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Epidemiology

Course of pain and fluctuations in pain related to suspected early hip osteoarthritis: the CHECK study

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Objectives: To evaluate the prevalence during a 10-year follow-up of clinically relevant fluctuations in pain and the course of hip pain in participants with hip complaints suspected to be early stage hip osteoarthritis (OA). To distinguish between participants with relevant fluctuations in pain and those without based on baseline characteristics.

Methods: Data were collected at baseline and after 2, 5, 8, and 10 years on 495 participants from the Cohort Hip and Cohort Knee Study (CHECK) with hip pain at baseline. Baseline demographic, anamnestic, and physical-examination characteristics were assessed. The primary outcome was levels of pain in the past week (scored using 0–10 Numeric Rating Scale) at follow-up assessments. Relevant fluctuation was defined as average absolute residuals greater than 1 after fitting a straight line to the participant's pain scores over time.

Results: The majority of the participants (76%) had stable or decreasing pain. Relevant fluctuations were found in 37% of the participants. The following baseline variables were positively associated with the presence of relevant fluctuations: higher levels of pain in the past week, use of pain transformation as a coping style, higher number of comorbidities, use of pain medication, and higher levels of high-sensitivity C-reactive protein. No associations were found for baseline radiographic hip OA or clinical hip OA.

Conclusion: During a 10-year follow-up, the majority of participants had stable or decreasing pain levels. In those participants with relevant fluctuation (37%), a limited number of baseline variables were associated with increased odds of having relevant fluctuations in pain.

Lay summary

Pain appears to be an important reason for consulting the general practitioner (GP) for hip osteoarthritis (OA) complaints. We know that hip pain remained quite stable over 10 years. Also is known that there is considerable variety between patients in pain. In this study, we found relevant pain fluctuations in 37% of primary care patients with hip complaints over a period of 10 years. The pain fluctuation was not associated with having osteoarthritis, neither radiographic hip OA (diagnosed based on a X-ray) or clinical hip OA (determined according to the American College of Rheumatology (ACR) criteria) at baseline. More research is needed to discover why some people experience fluctuations in time than others.

Key words: course, fluctuations, hip, osteoarthritis, pain, primary health care

Introduction

Pain appears to be an important reason for consulting the general practitioner (GP) for osteoarthritis (OA) complaints.[1] Recently, we published a study that showed that the level of pain in the Cohort Hip and Cohort Knee (CHECK) study as a group of participants suspected of hip OA remained quite stable over 10 years.[2] In a meta-analysis, the course of hip pain in OA patients was stable,[3] whereas other studies reported pain deteriorated slowly.[4, 5] Low educational level, more comorbidities, and high body mass index (BMI) were commonly reported predictors of increased pain.[6] Previous studies tried to explain the natural course of hip pain by defining trajectories through latent class growth analysis[7,8]; these studies hypothesized that the OA-population consists of homogeneous subgroups of patients, with stable mild and moderate progression in pain trajectories. These trajectories showed that the individual course of OA is variable: some patients showed stable disease symptoms or even improved disease symptoms, whereas others showed gradual deterioration, but those trajectories do not show fluctuations in pain.

Although OA is considered a chronic condition, studies showed that there is considerable variety between patients in pain, and weekly pain fluctuations have been identified.[9] Fluctuations in pain in hip and knee OA are reported to be associated with disability, poorer sleep quality, productivity losses, reduced quality of life (QoL), and higher healthcare resource use.[9-11] Treatment of OA flare-ups has proved to have positive effects on health-related QoL.[11] There is a wide variation in the definitions of OA flares, which, although focused on all symptoms of OA, predominantly emphasize on the measurement of pain.[12] Where OA flares tend to be episodic, with a duration ranging from minutes to hours to days, fluctuations in pain focus only on pain and on more long-term changes from stable pain trajectories. Understanding patient's patterns of hip OA-related pain and fluctuations in that

Key messages

- Overall pain remains quite stable in patients with hip osteoarthritis (OA).
- Relevant pain fluctuations were found in 37% of patients with hip complaints.
- Radiographic hip OA at baseline was not associated with relevant fluctuations.
- Clinical hip OA at baseline was also not associated with relevant fluctuations.

pain could help for the timing of medication use or other treatments.

