

Original Article

Gender related differences in pain in spinal cord injured individuals

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Study design: Out of a population of 456 patients with spinal cord injuries (SCI), 130 having pain were selected after matching, based on gender, age, American Spinal Injury Association (ASIA) impairment grade and level of lesion.

Objective: To investigate whether gender differences with regard to pain perception and prevalence exist in a population of patients following spinal cord injury.

Setting: Spinalis SCI Unit (out-patient clinic), Stockholm, Sweden.

Method: 130 patients suffering from pain were assessed over a 12-month period in a yearly health control.

Results: SCI women had a higher prevalence of nociceptive pain than men and their use of analgesics was greater. However, no differences between the sexes could be seen regarding pain and localization, onset, distribution, factors affecting pain, number of painful body regions, pain descriptors, ratings of pain intensities or in pain and life satisfaction.

Conclusion: This study showed that SCI men and women describe their pain very similarly. However, SCI women had a higher prevalence of nociceptive pain than men and their use of opiates and non-steroid anti-inflammatory drugs (NSAIDs) was greater.

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Introduction

Pain is described by spinal cord injured (SCI) patients as the worst problem,¹ far more disabling than the loss of motor and sensory function. Reports of pain prevalence differ between 34 and 94%,^{2–6} but it is most often described as present in around 60–65% of the SCI populations.^{2,7–11} This variability may depend on the population assessed, the type of survey¹² but also on the definition of pain.¹² Several studies have described pain prevalence, risk-factors, pain and medical variables and psychosocial scores in SCI populations,^{2–6,8–12} but since results vary from study to study there is no consensus. Pain seems to have an early onset after the injury,^{2–4,6,10} is reported mainly from below or at the level of the lesion,^{2,5,6,10} and is mostly classified as neurogenic/neuropathic.^{1,10,13} (The term neurogenic will be used throughout this paper). According to Ravenscroft and colleagues⁴ a higher incidence of pain is seen in patients with complete

injuries. However, others have reported a higher incidence in those with incomplete lesions^{6,8,10} and this has been supported by autopsy findings,¹⁴ further supported by the finding that patients with incomplete lesions have more severe pain than those with complete lesions.¹³

Age has previously been reported to influence the vulnerability to pain.^{15,16} Störmer² found a significant difference between age at injury and the presence of pain in SCI patients. Patients who had sustained their injury when young were less at risk of developing chronic pain. Demirel⁸ also found that SCI patients with continuing pain were older than those who were pain free.

In the non-spinal cord injured population, gender differences in pain perception and pain prevalence are often discussed. Several nociceptive pain conditions, for example migraine headaches, orofacial pain, fibromyalgia, abdominal pain and pelvic pain, are more common in women,¹⁷ as are some neurogenic pain conditions, such as reflex sympathetic dystrophy and post-herpetic neuralgia.¹⁷ Women also report greater severity and frequency of perceived pain than

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do men. Furthermore, women's pain is reported as longer lasting and present in a greater number of body regions compared to men's.^{18–20}

Often, epidemiological studies of spinal cord injured patients do not address gender differences.^{4,5,8} In a study by Störmer and colleagues² a tendency towards a higher prevalence of pain could be seen in women, even though this was not significant. However, Finnerup and colleagues⁶ reported significantly higher pain prevalence in men.

Objective

The aim of this study was to investigate whether gender differences regarding pain prevalence, the number of painful body regions, pain intensities, localization, onset, distribution, factors influencing pain, pain descriptors, pain quality, use of analgesics and pain and life satisfaction exist in a population of patients with SCI.

Methods and patients

Within the Spinalis SCI unit, an out-patient clinic, yearly health examinations are offered to all patients registered, ie those with a sustained spinal cord injury or with myelomeningocele. All patients are assessed by a physician, a physiotherapist, an occupational therapist, a nurse and a social worker, according to a standardized manual, The Spinal Injury Registry of Sweden (RYSS)²¹. These assessments are made in an out-patient setting and take 3–4 h. At the time of the study, the RYSS instrument was used in all Spinal Cord Injury Units in Sweden ($n=6$) in co-operation with regional hospitals with SCI care. Today this instrument is used nationwide in both Norway and Sweden and therefore has been re-named as the Nordic Spinal Cord Injury Registry. In addition to the assessment by the RYSS instrument, an additional pain questionnaire was filled in by the patient, in the presence of the assessing physician. This questionnaire included drawing a pain chart, describing pain character/s (including dysesthesia), the localization of pain, the number of painful body regions and the scoring of pain intensities. The scoring consisted of rating the 'mildest', the 'general' and the 'worst' intensity of all identified pain areas on a visual analogue scale (VAS), reading from 0 to 100 and marked at the ends with 'no pain' and 'unbearable pain'.

