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The demographics of pain after spinal cord injury: a survey of our model system.

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TITLE: THE DEMOGRAPHICS OF PAIN AFTER SPINAL CORD INJURY: A SURVEY OF OUR MODEL SYSTEM

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ABSTRACT:

Study Design: Survey

Objectives: Better understand the demographics of pain after spinal cord injury (SCI)

Setting: Academic Level 1 trauma center and SCI Model System

Methods: A survey including general demographic questions, questions of specific interest to the authors, the standardized SCI Pain Instrument (SCIPI), International SCI Pain Data Set, Basic form (ISCIPDS:B), Patient Reported Outcomes Measurement Information System (PROMIS) neuropathic 5a (PROMIS-Neur), and PROMIS nociceptive 5a (PROMIS-No).

Results: 81% of individuals with SCI experience chronic pain and 86% of individuals with pain have neuropathic pain. 55% of individuals had shoulder pain. Females and those who recall ≥5/10 pain during initial hospital stay had significantly higher PROMIS-Neur scores. Completeness of injury correlates inversely with degree of neuropathic pain. Those who recall ≥5 pain during initial hospital stay and those who reported the worst or second worst pain as being shoulder pain had significantly higher PROMIS-No scores. Lumbosacral injuries trended towards higher PROMIS-No scores and had the highest PROMIS-Neur scores. Those with tetraplegia were more likely to develop shoulder pain and those with shoulder pain had higher PROMIS-No scores.

Conclusions: Chronic pain is almost universal in patients with SCI. Pain is more commonly reported as neuropathic in nature and females reported more neuropathic pain than males. Physicians should monitor for nociceptive shoulder pain, particularly in those with tetraplegia. Patients with incomplete injuries or lumbosacral injuries are more likely to report higher levels of neuropathic pain and pain levels should be monitored closely. Those with more neuropathic

and nociceptive pain recall worse pain at initial hospitalization. Better understanding pain demographics in this population help screen, prevent and manage chronic pain in these patients.

Sponsorship: none

INTRODUCTION:

Chronic pain limits activities, decreases quality of life, and leads to significant impairment in individuals with spinal cord injury (SCI)[1–3]. Individuals with pain after SCI have a $22,545 increased cost burden per year compared to their SCI peers without pain[4] and the difficulty in treating this pain has been documented for years[5]. Pain after SCI is typically classified as nociceptive (which includes visceral and musculoskeletal pain), at-level-neuropathic, and below level neuropathic[6]. Neuropathic pain is generally regarded as the most frequent type of pain after SCI[7], although this remains disputed, with studies having up to 59% of those with SCI reporting musculoskeletal nociceptive pain [8]. The prevalence of chronic pain in this population varies from 13-96% depending on the study[3,8–11] and of severe pain from 20-58% [8,12]. The International Spinal Cord Injury Pain Classification System was developed in 2009, but experts were unable to estimate the prevalence of pain after SCI due to the variability between studies, suggesting the need for more and better data[6] which has since been reiterated[7,13]. Some data suggests incomplete lesions result in more chronic pain [8,11,14,15], though other studies paradoxically suggest complete lesions result in more chronic pain[16–18]. A metanalysis recently found no difference between groups[13]. Many studies suggest level of injury does not affect the prevalence of chronic pain, although others have suggested lumbosacral injuries are more painful[19].

This confusion originates from the lack of consistently used and validated instruments to measure pain. In a recent metanalysis of neuropathic pain after SCI that included 17 studies, Burke et al. found only two studies used validated instruments to measure neuropathic

pain[20]. To further delineate and add to the body of literature surrounding chronic pain after spinal cord injury, the authors of the current study developed a survey that included basic demographic questions, instruments to measure neuropathic pain after SCI, and specific questions assessing other types of pain that may be present in this population. Since pain is a subjective finding notoriously difficult to measure, a survey with validated pain instruments is one good way to assess the issues at hand and accurately evaluate the demographics surrounding pain after SCI.

METHODS:

Survey Development:

The authors evaluated existing reviews and metanalyses addressing the demographics of pain after spinal cord injury[6,13,20]. We then interviewed experts in the areas of spinal cord injury medicine, pain management, and survey statistics to solicit input on validated tools and potential questions that could be answered by this work. Based on this preliminary work, we developed a survey including general demographic questions, questions of specific interest to the authors, the standardized Spinal Cord Injury Pain Instrument (SCIPI), International Spinal Cord Injury Pain Data Set, Basic form (ISCIPDS:B), Patient Reported Outcomes Measurement Information System (PROMIS) neuropathic 5a (PROMIS-Neur), PROMIS nociceptive 5a (PROMIS-No), and PROMIS pain interference short form 8a (PROMIS-Int). The PROMIS instruments were designed to compare groups of individuals to the general population of the United States. A score of 50 represents the average population with a standard deviation of 10. The mean

