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ORIGINAL ARTICLE

Musculoskeletal pain reported by mobile patients with chronic kidney disease

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ABSTRACT

Background. Musculoskeletal pain has been reported as a clinical problem in patients with chronic kidney disease (CKD). The purpose of this study was to compare the frequency of musculoskeletal pain in patients with CKD and no mobility problems with a general population and to investigate the impact of pain on quality of life (QOL), physical activity and physical function.

Methods. Patients with CKD Stages 4 and 5 with or without a dialysis treatment and no mobility problems were included. Musculoskeletal pain in the shoulder/neck, back/low back and limbs and level of physical activity were measured using the Danish Health and Morbidity Survey and coded into dichotomous answers. QOL and physical function were measured using the kidney disease QOL questionnaire and the 30-s chair stand test, respectively. Data for the general population were collected in national registers and adjusted for age, gender and region.

Results. The patients ($n = 539$) had a mean age of 66 [95% confidence interval (CI) 65–67] years, 62% were men and they were treated with haemodialysis (HD) ($n = 281$), peritoneal dialysis ($n = 62$) or without dialysis ($n = 196$). The frequency of reported musculoskeletal pain in the patients did not exceed pain reported by the general population [e.g. pain in the limbs in patients undergoing HD versus a matched general population, 61% versus 63% ($P = 0.533$), respectively]. Pain in all measured body sites was associated with reduced QOL [e.g. pain in the limbs associated with a physical component scale β of -8.2 (95% CI -10.3 to -6.0), $P < 0.001$]. Pain in the limbs was associated with a reduced number of repetitions in the 30-s chair stand test [mean -1.7 (95% CI -3.0 to -0.4), $P = 0.009$]. Pain in the shoulder/neck was associated with reduced odds of being physically active [odds ratio 0.6 (95% CI 0.4 to 0.9); $P = 0.022$].

Conclusions. Musculoskeletal pain was not more frequently reported by patients with CKD and no mobility problems compared with the general population. However, as musculoskeletal pain was reported by up to two-thirds of the patient sample, healthcare professionals should remember to focus on this issue. The patients' pain was associated with negative impacts on QOL, level of physical activity and physical function.

Keywords: chronic kidney disease, haemodialysis, musculoskeletal pain, peritoneal dialysis, physical activity, physical function, quality of life

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INTRODUCTION

Previous studies have found that physical pain is a clinical problem in patients with chronic kidney disease (CKD) [1–3]. The pain may be reported as pain from several organs and body sites, among them the head, teeth, gastrointestinal system, peripheral nerves and dialysis access. The pain may also be reported as musculoskeletal pain and arise from renal osteodystrophy, renal myopathy or general rheumatic diseases including osteoarthritis. While pain has been proposed to be a common clinical problem in patients with CKD, it has not been investigated whether the patients report pain more often than matching general populations.

The pain may have negative impacts on the patients' quality of life (QOL), level of physical activity and physical functioning. However, patient populations with CKD have great variations in QOL, physical functioning and level of physical activity, and the impact of pain may vary between subgroups of patients with different clinical characteristics.

Physical inactivity is also a common problem in patients with CKD, and inactivity may have a crucial negative impact on health. In some patients with CKD, it may be difficult to achieve a sufficient level of physical activity due to different co-morbidities and clinical manifestations. The question remains whether patients with CKD and no mobility problems report musculoskeletal pain and their level of physical activity. Patients with no mobility problems may have conditions that reduce their level of activity; however, as they have no severe mobility restrictions, their functional status should not be a limitation.

The aim of this study was to compare the frequency of musculoskeletal pain in different body sites in patients with CKD and no mobility problems with a matched general population sample. The associations between musculoskeletal pain and QOL, physical activity and physical function were also investigated.

It was hypothesized that musculoskeletal pain was reported more frequently in patients with CKD and no mobility problems compared with a matched general population sample.

MATERIALS AND METHODS

This was a cross-sectional study with patient-reported outcomes that were compared with control groups constructed using data from the nationwide Danish Health and Morbidity Survey [4]. The patients' data were collected from April 2015 to May 2017 in the three departments of nephrology in the Capital Region, Denmark: Nordsjællands Hospital, Rigshospitalet and Herlev Hospital.