The condition was defined as pain, ache or unpleasantness present at least for the last two weeks or recurrent during at least four 2-week periods during the last year.²¹ The grading of the severity of the spinal cord injury was based on the American Spinal Injury Association's (ASIA) impairment scale, grading the injury from ASIA A (no motor or sensory function in the sacral segments S4–S5) to ASIA E (motor and sensory function are normal).²²

The study was approved by the ethical committee of the Karolinska Institutet in Stockholm, Sweden.

Subjects

During a 12 month period, all patients with a spinal cord injury who came for a yearly check-up were asked to participate in the study. Out of the population of 603 patients, 456 accepted the offer of a health control during this period of time and also agreed to participate in the study. Of the 456 patients, 340 (74.6%) had a traumatic injury and 116 (25.4%) a non-traumatic injury, 120 (26.3%) were females and 336 (73.7%) males. Mean age overall was 47.04 years, range 11–84. Mean age for females was 48.7 years, and for males 46.5 years.

Since gender, age and completeness of lesion can influence the perception of pain, we aimed at matching all females ($n=89$) with pain from the original sample of 456 patients, to males for age (± 3 years), ASIA grade and level of lesion (cervical, thoracic, lumbar/sacral) in order to detect gender differences. Sixty-five of these 89 women were successfully matched to a corresponding male, resulting in two groups of 65 patients each, with a mean age of 49.88 years (women 49.73 and men 50.04 years).

Statistics

Age at injury was demonstrated as mean values \pm standard deviation and tested with T-test for independent samples to evaluate differences between patients who developed lasting pain and those who did not. The different distribution of number of pain-locations between the sexes was evaluated with Fisher two-tailed exact test. The distribution of observed frequencies of nominal data was analyzed with the non-parametric Chi-square test with 1 degree of freedom throughout except for life satisfaction and sex differences in number of consumed pharmacological interventions where the non-parametric two-sample test Mann–Whitney U-test was used. The level of significance was set to 0.05.

Results

Prevalence of pain in the non-matched population consisting of 456 individuals

In this study¹⁰ 456 patients were assessed regarding perception of pain and its prevalence. Gender differences were found significant in the analysis of pain prevalence. Of the women 74.2% ($n=89$) reported pain compared to 60.1% of the men ($n=202$), $P=0.007$. When split into age categories, pain was seen to increase with age, and was most prevalent in women in the age group 50–59 years ($P=0.028$), after which it declined. Men's pain prevalence showed the same pattern but without the peak in the middle aged group (Figure 1). Patients with pain were of a significantly higher mean age (35.1 years, $SD \pm 16.24$) at injury than

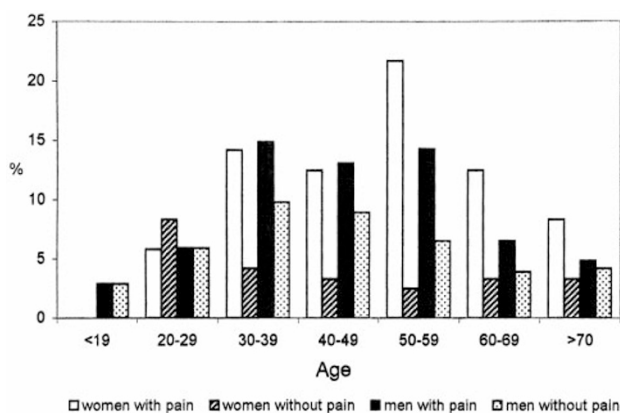


Figure 1 Comparison between men and women with and without pain split into age categories, with women and men being analyzed separately

those without (31.4 years, $SD \pm 18.05$), $P=0.027$. In our study we also found a higher prevalence of pain in ASIA D classified patients, $P=0.044$.

No correlations were found in this study regarding pain and etiology of injury (traumatic/nontraumatic), pain and time since injury, pain and level of lesion, pain and spasticity or in pain and contractures.

Results in the group consisting of 130 matched individuals

Onset of pain Most patients experienced pain within 3 months of their spinal cord injury. In 15 women and 25 men pain commenced more than 12 months after the injury, $P=0.057$ (Table 1).

