daily activities' ($r = 0.57$, $p < 0.0001$) and 'Personal relationships' ($r = 0.53$, $p < 0.0001$). The 'Sleep' and 'Mental status' scales exhibited less strong correlations with DLQI items. This was expected because the DLQI subheadings 'Leisure', 'Daily activities' and 'Personal relationships' cover areas of functioning, while the DLQI contains no questions related to sleep and has no focus on mental status and mental functions.

Correlation between CU-Q₂oL and Disease Activity

Disease activity, as determined by the UAS, was found to only moderately correlate with the CU-Q₂oL total score ($r = 0.40$, $p < 0.0001$) and with the DLQI score ($r = 0.37$, $p < 0.0001$). In figure 2, we present the distribution of patients in relation to quality of life impairment, as approached by the CU-Q₂oL, and disease activity, as approached by the UAS. Interestingly, there seems to be a group of patients with relatively low UAS that even so experience a remarkable impairment of their HRQoL. In order to investigate the ability of the CU-Q₂oL to discriminate between CSU patients with different severities of affection (known groups validity), we created three UAS groups (group 1: UAS7 0–14; group 2: UAS7 15–22; group 3: UAS7 23–42). Subsequently, we computed the HRQoL (fig. 3a). There was a statistically significant difference in the CU-Q₂oL total score between groups 1 and 2, but not between groups 2 and 3. Inversely, we created three CU-Q₂oL groups and assessed the UAS for each one. Notably, there is a wide range of UAS values in patients with a strong quality of life impairment (fig. 3b).

Predictors of HRQoL Impairment

Disease activity was found to be a significant predictor of the Greek CU-Q₂oL total and scale scores ($p < 0.01$). Age, gender and disease duration did not predict the total or scale scores with one exception. Sex was a significant predictor for the 'Mental status' scale ($p < 0.01$), with women being more severely affected.

Table 3. Results of the CFA and reliability analysis (internal consistency) for the six-scale structure of the Italian version of the CU-Q₂oL

CU-Q ₂ oL scale	CFA				Cronbach's α (95% CI)	Items
	χ^2 /d.f./p value	TLI	CFI	RMSEA		
Impact	24.4 9 0.004	0.906	0.943	0.125	0.845 (0.685–0.825)	Work Physical activities Sleep Spare time Social relations Eating
Sleep	10.2 5 0.068	0.943	0.971	0.098	0.822 (0.763–0.870)	Falling asleep Waking up at night Tired Concentration Nervous
Looks	18.0 5 0.003	0.786	0.893	0.155	0.656 (0.542–0.748)	Medication side effects Embarrassed by signs Embarrassed in public Cosmetics Limits clothes
Limits	*	*	*	*	0.562 (0.398–0.687)	Bad mood Limits food Sports
Swelling	*	*	*	*	0.629 (0.459–0.746)	Eyes swell Lips swell
Pruritus	*	*	*	*	0.789 (0.692–0.855)	Pruritus Wheals
Total model	505 215 <0.001	0.709	0.753	0.111	0.910 (0.884–0.933)	
* Cannot be calculated.						

Confirmatory Factor Analysis

The results of the CFA regarding the Italian and German scale structure are presented in tables 3 and 4, respectively. The results show that although the model fit is not ideal, the discrepancy is not high. Overall the model fit was found to be better for the German than the Italian model (RMSEA value 0.102 and 0.111, respectively). Regarding the factors, the data provided a perfect model fit for the German 'Sleep' scale (RMSEA = 0.000) and an acceptable model fit for the Italian 'Sleep' scale (RMSEA = 0.098). The criterion CFI > 0.9 was met for both 'Functioning' and 'Sleep' for the German model and for 'Impact on life activities' and 'Sleep' for the Italian model. Concerning the latter, the 'Looks' scale also presented a marginal CFI value (0.893).

