ORIGINAL ARTICLE

In subjects with chronic low back pain, does neuropathia exclusively correlated to neuronal compression? A correlation study of PainDETECT questionnaire and corresponding MRI and X-ray findings

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Abstract

Introduction Understanding the complex nature of low back pain (LBP) is crucial for effective management. The PainDETECT questionnaire is a tool that distinguishes between neuropathic (NeP), nociceptive (NoP), and ambiguous pain. This study aimed to investigate the relationship between pain classification and lumbar intervertebral degenerative parameters obtained from imaging.

Methods A cohort study was conducted involving 279 patients, aged 18 years and above, who completed PainDETECT questionnaires and underwent lumbar MRI and/or X-ray scans.

Results The study included 102 patients with NoP, 78 with ambiguous pain, and 99 with NeP. The NeP group had lower mean age (58.21 vs. 53.63, $p < 0.05$) and higher mean numerical rating scale score (7.9 vs. 5.9, $p < 0.001$) compared to the NoP group. A negative correlation was found between PainDETECT scores and pelvic incidence ($\tau = -0.177$, $p = 0.043$). The NeP group exhibited significantly higher severity of foraminal stenosis (U = 18.962, $p = 0.002$), spinal stenosis (U = 14.481, $p = 0.005$), and Pfirrmann grade (U = 14.221, $p = 0.028$) compared to the NoP group. A higher proportion of NeP patients had intervertebral disk bulge (96% vs. 78% vs. 78%, $p = 0.002$) and high-intensity zones (51% vs. 41% vs. 19%, $p < 0.001$) compared to those with NoP and ambiguous pain.

Conclusion NeP, as determined by the PainDETECT questionnaire, is associated with more severe neural compression, increased presence of discogenic disease and inflammatory disk severity, and decreased pelvic incidence. This pioneering study establishes a connection between pathological findings and pain categorization, providing clinicians with valuable guidance for formulating tailored management plans and reducing the need for unnecessary pharmacotherapy, imaging, and non-targeted surgical interventions.

Keywords Low back pain · PainDETECT · Neuropathic pain · Clinical imaging · Degenerative intervertebral disk

Introduction

Low back pain (LBP) is the leading cause of disability world-wide with more than 500 million people at one time significantly limited in their ability to undertake activities of daily living [1]. Additionally, this condition is also extremely debilitating, with an associated increase in depression, anxiety, and sleep disorders [2]. Australia spends roughly $4.8 billion dollars per year on management of LBP and is the most common condition keeping Australians aged 45–64 out of the workforce [3].

The nature of LBP is varied at each individual level and complex at systems level. At an individual level, it is

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hypothesized that pain is either generated via mechanical compression or chemical irritation via inflammatory biomarkers [4]. Nociceptive pain (NoP) results from activation of nociceptors that innervate ligaments, small joints, muscle tendons and other structures and may be a result of inflammatory response, mechanical compression, or autoimmune response [5–7]. Neuropathic pain (NeP) in the context of the lumbar spine is defined by the International Association for the Study of Pain as 'pain caused by a lesion or disease of the somatosensory nervous system' [8]. This can be a result of mechanical compression of radicular nerve tissues in the spinal canal or foramina or the action of inflammatory mediators that originate from the degenerated disk [5–7]. Different components of pain may individually or collectively contribute to the overall pain perception. Therefore, it is imperative to associate these pain classifications with underlying pathomechanisms able to be visibly observed on radiological imaging as the current understanding of the nature of LBP and leg pain is unclear, with high rates of degenerative changes visible on imaging in asymptomatic patients.

The PainDETECT questionnaire (supplementary 1) is a screening tool to discriminate between NeP and NoP on a 38 point scale, with 0–12 being negative of NeP, 12–18 being an ambiguous result and 19–38 being positive of NeP [9]. Validation was examined independently by pain specialists and revealed sensitivity, specificity, and positive predictive value all above 80% [10]. Although some authors have independently concluded the reliability of PainDETECT in distinguishing NeP [11], nonetheless, its use in the clinical setting is heavily debated with some studies showing PainDETECT to be a poor indicator of NeP [12]. To date, no studies have been conducted that analyze the association between the PainDETECT questionnaire and visible degenerative and stenosis findings observable on X-ray and MRI imaging in relation to the lumbar spine.