Instead of defining trajectories by longitudinal cluster analysis, the aim of our study is to define the pain trajectories by clinically relevant fluctuations over time. This study aimed to: (i) Provide the prevalence of relevant pain fluctuations over time and how do the overall course of pain develop? (ii) Distinguish between participants with relevant fluctuations in pain and without such fluctuations, do these groups differ at the baseline? Therefore, we used data of the CHECK study with a study population of people with hip complaints that either not yet consulted their GP about the symptoms or consulted them for the first time within six months prior to baseline.

Methods

General design

Data were obtained from the CHECK study; details of this cohort are published elsewhere.[13] The CHECK study is a prospective, 10-year follow-up cohort of 1002 individuals with hip and/or knee complaints suspected to be early stage hip and/or knee OA,[14] with measurements at baseline, after 2-, 5-, 8-, and 10-years follow-up. Individuals entered the cohort between October 2002 and September 2005. Participants were recruited by their GP or through advertisements and articles in local newspapers and on the Dutch Arthritis Foundation. Inclusion criteria were stiffness and/or pain of the knee and/or hip, aged 45–65, not having yet consulted their GP for these symptoms, or having their first consultation within 6 months before entry. Exclusion criteria were having any other pathologic condition that could explain the symptoms (e.g., other rheumatic disease, previous hip/knee joint replacement, congenital dysplasia, osteochondritis dissecans, intra-articular fractures, and septic arthritis), having a comorbidity that would not allow physical evaluation and/or follow-up >10 years, malignancy in the last 5 years, and inability to understand the Dutch language. Details for follow-up rate are published elsewhere.[15] Medical ethics committees approved the study, and participants gave informed consent.

Outcome variable

Pain was assessed using the Numeric Rating Scale (NRS) (0–10; higher score indicates more pain). The participants were asked to score the pain they experienced in their most affected joint over the past week (at baseline and at 2-year measurement). In the 5-, 8-, and 10-year measurements, the participants were asked to report pain related to the left and right hips for the past week. Of these two separate measurements, we used the highest score as the pain outcome. Preoperative data up to the last visit prior to hip replacement (HR) were used for participants who received HR. Relevant fluctuations in pain were defined based on deviations from the overall linear course of pain for each participant: first, a straight line was fitted to the available NRS-scores (baseline through 10 years of follow-up [3–5 measurements]) per participant (observed values). Secondly, the predicted values were obtained based on the NRS scores. The absolute difference between the observed and predicted values at each available time point (residual) was calculated. Participants with an absolute average residual (difference) above the minimal clinically important pain difference (>1 on a 0–10 scale) were defined as having relevant fluctuations.[16] If the absolute average residual was ≤1, participants were defined as having minor fluctuations. Two examples (one with relevant fluctuations in pain and one with minor fluctuations in pain) are shown in Supplementary Figures S1 and S2. The natural course of the pain was defined based on the slope of the straight line fitted (first step). A slope of >0.1 (1/10 = 1-point difference, defined as clinically relevant, divided by 10-year follow-up) was defined as a relevant increase in pain. A slope of <–0.1 was defined as a relevant decrease in pain. We defined the pain as stable if the slope was between –0.1 and 0.1. For the present study, we selected participants who reported hip pain (yes/no) at baseline. Participants with <3 pain measurements were excluded from the analyses.

