Objective: To evaluate spasticity and below-level spinal cord injury neuropathic pain after spinal cord injury in patients with, or without, damage to the lumbar spinal cord and roots.

Design/patients: Chart review of 269 patients with spinal cord injury from segments C1 to T11.

Methods: Patients were interviewed concerning leg spasticity and below-level spinal cord injury neuropathic pain in the lower trunk and legs. Damage to the lumbar spinal cord and roots was inferred where there was radiological evidence of a vertebral fracture, spinal stenosis or the narrowing of spinal foramina of a vertebra from thoracic 11 to lumbar 5, or; magnetic resonance imaging showing evidence of damage to the lumbar spinal cord and roots.

Results: Among 161 patients without damage to the lumbar spinal cord and roots, 87% of those with cervical spinal cord injury experienced spasticity, compared with 85% with thoracic spinal cord injury. The corresponding figures for patients in whom damage to the lumbar spinal cord and roots was present were 57% and 52%, respectively. Below-level spinal cord injury neuropathic pain was not associated with damage to the lumbar spinal cord and roots. In those patients with no damage to the lumbar spinal cord and roots, regression showed that neither outcome was significantly associated with the level of spinal cord injury.

Conclusion: The lack of segmental dependency for spinal cord injury and spasticity suggests mechanisms restricted mainly to the lumbar spinal cord. For below-level spinal cord injury neuropathic pain, additional mechanisms, other than lesions of the spino-thalamic tract, must be considered.

Key words: spinal cord injury; spasticity; neuropathic pain; lumbar spine stenosis.

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spasticity should be greater, as more disconnected spinal cord neurones contribute to the spasticity. BLSCIN pain, on the other hand, is thought to require a lesion of the spinothalamic tract. In this case, the resulting pain should be more prevalent where there is a large lesion of the tract, as in cervical SCI.

The primary objective of this study was, therefore, to investigate whether the prevalence of spasticity and BLSCIN pain is affected by SCI segmental level. Previous studies found a lower prevalence of spasticity where SCI level was lower, see Maynard et al. (3) and Skold et al. (4). In these studies, however, SCIs at the lumbar level were included. It is also possible that spasticity may not reflect the true overactivity of the neurones in the motor pathways. Can concomitant damage at lower spinal cord levels, e.g. the motor neurones and their axons, obscure the true prevalence? Lee & Lee (5) and Secil et al. (6) found motor neurone damage in persons with degeneration of the lumbar spine. To answer the primary objective, first it was necessary to determine whether the prevalence of spasticity in the legs of patients with an SCI at the cervical or thoracic level was affected by damage to the lumbar spinal cord and nerve roots (LSCR).

The question arises, as to whether spasticity and BLSCIN pain are dependent on specific lesions, e.g. of specific descending pathways, or whether there is an inclination to develop overactivity regardless of the neurones involved? In the first case, a large variation should occur in the relationship between spasticity and BLSCIN pain. In the latter case, more uniform changes should be prevalent. Previous studies have mapped the frequency of either spasticity or BLSCIN pain, but not the concurrence of these manifestations. The second objective was therefore to compare the pattern of overactivity of spasticity and BLSCIN pain among the patients.

### METHODS

Approximately 400 individuals with an SCI attend the Department of Rehabilitation Medicine in Gothenburg. Questions regarding spasticity and BLSCIN pain are routinely posed to patients, and suitable study participants were enrolled to this study from amongst them. Patients with an SCI at thoracic level 12 or injury to the lumbar or sacral segments were excluded to avoid instances of SCI in which lesions of the lumbar or sacral motor neurones were present. With SCI at these levels it is also difficult to differentiate BLSCIN pain from peripheral nerve pain.

Study participants have either; a radiological investigation of the spine covering thoracic vertebra 11 and all lumbar vertebra in order to find changes suggesting the possibility of damage to LSCR or a magnetic resonance imaging (MRI) with more direct evidence for damage to LSCR.

Participants included 269 patients with an SCI located between segments C1 and T11 (Table I). The time elapsed between injury and interview ranged from 1 to 64 years, with a mean of 15 years. SCI severity was determined according to the American Spinal Cord Injury Association Impairment Scale (AIS).

