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Chronic spontaneous urticaria activity, impact and control as well as their changes are strongly linked, and these links are not affected by angioedema or comorbid inducible urticaria – Results from the validation of the Polish Urticaria Control Test

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ABSTRACT

Background: Monitoring the effects of treatment on disease activity, impact, and control in patients with chronic spontaneous urticaria (CSU) is essential. We do not have enough information on how these features of CSU and its response to treatment are linked. Also, there is no information on how recurrent angioedema or coexisting chronic inducible urticaria (CIndU) affect their relation. The aim of this study was to analyse the link between disease activity, impact, and control in CSU patients and possible effects of recurrent angioedema and comorbid CIndU.

Methods: To perform these analyses, we validated the Polish version of the Urticaria Control Test (UCT) in 106 chronic urticaria patients. The relationship between CSU activity, impact, and control was assessed in regard to recurrent angioedema and coexisting CIndU.

Results: The Polish UCT showed high levels of validity, reliability, and sensitivity to change. Disease activity, impact, and control as well as their changes, assessed by the UAS, the CU-Q_2oL, and the UCT, respectively, were strongly correlated. Recurrent angioedema or comorbid CIndU did not significantly affect the link of CSU activity, impact, and control or the relation of their changes.

Conclusions: In CSU, there is a strong, albeit not perfect correlation of disease activity, impact, and control, which underlines the need to assess all 3 features of the disease in routine clinical practice. Recurrent angioedema and comorbid CIndU, which are both common and relevant in CSU, do not affect how disease activity, impact and control in patients with CSU are related to each other.

Keywords: Urticaria, Angioedema, UCT, Validation, Control

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INTRODUCTION

Chronic urticaria (CU) is a common disease characterized by the occurrence of itchy wheals, angioedema, or both for at least 6 weeks. It is divided into chronic spontaneous urticaria (CSU) and the heterogeneous group of chronic inducible urticaria (CIndU), where signs and symptoms occur spontaneously or in response to definite triggers, respectively.[1] CSU is characterized by the unpredictable occurrence of wheals, angioedema, or both, considerable daily fluctuations, and a significant impact on patient quality of life.[2] Therefore, the clinical disease status of CSU patients during a clinic visit usually does not reflect the actual activity, impact, and control of the disease.

Information on the activity, impact, and control of CSU is needed to guide treatment decisions. They should also be assessed to monitor the response to treatment, to secure that treatment goals are reached and to optimize treatment if needed. As of yet, we do not have enough information on how disease activity, impact, and control in CSU are linked. We know they are related, but the strength of the relation, the strength of the relation of their changes, and the impact of clinical features such as recurrent angioedema and CIndU are largely unexplored.[3]

Recurrent angioedema, an important clinical problem in daily practice and emergency medicine is one of the key features of CSU and also a major driver of patient health-related quality of life impairment. More than 50% of patients with CSU experience recurrent angioedema in addition to wheals and about 10% of CSU patients have isolated recurrent angioedema (without wheals).[4] CIndU comes with wheals and/or angioedema that occur in response to definite physical or chemical triggers, pressure in delayed pressure urticaria for example. Patients affected by CIndU are severely disabled by its signs and symptoms and the need to avoid relevant triggers. Up to 36% of CSU patients have comorbid CIndU.[5] However, there is little information on how recurrent angioedema and coexistent CIndU, in patients with CSU, affect how CSU disease activity, burden of disease, and disease control are linked.

At present, we have several tools to assess disease activity, impact and control in CSU. The Urticaria Activity Score (UAS) and the Chronic Urticaria Quality of Life questionnaire (CU-Q_2oL) are recommended by the EAACI/GA^{2}LEN/EDF/WAO guideline for urticaria as the standard tools for evaluating disease activity and quality of life impairment in CSU, respectively.[1] Both are useful instruments, but have important limitations. The UAS is a prospective tool that must be completed on a daily basis. Its results are, therefore, not instantly available at a patient's visit when treatment decisions need to be made.[6,7] Second, the UAS assesses the intensity of pruritus and the number of wheals, but not the frequency and severity of angioedema. Third, the UAS only works in CSU but not in CIndU patients: due to the varying exposure to triggers and the often considerable trigger avoidance behaviour of CIndU patients, the frequency and severity of symptoms alone is not a good reflection of CIndU patients disease activity.[8] The CU-Q_2oL is often considered too complicated for use in daily routine care, and its interpretation requires some experience. Therefore, the CU-Q_2oL is frequently used in clinical trials but less often in daily practice.[9,10] Finally, for both tools, the UAS and CU-Q_2oL, there are no accepted cut-off values available to guide treatment decisions. These limitations were major reasons for the development and validation of the Urticaria Control Test (UCT).