Current literature provides an uncertain conclusion in the relationship between radiological findings and pain related to the lumbar spine. Previous published studies exploring the use of PainDETECT in spinal clinical settings have yielded opposing conclusions. Therefore, it is interesting to ponder if there exists an association between pathological findings on radiology and NeP and NoP. This study aims to conduct an observational cohort study to explore the associations between radiological findings on MRI and X-ray and pain classifications assessed by the PainDETECT questionnaire to allow for an improved understanding into the pathophysiology and development of NoP and NeP.

Materials and methods

Study design and patient population

The study was IRB approved and conducted as a cohort study of adult patients (over 18 years of age) who presented to the Spine Service clinic at St George Private Hospital with completed PainDETECT questionnaire, MRI and/or X-ray scans. Written approval was granted by the original developer of the PainDETECT tool in an electronic format for the purpose of this study [9]. The most recent MRI and X-ray scans were used if multiple scans of the same patient were available in the database. All MRI scans, X-ray scans, radiology reports, demographic data and PainDETECT score were consecutively extracted. Patients were included if and only if they had chronic LBP (> 3 months) with or without leg pain. Patients were excluded if they had a history of lumbar spinal surgery prior to imaging and completing the PainDETECT form. Written informed consent was obtained from all patients to be included in the study.

Data collection

The standing lateral X-ray images, axial and sagittal T1W and T2W MRI scans of the lumbar spine were assessed, and data points were collected before reading the radiology report. SS was trained by an experienced spine surgeon and back pain researcher with extensive experience in interpreting radiological images (ADD). X-ray parameters for sagittal alignment are measured including cobb angle, sacral slope, pelvic tilt, and pelvic incidence. MRI degenerative and stenotic parameters include intervertebral disk (IVD) bulge, Pfirmann grade, endplate changes, high intensity zones (HIZ), spinal stenosis and foraminal stenosis. The specific measurement protocols of the degenerative/stenotic parameters are outlined in Table 1. In patients with multi-level degeneration, the parameter for the most severe level was extracted. The radiology reports were prepared by board certified radiologists.

Data points for ten percent of the patients were also measured by a second rater (ZG) to evaluate inter-rater reliability, and for a second time three weeks after initial extraction by the first author (SS) to evaluate intra-rater reliability. To enhance the quality and applicability of this study, each rater was blinded to their own measurements and findings of the other.

PainDETECT score and demographic data were extracted from the Spine Service PainDETECT RedCap database. PainDETECT was trichotomized into the NoP, ambiguous and NeP groups as defined by the PainDETECT questionnaire.