The cause of the cervical or thoracic SCI was traumatic in 194 patients, tumour in 19, vascular condition in 24, infection in 6, brain damage, e.g. traumatic injury or stroke. Of the participants, 106 were investigated by MRI, 149 by computed tomography (CT) scan and 14 by ordinary X-ray. Damage to LSCR was evidenced by degenerative or traumatic changes to a vertebra from T11 to L5. The changes looked for included vertebral fracture, spinal stenosis, narrowing of spinal foramina or extensive osteophytes in the foramina (Fig. 1). Stenosis was defined as more than one-third reduction in the spinal canal area. Narrow spinal foramina were defined rather arbitrarily as having an anterior-posterior width of less than 4 mm on axial CT scans (7, 8). Of the patients examined with MRI, 13 had direct damage to the lumbar spinal cord (apart from the SCI higher up); 8 had syringo-myelia, there was 1 distal effect related to a lumbar disc herniation, 1 at L5/S1 caused by a disarticulated coccyx, 1 with vertebral body destruction and 1 with ankylosing spondylitis.

Study participants have either; a radiological investigation of the spinal cord and roots (LSCR). In these studies, however, SCIs at the lumbar level were included. It is also possible that spasticity may not reflect the true overactivity of the neurones in the motor pathways. Can concomitant damage at lower spinal cord levels, e.g. the motor neurones and their axons, obscure the true prevalence? Lee & Lee (5) and Secil et al. (6) found motor neurone damage in persons with degeneration of the lumbar spine. To answer the primary objective, first it was necessary to determine whether the prevalence of spasticity in the legs of patients with an SCI at the cervical or thoracic level was affected by damage to the lumbar spinal cord and nerve roots (LSCR).

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### Table I. Characteristics of the patients with spinal cord injury

| Total | Spasticity | Troublesome spasticity | BLSCIN pain | Spasticity | Troublesome spasticity | BLSCIN pain |
|-------|------------|------------------------|-------------|------------|------------------------|-------------|
|       | n          | %                      | n           | %          | n                      | %           | n            | %           | n          | %                      | n           |
| Total | 269        | 74                     | 45          | 28         | 161                    | 86          | 53           | 30          | 108        | 55                     | 34          | 25           |
| Cervical SCI | 155    | 77                     | 51          | 28         | 101                    | 87          | 54           | 30          | 54         | 57                     | 44          | 24           |
| Thoracic SCI | 114    | 69                     | 38          | 29         | 60                     | 85          | 50           | 32          | 54         | 52                     | 24          | 26           |
| AIS A    | 84        | 80                     | 44          | 32         | 59                     | 86          | 49           | 24          | 25         | 64                     | 32          | 52           |
| AIS B    | 28        | 96                     | 68          | 32         | 26                     | 100         | 69           | 35          | 2         | 50                     | 50          | 0            |
| AIS C    | 39        | 82                     | 59          | 33         | 22                     | 95          | 73           | 45          | 17         | 65                     | 41          | 18           |
| AIS D    | 118       | 61                     | 36          | 23         | 54                     | 76          | 41           | 30          | 64         | 48                     | 33          | 17           |
| Traumatic SCI | 196   | 80                     | 49          | 31         | 132                    | 89          | 54           | 29          | 64         | 63                     | 41          | 36           |
| Non-traumatic SCI | 73    | 56                     | 34          | 21         | 29                     | 76          | 48           | 38          | 44         | 43                     | 25          | 9            |
| Male     | 204       | 76                     | 48          | 29         | 123                    | 89          | 54           | 31          | 27         | 43                     | 22          | 22           |

Characteristics of patients with or without suspected damage to lumbar spinal cord and roots. SCI: spinal cord injury; BLSCIN: below-level spinal cord injury neuropathic; AIS: American Spinal Cord Injury Association Impairment Scale; LSCR: lumbar spinal cord and roots; MRI: magnetic resonance imaging; CT: computerized tomography.
Spasticity was defined according to Pandyan et al. (9) as any involuntary muscle activity in the legs, as reported by the patient. Spasticity was considered troublesome where it interfered with daily life or where pharmacological treatment was deemed necessary. Sixty-nine patients received some sort of anti-spastic pharmacological treatment, e.g. oral baclofen (n = 31), oral diazepam (n = 14), intrathecal baclofen (n = 11) and/or botulinum toxin (n = 36).

