

Patients with Hidradenitis Suppurativa Suffer from Low Health-Related Quality of Life as Measured by the Generic 15D Instrument

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Keywords

Acne inversa · Hidradenitis suppurativa · Quality of life · International Hidradenitis Suppurativa Severity Score System · 15D

Abstract

Introduction: Hidradenitis suppurativa (HS) is a chronic inflammatory skin disease associated with various comorbidities and diminished quality of life (QoL). Among dermatological conditions, HS is reported to most severely diminish QoL. This study aimed to analyse the health-related QoL (HRQoL) of patients with HS in more detail by using generic to disease-specific HRQoL questionnaires. Correlations between the HRQoL measures and HS disease severity measures were assessed. **Methods:** We analysed the HRQoL and clinical severity of patients with HS ($N = 92$) treated in 5 Finnish hospitals using HRQoL measurement tools most often used in dermatological clinics, as well as the generic 15D instrument (standardized and self-administered 15-dimensional measure of HRQoL). The disease severity was assessed using the Hurley stage, International Hidradenitis Suppurativa Severity Score System, and disease severity evaluation by the investigator. **Results:** The mean 15D score of HS pa-

tients was low and comparable with that of patients with cancers. No correlation was found between HS severity measures and 15D score, indicating that even mild HS has a high impact on HRQoL. **Conclusions:** Our findings strengthen the understanding about HS as a debilitating disease and even compared with non-dermatological conditions and highlight the need of comprehensive care of patients with HS.

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Introduction

Hidradenitis suppurativa (HS) is a chronic disease with inflammatory changes in areas with apocrine glands. The disease presents as inflammatory nodules, abscesses, draining tunnels, and scarring [1]. Patients with HS have a heightened risk of several somatic [2] and psychiatric comorbidities [3]. Furthermore, a decreased life span was observed in a Finnish registry-based study [4]. HS is one of the dermatological conditions that most affects patients' quality of life (QoL) [5] and presents with several issues, such as pain and impairment in sex life [6].

An HS-specific QoL questionnaire was recently developed [7]. Until now, the Dermatology Life Quality Index

(DLQI) was used most to study the QoL of patients with HS [6]; however, the DLQI does not allow the direct comparison between the health-related QoL (HRQoL) effects in dermatological conditions and diseases in other areas. The 15D instrument is a generic, comprehensive, standardized, and self-administered 15-dimensional measure to assess HRQoL [8] that has been widely used in several areas of medicine, as well as to describe the HRQoL in the general population [9].

In this cross-sectional multicentre study, we analysed the effect of HS on the HRQoL by using both generic, skin disease and HS-specific instruments. The HRQoL of patients with HS was compared with that of age- and sex-standardized patients with psoriasis and the general population. We also studied the correlation of the recently described International Hidradenitis Suppurativa Severity Score System (IHS4) tool [10], Hurley stage, and clinical severity with the HRQoL scores.

Materials and Methods

Study Population

The study was conducted in 5 hospital dermatology clinics in Finland. The patients for this study were screened from recent patients with HS in each clinic. A letter of invitation was sent to the patients with the informed consent form. The patients who returned the signed informed consent were then invited on a study visit. On the study visit, the patients were first asked to complete the patient-reported outcome forms. Each patient was interviewed and examined by the investigator. The data from the chart review, interview, and clinical examination were gathered in an electronic case-reporting file system (Viedoc™, PCG Solutions AB, Uppsala, Sweden). All patients' data on demographics, education, economy, history of HS, smoking, alcohol consumption, comorbidities, and disease severity were collected based on chart review, interview of the patient, and clinical examination. The study protocol was approved by the Regional Ethics Committee of Tampere University Hospital (R16017/2016).

Clinical Evaluation

At the study visit, the disease severity was evaluated as mild, moderate, or severe (defined as "clinical severity") by an investigator. The number of inflammatory nodules, abscesses, and draining fistulas were counted, and these data were used later to determine the IHS4 [10] total score for each patient, albeit the scoring system was not yet published at the time the study was conducted. The IHS4 was considered mild, moderate, or severe if total scores were ≤ 3 , 4–10, or ≥ 11 , respectively [10]. Furthermore, a Hurley severity stage classification [11] was made for each patient.

