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ORIGINAL ARTICLE

# Osteoarthritis of the hip or knee: which coexisting disorders are disabling?

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**Abstract** Exercise therapy is generally recommended in osteoarthritis (OA) of the hip or knee. However, coexisting disorders may bring additional impairments, which may necessitate adaptations to exercise for OA of the hip or knee. For the purpose of developing an adapted protocol for exercise therapy in OA patients with coexisting disorders, information is needed on which specific coexisting disorders in OA are associated with activity limitations and pain. To describe the relationship between specific coexisting disorders, activity limitations, and pain in patients with OA of the hip or knee, a cross-sectional cohort study among 288 older adults (50–85 years of age) with OA of hip or knee was conducted. Subjects were recruited from three rehabilitation centers and two hospitals. Demographic data, clinical data, information about coexisting disorders (i.e., comorbidity and other disorders), activity limitations (WOMAC: physical functioning domain), and pain (visual analogue scale (VAS)) were collected by questionnaire. Statistical analysis included descriptive statistics and multivariate regression analysis. Coexisting disorders associated with activity limitations were chronic back pain or hernia, arthritis of the hand or feet, and other chronic rheumatic diseases (all musculoskeletal disorders); diabetes and chronic cystitis (non-musculoskeletal disorders); hearing impairments in a face-to-face conversation, vision impairments in long distances, and dizziness in combination with falling (all sensory impairments); and overweight and obesity. Coexistent disorders associated with pain were arthritis of the hand or feet, other chronic rheumatic diseases (musculoskeletal disorders), and diabetes (non-musculoskeletal disorder). Specific disorders coexisting next to OA and associated with additional activity limitations and pain were identified. These coexisting disorders need to be

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addressed in exercise therapy and rehabilitation for patients with OA of the hip or knee.

**Keywords** Activity limitations · Coexisting disorders · Comorbidity · Osteoarthritis · Pain

## Introduction

Osteoarthritis (OA) is one of the diseases with the highest rates of comorbidity [1]. Previous studies have reported comorbidity rates of 68% to 85% [2–5]. Diseases that frequently occur next to OA are diabetes, hypertension, and cardiovascular disorders; other disorders, including overweight and back pain, occur frequently as well [1, 4, 6]. Thus, coexisting disorders—defined as coexisting diseases and coexisting other disorders (e.g., overweight)—are highly prevalent in OA.

Exercise therapy is generally recommended in OA of the hip or knee: Exercise is effective in reducing activity limitations and pain in OA [7, 8]. However, coexisting disorders may bring additional impairments, which necessitate adaptations to the exercise protocol for OA of the hip or knee. For the future purpose of developing such an adapted protocol, information is needed on which specific coexisting disorders in OA are disabling, i.e., which coexisting disorders are associated with activity limitations and pain. Coexisting disorders causing activity limitations and pain are likely to cause restrictions to exercise therapy as well, necessitating adaptations in the exercise protocol.

Previously, we have reported which coexisting disorders are associated with additional activity limitations and pain in OA of hip or knee [5, 9]. In these studies, we used the Cumulative Illness Rating Scale (CIRS) [10–12] to assess coexisting disorders. The CIRS yields information on global categories of coexisting diseases, e.g., ear, eye, nose, and throat diseases or endocrine and metabolic diseases. Although quite informative, more detailed information on which specific coexisting disorders are disabling is required in order to be able to develop the exercise therapy protocol with adaptations for coexisting disorders. The objective of the study was to describe the relationship between specific coexisting disorders, activity limitations, and pain in patients with hip or knee OA.

## Methods

### Design

The present study is a secondary analysis of previously reported data [5]. The design of this cross-sectional study is summarized below. The reader is referred to the original publication for a more detailed description of the design [5]. The study was approved by the Medical Ethical Committee of the VU University Medical Centre, Amsterdam, the Netherlands.