Pain was analysed as either nociceptive or neurogenic according to Bryce et al. (10). Neurogenic pain was further categorized into peripheral, BLSCIN, and mixed pain. BLSCIN pain is located at least 3 segments below the level of injury and not according to the distribution of a nerve root or peripheral nerve. BLSCIN pain should not be aggravated by physical activity and, in the current study, questions were limited to pain in the lower trunk or legs. Sixty-four patients had BLSCIN pain. The
pharmacological treatment of BLSCIN pain followed a stepwise pattern. Gabapentin, pregabalin or clonazepam were given to 32 patients and, where this was insufficient, amitryptiline, nortriptyline or duloxetine was prescribed to 18 patients. Nineteen patients received opiate treatment.

Interviews took place between 2014 and 2019. The statistical significance of differences in the prevalence of spasticity and pain was tested using the χ² test Fisher exact test. Dependence on background factors was analysed by logistic regression (SPSS version 22) and statistical significance was set to p < 0.05 in all analyses.

The retrospective chart review was approved by the local ethics committee M2 (number 375-16).

RESULTS

Influence of damage to lumbar spinal cord and nerve roots

Of all 269 patients, 74% experienced spasticity, 45% found their spasticity troublesome and 28% reported BLSCIN pain (Table I). Damage to LSCR was found in 108 of the patients. These patients had a lower frequency of spasticity (55%) compared with those without damage (86%), whereas the frequency of BLSCIN pain was approximately the same. Binary logistic regression of the results for all 269 patients showed that spasticity, but not BLSCIN pain, had a significant and strong association with the absence of damage to LSCR (Table II).

Dependency on spinal level

The frequency of both spasticity and troublesome spasticity in the whole group (n = 269) appeared to be less frequent in cases where the SCI was at a lower thoracic level. This is demonstrated by the regression line in Fig. 2 (left diagram) and is in contrast to BLSCIN pain frequency, which was unaffected by segmental level of the SCI. On the other hand, this segmental relation was not present where only patients without damage to LSCR were included (Fig. 2, right diagram). Of these 161 patients, 87% of those with cervical SCI and 85% of those with thoracic SCI experienced spasticity. The corresponding figure for troublesome spasticity was 54% and 50%. A binary logistic regression of the group of patients without damage to LSCR showed that segmental level did not significantly influence these frequencies (Table III).

Association between spasticity and below-level spinal cord injury neuropathic pain

The association between spasticity and BLSCIN pain was tested in the group with no signs of damage to LSCR.

Table II. Binary logistic regression of the 3 outcomes in the whole group (n = 269). Variable(s) entered in step 1: damage to lumbar spinal cord and roots (LSCR), spinal cord segment, American Spinal Cord Injury Association Impairment Scale (AIS), traumatic injury, male sex, present age and years since injury. Reference AIS is AIS D.