The inclusion criteria were ≥18 years of age treated with chronic haemodialysis (HD) or peritoneal dialysis (PD) for a minimum 3 months or CKD Stages 4 and 5 [estimated glomerular filtration rate (eGFR) <30 mL/min/1.73 m^2 according to the patient records] without dialysis treatment, no hospital admission during the last month and physical function with a minimum walking distance of 50 m with a stick as a maximum aid. The exclusion criteria were dementia, serious psychiatric disorder defined by the authors and the inability to read and understand Danish.

Musculoskeletal pain was assessed using three questions from the Danish Health and Morbidity Survey [4]: 'Have you during the last 14 days had pain in the (i) shoulder/neck, (ii) back/low back and (iii) arm/leg/hand/foot (limbs). The participants could answer 'most of the time', 'some of the time' and 'no'. The answers were coded as in the Danish Health and Morbidity Survey into the dichotomous 'yes/no' to be comparable with answers from the general population. The participants' reported musculoskeletal pain was compared with the pain reported by the general population sample (n = 58 000) in the Capital Region, with age and gender distributions that matched the participants. Other physical pain was assessed using the same questions to measure the frequencies of headache and pain in the stomach, teeth, genital organs and ear/eye/nose/mouth. These questions to assess other physical pain were also developed by the Danish Health and Morbidity Survey. However, as the general populations' answers to these questions were not public, the patients' data were not compared with matched general populations.

The QOL was determined using the physical component summary (PCS) and mental component summary (MCS) scores and were calculated using the algorithms of the Kidney Disease Quality of Life Instrument version 1.3 (http://www.rand.org/health/surveys_tools/kdqol.html). The Danish version of the questionnaire includes the generic health-related QOL instrument Short Form 36, which provides data on different scales, among them the two summery scales (PCS and MCS) [5]. The scale scores range from 0 to 100 and higher scores indicates better health. The patients' QOL data were compared with data for the general population [6].

Leisure-time physical activity was measured using the Saltin–Grimby Physical Activity Level Scale [7]. The participants were asked, 'If we look at the past year, what would you say best describes your spare-time activities?' The response categories were (i) high-intensity sports several times during a week; (ii) minimum 4 h of exercise training weekly; (iii) minimum 4 h of moderate activity such as walking or cycling weekly; and (iv) read, watch television or other sedentary activities. The participants were categorized as being physically active if one of the three highest levels of activity was reported, while participants in the last category had a sedentary lifestyle.

Physical function was measured using the 30-s chair stand test from the senior fitness test [8]. The test required the patient to rise to a full standing position and return to a seated position as frequently as possible within a 30-s time frame, while maintaining their arms folded across their chest at all times. Physical function was tested only in patients undergoing dialysis, due to practical reasons.

Socio-economic status was determined using the patients' level of education. The question was taken from the Health and Morbidity Survey and the answers were coded into three levels (low, medium and high). Clinical data including recently tested haemoglobin, plasma albumin, C-reactive protein (CRP), plasma phosphate and eGFR were obtained from the patient records.

The study protocol was approved by the local ethical committee (H-6-2014-103) and by the Data Protection Agency. The participants gave informed consent and the study was in accordance with the Helsinki Declaration.

Statistics

The frequencies of musculoskeletal pain and physical activity reported by the patients were compared with age-, gender- and region-matched data from the general population using a chi-square test. The general population samples had the same distribution of age, gender and region as the patients, using the patients' age, gender and region as weights. The patients' QOL assessed by the PCS and MCS, and their physical function determined using the 30-s chair stand test were compared with age- and gender-matched general populations from Denmark [6] and the USA [7], respectively. The general population had the

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Table 1. Characteristics of all participants and in participants stratified by treatment