Table 1 Measurement protocols and example images/measurements for lumbar degenerative MRI and X-ray parameters
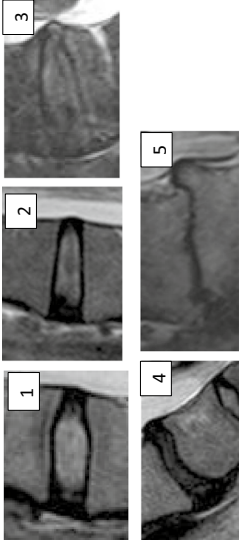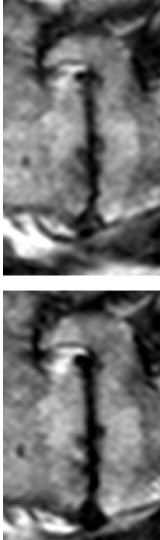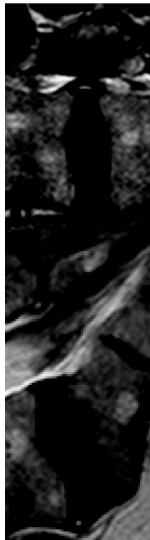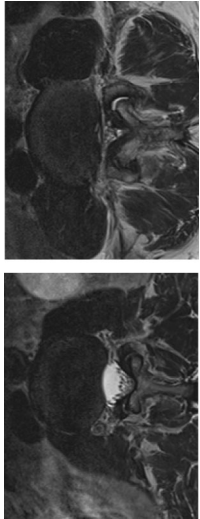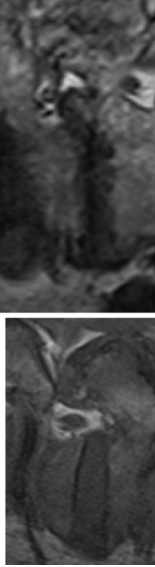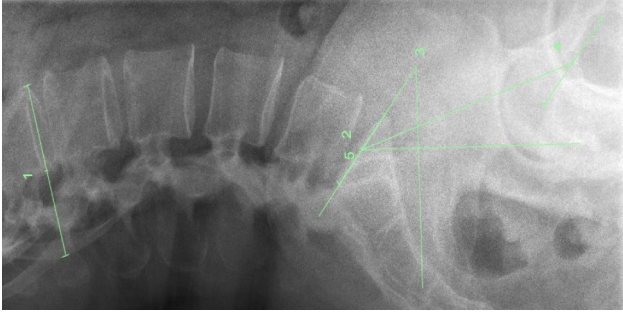
MRI parameter	Protocol	Example images
Pfirmann grade	Pfirmann classification of disk degeneration (assesses asymmetry in disk structure, distinction of nucleus and annulus, signal intensity and height of the disk. Ordinal scale of increasing pathology from I to V [13]	Pfirmann classification for IVD degeneration. 1: grade 1, 2: grade 2, 3: grade 3, 4: grade 4, 5: grade 5
Endplate changes	Hypointense, hyperintense or mixed bone marrow and vertebral endplate lesions visible on T1W and T2W MRI	Endplate signal changes on T2W MRI (left) and corresponding changes on T1W MRI (right)
High intensity zones	Lesion observed on T2W MRI where the signal intensity is at least 50% of the cerebrospinal fluid, contained within the annulus fibrosus and distinglty apart from the signal of the nucleus pulposus [14, 15]	Anterior HIZ on T2W MRI (left). Posterior HIZ on T2W MRI (right)
Spinal stenosis	Lee Y.G. et al. classification. Grade A = no stenosis. Grade B = moderate stenosis. Grade C = severe stenosis. Grade D = extreme stenosis. [16]	Grade A lumbar spinal stenosis (left). Grade D lumbar spinal stenosis with no epidural fat, CSF, or rootlets visible (right)

Table 1 (continued)

MRI parameter	Protocol	Example images
Foraminal stenosis	Lee S. et al. classification. Grade 0 = normal foraminal rootlet. Grade 1 = mild foraminal stenosis, Grade 2 = moderate foraminal stenosis, Grade 3 = severe foraminal stenosis [17]	Grade 0 foraminal stenosis (left). Grade 3 foraminal stenosis with complete nerve root collapse (right)
X-ray parameter	**Protocol**	
Sagittal alignment	Lumbar angle is the angle between the superior endplate of L1 and the superior endplate of S1. Sacral horizontal angle is the angle between the superior endplate of S1 and the horizontal. Pelvic tilt is the angle between the midpoint of the superior endplate of S1 and the midpoint of the centre of the femoral heads on standing x-ray. Pelvic incidence is the sum of sacral horizontal angle and pelvic tilt	Measurements required for sagittal alignment. 1 and 2: lumbar lordosis angle, 3: sacral horizontal angle, 4: line constructed between the midpoint of the femoral heads, 5: pelvic tilt. Note, all angle measurements are conducted automatically by *Inteleviewer*

