

# A secondary analysis of cross-sectional data including tender point examination and magnetic resonance imaging of the lumbar spine

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# Abstract

Consistency between back pain intensity and degenerative changes on magnetic resonance imaging (MRI) of the lumbar spine is poor. This study aimed to show whether tender point (TP) examination, used as a test for diffuse central sensitization, may add valuable information to clinical assessment of patients with low back pain (LBP).

This was a cross-sectional study including 141 patients with LBP on sick leave. Baseline measures comprised back pain, leg pain intensity, and LBP examination including TP examination. Degenerative MRI findings were assessed in a standardized manner and blinded for clinical data. The number of TPs was analyzed in relation to sex, widespread pain, radiculopathy, pain duration, and degenerative changes on MRI.

The number of TPs was positively associated with the female sex, widespread pain, and pain duration. It was negatively associated with degenerative manifestations and radiculopathy, the latter displaying a low level similar to that of the general population. A positive association between back pain intensity and TPs was present in patients with and without radiculopathy and in patients with substantial degenerative changes. Men with >7-8 TPs and women with >10-11 TPs had more back pain and similar or fewer degenerative changes than patients with few TPs (<3 and <6 TPs, respectively), thereby identifying 34% to 44% of patients with nonspecific LBP and 5% to 8% of patients with radiculopathy, respectively, with disproportionate back pain in relation to degenerative changes.

Supplemental TP examination improved clinical and MRI evaluation of patients with LBP. By using gender-specific cut points, patients with disproportionate back pain were identified, presumably indicating diffuse central sensitization.

**Abbreviations:**  $\beta$  = regression coefficient, CI = confidence interval, LBP = low back pain, MRI = magnetic resonance imaging, sd = standard deviation, TP = tender points, WP = widespread pain.

Keywords: diffuse central sensitization, hyperalgesia, low back pain, magnetic resonance imaging, nociplastic pain, tender point examination

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Supplemental Digital Content is available for this article

The datasets generated during and/or analyzed during the current study are publicly available.

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## 1. Introduction

Magnetic resonance imaging (MRI) of the lumbar spine is widely held to be too sensitive to identify a single cause of low back pain (LBP).<sup>[1]</sup> Disc degeneration increases with age and is caused partly by genetic factors.<sup>[2,3]</sup> Degenerative changes are only weakly associated with LBP. This is illustrated by the presence of disc degeneration in more than 50% of patients without LBP,<sup>[4,5]</sup> and lumbar disc herniation in mean 27% of patients without LBP.<sup>[4]</sup>

Medicine

Communication with a patient with normal MRI of the lumbar spine complaining of LBP may be difficult. High-intensity back pain causes much concern in patients and health providers, and higher back pain intensity has been shown to be associated with worse prognosis.<sup>[6]</sup> MRI of the lumbar spine may not help us understand back pain intensity, as the association between back pain intensity and the amount of degenerative changes on MRI of the lumbar spine is weak or nonexistent. This was shown in 170 cases planned for lumbar disc prosthesis<sup>[7]</sup> and in a follow-up cohort of surgery patients: Subsequent progressive adjacent disc degeneration 10 to 15 years after fusion surgery was not associated with disability or pain.<sup>[8]</sup> Thus, we need methods that may help us better understand disproportionate back pain intensity in relation to degenerative changes.

Tender point (TP) examination may be used as a supplementary clinical test in patients with LBP.<sup>[9–12]</sup> It was originally developed as a standardized method to assess diffuse hyperalgesia in chronic generalized pain conditions in order to classify—or not classify—the condition as fibromyalgia.<sup>[13]</sup>

In the general population, the median number of TPs is 3 in men and 6 in women.<sup>[14]</sup> In patients with LBP, we do not use TP examination to diagnose fibromyalgia but as a standardized measure to quantify diffuse hyperalgesia.<sup>[12]</sup> The test procedure in patients with LBP has been described in detail elsewhere.<sup>[15]</sup>

