PROTOCOL

Association between SF-36 parameters (physical and mental component summary) and PsA clinical and patient-reported measures

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BACKGROUND

Psoriatic Arthritis (PsA) is a chronic inflammatory disease including heterogenous manifestations involving joints, skin, entheses, and nails, together with patient-reported symptoms such as fatigue and pain leading to decreased quality of life (QoL) (1).

The diverse symptoms often complicate treatment as to improve QoL, and is often combined with a discrepancy in perception of disease activity between patients and physicians (2) indicating features fatigue, pain, disability, tender and swollen joint count to be of most importance contributing to this discrepancy (3). A few studies have indicated a possible change in individual symptoms to be associated with change in QoL (4) which might be important to include when treating PsA.

Treatment of PsA aim to decrease disease activity often by use medical therapies involving conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs) or biological DMARDs (bDMARDs). Available medical therapies are well-known to be effective in reducing inflammation of joints and skin (5), thus with minor effect in patient-reported fatigue (6). This is highly relevant as fatigue by PsA patients is deemed to be one of the most significant symptoms of disease (7, 8), and rated as the worst symptoms after pain and skin disease (9, 10).

This demonstrates the relevance of investigating different PsA symptoms influence on patient-reported QoL and how treatment might effect QoL measures in association with individual symptoms of PsA and disease activity.

Objective

The primary objective of this study is to investigate change in patient-reported QoL, assessed by the Short Form 36 (SF-36) questionnaire, in relation to change in individual manifestation of PsA and disease activity in response to treatment. The secondary objective includes an assessment of differences between change in physical and mental component score of SF-36 as a proxy for physical and mental health, respectively.

Hypothesis

It is hypothesized that individual symptoms of PsA have differentiated effect on patient-reported QoL and that treatment will improve QoL to the extent that treatment improves the specific symptom and disease activity.

METHODS

Literature search

Prior to initiating the study, a literature search on the topic was performed (24. September 2019). Following search string was used to search for existing literature on the link between disease activity and quality of life in patients with PsA: (psoriatic arthritis) AND (DAS28) AND (Quality of life)

Study design

This study is an observational cohort study including data from the PIPA cohort (11).

Participants

Patients initiating new treatment in Danish outpatient clinics of Rheumatology were invited to participate in the PIPA cohort study. Patients were included in the PIPA cohort if:

- Age ≥ 18 years
- Diagnosed with PsA fulfilling the CASPAR classification criteria
- Initiating new treatment due to disease flare

Patients participated in a baseline visits and a 4 month follow up visit. At both visits a clinical examination was conducted, including the evaluation of joints, skin, entheses and nails, and patients filled in questionnaires SF-36, health assessment questionnaire (HAQ), and visual analogue scale (VAS) measuring global health, fatigue and pain.

Additional inclusion criteria for the current study include patients having complete data on SF-36 at baseline and follow up.

Variable and outcome measures

This study examines change in patient-reported QoL in relation to change in disease outcome measures in response to treatment. SF-36 is included for the assessment of patient-reported QoL. The SF-36 survey scores QoL by 8 parameters (12). A high degree of covariation is seen between individual variables. It applies for four of the 8 parameters measured that they primarily measure physical health, and that physical disease often affect these parameters (13). Another four parameters primarily measure mental health which through comparison have shown to be affected by mental diseases (14). These are scored as the Physical Component Summary (PCS) and Mental Component Summary (MCS), respectively. Statistical coding to create summary component scores are described in the Danish SF-36 manual (14). SF-36 is compared to changes in clinical and patient-reported indices, 1) disease activity measured by disease activity score (DAS28CRP) evaluating swelling and tenderness of 28 joints and CRP, 2) psoriatic area severity index (PASI) assessing severity of psoriatic skin plaques by means of area involved together with degree of redness, scaling and induration of the plaque, 3) number of psoriatic nails (only finger nails will be included (0-10), 4) Spondyloarthritis Research Consortium of Canada (SPARCC) enthesitis index evaluating the presence of enthesitis in 16 sites, VAS patient measuring pain, fatigue and global health, respectively, on a 0-100 mm scale with '0' being no pain/fatigue/etc, and '100' being worst imaginable pain/fatigue/etc., 5) HAQ for the assessment of patients' ability to conduct daily activities as a measure for disability.

Primary outcome

Change in QoL (ΔSF-36) as a function of ΔDAS28CRP and Δpain/Δfatigue/ΔSPARCC/ΔHAQ/ΔPASI/Δnumber of nails comparing baseline and follow up.

DATA ANALYSIS

Baseline characteristics are given as medians with interquartile ranges (IQRs) and numbers with corresponding percentages. Delta values will be presented as changes (baseline minus follow up) with delta (Δ) values on XYZ-plots. Associations between ΔPCS and ΔMCS score, ΔDAS28CRP and Δpain / Δfatigue / ΔSPARCC / ΔHAQ / ΔPASI / Δnumber of nails, respectively, will be presented with fitted linear regression plane models.

Results will be presented in:

Table 1: Patient characteristics

Figure 1: XYZ-plots presenting DAS28CRP on the x-axis, ΔSF-36 on the y-axis, and Δpain / Δfatigue / ΔSPARCC / ΔHAQ / ΔPASI / Δnumber of nails on the z-axis.

Statistical analysis will be conducted with the statistical software R including packages 'plot3D' with XYZ-plots programmed with the following code:

<u>1) linear regressions are developed from XYZ values</u>

```
fit <- lm(z ~ x + y1)

2) values on xy grid are predicted
grid.lines = 15
x.pred <- seq(min(x, na.rm=TRUE), max(x, na.rm=TRUE), length.out = grid.lines)
y.pred <- seq(min(y1, na.rm=TRUE), max(y1, na.rm=TRUE), length.out = grid.lines)
xy <- expand.grid(x = x.pred,y1 = y1.pred)
z_pred <- matrix (nrow = grid.lines, ncol = grid.lines, data = predict(fit, newdata = data.frame(xy),interval = "prediction"))

3) fitted points for droplines are included and the 3Dplot is made
cbind(x, y, z)
table(complete.cases(cbind(x, y, z)))
fitpoints<- predict(fit)
scatter3D(x=DATA$x, y=DATA$y, z=DATA$z, bty="g", add=FALSE, main="[text]", xlab="[text]",ylab="[text]",zlab="[text]", pch=18, cex=1text, phi=10, theta=40, colvar = NULL, col = "darkblue", ticktype="detailed", surf = list(x=x.pred,y=y.pred,z=z.pred, facets=NA, fit=fitpoints))
```

ETHICAL CONSIDERATIONS

In accordance with Danish law, the study is approved by the Ethical Committee of the Capital Region of Denmark (J.no.: H-15009080) and meets GDPR requirement approved by the Capital Region of Denmark (J.no. 2012-58-0004). All patients have provided written informed consent to participate.

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