

# Skin-Related Quality of Life in HIV-infected Patients on Highly Active Antiretroviral Therapy

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## Abstract

*Background:* The overall health status and survival of HIV-infected patients has changed with the advent of highly active antiretroviral therapy (HAART). With this improved survival, there is a greater urgency to study quality-of-life issues.

*Objective:* Our objectives were to measure skin-related quality of life in a cohort of HIV-infected patients and to determine whether the use of highly active antiretroviral therapy is associated with improved skin-related quality of life.

*Methods:* We assembled a retrospective cohort of patients who were seen in our HIV-Dermatology Clinic at San Francisco General Hospital in June, July, or August of 1996. Eligible subjects were contacted by mail and asked (1) to complete a questionnaire (Skindex) and (2) to have a skin exam. Information on medication use and laboratory parameters was also collected.

*Results:* Of 107 eligible patients, 76 (71%) responded to the questionnaire; 60 patients were examined. Many patients had multiple skin conditions. For most diagnoses (except warts and onychomycosis), there were no consistent differences in Skindex scores of HIV-infected patients compared with scores of patients not known to be infected with HIV. Patients on HAART for longer duration had significantly lower Skindex scores (improved skin-related quality of life) compared with those on HAART for a shorter duration.

*Conclusion:* HAART is associated with improved quality of life with regard to HIV-associated skin diseases.

## Sommaire

*Antécédents:* L'état de santé général et le taux de survie des patients infectés par le VIH ont changé grâce à l'avènement de traitements antirétroviraux hautement actifs (HAART). Cette amélioration du taux de survie implique un besoin urgent d'étudier les questions relatives à la qualité de vie.

*Objectifs:* Mesurer la qualité de vie sur le plan dermatologique d'une cohorte de patients infectés par le VIH et déterminer si le recours à un traitement antirétroviral hautement actif est associé à une amélioration de la qualité de vie sur le plan dermatologique.

*Méthodes:* Nous avons rassemblé une cohorte rétrospective de patients qui étaient suivis dans notre clinique de dermatologie-VIH au *San Francisco General Hospital*, en juin, juillet ou août de 1996. Nous avons contacté par courrier les sujets admissibles et leur avons demandé (1) de remplir un questionnaire (Skindex) et (2) de se soumettre à un examen dermatologique. Également, nous avons recueilli de l'information sur la consommation des médicaments et les paramètres de laboratoire.

**Résultats:** Parmi les 107 patients admissibles, 76 (71%) ont retourné le questionnaire et 60 ont été examinés. Un grand nombre de patients présentaient multiples affections cutanées. Dans la plupart des diagnostics (sauf pour les verrues et les onychomycoses), les différences sont minimales entre les résultats du Skindex des patients infectés par le VIH et ceux des patients qui ne le seraient pas. Les patients qui ont suivi le traitement HAART pendant une plus longue durée accusent des résultats Skindex sensiblement inférieurs (meilleure qualité de vie sur le plan dermatologique) à ceux des patients ayant suivi un traitement HAART pendant une plus courte durée.

**Conclusion:** Le traitement HAART est associé à une qualité de vie améliorée en ce qui concerne les maladies dermatologiques liées du VIH.

The overall health status of HIV-infected patients has changed with the advent of highly active antiretroviral therapy (HAART).<sup>1-4</sup> This therapy has been responsible for a dramatic increase in survival of HIV-infected patients.<sup>5,6</sup> With this improved survival, there is a greater urgency to study quality-of-life issues. How do diseases and their treatments affect the lives of our HIV-infected patients? What aspects of disease bother them the most?

Most previous studies of skin diseases in patients infected with HIV were performed before HAART was available and did not assess the impact of skin disease on patients' quality of life.<sup>7-11</sup> Our objective was to measure skin-related quality of life in a cohort of HIV-infected patients. Since most of the patients in the cohort were taking HAART, we also examined whether more prolonged use of this treatment was associated with improved skin-related quality of life.