Covariates

The study included baseline medical history, physical examination, and radiographs of the hip to create variables that are available to the GP. The medical history was taken via questionnaires in which self-reported data were assessed. The demographic variables used were age, sex, height and weight (to calculate BMI), use of pain medication (none/paracetamol/aspirin/non-steroid anti-inflammatory drug/other), contact with a physiotherapist, and number of days per week physical activity (≥30 min/day). The number of comorbidities was defined by the presence of self-reported complaints, namely, asthma, chronic sinusitis, cardiovascular disease, high blood pressure, gastric ulcer, gallstones, liver disease, renal disease, diabetes, chronic cystitis, prolapse, thyroid gland disease, epilepsy, cancer, migraine, vertigo, severe skin disease, other chronic musculoskeletal diseases (including lower back pain, chronic inflammation of joints [i.e., rheumatoid arthritis], other chronic rheumatic diseases [>3 months], and disorders of neck/shoulder/elbow/wrist/hand). The WOMAC questionnaire was used to measure stiffness (0–8), pain (0–20), and physical functioning (0–68), with a higher score indicating worse health. Pain Coping Inventory (PCI) with six subscales was used to assess coping with pain. PCI measures active (transformation, distraction, and reducing demands) and passive (retreating, worrying, and resting) coping strategies.[17] On all subscales, a higher score means that when in pain, the coping strategy associated with the subscale is utilized more. The coping subscales are as follows. (i) Pain

transformation. This subscale focuses on reinterpreting and transforming pain, for example, 'I pretend the pain is not there' and 'I pretend the pain is less severe.' (ii) Distraction. This subscale focuses on distraction using physical activities (walking, cycling, or swimming) or other fun activities (music, reading, etc.). (iii) Reducing demands. This subscale assesses the extent to which patients make their activities less demanding ('I continue with less effort', 'I continue at a slower pace' and 'I continue with less precision'). (iv) Retreating. This subscale focuses on avoiding environmental stimuli, for example, 'I take care that I don't get upset' and 'I separate myself'. (v) Worrying. This subscale focuses on catastrophizing pain, for example, 'I focus on the pain all the time' and 'I start worrying'. (vi) Resting. This subscale assesses the level to which patients avoid physical activity when in pain ('I cease my activities' and 'I avoid physical exercise'). All six coping subscales are scored on a four-point Likert scale ranging from 1 (hardly ever) to 4 (very often) in terms of the frequency with which the strategies are applied when coping with pain.

During physical examination, participants were asked if they had morning stiffness of the hip (yes/no), hip pain (yes/no), and knee pain (yes/no). Pain during internal rotation of the hip was also asked (yes/no). At baseline, blood samples were collected to measure high sensitivity C-reactive protein (hs-CRP) and erythrocyte sedimentation rate (ESR). Clinical hip OA was determined according to the American College of Rheumatology (ACR) criteria which are: hip pain and all of the following criteria under [1] or [2]: [1] hip internal rotation ≥15°, pain present on internal rotation of the hip, morning stiffness of the hip ≤60 min, and age >50 years; [2] hip internal rotation <15°, and hip flexion ≤115° .[18] Standardized radiographs of the hips were collected and centrally scored[19] (sequence known) for OA features according to the Kellgren and Lawrence (KL) criteria.[20] All radiograph features in the hip showed good inter-observer reliability.[21] Radiographic OA (ROA) was defined as KL-grade ≥ 2. Information on HR was obtained from radiographs.

Statistics

Descriptive statistics were used to provide insight into the baseline characteristics. To obtain a normal distribution of hs-CRP and ESR, the natural logarithm was used. ANOVA or Pearson's χ^2-test was used to investigate how the included and excluded participants differed in characteristics. To explore whether we could identify distinctive baseline characteristics for participants with higher odds of relevant fluctuation in pain, univariate logistic regression analyses were performed to test whether there were statistically significant differences and to obtain crude odds ratios (OR). Next, separate multivariable models were run for each covariate of interest (each model adjusted for common participants characteristics [age, sex, and BMI]) in a multivariate model. The ORs represent the odds that the outcome (relevant fluctuations in pain) will be present in the participants with the particular characteristic, compared to the odds of having the outcome in the participants without that particular characteristic. Statistical analyses were performed using SPSS-V24.0 for Windows (SPSS Inc.) and Microsoft Excel-V2010.

