

Itch in patients with cutaneous T-cell lymphoma as a quality of life indicator



Rosanne Ottevanger, MD,^a Sylvia van Beugen, MSc, PhD,^b Andrea W. M. Evers, MSc, PhD,^b Rein Willemze, MD, PhD,^a Maarten H. Vermeer, MD, PhD,^a and Koen D. Quint, MD, PhD^a

Background: Cutaneous T-cell lymphoma (CTCL) is a chronic and progressive disease that has a major impact on quality of life (QoL).

Objectives: To describe the impact of the different stages of disease in patients with classical mycosis fungoides, folliculotropic mycosis fungoides, and Sézary syndrome on generic- and dermatology-specific QoL and the relation with itch.

Methods: A cross-sectional cohort study of patients with classical mycosis fungoides, folliculotropic mycosis fungoides, and Sézary syndrome was performed. Outcomes were the Skindex-29 score, Impact of Chronic Skin Disease on Daily Life which includes a visual analogue scale itch, and RAND-12.

Results: One hundred six patients with CTCL were included. Compared to the total mycosis fungoides group, patients with Sézary syndrome had significantly worse Skindex-29 scores. Patients with advanced disease had statistically higher scores for the symptom ($P = .007$), functioning ($P = .002$), and total score ($P = .012$). The degree of itching was strongly correlated with the total Skindex-29 score ($R = 0.713$, $P < .001$).

Conclusion: The different stages of CTCL can have a significant effect on multiple domains of generic- and dermatology-specific QoL. Itch was strongly correlated with QoL and therefore can be used as an overall QoL indicator. The effect on QoL, even in patients with early-stage disease, should not be underestimated. (JAAD Int 2022;9:57-64.)

Key words: cutaneous T-cell lymphoma; itch; mycosis fungoides; quality of life; RAND-12; Sézary syndrome; Skindex-29.

INTRODUCTION

Primary cutaneous T-cell lymphomas (CTCLs) comprise a heterogeneous group of diverse entities that present in the skin with no evidence of extracutaneous disease at the time of diagnosis.¹ Mycosis fungoides (MF) is the most common type

and mostly has an indolent clinical course. The different stages vary from localized patches/plaques to potential tumors.² Besides the classical MF (cMF), folliculotropic mycosis fungoides (FMF) is considered as a variant with distinctive clinical and pathological features that potentially has a more aggressive

From the Department of Dermatology, Leiden University Medical Center, Leiden, the Netherlands^a; and Institute of Psychology, Health, Medical and Neuropsychology Unit, Leiden University, Leiden, the Netherlands.^b

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were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Patient consent: Participants provided informed consent in order to participate in the study.

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Correspondence to: Rosanne Ottevanger, MD, Albinusdreef 2, 2333 ZA, Leiden, the Netherlands. E-mail: r.ottevanger@lumc.nl. 2666-3287

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disease course than cMF.³ Sézary syndrome (SS) is the leukemic variant, defined by the triad of erythroderma, lymphadenopathy, and blood involvement.¹

A recent systematic review shows that CTCL has a significant effect on quality of life (QoL), with a more profound effect in patients with more advanced disease.⁴ However, few studies account for the different stages of CTCL on the different domains of QoL.⁴ Awareness of the specific affected domains in patients with CTCL could help to improve QoL. Furthermore, the QoL in patients with FMF is not yet investigated.

Also, the QoL could also be more affected in newly diagnosed patients, which needs further elaboration as this could be clinically relevant.^{5,6} In daily practice, itch is a common but burdensome symptom and the relationship with QoL needs to be further assessed.⁴

The current study aims to describe the impact of the different disease stages in Dutch patients with cMF, FMF, and SS on the generic- and dermatology-specific QoL.

METHODS

This cross-sectional cohort study included patients in the outpatient clinic of the Department of Dermatology in the Leiden University Medical Center between September 1, 2020, and January 31, 2021, and was approved by the institutional review board (N20.052). Within the study period, 198 patients were approached for participation. Patients diagnosed with cMF, FMF, and SS were invited to complete questionnaires if they were aged >18 years and were able to provide a formal written consent. All included patients were diagnosed according to the clinicopathologic criteria of the World Health Organization-European Organization for Research and Treatment of Cancer.¹

Patients were asked to complete questionnaires related to their generic- and dermatology-specific QoL. In addition, baseline characteristics were extracted from their medical records.