The internal consistency of the German model was found to be excellent (Cronbach's α > 0.8) for the scales

'Functioning' and 'Sleep', while 'Itching/embarrassment' and 'Mental status' exhibited an adequate internal consistency (Cronbach's α > 0.7). For the remaining two scales the internal consistency was <0.7. The internal consistency of the Italian model was excellent for the scales 'Impact on life activities' and 'Sleep', acceptable for 'Pruritus' and minimally acceptable for 'Looks' (>0.65).

Discussion

It is nowadays well recognized that CSU substantially affects the HRQoL of patients. The extent of HRQoL impairment has been shown to be comparable with that of patients suffering from severe ischemic heart disease [8] and to be one of the highest among dermatologic disor-

Table 4. Results of the CFA and reliability analysis (internal consistency) for the six-scale structure of the German version of the CU-Q₂oL

Subscale	CFA				Cronbach's α (95% CI)	Items
	χ^2 /d.f./p value	TLI	CFI	RMSEA		
Functioning	23.5 10 <0.01	0.927	0.952	0.111	0.857 (0.812–0.895)	Work Physical activities Spare time Social relations Sports Medication side effects
Sleep	1.4 2 0.494	1	1	0.000	0.856 (0.807–0.896)	Sleep Falling asleep Waking up at night Tired
Itching/ embarrassment	45.2 2 <0.001	0.280	0.760	0.445	0.794 (0.723–0.850)	Pruritus Wheals Embarrassed by signs Embarrassed in public
Mental status	*	*	*	*	0.760 (0.670–0.828)	Concentration Nervous Bad mood
Swelling/eating	73.2 2 <0.001	*	0.271	0.572	0.582 (0.438–0.696)	Eyes swell Lips swell Eating Limits food
Limits looks	*	*	*	*	0.453 (0.202–0.625)	Cosmetics Limits clothes
Total model	457 215 <0.001	0.757	0.794	0.102	0.910 (0.884–0.933)	
* Cannot be calculated.						

ders [23]. A recent GA²LEN position paper recommended the use of evidence-based patient-reported outcome instruments, including HRQoL and disease activity measures, in clinical trials with urticaria patients [24]. Moreover, the current EAACI/GA²LEN/EDF/WAO guidelines on the definition, classification and diagnosis of urticaria [17] recommend the use of the disease-specific HRQoL instrument CU-Q₂oL as well as of the UAS for monitoring disease activity in CSU patients.

This study was performed in order to investigate the relation between quality of life impairment and disease activity in CSU patients by using the tools recommended by the guideline. However, a prerequisite for the application and acceptance of a patient-reported outcome instrument such as the CU-Q₂oL is that there is a validated language version available. Therefore, we initially trans-

lated, culturally adapted and validated the CU-Q₂oL for the Greek language and subsequently examined our CU-Q₂oL results with regard to the disease activity of the same patients.

The results of the EFA of the validation phase revealed a six-dimensional structure of the Greek CU-Q₂oL, which is in accordance with the original Italian, German and Polish versions [11, 13, 14], but different from the three-dimensional-structure of the Portuguese-Brazilian version [16]. The levels of internal consistency were satisfactory to excellent for all six identified dimensions ('Functioning', 'Sleep', 'Embarrassment', 'Eating/limits', 'Mental status' and 'Symptoms'). The level and pattern of correlations between the CU-Q₂oL and DLQI scores support the questionnaires' convergent validity. Notably, the 'Sleep' scale shows relatively low correlations to DLQI scores,

because the DLQI misses a question concerning sleep. However, our results as well as the results obtained from the German, Polish, Turkish and Brazilian population demonstrate that the impact of CSU on sleep is remarkable. This lack is a serious disadvantage of the DLQI when used in CSU patients, but also in other disorders that go along with pruritus. Interestingly, the CU-Q₂oL question focusing on medication side effects was found to load highest on the 'Sleep' scale. This is the first CU-Q₂oL language version with this allocation and makes perfect sense: It is well known that antihistamines, which are the first-line treatment for urticaria, may have an effect on the circadian sleep/wake cycle and the quality of sleep [25].