Results

Baseline measurements

Of all participants, 588 reported hip pain at baseline. In total, 495 of the 588 eligible participants were included. The 93 (16%) excluded participants either had <3 pain assessments or they were lost to follow-up. These 93 participants were significantly more likely to have an HR during the 10-year follow-up (Table 1). Table 1 presents the characteristics of the study population; mean age was 55.5 (SD5.2), mean BMI was 26.2 (SD4.1) kg/m^2, 82% were female, and overall the mean NRS-score was 3.7 (SD2.1). The mean NRS-score at 10 years was 3.0 (SD2.7).

Fluctuations in pain and the course of pain

Of the 495 participants, 185 (37%) participants had a clinically relevant fluctuation in reported pain and 310 (63%) participants had minor fluctuation in pain over the 10-year follow-up period (Fig. 1). Of those with relevant fluctuations in pain, 43% (n = 79/185) of them had decreasing pain (Fig. 1b), 29% (n = 53/185) stable pain levels (Fig. 1d), and 29% (n = 53/185) increasing pain (Fig. 1f). Minor fluctuations were observed in 63% (n = 310) of the participants. Of those with minor fluctuations in pain, 44% (n = 136/310) of the participants had decreasing pain (Fig. 1a), 35% (n = 107/310) stable pain (Fig. 1c), and 22% (n = 67/310) increasing pain (Fig. 1e). Baseline characteristics per group are presented in Supplementary Table S1. The majority of the participants showed decreasing pain (43%) or stable pain (32%).

Associated baseline variables

The univariate associations and the associations adjusted for age, sex, and BMI between baseline characteristics and the presence of relevant fluctuations in pain over 10 years are presented in Table 2. The adjusted baseline characteristics associated with a relevant fluctuation in pain over 10 years were higher level of pain [OR = 1.18 (95% CI 1.08–1.30)], use of pain transformation as a coping strategy [OR = 1.35 (95% CI 1.03–1.78)], presence of comorbidities [OR = 1.18 (95% CI 1.04–1.35)], the use of any pain medication [OR = 1.46 (95% CI 1.00–2.14)], and higher hs-CRP [OR = 1.22 (95% CI 1.02–1.46)] (Table 2). Neither the presence of ROA nor clinical hip OA was significantly associated with fluctuations in pain [OR = 1.21 (95% CI 0.72–2.05) and OR = 0.87 (95% CI 0.56–1.35), respectively] (Table 2).

Discussion

A substantial proportion of our participants with hip pain suspected to be hip OA showed clinically relevant fluctuations in pain. Stable mild pain or an improvement in the pain over the entire follow-up period was found in the majority of the participants. The presence of relevant fluctuations in pain was observed in all three pain courses over time. ROA and clinical hip OA were not associated with relevant fluctuations in pain. Our results suggest that certain baseline variables (higher level of pain, use of pain transformation as coping style, presence of comorbidities, use of any pain medication, and higher hs-CRP-levels) are associated with increased odds of relevant fluctuation in pain in participants with hip pain suspected to be hip OA.

This study is one of the first to uncover distinct pain groups with respect to fluctuations in pain over 10-year follow-up in

Table 1. Characteristics at baseline (2002–2005) of the study population.

