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Are painDETECT scores in musculoskeletal disorders associated with duration of daily pain and time elapsed since current pain onset?

Jean-Marie Berthelot*, Noura Biha, Christelle Darrieutort-Laffite, Benoît Le Goff, Yves Maugars

Abstract

Objectives: We aimed to compare painDETECT scores in outpatients seen in a rheumatology department over a 1-month period and search for correlations between painDETECT scores and the estimated duration of daily pain and time elapsed since the onset of current pain.

Patients and Methods: A total of 529 of 738 outpatients agreed to complete a set of questionnaires, including painDETECT.

Results: The mean painDETECT score was 14.14 ± 7.59, and 31% of the patients had painDETECT scores of >18. Fibromyalgia ranked first (21.2 ± 6.0), followed by osteoarthritis of the lower limbs (17.8 ± 8.2), back pain and radiculopathies (16.1 ± 6.8), osteoarthritis of the upper limbs (15.7 ± 8.1), spondylarthrosis (15.1 ± 7.2), entrapment neuropathies (14.1 ± 2.4), rheumatoid arthritis (13.8 ± 7.1), miscellaneous conditions (13.8 ± 8.2), tendinitis (13.4 ± 7.9), connectivitis (11.5 ± 6.7), and osteoporosis (8.5 ± 6.9). The duration of daily pain was much longer in patients with painDETECT scores of >18 (12.41 ± 8.45 vs 6.53 ± 7.45 hours) ($t = 0.0000$), but very similar painDETECT scores were observed for patients suffering from pain for less than 1 week (13.7 ± 8.2; 38% > 18), for 1 month (14.5 ± 8.2; 25% > 18), several months (12.7 ± 7.3; 23% > 18), 1 year (13.8 ± 7.7; 29% > 18), or several years (14.7 ± 7.4; 33% > 18).

Conclusion: PainDETECT scores differed little depending on the musculoskeletal condition, strongly correlated with the duration of daily pain, and appeared to be as high in patients with recent pain as in those suffering for years.

Keywords: PainDetect, Neuropathic, Musculoskeletal, Arthritis, Osteoarthritis, Back, Tendinopathies, Osteoporosis, Daily, Duration

1. Introduction

Pain is the most disabling symptom associated with most musculoskeletal disorders. However, its treatment is often disappointing, especially for back pain, osteoarthritis, and tendinitis. The relatively poor efficiency of analgesics for these conditions was first ascribed to ongoing nociceptive input, due to insufficient treatment of the triggering disorders. However, the frequent lack of association between pain levels and structural damage and/or disease activity later raised the hypothesis that musculoskeletal pain can also be maintained by the sensitization of peripheral nerves and/or the central nervous system (ie, by neuropathic pain). Neuropathic pain is presumed to result from abnormal neuronal activity of the somatosensory nervous system, but glial cell dysfunction may also contribute.[19] Neuropathic pain may develop at the site of injury, in the dorsal horn of the cell of the spinal cord, or at various synaptic regions in the brain that participate in the processing of somatosensory information. Several animal models of neuropathic pain have confirmed the validity of this concept[29] and allowed the identification of numerous targets, which can vary depending on the patient and trigger, making the topic very complex.[20]

The concept of neuropathic pain was first proposed for chronic back pain, with or without radiculopathies, as both disks and the zygapophyseal joint are surrounded by nerves which can be mechanically injured through compression or stretch. Questionnaires have been developed to better decipher the contribution of neuropathic components to pain, including the Douleur Neuropathique 4 (DNP4)[5] in 2005 and the painDETECT[12] in 2006. As expected, high scores on the DN4[2] and painDETECT[16] questionnaires were observed in chronic back pain, and comparisons of patients with high (>18) and low painDETECT scores found significant differences in sensory tactile discrimination thresholds

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and a wide range of behavioral domains.[36] The contribution of neuropathic pain to patient complaints was later extended to other chronic musculoskeletal conditions, including osteoarthritis, and inflammatory rheumatism. Indeed, despite the use of the most recent biological drugs, some patients with inflammatory rheumatism still suffer, despite the seemingly perfect control of inflammation in the joint and/or entheses.[27] This suggests that past inflammation and/or chronicity of pain may be more important than mechanical stress to induce sensitization of peripheral nerves and the central nervous system.[9] Thus, the contribution of the peripheral or central nervous system to these frustrating situations merits considerable interest.[9] Several studies have previously confirmed that high painDETECT scores can be observed in various musculoskeletal conditions. Some have also confirmed that neuropathic-like symptoms worsen the subjective rating of pain-related quality of life and highly influence function, for example, in osteoarthritis of the lower limbs (OA LL).[4] However, the magnitude and frequency of neuropathic pain have not been directly compared across all painful musculoskeletal conditions seen in the same setting and scarcely for certain conditions, such as tendinitis.