In patients with chronic LBP, localized or diffuse hyperalgesia is a sign of regional or diffuse central sensitization.<sup>[16]</sup> In patients with chronic LBP, central pain processing may resemble that of fibromyalgia.<sup>[17]</sup> In fibromyalgia, widespread pain often includes spinal pain, and fibromyalgia pain is explained by diffuse central sensitization, that is, altered pain processing resulting in generalized hyperalgesia, deep tissue hypersensitivity, and enhanced pain perception.<sup>[18-20]</sup> However, pain measurement techniques used in pain studies require advanced equipment and methods that are not available in daily clinical praxis. We have previously shown that back pain intensity in patients with LBP was positively associated with the number of TPs.<sup>[12,21]</sup> Furthermore, TPs was negatively associated with both disc height reduction on X-ray and with radiculopathy. In a validation study, we showed that in patients with nonspecific chronic LBP, TP examination was reliable although not precise, as reflected by 70% agreement within  $\pm 3$  TPs.<sup>[15]</sup>

In the present secondary analysis of data from patients with LBP on sick leave, all examined by MRI of the lumbar spine and by TP examination,<sup>[21]</sup> we wanted to elucidate whether it was possible to identify TP cut points to distinguish diffuse hyperalgesia from normal soft tissue sensitivity, whether back pain was also positively associated with TPs in subgroups, and whether it was possible to identify patients with disproportionate back pain, that is, back pain not explained by degenerative changes.

# 2. Methods

# 2.1. Design

This study is a secondary analysis of cross-sectional baseline data from a subset of patients participating in a controlled randomized clinical intervention study.

# 2.2. Patients

The patients in the present study participated in a controlled study<sup>[22]</sup> and were selected for a 1-year study period with consecutive MRI of the lumbar spine.<sup>[23]</sup> Prognostic factors<sup>[24]</sup> and associations between pain intensity and MRI findings have been reported previously.<sup>[21]</sup>

The following inclusion criteria for joining the intervention study were applied: part or full sick-listing from work for 4 to 12 weeks due to LBP with or without radiculopathy; LBP should be the prime reason for sick-listing and at least as bothersome as any possible pain elsewhere; age 16 to 60 years; referred from a welldefined area counting about 280,000 inhabitants; and being able to speak and understand Danish.

The following exclusion criteria were applied: unemployment; living outside the referral area; continuing or progressive radiculopathy constituting indication for surgery; low back surgery within the past year; previous lumbar fusion surgery; suspected cauda equina syndrome; progressive paresis or specific back disease (e.g., spondylolisthesis, severe scoliosis, inflammatory disorder, or cancer); pregnancy; known dependency on drugs or alcohol; and primary psychiatric disease.<sup>[22,23]</sup> At their first visit, patients completed a comprehensive questionnaire. Afterwards, a rehabilitation doctor (OKJ) made a patient-record and performed a clinical back examination and a TP examination. On the basis of symptoms and physical examination, the patients were classified as having nonspecific LBP or radiculopathy.<sup>[24]</sup>

# 2.3. MRI data

MRI of the lumbar spine, including T1- and T2-weighted sequences, was performed within 4 to 6 weeks after the primary clinical evaluation at the local hospital using a 0.7-T machine. A few MRIs were performed with similar techniques at hospitals nearby.

The classification into nonspecific LBP or radiculopathy was revised if MRI of the lumbar spine did not confirm clinical suspicion of radiculopathy. Afterwards, all MRIs were transformed to compact discs and data were blinded, except for identification number, and sent to a specialist in radiology who was blinded to the clinical data. MRI images were evaluated and described in accordance with a previously validated protocol.<sup>[25]</sup>

## 2.4. Questionnaire data

At the top of the questionnaire, a figure showed the LBP area from the 12th ribs to the inferior gluteal folds. A previously validated LBP rating scale was used.<sup>[26]</sup> The scale comprises a "sum score" based on three numeric rating scales indicating worst, average, and actual pain during the preceding 2 weeks. The 3 scales (0–10) were added to a back pain score (0–30) and a leg pain score (0–30).

Widespread pain (WP) was recorded using the Danish version of the General Health Questionnaire. WP was defined as an affirmative answer on 2 questions covering the preceding 2 weeks: Much bothered by pain or discomfort in neck, shoulders, arms, and hands; back, buttocks, legs, knees, and feet.