Variables	All	HD	PD	CKD Stages 4 and 5	P-value
n	539	281	62	196	
Gender (M/F), *n*/*n*	333/206	168/113	36/26	129/67	0.335
Age (years)	66 (65–67)	63 (61–65)	64 (61–68)	70 (69–72)	<0.001
BMI (kg/m^2)	26.2 (25.6–26.8)	25.5 (24.8–26.2)	25.8 (24.4–27.3)	29.0 (27.5–30.5)	<0.001
Renal disease, *n* (%)					0.269
Diabetes	65 (12)	31 (11)	5 (8)	29 (15)	
Hypertension	49 (9)	23 (8)	9 (15)	17 (9)	
Polycystic	29 (5)	18 (6)	5 (8)	6 (3)	
Glomerulonephritis	64 (12)	38 (14)	6 (10)	20 (10)	
Pyelonephritis	2 (<1)	2 (<1)	2 (3)	0 (0)	
Interstitial nephritis	7 (1)	4 (1)	1 (2)	1 (<1)	
Obstructive uropathy	17 (3)	9 (3)	5 (8)	7 (4)	
Nephrosclerosis	49 (9)	20 (7)	6 (10)	24 (12)	
Other/unknown/missing	257 (48)	136 (48)	29 (47)	92 (47)	
Haemoglobin (mmol/L)	7.3 (7.2–7.4)	7.1 (7.0–7.1)	7.2 (6.9–7.4)	7.8 (7.6–7.9)	<0.001
Plasma albumin (g/L)	36 (36–37)	36 (36–37)	33 (32–34)	37 (36–38)	<0.001
CRP (mg/L)	9.7 (7.7–11.7)	11.5 (8.4–14.5)	6.6 (4.1–9.0)	7.9 (4.7–11.1)	0.154
Plasma phosphate (mmol/L)	1.5 (1.5–1.6)	1.7 (1.6–1.7)	1.7 (1.6–1.9)	1.2 (1.2–1.2)	<0.001
eGFR (mL/min/1.73 m^2)				22 (21–23)	
Marital status, *n* (%)					0.026
Married/living with partner	324 (60)	154 (55)	42 (68)	128 (65)	
Living alone	200 (37)	118 (42)	16 (26)	66 (34)	
Missing	15 (3)	9 (3)	4 (7)	2 (1)	
Socio-economic status, *n* (%)					0.215
Low	119 (22)	63 (22)	8 (13)	48 (25)	
Medium	233 (43)	113 (40)	33 (53)	87 (44)	
High	162 (30)	89 (32)	15 (24)	58 (30)	
Missing	25 (5)	16 (6)	6 (10)	3 (2)	
Diabetes, *n* (%)					0.041
Yes	108 (20)	45 (16)	11 (18)	52 (27)	
No	243 (45)	135 (48)	24 (39)	84 (43)	
Unknown	188 (35)	101 (36)	27 (44)	60 (31)	

Data are presented as mean (95% CI) unless stated otherwise. Patients with CKD Stages 4 and 5 were not undergoing dialysis.

same distribution of age and gender as the patients using the patients' age and gender as weights.

Differences in categorical and continuous variables between the patient groups were analysed using a chi-square test and a one-way analysis of variance test, respectively. Student's *t*-test was used to analyse the differences between the patients' and general populations' QOL data. Differences in the number of rises in the 30-s chair stand test between patients treated with HD or PD were analysed using a Student's *t*-test.

The associations between the patients' musculoskeletal pain and PCS and MCS were analysed using multiple linear regression analyses. The analyses were adjusted for age, gender and treatment group (HD, PD and CKD Stages 4 and 5) and body mass index (BMI). The association between the patients' musculoskeletal pain and physical function (30-s chair stand test) in patients undergoing maintenance dialysis was analysed using a multiple linear regression analysis adjusted for age, gender, dialysis treatment (HD versus PD) and BMI.

Data are presented as numbers and percentages, mean [95% confidence interval (CI)], β (95% CI) or odds ratio (95% CI). Results were considered significant (two-tailed) when P-values were <0.05.

RESULTS

In the three departments of nephrology, 1408 potential participants were screened to be included in the study. Due to the study criteria, 692 patients were excluded, 716 patients were invited to participate and 539 agreed to participate in the study. The participants' characteristics are presented in Table 1. A total of 62% were men and the mean age was 66 (95% CI 65–67) years. The patients without dialysis treatments were older, had higher BMI and haemoglobin and a lower level of plasma phosphate compared with the patients that were treated with dialysis.

