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Original Article

The prevalence of neuropathic pain after non-traumatic spinal cord lesion

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Study design: Retrospective register study.
Objective: To investigate the predictive value of the following parameters for the development of neuropathic pain after non-traumatic spinal cord lesion: that is age at onset of spinal cord disease, gender, completeness of lesion, level of lesion, and aetiology.
Setting: A unit for patients with post-acute traumatic and non-traumatic spinal cord lesions in the greater area of Stockholm, Sweden.
Method: All patients with non-traumatic spinal cord lesions visiting the unit between 1995 and 2000 were classified according to the following: that is neuropathic pain at or below lesion level according to IASP criteria, age at time of the onset of the spinal cord symptoms, injury level, complete/incomplete injury, and aetiology. Results were analysed with χ^2 – analysis and logistic regression.
Results: In total, 38% had neuropathic pain, 15% had pain predominantly at the level of lesion, and 23% predominantly below the level of lesion. Of those with pain, 67% reported that the pain affected daily life. Women reported neuropathic pain below the level of lesion more often (40%) than men (13%). The prevalence was particularly high (64%) for patients with malignant spinal cord diseases. Neither age at onset of the spinal cord symptoms, nor complete/incomplete injury nor injury level had significant influence on the prevalence.
Conclusion: Neuropathic pain is common among patients with acquired non-traumatic spinal cord lesions regardless of aetiology, often causing severe problems in daily life.
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Keywords: non-traumatic spinal cord lesion; neuralgia; pain; prevalence; rehabilitation

Introduction

Non-traumatic spinal cord lesions (SCL) represent a significant portion of the patients admitted for spinal cord rehabilitation. They include a wide range of etiologies; spinal stenosis, malignant and non-malignant tumours, multiple sclerosis, infections and vascular disorders.[1–7] The relation between traumatic and non-traumatic SCL differs between investigations. The non-traumatic SCL have been reported to comprise 25% of all SCL in studies performed in Italy[8] and Germany,[9] 35% in England,[10] 39% in the US,[3] and 46% in Fiji.[11]

As for traumatic spinal cord injury, long-standing neuropathic pain is considered to be one of the most challenging problems after non-traumatic SCL. However, the frequency of neuropathic pain does not seem to have been systematically studied. Studies of traumatic injuries have shown a prevalence of neuropathic pain of about 40%,[12–15] and correlates positively with a greater age at the time of lesion, but not with the level of lesion, completeness of lesion, or with gender.[16,17] Whereas traumatic SCL occur primarily in young ages, it appears that at least some non-traumatic SCL affect older people more often. Therefore, the problem is expected to increase in the future as the number of elderly persons rise,[2] giving a sound, reason for a particular focus on this group.

The primary aim of the present study was to investigate the prevalence of long-standing neuropathic pain in patients with non-traumatic SCL at or below the level of lesion, supplementing our previous study of patients with traumatic spinal cord injury.[17] The following parameters were studied: that is non-traumatic SCL of different etiologies, age at the onset of SCL, gender, complete *versus* incomplete lesion (ASIA),[18] level of lesion, and combinations of these factors. Second, we studied the patients' opinion on the influence of neuropathic pain in daily life.

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Methods

All patients with non-traumatic SCL consulting the Spinal Cord Injury Unit ('Spinalis') at the Karolinska Hospital in Stockholm, Sweden during the years 1995–2000 were included in this retrospective register study. Patients were generally referred to the unit after treatment in the acute phase of the disease was completed. The Spinal Cord Injury Unit provides life long yearly check-ups to all adult patients with traumatic and non-traumatic SCL in the greater area of Stockholm, Sweden. A large number of data including pain was gathered for the database at the initial examination at the unit. More than half of the patients, 55/95 (58%), was examined within 1 year after the onset of the spinal cord lesion symptoms (range 2–38 years, mean 9.6 years).

The check-up included classification of the completeness of the lesion according to ASIA.[18] For the purpose of this study, the following generalisations within the ASIA system were made: that is those belonging to ASIA B–D were analysed together due to small patient numbers in group B and C, and patients who at the time of examination were classified as ASIA E were re-classified according to their initial classification (usually from ASIA E to ASIA D). Furthermore, the level of lesion was dichotomised as tetraplegia and paraplegia, respectively.

Five groups of non-traumatic SCL were selected for this investigation: that is vascular myelopathies (spinal infarction, artery–venous malformations, sequels after aorta aneurysm operations; $n=16$), spinal stenosis (cervical and lumbar; $n=25$), infections (viral or bacterial; $n=30$), benign tumours (meningeomas and lipomas; $n=13$), malignant tumours (gliomas, astrocytomas, ependymomas; $n=11$). Patients with spinal cord metastasis from primary neoplasms elsewhere in the body, multiple sclerosis, primary syringomyelia, and spina bifida were not included. Patients with metastasis and MS were regularly referred to other specialised clinics and the numbers were few in the database. Data on patients with spina bifida will be presented in a separate study.