As mentioned above, the Greek version of the CU-Q₂oL presents slight structural differences from the original Italian instrument, but also from all other published versions. These differences are expected and can be partially attributed to cultural peculiarities. Unfortunately, this fact makes direct comparisons or pooling of results difficult. In order to overcome this obstacle, we performed a CFA of the Italian and German structure. We chose the Italian questionnaire because it is the original instrument and the German one because it has a structure very similar to that of the Greek questionnaire, based on the results of our EFA. Our CFA results suggest that the Italian as well as the German versions' scale structure can also be applied for the Greek CU-Q₂oL. This finding is the key for its use in international multicenter studies.

Once the validation of the CU-Q₂oL was completed, we started to examine the relation of our CSU patients' HRQoL to their disease activity. Our results demonstrate that the CU-Q₂oL total scores and the UAS scores were only moderately correlated. Notably, this correlation was higher as compared to those of the DLQI and the UAS, again suggesting that the DLQI is not ideally suited for CSU patients. These findings are in line with earlier investigations that also found only moderate correlations in the German ($r = 0.39$), Turkish ($r = 0.48$) and Brazilian ($r = 0.39$) populations [15, 16, 26]. Interestingly, we could identify patients with relatively low UAS but high CU-Q₂oL scores. These data suggest that there are factors in addition to disease activity that also influence CSU patients' HRQoL. Indeed, Staubach et al. [9] reported that psychiatric comorbidity, such as depression and anxiety, influence HRQoL impairment, as assessed by Skindex-29, in patients with CSU. A moderate correlation between HRQoL and disease activity is not a unique finding for CSU patients, but has also been noticed in different (der-

matologic and other) conditions. For example, the DLQI score was found to have a relatively poor correlation with disease activity in an Italian population of psoriasis patients as well as in a Dutch population of atopic dermatitis patients [27, 28]. Additionally, moderate correlations between disease activity and HRQoL were found in subjects suffering from inflammatory bowel disease [29].

In addition, our results show that the CU-Q₂oL total score seems to be more sensitive to discriminate between CSU patients with different severities of affection when the UAS is relatively low. Interestingly, this result is in agreement with the Turkish validation study [15], where a statistically significant difference in the CU-Q₂oL total score was found between the first and second UAS quartile ($p < 0.05$), but not between the second and third ($p = 0.09$) and between the third and fourth ($p = 0.19$) quartile.

One limitation of our study is that we are not aware of any formal validation study of the Greek DLQI, which was used to test convergent validity of the Greek CU-Q₂oL in our project. Nevertheless, an official Greek language translation is available and this version has already been successfully applied in studies conducted in the Greek population [30]. Moreover, there is extensive experience concerning the application of DLQI to patients with urticaria [18, 23], and the DLQI is by far the most frequently applied HRQoL instrument in the field of dermatology. Therefore, we believe that it serves well the objects of our study. Moreover, patient selection bias in our study cannot be excluded, since the study was conducted in a tertiary referral hospital. An additional limitation is that the validation process was conducted in an adult population. For this reason, the Greek version of the CU-Q₂oL is not valid for use in children.

In conclusion, the Greek version of the CU-Q₂oL is a valid and reliable instrument that may be used in research but also in everyday clinical practice. It is important to note that HRQoL impairment and disease activity are only moderately correlated. Therefore, measures for both the CU-Q₂oL and the UAS should be applied in CSU patients in order to obtain a comprehensive picture of the actual disease status.

Disclosure Statement

The authors declare that there is no conflict of interest relating to this paper.

