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Gender disparities in health-related quality of life (HRQoL) in patients with cutaneous T-cell lymphoma

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ABSTRACT

Background: Patients with cutaneous T-cell lymphoma (CTCL) often experience debilitating symptoms that impair health-related quality of life (HRQoL). Existing evidence for HRQoL differences with respect to gender is conflicting.

Objective: To investigate potential gender differences in HRQoL for patients with CTCL.

Methods: We performed a cross-sectional study to assess HRQoL in patients with CTCL by partnering with the Cutaneous Lymphoma Foundation to distribute an electronic survey from February to April 2019.

Results: A total of 292 patient responses (66% women, mean age 57 years) were included in the analysis. Most of the cohort had early-stage (IA–IIA) (74%; 162/203) mycosis fungoides (MFs) (87%; 241/279), followed by Sézary syndrome (SS) (12%; 33/279). Women with CTCL experienced significantly worse HRQoL compared with men (Skindex-16: 51±26 vs. 36±26, $P \leq 0.001$; FACT-G: 69±21 vs. 77±16, $P = 0.005$). This gender difference was present even when controlling for stage of disease. Women experienced worse HRQoL in all three of the Skindex-16 subscales (symptoms: $\beta = 14.0$, $P \leq 0.001$; emotions: $\beta = 15.1$, $P \leq 0.001$; functioning: $\beta = 11.3$, $P = 0.006$), but only two of the four FACT-G subscales (physical: $\beta = -2.8$, $P \leq 0.001$; emotional: $\beta = -2.0$, $P = 0.004$).

Limitations: Due to the method of distribution of the survey, we were unable to estimate a participant response rate. Participants' diagnosis and stage were self-reported.

Conclusion: In this cohort women with CTCL experienced significantly worse HRQoL when compared to men. Additional studies are necessary to determine what factors contribute to this gender disparity.

Keywords: cutaneous T-cell lymphoma, gender disparity, health-related quality of life

Introduction

Primary cutaneous lymphomas (CL) are a heterogeneous group of non-Hodgkin lymphomas manifesting with a clonal proliferation of lymphocytes in the skin.[1,2] Cutaneous T-cell lymphoma (CTCL) is the most common CL subtype, representing approximately 75–80% of all CLs, with an incidence rate of 7.7 per 1,000,000 person-years.[3] The most common forms of CTCL include mycosis fungoides (MF) and Sézary syndrome (SS).[2] The clinical course of CTCL can span across years or even decades,[4] and health-related quality of life (HRQoL) is a key component in evaluating the success of patient care. Patients with CTCL can experience significantly impaired HRQoL due to intense pruritis, physical disfigurement, changes in functional status, and health distress.[5–7]

Healthy People 2020, a statement of national health objectives, defines a health disparity as a "particular type of health difference that is closely linked with social, economic, and/or environmental disadvantage".[8] Existing literature suggests health disparities play a role in a number of dermatologic conditions, and there is growing evidence for health disparities in CTCL.[9–13] However, existing literature are conflicted about differences in HRQoL by gender in CTCL. In this current study, we examined gender disparities in HRQoL in patients with CTCL.

What is known about this subject in regard to women and their families?

- Women often experience worse quality of life than men in a number of dermatologic conditions.
- Very few studies have addressed gender disparities in HRQoL among patients with CTCL.

What is new from this article as messages for women and their families?

- Women with CTCL experience significantly worse HRQoL compared to men at the same stage.
- Women experienced worse HRQoL in all 3 Skindex-16 subscales but only 2 of the 4 FACT-G subscales: physical and emotional wellbeing.

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Methods

A cross-sectional, anonymous electronic survey was administered between February and April 2019.[14] The survey was distributed via the Cutaneous Lymphoma Foundation (CLF) Facebook Group (approximately 1900 members at the time of distribution) and email listserv (approximately 1200 members). The study team did not directly access membership lists. Survey responses were collected and managed using REDCap electronic data capture tools at the University of Washington.[15,16] This study was determined to be exempt from review by the institutional review board of the University of Washington Human Division (STUDY00005784).

In addition to demographic items and items about participants' cutaneous lymphoma (type and stage), the visual analog scale for itch and 2 validated HRQoL instruments were used: Skindex-16 and Functional Assessment of Cancer Therapy (FACT-G).[17,18] Skindex-16 scores were calculated per Chren et al., transforming responses to a linear scale from 0 to 100. Total score and subscale scores were considered valid if at least 70% of the items had responses. Missing items in each subscale were imputed with the mean of the nonmissing items in the subscale. FACT-G scores were calculated according to the FACT-G Scoring Guidelines Version 4. Scores were calculated for each subscale and summed together to derive the total score, with lower scores indicating worse HRQoL. Subscale scores were considered valid if >50% of the items had responses (ie, ≥4 of 6 or 7 items per subscale). The total score was considered valid if >80% (≥22 of 27 items) had responses and all subscales were valid. Missing items in each subscale were imputed using the mean of nonmissing items in that subscale.