Disease stages were defined as early stage (IA-IIA) and late stage (\geq IIB without erythroderma). Patients with erythrodermic CTCL (with or without blood and/or lymph node involvement) including erythrodermic MF and FMF were considered as a separate group from the late-stage disease patients.⁴ As

erythrodermic patients experience a different impact on QoL than patients with late-stage disease, they could be considered as a distinct group from patients with late-stage disease (eg, patients with a small solitary tumor versus an erythrodermic patients).

The classic Charlson comorbidity index (CCI) was used to describe the degree of comorbidities. The CCI was calculated excluding the primary disease and was categorized into low (0-1) and high number of comorbidities (\geq 2).⁷

CAPSULE SUMMARY

- The different stages of cutaneous T-cell lymphoma can have a significant effect on the quality of life, even in patients with early-stage disease, which therefore should not be underestimated.
- Itch was strongly correlated with dermatology-specific quality of life and therefore can be used as an overall quality of life indicator.

Outcome measurements

For the different types and stages of CTCL, the outcomes were the dermatology-specific QoL measured by the Skindex-29, the RAND-12 as a generic QoL questionnaire, and the Impact of Chronic Skin Disease on Daily Life including a visual analogue scale itch.⁸⁻¹⁰

Statistical analysis

Statistical analysis was performed with IBM SPSS statistics 25 and reported following the Strengthening the Reporting of Observational studies in Epidemiology (STROBE) guidelines.¹¹ Sum scores for all items were calculated according to corresponding instrument manuals. Continuous data were reported as median and interquartile range (P₂₅-P₇₅) due to non-normal distribution and categorical data as number and percentage (%). Normality of data distribution was tested with the Kolmogorov-Smirnov test. There was no correction for missing values as all participating patients fully completed the questionnaires.

Disease impact of CTCL on QoL for cMF, FMF, and SS and at the different stages of disease (early, late, and erythrodermic disease) was compared using nonparametric bivariate Mann-Whitney *U* tests. Kruskal-Wallis test was used as a nonparametric test for continuous outcomes of 3 or more groups. Statistical tests were performed for the total group of patients, including the nonaffected patient category in case of the Skindex-29.

The clinical categories of the domains were compared using a chi-square or Fisher's exact test. Furthermore, differences in duration since the diagnosis (<2 years and \geq 2 years) and number of comorbidities were used to test for differences in the different domains.

The correlation between the degree of itching and the QoL was assessed using the Pearson's R

Abbreviations used:

CCI:	classic Charlson comorbidity index
cMF:	classical MF
CTCL:	cutaneous T-cell lymphoma
FMF:	folliculotropic mycosis fungoides
MF:	mycosis fungoides
PCS:	physical component score
QoL:	quality of life
SS:	sézary syndrome
STROBE:	Strengthening the Reporting of Observational studies in Epidemiology

correlation analysis. Statistical significance was assumed if $P < .05$.

RESULTS

Study population

In total, 106 patients with CTCL were included with a median age of 64 years (Table I). Most patients were diagnosed with early-stage cMF ($n = 43/106$; 41%). There were 35 patients (33%) with late-stage cMF or FMF (MF group) included in this study. All of these patients had stage IIB. Sixteen patients with erythrodermic CTCL (15%) were included. In this cohort, all participating patients with disease stage III/IV were erythrodermic.

There was no difference between cMF, FMF, or SS for gender ($P = .13$), comorbidities ($P = .36$), or the median time between completion of the questionnaires and time of diagnosis ($P = .24$).

Skindex-29

cMF, FMF, and SS. Overall, 58 patients (55%) were not affected on the total Skindex-29 score (Table II). The symptoms domain was not affected in 54 patients (51%), 52 (49%) were not affected regarding emotions, and 66 (63%) regarding functioning. In the cMF group, 37 (57%), 32 (49%), 45 (69%), and 40 patients (62%) were not affected in the symptoms, emotions, functioning, or total domains, respectively. In the FMF group, this was 13 (48%), 14 (52%), 16 (59%), and 14 (52%) for symptoms, emotions, functioning, and total score, respectively. In the SS group, 4 patients (29%) in the symptoms domain, 6 (43%) in the emotional domain, 5 (36%) in the functioning domain, and 4 patients (29%) with the total score were not affected.