The participants' musculoskeletal pain, QOL, level of physical activity and physical function are presented in Table 2. Pain in the neck/shoulder 'most of the time' was reported by 11%, pain in the back/low back 'most of the time' was reported by 18% and pain in the limbs 'most of the time' was reported by 20% of the patients. When those with pain in the neck/shoulder were compared with those without pain, more women than men reported pain (53% versus 39%, P = 0.002), whereas there were no differences in age, BMI, haemoglobin, plasma albumin, CRP, plasma phosphate and CKD treatment (data not shown) between the two groups. In those with and without back/low back pain, more women than men reported pain (66% versus 51%, P = 0.001) and the BMI was 26.9 ± 6.3 kg/m^2 versus 25.3 ± 5.3 kg/m^2 (P = 0.009), respectively, with no other differences in the aforementioned variables. In those with and without pain in the limbs, more women than men reported pain (71% versus 60%, P = 0.011), the BMI was 27.0 ± 6.6 kg/m^2 versus 24.9 ± 4.2 kg/m^2 (P ≤ 0.001) and haemoglobin was 7.4 ± 1.0 versus

Table 2. Musculoskeletal pain, QOL assessed using the PCS and MCS of the generic part of the KDQOL survey, physical activity and physical function in all participants and in participants stratified by treatment

Variables	All	HD	PD	CKD 4 and 5	P-value
N	539	281	62	196	
Pain in shoulder/neck (%)	45	47	33	45	0.151
Pain in back/low back (%)	57	55	47	62	0.105
Pain in limbs (%)	64	61	67	69	0.210
Physical component scale (0–100)	37 (36–38)	37 (35–38)	38 (35–41)	38 (36–39)	0.528
Mental component scale (0–100)	50 (49–51)	49 (48–50)	51 (48–54)	52 (51–54)	0.005
Physically active (%)	66	61	75	71	0.019
30-s chair stand test (*n*)	10.5 (9.8–11.1)	10.3 (9.7–11.0)	11.1 (9.5–12.6)		0.394

The 30-s chair stand test was only conducted in patients undergoing maintenance dialysis. Data are presented as mean (95% CI) unless stated otherwise. P between patient groups. KDQOL: Kidney Disease Quality of Life.