IVD intervertebral disk, *T1W* T1-weighted MRI, *T2W* T2-weighted MRI

Statistical analysis

Kruskal–Wallis H test was used to analyze the difference in PainDETECT scores for more than two groups. A post-hoc Mann–Whitney U test using a Bonferroni correction was used to analyze the difference in PainDETECT scores between paired groups. Pearson Chi square was used to analyse the independence of association. One way analysis of variance (ANOVA) was used to analyze the difference in continuous variables for more than two groups. A subgroup analysis of patients with no foraminal and spinal stenosis was conducted to determine the relationship between Pfirmann grade and PainDETECT. Inter-rater reliability was assessed using the intraclass coefficient estimates (ICC) based on single-rating, consistency, 2-way random effects model, and intra-rater reliability was assessed using ICC based on single-rating, absolute agreement, 2-way fixed effects model. ICC values of < 0.05, 0.5–0.75, 0.75–0.90, and > 0.90 indicated poor, moderate, good, and excellent reliability, respectively. Statistical analyses were conducted using the commercially available software SPSS (version 27, IBM Corporation, New York, USA). The level of statistical significance was set at 5% ($p = 0.05$).
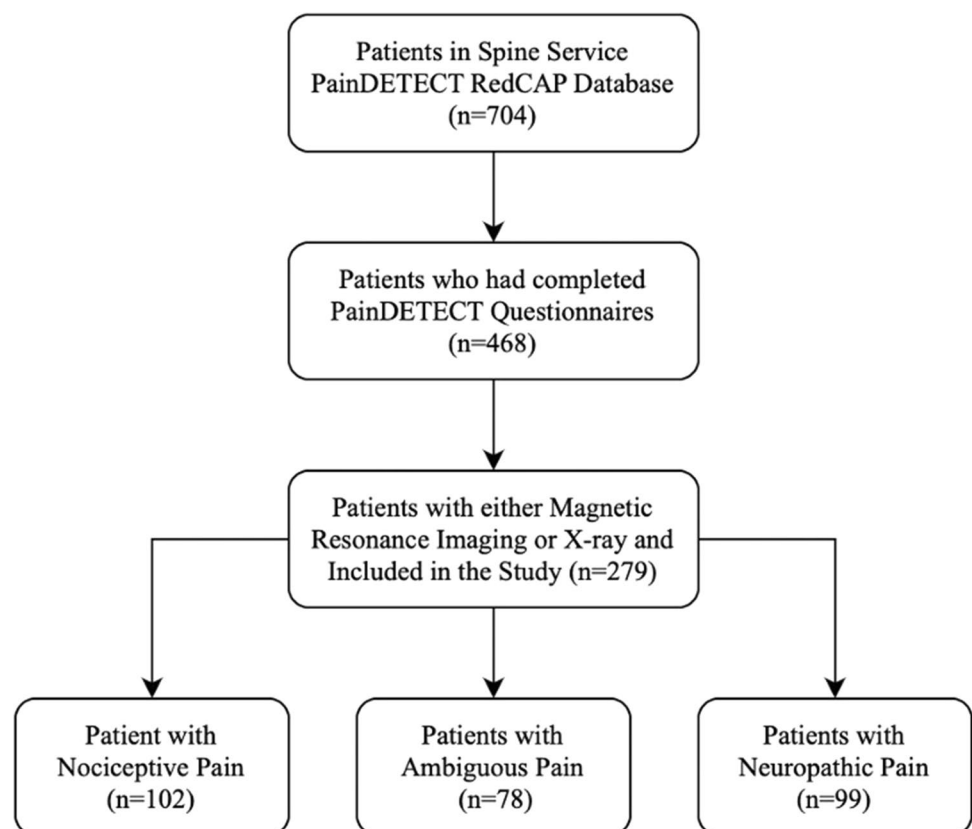
Results

Demographics

A flowchart depicting patient inclusion, exclusion, and separation into pain classification groups is shown in Fig. 1. Of the 279 patients included in the study, 102 had NoP, 78 had ambiguous and 99 had NeP based on the PainDETECT questionnaire scores. There was a statistically significant difference in mean age amongst the NoP, ambiguous, and NeP groups (58.21 ± 17.11 vs. 55.33 ± 16.45 vs. 53.63 ± 15.62, $p = 0.043$). The NeP group had highest mean numerical rating scale (NRS), then the ambiguous group and finally NoP group (7.9 ± 1.6 vs. 6.9 ± 1.6 vs. 5.8 ± 2.2, $p < 0.001$) (Table 2).

Relationship between radiological changes and pain classification

Kruskal–Wallis test showed that the distribution of foraminal stenosis ($H(2) = 12.742$, $p = 0.002$), spinal stenosis ($H(2) = 9.948$, $p = 0.007$) and Pfirmann grade ($H(2) = 6.823$, $p = 0.033$) was significantly different across the trichotomized pain classifications of NoP, ambiguous and NeP. Post hoc Mann–Whitney U test

Fig. 1. Flowchart Depicting the Inclusion of Participants in the Study
Flowchart representing the process of patient and exclusion of the study with the specific data on the number of patients included/excluded at each step. It also shows how the patients in the study were divided into nociceptive, ambiguous, and NeP categories as described by the PainDETECT questionnaire

