The Impact of Nail Psoriasis and Treatment on Quality of Life: A Systematic Review

Claire R. Stewart^a Leah Algu^b Rakhshan Kamran^c Cameron F. Leveille^d
Khizar Abid^b Charlene Rae^e Shari R. Lipner^f

^aWeill Cornell Medical College, New York, NY, USA; ^bFaculty of Health Sciences, McMaster University, Hamilton, ON, Canada; ^cMichael G. De Groote School of Medicine, McMaster University, Hamilton, ON, Canada; ^dDivision of Plastic Surgery, Department of Surgery, McMaster University, Hamilton, ON, Canada; ^eDepartment of Pediatrics, McMaster University, Hamilton, ON, Canada; ^fDepartment of Dermatology, Weill Cornell Medical College, New York, NY, USA

Keywords

Nail psoriasis · Quality of life · Systematic review · Indicators · Nail Psoriasis Severity Index · Psoriasis Area Severity Index · Dermatology Life Quality Index · Patient-reported outcome measures

Abstract

At least 80% of patients with psoriasis will have nail involvement during their lifetimes. Understanding quality of life (QoL) impact of this condition and associated treatments is of utmost importance. Study objectives were to review the available literature describing patient-reported QoL outcomes in nail psoriasis and relationship with disease severity and treatment. A literature search was performed for English-language articles published prior to August 1, 2020. Articles were included in the review if primary data and validated patient-reported outcome measures assessing QoL were presented, and nail involvement was specifically examined. Fifteen studies were included in the final analysis. Patients with nail psoriasis had higher Psoriasis Area Severity Index and Dermatology Life Quality Index scores than those with psoriasis without nail involvement. The largest percent

improvement in QoL score was associated with adalimumab. Studies investigating topicals, intralesionals, and systemic treatments were excluded since only biologic studies utilized validated patient-reported outcome measures. This review affirms that nail psoriasis is physically and emotionally distressing, warranting prompt treatment. Increased efforts are needed to address the impact of treatment on patient QoL using validated outcome measures that assess cosmetic, physical, and social problems.

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Introduction

Psoriasis is a chronic skin disorder affecting about 2% of the US population [1]. At least 80% of psoriasis patients will have nail involvement in their lifetimes, while an estimated 10% have isolated nail psoriasis [1]. Clinical findings include nail plate pitting, onycholysis, splinter hemorrhages, “oil spots,” and subungual hyperkeratosis. Yet the impact of nail psoriasis extends beyond aesthetics, as this condition causes pain, functional impairment, and embarrassment.

Fig. 1. Flow diagram of the study selection process.

While there is an expanding number of treatments for nail psoriasis, patient comorbidities, medication interactions, potential adverse effects, and costs must be considered [2]. Therefore, it is crucial to understand the impact of nail psoriasis on quality of life (QoL) to recommend treatment. Patient-reported outcome measures (PROMs) are useful tools to help patients vocalize their concerns. This review sought to evaluate the available literature describing the relationship of psoriasis severity and treatment with QoL outcomes as assessed by PROMs in nail psoriasis.

Materials and Methods

A search of the English-language literature published prior to August 1, 2020, for studies reporting QoL in patients with nail psoriasis was performed. MEDLINE and Embase databases were examined with the search terms “nail” and “QoL” (C.F.L.). Abstracts were screened by 2 researchers (R.K. and L.A.) using the exclusion criteria: not an original article, valid PROM not used, and outcomes not reported in patient subgroup with nail involvement. Full-text articles were reviewed by 2 researchers (R.K. and L.A.) with discrepancies resolved by a third (C.R.). References of articles were searched to identify additional articles that may have been missed, although no studies were added (C.F.L.). Data were ex-

tracted and confirmed by 2 researchers (C.S. and L.A.). Study design, population demographics, severity, and QoL scores were extracted. To measure evidence level, we used a 5-point scale with the following ratings: (1) randomized clinical trial or systematic review with meta-analysis; (2) controlled trial without randomization or prospective cohort trial; (3) case-control study or retrospective cohort study; (4) cross-sectional study or case series with more than 5 patients; and (5) case report.

Results

A total of 430 full-text articles were assessed for eligibility with 15 studies included in this analysis. The study selection process is detailed in Figure 1.