There were no statistical differences between patients with cMF and FMF regarding the Skindex-29 for all domains (symptoms, $P = .23$; emotions, $P = .63$; functioning, $P = .09$; and total score, $P = .18$) (Table II). cMF and FMF were therefore pooled (MF group). Compared to the MF group, patients with SS had significantly lower Skindex-29 scores on the symptoms ($P = .004$), functioning ($P = .005$), and total

($P = .019$) domains, but not on the emotional domain ($P = .35$).

Early-stage, late-stage, and erythrodermic CTCL. Patients with advanced disease had a higher disease burden for the symptoms domain ($P = .007$), functioning ($P = .002$) domain, and the total score ($P = .012$), but not for the emotional domain ($P = .28$) (Table II). The emotional domain was mildly affected across all stages and types of disease. Within the cMF and FMF groups, there were no statistical differences between patients with early- and late-stage disease on all domains of the Skindex-29. Patients with erythrodermic CTCL had higher Skindex-29 scores regarding symptoms ($P = .011$) and functioning ($P = .027$), but not for the emotions ($P = .62$) and total score ($P = .07$) compared to the MF group.

Time since diagnosis. Patients diagnosed with a CTCL < 2 years had lower dermatology-related QoL scores on all domains than patients diagnosed ≥ 2 years (symptoms, $P = .010$; emotions, $P = .007$; functioning, $P = .032$; and total score, $P = .006$) (Supplementary Tables, available via Mendeley at <https://doi.org/10.17632/w547r9366k.1>).

Comorbidities. In the higher CCI group, the Skindex-29 was more often affected regarding symptoms ($P = .013$), functioning ($P = .008$), and the total score ($P = .013$) compared to the lower CCI group, except for the emotions domain ($P = .27$) (Supplementary Tables).

RAND-12

cMF, FMF, and SS. Patients with SS had a statistically significantly lower physical component score (PCS) ($P = .003$) and mental component score (MCS) ($P = .041$) compared to the combined MF group (Table III). No statistically significant difference for PCS or MCS was found between the cMF and FMF group ($P = .44$ and $P = .07$, respectively).

Early-stage, late-stage, and erythrodermic CTCL. Overall, there was a lower PCS ($P = .001$) and MCS ($P = .048$) in the higher disease stages (Table III).

Within the cMF group, there was no statistical difference between patients with early- and late-stage disease for the PCS ($P = .33$) and the MCS ($P = .98$). This also accounted for the FMF group (PCS, $P = .35$ and MCS, $P = .27$), although these differences between early- and late-stage disease were considered clinically relevant based on the > 5 -point difference. Erythrodermic patients had a significantly lower PCS than patients with late-stage disease ($P = .019$), but not a statistically different MCS ($P = .09$).

Time since diagnosis. There was no statistical difference in patients diagnosed with a CTCL < 2

Table I. Patient characteristics

Patient characteristic	Total, N = 106	MF, N = 65	FMF, N = 27	SS, N = 14
Age	64 (53-72)	63 (55-71)	54 (41-73)	68 (63-78)
Age at diagnosis	59 (46-66)	56 (47-64)	50 (37-66)	65 (59-74)
Time since diagnosis				
<2 y	35 (33%)	18 (28%)	10 (37%)	7 (50%)
≥2 y	71 (67%)	47 (72%)	17 (63%)	7 (50%)
Gender				
Male	69 (65%)	43 (66%)	20 (74%)	6 (43%)
Female	37 (35%)	22 (34%)	7 (26%)	8 (57%)
CCI	1 (0-2)	1 (0-2)	0 (0-2)	2 (0-3)
0	50 (47%)	31 (48%)	14 (52%)	5 (36%)
1	21 (20%)	16 (25%)	3 (11%)	2 (14%)
2	16 (15%)	9 (14%)	5 (19%)	2 (14%)
3	12 (11%)	5 (8%)	4 (15%)	3 (21%)
4	5 (5%)	2 (3%)	1 (4%)	2 (14%)
5	2 (2%)	2 (3%)	-	-
Disease stage				
Early stage	55 (52%)	43 (66%)	12 (44%)	-
Late stage	35 (33%)	21 (32%)	14 (52%)	-
Erythrodermic	16 (15%)	1 (2%)	1 (4%)	14 (100%)

Numbers are displayed as number (%) or median (interquartile range).