Table 2 Demographics and clinical data

Parameter	Nociceptive	Ambiguous	Neuropathic	p Value	Total
Number of patients	102	78	99		279
Age (mean $\pm$ SD) (years)	58.21 $\pm$ 17.11	55.33 $\pm$ 16.45	53.63 $\pm$ 15.62	**0.043**	55.99 $\pm$ 16.56
Gender (M/F)	53/49	34/44	44/55	0.244	60/76
Numerical Rating Scale Score (mean $\pm$ SD)	5.8 $\pm$ 2.2	6.9 $\pm$ 1.6	7.9 $\pm$ 1.6	**< 0.001**	

Pearson chi-square test and independent t-test were used to assess association and compare differences between the nociceptive, ambiguous and neuropathic grousp as defined by the PainDETECT questionnaire

M male, *F* female, % percentage, *SD* standard deviation

revealed a higher foraminal stenosis severity (U = 18.962, p = 0.002), spinal stenosis severity (U = 14.481, p = 0.005) and Pfirmann grade (U = 14.221, p = 0.028) in the NeP group compared to the NoP group. With regards to all three MRI parameters there was no difference between the NeP and ambiguous group, and the ambiguous and NoP group (p > 0.05) (Table 3).

ANOVA showed no significant difference in pelvic tilt, sacral slope, pelvic incidence, and lumbar lordosis across NoP, ambiguous and NeP classifications. There was significantly higher number of NeP patients with intervertebral disk bulge compared to patients with NoP and ambiguous pain (96% vs. 78% vs. 78%, p = 0.002). There was significantly higher number of NeP patients with high intensity zones compared to patients with NoP and subsequently ambiguous pain (51% vs. 41% vs. 19%, p < 0.001). There was no association between pain classification and endplate changes (p = 0.776).

Subgroup analysis of patients without stenosis

Kruskal–Wallis test showed that the distribution of Pfirmann grade was significantly different across the trichotomized pain classifications of NoP, ambiguous and NeP in patients without foraminal or spinal stenosis (H(2) = 7.765, p = 0.021). Post hoc Mann–Whitney U test revealed a higher Pfirmann grade (U = 11.321, p = 0.020) in the NeP group compared to the NoP group. There was no difference between the NeP and ambiguous group, and the ambiguous and NoP group (p > 0.05).

Intra-rater and inter-rater reliability

The intra-rater reliability for all measurements methods of the lumbar degenerative parameters included in this study was good-to-excellent from 0.831 (0.670, 0.918) to 0.983 (0.189, 0.997) apart from IVD bulge which only had a moderate ICC of 0.738 (0.508, 0.870). The inter-rater reliability of the measurement methods was good-to-excellent from 0.752 (0.532, 0.877) to 0.979 (0.947, 0.991) (Table 4).

Table 3 Difference in radiological parameters between nociceptive, ambiguous and NeP as described by the PainDETECT questionnaire

	Nociceptive	Ambiguous	Neuropathic	Test statistic	p Value
Kruskal Wallis					
Foraminal stenosis (mean rank)	25.52	39.47	44.48	12.742	**0.002**
Spinal stenosis (mean rank)	42.98	37.17	28.50	9.948	**0.007**
Pfirmann grade (mean rank)	42.96	36.83	28.74	6.823	**0.033**
ANOVA					
Pelvic tilt (mean $\pm$ SD)	18.24 $\pm$ 5.97	15.66 $\pm$ 7.41	18.61 $\pm$ 7.43	0.753	0.475
Sacral slope (mean $\pm$ SD)	37.23 $\pm$ 6.82	35.49 $\pm$ 8.64	34.78 $\pm$ 11.10	0.737	0.628
Pelvic incidence (mean $\pm$ SD)	55.48 $\pm$ 8.86	51.16 $\pm$ 10.16	53.39 $\pm$ 11.22	0.469	0.483
Lumbar lordosis (mean $\pm$ SD)	47.40 $\pm$ 11.13	50.81 $\pm$ 17.29	46.66 $\pm$ 17.05	0.236	0.791
Pearson Chi square					
Endplate changes (Y/N)	15/66	11/43	18/60	0.507	0.776
Intervertebral disk bulge (Y/N)	63/18	42/12	75/3	12.75	**0.002**
High intensity zones (Y/N)	33/48	12/52	45/33	22.16	**< 0.001**

Kruskal Wallis, ANOVA and Pearson chi square tests were used to compare the differences of lumbar radiological parameters between nociceptive, ambiguous and NeP as described by the PainDETECT questionnaire