Patient-Reported Outcome Measures

Five PROMs were used to assess QoL, with Dermatology Life Quality Index (DLQI) most commonly used ($n = 10$). DLQI scores correlate as 0–1 no effect, 2–5 small effect, 6–10 moderate effect, 11–20 large effect, and 21–30 extremely large effect [3]. The minimal clinically important difference has been established as 4.0 [4]. The International Onychomycosis-Specific Questionnaire, while

designed to measure QoL in patients with onychomycosis, was used in 3 studies. This PROM is scored on a 0–100 scale with 100 representing the worst QoL [5]. The Nail Psoriasis QoL measure, Nail Assessment in Psoriasis and Psoriatic Arthritis Questionnaire (NAPPA-QoL), and NPQ10 Score were used in 1 study each. In the Nail Psoriasis QoL measure, scores range from 0 to 10 with 10 as most severe impact [6]. The NAPPA-QoL is a 20-item nail-specific QoL questionnaire assessing nail status, stigma, emotional, and everyday life impact [7]. The NPQ10 score is a nail-specific scale with scores ranging from 0 to 20 with higher scores indicating poorer QoL [8].

Demographics

The demographics of study populations were varied. The mean age of subjects across studies was between 43.3 and 57.5 years [6, 9–22]. Composition of females in study samples also varied from 19.2 to 63.0% [6, 9–22]. The mean duration of psoriasis in those with nail involvement ranged from 11.5 to 34.3 years [6, 9–22]. No studies included patients with comorbid onychomycosis.

Psoriasis Severity and Quality of Life

Eight studies compared clinician-assessed severity and DLQI in patients with and without nail involvement (Table 1) [9–15]. Severity was reported by Psoriasis Area Severity Index (PASI) and Nail Psoriasis Severity Index (NAPSI). Across studies, psoriasis with nail involvement was associated with significantly higher baseline PASI scores [9–15]. Nail involvement was also associated with significantly greater QoL impairment [9–15]. In studies with subgroup analysis by gender, women had higher PASI and DLQI scores than men [10, 12, 13].

Reich and Szepietowski [23] ($n = 30$) found that patients with nail psoriasis were most concerned with appearance and disease worsening; NailQoL scores were correlated with NAPSI in women, but not in men. Ortonne et al. [8] ($n = 795$) reported that female gender, shorter disease duration, and presence of both fingernail and toenail involvement were associated with worse QoL, as measured by the NPQ10 Scale; PASI and NAPSI scores were not reported. In addition, 86% of patients considered nail psoriasis to be bothersome, 87% as unsightly, and 59% as painful [8].

Treatment, Severity, and Quality of Life

Nine studies reported QoL data in combination with systemic biologic treatments (Table 2) [6, 9, 16–22]. Two randomized controlled trials received the highest Level 1 quality of evidence ranking; all other prospective, open-label studies received Level 2 [6, 22].

For all treatment modalities (infliximab, etanercept, adalimumab, ustekinumab, and secukinumab), authors reported statistically significant improvement in both NAPSI and QoL with treatment [6, 9, 16–22]. Ortonne et al. [8] reported that 72% of patients were dissatisfied with treatment, but specific therapies were not specified. Infliximab (5 mg/kg infusion at baseline, 2, 6, and every 8 weeks thereafter for 38 weeks) was associated with the greatest reported percentage improvement in NAPSI (94.1%) [16] which was 4.3 percentage points higher than the next highest scoring treatment, ustekinumab [21], and 48.8 percentage points higher than the lowest scoring treatment, secukinumab [22]. The ustekinumab dose was 45 mg for patients <100 kg and 90 mg for patients over 100 kg subcutaneous at baseline, 4, 16, and every 12 weeks thereafter for 40 weeks; secukinumab was dosed 300 or 150 mg subcutaneous weekly for 5 weeks and every 4–16 weeks [21].

While different parameters were used to assess QoL impact, multiple studies identified similar themes in specific domains of QoL that improved with treatment. Commonly mentioned themes across medications included improvement in symptoms, pain, functionality, and cosmetic appearance of nails, as well as improvements in personal relationships, business interactions, and ability to perform daily activities [16–18, 22].