CCI, Charlson comorbidity index; FMF, folliculotropic mycosis fungoides; MF, mycosis fungoides; SS, Sézary syndrome.

and ≥2 years for the PCS ($P = .42$) or MCS ($P = .25$) (Supplementary Tables).

Comorbidities. The PCS was statistically lower in the high comorbidity group ($P = .046$) compared to the low comorbidity group. The MCS showed no statistical differences for between groups ($P = .08$) (Supplementary Tables).

Impact of Chronic Skin Disease on Daily Life

cMF, FMF, and SS. There were no statistical differences for any of the subdomains in the ISDL between the cMF and FMF groups other than the FMF group having a higher score on the impact on relations domain than patients with cMF ($P = .009$).

In general, patients with SS had a trend toward a higher perceived burden of disease compared with the combined MF group (Supplementary Tables). However, compared to patients with SS, the combined MF group did not report lower degrees of stigmatization ($P = .91$), anxiety ($P = .27$), negative mood ($P = .41$), positive mood ($P = .96$), social network ($P = .07$), acceptance of their disease ($P = .32$), experienced benefits ($P = .27$), and impact on their partner ($P = .22$) or family ($P = .46$).

Early-stage, late-stage, and erythrodermic CTCL. Late-stage disease was more affected in skin status ($P \leq .001$), itching ($P = .001$), pain ($P = .001$), fatigue ($P = .044$), conscious scratching ($P = .013$), automatic scratching ($P = .016$), general impact on daily life ($P = .006$), activities ($P = 0.004$),

eating and sleeping ($P = .027$), relationships ($P = .013$), and helplessness ($P = .001$).

No statistical differences were found within the cMF group between early- and late-stage disease of any of the domains besides that patients with early-stage cMF reported less pain than late-stage patients (1 [1-1] versus 2 (1-3.5), $P = .021$).

Within the FMF group, no statistical differences were found between early and late stage on any domains. Only in the early-stage disease group, patients with FMF reported a higher degree of pain (1 [1-5]) than patients with cMF (1 [1-1]) ($P = .039$). No statistical differences were found within the late-stage disease group between cMF and FMF for any of the domains.

Time since diagnosis. Patients diagnosed with a CTCL <2 year scored higher on the itching ($P \leq .001$), pain ($P = .006$), fatigue ($P = .011$), conscious scratching ($P = .006$), automatic scratching ($P = .046$), scratching at night ($P = .001$), general impact ($P = .014$), activities ($P = .014$), relationships ($P = .001$), partner ($P = .003$), family ($P = .002$), and acceptance ($P = .016$) scales compared to patients diagnosed with CTCL ≥2 years (Supplementary Tables).

Comorbidities. Patients with high comorbidities reported higher degrees of itching ($P = .004$), pain ($P = .012$), fatigue ($P = .008$), and higher impact of activities ($P = .048$) but had higher acceptance of their disease ($P = .020$) than patients with low comorbidities (Supplementary Tables).

Table II. Skindex-29 scores categorized by the different types and stages of MF, FMF, and SS