# 2.5. Clinical data

Radiculopathy was defined as nerve root pain and at least 1 of the following signs: positive Lasègue  $\leq 60^{\circ}$ , missing or inhibited reflex, altered sensation in a dermatome, or paresis.<sup>[24]</sup>

TP examination:<sup>13</sup> A pressure, gradually increasing by 1 kg/s up to 4 kg, was applied by the thumb at 18 standardized spots on the body, symmetrically located on the neck, shoulders, forearms, second ribs, buttocks, and legs. Painful points were counted as TPs. The examination technique has been successfully validated in patients with LBP.<sup>[15]</sup>

## 2.6. Ethical approval

All patients signed informed consent as participants in a randomized clinical trial previously reported.<sup>[22]</sup> The study was approved by the Danish Data Protection Agency (No. 2007-41-1278).<sup>[22]</sup>

#### 2.7. Statistical analyses

Model checks showed that the conditions for using linear regression with TPs, pain intensity, or MRI variables as dependent variables were fulfilled.<sup>[27]</sup> Model checks included normality plots of residuals, residuals vs predicted values, and check of leverage and standardized residuals.

Linear regression analyses were therefore used for analyzing data, first with TPs as the dependent variable, second with pain variables or MRI variables as dependent variables and stratified for TPs. All analyses were adjusted for age and sex; and analyses with pain variables as dependent variables were also adjusted for WP and disc degeneration. Proportions were compared by Chi<sup>2</sup>-test and age differences were analyzed by Kruskal–Wallis' test. The disc height reduction sum score variable was dichotomized into 2 groups: one group with no or few degenerative changes (n=81), the other group with substantial degenerative changes (n=60).

All analyses were performed using STATA,<sup>[28]</sup> and a significance level of 5% was chosen.

## 3. Results

# 3.1. Characteristics of included patients

The median number of TPs was 6: 3.5 TPs in men and 8 TPs in women. About half of the patients reported pain duration of 3 months or less, but all had had pain for more than 4 weeks in accordance with the sick-listing criteria. Few patients had no degenerative changes on MRI, but spinal stenosis was infrequent (Table 1).

#### 3.2. TP associations

Unadjusted, the median WP, radiculopathy, and sex differences were 4 to 5 TPs. After adjustment, the differences fell to 2.3 to 2.5 (Table 2). The TP count was positively associated with pain duration, increasing with mean 2.1 TPs in patients whose pain lasted more than 6 months (adjusted). The TP count was negatively associated with disc degeneration (Table 2). Patients with radiculopathy had fewer TPs than patients with nonspecific LBP; the adjusted difference was mean 2.3. There was interaction between men and women, the association strongest in women (P < 0.027, Table 2, legend). The median number of TPs in men and women with radiculopathy was 3 (0–15) and 6 (0–13), respectively. The pattern is illustrated by Fig. 1: In both sexes, patients with WP and no radiculopathy had the highest TP counts, and patients with radiculopathy and no WP had the lowest TP counts.

When setting the upper cut points between radiculopathy and nonspecific LBP at 8 TPs in men and 11 TPs in women (Fig. 1), 2 of the male patients with radiculopathy had TPs above the cut point (5%) and 1 of the female patients with radiculopathy had TPs above the cut point (4.8%). The percentages were similar when setting the cut points one TP higher. When setting the cut points one TP lower (7 and 10 TPs, respectively), 3 men (7.5%) and 2 women (9.5%) above the cut points had radiculopathy. The percentages increased further when setting lower cut points. As the TP levels in the general population were similar to the TP levels in the present patients with radiculopathy, we may consider TPs elevated in patients with nonspecific LBP when >8 in men and >11 in women.

# 3.3. Tender points in relation to back pain, leg pain, and degenerative changes

Back pain intensity was associated with TPs as previously published (linear regression  $\beta = 0.35$ , P = .012).<sup>[21]</sup>Figure 2 (left) showed that this was also for patients with radiculopathy, as

## Table 1

# Characteristics of LBP population.

N=141 Clinical variables	
Sex:	
Women, n (%)	75 (53)
Men: :	66 (47)
Age, years, mean (sd)	41.6 (10.6)
Intensity of back pain, mean (sd)	17.7 (6.50)
Intensity of leg pain, mean (sd)	14.4 (8.30)
Radiculopathy, n (%):	
No (men 26, women 54)	80 (57)
Yes (men 40, women 21)	61 (43)
Widespread pain the preceding 2 wks, n (%)	
No	118 (84)
Yes	23 (16)
Tender points, median (IQ)	6 (3-10
Duration of pain, n (%)	
$\leq$ 3 mo	73 (53)
3–6	38 (27)
>6	27 (20)