When comparing reported percent improvement in QoL across treatment types, adalimumab had the greatest percent improvement from baseline. In 1 study, there was a 87.7% improvement in DLQI score, and in another study, a 88.2% improvement in Nail Psoriasis QoL Score [6, 19]. Of note, in a recent study by Kokolakis et al. [20], there was a lower percent improvement than Khobzey et al. [19] (60.0 vs. 88.2%) in DLQI. This difference may be due to the longer duration of disease in the study population investigated by Kokolakis et al. [19, 20]. In the study, using the Onychomycosis-Specific Questionnaire, the authors reported a mean improvement of 74.4% from baseline, while the studies reporting Nail Psoriasis QoL found 87.7% improvement [6, 18]. The percentage of patients with concomitant joint involvement ranged from 28.6 to 66.7% in these studies [6, 18–20].

Discussion

This review affirms that nail psoriasis is associated with both worse clinician-assessed severity and larger patient-reported QoL impact compared to psoriasis pa-

Table 1. Review of studies reporting the impact of nail involvement in psoriasis on QoL as measured by DLQI score

Reference	Country	Study design, inclusion criteria, and evidence level	Total N (with nail involvement, without)	Age Mean ± SD (range)	% female	Duration of psoriasis Mean ± SD, years		Severity Mean ± SD	DLQI Mean ± SD		Controlling for PASI, were DLQI values significant?		
						with nail involvement	without		with nail involvement	without			
Luger et al. [9]	Germany	Observational, open-label. Active but stable plaque psoriasis involving >10% of total BSA and a PGA of psoriasis of >3, and failed usual care (2)	711 (564, 145)	44.9 ^a (range nr)	28.3	22.3*	19.6	4.64	23.15 ^{a,*}	13.59 ^{a,*}	12.15 ^a	Yes	
Augustin et al. [10]	Germany	Cross-sectional. Patients >18 years with clinically confirmed psoriasis (4)	3,531 (F 511, 958) (M 894, 1,053)	51.1±14.8 (range nr)	42.4	23.1±15.8*	19.1±16.6	–	F 11.3±10.7*	9.5±7.1*	7.6±6.5	nr	
						21.4±13.6*	17.1±14.0	–	M 13.5±10.7*	8.6±7.1*	6.9±6.3		
Radtke et al. [11]	Germany	Cross-sectional. Patients >18 years with medically-verified psoriasis (4)	2,449 (1,761, 621)	57.0±11.7 (18–92)	44.8	34.3±13.9*	33.0±16.1	–	12.7*	7.2±6.4*	5.3±5.3	Yes	
Klaassen et al. [12, 13] [§]	The Netherlands	Cross-sectional. All members of the Dutch psoriasis association (4)	1,459 (total 963, 496) (F 464, 272) (M 489, 216)	57.5±13.6 (range nr)	51.1	32.4±15.3*	30.3±16.8	–	T 6.6±4.9* [†]	5.3±4.3 [†]	3.7±4.4	nr	
									F 6.8±4.9 [†]	5.3±4.7 [†]			
									M 6.4±4.9 [†]	5.2±3.8 [†]			
Kyriakou et al. [14]	Japan	Cross-sectional. Clinically diagnosed plaque psoriasis who had not received any systemic anti-psoriatic treatment or topical nail treatment for >1 year (4)	99 (54, 45)	43.9±13.7 (18–72)	48.5	18.9±10.1*	8.93±7.1	43.4±24.9	10.55±5.88*	5.11±3.25	4.4±2.9*	2.53±1.18	nr
Garbers et al. [15]	Brazil	Cross-sectional. Psoriasis without systemic treatment for 6 months (4)	40	50.7±12.2 (range nr)	62.5	Mean age of onset 37.4±12.0	Mean age of onset 37.4±12.0	–	The number of affected nails did not correlate linearly with PASI (Spearman's Rho = 0.23, <i>p</i> = 0.17)	For each affected nail, there is an increase in DLQI (Spearman's Rho = 0.43)* ^a		Yes	

DLQI, Dermatology Life Quality Index; PASI, Psoriasis Area Severity Index; SD, standard deviation; BSA, body surface area; PGA, Physician Global Assessment. [§] Klassen et al. reported the results of their questionnaire in 2, separate studies. ^a No SD reported. CAPASI, Self-administered Psoriasis Area and Severity Index. * Authors reported statistical significance.

DLQI, Dermatology Life Quality Index; PASI, Psoriasis Area Severity Index; SD, standard deviation; BSA, body surface area; PGA, Physician Global Assessment. [§] Klassen et al. reported the results of their questionnaire in 2, separate studies. ^a No SD reported. [†] SAPASI, Self-administered Psoriasis Area and Severity Index. * Authors reported statistical significance.

