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Fric Test Revisited: A Suggestion for a New Scoring System and Its Correlation with Urticaria Control Test and Dermatology Life Quality Index

Pelin Kuteyla Can Pırıl Etikan Utkan Kızıltaç Kübra Kızıltaç Ralfi Singer
Emek Kocaturk

Department of Dermatology, Okmeydanı Training and Research Hospital, Istanbul, Turkey

Keywords

Fric test · Inducible urticaria · Physical urticaria · Provocation test · Quality of life · Symptomatic dermographism · Urticaria Control Test

Abstract

Background: Fric test is a useful tool for the diagnosis and threshold testing for symptomatic dermographism. When threshold testing is not available, Urticaria Control Test (UCT) and Dermatology Life Quality Index (DLQI) might be used to assess disease control and quality of life (QoL) impairment, respectively. **Objectives:** In this study, we aimed to describe a new scoring system for the Fric test and evaluate the correlations of Fric scores with UCT, DLQI, and other disease activity assessment scores. **Method:** Provocation test with Fric Test 4.0 was performed in all patients at referral and at the 4th week. We considered a 4-grade rating score for Fric Test (0–4) [Total Fric Score (TFS)]. A positive response with all of the four pins suggested severe dermographism (TFS = 4), while a wheal with only the largest pin (4.5 mm) was considered as milder disease (TFS = 1). Treatment responses were evaluated with Fric Test 4.0, UCT, patient's global assess-

ment of disease severity (PatGA-VAS), the physician's global assessment of disease control (PhyGA-VAS), and DLQI at baseline and at the 4th week of treatment. The correlations of TFS with UCT, DLQI, PatGA-VAS, PhyGA-VAS at baseline as well as the changes in the mean scores after treatment (week 4) were performed. **Results:** The mean UCT and DLQI scores were 8.69 ± 3.40 and 7.88 ± 6.02 at the first visit. At the second visit, TFS decreased from a mean of 2.79 ± 1.68 to 1.91 ± 1.85 ($p < 0.001$), and UCT scores and PhyGA-VAS were increased ($p < 0.001$), while DLQI scores, PatGA-VAS, and pruritus scores decreased significantly ($p = 0.002$; $p = 0.001$; $p = 0.012$). There was a positive correlation between TFS and pruritus scores ($r = 0.378$) and DLQI scores ($r = 0.392$). TFS was found to have a negative correlation with UCT score ($r = -0.283$) and PhyGA-VAS ($r = -0.347$). **Conclusions:** This new Fric scoring system allows comparison with other tools and shows moderate correlations with most of the tools. Using disease-specific tools is recommended since they provide a subjective evaluation of disease severity, QoL impairment, and disease control.

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Introduction

Symptomatic dermographism (SD) (urticaria factitia, dermographic urticaria) is the most common subtype of physical urticaria (PU) with a prevalence of 1–5% in the general population [1–3]. SD constitutes about 50% of PU [4], and it is defined as the development of strip-shaped wheals and itching and/or burning within seconds to minutes following the shear force acting on the skin [1, 2, 4]. Wealing persists for 1.5–2 h [1, 4]. SD has to be distinguished from simple dermographism, which is characterized as the transient dermographic weal without itching [2, 4]. The disease has a long course, 6.5 years on average [1, 2, 4]. It affects everyday life and impairs quality of life (QoL) significantly [1, 4, 5]. The diagnosis is based on history and provocation testing [2, 6]. Provocation testing can be performed by a blunt smooth object (e.g., closed ballpoint pen tip, wooden spatula), the Fric test (longest pin), or a dermographic tester (36 g/mm²) [2]. But threshold testing is also needed to assess disease activity and treatment responses. Threshold testing may be performed either with the Fric test or a dermographic tester [2, 7]. When threshold testing is not possible, treatment response may be evaluated with Urticaria Control Test (UCT) [7, 8]. Although there is a specific QoL instrument for SD under development [2], Dermatology Life Quality Index (DLQI) can be used to assess QoL of patients with SD [7]. Treatment includes trigger avoidance and pharmacological treatment [2]. Guidelines recommend a stepwise approach starting with second-generation H1 antihistamines (sg-AHs), and it has been demonstrated that the same algorithm that is available for chronic spontaneous urticaria can be implemented in chronic inducible urticarias (CINDU) [9, 10].

