

Health-related quality of life and utility assessment among psoriasis patients in Hungary

Doctoral dissertation

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1. Introduction

Psoriasis is a chronic, autoimmune, papulosquamous dermatological disease. Adult prevalence is around 2%, genetics, age, environmental and geographical factors specifies the incidence.

The immune-mediated inflammation is caused by, on the one hand, the excessive reaction of the innate immune system, the antigen-presenting cell activation, and on the other hand, the abnormal, inflammatory response of the adaptive immune system. The clinical picture is characterized by the triad of erythema (redness), infiltration (thickness) and desquamation (exfoliation). Psoriasis can take on a variety of forms, and skin symptoms can either be localised or generalised. The disease has significant extracutaneous manifestations (e.g. metabolic syndrome, inflammatory bowel diseases, mental illnesses), and in about one-third of the patients psoriatic arthritis can be detected, often causing functional limitations and pain. Psoriasis is, therefore, associated with a notable impairment of health-related quality of life (HRQoL). The therapeutic palette of psoriasis includes local therapy, phototherapy, systemic synthetic/chemical and systemic biological therapies.

In psoriasis general HRQoL can be assessed by the EQ-5D health status questionnaire, whereas dermatology-specific HRQoL by the Dermatology Life Quality Index (DLQI). Disease severity is most commonly graded by Psoriasis Area and Severity Index (PASI). Health status of psoriasis patients can also be evaluated by utility measurement, which reflects the degree of preference of a specific health state or outcome. Health utility values can be used to calculate quality-adjusted life year (QALY). Measurement of utility values is especially

important from the health economic point of view, as health economic evaluations based on utilities (cost-utility analyses) aim to inform drug financing and health policy decision making.

In the 20-21th century the technological advancements in healthcare were accompanied by an enormous increase in healthcare costs. Reimbursement eligibility criteria in Hungary are specified by medical and financing protocols. In some of the benefits covered by the social insurance it is not enough to have a diagnosis, the therapy application is linked to certain degree of severity or health-related quality of life status. In clinical and financing decisions, the aforementioned health state, disease severity, HRQoL and utility measures have a paramount importance. Disease severity and dermatology-specific measures (e.g. PASI, DLQI) play a fundamental role in international medical guidelines and also in cost-effective allocation of healthcare resources (e.g. therapy indication, treatment follow up, therapy change, reimbursement eligibility criteria). Inadequate measurement methods may bias the quality of clinical decisions and lead to non-cost-efficient treatments. The use of proper standards describing patients' health status and HRQoL have now become essential tools to evidence based clinical decisions and effective resource allocations.

2. Objectives

2.1. Comparison of the measurement properties of EQ-5D-3L and EQ-5D-5L

Comparison of the EQ-5D questionnaire's earlier and newer versions, namely the EQ-5D-3L and the EQ-5D-5L quality of life questionnaires in psoriasis patients.

Hypotheses:

The new, improved version (EQ-5D-5L) of the EQ-5D general HRQoL questionnaire has better psychometric properties in psoriasis than the original version (EQ-5D-3L):

- a. It reduces ceiling effects and demonstrates a better informativity.
- b. It indicates a better correlation with PASI and DLQI indices.
- c. It performs a better known-groups validity.

2.2. Psoriasis health states evaluation by using time trade-off method

Evaluating the utility values of different psoriasis states by using time trade-off (TTO) method and in the light of this, assessing the validity of quality of life indices playing a central role in clinical and financial decision-making.

Hypotheses:

The validity of DLQI dermatology-specific quality of life index might be questionable in psoriasis:

- a. Utility values for health states with different DLQI total scores might be similar, and utility values with identical DLQI total scores may be different in patients with psoriasis.
- b. Patients with psoriasis generally evaluate the health states defined by the DLQI better than the normal population.

3. Methods

Our research was carried out in close collaboration between Department of Dermatology, Venereology and Dermatocology, Faculty of Medicine, Semmelweis University and the Department of Health Economics, Corvinus School of Economics, Corvinus University of Budapest. Ethical approval was obtained from the Semmelweis University Regional and Institutional Committee of Science and Research Ethics (Reference No. 58./2015).

3.1. Study design and patient population

Between September 2015 and June 2016, a cross-sectional survey was carried out among 238 patients. Consecutive in- and outpatients aged over 18 years or over with psoriasis were included. The diagnosis was established by two independent dermatologists. Informed consent was obtained from all patients participating in the study.