PROMIS-Neur scores for surveyed population was 55.2 while the mean PROMIS-No score was 52.0. Of note, the level of completeness of injury (AIS classification) was self-reported and not confirmed by physician examination or medical records review. The final survey consisted of a possible 80 questions, although most combination of answers did not result in the participant answering all 80 questions. A pilot test was conducted by the authors of the study as well as others from within the department to evaluate question clarity and software functionality. The goals of this survey were to a) collect demographic data as it relates to pain after SCI utilizing standardized tools; b) assess demographic information of specific interest to the authors; and c) compare multiple demographic parameters as they relate to measured outcomes using the validated instruments. The survey was thoroughly examined and approved by the Thomas Jefferson University Hospital institutional review board. We certify that all applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed during the course of this research. A formatted copy of the survey is available for review in appendix A.

Survey Distribution:

The survey was distributed via Survey Monkey to SCI consumer mailing lists maintained by Thomas Jefferson University as part of the SCI model systems program. Each participant received a link via email and completed the survey online. One patient was unable to independently complete the survey online and therefore completed it over the telephone. A reminder was sent six weeks after the initial invitation to participate. All survey responses remained anonymous and repeat responses were discounted by cancelling any duplicate IP

addresses. There was no time limit to complete the survey. There were no incentives offered for completing the survey. There were 705 individuals queried on the initial email and 711 on the second email.

Data Analysis:

To answer study objectives, participant data were grouped into neuropathic (SCIPI $\geq$2) or nociceptive (SCIPI <2). For specific analyses—particularly in questions with multiple answers, similar answers were grouped for analysis (i.e. multiple original age groups were combined to form <55 years of age and >55 years of age). Data on level of injury, completeness of injury, and other similar demographics were combined when no significant between group differences was found. The data were analyzed using individual Chi-Square or t-tests for continuous data. Fisher's Exact tests were used if expected values in categories fell below 5 in any cell. All data was calculated using SPSS v.25 (Armonk, NY).

RESULTS:

One hundred seventy-one responses were received, giving a response rate of 24%. 81% of respondents had chronic pain. As classified by the SCIPI, 86% of respondents with chronic pain were classified as having neuropathic pain. The mean PROMIS-Neur scores for the surveyed population was 55.2 while the mean PROMIS-No score was 52.0. Eighty-two percent of participants report having experienced pain during their initial hospitalization after their injury, 81% reported having chronic pain since that time, and 66% reported their primary chronic pain started immediately after their SCI. Most (56%) had constant and continuous pain that was

unpredictably intense (45%), continued on a daily basis (90%), and has gotten worse since initial injury (54%). Seventy percent of individuals with chronic pain had at least three separate body areas with pain. The median reported daily pain on the Stanford pain scale was 5/10 or "very distressing." The mode at initial injury was 3/10 or "tolerable" and the current mode of the surveyed sample was 4/10 or "distressing."

Seventy percent of the respondents were >55 years of age. There was no significant difference in the development of nociceptive vs neuropathic pain as categorized by the SCIPI based on age category (χ^2 = 0.942). Seventy-five percent of respondents were male. There was no difference between type of pain experienced (neuropathic versus nociceptive) when comparing males and females (χ^2 = 0.341), however, females mean neuropathic pain scores ($\overline{x} = 58.0$) was significantly higher than the male mean neuropathic pain score as measured by the PROMIS-Neur [($\overline{x} = 54.0$) (T = -2.053; p = .043)] (Table 1, Figure 1).

The most common mechanism of injury was motor vehicle accident (35%) followed by falls (30%). Twelve percent were due to penetrating injuries. Penetrating injuries did not influence the development of neuropathic or nociceptive pain on the SCIPI when compared to non-penetrating injuries (χ^2=0.138). However, those with penetrating injuries reported non-significantly higher PROMIS-No [($\overline{x} = 55.9$) and PROMIS-Neur ($\overline{x} = 57.5$) scores compared to their non-penetrating peers ($\overline{x} = 51.5$ and 55.1; T = -1.692 and -.869; p = .094 and .387) (Table 2).