15D Instrument

The generic 15D questionnaire was used to measure HRQoL. The questionnaire comprises the following dimensions: mobility, vision, hearing, breathing, sleeping, eating, speech (communication), excretion, usual activities, mental function, discom-

fort and symptoms, depression, distress, vitality, and sexual activity, with 5 ordinal levels on each. The single-index score (15D score), representing the overall HRQoL on a 0–1 scale (1 = full health and 0 = being dead), and the dimension level values, reflecting the goodness of the levels relative to no problems on the dimension (1) and to being dead (0), are calculated from the questionnaire by using a set of population-based preference or utility weights. The mean dimension-level values are used to draw 15D profiles for groups [8]. The estimated minimum clinically important change or difference in the 15D score is ± 0.015 on the basis that people can, on average, feel such a difference [12]. The HRQoL of patients was compared with that of a representative sample of an age- and sex-standardized general population ($N = 4,316$) from the National Health 2011 Health Examination Survey [9] and with that of age- and sex-standardized patients with psoriasis ($N = 145$) from the National Health 2000 Health Examination Survey [13].

Dermatology Life Quality Index

The DLQI, the most frequently used instrument in randomized controlled trials in dermatology [14], is a simple, validated questionnaire that consists of 10 questions. Each question has 4 possible answers, for a maximum of 3 points, and a total maximum score of 30. Higher scores indicate more severely affected HRQoL according to the following grade: no effect (0–1 points), small effect (2–5 points), moderate effect (6–10 points), very large effect (11–20 points), and extremely large effect (21–30 points).

Beck Depression Inventory 21

The Beck Depression Inventory 21 (BDI21) is one of the most widely used instruments for measuring depression symptoms. The questionnaire comprises items relating to depressive, cognitive, and physical symptoms. The BDI21 consists of 21 questions, and each question has 4 possible answers with a value of 0–3 assigned for each answer. Higher total scores indicate more severe depressive symptoms according to the following grade: normal (0–12 points), mild depression (13–18 points), moderate depression (19–29 points), and severe depression (≥ 30 points) [15].

Hidradenitis Suppurativa Symptom Assessment/Hidradenitis Suppurativa Impact Assessment

Hidradenitis Suppurativa Symptom Assessment (HSSA) and Hidradenitis Suppurativa Impact Assessment (HSIA) were recently developed to measure signs, symptoms, and impacts of HS, especially for treatment efficacy studies [16]. HSSA consists of 9 questions valued with check boxes from 0 to 10, where 0 is no symptoms and 10 is very severe symptoms. HSIA consists of 18 questions, 16 with similar scales as in HSSA and 2 questions assessing presence and absence from work and school.

Statistical Analyses

The descriptive statistics of patient characteristics are presented as means and standard deviations (SDs) and percentages. Pearson correlations were calculated between the scores of different instruments. Statistical significance of the differences between the groups in the means of variables was tested with independent samples t test. $p < 0.05$ was considered statistically significant. The analyses were conducted using SPSS Statistics, version 25.0 (IBM, Armonk, NY, USA).

Table 1. Demographics, lifestyle characteristics, disease, and HRQoL assessments of patients with HS (N = 92)

	Total	Female	Male
Demographic, mean ± SD			
Age, years	42.2±13.1	41.4±11.1	43.2±15.2
Age at onset (N = 88) ^a , years	25.2±11.7	23.8±9.9	27.1±13.6
Age at diagnosis, years	37.4±12.7	36.2±10.8	39.0±14.6
Diagnostic delay (N = 88) ^a , years	12.8±10.7	13.0±10.4	12.5±11.2
BMI	32.9±5.5	32.8±5.9	33.1±5.2
Lifestyle, n/N (%)			
Current smokers	53/92 (57.6)	24/51 (47.1)	29/41 (70.7)
Never smoked	15/92 (16.3)	13/51 (25.5)	2/41 (4.9)
Smoking at diagnosis	67/92 (72.8)	34/51 (66.7)	33/41 (80.5)
Mean weekly alcohol consumption, mean±SD, g	55.5±102.0	38.0±90.6	77.2±111.9
Median weekly alcohol consumption, g	12.0	6.0	48.0
Assessment tool, mean ± SD			
15D (N = 89) ^b	0.863±0.091	0.857±0.083	0.871±0.102
DLQI	7.50±6.18	7.90±6.02	7.00±6.42
BDI21	8.97±7.66	9.69±8.17	8.07±6.97
HSSA	3.81±2.64	3.67±2.56	3.99±2.75
HSIA	2.80±2.44	2.75±2.36	2.85±2.56
IHS4, mean ± SD	7.6±8.8	6.7±7.0	8.6±10.6
Clinical severity, n (%)			
Mild	44 (47.8)	24 (47.1)	20 (48.8)
Moderate	38 (41.3)	23 (45.1)	15 (36.6)
Severe	10 (10.9)	4 (7.8)	6 (14.6)
Hurley stage, n (%)			
1	16 (17.4)	9 (17.6)	7 (17.1)
2	62 (67.4)	36 (70.6)	26 (63.4)
3	14 (15.2)	6 (11.8)	8 (19.5)