HRQoL scores and gender were compared using the Wilcoxon rank-sum test or Fisher's exact test. Linear regression models were used to examine mean differences in Skindex-16 or FACT-G. *P*-Values less than 0.05 were considered statistically significant. β-values are mean differences in Skindex-16 or FACT-G per change in the corresponding variable; estimates were derived using linear regression models. All statistical analyses were performed using STATA (version 14.0; StataCorp) and R software (version 4.0.0; R Foundation for Statistical Computing).

Results

A total of 372 responses were received. An exact response rate could not be calculated due to the survey distribution methods but is estimated between 12 and 30% based on the maximum (3100) and minimum (1240) number of patients who could have viewed the survey link. Seventy-three respondents stopped before the end of the survey (19.6%). These surveys and 7 (1.7%) additional responses from patients with CBCL were excluded from the final analysis, leaving 292 participants (66% women, mean age 57 years). Demographics of this cohort have been previously published.[14]

Most of the cohort had early-stage (IA–IIA) (74%; 162/203) MF (87%; 241/279), followed by SS (12%; 33/279). Among our respondents, women experienced significantly worse HRQoL when compared with men (Skindex-16: 51 ± 26 vs. 36 ± 26, $P \leq .001$; FACT-G: 69 ± 21 vs. 77 ± 16, $P = .005$) (Tables 1 and 2). In Skindex, higher is worse HRQoL; in FACT-G, lower is worse HRQoL. This gender difference was present even when controlling for the stage of disease (early versus advanced). Women experienced worse HRQoL in all 3 of the Skindex-16 subscales (symptoms: $\beta = 14.8$, $P \leq .001$; emotions: $\beta = 17.0$, $P \leq .001$; functioning: $\beta = 13.2$, $P = .001$) but only 2 of the 4 FACT-G subscales (physical well-being: $\beta = -2.8$, $P \leq .001$; emotional well-being: $\beta = -2.0$, $P = 0.004$) (Tables 1 and 2).

Table 1

HRQoL as measured by Skindex-16 and FACT-G by gender

	All	Women	Men	*P* Value
Skindex-16				
Total score	46 ± 27	51 ± 26	36 ± 26	<0.001
Symptoms subscale	39 ± 30	43 ± 29	29 ± 29	<0.001
Emotions subscale	58 ± 29	63 ± 28	46 ± 29	<0.001
Functioning subscale	35 ± 32	40 ± 33	26 ± 29	0.001
FACT-G				
Total score	71 ± 19	69 ± 21	77 ± 16	0.005
PWB subscale	20 ± 6	19 ± 7	22 ± 6	<0.001
SWB subscale	19 ± 7	18 ± 7	19 ± 7	0.23
EWB subscale	15 ± 6	14 ± 6	16 ± 5	0.007
FWB subscale	18 ± 6	18 ± 7	19 ± 5	0.13

Values are mean ± SD unless otherwise specified.

EWB, emotional well-being; FWB, functional well-being; PWB, physical well-being; SWB, social/family well-being.

Table 2

Association of gender with HRQoL

	β[a] (95% CI)	*P* Value
Skindex-16		
Total score	15.1 (8.6, 21.6)	<0.001
Symptoms subscale	14.8 (7.7, 21.9)	<0.001
Emotions subscale	17.0 (9.9, 24.1)	<0.001
Functioning subscale	13.2 (5.3, 21.0)	0.001
FACT-G		
Total score	−7.7 (−12.5, −2.9)	0.002
PWB subscale	−2.8 (−4.4, −1.2)	<0.001
SWB subscale	−1.1 (−2.8, 0.6)	0.21
EWB subscale	−2.0 (−3.4, −0.7)	0.004
FWB subscale	−1.5 (−3.0, 0.0)	0.052

EWB, emotional well-being; FWB, functional well-being; PWB, physical well-being; SWB, social/family well-being.

[a]Regression coefficient, corresponding to the mean change in HRQoL score per change in the associated variable.