The UCT is an easy-to-administer and easy-to-complete four-item tool that retrospectively assesses disease control in patients with CSU, CIndU, or both with a clear cut-off value to aid and back treatment decisions.[11] Each of the 4 UCT questions has 5 possible answer options (scored with 0–4 points). The UCT score is calculated by summing up all 4 question scores. Accordingly, the UCT score ranges from 0 to 16 points, with 16 points indicating complete disease control, and 12 points or higher reflecting well-controlled disease.[11] Lower scores indicate poorly-controlled urticaria. The UCT was originally developed and validated in a German patient population and has subsequently been translated and linguistically validated in several other languages.[12–17]

The aim of this study was to analyse the relation between disease activity, control, and impact, especially in regard to recurrent angioedema and coexisting CIndU, in CSU patients. To perform these analyses, we first translated the UCT to Polish and then investigated the validity, reliability, screening accuracy, sensitivity to change and minimal clinically important difference (MCID) of the Polish UCT. Then, we assessed the relation of disease activity, impact and control as well as that of their changes in CSU patients, with subsequent analyses of the influence of angioedema and CIndU.

MATERIALS AND METHODS

Generation of the Polish version of the UCT

The German version of the UCT was independently translated into Polish by 2 native Polish speakers. These 2 Polish forward translations were reconciled and assessed for comprehensibility by a Polish dermatologist and an allergist specializing in urticaria. The final agreed upon version was independently back-translated into German by 2 bilingual translators and compared with the original German version of the UCT by the original author to assure conceptual equivalence of the Polish UCT version and to reduce possible discrepancies. After consensus on a final Polish translation was achieved, this version was subjected to cognitive debriefing in 12 CU patients (8 patients with CSU and 4 patients with CIndU). The cognitive debriefing did not reveal any requirement for changes in the Polish UCT version, and the final Polish UCT version was used for further analyses during a validation study (Table 1).

Study design - validation of the Polish version of the UCT

Polish CU patients aged 18–60 years attending Department of Internal Diseases with Division of Allergology from 2018 to 2019, were invited to participate in the validation study of the Polish UCT. We only included CSU patients with wheals, with or without angioedema, not CSU patients with recurrent angioedema without wheals. CSU patients with uncontrolled somatic or mental disorders were also excluded. CU therapy was provided to patients according to the current international guideline.[1]

All patients were assessed 3 times at 4-week intervals: baseline visit – to start disease activity documentation with the UAS; first and second follow up visit – to complete a questionnaire package. An overview on the study design is shown in Supplementary Figure 1.

Anchor outcomes – validation of the Polish version of the UCT

The UAS prospectively assesses the daily number of wheals (0–3 points) and intensity of pruritus (0–3 points) in CSU patients. It was completed for 4 weeks (UAS28) to match the 4-week recall period of the UCT.

Additionally, we assessed the patient's urticaria by using 2 visual analogue scales (VAS), each addressing the situation in the previous 4 weeks. The patient's global assessment of disease activity (Pat-VAS) consisted of a straight line with the extreme endpoints, ie, "no complaints at all" (0 cm) and "maximal intensity of complaints" (10 cm). The physician's global assessment of disease control (Phy-VAS) had the endpoints "not at all under control" (0 cm) to "completely under control" (10 cm).[11]

In parallel to the VAS ratings, evaluation of disease activity (categories: no complaints, mild complaints, moderate complaints, severe complaints), and disease control (categories: no control, little control, moderate control, good control, and complete control) during the previous 4 weeks was performed on a patient's Likert Scale (Pat-LS) and a physician's (Phy-LS).