Table 2. Review of studies reporting efficacy and QoL impact of various treatments in psoriasis with nail involvement

Reference	Country	Study design, inclusion criteria, and evidence level	N	Age Mean ± SD (range)	% female	Race/ethnicity	Disease duration, years	Treatment	Target	Study length, weeks	NAPSI Percent improvement from baseline	Quality of life Improvement from baseline	
												PROM	%
<i>Infliximab</i>													
Rigopoulos et al. [16]	Greece	Observational, open-label Psoriasis with nail involvement (2)	18	47.8±11.6 (32–60)	44.4	nr	Nails involved 3.9±1.1	Infliximab 5 mg/kg at baseline, 2, 6, and every 8 weeks thereafter	Finger nail 38	94.1*		International onychomycosis-specific questionnaire	71.2*
Shear et al. [17]	Canada	Observational open-label >18 years old with plaque psoriasis and physician and patient decision to start IFX treatment prior to enrollment (2)	516	46.4 (18–85)	33.5	83.5% Caucasian; 30.5% multi-racial, 0.5% black	–	Infliximab 5 mg/kg at weeks 0, 2, and 6, and then maintenance infusions every 8 weeks for 98 weeks	–	50	nr	DIQI	65.0*
<i>Etanercept</i>													
Luger et al. [9]	Germany	Observational, open-label Active but stable plaque psoriasis involving >10% of total BSA and a PGA of psoriasis of >3, and failed usual care (2)	564	44.9 (range nr)	28.3	nr	22.3	Etanercept 25 mg subcutaneously twice weekly	–	54	51.3*	DIQI	62.8*
<i>Adalimumab</i>													
Rigopoulos et al. [18]	Greece	Observational, open-label Severe plaque psoriasis or with psoriatic arthritis and cutaneous psoriasis with involvement of nails (2)	21	45.0±12.1 49.6±11.8 (28–71)	nr	nr	–	Adalimumab 80 mg at baseline, 40 mg at week 1 and 40 mg every 2 weeks thereafter subcutaneously	Finger nail 24	85.1*		International onychomycosis-specific questionnaire	74.4*
Khobzey et al. [19]	Slovenia	Observational open-label Adult with moderate-to-severe plaque psoriasis eligible for adalimumab therapy; NAPSI >10 (2)	501	47.0 (range nr)	37.3	99.6% Caucasian	15.7	Adalimumab 40 mg every other week	Finger and 52 toe nails	81.6*		DIQI	87.7*
<i>Ustekinumab</i>													
Elewski et al. [6]	USA	RCT. Adult with chronic (>6 months), moderate-to-severe plaque psoriasis and psoriasis in at least 1 fingernail (1)	217	46.7±12.0 (range nr)	15.7	94.9% Caucasian, 0.5% Asian, 4.6% other	11.5±9.4	Adalimumab 80 mg at baseline, then 40 mg every other week	Finger nail 26	Placebo	11.5	Nail psoriasis QoL Placebo	31.5
Kokolakis et al. [20]	Germany	Observational, open-label Adults with moderate-to-severe psoriasis with PASI >10 and DLQI >10 with involvement of the nail (2)	267	47±13.1	31.1	nr	27±12.8	Adalimumab 80 mg at baseline, then 40 mg at week 1 and then 40 mg in 2-week intervals for 2 years	Finger nail 96	68.6*	56.2*	Adalimumab	88.2*
<i>Secukinumab</i>													
Rigopoulos et al. [21]	Greece	Observational, open-label Plaque psoriasis and fingernail involvement who had failed systemic treatment in the past (2)	27	43.3±10.7 (32–60)	63.0	nr	Nails involved 2.2±1.2	Ustekinumab 45 mg for those <100 kg and 90 mg for those over 100 kg at baseline, 4, 16, and every 12 weeks thereafter	Finger nail 40	89.8*		International onychomycosis-specific questionnaire	79.2*
Reich et al. [22]	Germany	RCT. Moderate-to-severe plaque and nail psoriasis (1)	198	44.1±11.7 (range nr)	19.2	nr	17.7	Secukinumab 300 mg, 150 mg, or placebo subcutaneously once a week for 5 weeks and every 4 weeks thereafter	Finger and 16 toe nails	Placebo	10.8*	NAPPA-QoL Placebo	15.8*
										Secukinumab 150 mg	37.9*	Secukinumab 150 mg	49.9*
										Secukinumab 300 mg	45.3*	Secukinumab 300 mg	60.9*
PROM, patient-reported outcome measure; DLQI, Dermatology Life Quality Index; PASI, Psoriasis Area Severity Index; SD, standard deviation; NAPPA-QoL, Nail Assessment in Psoriasis and Psoriatic Arthritis Quality of Life questionnaire; QoL, quality of life; NAPSI, Nail Psoriasis Severity Index. * Authors reported statistical significance.													

