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REVIEW

Measuring Patient Quality of Life Following Treatment for Alopecia

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Abstract: Alopecia is a challenging problem for both physicians and patients in terms of diagnosis and treatment. Alopecia usually has negative effects on patients' emotional and psychological well-being. Several studies have examined the effect of alopecia on patients' health-related quality of life (HRQoL) and have consistently reported poor scores. However, deeper insight into the impact of alopecia on affected individuals and its measurement using HRQoL questionnaires is lacking in the literature. In this article, the methods for measuring the HRQoL of patients with alopecia were comprehensively reviewed. Their applications and limitations were also discussed.

Keywords: hair loss, health-related quality of life, questionnaire, instrument, disease-specific, patient-reported outcome

Introduction

Human hair may have little physiological importance, but its psychological counterpart is undeniable,[1] contributing significantly to a person's body image and attractiveness.[2,3] Hair loss, also known as alopecia, is a challenging problem for both physicians and patients worldwide. It is one of the common presenting symptoms in dermatological practice and is often a major source of distress for affected individuals. Numerous studies have been conducted to better understand its etiologies and pathophysiology and to find effective treatment options. There are several causes of hair loss, such as genetics, hormonal disorders, autoimmune disturbance, nutritional deficiency, and stress;[4–9] therefore, an organized and systematic approach is needed to accurately address patients' complaints. A thorough review of medical history, complete physical examination, laboratory investigation, and scalp biopsy are essential to establish a definitive diagnosis.

Alopecia can be categorized into two groups, ie, nonscarring and scarring. The main difference between them is that scarring alopecia is accompanied by follicular fibrosis, in contrast to nonscarring alopecia, where the follicular scar is not present.[10] Common nonscarring hair loss includes androgenetic alopecia (AGA), female pattern hair loss (FPHL), telogen effluvium, anagen effluvium, and alopecia areata (AA), whereas scarring alopecia, a permanent hair loss due to destruction of the hair follicles, is less frequently found and can be further divided into primary and secondary subtypes.[10] Primary scarring alopecia refers to a group of disorders that primarily affect hair follicles, such as lichen planopilaris (LPP), frontal fibrosing alopecia (FFA), chronic cutaneous lupus erythematosus, and central centrifugal cicatricial alopecia. In contrast, secondary scarring alopecia represents conditions

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involving the hair follicles as a bystander from any pathological processes of the surrounding tissues, such as inflammation, trauma, or infections.

Over the last decades, many therapeutic options for alopecia, including topical, intralesional, or systemic treatments, have been administered to regrow hair and to delay and stop the hair loss process. However, some medications, such as topical minoxidil and oral finasteride for AGA or corticosteroids for AA, may provide partial and temporary results and are associated with unwanted adverse effects.[7,11] In addition, treatments for some hair loss conditions, such as severe AA and many forms of scarring alopecia, are usually ineffective.[10,12,13] Hair restoration surgery is often the treatment in alopecic cases with unresponsiveness to medical therapy or irreversible hair loss. Evidence suggests that hair loss can cause significant impairment to patients' quality of life (QoL),[14,15] which is mostly experienced by the patients themselves. Therefore, the goals of the treatment of alopecia should involve not only the physical aspect of disease but also the psychosocial burden that the patients carry to help maximize the improvement of their QoL. Being able to measure patients' QoL should complement holistic patient care and facilitate the process of developing high-quality future therapeutic options through research. This article aims to review the current methods to measure the QoL of patients with alopecia and to provide insight into the current issues concerning QoL measurement in this patient group.

Health-Related Quality of Life and Its Measurement

QoL is a concept without a universally recognized definition; a widely used definition from the World Health Organization (WHO)[16] is as follows:

> individuals' perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns. It is a broad ranging concept, incorporating in a complex way individuals' physical health, psychological state, level of independence, social relationships, personal beliefs and their relationships to salient features of the environment.

The Economist Intelligence Unit regards nine factors as the determinants of quality of life, ie, material wellbeing, health, political stability and security, family life, community life, climate and geography, job security, political freedom, and gender equality.[17] In essence, QoL is a multidimensional concept involving many aspects of life that is difficult to measure comprehensively.[18] Thus, health-related QoL (HRQoL) can be defined as the area of QoL that encompasses only factors related to an individual's health,[19] and it will be the main topic of this review.