Baseline characteristics/factors	Included study population	Excluded study population[a]	*P*-value
Number of participants	495	93	
Age in years, mean (SD)	55.5 (5.2)	57.3 (5.3)	**<0.01**
Sex, n female (%)	408 (82)	67 (72)	**0.03**
Body Mass Index (kg/m^2), mean (SD)	26.2 (4.1)	25.8 (5.4)	0.37
Education level, *n* (%)			0.89
- Primary	89 (18)	18 (20)	
- Secondary	227 (47)	40 (44)	
- Higher	167 (35)	32 (36)	
Never smoked, *n* (%)	148 (31)	27 (30)	1.00
Use of alcohol, *n* (%)	381 (79)	65 (73)	0.21
Use of any pain medication, *n* (%)	204 (42)	46 (51)	0.11
Number of comorbidities, mean (SD)	1.7 (1.5)	1.4 (1.4)	0.09
Baseline NRS (0–10) last week, mean (SD)	3.7 (2.1)	3.8 (2.3)	0.49
Contact with a physiotherapist, *n* (%)	93 (19)	21 (23)	0.39
Coping style (range 1–4), mean (SD)			
Pain transformation	2.2 (0.7)	2.0 (0.7)	**0.02**
Distracting	2.3 (0.6)	2.2 (0.7)	0.39
Reducing demands	2.0 (0.6)	2.0 (0.7)	0.97
Resting	1.9 (0.5)	1.9 (0.6)	0.54
Worrying	1.6 (0.4)	1.6 (0.4)	0.51
Retreating	1.5 (0.5)	1.6 (0.5)	0.19
Morning stiffness in the hip <60min, *n* (%)	273 (55)	53 (57)	0.82
Knee pain, *n* (%)	368 (74)	50 (54)	**<0.01**
Physically active (>30 min) ≥3 times a week, *n* (%)	267 (56)	49 (55)	1.00
WOMAC			
• Pain (0–20), mean (SD)	5.4 (3.4)	5.8 (3.7)	0.34
• Stiffness (0–8), mean (SD)	2.8 (1.7)	3.0 (1.9)	0.31
• Physical function (0–68), mean (SD)	16.8 (11.9)	19.4 (12.4)	0.06
• Total sum score (0–100), mean (SD)	24.9 (15.9)	27.9 (17.0)	0.12
CRP, median (25–75 percentile)	1.4 (0.7–3.4)	1.2 (0.7–3.0)	0.17
ESR, median (25–75 percentile)	8.0 (5.0–13.0)	8.0 (5.0–13.0)	0.61
ROA either hip, *n* (%)	73 (15)	37 (40)	**<0.01**
ROA either knee, *n* (%)	59 (12)	17 (18)	0.13
Clinical hip OA[b] either hip, *n* (%)	123 (25)	37 (40)	**0.01**
Clinical knee OA[b] either knee, *n* (%)	183 (37)	23 (25)	**0.02**
HR after 10-year follow-up (total no.)	28 (6)	41 (44)	**<0.01**

Values are mean (standard deviation), median (25–75 percentile), or number (%). Differences in distribution between groups assessed with ANOVA or Pearson's χ^2 test as appropriate. Bold indicates *P*-value <0.05.
[a]Either lost to follow-up or ≤2 pain assessments.
[b]According to the clinical criteria of the American College of Rheumatology.
NRS = Numeric Rating Scale (0–10), WOMAC = Western Ontario and McMaster osteoarthritis index, hs-CRP = high-sensitivity C-reactive protein test, ESR = erythrocyte sedimentation rate, ROA = radiographic OA, HR = hip replacement.

individuals with hip pain suspected as hip OA in primary care. The strengths of this study are the population-based longitudinal design and the high response rate from baseline through follow-up. However, some limitations need to be discussed. First, selection bias due to loss to follow-up might have occurred. Our selective loss to follow-up and a reduction in the sample size might have led to biased results. The significantly different nature of the group of excluded participants can be explained by the fact that the people excluded because they had <3 measurement points were also more likely to have received an HR. It is possible that participants who received an HR have relevant fluctuations, but in this study we were not able to examine this hypothesis. A limitation to the data is that, although participants were asked where the pain was located (knee and/or hip; left and/or right), in the case of complaints in multiple joints participants were not asked which joint the NRS referred to. So for the baseline and measurement number 2, we do not know if the NRS-score we used to explain the course of pain is really hip pain. This could mean that we included not only participants with early hip complaints, but also participants with both early hip and knee complaints, and therefore, the NRS-score could also have applied to the knee pain. However, when we restricted the analysis to hip pain only and no knee

