

Observational Studies

Wang Dawu, Li Kaiting, Chen Dawei, Tao Yuzhang, Yi Weiwei*

Differences in risk factors for flare-ups in patients with lumbar radicular pain may depend on the definition of flare

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Abstract

Objectives – The objective was to determine whether specific physical activity (PA) or psychological stress factors are associated with different definitions of flare-ups (pain-defined flares [PDFs]: periods of increased pain lasting at least 2 h, when pain intensity is distinctly worse than it has been recently; and non-pain-defined flares [NPDFs]: obviously uncomfortable feelings, such as fatigue, loss of function, or emotional/psychosocial fluctuations, without major fluctuations in pain intensity based on 11-point scales) among people with lumbar radicular pain.

Methods – This was a case-crossover study. Participants with acute or subacute lumbar radicular pain completed serial face-to-face or online assessments for 6 weeks at 3-day intervals to determine whether they experienced sciatica flare-ups (PDF/NPDF) after specific types of PA or psychological stresses.

Results – A total of 152 participants were enrolled. There were 597 PDF and 323 NPDF case periods and 800 control periods. The odds of PDFs were increased by prolonged walking and standing, and the odds of NPPDFs were increased by prolonged sitting, mental distress, and depressed mood. According to the multivariable analyses, prolonged sitting (OR: 3.0, 95% CI: 1.7–5.5), prolonged walking (OR: 6.2, 95% CI: 3.9–9.9), and prolonged standing (OR: 5.6, 95% CI: 3.3–9.5) were significantly associated with the odds of PDFs, and prolonged sitting (OR: 3.4, 95% CI: 1.8–6.2), mental distress (OR: 6.7, 95% CI: 2.5–17.5), and depressed mood (OR: 5.8, 95% CI: 2.6–12.8) associated with the odds of NPPDFs.

Conclusions – Prolonged sitting, walking, and standing triggered the occurrence of PDF. Prolonged sitting, mental distress, and depressed mood triggered the occurrence of NPPDF.

Keywords: flare-ups, flare, lumbar radicular pain, sciatica, risk factors

1 Introduction

Low back pain (LBP) with or without radicular pain (also known as sciatica) is a fairly common health problem and a common cause of work disability [1–6]. Lumbar radicular pain is usually caused by compression or irritation of one of the lumbosacral nerve roots and is a common symptom of lumbar disc herniation. LBP has historically been classified as acute, subacute, or chronic. However, contemporary research highlights that LBP is often present as persistent and fluctuating, or episodic, and it rarely resolves completely without recurrence [7]. As a result, research has examined the trajectories of LBP, including fluctuations such as “flare-ups,” episodes, and recurrences [8–10]. LBP flare-ups have been defined as “periods of increased pain lasting at least 2 h, when the pain intensity is distinctly worse than it has been recently” [11,12]. There are different definitions of flare-ups, including “a worsening condition lasting from hours to weeks that is difficult to tolerate and generally impacts usual activities and/or emotions” [12,13]. Flare-ups are therefore characterized not only by an increase in pain but also by other factors, such as fatigue, loss of function, and psychosocial changes.

A variety of environmental and individual characteristics have been reported to increase the risk of LBP. A better understanding of the risk factors for flare-ups of LBP may provide important insights into the prevention and management of this condition. Numerous previous studies of risk factors associated with LBP and sciatica have been published. Suri et al. reported that prolonged sitting (>6 h) was a trigger for LBP flare-ups in adults with

* **Corresponding author: Yi Weiwei**, Department of Rehabilitation Medicine, The First Affiliated Hospital of Chongqing Medical University, 1 You-Yi Road, Chongqing 400016, P.R. China, e-mail: 13983440059@163.com, tel: +86-023-86528930

Wang Dawu, Li Kaiting, Chen Dawei, Tao Yuzhang: Department of Rehabilitation Medicine, The First Affiliated Hospital of Chongqing Medical University, Chongqing 400016, P.R. China

acute LBP. In contrast, activities involving physical exertion were not associated with an increased transient risk of flare-ups [14]. In older men with LBP and sciatica, even if LBP is associated with anatomical abnormalities, such as osteoporotic fractures, metastases, spinal stenosis, degenerative spondylolisthesis, and scoliosis, nonanatomical factors, such as age, social factors, obesity, and lifestyle factors, also seem to influence the subjective experience of pain [15–17]. Costa *et al.* reported that participants considered biomedical factors to be the main triggers of their LBP flare-ups, but some also cited nonbiomedical triggers. The most frequently reported reasons for experiencing flare-ups were active movements and static postures [9]. A recent study identified different risk factors for LBP flare-ups using different definitions, such as pain-defined flares (PDFs) or self-reported flares (SRFs) [12]. Poor sleep quality, fatigue, leisure time physical activity (PA), and fear of PA increased the risk for PDFs. Risk factors differed when the SRF definition was used.