HRQoL is considered a type of patient-reported outcome (PRO) measure, a term that denotes the outcomes evaluated directly by the patient, eg, measures of symptoms, satisfaction with treatment, and HRQoL.[20] PRO measures, along with observer-reported outcome measures, clinician-reported outcome measures, and performance outcome measures, are in turn the components of clinical outcome assessments (COAs).[21] To assess HRQoL, a regular patient interview may be carried out to gain some qualitative information, but this would not suffice if quantification of HRQoL is required for future use in either research or patient care. Therefore, HRQoL is usually assessed quantitatively using the measures described below.

HRQoL measures are usually classified into two major groups, ie, generic and specific measures. Generic measures are designed for general use in a wide range of interventions and conditions,[22] thus allowing comparisons between different diseases. They can be used to assess HRQoL in the general population as well as most health conditions, including alopecia. These generic HRQoL measures comprise two types: health profiles and health indices. Health profiles are the measures that attempt to quantify HRQoL on several dimensions by means of scores obtained from respondents through questionnaires (ie, instruments).[23] Many instruments have been developed for this purpose, eg, the Medical Outcomes Study 36-Item Short Form Health Survey (SF-36),[24] the Sickness Impact Profile (SIP),[25] the Nottingham Health Profile (NHP),[26] the Quality of Life Inventory (QOLI),[27] the Assessment of Quality of Life (AQoL) instrument,[28] and the Centers for Disease Control and Prevention Health-Related Quality of Life Measure (CDC HRQOL-14).[29] The World Health Organization Quality of Life assessment instrument (WHOQOL-100)[16] and its reduced version (WHOQOL-BREF),[30] although usually considered in this category, also contain domains other than health, such as the environmental domain, and thus may also be regarded as measures for general QoL (compared to HRQoL).

The other type of generic HRQoL measure is the health index, which is also known as utility. Its value normally ranges from 0 (corresponding to the worst possible health

or death) to 1 (corresponding to the best possible health), but negative values (corresponding to health states worse than death) are sometimes possible. Theoretically, utility is assessed by direct methods, namely, preference-based measures that include standard gamble and time trade-off. However, it can also be measured by indirect methods that use predefined population-based weights to calculate the utility from scores obtained from HRQoL instruments such as the EuroQoL 5-Dimension (EQ-5D),[31] the Health Utilities Index (HUI),[32] and the SF-6D (ie, a reduced version of the SF-36 developed for this purpose).[33] Utility can be used by itself, but more prominently, it is used for calculating the quality-adjusted life-years (QALY), which is the most widely recommended outcome measure for economic evaluation studies.[34]

Conversely, specific HRQoL measures are developed to suit either the disease/condition or the population of interest.[35] While disease-specific measures can collect some information peculiar to the disease of interest that their generic counterparts cannot, they are also more responsive,[22,36] ie, more sensitive for detecting differences or changes in disease status.[37] To measure the HRQoL of alopecia patients, dermatology-specific instruments may be used justifiably. The Dermatology Life Quality Index (DLQI),[38] Skindex-29[39] and its reduced versions (ie, Skindex-16[40] and Skindex-17[41]), and the Dermatology Quality of Life Scales (DQoLS)[42] are examples of dermatology-specific HRQoL measures. These instruments have been extensively reviewed elsewhere.[23,43,44] For patients with hair diseases, including alopecia, researchers have developed a number of hair-specific HRQoL measures. Their details are discussed in the following section.

Hair-Specific Health-Related Quality of Life Instruments

Although alopecia is considered a benign process, it has been demonstrated to have a serious impact on individuals' overall QoL. A variety of measures to assess the effects of alopecia on patients' lives have been introduced and validated in the literature. The details of some of the instruments discussed in this article are presented in Table 1.

Men's Hair Growth Questionnaire

The Men's Hair Growth Questionnaire (MHGQ) is a short instrument developed for male AGA patients. Initially, 17 questions were identified from a literature review, expert opinions, focus groups of patients, and the review of related questionnaires and then underwent a substantial reduction through tests for internal consistency, test-retest reliability, construct validity, and responsiveness. The final version contains seven individual items that do not belong to any particular domain or subscale. The MHGQ was primarily designed for clinical trials because the questions directly address the changes from baseline, with reference to the start of the study.[45]

Kingsley Alopecia Profile

The Kingsley Alopecia Profile (KAP) is an English instrument consisting of 15 questions on five-point Likert scales, with proposed bands of total scores for interpretation.[46] However, the process of its development was described in a thesis not accessible to us at the time of writing.[47]