### Study population

Participants were recruited from three rehabilitation centers and two hospitals (Departments of Orthopedics, Rheumatology, or Rehabilitation). Inclusion criteria were (a) diagnosis of OA of the hip or knee by medical specialist according to radiological criteria or clinical criteria of the American College of Rheumatology [13, 14], (b) 50 years of age or older, (c) referral to hospital or rehabilitation center less than a year before inclusion, (d) at least moderate functional problems (Lequesne algofunctional index score ≥5) [15], and (e) informed consent. Exclusion criteria were (a) 85 years of age or older, (b) insufficient understanding of the Dutch language, and (c) expected death due to fatal illness within 1 year after inclusion.

### Measurements

Patients were invited to a test location. The data used in the present study were gathered by means of interview (demographic and clinical data) and questionnaires (activity limitations, pain, and coexistent disorders). X-rays were used to evaluate radiological impairment of the hip or knee.

#### *Demographic and clinical data*

Demographic and clinical data were collected for each patient including age, gender, height, weight, location of OA, duration of complaints, other joint complaints, level of education, and marital status. Body mass index (BMI) was calculated (weight/height$^2$). If available, X-rays of the hip and knee recorded in the year before inclusion were scored on joint space width and osteophytes, following a standardized procedure [16, 17]. A 0–3 scale was used for rating the radiographs: 0=normal; 1=mild or 1–33% abnormal; 2=moderate or 34–66% abnormal; 3=severe or 67–100% abnormal. From these scores, Kellgren and Lawrence grades were calculated.

#### *Activity limitations and pain*

Activity limitations were measured using the physical functioning domain of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) (range 0–100) [18, 19]. WOMAC physical functioning score is a standardized score using the formula: ((68−total score on the physical functioning domain)×100)/68. A higher score on this standardized WOMAC stands for fewer activity

limitations. Pain at the time of assessment was rated on a visual analogue scale (VAS) (range 0–10). A higher score on VAS reflects more pain.

*Coexisting disorders*

Patients indicated the presence or absence of coexisting disorders in the year prior to the interview, using the list of the Dutch Bureau of Statistics (CBS). This list describes the most common chronic diseases and disorders in the Netherlands [20]. Based on expert consultation, impairments in vision and hearing were added to this list. Overweight was defined as 25 kg/m$^2$≤BMI<30 kg/m$^2$; obesity was defined as BMI≥30 kg/m$^2$. Coexisting disorders were categorized as musculoskeletal disorders, non-musculoskeletal disorders, sensory impairments, and overweight and obesity.

Statistical analyses

The presence of coexisting disorders, activity limitations, and pain was analyzed using descriptive statistics. Subsequent analyses were limited to those disorders that affected ≥5% of the study population. The association between coexisting disorders (present or absent) and activity limitations was evaluated in multivariate regression analyses, correcting for age and gender. Similar analyses were done for the association between coexisting disorders and pain, correcting for age and gender. An association was termed significant if the $p$ value was <0.05. For all analyses, the SPSS (version 14.0) was used [21]

## Results

Study population

Initially, 775 patients with osteoarthritis of the hip or knee that visited the department in the year prior to inclusion were contacted by mail and were asked to participate in the study. Of those patients that volunteered ($n$=364), 288 were included. Seventy-six patients were excluded because they did not meet the inclusion criteria. Reasons of exclusion were age ($n$=2), language ($n$=4), less than moderate functional problems ($n$=48), and referral longer than 1 year before inclusion ($n$=22). Analyses showed that there were no differences between the group of patients that were initially contacted ($N$=775) and the patients that were included in the study ($N$=288) with regard to age and gender. Some differences were found in the location of OA. Compared to our study population, patients that were initially contacted suffered less frequently from both hip and knee OA (6.2%) and more frequently from knee OA (59.5%) and hip OA (34.3%) [5].

Table 1 shows baseline characteristics of the study population. The majority of the study population was female (71,2%), the mean age was 66 (SD=8,7) years. The largest part of the subjects (48.4%) suffered from knee OA, 25.1% suffered from hip OA, and 26.5% had both hip and knee OA. The mean physical functioning score on the WOMAC was 56.5 (SD=19.6), and the mean pain score on the VAS was 4.8 (SD=2.6). Most patients (80%) were recruited from the departments of orthopedics; the other 20% originated from departments of rheumatology and departments of rehabilitation.