In this context, we first assessed the painDETECT scores of all patients seen in a representative sample of all outpatients from the rheumatology department of a tertiary care center to estimate how many had painDETECT scores of >18 and to search for significant differences in painDETECT scores between patients with various sources of musculoskeletal pain. This study did not aim to assess the specificity of painDETECT related to rheumatological diseases because we did not include sources of pain other than that from musculoskeletal disorders as controls. However, we addressed 2 specific questions. Indeed, whether the duration of daily pain and the time elapsed since the onset of the current pain episode correlate with neuropathic pain have not been addressed. We therefore recorded the duration of daily pain and time elapsed since the onset of current pain for all patients. Indeed, we tested 2 hypotheses: (1) longer daily nociceptive input may contribute to trigger changes in the dorsal spinal horn and/or brain, leading to higher painDETECT scores and (2) patients suffering for only a week or several months from their current pain should have lower painDETECT scores than those suffering for years.

Although both questionnaires perform similarly, we chose the painDETECT over the DN4 questionnaire for this study because roughly 10% of the outpatient visits in our center are devoted to ultrasound or X-ray-guided injections performed by busy physicians who are dressed for surgery and cannot perform a thorough medical examination during the procedure. Indeed, the painDETECT questionnaire is a patient-completed screening tool, whereas the DN4 is a clinician-administered questionnaire.

2. Patients and methods

All outpatients attending the same rheumatology unit (738) were asked to complete several questionnaires, including the 7-item version of the painDETECT during a 1-month period in 2018. This version was used (instead of the 9-item version) because the principal component analysis identified the 7 sensory items to be those driving the data structure of the questionnaire[12] and further studies showed that the 7-item version had greater reliability and more consistent item-level discrimination.[7]

The hospital anxiety and depression (HAD) scale was also used. The HAD comprises 14 items, 7 of which relate to anxiety symptoms and 7 to depressive symptoms. Each item is scored from 0 to 3. The scores for anxiety and depression can therefore vary from 0 to 21, depending on the presence and severity of the symptoms.[43] A score between 0 and 7 indicates the absence of symptoms of anxiety or depression. A score between 8 and 10 indicates the presence of a moderate degree of anxiety or depression, and a score of ≥11 indicates confirmed anxiety or depression. The studies concerning the accuracy of these thresholds have all shown them to be reliable.[3] The HAD can also be used as a 1 scale test (ie, mix of anxiety and depression) to measure the intensity of "emotional distress," with a recommended threshold of 16.[31]

Other parameters that were recorded were age, sex, familial history of chronic pain, RAPID3 score (which includes a 0–10 pain scale during the last week, 10 being the worst pain), mean length of daily pain, as subjectively and retrospectively estimated by patients, duration of sleep at night, fatigue on a 0 to 10 scale (0 meaning no fatigue and 10 the worst fatigue), and the social consequences of chronic pain, including work status. Given the remitting and relapsing nature of several disorders (eg, transient flares of calcifying tendinitis every 2 years) and retrospective design, patients were not requested to assess the entire duration of pain since the onset of each disorder. However, an estimation of duration of the disorder (time elapsed since its very first manifestation) and of the time elapsed since the onset of the current pain episode were requested.

Each physician was requested to indicate the main rheumatological condition leading to the patient visit from a list of 11 possible choices: (1) polyarthritis (rheumatoid arthritis and overlaps with peripheral psoriatic arthritis) (RA), (2) spondyloarthritis (including axial psoriatic rheumatisms) (SpA), (3) connectivitis (UCT), (4) osteoarthritis of the upper limbs, (5) OA LL, (6) back pain, with or without radiculopathy (Back), (7) osteoporosis (OP), with or without past fractures, (8) tendinitis (Tend), (9) entrapment neuropathies (Entrap), mostly carpal tunnel syndromes, which often combine musculoskeletal symptoms linked to tendon entrapment and neuropathic symptoms linked to median nerve entrapment[23]), (10) fibromyalgia (FM), and (11) miscellaneous disorders (Msc) (polymyalgia rheumatica, gout, chondrocalcinosis, Lyme disease, etc.).

Data were analyzed using SPSS 19-0 software. Student *t* test was used to compare means ($P < 0.01$), and Pearson test to determine correlations between quantitative variables. There were no missing values for the painDETECT scores because research assistants verified with the patients that the questionnaires had been completed in the waiting room before seeing the physician. Missing data for other variables were similarly rare (less than 5% for most items) and were not imputed.

Before their visits, all patients were informed both orally and by a form explaining the rationale of the questionnaires and had to provide their consent prior to completing them. This study was approved by a national ethics committee (Centre de Protection des Personnes, Sud-Méditerranée-1, May 26, 2017, ref: 1738).