Women's Androgenetic Alopecia Quality of Life Questionnaire

The Women's Androgenetic Alopecia Quality of Life Questionnaire (WAA-QOL) was developed from items regarding aspects of female patients' life affected by AGA, which were generated from a literature review, discussion with experts, and a focus group, with patients' feedback contributing to the revision. The final English version, consisting of 16 items that form only one domain, with a one-week recall period, was able to show high reliability (ie, internal consistency and test-retest reliability) but not responsiveness in the validation study (due to the intervention's lack of efficacy in the trial).[48] The formally translated Brazilian Portuguese version of the WAA-QOL has been thoroughly tested for validity and reliability.[49]

Hairdex

The original German version of Hairdex was a modification of Skindex-29 for use in female patients with diffuse alopecia and AGA in Germany. Patients' feedback also contributed to the revision and item reduction. The final version consists of 48 items that belong to five subscales (ie, domains) proven to determine the impact of hair loss on patients' lives, including emotions, functioning, symptoms, self-confidence, and stigmatization; the first three subscales are similar to the only three subscales of the original Skindex-29 instrument, while the last two were newly added. Hairdex can be completed within 15 minutes by most patients.[50] It has been translated and used in the USA,[51,52] India,[53] and Turkey,[54] but the processes of adaptation and validation were not detailed.

Table 1 Characteristics of Some Hair-Specific Health-Related Quality of Life Instruments Discussed in This Article

Instrument	Publication Year	Country of Origin	Language	Intended Patient Group	Recall Period	Number of Items	Scales for Items	Domains	Reliability
MHGQ	1998	USA	English	AGA in men	Since the start of treatment	17	4- to 7-point	Single	NR
WAA-QOL	2000	USA	English	AGA in women	1 week	16	7-point	Single	Cronbach's α 0.98, ICC 0.89
Hairdex	2001	Germany	German	AGA and diffuse alopecia	NR	48	5-point	5 (emotions, functioning, symptoms, self-confidence, stigmatization)	Cronbach's α 0.55–0.82 for each domain
WHGQ	2009	USA	English	AGA/ FPHL in women	Since the start of treatment	4	NR	Single	Cronbach's α 0.81, ICC 0.89
AAQ	2012	Japan	Japanese	AA	1 month	7	5-point	3 (restriction of activity, concealment, adaptation)	Cronbach's α 0.59–0.81 for each domain
Hair-Specific Skindex-29	2012	Spain	Spanish	FPHL in women	NR	29	5-point	3 (emotions, functioning, symptoms)	Cronbach's α 0.96, ICC 0.98
AASIS	2013	USA	English	AA	1 week	13	11-point	3 (interference, hair loss, other symptoms)	Cronbach's α 0.77–0.93 for each domain
AA-QLI	2013	Italy	Italian	AA	1 month	21	4-point	3 (subjective symptoms, objective signs, relationship)	NR
A-QLI	2016	South Africa	English	Alopecia	NR	19	4-point	3 (subjective symptoms, objective signs, relationship)	NR

Abbreviations: AA, alopecia areata; AAQ, Alopecia Areata Quality of Life; AA-QLI, Alopecia Areata Quality of Life Index; AASIS, Alopecia Areata Symptom Impact Scale; AGA, androgenetic alopecia; A-QLI, Alopecia Quality of Life Indicators; FPHL, female pattern hair loss; ICC, intraclass correlation coefficient; MHGQ, Men's Hair Growth Questionnaire; NR, not reported; WAA-QOL, Women's Androgenetic Alopecia Quality of Life Questionnaire; WHGQ, Women's Hair Growth Questionnaire.

Women's Hair Growth Questionnaire

The Women's Hair Growth Questionnaire (WHGQ) is a specific HRQoL instrument intended for use in female patients with AGA/FPHL. During its development, the initial 20 questions were identified from a literature review, focus groups of women with AGA/FPHL, and expert opinions. The patients' feedback from cognitive interviews was used to guide item revision and reduction to the final version of 4 items that assess growth of hair, amount of noticeable new hair, visibility of the scalp, and rate of hair loss since the start of the treatment. Good internal consistency, test-retest reliability, and responsiveness to change were shown.[55]

Alopecia Areata Quality of Life

The Alopecia Areata Quality of Life (AAQ) scale is a concise Japanese HRQoL instrument specific to AA that can be completed in two minutes. The preliminary questions were created from qualitative interviews, and the revisions were guided by patients' comments. After being tested for internal consistency and construct validity, the final version retains seven questions that contribute to three subscales, ie, restriction of activity, concealment, and adaptation, with a recall period of one month.[56]