In this study, we aimed to describe a new scoring system for the Fric test and evaluate the correlations of Fric scores with UCT, DLQI, and other disease activity assessment scores.

Materials and Methods

Patient Selection and Data Collection

Fifty-eight patients with SD were included in this prospective noncontrolled study. Patients above 17 years old who were referred to our UCARE (Urticaria Centers of Reference and Excellence) [11] center between November 2016 and June 2017 were enrolled in the study. The diagnosis of SD was confirmed by using Fric Test 4.0 by two different dermatologists.

Demographic characteristics including age, gender, and disease duration were noted. Patients that were on treatment other than standard doses of H1-AHs at the time of referral and patients

under immunosuppressive treatment or systemic steroids were excluded. Patients stopped using oral AHs at least 72 h prior to Fric testing.

Study Design and Evaluation of Treatment Responses Based on Disease Activity, Symptom Control, and QoL Tools

The same treatment algorithm recommended by the European Academy of Allergology and Clinical Immunology/Global Allergy and Asthma European Network/European Dermatology Forum/World Allergy Organization (EAACI/GA²LEN/EDF/WAO) [6] was implemented for all patients, and treatment responses were evaluated with Fric Test 4.0, UCT, patient's global assessment of disease severity (PatGA-VAS), the physician's global assessment of disease control (PhyGA-VAS), and DLQI at baseline and 4th week of treatment.

Provocation test with Fric Test 4.0 was performed in the patients with SD at referral and every visit. Fric Test 4.0 (Moxie, Berlin, Germany) was applied perpendicular to the skin of the volar forearm with a pressure that all pins made complete contact. A pruritic palpable clearly visible weal with a width of ≥ 3 mm measured 10 min after provocation was considered as a positive response. Positive weal responses were seen with pins 3.0 (4th pin), 3.5 (3rd pin), 4.0 (2nd pin), and 4.5 mm (1st pin) in length (online supplement file; see www.karger.com/doi/10.1159/000492970 for all online suppl. material). We considered a 4-grade rating score for the Fric test (0–4) (Total Fric Score [TFS]). A positive response with all of the four pins, suggested severe dermographism (TFS = 4), while a weal with only the largest pin (4.5 mm) was considered as milder disease (TFS = 1). Patients were also asked to rank the strength of pruritus from 0 to 10 where Fric 4.0 was applied, which gave the pruritus score (0–10).

The Turkish versions of DLQI [12] and UCT [13] were administered to SD patients. UCT has 4 questions, and each has 5 answer options which are scored between 0 and 4 points. Total UCT score was calculated by summing all 4 individual item scores (0–16 points). A score of ≥ 12 indicates well-controlled urticaria and a score of < 12 points indicates poor disease control [8]. DLQI scores were grouped as 0–1 = no effect at all on patient's life, 2–5 = small effect on patient's life, 6–10 = moderate effect on patient's life, 11–20 = very large effect on patient's life, 21–30 = extremely large effect on patient's life [14].

The PatGA-VAS and PhyGA-VAS [8] were also used to assess the strength of patient complaints and to assess the control of the disease during the previous 4 weeks. While PatGA-VAS is a 10-cm line with 2 ends with “no complaints” (0 cm) at one end and “maximal complaints” (10 cm) at the other, PhyGA-VAS is a tool with 2 ends which are “not at all under control” (0 cm) and “completely under control” (10 cm).

The correlations of TFS with UCT, DLQI, PatGA-VAS, PhyGA-VAS at baseline as well as changes in the mean scores after treatment (week 4) were analyzed.