3. Results

3.1. Patient characteristics

A total of 529 patients agreed to complete the painDETECT questionnaire. Their characteristics are shown in **Table 1**. According to patients, the mean duration since the first manifestation of their disorder was 9.2 ± 10.1 years, but this value varied widely. The mean duration since the first manifestations was 2.2 ± 3.0 years for miscellaneous disorders, 3.0 ± 1.1 years for entrapment neuropathies, 3.6 ± 3.0 years for tendinitis, 5.9 ± 7.9 years for back pain, 6.1 ± 6.4 years for OA LL, 7.12 ± 4 years for osteoarthritis of the upper limbs, 10.2 ± 4.8 years for connectivitis, 10.3 ± 9.6 years for OP, 11.9 ± 12.3 years

Table 1

Characteristics of the 529 patients.

Sex	28% males (n = 149), 72% females (n = 380)
Age (mean ± SD), y	53.5 ± 16.5
Disease duration (y)	9.2 ± 10.1
Work status	53% no longer working, including 38% retired and 15% with disablement benefits
Familial history of chronic pain	48%
Sleep duration (mean ± SD)	6.66 ± 1.37
Morning fatigue	68% already tired when awaking
Daily fatigue level [0–10]	5.3 ± 2.1
HAD score total	14.07 ± 7.23
HAD score anxiety	8.36 ± 4.16
HAS score depression	5.79 ± 4.00
RAPID3 [0–10]	5.06 ± 2.57
Mean pain in the last month [0–10]	5.79 ± 4.0
Max pain in the last month [0–10]	6.09 ± 2.76
Sharp pain at least once a day	75%
Daily duration of pain (h)	8.48 ± 8.26

HAD, hospital anxiety and depression.

for spondyloarthritis, 12.3 ± 10.8 years for rheumatoid arthritis, and 17.0 ± 5.2 years for fibromyalgia.

Classification of the patients according to the 11 main reasons for their visit is shown in **Table 2**. Only 13 patients were treated with strong opioids, 70 with weak opioids, and 11 with gabapentinoids, whereas 81 were treated with nonsteroidal anti-inflammatory drugs and 261 with acetaminophen.

3.2. painDETECT scores for the whole cohort and according to the physician's diagnosis

3.2.1. painDETECT scores for the whole cohort

The mean painDETECT score for the entire cohort was 14.14 ± 7.59. Within the cohort, 31% of patients had painDETECT scores of >18 (ie, probable neuropathic pain): 41 of 149 men (27%) and 124 of 380 women (33%); 57% of patients had painDETECT scores of >13 (ie, possible neuropathic pain): 84 of 149 men (56%) and 218 of 380 women (57%). The symptoms that contributed to the total painDETECT scores are shown in **Table 3**. There were few differences between male and female subjects. The only significant differences ($P < 0.01$) were for allodynia (1.38 ± 1.50 in women vs 1.0 ± 1.25 in men) and pain triggered by light pressure (2.66 ± 1.62 in women vs 2.24 ± 1.65 in men).

3.2.2. Results of painDETECT according to the main diagnosis

The painDETECT scores for each condition are shown in **Table 4** and **Figure 1**. There were no major differences according to most diagnoses, although painDETECT scores were positively associated with the diagnosis of fibromyalgia ($P = 0.013$) and osteoarthritis ($P = 0.03$) and negatively associated with the diagnosis of OP ($P = 0.002$).

3.3. Marked correlation between painDETECT scores and both the duration of daily pain and pain level during the last week

Mean pain during the last week was higher in patients with painDETECT scores of >18 (6.69 ± 2.09 vs 4.34 ± 2.66;

Table 2

List of the main source of pain for each of the 529 patients.

Condition	N	%	Females	Males
Spondyloarthritis	131	25.24	59	72
Rheumatoid arthritis	129	24.85	103	26
Osteoporosis	57	11	53	4
Back pain and radiculopathies	53	10.21	35	18
Osteoarthritis (16 upper limbs and 34 lower limbs)	50	9.63	42	8
Tendinitis	40	7.7	25	15
Miscellaneous	28	3.47	11	17
Connectivitis	22	4.23	18	4
Fibromyalgia	10	1.93	8	2
Entrapment neuropathies	9	1.74	6	3

Table 3

Contribution of the various symptoms to the final painDETECT score.

1. Burning sensation (stinging nettles): 2.62 ± 1.61
2. Pain triggered by slight pressure: 2.54 ± 1.64
3. Numbness: 2.18 ± 1.55
4. Tingling or prickling sensation: 2.10 ± 1.51
5. Sudden pain attacks: 2.00 ± 1.71
6. Pain induced by cold or heat: 1.94 ± 1.59
7. Pain induced by light touching: 1.27 ± 1.45

$P = 0.0001$). The duration of daily pain was also reported to be longer in patients with painDETECT scores of >18 (12.41 ± 8.45 vs 6.53 ± 7.45 hours; $P = 0.00001$) (**Fig. 2**).