Localization of pain Pain was experienced at the lesion level by 17 women and 21 men, and below it by 46 women and 47 men, ie in areas with decreased or no sensitivity. In 17 women and 21 men, pain was localized to areas above the level of injury, ie in areas with normal sensation (Table 1).

Pain distribution The patients were classified as having a diffuse distribution of pain (37 women and men), pain localized to a smaller area (22 women and 26 men) and segmental pain in one or more dermatomes (17 women and 20 men) (Table 1).

Factors affecting the perception of pain Around half of the women and men reported that mechanical factors influenced their pain. The same number of persons reported pain being unaffected by any observed factors (Table 1).

Number of painful body regions All patients were asked to describe how many different body areas (1–5) they could identify as painful (Table 2). On average women had 1.60 painful sites and men 1.72.

Scoring of pain intensities To assess the pain intensity, the 'mildest' pain, 'general' pain and 'worst' pain was rated for each located area on a VAS score. The median value for the mildest pain was 25 for both sexes, the general pain 48 in women and 46 in men, and the worst pain was rated 78 in women and 76 in men.

Pain descriptors Pain descriptors could be chosen from a given list with possibilities to use one's own expressions as well. Aching pain was the most commonly used descriptor in both men (47.4%, $n=31$) and women (43.1%, $n=28$). In women burning pain was reported by 22 (33.8%) compared with 16 men (24.6%). Seventeen men (26.1%) reported pricking pain compared to 12 women (18.5%) (Table 1).

Disturbance of daily life Employing the RYSS instrument, patients were asked the extent to which pain disturbed their daily life, using the categories,²¹ not at all; to some extent; a lot. Most patients were disturbed by their pain to some extent (30 women and 30 men) or a lot (19 women and 24 men) (Table 1).

Life satisfaction Life satisfaction was assessed with the Fugl–Meyer Life Satisfaction instrument.²³ The instrument contains nine questions and is self-rated, scoring from 1 (very dissatisfying) to 6 (very satisfying). One-third of the women ($n=22$) and half of the men ($n=36$) completed this questionnaire (Figure 2). There were no significant differences between the sexes but a tendency by women to rate family life higher than men could be identified, $P=0.056$.

Pain quality The types of pain were classified by the assessing physician into one of three different pain categories; neurogenic pain, nociceptive pain or mixed pain (ie presence of both neurogenic and nociceptive pain).^{21,24} Women were classified as suffering more often than men from nociceptive pain, $P=0.041$ (Table 1).

Use of pain relieving medication Fifty-three of the 130 patients (40.8%) used one or more pain relieving drugs. Mean value for the number of drugs used was 0.82 in women and 0.37 in men, $P=0.0025$. Significantly more women (53.8%) than men used pain medication (27.7%), $P=0.0024$. Major gender differences were also seen when looking at the varied choice of drugs (Table 2). Women used opiates ($P=0.0187$) and non-steroid anti-inflammatory drugs (NSAIDs) and other peripherally acting drugs ($P=0.0002$) to a much larger extent than men. Their consumption of NSAIDs was five times more common (32.3%) than men's (6.2%) and their use of opiates twice as common (36.9%) compared to men (18.5%). The use of anti-epileptic medication was very low in both sexes with only five men and one woman using this type of drug. Similarly only seven women and four men used anti-depressives as analgesics (Table 1).