Coexisting disorders

The presence of coexisting disorders in the study population is presented in Table 2. Eighteen coexisting disorders occurred in >5% of the sample (see Table 2). In the category of musculoskeletal disorders, coexisting conditions occurring in >5% of the patients included chronic back pain or hernia, 29.5%; arthritis of the hand or feet, 18.4%; and other chronic rheumatic diseases, 10.1%. In the category of non-musculoskeletal disorders, coexisting conditions occurring in >5% of the patients included hypertension, 31.9%; asthma or COPD, 15.6%; sinusitis, 12.2%; diabetes, 9.7%; thyroid disorders, 8.7%; severe cardiac disorder or coronary disease, 8%; severe bowel disorder, 6.6%; migraine, 6.6%; chronic cystitis, 5.6%; and prolapse in 8.3% of the female patients. In the category of sensory impairments, coexisting conditions occurring in >5% of the patients were hearing impairments in a group conversation,

**Table 1** Baseline characteristics ($N$=288)

| | |
|---|---|
| Gender: male, *n* (%) | 83 (28.8%) |
| Age, mean (sd) | 66 (8.7) |
| Body mass index, mean (sd), kg/m$^2$ | 27.8 (4.5) |
| Location OA | |
| Knee OA, *n* (%) | 139 (48.4%) |
| Hip OA, *n* (%) | 72 (25.1%) |
| Both, *n* (%) | 76 (26.5%) |
| Duration of complains (years), mean (sd) | 9.9 (10.7) |
| Physical functioning (WOMAC), mean (sd) | 56.51 (19.85) |
| Pain (VAS), mean (sd) | 4.81 (2.56) |
| Radiological impairment knee[a] | |
| K&L grade ≥2; *n* (%) | 118 (95.2) |
| Radiological impairment hip[b] | |
| K&L grade ≥2; *n* (%) | 83 (97.6) |

*N*, *n* number, *sd* standard deviation, *OA* osteoarthritis, *WOMAC*, Western Ontario and McMasters Universities Osteoarthritis Index, *VAS* visual analogue scale

[a] $N$=138 (from only a part of the included patients X-rays were available)

[b] $N$=90 (from only part of the included patients X-rays were available)

**Table 2** Presence of coexisting disorders

| | Present *n* (%) |
|---|---|
| Musculoskeletal disorders | |
| *Chronic back pain (>3 month) or hernia* | *85 (29.5)* |
| *Arthritis of the hands or feet* | *53 (18.4)* |
| *Other chronic rheumatic diseases (>3 month)* | *29 (10.1)* |
| Non-musculoskeletal disorders | |
| *Asthma or COPD* | *45 (15.6)* |
| *Sinusitis* | *35 (12.2)* |
| *Severe cardiac disorder or coronary disease* | *23 (8)* |
| *Hypertension* | *92 (31.9)* |
| (Consequences of) a stroke | 6 (2.1) |
| Peptic ulcer or duodenal ulcer disease | 10 (3.5) |
| *Severe bowel disorder (>3 month)* | *19 (6.6)* |
| Gallstones or inflammation of the gall bladder | 6 (2.1) |
| Liver disorder or cirrhosis of the liver | 0 (0) |
| Kidney stones (calculus renalis) | 7 (2.4) |
| Severe kidney disorder | 2 (0.7) |
| *Chronic cystitis* | *16 (5.6)* |
| *Prolapse (only females, N= 205)* | *17 (8.3)* |
| *Diabetes* | *28 (9.7)* |
| *Thyroid disorders* | *25 (8.7)* |
| Epilepsy | 2 (0.7) |
| *Migraine* | *19 (6.6)* |
| Severe skin disease | 4 (1.4) |
| Cancer and malignant diseases | 7 (2.4) |
| Sensory impairments | |
| *Hearing impairments in a group conversation (N= 286)* | *90 (31.5)* |
| *Hearing impairments in a face-to-face conversation (N= 287)* | *22 (7.7)* |
| *Vision impairments in short distances (N= 287)* | *77 (26.8)* |
| *Vision impairments in long distances (N= 287)* | *33 (11.5)* |
| *Dizziness in combination with falling* | *24 (8.3)* |
| Overweight and obesity (*N*=285) | |
| *Overweight (25≤BMI< 30)* | 149 (51.7) |
| *Obesity (BMI≥30)* | 68 (23.9) |

*N*=288, unless otherwise stated. Data in italics are present in >5%

31.5%; vision impairments in short distances and long distances, 26.8% and 11.5%, respectively; and dizziness in combination with falling, 8.3%. Overweight and obesity occurred in 51.7% and 23.9%, respectively.