15D, 15-dimensional questionnaire; BDI21, Beck Depression Inventory 21; BMI, body mass index; DLQI, Dermatology Life Quality Index; HS, hidradenitis suppurativa; HSSA, Hidradenitis Suppurativa Symptom Assessment; HSIA, Hidradenitis Suppurativa Impact Assessment; IHS4, International Hidradenitis Suppurativa Severity Score System; SD, standard deviation. ^aData available for 88 patients. ^bData available for 89 patients.

Table 2. Comorbidities in study population

Comorbidity	Total (N = 92), n (%)	Female (N = 51), n (%)	Male (N = 41), n (%)
Obesity	40 (43.5)	24 (47.1)	16 (39.0)
Cardiovascular disease	29 (31.5)	12 (23.5)	17 (41.5)
Skin condition	24 (26.1)	15 (29.4)	9 (22.0)
Other	21 (22.8)	17 (33.3)	4 (9.8)
Neurological disease	18 (19.6)	10 (19.6)	8 (19.5)
Psychiatric disorder	17 (18.5)	12 (23.5)	5 (12.2)
Diabetes	16 (17.4)	8 (15.7)	8 (19.5)
Sleep disorder	16 (17.4)	7 (13.7)	9 (22.0)
Respiratory disease	16 (17.4)	10 (19.6)	6 (14.6)
Metabolic disease and hormonal disorder	13 (14.1)	6 (11.8)	7 (17.1)
Joint disorder and musculoskeletal disease	11 (12.0)	8 (15.7)	3 (7.3)
Inflammatory bowel disease	3 (3.3)	3 (5.9)	0 (0.0)
Malignant disease	1 (1.1)	0 (0.0)	1 (2.4)
Autoimmune disease	1 (1.1)	0 (0.0)	1 (2.4)