Discussion

We found that in our cohort, women with CTCL experienced significantly worse HRQoL compared with men ($\beta = 14.2$; $P \leq .001$). Our findings are congruent with several recent studies. Sampogna et al.[6] reported that women treated for CTCL or CBCL experienced a worse HRQoL compared with men (OR = 1).[6] More recently, in the Prospective Cutaneous Lymphoma International Prognostic Index (PROCLIPI) study, Molloy et al.[19] reported women treated for MF or SS experienced a worse HRQoL compared with men ($\beta = 8.61$; $P = .003$).[19] In contrast, Porkert et al.[20] found no sex-specific differences in HRQoL, though the authors hypothesize that their finding may have been a result of "male predominance in the cohort."

The gender disparity we found among the patients with CTCL in this study is also consistent with studies investigating gender disparities in HRQoL in other chronic dermatological diseases. Women treated for psoriasis experience an impairment in HRQoL twice that observed in men.[21] Similarly, women with atopic dermatitis have worse HRQoL scores by means of the dermatology life quality index.[22] Gender-specific HRQoL disparities are also reported among patients with different types of cancers. A 1-year longitudinal study of patients with chronic lymphocytic leukemia, for example, found women experience globally worse HRQoL.[23,24] The gender disparities we found in our study adds to the growing body of evidence that gender disparities in HRQoL among patients with CTCL not only exist but also that gender disparities in CTCL are not unique to this particular disease.

We found women have worse HRQoL in all 3 of the Skindex-16 subscales but only 2 of the 4 in the FACT-G subscales. Using FACT-G, women reported worse physical and emotional well-being but no difference in social/family well-being and functional well-being when compared with men. Both Molloy et al.[19] and Sampogna et al.[6] also reported worse scores in the symptoms and emotions Skindex-16 subscales. Molloy et al.[19] reported women with CTCL experience worse HRQoL due to "more burning/stinging, pruritus, irritation and greater feelings of depression, shame, embarrassment and annoyance with their diagnosis."[19] This consistent gender disparity with respect to the experience of physical and emotional symptoms of living with CTCL across studies could be attributed to a number of socio-biological factors including biological difference, provider bias, trust gap, economic inequity, gender roles in society, or social genomics (the interaction between social environment and the functional activity of the genome). We find the increased emotional burden of CTCL for women of particular concern. In many cultures, women are subjected to a stigmatizing standard of beauty that may place a disproportionately high psychosocial burden on women with diseases affecting appearance.[25,26]

We found that compared to men, women reported worse functioning as measured by Skindex-16. In contrast, we did not find a gender difference in functional well-being as measured by FACT-G. This discrepancy between instruments may be related to the fact that Skindex-16 subscale questions on "function" focus on the particular effects of skin on quality of life and interaction with others, while FACT-G questions on "function" are more general in scope. This discrepancy between the Skindex-16 and FACT-G functional well-being subscale scores lends further urgency to the development and validation of a CTCL-specific HRQoL instrument.

Our study had a few limitations. The survey was distributed electronically and in a written form which may have been selected for populations that have higher socioeconomic status, increased access to technology, and higher educational level.[27] Sixty-six percent of our cohort identified as women, suggesting an over-representation of women, as CTCL generally has a higher incidence in men.[28] In addition, the majority (87%) of our cohort reported being treated for MF, which is higher than the estimated incidence rate of MF (54%) among patients with CTCL.[3] Due to the method of distribution of the survey, via email and Facebook, we were unable to estimate a participant response rate. In addition, participants' diagnosis and stage were self-reported, and given the anonymous survey design, we were unable to confirm this clinical data.

Previous literature suggests ongoing health disparities among gender and sexual minorities, including transgender, queer, and nonbinary individuals, underlying the importance of pursuing equitable research that benefits diverse patient populations.[29,30] We had only 2 respondents who identified their gender as "other," and we were not able to incorporate an analysis of these under-represented gender categories. Inconsistent terminology in our study and in the existing literature (female vs. woman, male vs. man, and gender vs. sex) also hinder our ability to analyze "gender" and "sex" as discrete categories and compare our data to previous literature.

In conclusion, we found that HRQoL is significantly worse for women with CTCL compared with men, even when adjusting for the stage of the disease. Additional research is necessary to clarify how individual factors contribute to these differences in HRQoL between men and women to disentangle the likely complex etiology of this gender disparity. A granular understanding of gender disparity among patients with CTCL is essential to help physicians and healthcare institutions provide the most equitable care to their patients to holistically improve HRQoL.

Conflicts of interest

None.

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Study approval

This study was determined to be exempt from institutional review board review by the University of Washington Human Subjects Division.

Author contributions

CWC, HMM, ETL, and MMS: Participated in research design, writing of the paper, and performance of the research. ET: Participated in research design, and writing of the paper. DSH Participated in data analysis.

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