## Association between coexisting disorders and activity limitations

Table 3 shows the relationship between specific coexisting disorders and activity limitations. Significantly more activity limitations were found in OA patients with chronic back pain or hernia ($p<0.05$), arthritis of the hand or feet ($p<0.05$), and other chronic rheumatic diseases ($p<0.05$) (all in the category of musculoskeletal disorders); with diabetes ($p<0.05$) and chronic cystitis ($p<0.05$) (category of non-musculoskeletal disorders); with hearing impairments in a face-to-face conversation ($p<0.05$), vision impairments in long distances($p<0.05$), and dizziness in combination with falling ($p<0.05$) (category of sensory impairments); and with overweight ($p<0.01$) and obesity ($p<0.05$).

## Association between coexisting disorders and pain

Table 3 also shows the relationship between coexisting disorders and pain. Arthritis of the hand or feet ($p<0.01$) and other chronic rheumatic diseases ($p<0.05$) (category of musculoskeletal disorders) and diabetes ($p<0.05$) (category of non-musculoskeletal disorders) were found to be significantly associated with more pain.

**Table 3** Association between coexisting disorders, activity limitations, and pain

| | Activity limitations (WOMAC) | Pain (VAS) |
|---|---|---|
| Musculoskeletal disorders | | |
| Chronic back pain (>3 month) or hernia | | |
| Present (mean (SD))[a] | 51.7 (18.2) | 5.0 (2.5) |
| Absent (mean (SD))[a] | 58.5 (20.2) | 4.7 (2.5) |
| *B* (95% CI)[b] | −6.4 (−11.5; −1.4)* | 0.3 (−0.4; 1.0) |
| $R^2$ | 0.033 | 0.008 |
| Arthritis of hands or feet | | |
| Present (mean (SD))[a] | 50.1 (20.3) | 5.8 (2.5) |
| Absent (mean (SD))[a] | 57.9 (19.5) | 4.6 (2.5) |
| *B* (95% CI)[b] | −7.4 (−13.4; −1.5)* | 1.2 (0.4; 1.9)** |
| $R^2$ | 0.032 | 0.037 |
| Other chronic rheumatic diseases (>3 month) | | |
| Present (mean (SD))[a] | 47.3 (18.3) | 5.9 (2.6) |
| Absent (mean (SD))[a] | 57.5 (19.8) | 4.7 (2.5) |
| *B* (95% CI)[b] | −10.0 (−17.6; −2.4)* | 1.1 (0.1; 2.1)* |
| $R^2$ | 0.035 | 0.023 |
| Non-musculoskeletal disorders | | |
| Asthma or COPD | | |
| Present (mean (SD))[a] | 55.2 (19.1) | 4.8 (2.6) |
| Absent (mean (SD))[a] | 56.7 (20.0) | 4.8 (2.6) |
| *B* (95% CI)[b] | −1.7 (−8.0; 4.7) | 0.0 (−0.8; 0.9) |
| $R^2$ | 0.012 | 0.005 |
| Sinusitis | | |
| Present (mean (SD))[a] | 54.5 (15.8) | 4.9 (2.6) |
| Absent (mean (SD))[a] | 56.8 (20.4) | 4.8 (2.6) |
| *B* (95% CI)[b] | −2.0 (−9.1; 5.1) | 0.1 (−0.8; 1.0) |
| $R^2$ | 0.012 | 0.006 |
| Severe cardiac disorder or coronary disease | | |
| Present (mean (SD))[a] | 51.2 (20.6) | 5.1 (2.8) |
| Absent (mean (SD))[a] | 57.0 (19.8) | 4.8 (2.6) |
| *B* (95% CI)[b] | −5.5 (−14.1; 3.1) | 0.4 (−0.7; 1.6) |
| $R^2$ | 0.012 | 0.008 |
| Hypertension | | |
| Present (mean (SD))[a] | 55.8 (21.9) | 4.9 (2.5) |
| Absent (mean (SD))[a] | 56.8 (18.8) | 4.8 (2.6) |
| *B* (95% CI)[b] | −0.6 (−5.6; 4.5) | 0.3 (−0.4; 0.9) |
| $R^2$ | 0.012 | 0.007 |
| Severe bowel disorder (>3 month) | | |
| Present (mean (SD))[a] | 54.3 (20.3) | 4.5 (3.2) |
| Absent (mean (SD))[a] | 56.7 (19.9) | 4.8 (2.5) |
| *B* (95% CI)[b] | −2.0 (−11.3; 7.2) | −0.4 (−1.6; 0.8) |
| $R^2$ | 0.012 | 0.007 |
| Chronic cystitis | | |
| Present (mean (SD))[a] | 45.2 (17.6) | 5.4 (2.9) |
| Absent (mean (SD))[a] | 57.2 (19.8) | 4.8 (2.5) |
| *B* (95% CI)[b] | −10.8 (−20.9; −0.7)† | 0.7 (−0.6; 2.1) |
| $R^2$ | 0.027 | 0.01 |
| Prolapse (females only) | | |
| Present (mean (SD))[a] | 47.0 (22.0) | 5.2 (2.9) |