To date, no studies have explored the risk factors for flare-ups in patients with lumbar radicular pain depending on how flare-ups is defined, such as PDFs and non-pain-defined flares (NPDFs). The aims of this study were to describe (i) the risk factors associated with flare-ups in people with lumbar radicular pain and (ii) the differences between risk factors for flare-ups using two different definitions: PDFs or NPDFs.

2 Methods

2.1 Study design

We used a case-crossover design to explore the risk factors for flare-ups in patients with lumbar radicular pain depending on the definition used (PDFs or NPDFs). Case-crossover studies involve each person functioning as their own control, eliminating between-person confounding by measured and unmeasured characteristics that remain constant over time [18]. This study design examines the transient effects of a brief exposure on the onset of an acute outcome. By design, each sciatica participant served as his or her own control, and so factors that were less likely to change within a short duration, such as age, sex, weight, socioeconomic status, lifestyle habits, and comorbidities, were automatically controlled for.

Two definitions of flare-ups (PDF and NPDF) were used. PDFs were defined as “periods of increased pain lasting at least 2 h, when the pain intensity is distinctly worse than it has been recently.” NPDFs were defined as

obviously uncomfortable feelings, such as fatigue, loss of function, or emotional/psychosocial fluctuations, without major fluctuation in pain intensity based on 11-point scales (Table S1, Supplementary Material). The first question (Select the number that best describes the **PAIN** you felt due to your lumbar radicular pain) is to respond to the PDF, and questions 2 (Select the number that best describes the **DIFFICULTY** you had in doing physical activities, such as walking, dressing, or preparing meals, etc., due to your lumbar radicular pain), 3 (Select the number that best describes the **FATIGUE** you felt due to your lumbar radicular pain), or 4 (Select the number that best describes the **DEPRESSED MOOD** you had due to your lumbar radicular pain) determine the NPDF. A >2-point increase over the usual intensity on an 11-point scale for radicular pain, difficulty, fatigue, or depressed mood was classified as a large fluctuation. The case period was defined as the 24 h prior to a PDF/NPDF. Similarly, the control period was defined as the 24 h that preceded a day with no flare-ups.

2.2 Participants

This descriptive study aimed to investigate the risk factors for flare-ups (PDF/NPDF). The incidence of PDF is approximately 2/3, while the incidence of NPDF is around 1/3 based on our clinical experience. The sample size estimation was based on the precision (width) of the 95% confidence intervals (CIs) of the proportions of expected events, and calculated using power analysis via SPSS software. The inclusion criteria were (i) patients with lumbar radicular pain, defined as pain radiating into the leg below the gluteal fold, also known as LBP with radicular pain, and lumbar MRI-confirmed disc herniation resulting in nerve root compression who developed sciatica; (ii) patients aged 18 years and older; and (iii) patients with a new episode of LBP with a radicular pain of duration ≤ 3 months, preceded by at least 1 month without LBP. The exclusion criteria were as follows: (i) clinical suspicion due to “red flag” conditions, including infection, fracture, or neoplasm; (ii) LBP without radicular pain; and (iii) previous spinal surgery, recent low back trauma, pregnancy, or severe active medical comorbidities. Participants reported their age, sex, employment status, and LBP history at their initial LBP consultation. Pain intensity was measured using an 11-point numerical rating scale (NRS) ranging from 0 (no pain) to 10 (worst imaginable pain). Participants completed the Oswestry Disability Index (ODI), the Fear-Avoidance Beliefs Questionnaire, and the PA subscale. This study was approved by the Ethics Committee of Chongqing Medical University (Decision number: 2021750). All study

protocols and procedures were conducted in accordance with the Declaration of Helsinki.