3.4. Correlations with other features

The painDETECT score was associated with other features: sleep duration ($r = -0.227$; $P = 0.0001$) (negative correlation), feeling already tired upon awaking ($r = 0.338$; $P = 0.0001$), global estimate of the activity of their disorder by the patient ($r = 0.504$: $P = 0.000$), the impact of pain on their ability to work ($r = 0.355$; $P = 0.0001$), on enjoying leisure activities ($r = 0.364$; $P = 0.0001$), and on their autonomy ($r = 0.390$; $P = 0.0001$), acceptance of their pain ($r = -0.223$; $P = 0.006$), and feeling that all efforts have not been made to relieve their pain ($r = -0.176$; $P = 0.008$) (negative correlation for both).

The painDETECT score also correlated with depression ($r = 0.310$; $P = 0.0001$) and anxiety ($r = 0.325$; $P = 0.0001$).

3.5. Lack of correlation with time elapsed since the onset of the current episode of pain

We observed nearly identical mean painDETECT scores (without clear differences according to underlying diagnoses) for the 13 patients suffering from their current pain for less than 1 week (13.7 ± 8.2; 38% > 18), the 8 suffering for 1 month (14.5 ± 8.2; 25% > 18), the 35 suffering for several months (12.7 ± 7.3; 23% > 18), the 42 suffering for 1 year (13.8 ± 7.7; 29% > 18), and the 431 suffering for several years (14.7 ± 7.4; 33% > 18) (**Fig. 3**).

Table 4

Results of pain-DETECT according to the 11 diagnoses.

Disorder	n	% PainDETECT > 18	Mean ± SD
Fibromyalgia	10	70%	21.2 ± 6.00
Osteoarthritis lower limbs	34	46%	17.77 ± 8.18
Back pain and radiculopathies	53	42%	16.13 ± 6.81
Osteoarthritis upper limbs	16	44%	15.68 ± 8.12
Spondyloarthritis	131	36%	15.11 ± 7.19
Entrapment neuropathies	9	0%	14.12 ± 2.42
Rheumatoid arthritis	129	27%	13.82 ± 7.10
Miscellaneous	28	39%	13.79 ± 8.18
Tendinitis	40	23%	13.36 ± 7.87
Connectivitis	22	25%	11.50 ± 6.67
Osteoporosis	57	9%	8.46 ± 6.88
Mean	529	31%	14.14 ± 7.59

4. Discussion

This study aimed to compare painDETECT scores in a representative sampling of outpatients with various musculoskeletal conditions seen in an outpatient rheumatology clinic and to test the 2 hypotheses that (1) longer daily nociceptive input is positively associated with higher painDETECT scores and (2) the time elapsed since the onset of the current episode of pain is also positively associated with higher painDETECT scores (ie, patients with a longer episode have higher painDETECT scores).

As expected, the painDETECT scores strongly correlated with the estimated duration of daily pain: 12.41 ± 8.45 hours for those with painDETECT scores of >18 vs 6.53 ± 7.45 hours for the others (**Fig. 2**). This result confirms that painDETECT may have prognostic value, as already observed on several occasions.[34] Longitudinal studies of painDETECT scores and duration of daily pain since the very beginning of the musculoskeletal conditions could help to decipher which is the egg and which is the hen because longer duration and severity of daily pain might precede the increase in the painDETECT score, whereas the opposite might be true because higher basal susceptibility of nerves or the spinal cord (responsible for higher painDETECT scores, even before the onset of the rheumatism) could further explain the longer daily duration of pain and/or more severe pain. The second hypothesis may be more consistent with our second observation.

Indeed, contrary to our initial hypothesis, painDETECT scores were nearly the same in patients whose current episode of pain lasted for only 1 week, 1 month, several months, 1 year, or several years. Although it cannot be ruled out that past episodes of pain in remitting and relapsing disorders may have presensitized either peripheral nerves or the central nervous system (to account for the high painDETECT scores since the first weeks of pain), the observation that painDETECT scores were no higher in patients suffering for several years suggests that painDETECT scores do not increase over time but may increase very quickly in some patients. This would be consistent with the observation previously made in an emergency department using the DN4 score, showing that 114 of 533 patients had a DN4 score of >4, although no details were given for the time elapsed since the onset of pain.[24] The retrospective assessment by patients on the length of their current episode of pain and the small number declaring to have suffered for 1 year or less (n = 98) in the present cohort are 2 limitations of the study. Thus, further prospective studies are needed to confirm this finding, by assessing painDETECT scores from the onset of various musculoskeletal conditions and at regular intervals thereafter.