Fifty-two percent of respondents had cervical spine injuries and most (68%) were incomplete injuries as classified by the international standards for classification of spinal cord injury (ISNCSCI) (grades B, C, D or E.) The breakdown of ASIA classification was as follows: 30% were ASIA A, 19% were ASIA B, 20% were ASIA C, 20% were ASIA D, and 0.58 % (1 responder) was ASIA E. There was no significant difference in pain type (neuropathic vs nociceptive) based on ASIA classification (χ^2 = 0.112). Those classified as ASIA C were more likely to be classified as nociceptive pain by the SCIPI than those in other ASIA classifications (20.5 % in C vs 12.2%, 9.1%, 10.7% for A, B, and D respectively). Mean nociceptive pain scores, as measured by the PROMIS-No, remained relatively stable across all ASIA classifications (A = 52.5, B = 51.0, C = 52.8, D = 50.2; p=.691; Table 3). However, subjects with progressively more incomplete injuries had higher mean PROMIS-Neur scores and trended toward significance (A = 52.1, B = 55.0, C = 55.8, D = 57.7; p=.161; Figure 2). Subjects classified as motor incomplete (ASIA C & D) had similar PROMIS-No scores ($\overline{x}$ =51.8) when compared to motor complete (AISA A & B) pain scores ($\overline{x}$ =52.0). Although not statistically significant, those with motor incomplete injuries reported higher PROMIS-Neur scores ($\overline{x}$ = 56.5) than motor complete ($\overline{x}$ =53.2) with a trend toward significance (p=.061).

There was no difference in reported pain type when grouping higher (cervical and thoracic) and lower (lumbar and sacral) levels of injury (χ^2 = 0.767). Lumbar and sacral injuries were associated with higher PROMIS-Neur ($\overline{x}$ =58.9 vs $\overline{x}$ = 54.7) and PROMIS-No ($\overline{x}$ =56.7 vs $\overline{x}$ = 51.5) scores when compared to cervical and thoracic injuries. Although this trend was noted,

the difference was not significant for PROMIS-Neur (T = -1.476, p .143) but trended towards significance for PROMIS-No (T = -1.977, P = .051).

Eighty-two percent of the surveyed population were >5 years from initial injury. Length of time since injury did not significantly impact the type of pain (χ^2 = 0.726), nor overall pain scores experienced. There was, however, a trend that respondents with injuries >5 years old had higher average PROMIS-Neur ($\overline{x}$ = 55.3) and PROMIS-No ($\overline{x} = 52.8$) scores when compared to injuries <5 years old ($\overline{x}$ = 54.4 and $\overline{x} = 49.2$), though this difference was not significant (T = -.376 , P = .708; T = -1.656, P =.101).

Similarly, patients with higher degrees of reported pain(>5) during their initial hospital stay did not have significantly different breakdown of pain type (nociceptive vs neuropathic pain) when compared to those with lower levels of reported pain (χ^2 = .320). Participants recalling >5 on the Stanford pain scale at initial hospital stay reported significantly higher PROMIS-Neur ($\overline{x}$ = 56.35) than respondents with Stanford pain scales <4 at initial hospital stays (($\overline{x} = 52.1$) (T =-2.114; p =.037) (Figure 3). Similarly, individuals who recall having >5 on the Stanford pain scale during their initial hospital stay reported significantly higher PROMIS-No scores ($\overline{x} = 53.2$) than those with <4 during their initial hospital stay ($\overline{x} = 48.8$) (T =-2.413; p =.018) (Figure 3).

Thirty-nine percent of respondents were employed to some degree, but there was no significant difference in type of pain based on employment status (χ^2 = 0.957). There was no

difference in PROMIS-No ($\overline{x}$ = 52.4 vs $\overline{x}$ = 51.4) or PROMIS-Neur ($\overline{x}$ = 55.5 vs $\overline{x}$ = 54.7 based on employment status (T = -.429 , P = .668; T = -.632, P = .529).

Fifty-five percent of respondents reported shoulder pain. Those with tetraplegia were more likely than those with paraplegia (thoracic, lumbar, or sacral injuries) to have shoulder pain (p=.049). Respondents who reported having their worst or second worst pain affect their shoulders had significantly higher PROMIS-No scores ($\overline{x}$ = 54.3 vs $\overline{x}$ = 50.6)(T =2.136; p =.030) but not PROMIS-Neur scores (Table 4).

A summary of SCIPI groups and variables can be reviewed in Table 1. PROMIS-Neur and PROMIS-No scores for each group can be reviewed in Table 2.

DISCUSSION:

Most individuals with SCI experience chronic pain regardless of mechanism of injury or ISNSCI scores. The demographics of this survey population are generally consistent with the population demographics of the those with SCI in the United States. Results of the current study suggest that most individuals with SCI (81%) have chronic pain and most of those (86%) experience neuropathic pain, which is within the range reported for most of the SCI pain literature [7,10,13,14,21].

Neuropathic pain after SCI is likely a unique phenotype of neuropathic pain that originates from disruption of spinal modulation pathways as opposed to similar 'neuropathic' conditions like a

peripheral nerve injury or post-stroke neuropathic pain[22]. Neuropathic pain manifests differently at and below the level of injury. Neuropathic pain at the level of injury is likely caused by injury to the nerve roots and spinal cord at that level as compared to neuropathic pain below the level of injury, which is likely related to disruption of longer neuronal pathways from the lesion[10,21].