Therapy effectiveness during the previous 4 weeks was assessed by patients (Pat-Therapy) and physicians (Phy-Therapy) as "effective" or "ineffective".[11]

To assess the patient's urticaria-related quality of life impairment, the Polish version of the CU-Q_2oL was used. The CU-Q_2oL is currently the only instrument available to assess urticaria-specific quality of life impairment. The total score of the CU-Q_2oL ranges from 0 to 100 points, with high values indicating a high degree of quality of life impairment.[18–21]

A

Test kontroli pokrzywki

Imię i nazwisko: **Data:**
Data urodzenia:
Instrukcja: Cierpi Pani/Pan na pokrzywkę. Poniższe pytania pomogą określić aktualny stan Pani/Pana choroby. Proszę uważnie przeczytać każde pytanie i wybrać jedną z pięciu odpowiedzi, która *najlepiej opisuje Pani/Pana odczucia* w odniesieniu do *ostatnich 4 tygodni.* Nad odpowiedziami *nie należy zastanawiać się zbyt długo*. Proszę o udzielenie odpowiedzi *na wszystkie pytania* zakreślając dla każdego z nich *tylko jedną odpowiedź*.

1. Jak bardzo w ciągu ostatnich 4 tygodni dokuczały Pani/Panu dolegliwości związane z pokrzywką (świąd, bąble i/lub obrzęki)?
   O bardzo mocno O mocno O umiarkowanie O nieznacznie O wcale
2. Jak bardzo pogorszyła się Pani/Pana jakość życia w ciągu ostatnich 4 tygodni z powodu pokrzywki?
   O bardzo mocno O mocno O umiarkowanie O nieznacznie O wcale
3. Jak często leczenie pokrzywki w ciągu ostatnich 4 tygodni nie było wystarczająco skuteczne aby opanować objawy choroby?
   O bardzo często O często O czasami O rzadko O wcale
4. W jakim stopniu udawało się Pani/Panu w ciągu ostatnich 4 tygodni utrzymywać objawy pokrzywki pod kontrolą?
   O wcale O słabo O umiarkowanie O dobrze O całkowicie

B

Urticaria Control Test

Patient name: **Date:**

Date of birth:

Instruction: You suffer from urticaria. The questions below allow to assess your current disease status. Please read each question carefully and choose one answer from the five options that best fits your feelings in the last four weeks. Please don't think about the answers for a long time. Remember to answer all questions and to provide only one answer to each question.

1. How much have you suffered from symptoms of urticaria (itch, hives and/or oedema) in the last 4 weeks?
   O very much O much O somewhat O a little O not at all
2. How much was your quality of life impaired by the urticaria in the last 4 weeks?
   O very much O much O somewhat O a little O not at all
3. How often was the treatment for urticaria not enough effective to control disorder symptoms in the last 4 weeks?
   O very often O often O sometimes O seldom O not at all
4. How well have you had your urticaria symptoms under control in the last 4 weeks?
   O not at all O a little O somewhat O well O very well

Table 1. Polish version of Urticaria Control Test (A) with an English working translation (B)

Assessment of clinimetric properties of the Polish version of the UCT

The internal consistency of the Polish UCT was examined by computing Cronbach's α coefficient. Cronbach's α coefficient was interpreted as unacceptable (<0.60), poor (0.60–0.65), questionable (0.65–0.70), acceptable (0.70–0.80), good (0.80–0.90), or excellent (>0.90) (20).

To assess the convergent validity of the Polish UCT, we correlated its scores (Spearman's correlation) with anchor outcomes, ie, UAS28, Pat-VAS, Phy-VAS, and the CU-Q_2oL total score. Spearman's rank correlation coefficient was interpreted as weak (0.2–0.4), moderate (0.4–0.6), strong (0.6–0.8), or very strong (>0.8).

To determine the known-groups validity and banding of the Polish UCT, we calculated Polish UCT values for patients with different levels of disease status as assessed by the Pat-LS and Phy-LS as well as Pat-Therapy and Phy-Therapy. To assess the capacity of Polish UCT to discriminate patients with different levels of disease activity, the patients were stratified with regard to their UAS28 results into four groups: 0–6, 7–24, 25–64, ≥65.[11,16]

The UCT's test-retest reliability was assessed in stable patients (no change in the Pat-LS values) from the first to the second follow-up visit. Intraclass correlation coefficient (ICC) value of 0.5–0.7 was interpreted as moderate-to-good reproducibility, while values > 0.7 were regarded to indicate excellent reproducibility.[11]

To assess the sensitivity to change of the Polish UCT, we computed and subsequently correlated the score changes of the UCT, UAS28, CU-Q_2oL, Pat-VAS, and Phy-VAS between first and second follow-up visit.