The survey comprised of a paper-based questionnaire, first part was completed by the patients and the second part by their dermatologists. Patients were asked about socio-demographic characteristics, medical history was recorded, and patients' general health (EQ-5D-3L, EQ-5D-5L, EQ VAS), dermatology-specific HRQoL (DLQI) and health state utility (10-year time trade-off) was assessed. Due to lack of Hungarian value sets, the United Kingdom/England tariffs were used to calculate EQ-5D-3L and EQ-5D-5L utilities (range: -0.594-1 and -0.281-1, respectively). Furthermore, patients evaluated three hypothetical health states described by the DLQI by TTO, in a randomized order. Dermatologists provided data about

clinical characteristics, disease duration, disease severity (PASI) and treatments.

3.2. The psychometric analysis of EQ-5D-3L and EQ-5D-5L

Both EQ-5D instruments assess general aspects of health comprising five dimensions in its descriptive part, namely mobility, self-care, usual activities, pain/discomfort and anxiety/depression. The original version of the questionnaire, the EQ-5D-3L has three response levels (no problems, some problems, extreme problems), the new version, the EQ-5D-5L has five response levels (no problems, slight problems, moderate problems, severe problems, extreme problems) in each dimension. The second part of the EQ-5D (EQ VAS) records the respondent's self-rated health on a vertical health thermometer (range: 0-100) where the endpoints are labelled the worst and the best imaginable health state.

Following the methodology used in previous studies of various chronic diseases and normal population, the psychometric analysis of EQ-5D-3L and EQ-5D-5L was performed, such as feasibility, ceiling effect, redistribution properties (inconsistent response pairs), discriminatory power (informativity), convergent validity and known-groups validity.

3.3. Utility values for patients' own and for the hypothetical DLQI health states

The time trade-off method involves a hypothetical decision between two alternatives: a shorter life in impaired health or a longer life in full health.

As a warm-up task, patients were asked to compare their own health state with the hypothetical DLQI defined health states. Patients evaluated their own and three further hypothetical DLQI defined health states in a randomized order by using time trade-off method. The timeframe of the time trade-off was set at 10 years similarly to the study targeting the general public, where the given up time unit was one year, 6 months between 0 and 1 year. The patients imagined living in their actual condition for the next 10 years, after which they would die, then the patients were asked to decide how many years they would give up to regain full health. In our study the utility scores were anchored between 0 (as bad as dead) and 1 (full health), utility was calculated by extracting the tenth of the given up time from one.

Overall, seven hypothetical DLQI health states were evaluated, three DLQI score of 11 points (L1-L3, where L refers to large impact on HRQoL), three DLQI score of 6 points (M1-M3, where M refers to moderate impact on HRQoL) and one DLQI score of 16 points (where S refers to severe impact on HRQoL). The DLQI differences between hypothetical health states (5 points) were larger than the minimal clinically important difference (MCID) in psoriasis (4 points).

Utility values were also compared to the values previously obtained from the normal population sample.

4. Results

4.1. Characteristics of the patient population

A total of 238 patients were enrolled in the study, with a mean age of 47.44 years (SD: 15.20, minimum 18, maximum 86), the average disease duration was 18.10 years (SD: 12.34, minimum 3 months, maximum 52 years). A slight male dominance was observed (male: N=149, 62.6%, female: N=89, 37.4%). The majority of the patients were outpatients (N=211, 88.7%), minority were hospitalized at the Dermatology, Venereology and Dermatooncology Clinic due to psoriasis (N=27, 11.3%).

The study population had a higher level of education compared to the Hungarian population aged 15-74.

According to disease severity 62 patients (26.9%) had mild, 174 patients (73.1%) had moderate-to-severe psoriasis.

The proportion of the treatments were the following: none (N=8, 3.4%), topical only (N=91, 38.2%), phototherapy (N=1, 0.4%), systemic, non-biological (N=51, 21.4%), biological (N=87, 36.6%).

Mean PASI score (range: 0-72) was 8.68 (SD: 9.19), mean DLQI score (range: 0-30) was 7.13 (SD: 7.36). The quality of life measures provided the following average scores: EQ-5D-3L score (range: -0.594-1) was 0.77 (SD: 0.26), EQ-5D-5L score (range: -0.281-1) was 0.84 (SD: 0.19) and EQ VAS score (range: 0-100) was 72.46 (SD: 20.27). The EQ-5D-3L index scores were compared to the age- and gender-matched Hungarian population norm, the differences were significant for females aged between 18-24 and 25-34 years, and males aged between 25-34 years ($p < 0.05$). The mean time trade-off utility value for patients' own health state was 0.93 (SD: 1.60).