MRI variables	n (%)	Sumscore mean (sd)
Nucleus signal change		7.1 (1.67)
Absent (hyper-intense or with	18 (13)	
band)		
Osteophytes		2.6 (2.42)
Absent	45 (32)	
Disc height reduction		2.7 (2.31)
Absent	28 (20)	
High intensity zone		1.1 (0.90)
Absent	42 (30)	
Protrusion/ herniation		4.2 (2.57)
Absent	15 (11)	
Bulging	23 (16)	
Protrusion		
Broad	7 (5)	
Focal	48 (34)	
Extrusion	40 (28)	
Sequestration	8 (6)	
MRI nerve root involvement $^*$		1.4 (1.35)
Absent	52 (37)	
Touch	31 (22)	
Displacement	37 (26)	
Compression	21 (15)	
Spinal stenosis		0.2 (0.76)
Absent	123 (87)	
Modic changes (volume)		3.4 (3.61)
Absent	57 (40)	

IQ=interquartile range, sd=standard deviation. The degenerative changes described in detail elsewhere.  $^{\left[ 23\right] }$ 

\* Touch: contact between disc herniation and nerve root; displacement or compression: the nerve root is displaced or compressed by the disc herniation, respectively.

almost no difference was seen between the slopes of the regression lines representing radiculopathy and nonspecific LBP. Similarly, back pain was also positively associated with TPs in patients with substantial degenerative changes [Fig. 2 (right)].

Unadjusted, back pain intensity was higher in patients with WP than in patients without WP, the difference was 4.1 (1.1; 7.0), P < .001. This difference was reduced after adjustment by TPs: 2.3 (-0.8; 5.5), P = .149; and was further reduced after adjustment by age, sex, and disc degeneration: 1.9 (-1.3; 5.2), P = .238 (linear regression with back pain intensity as dependent variable).

In order to show how the intensity of pain, radiculopathy, and degenerative changes on MRI varied in relation to TPs, we

Table 2	
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## Tender point associations.

N=138	Univariate		Multivariate	
	β <b>95% Cl</b>	Р	β <b>95% Cl</b>	Р
Pain duration 1–3 months $n = 73$	ref.		ref.	
3–6 mo n=38	1.9 (0.17-3.56)	.031	1.6 (0.23-2.89)	.022
> 6  mo  n = 27	4.4 (2.46-6.28)	<.001	2.1 (0.46-3.71)	.012
Widespread pain, ref. not present	4.3 (2.35-6.26)	<.001	2.4 (0.64-4.12)	.008
Radiculopathy, ref. not present	-4.2 (-5.62 to -2.86)	<.001	-2.3 (-3.51 to -1.06)	<.001*
Disc height red., sum score, ref. 0	-0.7 (-1.02 to -0.40)	<.001	-0.4 (-0.67 to -0.16)	.002
Sex, ref. men	4.5 (3.21–3.77)	<.001	2.5 (1.24–3.77)	<.001
Age (per yr), ref. 18	-0.1 (-0.19 to -0.054)	.001	-0.04 (-0.10 to 0.01)	.129
			Adjusted $R^2 = 0.47$	7

Univariate and multivariate linear regression analyses with tender points as dependent variable. Missing values 3 (pain duration).

 $\beta = \text{Regression coefficients}, Cl = 95\%$  confidence interval.

\* Interaction analysis showed interaction of sex, adjusted β for men and women, -1.1 and -4.0, respectively (P<.027). No interaction was found for the other variables.

divided the patients into 3 TP subgroups, LOW, MED (intermedium), and HIGH with different cut points in men and women; men LOW < 3, MED 3 to 8, HIGH > 8; women LOW < 6, MED 6 to 11, HIGH > 11 (Table 3).