The patients were divided in five age groups: 0–19 ($n=11$), 20–29 ($n=16$), 30–39 ($n=18$), 40–49 ($n=15$), and 50 years of age and older ($n=35$). For the analysis of age in relation to the prevalence of neuropathic pain as well as patients rating of pain as a problem in daily life, the patients were divided into two groups, aged 0–39 years, and 40 years and older. This was due to the rather small numbers of patients in the above groups.

The pain was classified by the examining neurologist as neuropathic when it met the criteria presented by the IASP task force.[19] Criteria used were pain without primary relation to movements or sign of inflammation, presence of sensory disturbances to pin prick and touch within the painful territory, corresponding to the SCL. When pain was present, it was classified as above level neuropathic pain, at level neuropathic pain, and below level neuropathic pain (see also Siddall *et al*[20]). Pain characteristics (lancinating, dysestehesia, etc.) were not systematically recorded in the database. Data on patients experience of neuropathic pain as a problem in daily life was obtained by interview during the first visit to the unit.

Analysis of data

Groups and sub-groups are presented as absolute numbers and percentages. Comparisons between groups were made by χ^2-tests or by Fischer's exact test when the numbers were too small to allow χ^2-test. Even smaller samples were not analysed statistically or were grouped before analysis. Logistic regression was used to quantify the association between some of the possible risk factors (gender, level of lesion, completeness of SCL). $P<0.05$ were considered significant.

Results

Structure of patient samples

The prevalence of complete and incomplete SCL was similar in the youngest age group (0–19 years). In all older age groups, incomplete SCL clearly dominated (Table 1).

Patients with malignant tumours had the lowest mean-age (16 years), and vascular myelopathies the highest mean age (54 years) at time of the diagnosis of the SCL (Table 2). Patients with malignant tumours also

Table 1 Prevalence of neuropathic pain in different age classes as a function of gender, complete/incomplete lesion (ASIA), and level of lesion

Age groups	*0–19*	*20–29*	*30–39*	*40–49*	*50*	*Total*
Men	3/9	2/11	3/10	3/9	7/21	18/60 (30%)
Women	1/2	3/5	4/8	5/6	5/14	18/35 (51%)
Para A–E	4/9	3/12	3/10	7/14	7/23	24/68 (35%)
Tetra A–E	0/2	2/4	4/8	1/1	5/12	12/27 (44%)
ASIA A	1/6	0/0	0/0	1/2	2/3	4/11 (36%)
ASIA B–E	3/5	5/16	7/18	7/13	10/32	32/84 (38%)
Tetra A	0/2	0	0	0	0	0/2
Tetra B–E	0/1	2/4	4/9	1/1	5/11	12/26 (46%)
Para A	1/4	0/0	0	1/2	1/3	3/9 (33%)
Para B–E	3/4	3/12	3/9	6/11	6/22	21/58 (36%)

had a high frequency of complete SCL (ASIA A; 4/11) compared to the other diagnostic groups.

Prevalence of neuropathic pain

In total 36/95 (38%) of the patients met the criteria for neuropathic pain, 14/36 (39%) reported at level pain primarily, and 22/36 (61%) primarily below level pain. No patients had above level neuropathic pain. Detailed results are shown in Tables 1, 3 and 4.

There was no statistically significant difference in the prevalence of neuropathic pain between those diagnosed at ages up to 39 years (16/45, 36%) and those aged 40 years and above (20/50, 47%; $\chi^2 = 1.30$, df = 1; for details, see Table 1, Figure 1).

There was no statistically significant difference in the prevalence of unspecified neuropathic pain between women (18/35, 51%) and men (18/60, 30%; $\chi^2 = 1.88$, df = 1; Figure 2). At level pain was diagnosed in 4/35 (11%) of the women, and in 10/60 (17%) of the men (NS, $\chi^2 = 0.36$, df = 1). Below-level pain was diagnosed in 14/35 (40%) of the women, and in 8/60 (13%) of the men. The latter difference was significant ($\chi^2 = 5.27$, df = 1, Figure 2).

The frequency of neuropathic pain was similar between those with complete lesion (ASIA A; 4/11, 36%) and those with incomplete lesion (ASIA B–D; 32/84, 38%; Figure 2). Similar prevalence's were found also when comparing patients with tetraplegia (12/27, 44%) and paraplegia (24/68, 35%).