Our results suggest that the completeness of the SCI correlates inversely with the degree of neuropathic pain experienced—complete injuries had a lower mean pain score compared to those with progressively more incomplete injuries (Table 2). This may be related to the way descending modulation pathways in the spinal cord are disrupted by injury, creating intermittent, incomplete, and abnormal transmission of signal across the damaged area of the cord. A similar mechanism is proposed to explain why spasticity is worse in incomplete spinal lesions[23]. As previously noted, level of completeness was recorded by patient report and not confirmed with examination or medical record review as such measures are unlikely to significantly impact the overall accuracy of the data collected. This population is knowledgeable about their injuries and the aforementioned classification system. Given the frequency that patients report such scores, there is a high degree of confidence in the accuracy of these responses. Though, a small degree of error is introduced and may contribute to some uncertainty in our final data analysis.

In addition to pain at and distal to the level of injury, patients with SCI often develop shoulder pain, regardless of the level of injury. Those who rated the shoulder as their first or second

most painful area reported higher PROMIS-No scores than the rest of our population. Individuals with paraplegia often develop nociceptive shoulder pain from overuse[24]. Years of relying on the shoulder girdle for weight shifts, transferring, and mobility (propelling a manual wheelchair) can lead to a spectrum of rotator cuff pathology. From acute tendonitis to chronic complete rotator cuff tears, these injuries can all result in chronic shoulder pain[25].

In the current study, those with tetraplegia were significantly more likely than those with paraplegia to report shoulder pain. Alternatively, individuals with higher cervical injuries (C3-5) may develop shoulder pain secondary to spasticity and shoulder subluxation. In addition to pain, a weak shoulder struggles to position the hand in space to perform activities of daily living[26]. This abnormal scapular kinesis may lead to the entire spectrum of rotator cuff pathology seen in paraplegia. Scapular dyskinesis is a well-known etiology of shoulder pain, but may be secondary to other conditions[27,28]. Higher levels of injury may result in decreased shoulder range of motion. This has been linked to increased shoulder pain in this population[29]. Functional substitution of stronger muscle groups such as the trapezius may lead to suboptimal positioning of the scapula further predisposing the shoulders to injury. Taken in total, the current study suggests the shoulder is a common pain generator and the shoulder pain experienced by both those with paraplegia and tetraplegia is more consistent with nociceptive pain than neuropathic pain.

With regard to level of injury, lumbar or sacral injuries trended towards having more nociceptive pain and also reported the highest PROMIS-Neur scores of any subgroup analyzed,

268 although the mean score was not significantly different from that of the cervical/thoracic
269 group. There is some literature that cauda equina injuries are particularly painful[14]. It is
270 suspected that both of these differences would have been significant if the number of subjects
271 was higher, as there were only 17 lumbar/sacral injuries in our sample.
272
273 Females reported significantly higher levels of neuropathic pain (PROMIS-neur), but not
274 nociceptive pain (PROMIS-no). However, there was a similar distribution of females and males
275 with neuropathic and nociceptive pain ($\chi^2 = 0.341$). As such, sex did not predispose patients to
276 developing neuropathic or nociceptive pain. It is possible this is not a true reflection of the
277 demographics of women with SCI as our sampled population was heavily skewed in favor of
278 males. It has been noted in prior studies, however, that women report more below-level
279 neuropathic pain after SCI in the past[30]. This phenomenon has also been noted with other
280 neuropathic conditions such as polyneuropathy[31]. Some suggest sex may be an important
281 factor in the modulation of pain[32,33]. Additionally, a review on prevalence of chronic pain
282 after SCI found sex to have a small impact on the experience of pain[13].
283
284 Understanding the trajectory of the pain course is of vital importance to those who treat SCI
285 related pain. The current study was not designed to track pain over time, however, there was a
286 correlation between the recollection of a painful acute hospital stay and current levels of
287 neuropathic and nociceptive pain. This may suggest that those with more pain at the onset of
288 injury will also experience more chronic pain. Alternatively, there could be recall bias where
289 those who develop more chronic pain recall always being in more pain. This distinction is

important as it may impact patient prognosis, goals and expectations. A longitudinal study tracking pain severity over time would help elucidate this question.

The current study is not without limitations. This survey was distributed through our model system database which covers the Delaware Valley and could introduce regional bias. There were a number of statistical categories, mainly those assessing nociceptive pain, where our sample size was small enough to introduce the possibility of Type II error. Additional studies with larger samples size spanning a broader part of the country would be warranted to eliminate the possibility of a regional bias, better understand how sex impacts pain in patients with SCI, and compare the quality and severity of pain to the level of injury.