Adjusted for WP, sex, age, and disc degeneration, patients in subgroup HIGH reported more back pain than patients in subgroup LOW. Degenerative changes in subgroup HIGH were fewer than in subgroup LOW, though not statistically significant so for nucleus signal intensity, HIZ, osteophytes, and spinal stenosis. The adjusted mean difference in back pain between subgroup HIGH and LOW was 3.6 (0.3–6.9) (3.9 in men and 4.3 in women, no interaction, P > .5) (Table 3). In subgroup MED, we observed a tendency to more back pain in spite of less degenerative changes, but no statistically significant differences were observed. When setting the cut points 1 TP lower (7 TPs in men and 10 TPs in women), back pain intensity was also higher in subgroup HIGH than in subgroup LOW [median difference  $\beta$  = 3.1 (0.0–6.1), *P*=.047], and similar associations were found for degenerative changes (analyses not shown). When setting cut points lower than 7 and 10, no statistically significant differences were seen. When using 8 and 11 TPs as cut points, 27 (34%) of the patients with nonspecific LBP and 3 (5%) of patients with radiculopathy belonged to subgroup HIGH. Twenty of these 30 patients were women. When using 7 and 10 TPs as cut points, 44% with nonspecific LBP and 8% of patients with radiculopathy belonged to subgroup HIGH, and 27 of these 40 patients were women.

The proportion of patients with radiculopathy decreased from LOW through HIGH, supporting the tendency toward a negative association with leg pain. Mean age increased from HIGH



Figure 1. Box plots showing tender point distribution in different subgroups of the present study group of 141 patients. The boxes include 25% to 75% of the distributions, and the whiskers define 1% and 99% limits. Outliers presented by dots. Only 4 women and 1 man both had radiculopathy and widespread pain. 1. +widespread pain<sup>\*</sup>, -radiculopathy. 2. +widespread pain<sup>\*</sup>, +radiculopathy. 1. -widespread pain<sup>\*</sup>, -radiculopathy. 1. -widespread pain<sup>\*</sup>, +radiculopathy. <sup>\*</sup>the preceding two weeks.



Figure 2. Associations between tender points and back pain intensity in patients with and without radiculopathy (left), and in patients with and without substantial degenerative changes (right). Fitted values and 95% confidence intervals of standard error of the means. The confidence intervals were wide in the upper spectrum of TPs in patients with radiculopathy and substantial degenerative changes due to few of these patients with many TPs.

through LOW, reflecting the positive association between degenerative changes and age (Table 3).

More than 10 TPs were present in 31 patients (22.0%), and WP was present in 23 patients (16.3%). Both conditions were present in 11 patients (7.8%), 8 of whom had pain duration >3 months. Seven of these 8 patients also had degenerative changes on MRI.

Eleven patients, 3 men and 8 women, had no degenerative manifestations on MRI; 5 belonged to the MED subgroup; 6 to the HIGH subgroup. Only 1 of these patients had WP and >10 TPs and pain duration >3 months.

As summarized in Table 2, both radiculopathy and degenerative changes were negatively associated with TPs. Detailed analyses of the associations between these three variables are shown in Supplemental Digital Content (Appendix, http://links. lww.com/MD/E858).

#### 4. Discussion

Diffuse central sensitization assessed by standardized TP examination added valuable information to the clinical assessment of patients with LBP. The TP levels were higher in women and in patients with WP the preceding 2 weeks, and they were lower in men and in patients with many degenerative changes. The TP levels were especially low in patients with radiculopathy who displayed levels similar to those that have been found in the general population.

Back pain intensity was not only positively associated with TPs among patients with nonspecific LBP but also among patients with radiculopathy and patients with substantial degenerative changes.

The statistical significance of the association between back pain and WP disappeared after adjustment for TPs.

# Table 3

Analyses of differences between the 3 TP categories defined at the top of the table.						
TP category Men, n=66 Women, n=75	LOW, n=46 <3 (n=27) <6 (n=19)	MED, n=65 3–8 (n=29) 6–11 (n=36)		HIGH, n=30 >8 (n=10) >11 (n=20)	Р	
Mean age (sd) Radiculopathy, n (%)	45.2 (7.89) 26 (56.5)	40.9 (11.4) 32 (49.2)		37.7 (10.9) 3 (10.0)	.011 <sup>*</sup> <.001	
Linear regression analyses		β <b>(95% Cl)</b>	Р	β <b>(95% Cl)</b>	Р	
Back pain, N=135	ref.	1.6 (-1.00 to 4.10)	.231	3.6 (0.31–6.86)	.032	
Leg pain, N=137	ref.	-0.3 (-3.54 to 2.90)	.846	-4.2 (-8.34 to 0.02)	.051	
Nucl. signal intensity	ref.	-0.18 (-0.80 to 0.43)	.558	-0.16 (-0.93 to 0.61)	.680	
Osteophytes	ref.	-0.15 (-0.99 to 0.70)	.729	-0.67 (-1.72 to 0.39)	.214	
Disc height reduction	ref.	-0.50 (-1.33 to 0.35)	.250	-1.52 (-2.57 to -0.48)	.005	
High intensity zone	ref.	0.05 (-0.29 to 0.40)	.751	-0.32 (-0.74 to 0.11)	.143	
Disc protrusion/ extrusion/seq.	ref.	-0.69 (-1.62 to 0.24)	.143	-1.68 (-2.83 to -0.52)	.005	
MRI nerve root involvement	ref.	-0.35 (-0.83 to 0.14)	.160	-0.91 (-1.52 to -0.30)	.004	
Spinal stenosis	ref.	0.05 (-0.24 to 0.33)	.741	-0.10 (-0.45 to 0.26)	.591	
Modic changes	ref	-0.43 ( $-1.69$ to 0.83)	.503	-1.60 ( $-3.18$ to $-0.03$ )	046	