## Patients and Methods

### Patient Samples

We assembled a retrospective cohort of patients who were seen in our HIV-Dermatology Clinic at San Francisco General Hospital in June, July, or August of 1996. Our rationale was that this time period marked the beginning of widespread release and use of protease inhibitors, and most eligible patients likely began therapy with these agents around that time. Patients in this clinic were referred from HIV clinics as well as from community primary care clinics. All patients were considered eligible unless data about their CD4 counts or viral load were not available or unless a patient had been on protease inhibitor therapy for greater than 3 months prior to the start of the study. Patients taking at least two nucleoside analogs and at least one protease inhibitor or non-nucleoside reverse transcriptase inhibitor were defined as being on HAART therapy.

Eligible subjects were contacted by mail during the period from January 1998 through May 1998 and asked (1) to complete a questionnaire and (2) to come to clinic for a skin examination. Patients who were unable to come to clinic were asked only to mail back the questionnaire. Patients who did not respond to the mail request were sent a reminder letter. The study was approved by the Committee on Human Research at the University of California, San Francisco.

Skin-related quality of life in the patient sample was compared with that of a previously assembled sample of dermatology patients who were not known to be infected with HIV. This group consisted of consecutive patients waiting for appointments in general dermatology practices in Cleveland, Ohio, whose responses were used in the psychometric testing of Skindex.<sup>12</sup>

### Measures

Demographic information, baseline CD4 count, most recently available CD4 count and viral load data, and medication history were obtained from the medical record or from the hospital's computerized information system. Dermatologic examinations were conducted by one of the authors (TM or TB), all of whom have extensive expertise in HIV dermatology. The examinations included assessments of the skin, hair, nail, oral, and genital areas. All skin diseases were noted on a standardized form.

The questionnaire consisted of 45 items and included Skindex, a validated 29-item instrument to measure the effects of skin diseases of any type on patients' quality of life.<sup>12</sup> Three of us (TG, TM, PM) reviewed the items of Skindex to determine if they adequately assessed possible skin-related concerns specifically of HIV-infected patients.<sup>13</sup> Based on this review, we added one HIV-specific item to the parent Skindex instrument: "My skin condition makes it difficult for me to concentrate." Patients also responded to an open-ended question: "What is it about your skin condition that bothers you the most?" In addition, patients responded to four items of the health distress scale of the MOS-HIV, a validated generic instrument for measuring quality of life in HIV-infected patients.<sup>14</sup> The aim of the health distress questions is to measure discouragement, despair, and fear about health problems. The MOS-HIV has been validated for several subsets of HIV-infected patients, including those with early asymptomatic disease, and injection drug users. Finally, we asked patients whether they had ever taken any of four common protease inhibitor agents.

### Scoring and Statistical Analysis

Our overall analytic strategy was to measure the skin-related quality of life of the patients and to determine its relation to the duration of HAART therapy.

To document the kinds of skin diseases diagnosed in

this population, we reported all diagnoses although a given patient often had more than one diagnosis. To compare patients by diagnosis, we categorized patients according to the diagnosis that was bothering the patient the most, in the judgment of the dermatologist. Six diagnostic categories were defined: onychomycosis, inflammatory skin diagnoses (such as eczematous dermatitis or seborrheic dermatitis), isolated benign lesions (such as actinic keratosis or lentigo), warts or molluscum contagiosum, condyloma accuminata, and skin problems that were primarily related to appearance (such as hyperpigmentation). To compare patients taking HAART for different durations, we assigned patients to two categories: "early start" if they had started these medications before or during November 1996 (within the first 6 months of the study) and as "late start" if they had started them after November 1996.

Results for Skindex are reported as three scale scores representing three specific aspects of quality of life (symptoms of skin diseases, effects of skin diseases on functioning, and effects on emotions). Each scale score is the mean of items comprising a scale, as previously described.<sup>12</sup> A composite score was also calculated as the mean of the item responses. Scores vary from 0 to 100; higher Skindex scores indicate greater effects on quality of life. Responses to the open-ended question regarding how patients were most bothered by their skin disease were evaluated, categorized, and rank-ordered by one of us (PM).