| Outcome                  | p-value | Exp(B) | 95% CI for Exp(B) |
|--------------------------|---------|--------|-------------------|
| Spasticity               |         |        |                   |
| LSCR damage              | 0.001   | 0.309  | 0.160 0.600       |
| Spinal cord segment      | 0.095   | 0.951  | 0.897 1.009       |
| AIS                       | 0.048   |        |                   |
| AIS A                    | 0.306   | 1.527  | 0.679 3.438       |
| AIS B                    | 0.080   | 6.629  | 0.799 54.981      |
| AIS C                    | 0.020   | 3.330  | 1.209 9.173       |
| Traumatic injury         | 0.120   | 1.785  | 0.860 3.706       |
| Male                     | 0.408   | 1.347  | 0.665 2.727       |
| Current age              | 0.193   | 0.987  | 0.968 1.006       |
| Years since injury       | 0.289   | 1.014  | 0.988 1.041       |
| Constant                 | 0.031   | 4.887  |                   |
| Troublesome spasticity   |         |        |                   |
| LSCR damage              | 0.121   | 0.629  | 0.350 1.130       |
| Spinal cord segment      | 0.040   | 0.947  | 0.898 0.997       |
| AIS                       | 0.013   |        |                   |
| AIS A                    | 0.385   | 1.357  | 0.681 2.705       |
| AIS B                    | 0.026   | 3.022  | 1.142 7.996       |
| AIS C                    | 0.005   | 3.186  | 1.412 7.189       |
| Traumatic injury         | 0.263   | 1.471  | 0.748 2.893       |
| Male                     | 0.412   | 1.297  | 0.697 2.416       |
| Current age              | 0.522   | 0.994  | 0.978 1.011       |
| Years since injury       | 0.199   | 0.987  | 0.967 1.007       |
| Constant                 | 0.847   | 1.129  |                   |
| Below-level spinal cord injury neuropathic pain |         |        |                   |
| LSCR damage              | 0.407   | 0.759  | 0.396 1.456       |
| Spinal cord segment      | 0.422   | 1.023  | 0.967 1.083       |
| AIS                       | 0.322   |        |                   |
| AIS A                    | 0.192   | 1.646  | 0.779 3.479       |
| AIS B                    | 0.228   | 1.866  | 0.677 5.142       |
| AIS C                    | 0.102   | 2.025  | 0.869 4.719       |
| Traumatic injury         | 0.051   | 2.152  | 0.997 4.646       |
| Male                     | 0.919   | 0.965  | 0.491 1.899       |
| Current age              | 0.235   | 1.011  | 0.993 1.030       |
| Years since injury       | 0.007   | 0.969  | 0.947 0.992       |
| Constant                 | 0.004   | 0.128  |                   |

Table III. Binary logistic regression of the outcomes in the group without damage to lumbar spinal cord and roots (LSCR) (n = 161). Variable(s) entered on step 1: spinal cord segment, American Spinal Cord Injury Association Impairment Scale (AIS), traumatic injury, male sex, present age and years since injury. Reference AIS is AIS D.

| Outcome                  | p-value | Exp(B) | 95% CI for Exp(B) |
|--------------------------|---------|--------|-------------------|
| Spasticity               |         |        |                   |
| Spinal cord segment      | 0.601   | 0.975  | 0.887 1.072       |
| AIS                       | 0.105   |        |                   |
| AIS A                    | 0.276   | 1.845  | 0.613 5.554       |
| AIS B                    | 0.071   | 7.403  | 0.843 64.976      |
| AIS C                    | 0.068   | 7.284  | 0.862 61.540      |
| Traumatic injury         | 0.547   | 1.453  | 0.431 4.901       |
| Male                     | 0.353   | 1.649  | 0.574 4.740       |
| Current age              | 0.485   | 0.987  | 0.952 1.023       |
| Years since injury       | 0.629   | 0.991  | 0.955 1.028       |
| Constant                 | 0.166   | 4.706  |                   |
| Troublesome spasticity   |         |        |                   |
| Spinal cord segment      | 0.677   | 0.985  | 0.917 1.058       |
| AIS                       | 0.020   |        |                   |
| AIS A                    | 0.155   | 1.858  | 0.790 4.370       |
| AIS B                    | 0.013   | 3.909  | 1.332 11.468      |
| AIS C                    | 0.010   | 4.462  | 1.423 13.991      |
| Traumatic injury         | 0.765   | 1.164  | 0.430 3.155       |
| Male                     | 0.932   | 1.037  | 0.454 2.367       |
| Current age              | 0.458   | 1.010  | 0.984 1.036       |
| Years since injury       | 0.012   | 0.966  | 0.941 0.993       |
| Constant                 | 0.588   | 0.637  |                   |

95% CI: 95% confidence interval.
DISCUSSION

This study shows that patients with a cervical or thoracic SCI concurrent with signs of damage to LSCR have a lower prevalence of spasticity. As expected, no such association was found for BLSCIN pain. In the group without damage to LSCR, the SCI level had no significant effect on spasticity, troublesome spasticity and BLSCIN pain. Spasticity and BLSCIN pain were not associated.