Statistical Analysis

Statistical analyses were performed using the SPSS software version 22.0 (Statistical Package for Social Sciences). All numerical variables were reported as the mean $\pm$ standard deviation, median (25th–75th percentile), minimum, maximum, frequency, and percentages. The levels of significance values were for differences in the mean UCT, DLQI, TFS, pruritus scores, PhyGA-VAS, and PatGA-VAS following the stepwise treatment approach. They were

calculated by the Wilcoxon signed rank test. Bivariate correlation statistics (Spearman rank correlation) was performed to determine the correlations between TFS and other parameters. Correlations were expressed as Spearman correlation coefficients. $r < 0.3$, $0.3-0.6$, and >0.6 were defined as weak, moderate, and strong, respectively. Statistical significance was achieved at $p < 0.05$ and $p < 0.01$. All analyses were performed using nonparametric methods.

Results

Patient Characteristics

Table 1 shows the demographic data of the patients and Fric responses at referral.

Fric Test, UCT, DLQI, PatGA-VAS, and PhyGA-VAS Scores of Patients

Treatment with sg-AH (either single dose or up dosing/combination treatment) resulted in significant increase in the mean UCT scores, PhyGA-VAS ($p < 0.001$), and significant decrease in DLQI scores, PatGA-VAS, and pruritus scores ($p = 0.002$; $p = 0.001$; $p = 0.012$). TFS also significantly decreased from a mean of 2.79 ± 1.68 to 1.91 ± 1.85 between the two visits ($p < 0.001$) (Table 2). The impact of SD on patient's life is shown in Table 2, as demonstrated by bands of DLQI. The number of patients and weal responses induced by Fric Test 4.0 at the 1st and 2nd visits are shown in Figure 1.

Correlation of Total Fric Score and UCT with Other Tools in All Patients

At referral, there was a significant positive correlation between TFS and pruritus score ($r = 0.378$, $p = 0.003$) and DLQI score ($r = 0.392$, $p = 0.002$). TFS was found to have a significant negative correlation with UCT score ($r = -0.283$, $p = 0.031$) and PhyGA-VAS ($r = -0.347$, $p = 0.008$). But when the correlation of change in the mean TFS with the mean change in other tools between 1st and 2nd visits was analyzed, there was a significant positive correlation observed between mean change in TFS and DLQI ($r = 0.405$, $p = 0.002$), and a significant negative correlation was observed between mean change in TFS and PhyGA-VAS ($r = -0.259$, $p = 0.049$). No significant correlations were identified between mean change in TFS and mean change in other tools. (UCT $r = -0.215$, $p = 0.106$, pruritus score $r = 0.232$, $p = 0.079$, PatGA-VAS $r = 0.243$, $p = 0.066$). UCT has a negative correlation with DLQI ($r = -0.523$, $p < 0.001$), pruritus score ($r = -0.285$, $p = 0.03$), and PatGA-VAS ($r = -0.753$, $p < 0.001$), and a positive correlation with PhyGA-VAS ($r = 0.839$, $p < 0.001$). Mean UCT change was also correlated with the

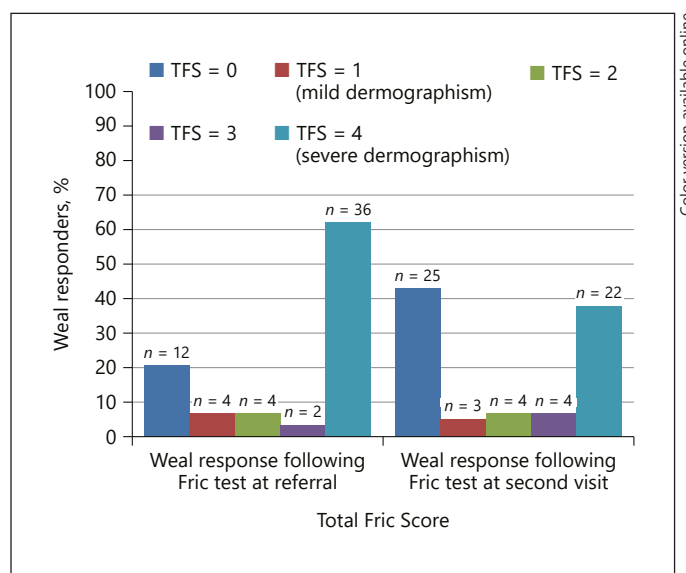


Fig. 1. Weal responses induced by Fric Test 4.0 at the 1st and 2nd visits.