The third objective of this study was to compare the painDETECT scores according to the diagnosis leading to the visits, including disorders that have been thus far poorly assessed as a possible source of neuropathic pain, such as entrapment neuropathies, tendinopathies, and OP.

The observation that 27% of RA patients had painDETECT scores of >18 is not surprising. Indeed, although a Japanese study on 300 RA patients showed that only 3.0% had painDETECT scores of >18,[18] this was a striking exception. Another study on 115 early patients with RA showed that 13% already had painDETECT scores of >18,[32] and a study on 7,054 Danish patients, including 3826 with RA, 1180 with PsA, and 1093 with SpA, showed that 20% of patients with RA had scores of >18 (as well as 28% of those with PsA and 21% with SpA).[30]

Similarly, although a study of 105 SpA patients showed that only 14.2% had painDETECT scores of >18,[8] other studies reported much higher percentages. For example, painDETECT scores of >18 were found for 33.5% of patients with axial SpA.[15]

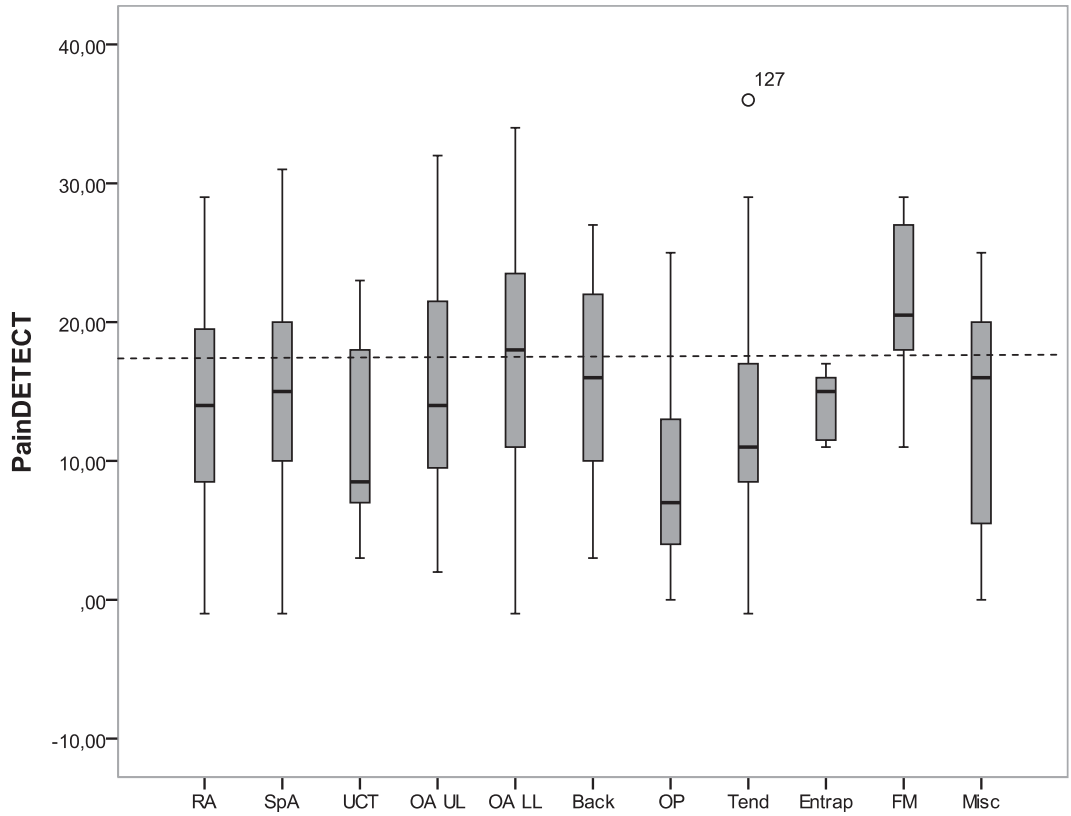

Figure 1. Boxplots showing the distribution of painDETECT scores according to the 11 possible diagnoses. Boxplots represent median and quartiles below or above the median; whiskers show either the minimum or maximal values, or one and a half times the interquartile range, in case of outliers (very low or very high values) which appear as round circles. The dashed line represents the threshold of 18. Back, back pain with or without radiculopathies; Entrap, entrapment neuropathies; FM, fibromyalgia; Misc, Miscellaneous conditions (Lyme disease, genetic disorders, etc.); OA LL, osteoarthritis of lower limbs; OA UL, osteoarthritis of upper limbs; OP, osteoporosis; RA, rheumatoid arthritis; SpA, spondyloarthritis; Tend, tendinopathies; UCT, connectivitis (lupus, Sjögren's, etc…).