Differences in back pain, leg pain, and MRI variables were analyzed by linear regression analyses. Dependent variables displayed in the left column. The linear regression analyses for back pain and leg pain were adjusted by age, sex, widespread pain, and disc height reduction. The linear regression analyses for MRI variables were adjusted by age and sex, and there were no missings (N=141). Missing values 6 (back pain) and 4 (leg pain).

<sup>\*</sup> Differences in mean age analyzed by Kruskal-Wallis test, and differences in proportions of patients with radiculopathy in subgroups analyzed by Chi<sup>2</sup>-test.

When defining the upper TP cut points at 7 to 8 in men and 10 to 11 in women, 34% to 44% of patients with nonspecific LBP had TPs above the cut points, and 5% to 8% of patients with radiculopathy had TPs above the cut points. These patients reported more back pain than patients with fewer TPs. Notwithstanding having more back pain, patients with TPs above the upper cut points had less degenerative changes than patients with few TPs, not only in terms of disc height reduction but also in terms of disc protrusions, MRI nerve root involvement, and Modic changes, that is, an indication of disproportionate back pain in relation to degenerative changes.

As the number of TPs is a measure of diffuse and remote hyperalgesia, we assume that diffuse central sensitization was responsible for the higher back pain intensity in patients with many TPs than in patients with fewer TPs. The positive association between TPs and pain duration supported this notion, as the time factor is well documented in the process of diffuse central sensitization.<sup>[20]</sup> According to the present data, 7 to 8 TPs in men and 10 to 11 TPs in women seemed to represent a transitional zone between normal soft tissue sensitivity and hyperalgesia. In the intermediate TP subgroup (MED), the tendency toward an increase in back pain and a decrease in degenerative changes may indicate that central sensitization was also present in a few of the patients with fewer than 8 for men and fewer than 11 TPs for women. The lack of sharp cut points between diffuse sensitization and no sensitization is in accordance with the literature.<sup>[29,30]</sup> However, in daily use, it is practical to have cut points or transition zones to help distinguish normal soft tissue sensitivity from hyperalgesia.

The positive association between back pain and TPs demonstrated here may help explain high back pain intensity in some patients with no or few degenerative findings on MRI of the lumbar spine. These patients seem to perceive more back pain in spite of having no or few degenerative changes. Likewise, little back pain intensity in patients with few TPs may also help explain why some patients with substantial degenerative changes experience no pain, whereas others do.

Patients with radiculopathy had few TPs, like the general population. We have no definite explanation for this finding, but speculate that radiculopathy could be a more specific pain condition than nonspecific LBP. We also may hypothesize that nerve root pain has a certain direct effect on the nociceptive system, albeit this was not elucidated in the present study.

Our data confirmed sex-specific and WP differences of TPs in the general population.<sup>[14]</sup> Although TPs in the general population may be lower than 3 in men and 6 in women,<sup>[31]</sup> we believe that these median general population levels are duly documented.<sup>[14]</sup> In the present study, the overall TP level was higher, a finding also demonstrated for other nonspecific regional pain conditions.<sup>[32]</sup> To our knowledge, the present finding of a negative association between TPs and radiculopathy has not been demonstrated elsewhere, except in the large patient group to which the present patient group belonged.<sup>[12]</sup>

# 4.1. Other LBP studies on central sensitization

A positive association between back pain and TPs was also demonstrated in 2 population studies,<sup>[9,10]</sup> the latter only including women. Another study showed negative associations between LBP intensity and the pain-pressure threshold at the forehead and thumbnail.<sup>[31]</sup> Thus, there is some evidence that

diffuse or remote hyperalgesia is positively associated with back pain intensity in patients with LBP.