Skindex-29 Disease Cutoff point	Symptoms				Emotions				Functioning				Total			
	Mild ≥39	Moderate ≥42	Severe ≥52	Sum	Mild ≥24	Moderate ≥35	Severe ≥39	Sum	Mild ≥21	Moderate ≥32	Severe ≥37	Sum	Mild ≥25	Moderate ≥32	Severe ≥44	Sum
Total group	7 (7%)	19 (18%)	26 (25%)	36 (21-52)	22 (21%)	6 (6%)	26 (25%)	25 (13-38)	16 (15%)	4 (4%)	20 (19%)	10 (2-30)	11 (10%)	21 (20%)	16 (15%)	22 (11-38)
Early (n = 55)	5 (9%)	10 (18%)	9 (16%)	32 (21-46)	15 (27%)	1 (2%)	10 (18%)	23 (13-30)	6 (11%)	1 (2%)	7 (13%)	6 (0-21)	6 (11%)	10 (18%)	3 (96%)	20 (11-31)
Late (n = 35)	1 (3%)	7 (20%)	8 (23%)	36 (21-50)	5 (14%)	3 (9%)	11 (31%)	25 (13-43)	6 (17%)	2 (6%)	7 (20%)	13 (2-33)	3 (9%)	7 (20%)	7 (20%)	24 (9-43)
Erythrodermic (n = 16)	1 (6%)	2 (13%)	9 (56%)	59 (37-74)	2 (13%)	2 (13%)	5 (33%)	31 (19-46)	4 (25%)	1 (6%)	6 (38%)	29 (17-52)	2 (13%)	4 (25%)	6 (38%)	39 (24-54)
MF group	6 (9%)	11 (17%)	11 (17%)	32 (20-48)	16 (25%)	4 (6%)	13 (20%)	25 (13-36)	10 (15%)	1 (2%)	9 (14%)	6 (0-27)	7 (11%)	11 (17%)	7 (11%)	21 (9-34)
Early (n = 43)	5 (12%)	8 (19%)	5 (12%)	32 (21-46)	13 (30%)	1 (2%)	7 (16%)	23 (10-30)	6 (14%)	1 (2%)	5 (12%)	4 (0-25)	5 (12%)	8 (19%)	2 (5%)	18 (11-31)
Late (n = 21)	1 (5%)	3 (14%)	5 (24%)	36 (16-54)	3 (14%)	3 (14%)	5 (24%)	25 (14-39)	4 (19%)	-	3 (14%)	10 (1-26)	2 (10%)	3 (14%)	4 (19%)	22 (9-36)
Erythrodermic (n = 1)	-	-	1 (100%)	64	-	-	1 (100%)	53	-	-	1 (100%)	52	-	-	1 (100%)	55
FMF group	1 (4%)	6 (22%)	7 (26%)	39 (25-57)	4 (9%)	-	9 (33%)	23 (10-45)	3 (11%)	2 (7%)	6 (22%)	19 (4-33)	3 (11%)	6 (22%)	4 (15%)	24 (15-43)
Early (n = 12)	-	2 (17%)	4 (33%)	39 (23-60)	2 (17%)	-	3 (25%)	23 (15-43)	-	-	2 (17%)	9 (3-19)	1 (8%)	2 (17%)	1 (8%)	22 (16-34)
Late (n = 14)	-	4 (29%)	3 (21%)	39 (24-52)	2 (14%)	-	6 (43%)	28 (10-48)	2 (14%)	2 (14%)	4 (29%)	27 (8-43)	1 (7%)	4 (29%)	3 (21%)	31 (11-46)
Erythrodermic (n = 1)	1 (100%)	-	-	39	-	-	-	23	1 (100%)	-	-	23	1 (100%)	-	-	27
SS group (n = 14)	-	2 (14%)	8 (57%)	59 (35-76)	2 (14%)	2 (14%)	4 (29%)	31 (17-42)	3 (21%)	1 (7%)	5 (36%)	29 (15-53)	1 (7%)	4 (29%)	5 (36%)	39 (21-51)

Numbers are displayed as number (%) or median (interquartile range).

The Skindex-29 is a validated 29-item questionnaire that specifically addresses the QoL in patients with skin disease.⁸ Individual items measure the frequency of affected QoL on 5 levels using 5-point scales ranging from 1 ('never') to 5 ('all the time'). The individual items can be categorized into 3 separate domains: symptoms, emotions, functional limitations, and as a total score. Each of the domains have suggested cutoff points.

Cutoff points for the Skindex-29: These are ≥39, ≥42, and ≥52 for mild, moderately, and severely impaired for the symptoms domain; ≥24, ≥35, and ≥39 for emotions domain; and ≥21, ≥32, and ≥37 for the functional limitation domain, respectively. The cutoff points for the total Skindex-29 score is ≥25 for mild, ≥32 for moderate, and ≥44 for severe impairment. In case of scores below the lowest cutoff, category for mildly impaired was regarded as not affected.

Patients who scored in the unaffected category were not described in the categorical descriptions in Table I. The percentage of patients within the mild, moderate, or severe groups are described as the percentage of the whole group (including the unaffected category).

FMF, Folliculotropic mycosis fungoides; MF, mycosis fungoides; SS, Sézary syndrome.