2.3 Exposure assessment

The participants completed face-to-face interviews or online surveys. The participants reported whether they had PDFs or NPPDFs, and whether they had engaged in specific types of PA exposures during the past 24 h prior to a PDF/NPDF or a day with no flare-ups, including prolonged sitting (>1 h), prolonged standing (>1 h), prolonged walking (>half an hour), manual handling of objects (10 kg), driving (>1 h), frequent bending, frequent twisting, frequent lifting ($\geq 1/2$ of the day as frequent) [16], mental distress, depressed mood, and dissatisfaction with life. To avoid confusion in the risk factor analysis, we did not include both PDF and NPPDF on the same day in same participant. Subsequent surveys reassessed triggers and flare-ups at 3-day intervals after the first survey, for a maximum of 15 surveys completed during the 6-week follow-up. All participants received standard medical care for acute LBP with radicular pain as per clinical practice guidelines.

2.4 Statistical analysis

Only participants with both case and control periods were included in the analysis. Participant characteristics were reported using descriptive statistics. Continuous variables were expressed as mean (standard deviations [SDs]), and categorical variables are expressed as numbers and percentages. Comparisons of categorical variables (sex, BMI, history of prior LBP history, history of prior lumbar radicular pain, and employment status) were conducted using the χ^2 test or Fisher's exact test, as appropriate. Numerical data (age, duration of symptoms, NRS score, ODI score, and fear avoidance belief questionnaire score) were analysed using an unpaired *t*-test or the Mann–Whitney *U*-test, as appropriate. We calculated crude odds ratios (ORs) and 95% CIs for associations between triggers over the past 24 h and the risk of PDFs and NPPDFs, respectively, using univariate analysis. Next, based on the univariate analysis, factors with statistical significance and approximate significance were included in the multivariate conditional logistic regression analyses.

In addition, we performed sensitivity analyses by treating recurrent flare events within each person as a cluster, constructing the conditional likelihood on a person/flare level, and restricting analyses to the first reported flare-up for each participant.

Data were analysed using IBM® SPSS® statistics software, version 24 (IBM SPSS Statistics for Mac, version 24.0., IBM Corp., Armonk, NY, USA). A *p*-value <0.05 was considered to indicate statistical significance.

3 Results

This case-crossover study included 152 participants recruited from the outpatient clinic or who were admitted to the Department of Rehabilitation Medicine, the Affiliated Hospital of Chongqing Medical University between August 2022 and May 2023 (Figure 1). The characteristics of the study sample (*n* = 178) are presented in Table 1. The mean (SD) age of the participants was 49(15.5) years, and 49% of the participants were male. Participants who were included in the case-crossover analysis (*n* = 152) had similar characteristics to those who were not included. Of the 1,831 surveys (1,108 face-to-face surveys by 152 participants, 723 online surveys by 114 participants) completed by participants in the case-crossover analysis, a total of 1,031 flare-up days were identified, and 111 flare periods were excluded for having both PDF and NPPDF on the same day in same participant. This left 920 case periods, being 597 PDF and 323 NPPDF case periods, and 800 control periods during the 6-week follow-up, with an average of 12 completed surveys per participant.

3.1 Risk factors for PDF

The absolute number of triggers reported during flare periods was low for many of the triggers studied (Table 2). Prolonged walking (>half an hour) and prolonged standing

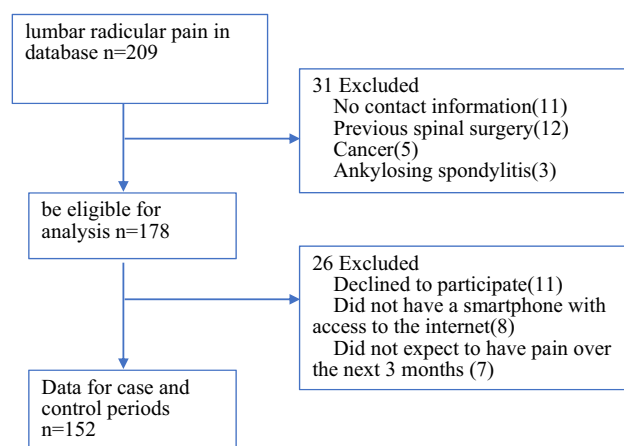


Figure 1: Flow diagram for the inclusion and exclusion of patients with lumbar radicular pain.