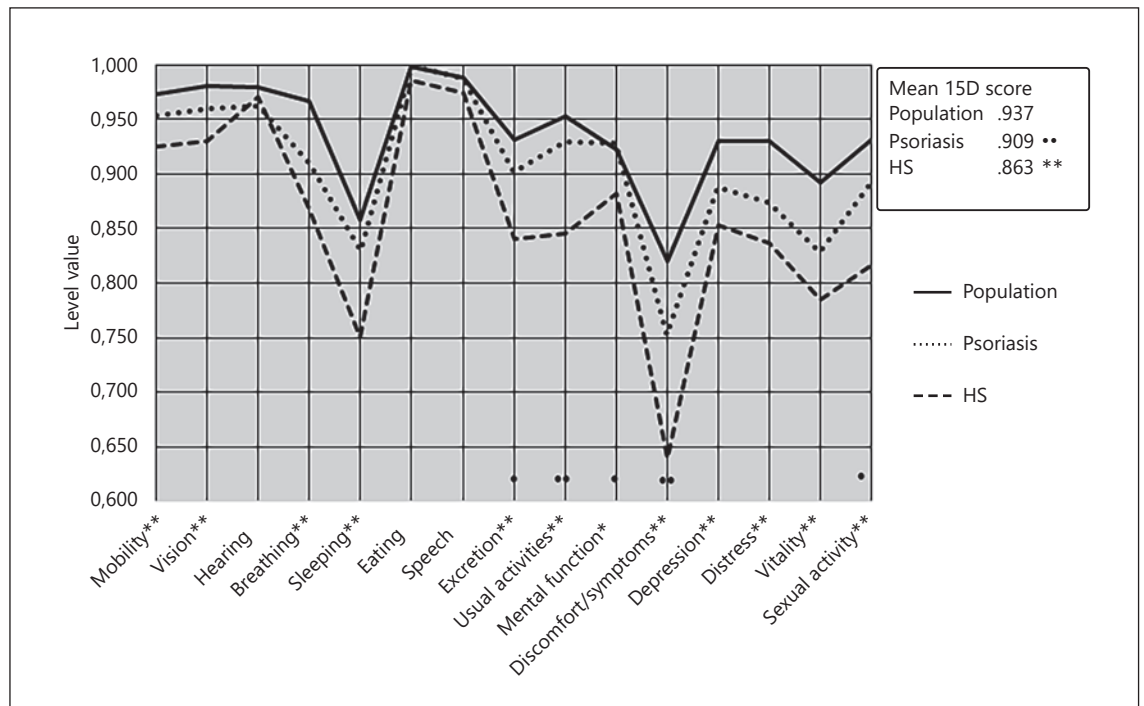


Fig. 1. Mean 15D scores and profiles of patients with HS ($N = 89$), age- and sex-standardized cohorts of the Finnish general population ($N = 4,316$) [9], and patients with psoriasis ($N = 145$) [13]. Statistical significance of the difference in the means between the general population and patients with HS: * $p < 0.05$, ** $p < 0.01$. Statistical significance of difference in the means between patients with psoriasis and those with HS: • $p < 0.05$, •• $p < 0.01$. 15D, 15-dimensional questionnaire; HS, hidradenitis suppurativa.

Table 3. Pearson correlations between the scores of different instruments

	15D	DLQI	BDI21	HSSA	HSIA	Clinical severity	Hurley stage	IHS4
15D	1							
DLQI	-0.553**	1						
BDI21	-0.727**	0.517**	1					
HSSA	-0.303**	0.780**	0.329**	1				
HSIA	-0.517**	0.902**	0.519**	0.856**	1			
Clinical severity	-0.212*	0.500**	0.149	0.456**	0.437**	1		
Hurley stage	-0.159	0.276**	0.102	0.248*	0.248*	0.632**	1	
IHS4	-0.103	0.355**	-0.008	0.373**	0.322**	0.637**	0.420**	1

15D, 15-dimensional questionnaire; BDI21, Beck Depression Inventory 21; DLQI, Dermatology Life Quality Index; HSSA, Hidradenitis Suppurativa Symptom Assessment; HSIA, Hidradenitis Suppurativa Impact Assessment; IHS4, International Hidradenitis Suppurativa Severity Score System. ** Correlation is significant at the 0.01 level (2-tailed). * Correlation is significant at the 0.05 level (2-tailed).

Results

Demographics and lifestyle data of the 92 patients included are presented in Table 1. Obesity and cardiovascular diseases were the most often found comorbidities (Table 2). The mean (SD) 15D score of patients with HS

was 0.863 (0.091) (Table 1; Fig. 1), lower than that of the age- and sex-standardized population 0.937 (0.016) and that of age- and sex-standardized patients with psoriasis 0.909 (0.082) (Fig. 1). These differences between the groups are statistically significant ($p < 0.01$) and clinically important. Only 2.2% (2/89) of patients obtained a 15D

score of 1.0 suggesting full health. Apart from hearing, eating, and speech (communication), patients with HS were statistically significantly worse off than the age- and sex-standardized population on all 15D dimensions. The biggest absolute differences were seen on the dimensions of sleeping, excretion, usual activities, and discomfort and symptoms, as well as on the psychical dimensions. Compared with age- and sex-standardized patients with psoriasis, those with HS were statistically significantly worse on the dimensions of excretion, usual activities, mental function, discomfort and symptoms, and sexual activity (Fig. 1).

The 15D scores had an especially high correlation with the BDI21 scores, a high correlation with the DLQI and HSIA scores, and a somewhat lower correlation with the HSSA scores. There was no statistically significant correlation with the IHS4 scores and Hurley stage. The HSSA and HSIA scores correlated very strongly between each other and with the DLQI scores. The correlation of IHS4 was strong with the clinical severity assessed by the physician (Table 3).

Discussion

The QoL in patients with HS has mostly been studied by using the skin disease-specific DLQI, which allows comparison with other skin diseases but does not allow comparison with other chronic and non-chronic states, healthy control populations [17], or quality-adjusted life year-based health economic evaluation of different interventions. The use of generic HRQoL tools thus far has been sparse in HS studies [17]. Although the 15D has been previously used in a small population of 26 patients with HS [18], our study, to the best of our knowledge, is the first one to describe the correlations of this generic instrument with other HRQoL measures and disease severity measures in HS disease. In our study, patients with HS had a 15D total score even lower (0.863) than previously described (0.882 ± 0.083 [18]); the score corresponds to total scores in diseases such as prostate cancer (0.897 and 0.855 for locally advanced and metastatic, respectively [19]), metastatic breast cancer (0.82 [20]), inflammatory bowel disease (0.874 [21]), and axial spondyloarthritis (0.85 [22]). However, comparisons should be made with caution because the sex and age distribution in these populations may differ from our population.