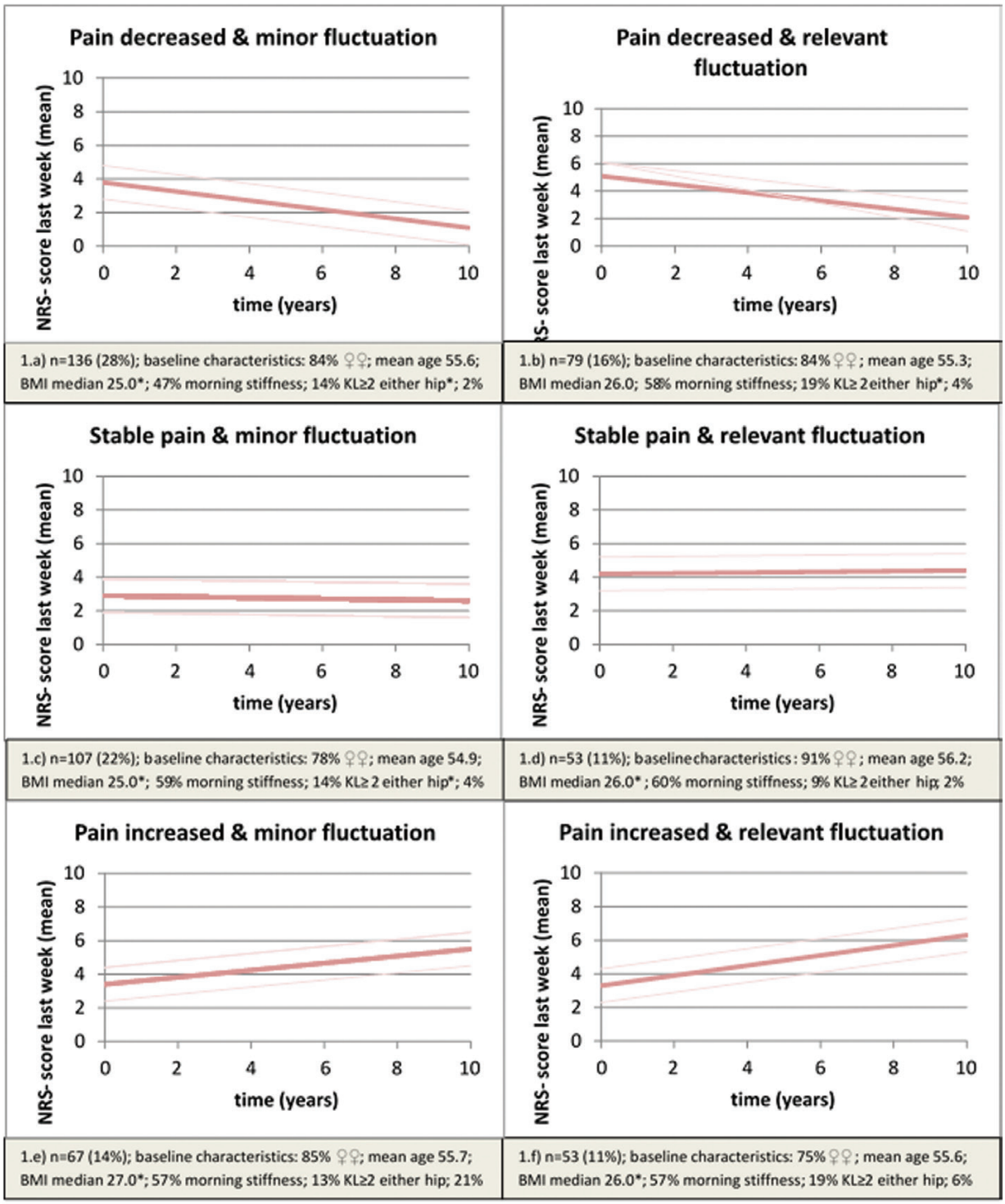

Figure 1. (a) to (f) describe the course of pain past week (mean NRS-score) classified based on pain slopes (>0.1 as clinically relevant increase in pain, <−0.1 as clinically relevant decrease in pain, and slopes between −0.1 and 0.1 as stable pain (thick line) and on the fluctuations in pain. There were some missing values in all figures (*1–4 missing participants).