Table 1: Characteristics of acute and subacute participants with lumbar radicular pain

	Eligible participants (<i>n</i> = 178)	Included in case-crossover analysis (<i>n</i> = 152)	Not included in case-crossover analysis (<i>n</i> = 26)
	Mean (standard deviation) or <i>n</i> (%)		
Age, year	48.9(15.3)	47.5(15.9)	49.4(14.8)
Sex (% male)	87(48.9%)	81(53.3%)	15(57.7%)
<25 kg/m ²	143(80.3%)	125(82.2%)	21(80.8%)
≥25 kg/m ²	35(19.7%)	27(17.8%)	5(19.2%)
Duration of symptoms, days	16(15.0)	14(15.3)	15(16.6)
Prior low back pain history (%)	163(91.6%)	141(92.8%)	25(96.1%)
Prior lumbar radicular pain history (%)	63(35.4%)	46(30.3%)	7(26.9%)
Full- or part-time employment	126(70.8%)	95(62.5%)	17(65.4%)
Retired	24(13.5%)	25(16.4%)	4(15.4%)
Unemployed	15(8.4%)	24(15.8%)	2(7.7%)
Disabled	13(7.3%)	8(5.3%)	3(11.5%)
NRS (0–10)	6.9(2.5)	7.2(2.4)	7.5(2.3)
ODI (0–100)	59(26)	61(23)	65(25)
Fear avoidance beliefs questionnaire, PA subscale	13.9(4.9)	14.8(4.6)	14.0(5.1)

BMI: body mass index; NRS: numerical rating scale; ODI: Oswestry Disability Index; PA: physical activity.

Table 2: Analyses of associations between potential risk of PDF during an acute and subacute lumbar radicular pain

	No. (%) of PDF periods (<i>n</i> = 597)	No. (%) of control periods (<i>n</i> = 800)	Univariate ORs (95% CI)	Multivariate ORs (95% CI)
Physical activities				
Prolonged sitting (>1 h)	84(14.1%)	76(9.5%)	1.6(0.9–2.7)	3.0(1.7–5.5)
Prolonged walking (>half an hour)	242(40.5%)	117(14.6%)	4.0(2.6–6.1)	6.2(3.9–9.9)
Prolonged standing (>1 h)	154(25.8%)	84(10.5%)	3.0(1.8–4.8)	5.6(3.3–9.5)
Manual handling of objects <10 kg	19(3.2%)	16(2.0%)	1.5(0.5–4.8)	
Manual handling of objects ≥10 kg	14(2.3%)	16(2.0%)	1.1(0.3–3.7)	
Time driving (for >1 h)	11(1.8%)	14(1.8%)	1.1(0.3–4.0)	
Frequent bending	8(1.3%)	11(1.4%)	1.0(0.2–4.5)	
Frequent twisting	16(2.7%)	14(1.8%)	1.6(0.5–5.4)	
Frequent lifting	19(3.2%)	22(2.8%)	1.2(0.4–3.3)	
Psychological stress				
Mental distress	21(3.5%)	19(2.4%)	1.6(0.6–4.3)	
Depressed mood	27(4.5%)	33(4.1%)	1.1(0.5–2.6)	0.9(0.3–2.3)
Dissatisfaction with life	14(2.3%)	27(3.4%)	0.7(0.2–2.0)	

PDF: pain-defined flare-ups.

The bold values mean potential risk with statistically significant associations with PDF.

(>1 h) in the past 24 h were activities that were significantly associated with PDFs, conferring a fourfold and threefold increased risk of flare-up compared to not walking and standing for prolonged periods (OR: 4.0, 95% CI: 2.6–6.1; OR: 3.0, 95% CI: 1.8–4.8, respectively). For most physical activities involving physical exertion (except for walking and standing), the frequency of triggers reported during

flare periods was similar to that reported during control periods. Variables related to psychological stress were not associated with PDF (Table 2). According to the multivariable logistic analyses, prolonged sitting (OR: 3.0, 95% CI: 1.7–5.5), prolonged walking (OR: 6.2, 95% CI: 3.9–9.9), and prolonged standing (OR: 5.6, 95% CI: 3.3–9.5) were independently and significantly associated with PDF risk (Table 2).

Table 3: Analyses of associations between potential risk of NPDF during an acute and subacute lumbar radicular pain