In summary, this survey suggests neuropathic pain is the predominate pain after spinal cord injury. In our sample, 81% of individuals experience chronic pain and 86% of those with pain are classified as having neuropathic pain. Overall, individuals with SCI report higher levels of neuropathic and nociceptive pain compared to the general United States population. Those who reported higher levels of current nociceptive and neuropathic pain were more likely to report higher levels of pain during their initial hospital stay. Females were more likely to report higher levels of neuropathic pain but not nociceptive pain than males. Incomplete injuries trended toward producing a phenotype with more neuropathic pain and possibly nociceptive pain than complete injuries and lumbar/sacral injuries trended toward producing a phenotype with more nociceptive pain. Shoulder pain afflicted 55% of individuals surveyed. Those with tetraplegia were more likely to develop shoulder pain than those with paraplegia and those

who reported their first or second worst pain to be shoulder pain had significantly higher nociceptive pain scores. Understanding these pain demographics will enable physicians to better predict complications, take down barriers to improvement, and optimize care for patients with SCI.

DATA ARCHIVING: Data has been stored in a secured Survey Monkey account

CONFLICT OF INTERESTS: None

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FIGURE LEGENDS:

FIGURE 1: Women report higher levels of neuropathic pain but not nociceptive pain after SCI
FIGURE 2: Neuropathic and Nociceptive pain scores based on ASIA level
FIGURE 3: Neuropathic and Nociceptive Pain scores based on recall of degree of pain during initial hospitalization

TABLES and FIGURES:

TABLES:

Table 1: Categorical Variation in Pain Quality

Sub-Group		Number of patients	Neuropathic Pain Group	Nociceptive Pain group	Chi Squared Value	Significance value
Age	<55	70	60	10	.005	.942
	>55	65	56	9		
Sex	Male	94	79	15	.908	.341
	Female	41	37	4		
Mechanism of Injury	Penetrating	14	14	0	3.402	.183
	Non-penetrating	117	98	19		
AISA Classification	A	41	36	5	8.930	.112
	B	22	20	2		
	C	39	31	8		
	D	28	25	3		
Completeness	Complete (ASIA A/B)	63	56	7	.767	.381
	Incomplete (AISA C/D)	67	56	11		
Level of Injury	Cervical or thoracic	118	101	17	.086	.770
	Lumbar or sacral	17	15	2		
Time Since Injury	≤5 years	24	20	4	.123	.726
	>5 years	108	93	15		
Degree of pain at initial stay	<5	37	30	7	.989	.320
	≥5	98	86	12		
Employment status	Yes	49	42	7	.003	.957
	No	86	74	12		

*Neuropathic and nociceptive pain groups derived from SCIPI (neuropathic = SCIPI $\geq$2; nociceptive = SCIPI <2).
ASIA = American Spinal Injury Association [Impairment Scale]

Table 2: Pain Severity

Sub-Group		Mean Neuropathic Pain Score	T-value	p-value	Mean Nociceptive Pain Score	T-value	p-value
Age	<55	56.0	.906	.367	52.9	1.042	.300
	>55	54.3			51.1		
Sex	Male	54.0	-2.053	.043^	52.0	.008	.994
	Female	58.0			52.0		
Mechanism of Injury	Penetrating	57.5	-.869	.387	55.9	-1.692	.094
	Non-penetrating	55.1			51.5		
Completeness	Complete (ASIA A/B)	53.2	-1.891	.061†	52.0	.113	.910
	Incomplete (ASIA C/D)	56.6			51.8		
Level of Injury	Cervical or thoracic	54.7	-1.476	.143	51.5	-1.977	.051†
	Lumbar or sacral	58.9			56.7		
Time Since Injury	≤5 years	54.4	-.376	.708	49.2	-1.656	.101
	>5 years	55.3			52.8		
Degree of pain at initial stay	<5	52.2	-2.144	.037^	48.8	-2.413	.018^
	≥5	56.4			53.3		
Employment status	Yes	54.7	-.429	.668	51.4	-.632	.529
	No	55.5			52.5		

*Neuropathic and nociceptive pain scores derived from neuropathic 5a (PROMIS-Neur), PROMIS nociceptive 5a (PROMIS-No) values. ASIA = American Spinal Injury Association [Impairment Scale]

^statistical significance (p <.05)