Table 2 Mean-age at the time of the diagnosis of the SCL, prevalence of at level and below level neuropathic pain (NP), and patients rating of pain as a problem in daily life in the different etiologic sub-groups

Etiologic subgroups	*Mean years of age*	*Complete/incomplete lesion/all*	*Level of lesion tetra/ para/all*	*At level NP/ below level NP/all*	*Pain is a problem in daily life/all with NP*
Vascular diseases	53.7 (16–79)	2/14/16	1/15/16	4/2/16	5/6
Spinal stenosis	46.0 (23–84)	0/25/25	14/11/25	6/5/25	8/11
Infections	43.0 (11–75)	4/26/30	5/25/30	2/7/30	5/9
Benign tumours	36.9 (17–82)	1/12/13	4/9/13	1/2/13	2/3
Malignant tumours	16.3 (0–84)	4/7/11	3/8/11	1/6/11	5/7
All patients	41.7 (0–47)	11/84/95	27/68/95	14/22/95	25/36

Table 3 Prevalence of *at level* neuropathic pain in different age classes as a function of gender, complete/incomplete lesion (ASIA) and level of lesion

Age groups	*0–19*	*20–29*	*30–39*	*40–49*	*50–*	*All*
Men	1/9	0/11	3/10	2/9	4/21	10/60 (17%)
Women	0/2	1/5	1/8	0/6	2/14	4/35 (11%)
Para A–E	1/9	1/12	1/10	1/14	2/23	6/68 (9%)
Tetra A–E	0/2	0/4	3/8	1/1	4/12	8/27 (30%)
ASIA A	0/6	0/0	0/0	0/2	1/3	1/11 (9%)
ASIA B–E	1/5	1/16	4/18	2/13	5/32	13/84 (15%)
Tetra A	0/2	0/0	0/0	0/0	0/0	0/2
Tetra B–E	0/1	0/4	3/9	1/1	4/11	8/26 (31%)
Para A	0/4	0/0	0/0	0/2	1/3	1/9 (11%)
Para B–E	1/4	1/12	1/9	1/11	1/22	5/58 (9%)

Table 4 Prevalence of *below level* neuropathic pain in different age classes as a function of gender, complete/incomplete lesion (ASIA) and level of lesion

Age groups	*0–19*	*20–29*	*30–39*	*40–49*	*50–*	*All*
Men	2/9	2/11	0/10	1/9	3/21	8/60 (13%)
Women	1/2	2/5	3/8	5/6	3/14	14/35 (40%)
Para A–E	3/9	2/12	2/10	6/14	5/23	18/68 (26%)
Tetra A–E	0/2	2/4	1/10	0/1	1/12	4/27 (15%)
ASIA A	1/6	0/0	0/0	1/2	1/3	3/11 (27%)
ASIA B–E	2/5	4/16	3/18	5/13	5/32	19/84 (23%)
Tetra A	0/2	0/0	0/0	0/0	0/0	0/2
Tetra B–E	0/1	2/4	1/9	0/1	1/11	4/26 (15%)
Para A	1/4	0/0	0/0	1/2	1/3	3/9 (33%)
Para B–E	2/4	2/12	2/9	5/11	4/22	15/58 (26%)

The prevalence's of at level and below level neuropathic pain among the different diagnostic groups can be seen in Table 2. Although groups were too small for statistical analysis, it was noted that patients with benign and malignant tumours and infections appeared to have below-level pain more often than patients with spinal stenosis and vascular myelopathies (Table 4).

Logistic regression was used to analyse the contribution of single variables after adjusting for other variables. Results are shown in Table 5. Female gender tended to be a predictor for neuropathic pain ($P=0.06$). However, no statistically significant contribution to the prevalence was found for the different diagnostic groups, complete/incomplete lesions, or for tetra- and paraparesis (Table 5).

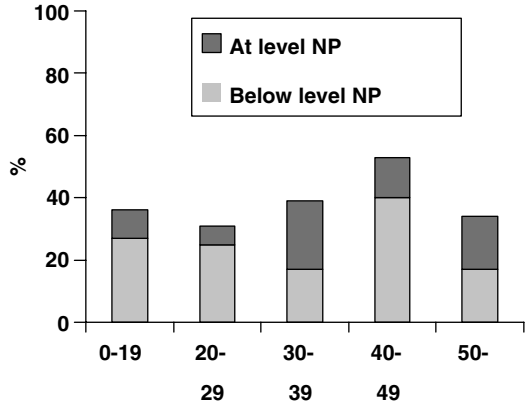

Figure 1 Most prominent type of neuropathic pain in the different age groups

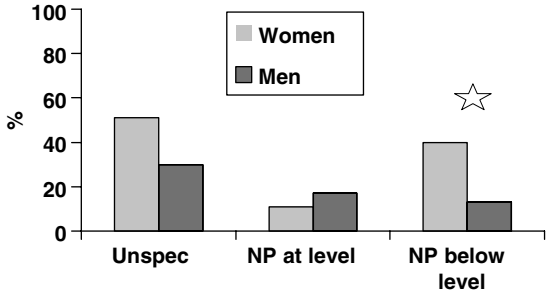

Figure 2 Prevalence of at level and below level neuropathic pain among women and men. Star indicates statistically significant difference