**Table 3** (continued)

| | Activity limitations (WOMAC) | Pain (VAS) |
|---|---|---|
| Absent (mean (SD))[a] | 56.4 (19.7) | 4.8 (2.6) |
| *B* (95% CI)[b] | −9.0 (−18.9; 0.9)*** | 0.4 (−0.9; 1.7) |
| $R^2$ | 0.03 | 0.005 |
| Diabetes | | |
| Present (mean (SD))[a] | 49.5 (18.2) | 5.9 (2.2) |
| Absent (mean (SD))[a] | 57.3 (19.9) | 4.7 (2.6) |
| *B* (95% CI)[b] | −8.2 (−15.9; −0.4)* | 1.2 (0.2; 2.2)* |
| $R^2$ | 0.026 | 0.024 |
| Thyroid disorders | | |
| Present (mean (SD))[a] | 51.4 (22.6) | 5.6 (2.8) |
| Absent (mean (SD))[a] | 57.0 (19.6) | 4.7 (2.5) |
| *B* (95% CI)[b] | −5.8 (−14.2; 2.6) | 1.1 (0.0; 2.1)*** |
| $R^2$ | 0.018 | 0.018 |
| Migraine | | |
| Present (mean (SD))[a] | 56.6 (20.8) | 4.5 (2.6) |
| Absent (mean (SD))[a] | 56.5 (19.8) | 4.8 (2.6) |
| *B* (95% CI)[b] | 0.1 (−9.2; 9.5) | −0.4 (−1.6; 0.8) |
| $R^2$ | 0.012 | 0.007 |
| Sensory impairments | | |
| Hearing impairments in a group conversation | | |
| Present (mean (SD))[a] | 55.4 (19.1) | 4.6 (2.7) |
| Absent (mean (SD))[a] | 57.0 (20.2) | 4.9 (2.5) |
| *B* (95% CI)[b] | −0.9 (−6.0; 4.2) | −0.3 (−0.9; 0.4) |
| $R^2$ | 0.011 | 0.004 |
| Hearing impairments in a face-to-face conversation | | |
| Present (mean (SD))[a] | 46.7 (19.9) | 5.6 (2.8) |
| Absent (mean (SD))[a] | 57.2 (19.7) | 4.8 (2.5) |
| *B* (95% CI)[b] | −9.6 (−18.4; −0.8)* | 1.0 (−0.1; 2.2)*** |
| $R^2$ | 0.027 | 0.016 |
| Vision impairments in short distances | | |
| Present (mean (SD))[a] | 54.1 (19.8) | 5.0 (2.6) |
| Absent (mean (SD))[a] | 57.3 (19.8) | 4.8 (2.6) |
| *B* (95% CI)[b] | −2.9 (−9.1; 2.3) | 0.3 (−0.4; 1.0) |
| $R^2$ | 0.016 | 0.007 |
| Vision impairments in long distances | | |
| Present (mean (SD))[a] | 47.6 (19.1) | 5.2 (2.5) |
| Absent (mean (SD))[a] | 57.6 (19.7) | 4.8 (2.6) |
| *B* (95% CI)[b] | −9.0 (−16.3; −1.6)* | 0.6 (−0.4; 1.6) |
| $R^2$ | 0.031 | 0.01 |
| Dizziness in combination with falling | | |
| Present (mean (SD))[a] | 45.4 (23.4) | 5.7 (2.9) |
| Absent (mean (SD))[a] | 57.5 (19.2) | 4.7 (2.5) |
| *B* (95% CI)[b] | −11.2 (−19.6; −2.8)** | 1.1 (0.0; 2.2)*** |
| $R^2$ | 0.035 | 0.019 |
| Weight | | |
| Overweight (25≤BMI<30) | | |
| Present (mean (SD))[a] | 54.7 (19.1) | 4.9 (2.6) |
| Absent (mean (SD))[a] | 62.7 (19.0) | 4.4 (2.6) |
| *B* (95% CI)[b] | −8.0 (−13.7; −2.4)** | 0.5 (−0.3; 1.2) |