Table 1 Pain and assessed variables in 65 women and 65 men

Description	Women		Men		P
	%	n	%	n	
Onset of pain					
within 3 months	78.5	51	69.2	45	ns
3–6 months	4.6	3	7.7	5	ns
6–12 months	6.2	4	7.7	5	ns
more than 12 months post injury	23.1	15	38.5	25	ns
Localization of pain					
above the level of lesion (normal sensation)	26.2	17	32.3	21	ns
at the level of lesion	26.2	17	16.9	11	ns
below the level of lesion (decreased sensation)	70.8	46	72.3	47	ns
at and below the level of lesion	6.2	4	7.7	5	ns
above, at and below the level of lesion	0	0	3.1	2	ns
Pain distribution					
diffuse distribution	56.9	37	56.9	37	ns
segmental distribution	26.2	17	30.8	20	ns
non-segmental, radiating	4.6	3	1.5	1	ns
pain localized to a smaller area	33.8	22	40	26	ns
Factors influencing the perception of pain					
mechanical (body position, effort etc)	47.7	31	55.4	36	ns
internal factors (infection, fever, stress etc)	4.6	3	3.1	2	ns
external factors (temperature, low barometer pressure etc)	7.7	5	9.2	6	ns
internal and external factors	6.2	4	4.6	3	ns
mechanical and other factors	13.8	9	9.2	6	ns
no factors observed	49.2	32	46.2	30	ns
Pain disturbs my daily life					
not at all	18.4	12	13.8	9	ns
to some extent	46.1	30	46.1	30	ns
a lot	29.2	19	36.9	24	ns
missing data	6.1	4	3.0	2	
Pain descriptors					
aching	43.1	28	47.4	31	ns
burning	33.8	22	24.6	16	ns
pricking	18.5	12	26.1	17	ns
pressing	18.5	12	23.1	15	ns
throbbing	13.8	9	20.0	13	ns
radiating	4.6	3	3.1	2	ns
pulsating	3.1	2	3.1	2	ns
various characters	3.1	2	6.2	4	ns
dysesthesia	1.6	1	1.6	1	ns
Pain quality					
neurogenic	43	28	52.3	34	ns
mixed	24.6	16	29.2	19	ns
nociceptive	30.7	20	15.3	10	*
missing data	1.5	1	3.0	2	
Use of analgesics					
total use of analgesics	53.8	35	27.7	18	**
opiates	36.9	24	18.5	12	*
NSAIDs and other peripherally acting drugs	32.3	21	6.2	4	***
anti-epileptic drugs	1.5	1	7.7	5	ns
anti-depressive drugs	10.8	7	6.2	4	ns

Since patients could suffer from more than one painful bodysite, and all reported pain being presented, some of the figures exceed 100%. Regarding the use of analgesics some of the patients used more than one drug. Missing values exists in information collected from the data records. * $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$

Discussion

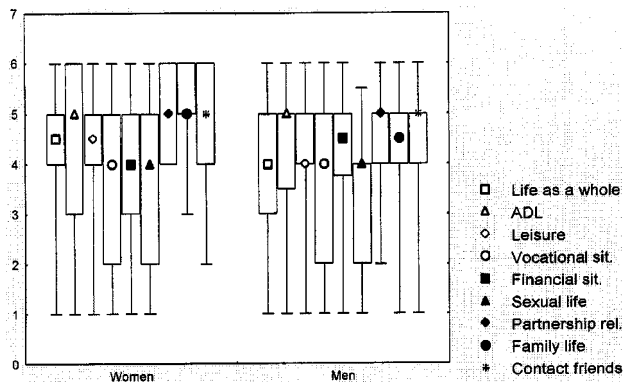
In this study we found a higher prevalence of nociceptive pain in SCI women than in SCI men. SCI women also had higher consumption of opiates and NSAIDs. However, there were no differences with regard to onset of pain, pain descriptors, number of

affected body regions, factors influencing pain, rating of pain intensities and life satisfaction in this age-, gender-, level of lesion- and completeness of lesion matched population of SCI patients.

We were unable to detect any gender differences regarding pain and life satisfaction, but the amount of responders was very low, only one-third of the women

Table 2 Number of painful body regions in 65 women and 65 men with pain

	1		2		3		4		5	
	%	n	%	n	%	n	%	n	%	n
Women	60.0	39	27.7	18	7.7	5	1.5	1	3.1	2
Men	53.8	35	26.1	17	15.4	10	3.1	2	1.5	1

**Figure 2** Rating of Life Satisfaction according to Fugl-Meyer in 22 women and 36 men with pain

and half of the men had completed the questionnaire, making it difficult to draw conclusions from this material. In our study 'aching pain' was the most commonly used word descriptor, the same as in two studies by Turner and colleagues.^{5,9} This contrasts with others who have reported burning pain,² pricking and tingling pain⁶ as the most frequently used words. The descriptor 'aching pain' was in our study used by more men than women and 'burning pain' by more women than men, even though these differences were not significant. However, a recent study has investigated the use of pain descriptors when classifying SCI pain and concluded that verbal descriptors alone are not sufficient for pain classification.²⁵