pain at baseline, we found similar results (albeit with less power; Supplementary Table S2). Another limitation of our study is that we used measurements with time intervals of 2–3 years and that we may therefore have missed important fluctuations in between. A more frequent NRS-assessment would have led to a more detailed estimation of the fluctuations and the course of pain.

Relevant fluctuations in pain were observed in 185 participants (37%) in the present study. The percentage in our study is lower compared to other studies. A 12-week follow-up study reported weekly fluctuations of (WOMAC-)pain in 49% of their participants, aged ≥50 (mean age 65) with physician-diagnosed hip and/or knee OA, and recruited across primary care and rheumatology practices.[9] Another study observed

Table 2. Univariate and adjusted analysis for associations with the presence of relevant fluctuations in pain (*n* = 185) compared to minor fluctuations in pain (*n* = 310) over 10-year follow-up.

Baseline variables	Univariate analysis			+ adjustment for sex, age and BMI		
	OR	CI (95%)	*P*-value	OR	CI (95%)	*P*-value
Female	1.10	0.68–1.77	0.72	1.14	0.70–1.86	0.60
Age	1.01	0.98–1.05	0.60	1.01	0.97–1.05	0.61
BMI	1.05	1.00–1.09	0.06	1.05	1.00–1.09	0.05
Education (primary is ref)						
Secondary	1.07	0.65–1.77	0.79	1.12	0.68–1.86	0.66
- Higher	0.68	0.40–1.16	0.16	0.75	0.43–1.29	0.29
Number of comorbidities	**1.21**	**1.06–1.37**	**<0.01**	**1.18**	**1.04–1.35**	**0.01**
Knee pain	1.07	0.70–1.63	0.76	1.04	0.68–1.60	0.85
Morning stiffnessinhip	1.23	0.85–1.78	0.27	1.22	0.84–1.77	0.30
Activities 30min ≥ 3timesa week	1.06	0.73–1.53	0.77	1.09	0.75–1.58	0.66
Paid work	0.90	0.62–1.31	0.57	0.92	0.61–1.40	0.71
Missed work duetohip/knee problems?	0.79	0.33–1.91	0.60	0.73	0.30–1.82	0.50
Contact with a physiotherapist	1.14	0.71–1.80	0.59	1.12	0.70–1.80	0.65
Duration of complaints	1.00	0.99–1.00	0.37	1.00	0.99–1.00	0.21
NRS last week	**1.19**	**1.09–1.30**	**<0.01**	**1.18**	**1.08–1.30**	**<0.01**
Pain during walking	1.48	1.01–2.19	0.05	1.41	0.95–2.08	0.09
Pain during shopping	1.37	0.91–2.07	0.13	1.30	0.86–1.97	0.21
Pain coping strategies						
Pain transformation	**1.38**	**1.05–1.81**	**0.02**	**1.35**	**1.03–1.78**	**0.03**
Distracting	1.11	0.83–1.48	0.48	1.06	0.79–1.43	0.69
Reducing demands	1.26	0.94–1.69	0.13	1.25	0.93–1.82	0.14
Resting	1.12	0.78–1.63	0.54	1.03	0.70–1.51	0.88
Worrying	1.33	0.84–2.10	0.22	1.25	0.79–1.99	0.35
Retreating	0.93	0.62–1.39	0.72	0.88	0.58–1.32	0.53
Use of any pain medication	**1.53**	**1.05–2.21**	**0.03**	**1.46**	**1.00–2.14**	**0.05**
Painful internal rotation, either hip	0.96	0.66–1.38	0.81	0.89	0.62–1.30	0.56
(Natural logarithm of) hs-CRP	**1.29**	**1.09–1.51**	**<0.01**	**1.22**	**1.02–1.46**	**0.03**
(Natural logarithm of) ESR	1.02	0.80–1.30	0.88	0.93	0.70–1.23	0.61
KL≥2, either hip	1.19	0.72–1.97	0.51	1.21	0.72–2.05	0.48
KL≥2, either knee	1.27	0.85–2.54	0.17	1.40	0.80–2.43	0.24
Clinical hip OA[a], either hip	0.93	0.61–1.42	0.73	0.87	0.56–1.35	0.53
Clinical knee OA[a] , either knee	1.37	0.94–2.00	0.10	1.25	0.84–1.85	0.27