4.2. Comparison of the measurement properties of EQ-5D-3L and EQ-5D-5L

The EQ-5D-5L performed a better feasibility and ceiling effect than the EQ-5D-3L. Evaluating ceiling effect (EQ-5D-3L vs. EQ-5D-5L) self-care showed the highest (85.7% vs. 81.9%) and pain/discomfort the lowest (49.6% vs. 46.6%) percentage of patients without any complaint. The inconsistency – where the EQ-5D-3L response is two or more levels away from the EQ-5D-5L response – was low, and it was observed in a minor subgroup of the patients (16%). The highest rate of inconsistent responses was measured in anxiety/depression dimension (6.3%). The EQ-5D-5L index showed higher absolute informativity across all five dimensions and a better relative informativity in mobility, self-care and usual activities dimensions. The correlation between the two EQ-5D indices, and the PASI, the DLQI, and between the EQ-5D-5L index and the EQ VAS was moderate, while EQ-5D-3L index and EQ VAS produced a moderate-to-strong correlation indicating an overall good convergent validity. Known-groups validity was evaluated for EQ-5D-3L and EQ-5D-5L, both versions were able to discriminate between groups of patients based on gender, most clinical subtypes (EQ-5D-5D: 5/7 vs. EQ-5D-3L: 4/7), number of clinical subtypes and treatments, but not between age groups ($p < 0.05$). The presence of nail, scalp psoriasis and psoriatic arthritis resulted in the highest difference in both EQ-5D-3L and EQ-5D-5L index scores.

4.3. Utility values for patients' own and for the hypothetical DLQI health states

During the study the patients performed 704 comparisons (worse, being the same, better) between their own health and the hypothetical DLQI health states, with 10 (1.4%) missing responses. The majority (N=463, 65.8%) of the judgements were correct, overestimation (N=159, 22.6%) and underestimation (N=82, 11.6%) occurred in few cases.

For the seven hypothetical health states, the total number of valid health state valuations was 699 (97.9%), with 15 (2.1%) missing answers. The mean utility values ranged from 0.83 (L1) to 0.91 (M2), utility scores were found to be homogenous across the seven hypothetical health states. In 11 out of the 15 comparisons across health states with DLQI differences larger than minimal clinically important difference, there was no statistically significant difference in utility values. Furthermore, in one out of the six comparisons across health states with identical DLQI scores a statistically significant difference was found in utilities.

Mean utilities assessed by psoriasis patients were higher for all seven health states in comparison with values from the general public. In the general population sample, 'full health' (utility=1) answers ranged between 9.6% and 22.3%, whereas the same proportion for psoriasis patients was between 30.6% and 44.1% (corresponding to S and M2 health states, respectively). The highest proportion of 'as bad as dead' (utility=0) responses was 2% (L1) among psoriasis patients and 12% (M1) among general public. The maximum difference in mean utilities across the seven health states was smaller for psoriasis patients than for general public (0.08 vs. 0.19).

5. Conclusions

5.1. Comparison of the measurement properties of EQ-5D-3L and EQ-5D-5L

Hypotheses:

The new, improved (EQ-5D-5L) version of the EQ-5D general quality of life questionnaire has better psychometric properties in psoriasis than the original version (EQ-5D-3L):

a. It reduces ceiling effects and demonstrates a better informativity.

EQ-5D-5L performed a lower ceiling effect comparing to EQ-5D-3L in four dimensions of the EQ-5D with the exception of anxiety/depression.

The EQ-5D-5L index indicated a higher absolute informativity across all five dimensions and a better relative informativity in mobility, self-care and usual activities dimensions.

b. It indicates a better correlation with PASI and DLQI indices.

The correlation analysis between the PASI and the EQ-5D-5L showed a better convergent validity in all five dimensions compared to EQ-5D-3L.

As for the correlation analysis between DLQI and the EQ-5D questionnaires, EQ-5D-5L performed better in mobility, self-care and usual activities dimensions.

c. It performs a better known-groups validity.

EQ-5D-5L performed slightly better than EQ-5D-3L during known-groups validity investigation. Both versions were able

to discriminate between genders, most clinical subtypes, number of clinical subtypes and treatments, especially in the presence of nail, scalp psoriasis and psoriatic arthritis.

5.2. Psoriasis health states evaluation by using time trade-off method

Hypotheses:

The validity of DLQI dermatology-specific quality of life index is questionable in psoriasis:

a. Utility values for health states with different DLQI total scores might be similar, and utility values with identical DLQI total scores may be different in patients with psoriasis.

Health states with different DLQI total scores were similar (15/11), health states with identical DLQI scores were evaluated to be different (6/1). Summing it up, in 12 out of 21 pairwise comparisons difference were found between DLQI scores and utilities. Our study confirms the results of a previous study based on Hungarian general population that found discrepancy between DLQI values and utility scores.

b. Patients with psoriasis generally evaluate the health states defined by the DLQI better than the normal population. According to the literature and our expectations mean utilities assessed by psoriasis patients were higher for all seven health states compared to the general population.

6. Bibliography of the candidate's publications

6.1. Publications related to the thesis

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