Differences between groups were evaluated using chi-square or *t*-test analyses. Multiple linear regression analyses were used to analyze Skindex composite scores controlling for duration of HAART use (early vs. late start), number of skin diagnoses, and diagnostic category. Statistical analysis was performed with Excel (Microsoft Corp., Redmond, WA) and Statistical Package for the Social Sciences (SPSS) (SPSS, Inc., Chicago, IL).

## Results

Of the 191 patients who were seen in the clinic during June–August 1996, 66 patients were excluded for lack of CD4 count or viral load or they had used protease longer than 3 months. Eight patients were deceased, and for 10 patients no home address was available. The final eligible sample who were contacted consisted of 107 patients (56% of the total number of patients seen in clinic). Of this eligible group, 76 patients (71%) responded to the questionnaire. Of these 76 patients, 60 (79% of those on whom surveys were available) were examined.

Patients ranged in age from 29 to 65 years (mean = 42 years) (Table I). Patients were mainly white (66%), male (99%), and homosexual (87%). Most patients (76%) had CD4 counts above 200 mm<sup>3</sup> and in almost half (46%) the viral load was undetectable. Mean CD4 count at baseline was 267 mm<sup>3</sup> and improved to 354 mm<sup>3</sup> at the most recent measure. The majority of patients (91%) reported that they had taken HAART at some time. This number

**TABLE I**

**Patient characteristics (n = 76)**

<b>Age</b>	
Mean	42
Range	29–65
<b>Sex</b>	
Men	75 (99%)
<b>Ethnicity</b>	
White	50 (66%)
Hispanic	16 (21%)
Black	6 (8%)
Asian	2 (3%)
Other	1 (1%)
<b>HIV risk factors</b>	
Sex	66 (87%)
IVDA and sex	6 (8%)
Blood products and sex	3 (4%)
Unknown	3 (4%)
<b>CD4 counts (mm<sup>3</sup>)</b>	Mean = 354
<50	2 (3%)
50–199	19 (25%)
200–499	36 (47%)
>500	18 (24%)
<b>Viral loads (log)</b>	Median = 4.3
<2.7 (undetectable)	35 (46%)
2.7–4	22 (29%)
4–5	15 (20%)
>5	3 (4%)
<b>HAART use</b>	
Never used	6
Early start (6 months)	49
Late start (after 6 months)	20
<b>Health status</b> (in general would you say your health is:)	
Excellent	3 (4%)
Very Good	28 (37%)
Good	33 (43%)
Fair	10 (13%)
Poor	1 (1%)
<b>Quality of life</b> (How have things been going for you?)	
Very good: could hardly be better	9 (12%)
Pretty good	31 (41%)
Good and bad parts about equal	27 (36%)
Pretty bad	6 (8%)
Very bad: could hardly be worse	1 (1%)

was 100% concordant with records of medication use in the patients' charts. Of the patients taking HAART, 64% had started these medications within the first 6 months of the study (early start).

Ninety percent of the patients reported that their general health was "good," "very good," or "excellent," and

TABLE II

Skin exams ( <i>n</i> = 60)	
Number of skin diagnoses	Number (%) of patients
0	4 (7%)
1	2 (3%)
2	12 (20%)
3	13 (22%)
4	15 (25%)
5	13 (22%)
6	1 (2%)
<b>Skin diagnoses</b>	
Onychomycosis	20 (33%)
Warts (includes verruca vulgaris and flat warts)	16 (27%)
Seborrheic dermatitis	14 (23%)
Tinea pedis	12 (20%)
Condyloma	12 (20%)
Postinflammatory pigment alteration	12 (20%)
Eczema	7 (12%)
Bacterial folliculitis	7 (12%)
Molluscum contagiosum	6 (10%)
Hyperpigmentation of nails or oral mucosa	6 (10%)
Actinic keratosis	6 (10%)
Xerosis	5 (8%)
Dermatofibroma	5 (8%)
Keratosis pilaris	5 (8%)
Kaposi's sarcoma	4 (7%)