An OR > 1 indicates an increased odds for more fluctuation in pain. Bold indicates *P*-value <0.05.
BMI = body mass index, NRS = Numeric Rating Scale (0–10), hs-CRP = high-sensitivity C-reactive protein test, ESR = erythrocyte sedimentation rate, KL = Kellgren and Lawrence score.
[a]According to the clinical criteria of the American College of Rheumatology (ACR) at baseline, OR = Odds ratio, CI = confidence interval. All variables are baseline variables.

fluctuations in daily pain assessments in 41% of their participants with hip OA, according to clinical and radiological criteria and/or clinical criteria of ACR (follow-up: 28 days).[22] These participants, with hip OA according to clinical and radiological criteria and/or clinical criteria of ACR, needed an analgesic treatment for at least 1 week and were on average older (mean age 68.4) compared to our population.[22] In a study of 106 participants with rheumatic diseases (49% diagnosed with OA [not further specified]), 34% showed fluctuation in pain based on daily measurements.[23] The lower percentage in our study is possibly due to fewer assessments and longer time intervals between the measurements or due to the different study populations. Clinical hip OA and hip ROA at baseline were not associated with fluctuations in pain, implying that the presence of hip OA at baseline does not seem to be important for the presence of relevant fluctuations in pain over 10 years. Similar results were found for knee OA.[24]

In the present study, we found that participants with an active coping style with a high score for pain transformation (the person pretends the pain is absent or less intense than it actually is) had higher odds of having relevant fluctuations in pain over time. Previous research showed that participants with an active coping style strive to maintain their function and self-manage the pain.[25] The association between an active coping style and relevant fluctuations in pain could be explained by the fact that transforming the pain is beneficial in itself, but excessive use of this coping style is more

harmful because warning signs are ignored. We found that a higher level of hs-CRP was associated with fluctuations in pain. A higher level of hs-CRP might be linked mechanically to a more inflammatory type of OA[26] and subsequent periodic higher pain levels. Use of any pain medication was also found to be associated with fluctuations in pain. This is in line with research in flares in knee OA that found that patients in the flare-up group used more analgesics.[27] Another study found that use of pain medication was associated with pain flares in response to a repeated Sit-to-Stand activity in hip OA patients.[28]

For patients with minor fluctuations, it seems justified to retain the current approach and treatment (in general practice: lifestyle, education, and pain medication).[29-31] Clinical awareness of the GP for patients with higher odds of relevant fluctuations is important and could possibly help these patients to manage their disease better, which could possibly result in improved QoL.

Further studies are needed to replicate our findings and to further explore if those variables can be used as predictors for fluctuation in pain. Future studies are also needed to investigate the prognosis for these patients with relevant fluctuations in pain, how these relevant fluctuations are related to flares, and how to treat this group of patients optimally.

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Supplementary material

Supplementary material is available at *Family Practice* online.

Authors' contributions

ACB, DS, and SBZ contributed to the conception and design of this study. ACB, DS, and SBZ contributed to the analysis of the data. All authors contributed to the interpretation of the data. Article drafts were written by ACB and critically revised by all authors. The final version of the article was approved by all authors.

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Conflict of interest

None declared.

Data availability

Datasets analyzed during the current study are available from the corresponding author on reasonable request.

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