In a cross-sectional study,<sup>[33]</sup> central sensitization was identified in 48% of a population with chronic LBP by using the 2011 fibromyalgia survey.<sup>[34]</sup> The pressure pain thresholds on the thumbnail and the L5-S1 interspace in patients meeting the fibromyalgia criteria were significantly lower than those in patients not meeting these criteria.

In another cross-sectional study,<sup>[20]</sup> altered pain processing was demonstrated in chronic LBP, but not to the same extent as in fibromyalgia, which is in accordance with the present findings.

In a third study,<sup>[35]</sup> an algorithm was proposed to identify diffuse central sensitization in patients with LBP. The authors stated that diffuse tenderness was an important clinical finding, but a standardized measurement of diffuse tenderness was not included in the algorithm. We consider a high TP count, as defined here, a more precise measure of remote and diffuse hyperalgesia than the clinical observation of diffuse tenderness. The TP examination includes no points located at the lower back.

# 4.2. Widespread pain and fibromyalgia

According to the 1990 fibromyalgia criteria,<sup>[13]</sup> chronic WP was defined as pain on both sides of the body, pain above and below the waist, and axial pain. The pain had to be present for at least 3 months. According to the most recent 2016 fibromyalgia criteria,<sup>[36]</sup> WP was defined as pain the past week in a proportion of 19 body sites, either >6 or 4 to 6 sites, depending on the amount of other fibromyalgia symptoms (symptom severity scale). Furthermore, 4 of 5 regions must be involved, and the symptoms generally should have been present for 3 months or more.

In the present study, 9 patients (6.4%) had a fibromyalgia-like condition according to the 1990 criteria<sup>[13]</sup> as they had >10 TPs, pain duration >3 months, and WP. This is within the reference interval for fibromyalgia in the general population (2–8%),<sup>[30]</sup> although WP in the present study covered only the preceding 2 weeks. However, degenerative spinal manifestations were present in 7 of these patients and may therefore be hypothesized to be a competing cause of pain. It should be added that we do not know the prevalence of fibromyalgia in the present study group if tested by the 2016 fibromyalgia criteria.<sup>[36]</sup>

## 4.3. Tender points and trigger points

In the present study, TP examination was used as a supplemental diagnostic tool in patients with LBP to estimate diffuse hyperalgesia in a standardized way, discussed in detail elsewhere.<sup>[12,15]</sup> Therefore, it was used also in patients with pain duration of less than 3 months, although the examination technique originally was developed for diagnosing fibromyalgia, a diagnosis requiring that pain lasts more than 3 months.<sup>[13]</sup>

According to the 1990 fibromyalgia consensus study,<sup>[13]</sup> the upper limit for the normal range of TPs was set at 10. However, that cut point may not be relevant for men, as 89% of the included patients were women. The results of the present study may argue for the use of gender-specific TP cut points.

TPs are often mistaken for myofascial trigger points. However, a myofascial trigger point is defined as localized tenderness in a muscle and the presence of a taut band or nodulus,<sup>[37]</sup> thus quite different from the definition of a TP.<sup>[13]</sup> Furthermore, trigger points are detected with the purpose of instituting localized

treatment in contrast to the present use of the TP count as a measure of diffuse hyperalgesia. Finally, a recent systematic review<sup>[37]</sup> concluded that detection of myofascial trigger points was unreliable, notwithstanding that localized tenderness was moderately reproducible. Thus, the definition and potential use of trigger points are quite different from those of TPs.