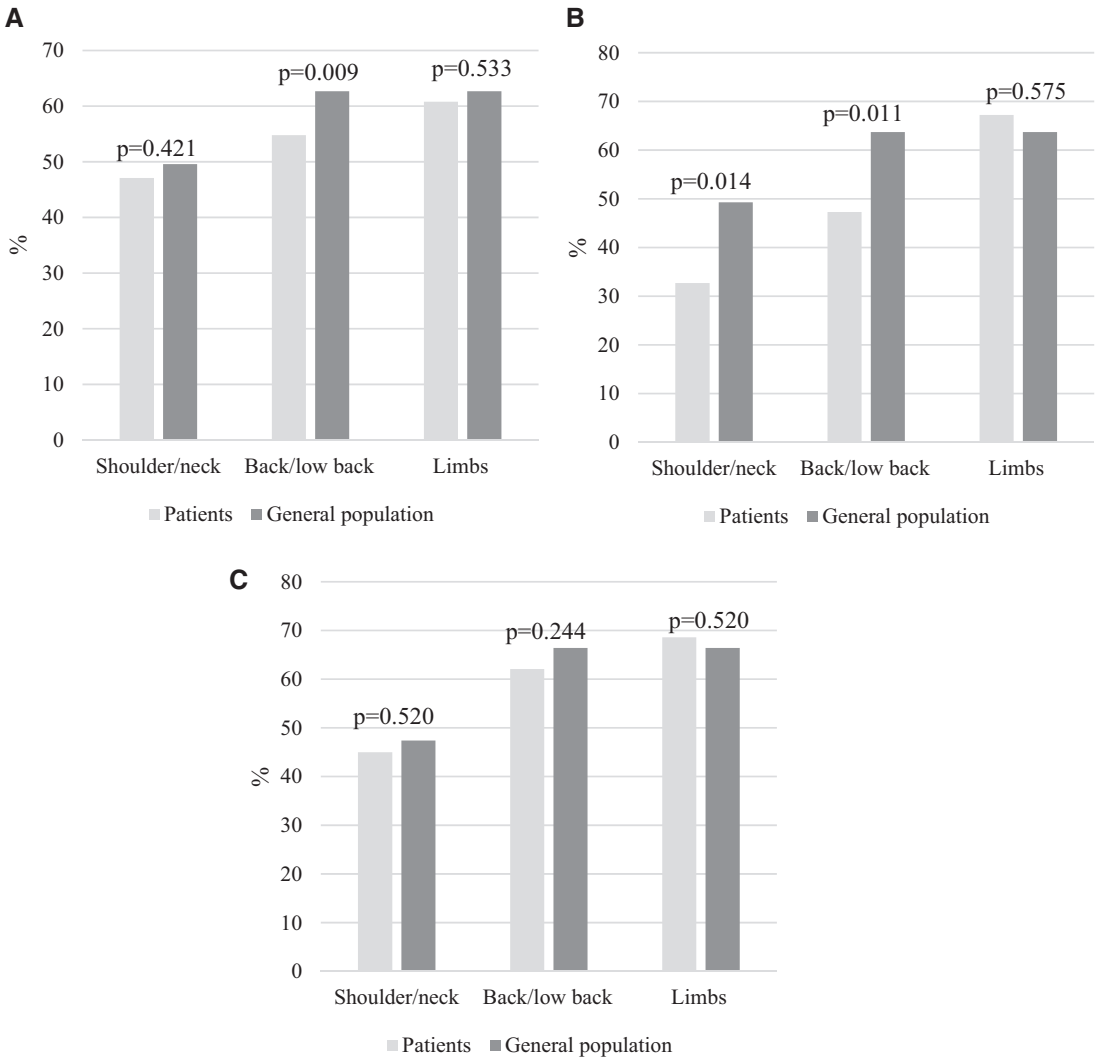

FIGURE 1: Musculoskeletal pain in participants (**A**) receiving maintenance HD compared with age-, gender- and geographical region–matched individuals from the general population; (**B**) receiving maintenance PD compared with age-, gender- and geographical region–matched individuals from the general population and (**C**) with CKD Stages 4 and 5 not receiving dialysis compared with age-, gender- and geographical region–matched individuals from the general population.

7.2 ± 0.8 mmol/L (P = 0.042), respectively, with no other differences. The MCS score was significantly elevated in patients without dialysis treatment compared with those undergoing maintenance dialysis. The patients treated with PD had the greatest percentage of physically active patients.

In Figure 1A–C, the frequencies of musculoskeletal pain in the patients are presented together with data for matching general populations. In patients treated with HD, the reported pain prevalence in the back/low back was reduced compared with the general population (55% versus 63%, P = 0.009). In patients

treated with PD, the reported pain prevalence in the neck/shoulder and back/low back was reduced compared with the general population (33% versus 49%, P = 0.014 and 47% versus 64%, P = 0.011, respectively). There were no differences in the musculoskeletal pain reported by the patients with CKD without a dialysis treatment and the matched general population.

Other physical pain data are presented in Table 3. Headache was more often reported by patients undergoing dialysis compared with patients without dialysis treatment (34% versus 21%, P = 0.008).

In Figure 2A and B, the QOL reported by the patients is presented together with data for matching general populations. The PCS scores were reduced in patients treated with HD, PD and CKD without a dialysis treatment compared with the matching general populations [37 (95% CI 35–38) versus 47 (47–48), P < 0.001; 38 (35–41) versus 47 (46–47), P < 0.001 and 38 (36–39) versus 46 (45–46), P < 0.001, respectively]. The MCS scores were reduced in patients treated with HD, PD and CKD without a dialysis treatment compared with the matching general populations [49 (95% CI 48–50) versus 55 (54–55), P < 0.001; 51 (48–54) versus 55 (54–55), P = 0.008 and 52 (51–54) versus 55 (55–55), P = 0.002, respectively].