Receiver operating characteristic (ROC) curve analyses and area under the curve (AUC) were used to evaluate the screening accuracy of the Polish UCT, ie, its ability to differentiate urticaria patients into those with poorly-controlled disease (answer options: no control, little control or moderate control) and well-controlled disease (answer options: good control or complete control) according to Phy-LS results. The cut-off value for well-controlled urticaria against poorly controlled urticaria was assessed. AUC values of 1, 0.9, 0.8, 0.7, and 0.5 were categorized as perfect, excellent, good, fair, and no better than chance, respectively.[11,16]

The MCID is the minimal difference in a score that patients perceive as a clinically relevant change. To assess the MCID, we applied an anchor-based approach by using Pat-LS as an external anchor for the MCID determination.[7] We correlated UCT changes and Pat-LS changes under the category of "improvement" (1 level improvement in Pat-LS) and "no improvement" (no improvement or worsening in Pat-LS).

Assessment of the relation between disease activity, impact, and control and the effect of angioedema and CIndU

In order to better characterize the link between disease activity, impact, and control and the specific role of recurrent angioedema or CIndU, we computed correlations between the UCT, UAS28, and CU-Q_2oL scores at the first visit and of score changes between the first and second follow-up visit. We also calculated these correlations after controlling for the presence or absence of recurrent angioedema and comorbid CIndU.

Statistical analysis

Kruskal-Wallis, U Mann-Whitney, Pearson, Spearman tests, and partial correlations (for controlling for angioedema and CIndU) were used for statistical analyses (Statistica 13.1, Statsoft, USA).

RESULTS

One-hundred-six of the 121 initially enrolled patients completed the study (Supplementary Table 1). Fifteen subjects were excluded from the analysis because of highly incomplete data sets. All analyzed outcome measures improved between the first and second follow-up visit, with increased UCT and Phy-VAS values and decreased UAS28, CU-Q_2oL, and Pat-VAS values (Table 2).

The internal consistency, convergent and known-groups validity of the Polish UCT is high, and its test-retest reliability is excellent

The Cronbach's α value of the Polish UCT was 0.88, indicating an excellent internal consistency reliability. In the convergent validity analyses,

	Median	IQR	*p-value*
UCT 1st assessment	9	4–11	<0.01
UCT 2nd assessment	12	6–14	
UAS28 1st assessment	64	40–92	<0.01
UAS28 2nd assessment	52	22–80	
CU-Q_2oL 1st assessment	38	24–58	<0.01
CU-Q_2oL 2nd assessment	33.1	17–50	
Pat-VAS 1st assessment	5.5	3–7	<0.01
Pat-VAS 2nd assessment	3.5	2–6	
Phy-VAS 1st assessment	6	3–8	<0.01
Phy-VAS 2nd assessment	7.5	4–9	

Table 2. Results of the applied patient-reported outcome measures at the first and the second assessment. *UCT, Urticaria Control Test; UAS28, Urticaria Activity Score 28 day summary; CU-Q_2oL, Chronic Urticaria Quality of Life Questionnaire; Pat-VAS, Patient's self-rated disease activity on a visual analogue scale; Phy-VAS, Physician's rating of disease control on visual analogue scale; IQR, interquartile range. The decrease in the values of the UAS28, CU-Q2oL, and Pat-VAS as well as the increase in the values of the UCT and Phy-VAS indicate improvement of the disease status*

strong correlations were found between the UCT and the anchor outcomes (Table 3). The correlations of the UCT were higher with other patient-reported outcomes as compared to physician-based assessments.

The UCT was able to differentiate patient subgroups with different levels of disease activity, disease control, and therapy effectiveness (Table 4). Patients with higher disease activity (UAS28 and Pat-LS) had lower UCT values, indicating lower levels of disease control. In addition, patients with an ineffective treatment (patients self-rating and physician rating) showed low UCT values as compared to patients with a good treatment response.

The results of 28 patients in whom no changes in Pat-LS values were observed between the first and second follow-up visits, indicating stable disease, were included in the test-retest reliability assessment. The ICC was 0.97 (95% confidence interval: 0.95–0.99) reflecting excellent reproducibility and test-retest reliability.

The sensitivity to change of Polish UCT is high, its MCID is 3, and its cut-off for well controlled disease is 12

The Polish UCT was sensitive to detect changes in disease control, with strong or very strong correlations between its changes and those of the UAS28, CU-Q_2oL total score, Phy-VAS and Pat-VAS scores (Table 5). The correlations of the changes of UCT scores were higher with those of other patient-reported outcomes as compared to those of physician-based assessments.