53% reported that their overall quality of life was “pretty good” or “very good—could hardly be better.” On the health distress scale of the MOS-HIV, however, patients in this sample had significantly lower scores (indicating worse health status) than published values for asymptomatic patients and for “early ARC” patients (69.4 vs. 81.4 and 76.3 for asymptomatic and “early ARC” patients, respectively,  $p > 0.001$ ).<sup>14</sup>

On examination, the majority of patients had multiple skin diseases: 42 (55%) had three or more skin diagnoses, with the most being six diagnoses in one patient (Table II). Only 4 patients had a normal exam. The most common skin conditions were onychomycosis (present in 20 patients, 33%), warts (in 16 patients, 27%), and seborrheic dermatitis (14 patients, 23%).

In all diagnostic categories except warts and onychomycosis there was no consistent difference in Skindex scores of HIV-infected patients compared with those not known to be infected with HIV, although the small sample size limits the power to make statistical comparisons. Patients with warts and onychomycosis had higher scores in all three categories of symptoms, emotions, and functioning (indicating a worse skin-related quality of life) compared with the group not known to be HIV-infected (Table III).

TABLE III

Mean Skindex scores ( $\pm$ SD) of patients with selected dermatological diagnoses and persons without skin disease <sup>a</sup>			
Diagnosis (number of patients)	Symptom score	Emotions score	Functioning score
<b>Warts</b>			
Patients infected with HIV (6)	38 ( $\pm$ 23)	52 ( $\pm$ 38)	41 ( $\pm$ 32)
Patients not known to be infected with HIV (24)	23 ( $\pm$ 18)	22 ( $\pm$ 16)	6 ( $\pm$ 13)
<b>Onychomycosis</b>			
Patients infected with HIV (4)	53 ( $\pm$ 32)	47 ( $\pm$ 27)	35 ( $\pm$ 31)
Patients not known to be infected with HIV (31)	34 ( $\pm$ 22)	26 ( $\pm$ 22)	11 ( $\pm$ 13)
Norms <sup>b</sup> (107)	14 ( $\pm$ 12)	9 ( $\pm$ 13)	4 ( $\pm$ 8)

<sup>a</sup> All scales are scored from 0 (no effect) to 100 (maximal effect). Patients with HIV differed from those not known to be HIV-infected,  $p < 0.05$ .

<sup>b</sup> Persons not known to be infected with HIV and without skin disease.

TABLE IV

Answers to the question: “What is it about your skin problem that bothers you the most?” ( <i>n</i> = 98)		
	Categorized responses	Number (%) of mentions
Appearance	40	(41%)
Itching	18	(18%)
Recurrence, chronicity	15	(15%)
Concern about worsening	8	(8%)
Dry skin	7	(7%)
<b>Other</b>		
Symptom-related	6	(6%)
Emotion-related	4	(4%)

Only 18 patients (23%) responded that their skin condition “sometimes,” “often,” or “all the time” made it difficult for them to concentrate. The most common diagnoses in these patients were warts (33%) and inflammatory skin diseases (25%). In these patients, the mean number of skin diagnoses was similar to those stating that they never or rarely had difficulty concentrating (1.7 vs. 2.1,  $p = 0.40$ ).

In response to the open-ended question: “What is it about your skin condition that bothers you most?,” there were 98 mentions by 68 patients (80%) (Table IV). Of these mentions, 47 (48%) did not report specific quality-of-life effects of skin disease (e.g., appearance, dry skin). Of the remaining 51 mentions, 36 (71%) were about constructs addressed in the parent Skindex instrument. The remaining 15 mentions were about recurrence or chronicity of skin problems. No patient responded that the skin problem made it difficult to concentrate. Eighteen percent of patients mentioned itching as their most bothersome symptom. These responses are similar to those of patients not known to be affected by HIV.<sup>13</sup>

TABLE V

Skindex scores: comparison of patients with early vs. late start HAART use			
	Early start (n = 49)	Late start (n = 20)	p value
Emotions	30	46	0.009
Symptoms	28	47	0.0008
Function	21	38	0.001

Patients who had started HAART therapy sooner (early start) had significantly lower Skindex scale scores (indicating better skin-related quality of life) than other patients (Table V). Although CD4 count and viral load did not correlate significantly with Skindex scores, the trend was toward improved scores with higher CD4 count and lower viral load values. In a multivariate regression model controlling for duration of HAART use (early vs. late start), number of skin diagnoses, and diagnostic category, duration of HAART use was significantly associated with lower Skindex composite scores ( $p < 0.01$ ).