The frequencies of physically active participants are presented in Figure 3. Sixty-one percent of the patients undergoing HD were physically active versus 80% in the matching general population (P < 0.001). There were no differences between the frequencies of physically active patients treated with PD and without a dialysis treatment compared with matching general populations.

In the 30-s chair stand test, the patients treated with HD and PD performed fewer rises compared with the matching general populations [10.3 (95% CI 9.7–11.0) versus 14.4 (14.2–14.6), P < 0.001 and 11.1 (9.5–12.4) versus 14.4 (14.1–14.7), P < 0.001, respectively] (Figure 4).

Pain in the shoulder/neck, back/low back and limbs was associated with reduced PCS and MCS scores (Table 4). Pain in the shoulder/neck was associated with reduced odds of being physically active, whereas pain in the back/low back and limbs was not associated with physical activity levels (Table 5). Pain in the limbs was associated with fewer rises in the 30-s chair stand test, whereas pain in the shoulder/neck and back/low back was not associated with the number of rises in the chair stand test (Table 4).

Table 3. Other physical pain in all participants and in participants stratified by treatment

Variables	All	HD	PD	CKD 4 and 5	P-value
n	539	281	62	196	
Headache (%)	29	34	34	21	0.008
Pain in stomach (%)	21	24	25	15	0.069
Pain in teeth (%)	10	10	11	9	0.937
Pain in genital organs (%)	9	10	7	9	0.813
Pain in ear/eye/nose/mouth (%)	23	20	28	25	0.273

Patients with CKD Stages 4 and 5 were not undergoing dialysis.

DISCUSSION

This study found that the frequency of musculoskeletal pain in patients with CKD and no mobility problems was reported by a minimum of two-thirds of the participants. The pain reported by the patients did not exceed the frequency of pain reported by a matched general population. The reported musculoskeletal pain was associated with reduced QOL. Pain in the limbs was associated with reduced physical functioning and pain in the shoulder/neck was associated with reduced odds of being physically active.

While pain in patients with CKD may be reported often in clinical practice, this study found that musculoskeletal pain may not be more frequently reported by mobile patients compared with matched general populations. Thus, in general, musculoskeletal pain may not be an additional barrier to physical activity in mobile patients with CKD compared with general populations. However, the comparison of pain between the patients in the present study and the general population should be interpreted with caution, as severity and duration >14 days were not investigated. A minimum of 64% of the patients reported musculoskeletal pain in at least one tested body site and pain may have important clinical implications and need further focus in clinical practice in this seriously ill patient group. The present study found reduced QOL in the patients compared with the general population, a result that has been found in several previous studies [9–11]. The participants' QOL was reduced even though it was reported by a selected patient sample with a lower limit of physical functioning. As QOL was associated with musculoskeletal pain, and to increase patients' QOL, staff should remember to keep focus on the individual patient's musculoskeletal pain.

While pain in the neck/shoulder was associated with a reduced level of physical activity, the causal explanation was not investigated in this study. However, since physical activity is part of the pain treatment in patients with rheumatic diseases [12, 13], exercise training may have positive impacts on musculoskeletal pain in patients with CKD. Previous studies have shown reduced bodily pain after exercise training programmes in patients undergoing HD [14, 15]. Bodily pain has been measured using a scale of the Short Form 36 questionnaire, and this scale may comprise other reports of pain than those from the musculoskeletal system. The bodily pain scale scores may, however, be dominated by reports of musculoskeletal pain, an assumption that was supported by the present study where musculoskeletal pain was reported more often than other physical pain (headache, etc.).

Pain in the limbs was associated with lower physical functioning and it may most likely be pain in the lower limbs that was associated with this outcome. As the study also found that the patients' physical function measured using the 30-s chair stand test was significantly reduced compared with matching controls, there is an additional need to focus on patients' musculoskeletal pain in clinical practice to optimize the ability to perform physical activity. The reported pain in the lower limbs may arise from peripheral neuropathy [16], which may negatively affect physical function.

Thus future studies should investigate the effects of exercise programmes in those patients with CKD who report musculoskeletal pain. Whether exercise training reduces musculoskeletal pain and thereby improves QOL and physical function in patients with CKD would also be relevant to investigate.