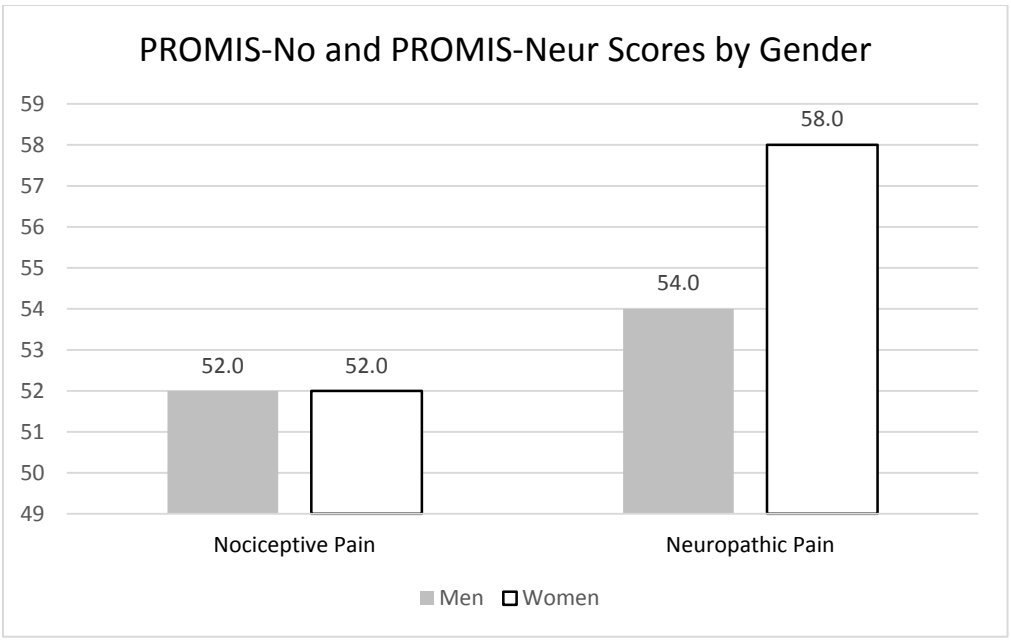
†trending towards statistical significance (p>.05 and <.10)

Table 3: Pain Severity by ASIA Classification

		Mean Neuropathic Pain Score	ANOVA Significance	Mean Nociceptive Pain Score	ANOVA Significance
AISA Score	A	52.1	.161	52.5	.691
	B	54.9		51.0	
	C	55.8		52.8	
	D	57.7		50.2	

*Neuropathic and nociceptive pain scores derived from neuropathic 5a (PROMIS-Neur), PROMIS nociceptive 5a (PROMIS-No) values. ASIA = American Spinal Injury Association [Impairment Scale].

FIGURE 1:



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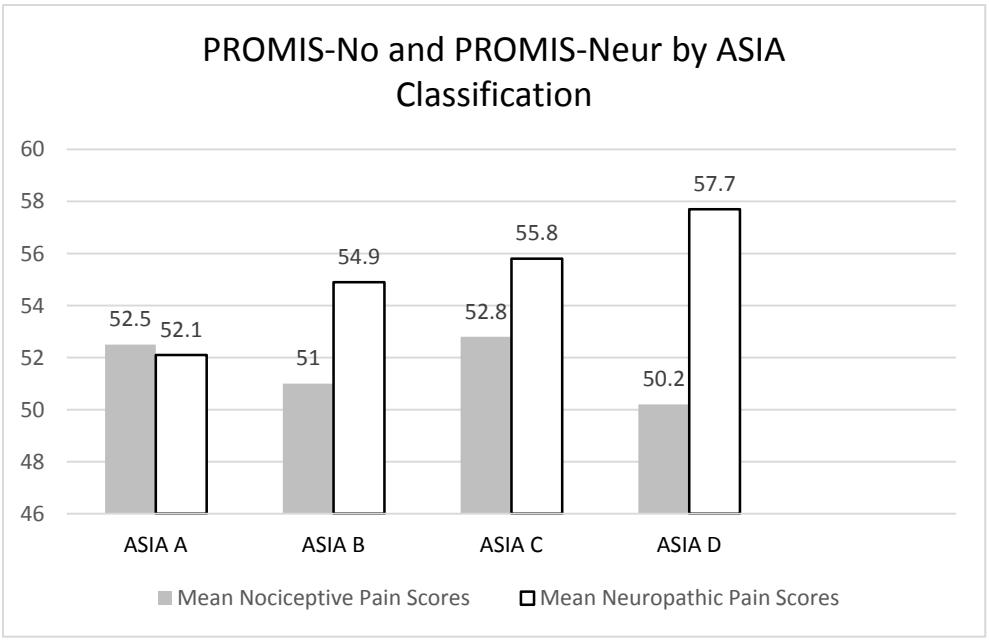
453 **FIGURE2:**