The mean (±SD) change in the UCT value, when a minimal improvement of disease activity (1-step improvement in Pat-LS) was reported by the patients, was found to be 3.3 ± 2.3 points. In contrast, in patients with no change in Pat-LS, the mean ± SD change in the UCT value was 0.4 ± 1.6 points.

Variable	UCT	
	R Spearman	*p-values*
UAS28	−0.68	<0.01
CU-Q_2oL	−0.72	<0.01
Phy-VAS	0.63	<0.01
Pat-VAS	−0.74	<0.01

Table 3. Convergent validity of the Polish Urticaria Control Test (UCT). *UAS28, Urticaria Activity Score 28 days summary; CU-Q_2oL, Chronic Urticaria Quality of Life Questionnaire; Phy-VAS, Physician's rating of disease control on visual analogue scale; Pat-VAS, Patient's self-rated disease activity on a visual analogue scale; R, Spearman correlation coefficient: negative in case of reciprocal correlation and positive in case of convergent correlation*

	N	UCT		*p-value*
		Median	IQR	
UAS28				<0.01
≤6	16	16	14–16	
7–24	32	12	11–13	
25–64	34	9	7–11	
≥65	24	7	2–8	
Pat-LS				<0.01
No complaints	18	16	14–16	
Mild complaints	37	12	11–14	
Moderate complaints	28	9	8–10	
Severe complaints	23	5	1–6	
Phy-LS				<0.01
No control	18	5	0–7	
Little control	29	9	4–10	
Moderate control	22	12	8–13	
Good control	24	14	12–14	
Complete control	13	16	15–16	
Pat-Therapy				<0.01
Effective	58	12	10–14	
Ineffective	48	7	3–9	
Phy-Therapy				<0.01
Effective	63	12	11–14	
Ineffective	43	8	4–8	

Table 4. Banding and known groups validity of the Polish Urticaria Control Test (UCT). *UAS28, Urticaria Activity Score 28 day summary; Pat-LS, Patient's self-rated disease activity on a Likert Scale; Phy-LS, Physician's rating of disease control on a Likert Scale; Pat-Therapy, Patient's self-rated of therapy effectiveness; Phy-Therapy, Physician's assessment of therapy effectiveness; IQR, interquartile range;* p-values for Kruskal-Wallis test

Variable	Δ UCT	
	R Spearman	*p*
Δ UAS28	−0.84	<0.01
Δ CU-Q_2oL	−0.70	<0.01
Δ Phy-VAS	0.62	<0.01
Δ Pat-VAS	−0.74	<0.01

Table 5. Sensitivity to change of the Polish Urticaria Control Test (UCT). Δ, *changes in scores between 1st and 2nd FU visit; UAS28, Urticaria Activity Score 28 day summary; CU-Q_2oL, Chronic Urticaria Quality of Life Questionnaire; Phy-VAS, Physician's rating of disease control on visual analogue scale; Pat-VAS, Patient's self-rated disease activity on a visual analogue scale; R, Spearman correlation coefficient*

Cut-off value	Phy-LS	
	Sensitivity (%)	Specificity (%)
<9	98	44.5
<10	96	53.9
<11	92.5	62.3
<12	**89.0**	**74.9**
<13	68.9	88.1
<14	49.3	100
AUC (95% CI)	0.91 (0.85–0.97)	

Table 6. Cut-off values for the Urticaria Control Test (UCT) for screening patients for poorly-controlled disease. *Phy-LS, Physician's global assessment of disease control; AUC, Area Under the Curve; CI, Confidence Interval*

ROC curve analyses identified an UCT value of 12 to have the best balance of sensitivity (89%) and specificity (75%) to distinguish well-controlled CSU (≥12 points) from poorly-controlled CSU (<12 points) with an AUC of 0.91, ie, with high accuracy (95% CI: 0.85–0.97) (Table 6, Supplementary Figure 2).

In CSU, disease activity, quality of life impairment, and disease control are strongly correlated

Disease activity (UAS), impact (CU-Q20L), and control (UCT) in patients with CSU were strongly correlated (all R coefficients >0.6, all $p < 0.01$), with UCT: CU-Q_2oL showing the highest correlation ($R = -0.72$; $R = 0.66$ for UCT:UAS28 and 0.62 for UAS28:CU-Q_2oL; Table 7). Changes in the UCT, the UAS28 and the CU-Q_2oL between the first and second follow up visit were also strongly correlated (Table 8).