The presence of current depressive symptoms has been reported to markedly reduce HRQoL as measured by 15D, e.g., in primary care patients [23]. The mean

BDI21 score in our population was 8.97 (SD 7.66) corresponding to “no depression.” However, up to 13.1% of these cases had BDI21 scores of 19–63, denoting moderate to severe signs of depression, and 16.3% had BDI21 scores of 13–18, denoting mild signs of depression. Also in our population, the 15D scores had a high correlation with the BDI21 scores (Table 3). In addition, as many as 18.5% (17/92) of our patients had diagnosed psychiatric comorbidity (including depression and anxiety), which is comparable with findings from the studies from Finnish national registries [3].

As in previous studies, we found no relationship for the generic HRQoL instrument with the severity measures of HS, including Hurley staging and the IHS4 [24]. In our study, the mean DLQI score was 7.50 (SD 6.18), indicating moderate effects in QoL. We found a weak correlation of the DLQI with Hurley staging and IHS4 disease severity measures, while correlation was moderate with the clinical severity. These findings are in line with previous reports [10, 17].

The strength of our study is that all the study subjects were carefully interviewed and examined by a dermatologist. In addition, several different methods were used to measure the HRQoL. Although our population was based on patients treated in a hospital, we assume that the study population well represents the majority of patients diagnosed with HS because in Finland, most patients with HS are treated in public health care. Patients treated by private dermatologists are a small minority of all patients and do not markedly deviate from patients treated in hospital polyclinics.

HS is one of the most debilitating skin diseases [25, 26]. With the use of the generic 15D instrument, we show in this study that HS has a remarkable effect on HRQoL, also when compared with diseases of other disease groups. These effects seem to be independent of HS disease severity as they are present even in mild disease. This finding should raise the understanding of the burden of patients with HS and their need for comprehensive care.

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Statement of Ethics

The study protocol was approved by the Regional Ethics Committee of Tampere University Hospital (R16017/2016), and the study was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. Patients for this study were screened from recent patients with HS in each clinic. A letter of invitation was sent to the patients with the informed consent form. The patients who returned the signed informed consent were invited on a study visit.

Conflict of Interest Statement

Dr Huilaja has received educational grants from CSL Behring, Shire, Janssen-Cilag, Novartis, AbbVie, and LEO Pharma and honoraria from AbbVie, Takeda, Novartis, Sanofi Genzyme, and UCB Pharma for consulting and/or speaking and is an investigator for AbbVie. Dr. Tiina Lipitsä has received educational grants from AbbVie and is an investigator for AbbVie. Dr. Rauno Harvima has received educational grants from AbbVie. Dr. Armi Vihervaara has received educational grants from AbbVie, Janssen, Novartis, and Celgene. Dr. Rafael Pasternack has received educational grants from AbbVie, Janssen, LEO Pharma, Novartis, and Sanofi Genzyme and honoraria from AbbVie, Bristol Myers Squibb, Eli Lilly, Janssen, Novartis, Sanofi Genzyme, and UCB for consulting and/or speaking; participated in clinical studies sponsored by AbbVie, Novartis, Eli Lilly, and Regeneron; and is an investigator for Abb-

Vie. Harri Sintonen is the developer of the 15D instrument and obtains royalties from its electronic versions. Martta Ranta and Mirikka Hirvonen are employees of AbbVie and may or may not own AbbVie shares. The sponsor of this study, AbbVie, participated in the study design, study research, collection, analysis and interpretation of data and writing, reviewing, and approval of this publication. All authors had access to the data and participated in the development, review, and approval and decision to submit this publication.

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Author Contributions

R.P., M.R., and H.S. contributed to the study design; R.P., T.L., A.V., R.H., and L.H. participated in acquisition of the data. All the authors contributed to analysis of the data. M.J.H., R.P., H.S., and L.H. wrote the first version of the manuscript. All the authors participated in the critical revision of the manuscript and have accepted the final version of the manuscript.

Data Availability Statement

The data that support the findings of this study are not publicly available due to their containing information that could compromise the privacy of research participants but are available from the corresponding author L.H. upon reasonable request.

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