Patients rating of the pain as a problem in daily life

Of those with neuropathic pain, 24/36 (67%) reported that the pain was 'a severe problem' or 'a problem to some extent' in their daily life (Table 6). Patients diagnosed with neuropathic pain in the younger age group reported pain as a problem in daily life less often than the older age group (0–39 years, 7/16, 44%; 40 years and older, 17/20, 85%; $\chi^2=6.82$, $P=0.01$, df = 1). Women reported that pain was a problem in daily life more often than men did (women, 15/18, 83%; men, 9/18, 50%; $\chi^2=4.5$, $P=0.05$, df = 1). No apparent differences were found, however, when comparisons were made between paraplegics (16/24, 66%) and tetraplegics (8/12, 66%), or in patients with incomplete (21/32, 66%) and complete lesions (3/4). Likewise, no differences were found between patients in the different diagnostic groups ($\chi^2=2.28$, df = 4).

Discussion

The results of the present study show that in all 38% of the patients with non-traumatic SCI suffer from neuropathic pain. Furthermore, below level pain was more frequent than at level pain, females had below-level neuropathic pain more often than males and neuropathic pain was particularly frequent in patients with malignant diseases. Approximately 70% of the patients who suffered from neuropathic pain said that the pain was a problem in their daily life.

Table 5 Logistic regression odds ratio and *P*-values

	Odds ratio	P-*value*
Complete/incomplete SCI	1.22	1.00
Paraplegia/tetraplegia	0.79	0.83
Gender female/male	2.45	0.06

Table 6 Rating of pain as a problem in daily life

All patients	*Number of patients with NP*	*Pain rated as a problem in daily life*	*NP is not a problem in daily life*
All included patients	36	24/36 (67%)	8/36 (33%)
Men	18	9/18 (50%)	9/18 (50%)
Women	18	15/18 (83%)	3/18 (17%)
Tetraplegics	12	8/12 (66%)	4/12 (34%)
Paraplegics	24	16/24 (66%)	8/24 (34%)
Complete SCL	4	3/4	1/4
Incomplete SCL	32	21/32 (66%)	11/32(34%)
Age over 39 years at the time of lesion	16	7/16 (44%)	9/16 (56%)
Age under 39 years at the time of lesion	20	17/20 (85%)	3/20 (15%)

Methodological issues

The results obtained here reflect the patient referral system and may not be generally applicable. For instance, the present material does not include patients with metastasis affecting the spinal cord, multiple sclerosis, primary syringomyelia or motor neuron diseases because they usually are referred to medical services at other clinics.

All patients included were examined at their first visit to the Spinalis Clinic by a neurologist specialised in spinal cord disorders using the standard criteria presented by the IASP task force for identifying neuropathic pain.[19,20] Another specialist was consulted for a second opinion in selected cases when the pain analysis was considered to be difficult. In general, the reliability was high, indicating an acceptable precision in the diagnosis. The database does not contain data on pain characteristics and we are therefore, unable to study possible relations of detailed symptoms to etiologies.

It is reasonable to believe that the predisposition of the individual to report pain is influenced by environmental and psychological factors. In the present study, patients were told to report pain regardless of intensity and regardless of whether it was considered to be a problem in daily life or not. This method is therefore, likely to give a higher frequency of pain reports than studies in which only patients spontaneously complaining of pain were included.

In this study only the dominating type of neuropathic pain was reported. It is therefore, reasonable to assume that our presentation is an underestimation of the true number of cases with combined at level and below level neuropathic pain. This should not change our major conclusions, however.

All patients in this study were examined at a yearly check-up at the Spinalis Unit, Karolinska Hospital, and the data was, in most cases, gathered within a year after the diagnosis of the non-traumatic SCL. At level pain after traumatic spinal cord injury has been reported to begin early after the injury.[21] In agreement with this, our impression was that most patients in the present study reported that the neuropathic pain started within months after the SCL. We do not, however, have data on the first symptoms of the disease and the possible delay until neuropathic pain appeared. Furthermore, like Siddall *et al*,[21] we found that when neuropathic pain is present it usually persists. Thus, the prevalence of neuropathic pain reported here is likely to represent both an established and a long-term situation.