In CSU patients, recurrent angioedema and coexisting CIndU do not affect how disease activity, quality of life impairment, and disease control are linked

The correlations of disease activity, quality of life impairment, and disease control were very similar in patients with and without recurrent angioedema (maximum change in $R = 0.03$) as well as in patients with or without comorbid CIndU (maximum change in $R = 0.02$) (Table 7). Recurrent

UCT – CU-Q2oL	$R = -0.72$	$p < 0.01$
	$R^* = -0.75$	$p^*<0.01$
	$R^{**} = -0.73$	$p^{**}<0.01$
UCT – UAS28	$R = -0.66$	$p < 0.01$
	$R^* = -0.64$	$p^*<0.01$
	$R^{**} = -0.64$	$p^{**}<0.01$
UAS28 – CU-Q2oL	$R = 0.62$	$p < 0.01$
	$R^* = 0.61$	$p^*<0.01$
	$R^{**} = 0.60$	$p^{**}<0.01$

Table 7. Relation between disease activity, impact, and control in chronic spontaneous urticaria patients. *UCT, Urticaria Control Test; UAS28, Urticaria Activity Score 28 day summary; CU-Q_2oL, Chronic Urticaria Quality of Life Questionnaire; R, correlation coefficient; p, statistical significance value; *, adapted values after controlling for recurrent angioedema using partial correlation; **, adapted values after controlling for coexisting chronic inducible urticaria using partial correlation*

Δ UCT – CU-Q2oL	R = −0.71	p < 0.01
	R* = −0.73	p*<0.01
	R** = −0.72	p**<0.01
Δ UCT – UAS28	R = −0.84	p < 0.01
	R* = −0.81	p*<0.01
	R** = −0.82	p**<0.01
Δ UAS28 – CU-Q2oL	R = 0.65	p < 0.01
	R* = 0.64	p*<0.01
	R** = 0.62	p**<0.01

Table 8. Relation between disease activity, control and impact in chronic spontaneous urticaria patients. *(Δ, changes in scores between 1st and 2nd FU visit; UCT, Urticaria Control Test; UAS28, Urticaria Activity Score 28 day summary; CU-Q_2oL, Chronic Urticaria Quality of Life Questionnaire; R, correlation coefficient; p, statistical significance value; *, adapted values after controlling for recurrent angioedema using partial correlation; **, adapted values after controlling for coexisting chronic inducible urticaria using partial correlation)*

angioedema or coexisting CIndU also did not affect the correlation of changes in disease activity, quality of life impairment and disease control (Table 8).

DISCUSSION

This study confirms that disease activity, impact, and control in CSU are strongly linked, and we are among the first to show that their changes are strongly correlated as well. Importantly, we show for the first time that the strength of these correlations is unaffected by the presence or absence of recurrent angioedema or coexisting CIndU, demonstrating their stability across major CSU subpopulations. Finally, we report the newly validated Polish UCT and its clinimetric properties.

The Polish version of the UCT is very similar to the original UCT in its validity, reliability, sensitivity to change, MCID, and cut-off for well-controlled disease.[11,22] Our results demonstrate high levels of validity, reproducibility, and reliability of the Polish UCT, comparable to other studies and other versions of the UCT and indicating excellent reproducibility.[11,16] Additionally, like other language versions, the newly developed Polish UCT showed significant correlations with anchor tools assessing disease activity and impact, ie, we found negative correlations with UAS28, CU-Q_2oL, and Pat-VAS as well as positive correlations with Phy-VAS.[11,13,16]

An important aspect of our study is that we assessed the Polish UCT's cut-off value and its MCID. Notably, we found the same cut-off value to discriminate well-controlled (≥12 points) and poorly-controlled (<12 points) disease as previous studies with other language versions (German, Arabic, Korean, and Turkish), which indicates methodological coherence.[11,14–16] Additionally, we confirm the previously published MCID of 3 points. Most of the previous studies demonstrated the same MCID.[13,16,23] Accordingly, our results indicate that the Polish UCT performs similarly to previously reported language and country versions of the UCT. Differences in comparison with other studies probably resulted from the anchors used in determining the response. Other levels were determined in studies in which 3 control steps were used.[15] Additionally, these differences may result from different conditions related to patient enrolment and kind of therapy, which impact on symptom improvement.[15]

Disease control is a major treatment goal in CSU. At present, it is largely unclear how treatment-induced changes in the UAS, UCT, and CU-Q_2oL compare. There are, actually, very few studies on this. A German study showed a strong correlation between disease control and activity as well as strong correlation of changes in these parameters.[3] In a Japanese study, the UCT correlated stronger than UAS with quality of life assessed with the dermatology life quality index (DLQI).