This study showed that even though the participants had no mobility problems, the percentage of physically active participants was significantly reduced in patients undergoing HD compared with a general population. Physical inactivity is related to several health problems, among them development of insulin resistance and type 2 diabetes, cardiovascular diseases and an elevated mortality risk [17, 18]. Moreover, physical inactivity

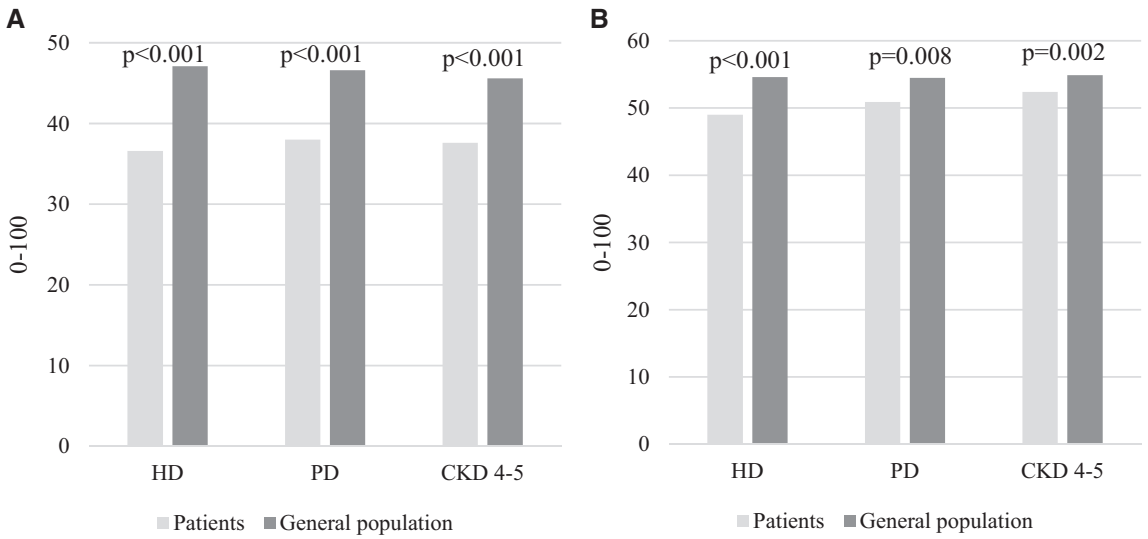

FIGURE 2: QOL determined as (**A**) PCS reported by the patients compared with age- and gender-matched individuals from the general population. Patients with CKD Stages 4 and 5 were not receiving dialysis. (**B**) MCS reported by the patients compared with age- and gender-matched individuals from the general population. Patients with CKD Stages 4 and 5 were not receiving dialysis.

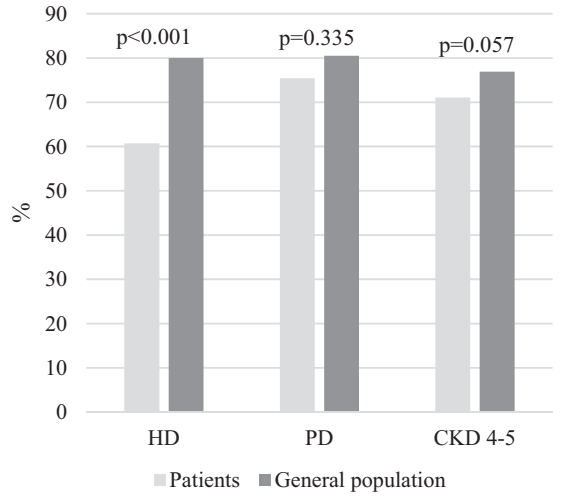

FIGURE 3: Physically active participants compared with age-, gender- and geographical region–matched individuals from the general population. Data are presented for the participants stratified by treatment. Patients with CKD Stages 4 and 5 were not receiving dialysis.