This cohort appears to be representative; the prevalence of spasticity or BLSCIN pain was similar to the previous studies (3, 4, 11, 12). The prevalence of BLSCIN pain may have been underestimated, as evoked neurogenic pain was not included. The prevalence of spasticity may also have been underestimated, as patients experiencing muscle stiffness may have given negative answers to questions regarding involuntary muscle activity. Finnerup (13) advocates more detailed investigations regarding spasticity and pain descriptors. Radiological determination of vertebral damage was estimated visually and was therefore necessarily subjective. This may have resulted in an underestimation of degenerative changes in the spine. There is no universally accepted definition as to when a foraminal stenosis is to be considered significant, and most studies prefer to measure the height using sagittal images. This measurement should preferably be carried out with the patient in a sitting position. The best method for finding evidence of damage to LSCR may be neurophysiological. In patients with lumbar stenosis, Lee & Lee (5) found that the results of electromyographic tests in leg muscles were more closely correlated with leg weakness than damage found in MRI examinations of the lumbar spine. Perhaps all of the patients in this study with AIS A to AIS C, and without spasticity, had some degree of LSCR damage. It is possible that neurones in motor pathways will develop overactivity in all patients with a substantial SCI above the motor neuronal level.

Since no association was found between spasticity and BLSCIN pain, they appear not to share common mechanisms, such as a general predisposition to develop neuronal overactivity after central nervous system (CNS) damage. The drugs that reduce spasticity and BLSCIN pain are also different: baclofen the main drug used for depressing spasticity has only a minor effect on BLSCIN. Correspondingly, the main drugs used for BLSCIN pain gabapentinoids or tricyclic antidepressants have only minor effects on spasticity (see Finnerup (13) for references). It therefore seems justified to discuss spasticity and BLSCIN pain separately.

The segmental level of the SCI in the group with no damage to LSCR was found to bear no relation to spasticity. This implies that very few neurones in spinal segments higher up (below the SCI but above the lumbar segments) contribute to leg spasticity. It also suggests that the neurones contributing to leg spasticity are located within the lumbar or sacral segments; this could be the motor neurones or lumbar/sacral interneurones (Fig. 2). Jankowska & Hammar (2) discusses possible interneuronal reflex arcs contributing to spasticity: since alpha-2 adrenergic agonists have an antispastic effects in patients with SCI and that the depressive effects of these agonists is mainly on group II interneurones and not on the motor neurones, they argue for interneuronal overactivity as a major cause for spasticity.

### Table IV. Differences in prevalence of spasticity and below-level spinal cord injury neuropathic (BLSCIN) pain tested using χ2 test (Fisher’s exact test). Results for the group without damage to lumbar spinal cord and roots (LSCR) (n = 161). Table shows the number of patients with spasticity and BLSCIN pain

| Spasticity: | BLSCIN pain | Fisher’s test | p   |
|------------|-------------|---------------|-----|
| Yes ( %)   | 49 (30) [23–38] | 112 (70) [62–77] |     |
| No ( %)    | 6 (27) [6–48] | 43 (31) [23–39] |     |
| BlSCIN pain | 96 (69) [61–77] | 9 (6) [0–20] | p = 0.8 |
| Troublesome spasticity: | 28 (33) [22–44] | 57 (67) [56–78] |
| Yes ( %)   | 21 (28) [17–38] | 55 (72) [62–83] |     |
| No ( %)    | 9 (12) [6–18] | 4 (6) [0–14] |     |

95% CI: 95% confidence interval.
Since BLSCIN pain (experienced below the SCI level) is also present in complete SCI, some of the neural alterations must be localized above the lesion. It is considered that BLSCIN pain requires a lesion of the spinothalamic tract and may be caused by neuronal overactivity at several levels in the spinal cord and brain, including in the thalamus. If BLSCIN pain was dependent only upon a lesion of the spinothalamic tract, then a cervical SCI should cause a more extensive deafferentation in the thalamus compared with a lower SCI. However, BLSCIN pain was not more prevalent in cases of cervical SCI. The lack of correlation between segmental level and pain could be explained by overactivity in neurones located just above the SCI. Vierck (14) suggests that BLSCIN pain is caused by a combination of different neural mechanisms. He suggests that the main mechanism is damage to pathways from the dorsal horn to reticular nuclei in the brainstem. This system is considered to consist of chains of propriospinal interneurons conveying impulses from C-fibre afferents, impulses that are experienced as diffuse widespread pain.