**Table 3** (continued)

| | Activity limitations (WOMAC) | Pain (VAS) |
|---|---|---|
| Obesity (BMI≥30) | | |
| Present (mean (SD))[a] | 54.1 (21.4) | 5.0 (2.6) |
| Absent (mean (SD))[a] | 62.7 (19.0) | 4.4 (2.6) |
| *B* (95% CI)[b] | −8.6 (−15.3; −1.9)* | 0.6 (−0.3; 1.5) |
| $R^2$ | 0.041 | 0.014 |

*WOMAC* Western Ontario and McMaster Universities Osteoarthritis Index, *VAS* visual analogue scale, *B* regression coefficient, *95% CI* 95% confidence interval

*$p<0.05$; **$p<0.01$; ***$p<0.1$

[a] Observed value

[b] Adjusted value for age and sex

## Discussion

The aim of this study was to describe the relationship between specific coexisting disorders, activity limitations, and pain in patients with OA of the hip or knee. We have previously reported that "symptoms of other musculoskeletal disorders" occur frequently in OA [5]: We have now found chronic back pain or hernia, arthritis of the hands or feet, and other chronic rheumatic diseases to be associated with activity limitations. In our previous study, we found "endocrine and metabolic diseases" to be associated with activity limitations: We now discovered that this applies to diabetes. We also found "other urogenital diseases" to be associated with activity limitations [5]: We now discovered that this applies in particular to chronic cystitis. Previously, we found "ear, eye, nose, and throat diseases" to be associated with activity limitations [5]: We have now observed that this applies in particular to hearing impairments in a face-to-face conversation and vision impairments in long distances. We also found dizziness in combination with falling to be associated with activity limitations. Finally, overweight and obesity were found to be related to activity limitations.

Regarding coexistent disorders and pain, we have now found arthritis of the hands or feet and other chronic rheumatic diseases to be associated with pain. Previously we did not find a relationship between endocrine and metabolic diseases and pain [5]; however, we now found an association between diabetes and pain.

Coexisting disorders may bring additional impairments, which necessitate adaptations to exercise for patients with OA of the hip or knee. For the future purpose of developing a protocol for exercise in OA patients with coexisting disorders, information is needed on which specific coexisting disorders in OA are associated with activity limitations and pain. The present study brings highly relevant new information in this respect. To our knowledge, this is the first study suggesting that hearing impairments, vision impairments, dizziness, and chronic cystitis need to be addressed in order to optimize functioning of patients with OA. Only Peters et al. have previously reported on the (near significant) relationship between eye diseases and future disability in patients with knee OA [22]. The present results shows that coexisting sensory impairments in hearing, vision, and balance, as well as motor impairments in bladder control (in the case of cystitis), have impact on functioning of patients with OA of the hip or knee: Apparently, these impairments need to be addressed in the rehabilitation of OA patients.