Table 1. Demographic data and Fric test responses of patients with symptomatic dermographism at referral ($n = 58$)

<i>Age, years</i>	
Min-max (median)	17–72 (38.5)
Mean $\pm$ SD	36.9 $\pm$ 12.38
<i>Gender</i>	
Male	18 (31%)
Female	40 (69%)
<i>Duration of disease, months</i>	
Min-max (median)	2–240 (18)
Mean $\pm$ SD	31.8 $\pm$ 46.22
<i>Fric test at referral</i>	
<i>A positive response with:</i>	
None of the pins (TFS = 0)	12 (20.7%)
First pin (4.5 mm) (mild dermographism) (TFS = 1)	4 (6.9%)
First two pins (TFS = 2)	4 (6.9%)
First three pins (TFS = 3)	2 (3.4%)
All four pins (TFS = 4) (including 3-mm pin) (severe dermographism)	36 (62.1%)
SD, standard deviation; TFS, Total Fric Score.	

mean change in DLQI ($r = -0.410$, $p = 0.001$), PatGA-VAS ($r = -0.400$, $p = 0.002$), and PhyGA-VAS ($r = 0.687$, $p < 0.001$). No correlation was observed between mean change in UCT and pruritus score ($r = -0.126$, $p = 0.347$).

Table 2. Mean UCT, DLQI, bands of DLQI scores, pruritus scores, TFS, PatGA-Vas, and PhyGA-Vas of patients with symptomatic dermographism ($n = 58$)

	1st visit	2nd visit	<i>p</i> value
<i>UCT score</i>			
Min-max (median)	2–16 (8)	12–16 (12)	0.00000025
Mean ± SD	8.69±3.40	11.69±3.27	
<i>DLQI score</i>			
Min-max (median)	0–23 (6.5)	0–27 (3)	0.002
Mean ± SD	7.88±6.02	5.66±6.18	
<i>Pruritus score</i>			
Min-max (median)	0–10 (5)	0–10 (1)	0.012
Mean ± SD	4.17±3.4	2.93±3.45	
<i>TFS</i>			
Min-max (median)	0–4 (4)	0–4 (2)	0.000263
Mean ± SD	2.79±1.68	1.91±1.85	
<i>PatGA-Vas</i>			
Min-max (median)	0–9 (5)	0–10 (3)	0.001
Mean ± SD	4.74±2.36	3.64±2.52	
<i>PhyGA-Vas</i>			
Min-max (median)	2–10 (6)	2–10 (8)	0.000004
Mean ± SD	5.78±2.22	7.21±2.12	
<i>Bands of DLQI scores</i>			
No effect at all on patient's life	6 (10.3%)	15 (25.9%)	
Small effect on patient's life	19 (32.8%)	23 (39.7%)	
Moderate effect on patient's life	18 (31%)	13 (22.4%)	
Very large effect on patient's life	13 (22.4%)	4 (6.9%)	
Extremely large effect on patient's life	2 (3.4%)	3 (5.2%)	

DLQI, Dermatology Life Quality Index PatGA-VAS, Patient's Global Assessment of Disease Severity; PhyGA-VAS, Physician's Global Assessment of Disease Control; SD, Standard Deviation; TFS, Total Fric Score; UCT, Urticaria Control Test.

Discussion

SD is a debilitating condition and the most common form of CINDU that impairs QoL significantly [15, 16].

Although UCT, DLQI, VAS, and threshold testing may be used to evaluate disease activity and impact on QoL in CINDUs [7, 8, 17], the correlations between these tools have not been investigated. The EAACI/GA²LEN/EDF/UNEV (urticaria network e.V.) guidelines for the definition, diagnostic testing, and management of CINDU recommend determining disease activity and treatment response by measuring critical trigger thresholds [2]. Threshold testing can be performed by available instruments, a calibrated dermatographometer (HTZ Limited, New Addington, UK) [2, 18, 19], Fric Test 3.0 (Biomedizinische Werkstatte der Charite, Berlin, Germany) [7, 18] or Fric Test 4.0 (Moxie, Berlin, Germany) [3].