Therefore, the 36% of SpA patients with painDETECT scores of >18 in our cohort are consistent with previous findings.

Previous studies, either in RA or SpA, showed that high painDETECT scores were generally not associated with greater inflammation (C-reactive protein and erythrocyte sedimentation rate) but strongly correlated with the patients' global assessment.[14] This was also true for our cohort ($P = 0.000$).

In our study, 44% and 46% of patients with osteoarthritis of the upper and lower limbs, respectively, had painDETECT scores of >18, higher than that reported in a survey of population-based study of patients reporting of knee pain in the United Kingdom, in which 13.65% of patients had painDETECT scores of >18.[10] However, even higher scores have been reported in knee osteoarthritis, with 66.7% of Turkish patients with neuropathic pain, based on the painDETECT scale (46.7% of patients based on DN4 scale).[1] Such discrepancies based on the setting are sufficiently large to suggest that cultural bias could contribute to overresponding to some questions. Responses could be accordingly more finely weighted.[6]

In our sample of patients, 42% with back pain had painDETECT scores of >18. This is in the range of previous estimations: 36.6%[11] and 32.5%.[25] Even higher percentages were reported in a study of 215 patients with chronic low back pain, with or without leg pain, as up to 164 (76.3%) were classified as suffering from neuropathic pain, assuming the physician-made diagnosis as the gold standard, whereas painDETECT showed excellent discrimination, with an area under the curve of >0.8 (also observed for the DN4 score).[16]

PainDETECT has so far been studied once in patients with OP. The study of 113 patients with previous osteoporotic fracture(s) found that painDETECT scores were suggestive of neuropathic pain in only 15% of patients,[13] consistent with our results of 9% of patients, with or without a previous osteoporotic fracture.

Surprisingly, none of our patients with entrapment neuropathies had painDETECT scores of >18, although the mean score was 14.12 ± 2.42. In a previous study on 34 patients with carpal tunnel syndromes, only 3 (8%) had scores of >18, and the mean painDETECT score was also low (9.4 ± 7.8). Strikingly, there was no significant correlation between terminal latency and the pain DETECT score.[35]

A study of 282 patients with chronic lower-limb tendinopathy, with a median duration of symptoms of 24.0 months, showed the median painDETECT score to be 14.0%, and 28% of respondents had scores of >18.[42] We obtained very similar results: a mean score of 13.36 ± 7.87, and 23% of patients with painDETECT scores of >18.

Overall, these observations, and previous estimations of 41.1% for the prevalence of neuropathic pain in soft tissue syndromes,[11] confirm that painDETECT scores can be high in all musculoskeletal conditions.

The observation that painDETECT scores can be high without overt lesions of the peripheral nervous system is somewhat puzzling, moreover as lower painDETECT scores were observed in entrapment neuropathies. Indeed, the painDETECT questionnaire was developed to identify significant neuropathic components.[36]