Table III. The PCS and MCS of the RAND-12 according to disease and disease stage of MF, FMF, and SS

RAND-12	PCS (0-100)	MCS (0-100)
Total group (N = 106)	53 (46-57)	49 (40-54)
Early (n = 55)	56 (50-57)	51 (43-56)
Late (n = 35)	53 (42-56)	48 (39-56)
Erythrodermic (n = 16)	41 (35-52)	41 (30-52)
MF group (N = 65)	54 (49-57)	51 (44-56)
Early (n = 43)	55 (60-57)	51 (44-56)
Late (n = 21)	54 (45-56)	51 (41-57)
Erythrodermic (n = 1)	48	42
FMF group (N = 27)	53 (42-57)	47 (36-53)
Early (n = 12)	56 (49-57)	50 (39-55)
Late (n = 14)	52 (38-57)	44 (35-51)
Erythrodermic (n = 1)	34	42
SS group (N = 14)	41 (35-52)	40 (30-52)

Numbers are displayed as number (%) or median (interquartile range).

The RAND-12 Health Survey (RAND-12) is a shorter version of the RAND-36 questionnaire and is a validated instrument that measures the impact of disease with a physical component score (PCS) and mental component score (MCS). The 2 domains range from 0 to 100, with higher scores correlating with a better health status, with a score differences of 3 to 5 points being considered clinically meaningful.

FMF, Folliculotropic mycosis fungoides; MF, mycosis fungoides; SS, Sézary syndrome.

Itch score

The itch score conducted in the ISDL showed that within the cMF group patients with early-stage disease did not have a statistically different itch scores compared to late-stage disease ($P = .23$). This was also the case for patients with FMF ($P = .47$). Also, the itch score did not differ in the early-stage patients with cMF and FMF ($P = .13$) and in the late-stage disease patients with cMF and FMF ($P = .75$) (Supplementary Tables). Patients with a more recent diagnosis and higher CCI had a higher visual analogue scale itch ($P = .006$ and $P = .001$, respectively) (Supplementary Tables).

Correlations between itch and QoL. The itch scale of the ISDL was strongly correlated with the total Skindex-29 score ($R = 0.713$, $P < .001$) (Fig 1) and the symptom domain of the Skindex-29 ($R = 0.78$, $P < .001$) and moderately with the emotional ($R = 0.560$, $P < .001$) and functional score ($R = 0.599$, $P < .001$). The degree of itching was very weakly associated with the PCS of the RAND-12 ($R = -0.186$, $P = .06$) and weakly associated with the MCS ($R = -0.307$, $P = .001$).

DISCUSSION

This study shows that cMF, FMF, and SS can have a significant effect on multiple domains of generic-

and dermatology-specific QoL; however, QoL is not affected in approximately half of the patients regarding dermatology-specific QoL. The affected QoL varied between patients within the different stages of the CTCL types. Patients with more advanced disease and those with a more recent diagnosis of a CTCL were more affected regarding symptoms and functioning. However, the emotional domains were consistently affected in half of the patients across cMF, FMF, SS, and all different stages of disease. Itch was strongly associated with a more impaired skin-related QoL. The results illustrate that the effect of CTCL on QoL, even in some patients with early-stage disease, should not be underestimated.

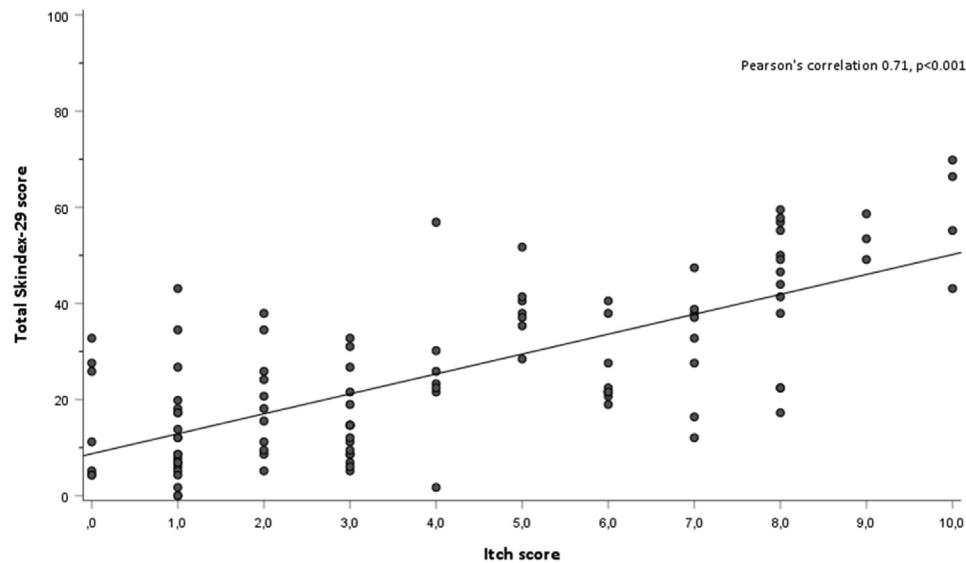
In line with previous studies, QoL in patients with late-stage disease were more affected in the symptoms and functioning domains than early-stage patients.^{5,6,12-14} Despite patients with erythrodermic CTCL reporting the most severe impact on QoL, some erythrodermic patients were only mildly affected.