## Discussion

In this study we examined skin-related quality of life in a sample of HIV-infected patients by using Skindex, a generic measure for all skin diseases, and a variety of HIV-specific items. Patients in our study were relatively healthy by self report and laboratory assessment (71% with CD4 count  $> 200 \text{ mm}^3$  and 46% with viral load  $> 500 \text{ mm}^3$ ; increased mean CD4 count from  $267 \text{ mm}^3$  at baseline to  $354 \text{ mm}^3$  most recent). The profile of skin disease in our patients was similar to that seen in other published studies of skin disease in HIV-infected patients<sup>7-11</sup> prior to the availability of HAART (the majority had less than two skin diagnoses and they had inflammatory skin disease). Despite the high prevalence of multiple skin conditions, however, we found that for most diagnoses there were no consistent differences in Skindex scores of HIV-infected patients compared with those not known to be infected with HIV.

HIV-infected patients with warts and onychomycosis had higher Skindex scores (indicating worse skin-related quality of life) than did those patients not known to be infected with HIV. The especially recalcitrant nature of these diseases in HIV-infected patients may explain the notable impact on skin-related quality of life. Both warts and onychomycosis have been associated with HIV,<sup>15-17</sup> and there is some suggestion that the prevalence or severity of warts may be increased with HAART.<sup>18</sup> Although new oral therapies are available for onychomycosis, HIV-infected patients on multiple medications may not be able to take the medications.

Pruritus without any underlying skin disease has been reported as a significant problem in HIV-infected patients and may worsen with some protease inhibitors. When

asked specifically about itching, the majority of patients responded that they sometimes, often, or all the time had itching, and 18% of the patients in our cohort remarked that itching was their most bothersome skin symptom. We were unable to find any specific skin diagnoses in the group of patients with itching as a major complaint.

The majority of skin-related concerns were addressed by the generic Skindex. Only 23% of the respondents felt that their skin condition sometimes, often, or all the time made it difficult for them to concentrate; we were unable to identify any specific skin disease in this subgroup.

Studies done prior to the availability of HAART have indicated that skin disease in HIV patients is more severe and recalcitrant to treatment.<sup>7-11</sup> More recent case reports have highlighted the role of HAART in the resolution of some skin disease such as molluscum, Kaposi's sarcoma, and other infectious skin diseases.<sup>19-21</sup> In patients who still have skin disease after starting on HAART, it is unclear what impact that disease has on quality of life. Studies have shown improved overall quality of life in HIV-infected patients with the addition of a protease inhibitor to their medication regimen regardless of their virologic response.<sup>1,2</sup> We had postulated that longer HAART would be associated with better skin-related quality of life. Indeed, patients on HAART for longer duration had significantly lower Skindex scores (improved skin-related quality of life) compared with those on HAART for a shorter duration.

There are limitations to our study. The relatively small sample size may have restricted our ability to find true differences between HIV-infected patients and those not known to be infected with HIV. Like most HIV-infected patients seen in San Francisco, our sample is primarily gay, white, and male. Although response rates for the questionnaire and skin exam were good, the patients who responded to the questionnaire and who agreed to be examined may have been healthier, more compliant, or more concerned about their skin. Lastly, we cannot conclude that HAART itself was the cause of improved skin-related quality of life because we were unable to compare Skindex scores before and after initiation of HAART; other factors may have been involved.

Skin disease has been an important aspect of HIV infection since the early recognition of the disease. With improved treatment and survival, quality of life is emerging as an important health outcome. Further studies looking at changes in skin-related quality of life over time and with various treatments will provide dermatologists with important information about the care of HIV-infected patients.

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