	No. (%) of NPDF periods (<i>n</i> = 323)	No. (%) of control periods (<i>n</i> = 800)	Univariate	Multivariate
			ORs (95% CI)	ORs (95% CI)
Physical activities				
Prolonged sitting (>1 h)	65(20.1%)	76(9.5%)	2.4(1.3–4.4)	3.4(1.8–6.2)
Prolonged walking (>half an hour)	49(15.2%)	117(14.6%)	1.0(0.6–1.9)	
Prolonged standing (>1 h)	41(12.7%)	84(10.5%)	1.2(0.6–2.3)	1.5(0.8–3.0)
Manual handling of objects <10 kg	14(4.3%)	16(2.0%)	2.1(0.6–7.1)	
Manual handling of objects ≥10 kg	16(5.0%)	16(2.0%)	2.6(0.8–8.1)	
Time driving (for >1 h)	14(4.3%)	14(1.8%)	2.5(0.7–9.0)	
Frequent bending	8(2.5%)	11(1.4%)	1.9(0.4–8.5)	
frequent twisting	16(5.0%)	14(1.8%)	3.1(0.9–10.3)	
Frequent lifting	14(4.3%)	22(2.8%)	1.6(0.5–4.9)	
Psychological stress				
Mental distress	35(10.8%)	19(2.4%)	5.0(2.0–13.0)	6.7(2.5–17.5)
Depressed mood	49(15.2%)	33(4.1%)	4.2(2.0–9.0)	5.8(2.6–12.8)
Dissatisfaction with life	22(6.8%)	27(3.4%)	2.1(0.8–5.3)	

NPDF: non-pain-defined flare-ups.

The bold values mean potential risk with statistically significant associations with NPDF.

3.2 Risk factors for NPDF

The ORs (95% CIs) of each variable for the case and control days preceding an NPDF or nonflare day are presented in Table 3. Prolonged sitting (>1 h) (OR: 2.4, 95% CI: 1.3–4.4), mental distress (OR: 5.0, 95% CI: 2.0–13.0), and depressed mood (OR: 4.2, 95% CI: 2.0–9.0) in the past 24 h were significantly associated with NPDFs, conferring a twofold, fivefold, and fourfold increased risk of NPDFs. For all physical activities involving physical exertion except for sitting, the frequency of triggers reported during flare periods was similar to that reported during control periods. Variables related to psychological stress were significantly associated with NPDFs except for dissatisfaction with life. According to multivariable logistic analyses, prolonged sitting (OR: 3.4, 95% CI: 1.8–6.2), mental distress (OR: 6.7, 95% CI: 2.5–17.5), and depressed mood (OR: 5.8, 95% CI: 2.6–12.8) were independently and significantly associated with NPDF risk (Table 3).

The sensitivity analyses yielded results that were not materially different from those of the primary analyses, although the precision of the risk estimates decreased in the analyses restricted to the first flare-ups, as expected owing to the smaller number of flare events included (online Supplementary material).

4 Discussion

Our study demonstrated that there are different risk factors for flare-ups in patients with lumbar radicular pain

depending on whether the flare is defined as a PDF or an NPDF. Prolonged sitting (>1 h), prolonged walking (>half an hour), and prolonged standing (>1 h) triggered PDFs. However, prolonged sitting (>1 h), mental distress, and depressed mood triggered NPDFs. Therefore, prolonged sitting triggered both PDFs and NPDFs.

Parreira et al. previously performed an overview of risk factors evaluated for their association with LBP and sciatica [19]. Their results showed that exposure to a range of factors pertaining to the individual, poor general health, physical or psychological stress significantly increased the risk of LBP and sciatica. The associations between PA and psychological stress and lumbar radicular pain were also noted in an earlier study [20]. The findings of this study are consistent with these earlier reports and demonstrate that PA and stress or depression trigger LBP and sciatica flare-ups. Similar to Costa's findings relating to risk factors for low back pain flares [12], this study revealed that risk factors for flare-ups vary depending on the different definitions of flare. These findings built upon earlier work by further demonstrating that prolonged sitting (>1 h), prolonged walking (>half an hour), and prolonged standing (>1 h) triggered PDFs, and prolonged sitting (>1 h), mental distress, and depressed mood triggered NPDFs for patients with lumbar radicular pain who developed sciatica.

The categories of risk factors for flare-ups in patients with sciatica in the present study, such as PA and psychological stress, are similar to the categories of risk factors for low back pain reported by Parreira et al. [19]. While PA categories consisted of sitting (>2 h), prolonged standing

(>2 h), and prolonged walking (>2 h) for low back pain patients according to Parreira's review, the duration of PA in the present study was shorter, and PA consisted of sitting (>1 h), prolonged standing (>1 h), and prolonged walking (>half an hour). This means that there are significant differences in the intensity of PA between patients with the low back pain only and those with sciatica, with patients with lumbar radicular pain who develop sciatica requiring less intense PA to induce flares than patients with low back pain alone. In other words, shorter periods of PA can induce and aggravate sciatica.