References

- Zuberbier T, Balke M, Worm M, Edenharter G, Maurer M: Epidemiology of urticaria: a representative cross-sectional population survey. *Clin Exp Dermatol* 2010;35:869–873.
- Gaig P, Olona M, Muñoz Lejarazu D, Caballero MT, Dominguez FJ, Echechipia S, Garcia Abujeta JL, Gonzalo MA, Leonart R, Martinez-Cocera C, Rodriguez A, Ferrer M: Epidemiology of urticaria in Spain. *J Investig Allergol Clin Immunol* 2004;14:214–220.
- Zuberbier T, Chantraine-Hess S, Hartmann K, Czarnetzki BM: Pseudoallergen-free diet in the treatment of chronic urticaria. A prospective study. *Acta Derm Venereol* 1995;75:484–487.
- Hide M, Francis DM, Grattan CE, Hakimi J, Kochan JP, Greaves MW: Autoantibodies against the high-affinity IgE receptor as a cause of histamine release in chronic urticaria. *N Engl J Med* 1993;328:1599–1604.
- Wedi B, Raap U, Kapp A: Chronic urticaria and infections. *Curr Opin Allergy Clin Immunol* 2004;4:387–396.
- Maurer M, Weller K, Bindslev-Jensen C, Gimenez-Arnau A, Bousquet PJ, Bousquet J, Canonica GW, Church MK, Godse KV, Grattan CE, Greaves MW, Hide M, Kalogeromitros D, Kaplan AP, Saini SS, Zhu XJ, Zuberbier T: Unmet clinical needs in chronic spontaneous urticaria. A GA²LEN task force report. *Allergy* 2011;66:317–330.
- WHOQOL Group: Study protocol for the World Health Organization project to develop a Quality of Life assessment instrument (WHOQOL). *Qual Life Res* 1993;2:153–159.
- O'Donnell BF, Lawlor F, Simpson J, Morgan M, Greaves MW: The impact of chronic urticaria on the quality of life. *Br J Dermatol* 1997;136:197–201.
- Staubach P, Eckhardt-Henn A, Dechene M, Vonend A, Metz M, Magerl M, Breuer P, Maurer M: Quality of life in patients with chronic urticaria is differentially impaired and determined by psychiatric comorbidity. *Br J Dermatol* 2006;154:294–298.
- Ozkan M, Ofiaz SB, Kocaman N, Ozseker F, Gelincik A, Buyukozturk S, Ozkan S, Colakoglu B: Psychiatric morbidity and quality of life in patients with chronic idiopathic urticaria. *Ann Allergy Asthma Immunol* 2007;99:29–33.
- Baiardini I, Pasquali M, Braidò F, Fumagalli F, Guerra L, Compalati E, Braga M, Lombardi C, Fassio O, Canonica GW: A new tool to evaluate the impact of chronic urticaria on quality of life: chronic urticaria quality of life questionnaire (CU-QoL). *Allergy* 2005;60:1073–1078.
- Valero A, Herdman M, Bartra J, Ferrer M, Jauregui I, Davila I, del Cuavillo A, Montoro J, Mullol J, Sastre J, Canonica GW, Baiardini I: Adaptation and validation of the Spanish version of the chronic urticaria quality of life questionnaire (CU-Q2oL). *J Investig Allergol Clin Immunol* 2008;18:426–432.
- Mlynek A, Magerl M, Hanna M, Lhachimi S, Baiardini I, Canonica GW, Brzoza Z, Kasperska-Zajac A, Rogala B, Zalewska-Janowska A, Zuberbier T, Maurer M: The German version of the chronic urticaria quality-of-life questionnaire: factor analysis, validation, and initial clinical findings. *Allergy* 2009;64:927–936.
- Brzoza Z, Badura-Brzoza K, Mlynek A, Magerl M, Baiardini I, Canonica GW, Weller K, Kocaturk E, Kalogeromitros D, Zalewska-Janowska A, Zuberbier T, Maurer M: Adaptation and initial results of the Polish version of the GA²LEN chronic urticaria quality of life questionnaire (CU-Q2oL). *J Dermatol Sci* 2011;62:36–41.
- Kocaturk E, Weller K, Martus P, Aktas S, Kavala M, Sarigul S, Baiardini I, Canonica GW, Brzoza Z, Kalogeromitros D, Maurer M: Turkish version of the chronic urticaria quality of life questionnaire: cultural adaptation, assessment of reliability and validity. *Acta Derm Venereol* 2012;92:419–425.