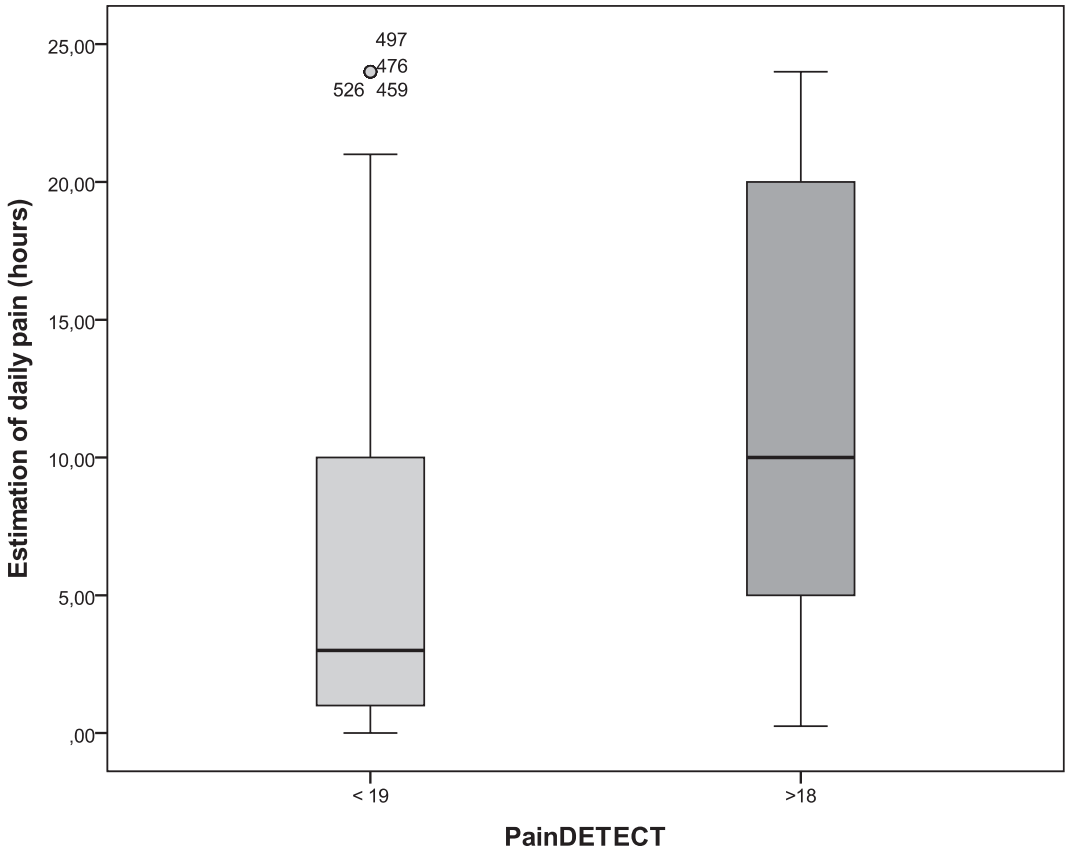

Figure 2. Patients' estimation of their daily duration (in hours) of pain. Boxplots represent median and quartiles below or above the median; whiskers show either the minimum or maximal values, or one and a half times the interquartile range, in case of outliers (very low or very high values) which appear as round circles.

The first explanation could be a poorer ability of painDETECT to detect neuropathic components than previously thought. A recent study suggested that painDETECT was not sensitive and performed poorly among 44 patients diagnosed with definite neuropathic pain following clinical examination (based on the 2016 International Association for the Study of Pain Special Interest Group on Neuropathic Pain Grading System). Indeed, only 8 of 44 patients (18%) had painDETECT scores of >18.[17] Conversely, another study concluded that painDETECT may lack specificity and be too sensitive because 55 of 120 patients (45%) with chronic pain for a variety of reasons had painDETECT scores of >18, whereas only 11 (20%) were also classified as probable or definite neuropathic pain using the same new reference standard as that used in the previously mentioned study.[41] Such discrepancies may be partially related to the usual mix of nociceptive and neuropathic pain in a single patient and the poorer accuracy of painDETECT in this context than in the first study (in which the gold standard used was the assessment of the pain type based on an examination by 2 experienced pain specialists). Indeed, in the first study, the percentage specificity of painDETECT was 85% and 80%, respectively,[12] but lower scores were later observed in patients who were not previously examined as probably suffering (or not) from neuropathic pain.[26] This has led some authors to recently conclude that the validity of screening tools for neuropathic pain (such as painDETECT) needs to be proven in patients with pain who were not prestratified on the basis of the target outcome of probable neuropathic pain or nonneuropathic pain (ie, suffering from an equal mix of neuropathic pain and ongoing nociceptive pain).[38] The DN4 questionnaire may be more accurate in this situation, although it is less patient friendly (because the DN4 is a physician-administered tool).[38]

The second explanation could be that low-grade inflammation following lesions in musculoskeletal tissues can drive the granulation of tissues in some patients only. This could lead to the sprouting of tiny vessels and nerves in the scar area (as observed in chronic tendinitis[33] and back pain[21]) following distal release of various chemokines or growth factors, such as nerve growth factor.[22] However, this hypothesis is somewhat at odds with another unexpected finding of our cohort because the mean and median values of painDETECT appeared to be nearly identical in patients whose current pain episode began 1 week, 1 month, several months, 1 year, or several years before, based on their retrospective judgment (**Fig. 3**). Indeed, functional and very early changes in peripheral nerves or the central nervous system (ie, more neuroplastic than neuropathic, such as epigenetic changes in neurons and/or glial cells) could account more for the painDETECT scores than the sprouting of new nerves or anatomical lesions (such as those induced in entrapment neuropathies by chronic nerve compression or ischemia). For example, dysregulation of transcriptional repressors, such as neuron restrictive silencer factor, contributes to neuropathic pain through epigenetic mechanisms[37] and repression (by neuron restrictive silencer factor) of Nav1.8, leading to hypoesthesia and the repression of mu-opioid receptor genes, resulting in the loss of endorphins and morphine analgesia.[39]

This study had several limitations: (1) this population may not be representative of patients seen in private practice; (2) patients with the most severe and active forms of inflammatory