PROM, patient-reported outcome measure; DIQI, Dermatology Life Quality Index; PASI, Psoriasis Area Severity Index; SD, standard deviation; NAPPA-QoL, Nail Assessment in Psoriasis and Psoriatic Arthritis Quality of Life questionnaire; QoL, quality of life; NAPSI, Nail Psoriasis Severity Index. * Authors reported statistical significance.

tients without nail involvement. Furthermore, the reviewed studies confirm that treatment of nail psoriasis leads to improved QoL. In our review, adalimumab was associated with the greatest percentage improvement in health-related QoL.

Some clinical trials have incorporated PROMs, however, analyzing patient QoL with validated outcome measures should be standard [24]. Our study also raised concerns as to whether existing PROMs can adequately evaluate the impact of nail changes. Though all studies found that DLQI is higher in patients with nail involvement, the differences in scores ranged from 1.2 to 1.9, which is below the minimal clinically important difference [4]. These findings contrast with clinical practice, in which patients with nail disorders have aesthetic, physical, and social disabilities. The DLQI, which is designed for general skin conditions, may not have relevant content validity to measure the outcomes most important in nail psoriasis. In a review of health-related QoL in patients with nail disorders, Reich and Szepletowski [23] pointed out that when DLQI is applied to patients with both skin and nail involvement, the instrument cannot differentiate between the influence of nail versus skin changes on QoL. Since no studies excluded patients with psoriatic arthritis, it is not clear whether improvement in QoL scores was attributable to improvement in nail or joint symptoms. Only 3 studies utilized nail psoriasis-specific PROMs, thus limiting our comparisons.

This study is subject to several limitations. The lack of literature evaluating QoL and meeting our screening criteria limits the generalizability of our findings. None of the studies included children and only the studies by Radtke et al. [11] and Shear et al. [17] included adults over the age of 75, despite nail psoriasis being a concern in both pediatric and older patients. In the Joint American Academy of Dermatology – National Psoriasis Foundation guidelines for the treatment of psoriasis in pediatric patients, Menter et al. [25] recommended for consideration of the impact of disease on the “physical, social, and psychological QoL and/or activities of daily living” when determining the severity of psoriasis in children. Additionally, they highlighted the use of the Children’s DLQI, a derivative of the DLQI designed for patients aged 4- to 11-year old – a recommendation that we support for future research in this subgroup [25, 26]. Another limitation is that topicals, intralesionals, and systemics were excluded; only studies investigating biologic therapies met inclusion criteria for our review. Additionally, only 2 studies reported whether patients had previous exposure

to biologics, though others did indicate that there was a washout period [17, 22]. If patients had failed treatment with other biologics, they may have had more severe disease with poorer QoL. The strength of evidence for the treatment studies was quite high, and the risk of bias was deemed to be low.

Conclusions

This review confirms that nail psoriasis is physically and emotionally distressing, warranting prompt and adequate treatment. However, the paucity of data limited types of treatments included in our analysis highlight the necessity of further research. While future studies should include PROMs as metrics to incorporate the patient perspective of the social, emotional, and functional impact of nail psoriasis, it is crucial that these PROMs capture the aspects most important to the patient and have content validity for use in nail psoriasis.

Statement of Ethics

Ethics approval was not required for this systematic review because all data was publicly available.

Conflict of Interest Statement

The authors have no conflicts of interest to disclose.

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Author Contributions

Claire Stewart was responsible for data extraction, writing of the manuscript, and figure creation. Leah Algu screened abstract and full-text articles and conducted data extraction. Rakhshan Kamran screened abstract and full-text articles. Cameron Leveille conducted publication search and organized search results. Khizar Abid found and organized full-text articles. Charlene Rae oversaw coordination and created the data extraction sheet. Shari Lipner is the senior author who conceived the study and wrote the manuscript. All authors reviewed the manuscript.

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