The similarities and differences in the risk factors for flare-ups in lumbar radicular pain patients are noteworthy given that different definitions of flare-ups (PDFs or NPPDFs) were used. Prolonged sitting (>1 h) is a common risk factor for both PDFs and NPPDFs. Although other physical activities (manual handling of objects, driving, and frequent lifting) were not significantly associated with flare-ups in our study, it is possible that participants with sciatica rarely engage in such heavy PA, biasing effect estimates toward the null and decreasing our ability to detect associations. The majority of patients with lumbar radicular pain may perform only basic activities of daily living. Mental distress and depressed mood represent important and complex risk factors for NPPDF-related lumbar radicular pain. A common theory holds that depression is a psychiatric disorder with various symptoms and is often accompanied by unexplained painful somatic symptoms [21]. As argued by Torta and Munari, depression may reduce the pain threshold and sensitize pain perception [22].

The data of risk factors for flare-ups in patients with lumbar radicular pain in this study were collected by face-to-face interviews or online survey. The majority of our participants (114/152) could complete the survey by both face-to-face and online methods, and a few participants (38/152) by only face-to-face interview. Significantly older and more dumpphone users were found in the only face-to-face surveys compared both face-to-face and online surveys. Overall, assessments of face-to-face validity were similar to online.

This study presents novel information about differences in risk factors for flare-ups in patients with lumbar radicular pain, depending on the different definitions of flare-ups used; this information may be useful for clinicians. First, prolonged sitting (>1 h) is a common risk factor for both PDFs and NPPDFs in individuals with sciatica. Prolonged sitting may increase flare-ups in sciatica patients, particularly NPPDFs. Second, clinicians should be aware that increases in flare-ups of radicular pain (PDF) may be related to PA, such as prolonged standing (>1 h) and prolonged walking (>half an hour), consistent with the characteristics of low back pain with radicular pain. Finally, the findings that mental distress

and depressed mood are major risk factors for NPPDFs, could influence clinicians' decisions to pay attention to patients' emotional states and provide timely psychological support in time for sciatica patients with lumbar radicular pain. In short, a better understanding of these risk factors provides a logical rationale for the development of more effective prevention strategies.

This study has several limitations. First, although the case-crossover design is an epidemiologic technique with distinct strengths for assessing the change in the risk of an acute event during a brief interval after exposure to a transient risk factor, there are some limitations of this study design. Such as incomplete data on exposures, overestimating exposures immediately prior to the outcome, and underestimating exposures during control intervals [23]. Second, the duration of our flare-up survey period, which spanned more than 3 days, was excessively long and may compromise the authenticity of determining the cause of the incident. Flare-ups reported more than a few hours (more than 3–4 h) after flare onset are problematic because when reporting such flares, participants often mistakenly report the consequences of a flare (things they have done or experienced because of the flare) as they happened before the flare. Future studies examining pain fluctuations should incorporate a longitudinal design to better characterize the quantitative changes in pain intensity typical of flare-ups, and to identify flare-ups prospectively, thereby avoiding the possible biases of retrospective flare-up assessments used in the present study. Last, although we excluded for having both PDF and NPPDF on the same day in same participant, we examined the occurrence of either only PDFs or only NPPDFs in terms of the participants' respective risk factors. However, there may be an inherent logical connection between PDFs and NPPDFs, or a vicious cycle between PDFs and NPPDFs. Indeed, increased pain intensity can lead to functional limitations and depressed mood. For example, a PDF on a previous day may lead to an NPPDF the next day. In fact, increased pain intensity can result in functional limitations and a depressed mood. This can create major problems in pain research. Future research should better clarify the differences and connections between PDFs and NPPDFs.

5 Conclusions

This study of participants with acute lumbar radicular pain revealed that prolonged sitting (>1 h), prolonged walking (>half an hour), and prolonged standing (>1 h) increased risk for PDFs, and prolonged sitting (>1 h), mental distress, and depressed mood increased the risk for NPPDFs.

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Research ethics: The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Ethics Committee of Chongqing Medical University (Decision number: 2021750).

Informed consent: Informed consent was obtained from all individuals included in this study, or their legal guardians or wards.

Author contributions: The authors have accepted responsibility for the entire content of this manuscript and approved its submission. Wang Dawu and Yi Weiwei designed the study; Wang Dawu and Li Kaiting wrote the main manuscript text; Chen Dawei prepared Figure 1 and Supplementary tables; Tao Yuzhang prepared Table 1–3. All authors reviewed the manuscript.

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Data availability: The raw data can be obtained on request from the corresponding author.

Artificial intelligence/Machine learning tools: Not applicable.

Supplementary Material: This article contains supplementary material (followed by the link to the article online).

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