It was remarkable that the emotional domain was relatively consistently affected across the different disease stages. The difference between early- and late-stage disease of the emotional domain scores was more pronounced in the study by Herbosa *et al* and Porkert *et al*.^{6,14} This could be due to sample size limitations, cultural differences, or differences in the clinical guidance of patients. Furthermore, the emotional domain could be more affected by the diagnosis “lymphoma” independently of the disease stage.

This study is the one of the few studies in the literature to separately report on patients with erythrodermic CTCL and therefore provide a more detailed insight into the effect of the different stages of disease on QoL. In addition, to our knowledge, this is the first study to report on QoL in the different stages of disease of patients with FMF. Few differences were found between the cMF and FMF groups, probably because early cMF and early FMF both have an indolent disease course.

Itch seems to be an important symptom that correlates with an impaired QoL.¹⁵ Therefore, optimal symptom control of itching is important as itching can have a profound effect on quality of sleep and mood, which consequently can affect multiple other domains.¹⁶ However, it is known that itching can be a difficult symptom to treat and is subject to high interindividual differences.¹⁷

Furthermore, patients with a more recent diagnosis of a CTCL were more affected in the symptoms and functioning domains and had more intense itch. This could be due to the fact that it takes time for



A coefficient of 0-0.19 was considered very weak, 0.2-0.39 weak, 0.40-0.59 moderate, 0.60-0.79 strong, and 0.80-1.0 very strong.

Fig 1. Cutaneous T-cell lymphoma. Scatterplot and Pearson's R correlation of the itch score and the total Skindex-29 score.

therapies to have an effect and establish disease regression/stabilization and proper symptom control. However, illness perception and coping strategies can evolve over time.¹⁸ This could be important to realize and provide additional support in the early phase of treatment. Future studies would benefit from evaluating the QoL over time in newly diagnosed patient and measure the effect of different therapies.

Limitations in the current study are the influence of selection bias in nonresponders and the fact that the current and prior treatments and their benefits/side effects were not taken into account.

This broad assessment of QoL on multiple domains provides a useful insight in the influence of cMF, FMF, and SS and their different stages of disease on QoL. Evaluation of QoL should be integrated in the daily routine as the disease can severely affect QoL.¹⁴ Together with an assessment of the QoL, disease severity, and patients' treatment goals, the best treatment decision can be made. By assessing QoL domains, a timely referral to social workers, psychologists, or sexologists can be made if necessary.

CONCLUSION

The different stages of cMF, FMF, and SS can have a significant effect on multiple domains of generic- and dermatology-specific QoL. Itch strongly correlates with a more impaired dermatology-specific QoL and therefore can be used as an overall QoL

indicator. Patients with advanced disease and those with a more recent diagnosis were more affected regarding symptoms and functioning. The effect of CTCL on QoL, even in some patients with early-stage disease, should not be underestimated.

Transparency statement

The guarantors affirm that the manuscript is an honest, accurate, and transparent account of the study being reported, that no important aspects of the study have been omitted, and that any discrepancies from the study as originally planned (and, if relevant, registered) have been explained.

Access to data and data analysis

RO, KQ, and MV had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Data sharing statement

Relevant anonymized data on individual patients for meta-analysis purposes can be provided upon reasonable request to the principal investigator.

Conflict of interest

None declared.

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