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455 **FIGURE 3:**

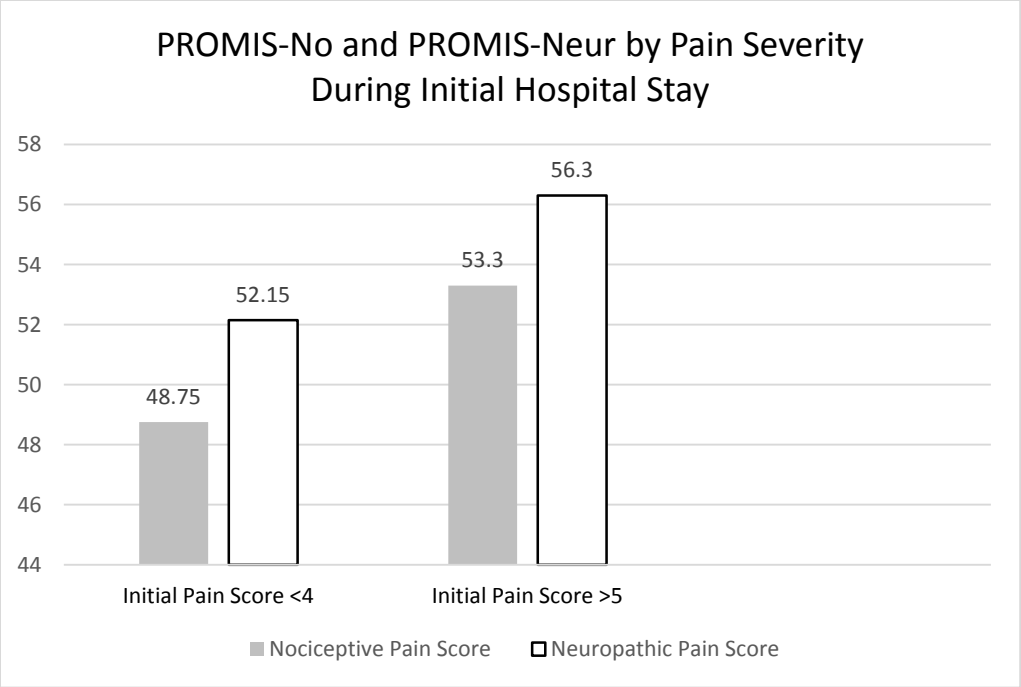

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FIGURE 1: Women report higher levels of neuropathic pain but not nociceptive pain after SCI

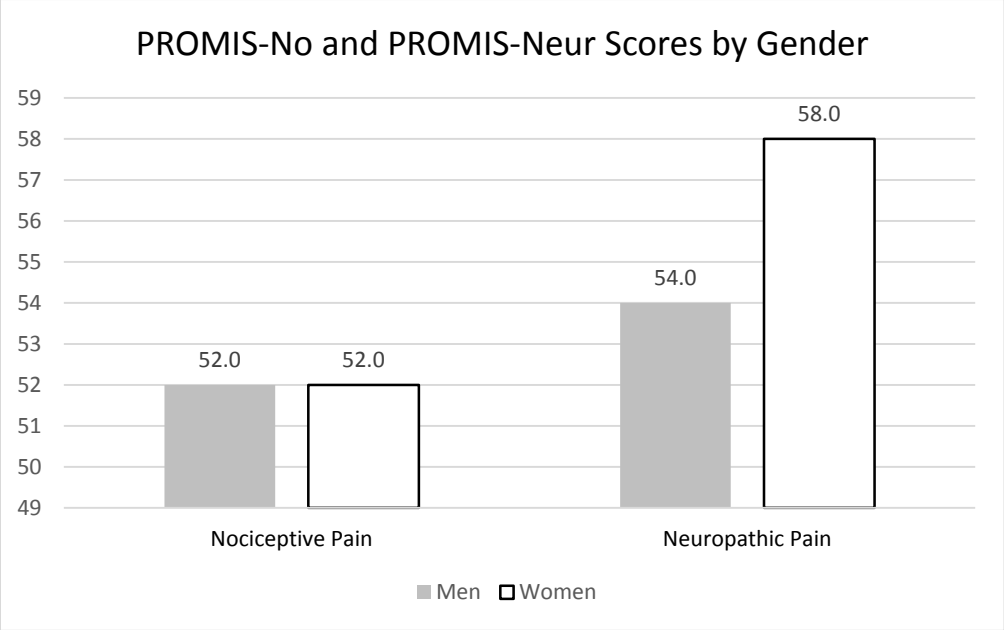


FIGURE2:

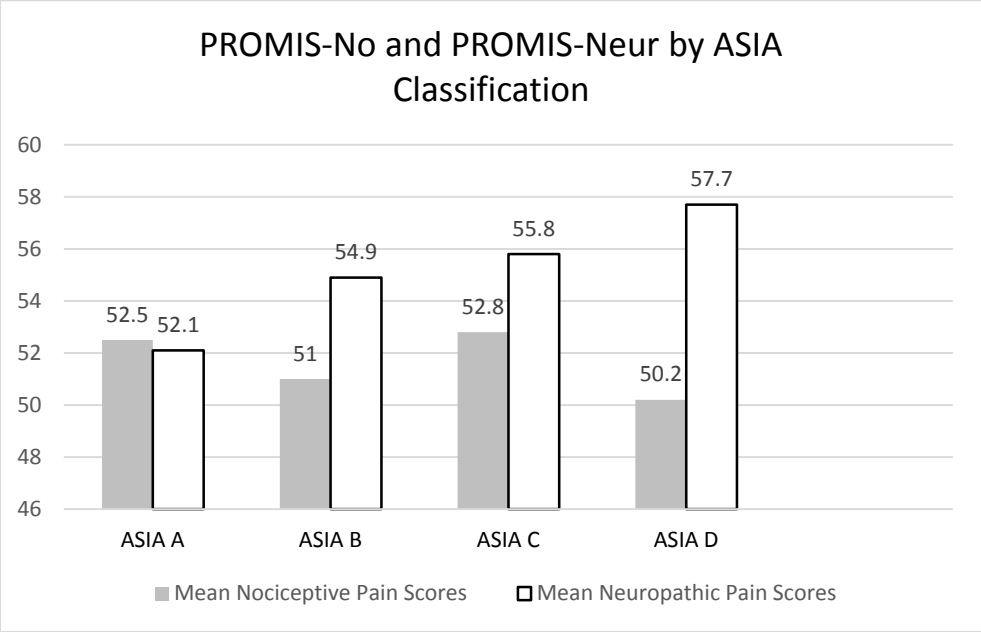
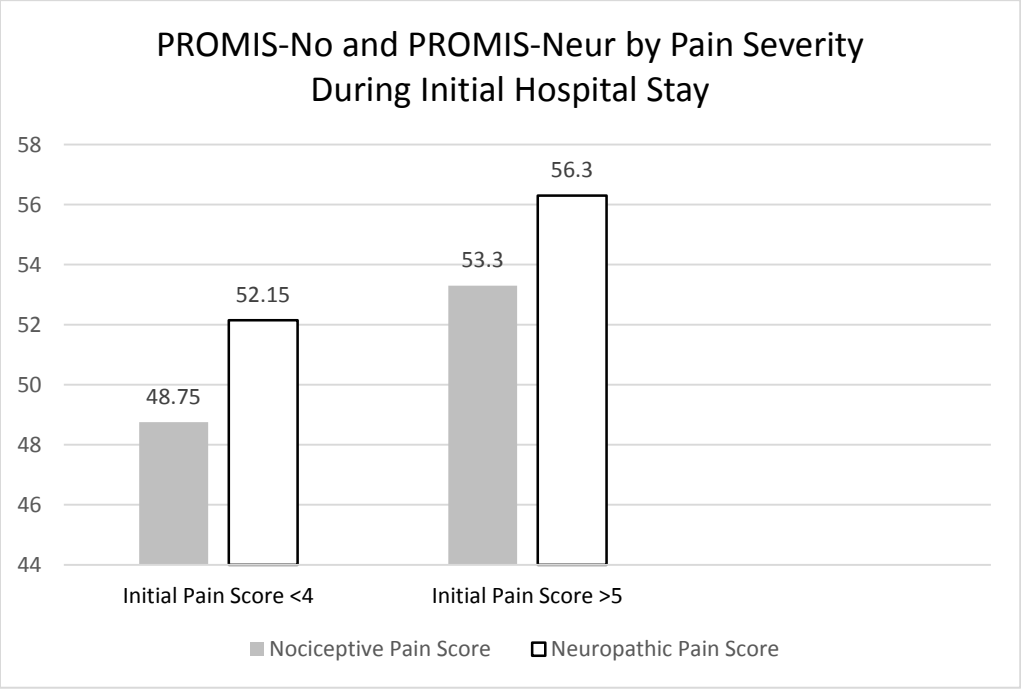

PROMIS-No and PROMIS-Neur by ASIA Classification
60
58
56
54
52
50
48
46
52.5
52.1
51
54.9
52.8
55.8
50.2
57.7
ASIA A
ASIA B
ASIA C
ASIA D
Mean Nociceptive Pain Scores
Mean Neuropathic Pain Scores

FIGURE 3:


PROMIS-No and PROMIS-Neur by Pain Severity During Initial Hospital Stay
58
56
54
52
50
48
46
44
48.75
52.15
53.3
56.3
Initial Pain Score <4
Initial Pain Score >5
Nociceptive Pain Score
Neuropathic Pain Score

TABLES:

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