Hair-Specific Skindex-29

Skindex-29 was modified to assess the HRQoL of Korean male patients with AGA by replacing the words "skin" with "scalp" and "skin condition" with "AGA" and was renamed the Hair-Specific Skindex-29.[57] Details on the processes of Korean translation, adaptation, and validation were not available. Nevertheless, Skindex-29 underwent a formal translation and cross-cultural adaptation to Spanish and was thoroughly tested for validity and

reliability by Spanish female patients with FPHL, with satisfactory face validity, construct validity, and test-retest and internal consistency. Factor analysis showed 3 domains similar to those of the original Skindex-29.[58] Responsiveness to change was subsequently shown in a longitudinal study.[59] The Hair-Specific Skindex-29 has also been adapted for use in India[60] and Russia,[61] but details on the processes of adaptation and validation were not available.

Alopecia Areata Symptom Impact Scale

The Alopecia Areata Symptom Impact Scale (AASIS) was developed for AA in English using retrospective data of responses to 125 items of several HRQoL instruments, including Skindex-16 and the DLQI, from 1649 patients who participated in the National Alopecia Areata Registry of the USA as the input. Extensive reduction of items was carried out by means of cluster analysis and clinical experts' reviews to yield the final 13 items grouped into 3 subscales, ie, interference, hair loss, and other symptoms, with good internal consistency. Cognitive debriefing of participants showed acceptable content validity.[62,63]

Alopecia Areata Quality of Life Index

The Alopecia Areata Quality of Life Index (AA-QLI) is a disease-specific HRQoL instrument for AA in Italian that contains 21 items contributing to three domains, ie, subjective symptoms, objective signs, and relationships, with a recall period of one month. The questions were reported as being guided by answers from AA patients about the impact of AA and its treatment on their lives, but the processes of qualitative study and tests for reliability were not detailed. Good concurrent validity was shown between the total scores of the AA-QLI and the DLQI. Calculation of an index from the scores using the weights derived from structural equation modeling was also proposed.[64]

Alopecia Quality of Life Indicators

Alopecia Quality of Life Indicators (A-QLI) is an adaptation of the abovementioned AA-QLI (which is specific to AA) to be used with alopecia patients in general. However, the authors acknowledged a concern over its selection bias because the development was based on a pilot study in 50 South African women with alopecia, of which LPP/FFA was the most prevalent type. This might affect the generalizability in other populations of alopecia patients. The items were quite similar to those of the AA-QLI, but with the number of questions reduced from 21 to 19, while the three domains of the AA-QLI were retained with good internal consistency. Weighting factors for calculating an index were also proposed.[65]

Skindex-16 for AA

Skindex-16 for AA is a modification of Skindex-16 for use in patients with AA[66] whose development is still ongoing.[67]

To seek information on HRQoL measures, in addition to using regular search engines, there are also certain online information sources that focus on COAs (among them, HRQoL measures), such as PROQOLID (https://eprovide.mapi-trust.org/about/about-proqolid), which is an online database designed for searching COAs, and the COnsensus-based Standards for the selection of health Measurement Instruments (COSMIN) Database of Systematic Reviews (https://database.cosmin.nl/), which is a database dedicated to systematic reviews of outcome measurement instruments. Although not exhaustive, these tools may be considerably helpful in finding appropriate instruments of COAs to suit one's need, such as for clinical practice or research.

Applications of Health-Related Quality of Life Measures

The most prominent application of HRQoL measures is probably their use in clinical research, which is the area for which most HRQoL measures were developed. The benefit of measuring HRQoL in clinical research is obvious, as HRQoL, along with other PRO measures, represents the patients' perceptions about the effects of the disease and its treatment. Without measuring HRQoL, researchers could fail to capture the other dimensions of those effects that are also important to the patients. HRQoL measures have been progressively developed and used over the past decades in clinical studies,[68] both observational and experimental. HRQoL information from healthcare research may also help in estimating the burden of disease, interpreting outcomes of clinical studies, and determining the cost-effectiveness of treatments.[69] Moreover, regulatory agencies such as the US Food and Drug Administration and the European Medicines Agency recognize PRO measures, including HRQoL, in their drug evaluation process and claim substantiation. Their guidelines regarding the expected properties of PRO measures for this purpose have been

provided.[20,70] HRQoL measures, including DLQI, have been used for labeling several drugs.[71]

HRQoL measurement has also been increasingly encouraged to be incorporated into routine clinical practice to aid clinicians' treatment decision making.[72] As the perception of disease status by clinicians and patients may not always be congruent,[73,74] an explicit HRQoL assessment should provide clinicians with valuable information to support clinical decision making. Other possible benefits, such as its potential to improve clinician-patient communication, awareness of the skin disease burden, efficiency of the consultation, and clinical service administration,[75] may also be relevant.