Discussion

This study used a cohort analysis to examine the association between PainDETECT score and the different classifications of NeP (PainDETECT > 18), ambiguous (12 < PainDETECT < 19) and NoP (PainDETECT < 13) pain as described by the PainDETECT Questionnaire [9]. Additionally, degenerative, and stenotic parameters were evaluated from MRI and gravity-loaded standing x-rays. Of the 279 patients included, 102 had predominantly NoP, 78 had ambiguous and 99 had predominantly NeP. The results showed that patients in the NoP group (58.21 ± 17.11) had the highest mean age followed by ambiguous (55.33 ± 16.45) and NeP group (53.63 ± 15.62). This finding supports the postulation that NoP is associated with global degeneration of the lumbar spine, which is more prevalent in the older population, and that the putative pathological causes of NeP are less age dependent [18]. In this study patients in the NeP group had the highest NRS followed by the ambiguous and NoP group, which corresponds with previous literature that NeP LBP experience higher levels of pain, disability, and reduced quality of life [19].

The mechanism of nervous system response to disk degeneration is heavily debated by researchers. Traditionally, studies have described the progression of low back pain as disk degeneration simulating the nociceptors of the anulus fibrosus (AF) resulting in NoP discogenic pain which progresses to NeP when degeneration leads to herniation causing pressure on the adjacent nervous tissue [20]. Interestingly, our study found that patients with NeP had a higher Pfirmann grade compared to patients with NoP pian, positing disk degeneration alone can cause NeP. Nerve endings of the sinuvertebral nerve in degenerated disks have been found to penetrate into the deeper layers of the AF and can even extend into the NP [21]. This is pathoanatomically correlated to discogenic LBP and under repetitive trauma and mechanical stress can result in chronic increase in levels of inflammatory mediators in the IVD. Miyagi et al. demonstrated increase in calcitonin gene-related peptide expression contributing to increase severity of pain and neuronal remodelling, ultimately aiding in the pathogenesis of NeP [22]. The finding of HIZs in patients with NeP also demonstrates the hyperinflammatory state of a degenerated disk. Our study found that there was a higher prevalence of HIZs in patients with NeP compared to NoP and ambiguous pain. HIZs have been proposed to be fluid filled zones in the AF as a result of an inflammatory process and is related to extradural inflammation [5]. Studies have linked upregulation of macrophages in HIZs which results in proliferation of tumour necrosis factor alpha (TNF-a), Interleukin 1 and prostaglandin E2, consequently, causing further neuronal damage and nerve regeneration [23]. Biomechanical and mechanical factors arising from a deteriorated disk influences the pain process of nerve roots and the dorsal root ganglia, ultimately aiding in NeP pathogenesis. Future studies should incorporate other measures of degeneration and inflammation including facet joint arthrosis and paraspinal muscle fat infiltration level.

Mechanically, a herniated disk represented as a disk bulge on MRI can cause compression resulting in spinal and foraminal stenosis. Spinal and foraminal canal narrowing results from degenerative changes of the spine, leading to compression or ischemia of the lumbosacral nerve roots. Consequently, morphological changes can occur to the patient's nerve roots leading them to present clinically with NeP [24]. This pathway is supported by our study as patients in the NeP group had a higher severity of foraminal stenosis, spinal stenosis and prevalence of disk bulges compared to the NoP group. A positive relationship between PainDETECT score and foraminal and spinal stenosis severity was also observed in our study. However, acute mechanical nerve compression alone does not cause NeP but commonly leads to NoP lumbar radiculopathy, which is often resolved after

Table 4 Intraclass correlation coefficients for lumbar radiological parameters

Parameter	Intra-rater analysis (ICC, 95% CI)	Inter-rater analysis (ICC, 95% CI)
Foraminal stenosis	0.925 (0.846, 0.965)	0.898 (0.792, 0.952)
Spinal stenosis	0.885 (0.769, 0.945)	0.935 (0.865, 0.970)
Pfirmann grade	0.922 (0.808, 0.966)	0.937 (0.869, 0.971)
Intervertebral disk bulge	0.738 (0.508, 0.870)	0.752 (0.532, 0.877)
Endplate changes	0.831 (0.670, 0.918)	0.836 (0.677, 0.921)
High intensity zones	0.931 (0.858, 0.967)	0.864 (0.727, 0.935)
Lumbar lordosis	0.983 (0.189, 0.997)	0.979 (0.947, 0.991)
Pelvic tilt	0.880 (−0.026, 0.973)	0.847 (0.696, 0.926)
Sacral slope	0.919 (0.106, 0.980)	0.885 (0.768, 0.945)
Pelvic incidence	0.941 (0.091, 0.987)	0.919 (0.833, 0.962)