We have used the ASIA classification even though this classification was initially created for traumatic spinal cord injuries.[18] We do not know to what extent this classification is relevant also for non-traumatic SCL. One difference, which might be important, is that non-traumatic SCLs tend to be incomplete more often than traumatic injuries. Thus, in the present study of non-traumatic SCL only 12% were complete, whereas 39% were found to be complete in our previous study of traumatic spinal cord injury.[17]

Neuropathic pain, aetiology, and age

The patients in the present study were divided into five aetiological subgroups. In all 95 patients were included. In particular, the patients in the tumour subgroups were few and the detailed data for this subgroup must be interpreted with caution.

Patients with malignant tumours had a mean age of 16.3 years at the time the spinal cord symptoms appeared, which is considerably lower than the corresponding age for the studied group as a whole (41.7 years). Most of these patients had malignant astrocytoma, which mostly affects children.[22] Even though the material is small, these comparatively young patients tended to have neuropathic pain more often than patients in the other aetiologic subgroups. This could be an explanation to the finding that the age at the time of diagnosis was not a predictor for the development of neuropathic pain in this study of non-traumatic SCL, whereas higher age was found to be a significant contributor in our previous study of the prevalence of neuropathic pain after traumatic injury.[17]

Patients in the subgroup with vascular myelopathies had the highest mean age among the diagnostic subgroups studied (53.7 years of age). This is to be expected since the diagnoses in this subgroup (infarction, aorta-aneurysms, and other vascular myelopathies) mainly affects persons above the age of 50.[7]

Neuropathic pain and gender

The male dominance among the patients with traumatic spinal cord injury (79.5%) collected in the same clinic,[17] was not as evident among the non-traumatic SCL patients (37%). The male dominance in the traumatic group is likely due to higher exposure to violent accidents. Furthermore, whereas no difference in the prevalence of neuropathic pain was found in our previous study of traumatic spinal cord injury patients,[17] a clear dominance among women was evident in the present study of non-traumatic SCL patients.

A number of experimental, clinical and epidemiological studies have shown that men and women experience pain differently; for review see Berkley.[23] For experimentally delivered somatic stimuli, females have lower thresholds, greater ability to discriminate, higher pain ratings and less tolerance of noxious stimuli than males. The gender difference found in the present study was therefore not unexpected, even though there are, to our knowledge, no previous reports on gender differences in the prevalence of neuropathic pain. A higher female prevalence of nociceptive pain after SCI has been reported.[16,24] One possibility is that the males who suffered a traumatic SCI belong to a male subgroup that are more prone to develop neuropathic pain than other men, and are perhaps associated with a more risky way of living. This would not apply to men with non-traumatic SCI. There is no scientific support for this hypothesis, however.

Neuropathic pain and complete/incomplete SCL, level of SCL

In the present study, 11/95 (12%) patients had a complete spinal cord lesion (ASIA A) compared to 162/402 (40%) in our previous study on traumatic spinal cord injuries.[17] This difference was significant ($X = 27.92$, $df = 1$, $P = 0.001$), and is likely to reflect differences related to the pathogenesis. Like our previous study of patients with traumatic SCI,[17] we did not see any difference in the prevalence of neuropathic pain between complete and incomplete SCL and found only small differences in the frequency of neuropathic pain between paraplegic and tetraplegic patients.

Interference of pain on the quality of daily living

Pain is one of the most important factors interfering with daily life activities after SCL.[15] This is most likely to include neuropathic pain as an important component. We therefore, used the opportunity to ask the patients in this study to rate how much the pain affected their daily life. In total, 67% of those with pain answered that pain affected their life a lot ('much' or 'to some extent'), corresponding to 26% of all patients in the study. We cannot discern, however, to what extent this finding reflects the contribution of neuropathic pain rather than a mixture of neuropathic and non-specified pain. Although not formally examined in this study, a common statement among patients who reported that the pain did not affect their life was that they had got used to the pain and therefore, did not think much about it. Our results show a lower rate of distress caused by the pain than those of Anke *et al*,[25] who found that the pain caused significant psychosocial stress in 46% of the patients.

Taken together, the findings confirm that the neuropathic pain associated with acquired SCL is a major cause of distress and always deserves careful attention in spinal cord units. Patients of female gender and those with malignant tumours are particularly prone to develop neuropathic pain whereas contribution from age at the time of the onset of symptoms and level of lesion seem to be less important.

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