The lower prevalence of spasticity in patients with LSCR damage points to the possibility that degeneration of the lumbar spine contributes peripheral paresis on top of the central paresis of the legs in elderly patients. This study also suggests that future studies of the neuronal mechanisms behind spasticity should mainly be directed to the lumbar segments. The suggested localization of a pain generator just above the level of the SCI supports further investigation into the use of intrathecal gabapentin. Previous attempts by Rauck et al. (15) to treat peripheral neuropathic pain with intrathecal gabapentin failed, but further study is warranted in effect on BLSCIN pain of intrathecal gabapentin injection just above the level of the SCI.

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REFERENCES

1. Bellardita C, Caggiano V, Leiras R, Caldeira V, Fuchs A, Bouvier J, et al. Spatiotemporal correlation of spinal network dynamics underlying spasms in chronic spinalized mice. Elife 2017; 6: e23011.
2. Jankowska E, Hammar I. Spinal interneurones; how can studies in animals contribute to the understanding of spinal interneuronal systems in man? Brain Res Brain Res Rev 2002; 40: 19–28.
3. Maynard FM, Karunas RS, Waring WP, 3rd. Epidemiology of spasticity following traumatic spinal cord injury. Arch Phys Med Rehabil 1990; 71: 566–569.
4. Skold C, Levi R, Seiger A. Spasticity after traumatic spinal cord injury: nature, severity, and location. Arch Phys Med Rehabil 1999; 80: 1549–1557.
5. Lee JH, Lee SH. Physical examination, magnetic resonance image, and electrodiagnostic study in patients with lumbar-sacral disc herniation or spinal stenosis. J Rehabil Med 2012; 44: 845–850.
6. Secil Y, Ekinci AS, Bayram KB, Incesu TK, Tokucoglu F, Gurgor N, et al. Diagnostic value of cauda equina motor conduction time in lumbar spinal stenosis. Clin Neurophysiol 2012; 123: 1831–1835.
7. Beers GJ, Carter AP, Leiter BE, Tilak SP, Shah RR. Interobserver discrepancies in distance measurements from lumbar spine CT scans. AJR Am J Roentgenol 1985; 144: 395–398.
8. Ciric I, Mikhael MA, Tarkington JA, Vick NA. The lateral recess syndrome. A variant of spinal stenosis. J Neurosurg 1980; 53: 433–443.
9. Pandyan AD, Gregoric M, Barnes MP, Wood D, Van Wijck F, Burridge J, et al. Spasticity: clinical perceptions, neurologi- cal realities and meaningful measurement. Disabil Rehabil 2005; 27: 2–6.
10. Bryce TN, Biering-Sorensen F, Finnerup NB, Cardenas DD, Defrin R, Lundeberg T, et al. International spinal cord injury pain classification: part I. Background and description. March 6–7, 2009. Spinal Cord 2012; 50: 413–417.
11. Siddall PJ, McClelland JM, Rutkowski SB, Cousins MJ. A longitudinal study of the prevalence and characteristics of pain in the first 5 years following spinal cord injury. Pain 2003; 103: 249–257.
12. Werhagen L, Budh CN, Hulting C, Molander C. Neuropathic pain after traumatic spinal cord injury – relations to gender, spinal level, completeness, and age at the time of injury. Spinal Cord 2004; 42: 665–673.
13. Finnerup NB. Neuropathic pain and spasticity: intricate consequences of spinal cord injury. Spinal Cord 2017; 55: 1046–1050.
14. Vierck C. Mechanisms of below-level pain following spinal cord injury. J Pain 2019 Sep 5. [Epub ahead of print].
15. Rauck R, Coffey RJ, Schultz DM, Wallace MS, Webster LR, McCarville SE, et al. Intrathecal gabapentin to treat chronic intractable non-cancer pain. Anesthesiology 2013; 119: 675–686.