- Dias GA, Pires GV, Valle SO, Franca AT, Papi JA, Dortas SD Jr, Levy SA, Baiardini I, Canonica GW: Cross-cultural adaptation of the Brazilian-Portuguese version of the chronic urticaria quality-of-life questionnaire – CU-Q2oL. *Allergy* 2011;66:1487–1493.
- Zuberbier T, Asero R, Bindslev-Jensen C, Walter Canonica G, Church MK, Gimenez-Arnau A, Grattan CE, Kapp A, Merk HF, Rogala B, Saini S, Sanchez-Borges M, Schmid-Grendelmeier P, Schunemann H, Staubach P, Vena GA, Wedi B, Maurer M: EAACI/GA²LEN/EDF/WAO guideline: definition, classification and diagnosis of urticaria. *Allergy* 2009;64:1417–1426.
- Lennox RD, Leahy MJ: Validation of the Dermatology Life Quality Index as an outcome measure for urticaria-related quality of life. *Ann Allergy Asthma Immunol* 2004;93:142–146.
- Bentler PM, Bonett DG: Significance tests and goodness of fit in the analysis of covariance structures. *Psychol Bull* 1980;88:588–606.
- Bollen KA: A new incremental fit index for general structural equation models. *Sociol Methods Res* 1989;17:303–316.
- Browne MW, Cudeck R: Alternative ways of assessing model fit. *Sociol Methods Res* 1992;21:230–258.
- Streiner DL, Norman GR: Health Measurement Scales: A Practical Guide to Their Development and Use. Oxford, Oxford University Press, 1995.
- Basra MK, Fenech R, Gatt RM, Salek MS, Finlay AY: The Dermatology Life Quality Index 1994–2007: a comprehensive review of validation data and clinical results. *Br J Dermatol* 2008;159:997–1035.
- Baiardini I, Braidò F, Bindslev-Jensen C, Bousquet PJ, Brzoza Z, Canonica GW, Compalati E, Fiocchi A, Fokkens W, Gerth van Wijk R, Gimenez-Arnau A, Godse K, Grattan C, Grob JJ, La Grutta S, Kalogeromitros D, Kocaturk E, Lombardi C, Mota-Pinto A, Ridolo E, Saini SS, Sanchez-Borges M, Senna GE, Terreehorst I, Todo Bom A, Toubi E, Bousquet J, Zuberbier T, Maurer M: Recommendations for assessing patient-reported outcomes and health-related quality of life in patients with urticaria: a GA²LEN taskforce position paper. *Allergy* 2011;66:840–844.
- Church MK, Maurer M, Simons FE, Bindslev-Jensen C, van Cauwenberge P, Bousquet J, Holgate ST, Zuberbier T: Risk of first-generation H(1)-antihistamines: a GA²LEN position paper. *Allergy* 2010;65:459–466.
- Weller K, Church MK, Kalogeromitros D, Krause K, Magerl M, Metz M, Pisarevskaja D, Siebenhaar F, Maurer M: Chronic spontaneous urticaria: how to assess quality of life in patients receiving treatment. *Arch Dermatol* 2011;147:1221–1223.
- Mazzotti E, Picardi A, Sampogna F, Sera F, Pasquini P, Abeni D: Sensitivity of the Dermatology Life Quality Index to clinical change in patients with psoriasis. *Br J Dermatol* 2003;149:318–322.
- Haeck IM, ten Berge O, van Velsen SG, de Bruin-Weller MS, Buijnzeel-Koomen CA, Knol MJ: Moderate correlation between quality of life and disease activity in adult patients with atopic dermatitis. *J Eur Acad Dermatol Venereol* 2012;26:236–241.
- Gray WN, Denson LA, Baldassano RN, Hommel KA: Disease activity, behavioral dysfunction, and health-related quality of life in adolescents with inflammatory bowel disease. *Inflamm Bowel Dis* 2011;17:1581–1586.
- Antoniou C, Stefanaki I, Stratigos A, Moustou E, Vergou T, Stavropoulos P, Avgerinou G, Rigopoulos D, Katsambas AD: Infliximab for the treatment of psoriasis in Greece: 4 years of clinical experience at a single centre. *Br J Dermatol* 2010;162:1117–1123.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.