#### 4.4. Usefulness

A method for assessing diffuse central sensitization in patients with LBP may improve clinical care in these patients, especially if it is quick to use and is implementable in clinical praxis. Since our first publication on this subject,<sup>[12]</sup> we have used TP examination routinely in patients with LBP, and our experiences are as follows:

First, it may help deliver reassuring information to the patient, which is important in patients with nonspecific LBP, for example, "the pain does not reflect dangerous damage, but is caused by sensitization or disturbed pain regulation," followed by an explanation of the fibromyalgia-like pain mechanism. Second, it may help distinguish atypical radiculopathy from classic radiculopathy, for example, if there are many TPs and sparse findings on MRI, diffuse leg symptoms or diffuse clinical signs may be due to central sensitization rather than caused by radiculopathy. Third, it may help the doctor and the patient in choosing the most appropriate treatment: If diffuse central sensitization is present, conservative treatment may be preferable, when surgery is not absolutely indicated,<sup>[38]</sup> and aerobic exercise training may be preferable to strength training.<sup>[38]</sup> Fourth, it also may guide the choice of the most relevant treatment when pharmaceutical treatment is considered. Tricyclic antidepressants (especially amitriptyline) and duloxetine have documented effects in conditions characterized by diffuse central sensitization.[16,39] The use of TP examination is furthermore supported by the 1-year prognostic value of the TP count in sick-listed patients with LBP.<sup>[24]</sup>

## 4.5. Strengths

Clinical evaluation and TP examination were performed by one person (OKJ) and were performed without knowing the results of MRI of the lumbar spine. The digital TP examination has been validated previously.<sup>[15]</sup> MRI was described in a standardized manner without access to clinical information. The patients were referred according to well-defined criteria including sick-listing for 1 to 3 months, minimizing the risk of selection bias due to radiculopathy.

## 4.6. Limitations

The number of patients was limited based on pragmatism (available consecutive, standardized MRI description), not defined by power calculation. The low level of TPs in patients with radiculopathy should be replicated in larger patient samples. Our results point to a positive association between TPs and back pain intensity in subgroups; however, a higher number of patients will be needed to confirm this finding.

Digital TP examination in patients with LBP, although reliable, is not precise.<sup>[15]</sup> Furthermore, apart from the associations presented here, TPs may also reflect bodily distress, psychological distress,<sup>[12]</sup> and poor sleep,<sup>[14]</sup> aspects that were not included in the present analyses. Except for poor sleep, these associations have been analyzed and presented previously.<sup>[12]</sup>

WP the preceding 2 weeks may not be a sufficient WP measure, and it is different from the chronic WP measure used in the 1990 fibromyalgia criteria<sup>[32]</sup> and from the one used in the 2016 fibromyalgia criteria.<sup>[36]</sup>

The study was cross-sectional. No final conclusions can therefore be drawn regarding causal relationships between back pain intensity and TPs. Furthermore, we have studied only diffuse central sensitization. Regional central sensitization may also cause persistent and disproportional LBP.<sup>[20,30]</sup> Finally, the conclusions may not apply for patients not included in the present study, for example, patients with LBP with pain duration shorter than 4 weeks, patients at work, or patients with specific back disease.

# 4.7. Test perspectives

The TP examination technique has to be learned, evaluated, and exercised sufficiently often to be reliable with acceptable precision.<sup>[40]</sup> Nonetheless, digital TP examination is simple and quick to perform in connection with a LBP examination. It takes less than 5 minutes.<sup>[15]</sup> The examination technique may be suitable for physiotherapists and chiropractors trained in soft tissue palpation.

TP examination was originally developed for classifying WP patients with fibromyalgia and has been criticized for its low reliability because of bias induced by patient expectations or by test imprecision.<sup>[41]</sup> We believe that the method is more reliable in patients with LBP who cannot know what is preferable, many or few TPs.

# 5. Conclusion

Digital TP examination added valuable information to the clinical and MRI assessment of patients with LBP on sick leave. A high TP count (>7-8 in men, >10-11 in women) could identify patients with diffuse central sensitization, including 34% to 44% of patients with nonspecific LBP and 5% to 8% of patients with radiculopathy. In spite of similar or fewer degenerative changes on MRI, these patients reported more back pain than patients with few TPs (<3 in men <6 in women). The TP level was lowest in patients with TPs, and this was also so in subgroups with radiculopathy or substantial degenerative changes. Thus, TP examination improved the understanding of LBP as well as communication with and treatment of patients with LBP. However, further studies are needed to confirm these findings and to define more specifically the role of WP in LBP.

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## Author contributions

Conceptualization: OKJ, KS, CVN. Data curation: OKJ, CVN. Formal analyses: OKJ. Funding acquisition: CVN. Investigation: OKJ. Methodology: OKJ, KS, CVN. Project administration: OKJ, CVN. Supervision: KS, CVN. Writing – original draft: OKJ.

Writing – review & editing: OKJ, KS, CVN.

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