In this study, we used the Fric Test 4.0 dermatographometer, which is a validated instrument for diagnosis and threshold testing of SD. It is a flat plastic comb with 4 round-ended plastic pins with, respectively, 3.0, 3.5, 4.0, and 4.5 mm in length and in 3 mm diameter. Fric Test 4.0 has positive wealing responses similar to Fric Test 3.0, which is a former 6-pin Fric testing device with lengths of 2.5, 3.0, 3.5, 4.0, 4.5, and 5.0 mm (pins 1–4 of Fric Test 4.0, [length 3.0–4.5 mm] were similar to 3rd to 6th pins of Fric Test 3.0 [length 3.5–5.0 mm]). Fric Test 4.0 has 100% sensitivity and specificity for diagnosing the patients with SD and has similar responses with Fric Test 3.0 [3]. Schoepke et al. [3] numbered the pins of Fric test as 1–4, with lengths of 3.0, 3.5, 4.0, and 4.5 mm, and they compared the number of patients with response to each pin of the device but did not use a scoring system. Unlike Schoepke et al. [3], we used TFS which provides objective statistical analyses

of the treatment responses and allows comparison with other QoL and disease scoring tools. In this study, we demonstrated correlations of the Fric score with other tools (pruritus score [$r = 0.378$, $p = 0.003$], DLQI score [$r = 0.392$, $p = 0.002$], UCT score [$r = -0.283$, $p = 0.031$], PhyGA-VAS [$r = -0.347$, $p = 0.008$]), which has not been studied before. There are no similar studies in the literature that we may compare our findings with, but Maurer et al. [20] in a recent study evaluated the efficacy of omalizumab in SD. In that study, DLQI and critical friction thresholds (CFTs) were used as efficacy measures. Absence of weal with strongest friction strength (grade 4) was defined as complete response, while reduction of 2 or more Fric test grades was defined as partial response. The mean changes in these two tools were also evaluated. And they showed that treatment markedly reduces trigger thresholds and improves DLQI in patients with AH-refractory SD. Mean CFT at the baseline was 3.5 ± 0.8 , and DLQI was 11.1 ± 6.1 , which shows a very large effect on QoL [20]. In our study, mean TFS was 2.79 ± 1.68 , and DLQI was 7.88 ± 6.02 , which indicates a moderate effect on patient's life. Mean DLQI and CFT were higher than in our study because they included the AH-refractory cases to evaluate the efficacy of omalizumab in SD [20].

Although a specific QoL instrument for SD is under development [2, 7], currently DLQI may be used to assess QoL of patients with SD [7, 21]. In a survey, 42% (38/91) of SD patients claimed that QoL was significantly impaired and 7% (6/91) stated that a normal life was not possible [1]. In our study, SD caused a very large and an extremely large effect on life in 22.4 and 3.4% of patients, respectively (DLQI scores between 11 and 20 indicate very large effect, while 21–30 show extremely large effect on patient's life [14]).

UCT is a tool that evaluates disease control using four questions which determine the efficacy of treatment, overall disease control, QoL and control of signs and symptoms of the disease over the past 4 weeks. This validated instrument is suitable to introduce both patients with chronic spontaneous urticaria and patients with CINDU [6, 7]. VAS is also another objective tool that may be used to assess disease severity and response of symptoms to treatment [17].

Pruritus is the major diagnostic criterion that distinguishes SD from simple dermographism. A wheal response without itch indicates simple dermographism [2]. The Fric test can also be used to differentiate the two entities. In the study by Schoepke et al. [1], wheals were associated with pruritus in 95% of the patients. The mean pruritus VAS was 7.06 ± 0.24 [1], while it was 4.17 ± 3.4

in our study. It is lower in our study than in the mentioned study. The reason for that might be that Schoepke et al. [1] evaluated the intensity of the pruritus based on a questionnaire, and we evaluated the pruritus VAS following the Fric test. Another study also reported the mean pruritus score as 3.53 ± 0.40 following Fric Test 4.0 [3], which was also compatible with our result.