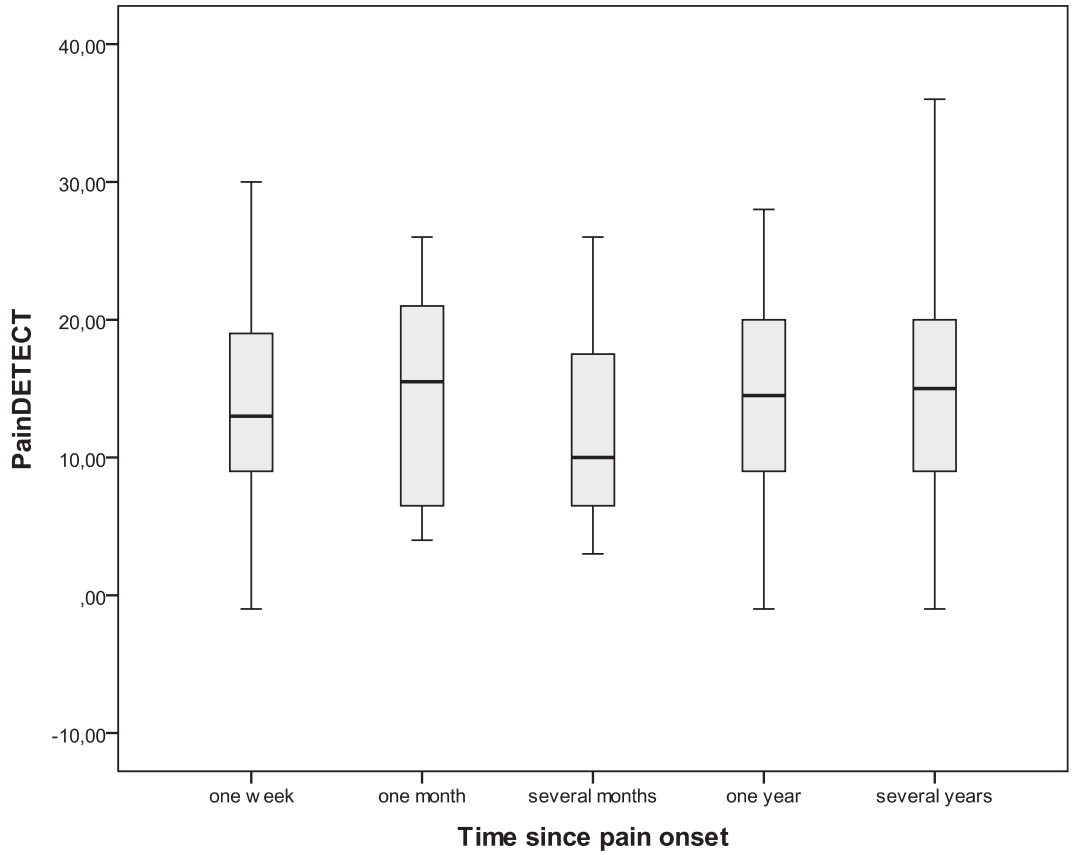

Figure 3. PainDETECT is not associated with time elapsed since pain onset. Boxplots represent median and quartiles below or above the median; whiskers show the minimum or maximal values.

rheumatism or osteoarthritis were probably overrepresented; (3) physicians were asked to select the main condition leading to the outpatients visits, whereas some patients may have had several disorders, and comorbidities, such as diabetes, were not sought out as other possible sources of high painDETECT scores; (4) patient estimations of their daily pain and the time elapsed since the onset of their current pain were both subjective and retrospective; and (5) only 98 of 529 patients declared that their current episode of pain lasted for 1 year or less.

However, our findings confirm that high painDETECT scores (1) can be found in nearly all musculoskeletal conditions, (2) are associated with much longer duration of daily pain, and (3) can occur early after the onset of the current pain episode but may not worsen over time. If painDETECT truly measures neuropathic pain, this finding does not support the hypothesis that the cumulative amount of nociceptive input is important for triggering neuropathic pain.

Further studies mixing various musculoskeletal conditions could longitudinally assess both painDETECT (and/or DN4) scores and daily pain duration (eg, using a diary to assess it prospectively), early after the onset of a new pain episode to reproduce, or not, these findings. Similar observations would suggest that high painDETECT scores do not require lasting anatomical lesions in peripheral nerves or the central nervous system but may rather result from early epigenetic changes[37,40] and/or genetically encoded traits, leading to more rapid sensitization of neurons or glial cells. Genetic traits indeed appeared to be nearly as important as environmental or traumatic influences for high painDETECT scores in a recent large epidemiological study of 4324 people and 1357 twins, which concluded that, as for chronic widespread pain, high painDETECT scores were best explained by a combination of similar heritable traits, accounting for 37% (95% CI: 23%–50%) of the variance, and unique environmental factors, accounting for 63% (95% CI: 49%–79%).[28]

Disclosures

The authors have no conflict of interest to declare.

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