Furthermore, similar relations were demonstrated when analyzing parameter changes.[24] This was explained by the fact that one of the UCT's questions is on quality of life impairment, but other factors may have contributed.[24]

To the best of our knowledge this study is only the third to analyse the relationships of disease activity, impact, and control in CU. Furthermore, it must be underlined that, contrary to the Japanese study, we used an urticaria-specific quality of life questionnaire.[24] We observed a stronger correlation between the UCT and the CU-Q_2oL in comparison to the UAS and the CU-Q_2oL relation, with lack of a significant influence of angioedema and comorbid CIndU. We are not surprised by the lack of CIndU effects on the relations of the outcomes analyzed as this type of CU is not taken on board in the UAS and CU-Q_2oL. On the other hand, surprisingly, we did not observe any influence of angioedema. Angioedema factors into the results of both, the UCT and the CU-Q_2oL, but not the of UAS. The most likely explanation for the fact that angioedema did not influence the relationship of these measure or their changes is that we only included, in our study, CSU patients with wheals (with or without angioedema) and not patients with recurrent angioedema without wheals. In most patients with CSU who present with wheals and angioedema, recurrent angioedema frequency and activity is linked to the intensity of whealing, and changes in one usually parallel those of the other.

The strength of our study is that we provide precise data on the relation between disease control, activity and impact and the possible role of angioedema and CIndU in this dependency. To explore this relationship, we performed a careful and structured translation of the UCT into Polish including cognitive debriefing and examination of all major clinimetric properties relevant for the use and interpretation of the Polish UCT in clinical trials and routine care. One limitation of our work is that we did not include children and adolescents, for which the tools used were not designed or validated. Another limitation is that we did not include in our study CSU patients with isolated angioedema. Additionally, in the group of patients with comorbid angioedema we did not use angioedema-focused questionnaires as these tools are not validated into Polish.

In conclusion, we report the Polish version of the UCT and its validation, and in doing so, we confirm that it is a valuable and reliable tool for assessing the disease status of patients with CSU in terms of the control they have of their disease. More importantly, we demonstrate that the activity and the impact on QoL and the levels of disease control that CSU patients have over their disease as well as their changes are linked to each other strongly, yet not perfectly. This supports the recommendation to assess all 3 of these patient-reported outcomes in routine clinical practice, before and after the initiation of therapy. Importantly, this is a valid approach across different subgroups of CSU patients, ie, patients with and without comorbid CIndU and CSU patients who develop wheals with or without angioedema. Further studies are needed to better understand how disease activity, impact and control as well as their changes are linked in pediatric patients with CSU and in CSU patients with angioedema but without wheals.

Abbreviations

AUC, area under the curve; CIndU, chronic inducible urticaria ; CSU, chronic spontaneous urticaria; CU-Q_2oL, Chronic Urticaria Quality of Life questionnaire; CU, chronic urticaria; DLQI, dermatology life quality index; MCID, minimal clinically important difference; Pat-LS, patient's Likert Scale; Pat-VAS, patient's global assessment of disease activity; Phy-LS, physician's Likert Scale; Phy-VAS, physician's global assessment of disease control; ROC, receiver operating characteristic; UAS, Urticaria Activity Score; UCT, Urticaria Control Test; VAS, visual analogue scale.

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Authors' contributions

ZB, KBB, MM and KW designed the study and wrote the manuscript. ZB and KBB collected the data. ZB, KBB and TH performed the statistical analysis and interpretation of the results. All authors read and approved the final manuscript.

Ethical approval

The study was approved by the Ethics Committee of the Medical University of Silesia, Katowice, Poland (KNW/0022/KB1/18/15).

Consent for publication
This manuscript is original, has not been published before, is not currently being considered for publication elsewhere, and has not been posted to a preprint server.
Authors' consent for publication was obtained.

Availability of data and materials
Data are available on reasonable request.

Declaration of competing interest
Authors declare no conflict of interest.

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Appendix A. Supplementary data
Supplementary data to this article can be found online at https://doi.org/10.1016/j.waojou.2022.100635.

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