In non-SCI populations, women often report more numerous pain locations than men^{17,19} and more severe pain.¹⁸ This was not the case in our study, where no differences were found. But the greater prevalence of pain in women in our population of 456 individuals is supported by epidemiological studies of gender differences in general.^{17,20} The underlying reasons are largely unknown. Several studies emphasize that no difference in sensitivity is apparent sex-wise in pain thresholds tested pre-pubertally, while a significant increase is noted in women post-pubertally.^{26,27} This could come about through increased levels of gonadal hormones^{3,19,28-30} The increased pain prevalence seen in this study amongst women aged between 50 and 59 years could possibly be explained by fluctuating menopausal hormone levels. Differences in body composition (women have a higher

percent of body fat and smaller muscle mass) could be a contributing factor, and could have importance in eg musculo-skeletal conditions.²⁸ Size, eg height and body surface, is less likely to contribute.^{27,31} Another reason why women appear to exhibit greater and more frequent pain could be that it is habitually more socially acceptable. It is possible that men and women differ in their acknowledgement of pain as well as in evaluating and interpreting bodily discomfort.^{20,32} This is supported by Canli and colleagues³³ showing that women have better emotional memory than men.

In other patient groups women and men describe symptoms and signs of various pain disorders in different ways, eg in coronary diseases.³² This has led to differences in aggressiveness in treating the disease. Different ways of expressing pain might have an impact on the choice of pharmacological treatment, but in our study the differences in choice of analgesics cannot be explained thus, since men and women described their pain very similarly. In the extensive review by Unruh in 1996¹⁸ she declares that no evidence for gender differences in the amounts of analgesics used has been found in non-SCI populations, but our findings were in contrast to this. 53.8% of the women used one or more pain relieving drug compared to 27.7% of the men. NSAIDs and other peripherally acting drugs were more commonly used by women (32.3 vs 6.2%), as were opiates (36.9 vs 18.5%). The small use of anti-depressive and anti-epileptic drugs was surprising, although this was also noted in a recent Danish study.⁶ 10.8% of the women used anti-depressive medication for analgesia compared to 6.25 of the men, and only 1.5% of the women and 7.7% of the men used anti-epileptic drugs. In our study neurogenic pain was the most frequently diagnosed type of pain in both men and women. But as many as 20 women and 10 men were being classified as suffering from nociceptive pain, mixed pain unregarded. In this respect women seem to be classified as suffering more often from nociceptive pain than men. But why this increased prevalence of pain in SCI women is restricted to nociceptive pain alone and does not include neurogenic pain we are unable to explain. No gender differences could be detected in the classification of mixed or neurogenic pain or in onset, distribution, localization, pain descriptors and factors influencing pain. Still the use of opiates and NSAIDs differed significantly between the sexes and we found this hard to explain simply by the greater incidence of nociceptive pain in women alone. The reason behind the women's greater use of analgesics could not be explained either by age, level of lesion or completeness of lesion since the patients in this study were matched in these.

Pain in patients with SCI can be of both neurogenic and nociceptive quality. The 'golden standard' in treating pain is by use of NSAIDs and opiates for nociceptive pain and anti-depressive or anti-epileptic drugs for neurogenic pain. Some study results, however, show effects from opiates given intrathecally

or in i.v. infusions.³⁴ According to a review in Pain Clinical updates³⁴ effectiveness in treating neurogenic pain orally has been achieved in the use of antidepressants, anti-convulsants and NMDA (N-methyl-D-aspartate)-receptor antagonists. Unfortunately, there are few studies that have assessed, in a randomized controlled way, the effect of both pharmacological and non-pharmacological treatments of neurogenic pain.

Nothing in this study can totally explain the gender differences found in the diverse use of analgesics. There are studies showing gender differences in the responses to both physical and pharmacological treatment, especially to opiates but also to transcutaneous electric nerve stimulation (TENS). Women seem to respond better to κ -mediated and men to μ -mediated treatment.^{14,35–38} Since most traditional opiates used today work mainly on the μ -receptors, opiates are likely to be less effective in women and therefore less used in their treatment. No studies (to our knowledge) have assessed possible gender differences in the effects of treatment with anti-epileptic or anti-depressive drugs, but it would be interesting to investigate if this partly accounts for the differences found in this study.

Conclusion

In our study population we found that: (1) SCI women have a higher prevalence of nociceptive pain than men; (2) SCI men and women perceive and describe their pain similarly regarding the number of painful body regions, pain intensities, localization, onset, distribution, factors influencing pain and life satisfaction; and (3) SCI women use more analgesics than men, i.e. opiates and NSAIDs.

Differences shown in this study and many others are of interest, not only for identifying the patients at risk of developing chronic pain but also for choosing the optimal treatment. The assessment of the patients' clinical pain is of great importance since this may lead to different treatment strategies. Gender differences in the perception of different drugs' effect raise another important issue that needs further addressing.

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