ICC Intraclass correlation coefficient, *CI* confidence interval

a discectomy when the nerve is decompressed [25]. A large number of inflammatory and signalling pathways that play a role in NeP are hypothesized to be stimulated as a result of nerve damage. For example, TNF-alpha, a proinflammatory cytokine found in HIZs, is also upregulated in endoneurial macrophages and Schwann cells following neuronal injury which results in NeP pain [26]. Existing literature has identified variations in the manifestation of NeP. Injuries proximal to the dorsal root ganglia (DRG) have been associated with a higher incidence of chronic NeP compared to injuries distal to the DRG [27]. To enhance our understanding of NeP and its diverse presentations, future studies should consider incorporating comprehensive analyses of the extent, location, and duration of compression. By examining radiological findings in conjunction with these factors, researchers can gain valuable insights into the distinct manifestations of NeP among patients.

This study was the first to introduce sagittal alignment measurements on X-ray. None were significantly associated with NeP apart from pelvic incidence, which was shown to be negatively correlated with PainDETECT score. Studies have shown pelvic incidence to be lower in patients with spinal stenosis, foraminal stenosis and chronic LBP [28]. This demonstrates that neuropathia is possibly a local disk based segmental issue with no associations to sagittal imbalance and NoP is mechanical in origin.

Low back pain is complex and multi-faceted. We posit that whilst compression itself is associated with neuropathia it is not exclusive to NeP. Disk degeneration and the resulting proinflammatory state of the degenerated disk are also drivers of neuropathia. Ultimately, it is imperative for future longitudinal prospective studies to investigate the possibility of the existence of a causal pathological pathway between disk degeneration, stenosis, inflammation, and NeP pain, or if all are independent causes of NeP pain and exist simultaneously. This will allow surgeons to identify problematic patients and develop potential predictors for beneficial treatment outcomes, enhancing the customization of spinal treatments.

The results of this study were impacted by certain limitations. Firstly, the study did not have any follow ups, meaning the progression of patient's clinical and radiological parameters were not analysed over time and compared between the pain groups. Socioeconomic measures and certain patient demographic information such as body mass index, smoking status etc. was not recorded. The population only included patients who presented to a tertiary spinal clinic, therefore, the prevalence of patients who have lower limb NeP pain without a spinal pathology is difficult to assess. To further explore the concept of NeP a prospective registry needs to be established to allow for longitudinal tracking of individual patients to determine whether radiological parameter can reliably predict NeP, based on the concordance between surgeon's assessments and objective Pain DETECT scores alongside actual radiological findings. This will provide valuable insights into optimizing pain diagnosis and treatment strategies.

Conclusion

NeP group had lowest mean age and exhibited more severe pain levels compared to the NoP group. Positive correlations were observed between PainDETECT scores and foraminal stenosis, spinal stenosis, and Pfirmann grade. Conversely, a negative correlation was found between PainDETECT scores and pelvic incidence. Furthermore, the NeP group had significantly higher severity of foraminal stenosis, spinal stenosis, and Pfirrmann grade compared to the NoP group. Moreover, a higher proportion of NeP patients displayed intervertebral disk bulge and high-intensity zones compared to those with NoP and ambiguous pain. These results emphasize the multifactorial nature of NeP and highlight the importance of considering various pathological factors beyond neuronal compression in the evaluation and management of individuals with back and leg pain. Future research should continue to explore the complex interactions between these factors to gain a more comprehensive understanding of NeP and inform more targeted treatment approaches for individuals experiencing chronic LBP.

Declarations

Conflict of interest All authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Ethical approval IRB approval was obtained from the Human Research Ethics Committee of the University of Wollongong (HREC No. 2020/329) and the University of New South Wales (HC210096) for retrospective collection of anonymized patient's lumbar MRI scans, X-ray scans, radiology reports, and PainDETECT data from digital archives.

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