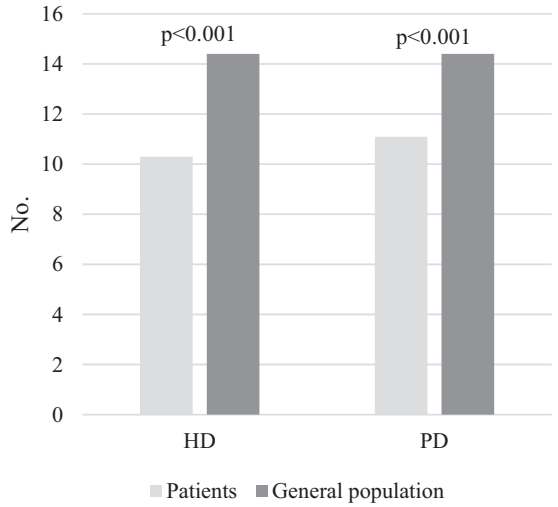

FIGURE 4: Physical function of the participants compared with age-, gender- and geographical region–matched individuals from the general population. Data are presented for all participants and for the participants receiving maintenance HD or PD.

also has a crucial negative impact on physical function. Indeed, physical functioning is important in relation to performing physical activity and staying mobile and independent of physical help from other people.

The clinical implications of this study are that strategies to elevate the level of physical activity are needed. Interventions with exercise training have the potential to increase the reduced QOL [19–21] and physical function measured using the chair stand test [14, 22].

This study investigated patients with no mobility problems only and it is unknown how the rest of the patient population would report musculoskeletal pain compared with age- and gender-matched general populations. It could be hypothesized that those patients with more disabilities would report musculoskeletal pain more often. Furthermore, reduced QOL, physical inactivity and low physical function are most likely an even greater problem in those patients who were not included in this study.

The study was limited by only measuring physical activity as self-reported data and by measuring musculoskeletal pain in the limbs that were not differentiated between upper and lower limbs. However, the two ways of measuring physical activity level and musculoskeletal pain in the limbs made it possible to compare the patients' data with data from a general population. Another limitation was that the underlying reasons for the musculoskeletal pain were not investigated.

In conclusion, musculoskeletal pain was not more frequently reported by patients with CKD compared with general populations. However, musculoskeletal pain was reported by at least two of three patients and it was associated with reduced QOL. Pain in the shoulder/neck was associated with lower odds of being physically active. In patients undergoing dialysis, pain in the limbs was associated with lower physical function, which

Table 4. Multiple linear regression analyses of the associations between the exposure outcomes musculoskeletal pain and the outcome variables PCS and MCS of the KDQOL survey and physical function determined using the 30-s chair stand test

Variables	PCS		MCS		30-s chair stand test	
	β (95% CI)	P-value	β (95% CI)	P-value	β (95% CI)	P-value
Pain in shoulder/neck	−3.6 (−5.9 to −1.3)	0.002	−3.4 (−5.6 to −1.2)	0.003	−0.8 (−2.1 to 0.5)	0.221
Pain in back/low back	−4.3 (−6.5 to −2.0)	<0.001	−4.5 (−6.8 to −2.3)	<0.001	−0.6 (−1.9 to 0.7)	0.348
Pain in limbs	−8.2 (−10.3 to −6.0)	<0.001	−3.3 (−5.6 to −1.1)	0.004	−1.7 (−3.0 to −0.4)	0.009

The analyses of the two component scales were adjusted for age, gender, BMI and treatment group (HD or PD versus CKD Stages 4 and 5 without dialysis treatment). The analysis of the 30-s chair stand test was only performed on patients undergoing maintenance dialysis and it was adjusted for age, gender, BMI and treatment group (HD versus PD). KDQOL: Kidney Disease Quality of Life.

Table 5. Multiple logistic regression analyses of the association between the exposure variables musculoskeletal pain and the outcome variable physical activity

Variables	Physical active OR (95% CI), P-value
Pain in shoulder/neck	0.6 (0.4–0.9), 0.022
Pain in back/low back	0.9 (0.6–1.4), 0.596
Pain in limbs	0.7 (0.4–1.1), 0.092

All analyses were adjusted for age, gender, BMI and treatment group (HD or PD versus CKD Stages 4 and 5 without dialysis treatment). OR: odds ratio.

was significantly reduced in patients compared with the general population.

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CONFLICT OF INTEREST STATEMENT

None declared.

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