It is well known that OA is associated with other musculoskeletal disorders [23]. In contrast, very little information is available on the impact of coexisting musculoskeletal disorders on activity limitations and pain. Cimmino et al. describe greater pain in patients with generalized OA than in patients with hip or knee OA alone [24]. The present study found an association between arthritis of the hand or feet, "other" chronic rheumatic diseases, chronic back pain or hernia, and activity limitations. We also found a relationship between arthritis of the hand or feet, other chronic rheumatic diseases, and pain.

The present study confirms earlier observations on the impact of diabetes, overweight, and obesity on activity limitations in OA. Diabetes causes physiological restrictions to exercise therapy [25], whereas overweight and obesity introduce behavioral restrictions to exercise [26]. Combining exercise therapy with a weight loss program has been shown to result in moderately improved outcome, compared to exercise therapy alone [27]. Further work on adaptations to exercise therapy for OA patients with diabetes, overweight, and obesity is urgently required, because of the high prevalence and the functional impact of these coexisting disorders.

In our previous study, we found 54% of the study population to have cardiac diseases, and a significant relationship with activity limitations was found [5]. Caporali et al. found cardiac diseases (myocardial infarction

and/or angina pectoris) to influence pain, quality of life, and joint function in OA patients [4]. Ettinger et al. also describe a higher likelihood of disabilities in OA patients with heart diseases [28]. In the present study, no significant relationship was found between cardiac diseases and activity limitations or pain. A likely explanation is that subjects rated the presence of "severe heart diseases or coronary diseases." This item might have implicated a too serious stage of disease, causing us to miss patients with mild or moderate heart disease. Despite our present results, adaptations for cardiac disease in exercise therapy for OA patients seem to be required.

The number of coexisting disorders associated with activity limitations ($n$=10) was larger than the number of coexisting disorders associated with pain ($n$=3). It seems that coexisting disorders easily impact on activity limitations, while the impact on pain is less strong. Future research is needed to elucidate the mechanisms of how coexisting disorders have an impact on activity limitations and pain. This research may also clarify the differential impact of coexisting disorders on activity limitations and pain.

Some limitations of the present study need to be discussed. Firstly, we relied on self-report to assess coexisting disorders, instead of medical record review. However, self-reported coexisting disorders tend to correspond rather well with coexisting disorders derived from medical record review [29]: The percentage of agreement exceeded 90% for all coexisting disorders except for tumors; the kappa statistic ranged from 0.35 to 0.85, reflecting fair to substantial agreement. Fair agreement (kappa <0.40) was found for ulcer disease, end organ damage resulting from diabetes, and connective tissue disease (not assessed in the present study); substantial agreement (kappa >0.60) was found for myocardial infarction, stroke, and renal disease. Thus, self-report on coexisting disorders seems to be valid, with some exceptions noted above. Secondly, in assessing coexistent disorders, we used the list of the Dutch Bureau of Statistics (CBS). Unfortunately, this list did not include psychiatric disorders. From previous studies, it is known that depression plays an important role in developing activity limitations [30, 31]. Thirdly, patients included in this study were recruited from hospitals and rehabilitation centers; these patients may have received some form of rehabilitation. Thus, the results of the present study cannot be generalized to the general population suffering from OA. Nevertheless, the results are applicable to the group of patients consulting in hospitals and rehabilitation centers: This is a highly relevant group. Fourthly, the study focused on patients with OA of the hip or knee. We did not have information on a reference group of subjects without OA or subjects with another index disease. In subjects without OA and subjects with another index disease, comorbidity is likely to be associated with activity limitations and pain as well. In future studies, it would be interesting to compare impact of comorbidity in OA patients and other subjects. Finally, we did not adjust the analysis for multiple comparisons: This could easily result in false-negative errors (type II errors) because of the limited number of subjects with a specific coexisting disorder. It is acknowledged that this may have introduced some risk of false-positive errors (type I errors).

In conclusion, specific disorders coexisting next to OA and associated with additional activity limitations and pain were identified. These coexisting disorders need to be addressed in exercise therapy and rehabilitation for patients with OA of the hip or knee.

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