We also assessed the correlations between UCT and other parameters which assess the patient's situation in the last 4 weeks; and we have shown that they are more strongly correlated with UCT than with TFS. This might be due to the assessment time period of these tools; while TFS evaluates the time the patient came to the doctor's office, UCT evaluates the last 4 weeks. UCT has a moderately negative correlation with DLQI and strong correlations with PatGA-VAS and PhyGA-VAS. Mean UCT change also has moderate correlations with mean change in DLQI and PatGA-VAS, and a strong correlation with mean change in PhyGA-VAS. Again, the reason for moderate correlations with the DLQI might be linked to the time of assessment, which is the last week for the DLQI.

In this study, we found that TFS is an objective, practical disease-specific scoring system that has moderate positive correlations with pruritus score, DLQI score and a weak negative correlation with UCT score and a moderate negative correlation with PhyGA-VAS. However, the mean changes in TFS score had only significant moderate correlations with DLQI and negative weak correlations with PhyGA-VAS, but not with UCT, pruritus score, and PatGA-VAS. The lack of correlations between mean changes in TFS and those tools at the 1st and 2nd visits is thought to be due to stopping H1-AHs 3 days prior to the visits (when Fric tests are undertaken). But we have also shown that in some patients weal responses had changed from all of the pins to none of the pins following the sg-H1-AH treatment, which also proves that Fric Test 4.0 is a reliable tool to evaluate treatment response. At referral, 36 (62.1%) patients had a TFS of 4 (positive weal response with all of the pins meaning severe dermographism), while 46 (79.3%) of the patients had positive weal response with the first pin. Mehta et al. [22] reported that only 4 subjects had severe response on the Fric test (all four pins positive), while positive response with the largest pin was found in 28 (93.3%) of the SD patients. Schoepke et al. [3] reported that 50% of the patients had positive weal responses with all of the pins, while all of the patients had positive weal response with the longest pin ($n = 30$).

We believe that we made a mistake by having the patients wean off the AHs prior to Fric testing at the second visit; that resulted in false-positive testing or a wrong in-

terpretation of the treatment responses (as if the AH did not work). If the patients were under AH treatment during Fric testing, then we would be able to evaluate the suppressing effect of the AH and thereby its efficacy. Therefore, we recommend stopping AHs before Fric testing for provocation but not to stop for evaluating treatment responses (threshold testing). On the other hand, all scores and scales except TFS and pruritus score actually assess previous 4 weeks, so discontinuation of AHs 3 days before the evaluation does not seem to affect these scores and scales. Mehta et al. [22] stated that cessation of AHs for 3 days (48–72 h) before the treatment would be an acceptable time for assessment of Fric test response in symptomatic patients except for the drugs like doxepin.

In conclusion, we suggest using the Fric scoring system we introduced in other studies as it provides an objective assessment of the treatment responses by providing a numerical score and enables comparison with other tools. Using disease-specific instruments and QoL measures ensures a better patient care.

Statement of Ethics

This study was approved by Okmeydanı Training and Research Hospital Institutional Review Board (IRB protocol approval number: 525, 48670771-514.10, 11.10.2016) and was conducted according to the principles of the Declaration of Helsinki. All participants gave signed informed consent.

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Author Contributions

All authors read and approved the manuscript and agreed to the submission of the manuscript to the *Journal*.

E.K., *P.K.C.* contributed to the conception and design of the study, editing the figures, and preparation, drafted the article and critically revised the manuscript. *P.K.C.*, *P.E.* contributed to the acquisition and interpretation of the data. *P.K.C.* contributed to analysis of the study. *E.K.*, *P.K.C.*, *P.E.* revised and approved the final version of the manuscript. *U.K.*, *K.K.* contributed to the acquisition and interpretation of the data and revised critically and approved the final version of the manuscript. *R.S.* contributed to interpretation of the data and revision of the manuscript. *R.S.* approved the final version of the manuscript.

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