Current Usage of Health-Related Quality of Life Instruments in Clinical Trials of Alopecia

To gain an impression of the current situation of how HRQoL is measured to assess the effects of treatments for alopecia, we conducted a literature review of parallel randomized controlled trials (RCTs) on any intervention used for treating alopecia of any type that were indexed in PubMed and Embase in the past half-decade (ie, from 2016 to May 2021). Sixty-one parallel RCTs from every continent were identified. They were conducted on alopecia patients diagnosed with AA, AGA, FPHL, telogen effluvium, chemotherapy-induced alopecia, LPP, or trichotillomania and evaluated a wide range of interventions, including oral drugs, topical drugs, cosmeceuticals, medical procedures, laser and light therapies, acupuncture, injections with neurotoxin, stem cells, platelet-rich plasma, and some combinations thereof. Only eight RCTs (13.1%) measured HRQoL as a study outcome using a generic (ie, QOLI[76]), dermatology-specific (ie, DLQI[77–79]), or hair-specific HRQoL instrument (ie, AASIS[80,81] or WAA-QoL[82,83]). Among these eight studies, the patients were blinded in four.[76,79–81] The patients in the other four studies were aware of the treatment given.

These findings suggest that HRQoL is rarely measured in RCTs of alopecia treatments. Blinding of study participants is also surprisingly underused.

Some Issues Concerning the Use of Health-Related Quality of Life Measures in Alopecia Patients

As demonstrated above, HRQoL measurement is an area that is still underappreciated in clinical trials on alopecia patients, despite the considerable number of hair-specific HRQoL instruments available. This problem could be addressed by the advent of a core outcome set, ie, a minimum set of outcome measures that have been agreed upon to be important and necessarily reported in all clinical trials for a specific condition,[84] which should standardize the types of outcome measures used and promote comparability of results across trials evaluating the same disease.[85–88] Core outcome sets have been developed for several skin diseases,[89] but one for hair loss/nonscarring alopecia is still under development.[90] However, the Alopecia Areata Consensus of Experts (ACE) group has proposed a consensus on the outcome measures for AA patients, which recommended that measurement of HRQoL is required in clinical trials.[91] If core outcome sets for alopecia have been successfully developed and complied with, the problem might be resolved to some extent. Nevertheless, for clinical trials using split-scalp, intraindividual comparisons, it should be difficult to apply HRQoL measurements because each patient, whose HRQoL is measured once, receives more than one treatment.

Moreover, bias in HRQoL measurement does not seem to be rigorously avoided. HRQoL is assessed by the patients themselves. Therefore, failure to blind the patients results in an increased risk of measurement bias. The sequence of measurement of multiple outcomes on the same visit can also be important. It is recommended that PRO assessments should be completed before the outcomes by other parties, such as clinician-reported outcomes or objective measures, are assessed. Otherwise, the patient's responses to PRO measures may be influenced by their knowledge of those outcomes.[70] Methodological weaknesses in the conduct of clinical trials can undermine the validity of the study, of which the results may consequently deviate from the truth.

Another issue of concern for HRQoL instruments is that they are developed and validated for a specific group of people or patients. Validity might not be retained if the instrument was modified or used with people different from the intended population or even when the mode of administration was changed, eg, from paper to electronic format or from an interview to self-administration. In these situations, the instrument should be validated again to ensure its ability to measure what it is designed for.[70]

In addition, although measurement of HRQoL in clinical practice should also be encouraged because of the potential benefits, the burden of using HRQoL to both

clinicians and patients may be a barrier against its use.[75] Therefore, shorter instruments, which impose less burden, with acceptable psychometric properties might gain advantages in this regard.

Conclusions

There are several dermatology- and hair-specific HRQoL instruments available, some of which are well developed and possess good measurement properties. However, underuse of these instruments in both clinical trials and clinical practice and a lack of standardization and regulation of their use are current issues. Core outcome sets should be developed for clinical trials on alopecia, and measuring HRQoL in clinical practice should be encouraged.

Disclosure

The authors report no conflicts of interest in this work.

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