Classification of Chronic Neck Pain as Neuropathic, Nociceptive or Mixed According to Different and a Composite Categorization System(s): A Longitudinal Cohort Study

COL Richard Liu, MD,[1] Connie Kurihara, RN,[1] Hueting Tsai, PhD,[2] MAJ Peter J. Sylvestri, DO;[1] Michael I. Bennett, MD,[3] Paul F. Pasquina, MD,[4] Steven P. Cohen, MD[1,4,5]

[1] Department of Anesthesiology, Walter Reed National Military Medical Center, Bethesda, MD; [2] Dept. of Oncology, Georgetown University School of Medicine, Washington, DC; [3] Dept. of Palliative Medicine, Leeds Institute of Health Sciences School of Medicine, Leeds, UK; [4] Dept. of Physical Medicine & Rehabilitation, Uniformed Services University of the Health Sciences, Bethesda, MD; Depts. of Anesthesiology and Physical Medicine & Rehabilitation, Uniformed Services University of the Health Sciences; [5] Depts. of Anesthesiology & Critical Care Medicine and Physical Medicine & Rehabilitation, Johns Hopkins School of Medicine, Baltimore, MD

Address correspondence to:
Steven P. Cohen
550 North Broadway, Suite 301
Baltimore, MD 21205
Tel +1 410 955 1822
Fax +1 410 614 7592
E-mail: scohen40@jhmi.edu

The first 2 authors contributed equally to the manuscript

Funded in part by the Centers for Rehabilitation Sciences Research, Bethesda, MD. The role of the funding sources was to provide support for research personnel.

The opinions or assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the Dept. of the Army or the Dept. of Defense.

Conflicts of interest: All authors report no conflicts of interest

Abstract

Neck pain exerts a steep personal and socioeconomic toll, ranking as the 4th leading cause of disability. The principal determinant in treatment decisions is whether pain is neuropathic or mechanical, as this affects treatment at all levels. Yet, no study has sought to classify neck pain as such. To address this, 100 participants referred to an urban, academic military treatment facility with a primary diagnosis of neck pain were enrolled and followed for 6 months. Pain was classified as neuropathic, nociceptive or mixed using painDETECT and s-LANSS instruments, as well as physician designation. The final classification was based on a system consisting of all 3 systems, slightly weighted towards physician's judgment, which is considered the reference standard. We found that 50% of participants were classified as having mixed pain, 43% as having nociceptive pain and 7% with primarily neuropathic pain. Concordance was high between the various classification schemes, ranging from a low of 62% between painDETECT and physician designation for mixed pain, to 83% concordance between s-LANSS and the 2 other systems for neuropathic pain. Individuals with neuropathic pain reported higher levels of baseline disability, were more likely to have a co-existing psychiatric illness, and underwent surgery more frequently than other pain types, but were also more likely to report greater reductions in disability after 6 months. We conclude that although purely neuropathic pain comprised a small percentage of our cohort, half the participants had at least some component. There was significant overlap between the various classification schemes, validating the instruments.

Introduction

Neck pain exerts a substantial socioeconomic toll that transcends geographic and cultural boundaries. According to the 2010 Global Burden of Disease assessment, neck pain ranks as the fourth leading cause of disability in the U.S.[28] In a systemic review on the epidemiology of neck pain, Fejer et al.[11] reported a mean annual prevalence rate of 37.2%, and a lifetime prevalence rate of around 50%. In the armed forces population, approximately 1% of evacuations from theaters of operation involve a primary diagnosis of neck pain, with only 16% of service members returning to their unit.[8,9]

Neck pain is a symptom, not a diagnosis. The etiologies of neck pain are often multifactorial and difficult to identify, though trauma accounts for a significant proportion.[4,6] The heterogeneous nature of neck pain translates into inherent treatment challenges in treatment, which has led to concerted efforts to better categorize and classify the symptom. There are numerous ways to classify neck pain, with categorization into neuropathic and nociceptive pain being perhaps the most relevant, as this has treatment implications at multiple levels (e.g. medical and surgical therapy, referral patterns). For example, common examples of neuropathic pain such as radiculopathy and spinal stenosis are best treated with adjuvants, and for refractory cases epidural steroids and decompression, whereas nociceptive pain conditions such as facet arthropathy and soft-tissue injury may be more likely to respond to nonsteroidal anti-inflammatory drugs, muscle relaxants and facet denervation. Studies also suggest that neuropathic pain may be associated with poorer quality of life than comparable degrees of nociceptive pain.[25] Since the turn of the millennium, several instruments have been developed and validated to facilitate the categorization of myriad pain conditions into

neuropathic and non-neuropathic groupings, such as PainDETECT, s-LANSS (self-completed Leeds Assessment of Neuropathic Symptoms and Signs pain scale) and DN4.[2,3,5,13] There have been over a dozen studies that have used these instruments and other methods to separate low back pain into neuropathic and nociceptive pain. These studies have reported prevalence rates of a neuropathic pain component ranging from 17% to more than 50%,[1,10,24] with one structured review reporting an aggregate rate of 36.6% in 13,518 patients.[12] However, despite its global impact, no study has sought to validate these instruments for neck pain, or sought to quantify the relative proportions that constitute neuropathic and nociceptive pain. This is important, as neck pain may contain different pathoanatomical mechanisms than low back pain, and present unique treatment considerations.[7] The objectives of this longitudinal cohort study were to determine the proportions of patients with a primary pain complaint of neck pain that are neuropathic, nociceptive and mixed in nature; to determine whether treatment, and possibly outcome differences differ between neuropathic and nociceptive neck pain; and to determine the validity of the s-LANSS[3] and painDETECT[13] questionnaires to identify various forms of chronic neck pain by comparing it to a physician-designated reference standard. We hypothesized that neuropathic pain would be associated with greater levels of disease burden, and require higher amounts of resource utilization than nociceptive and mixed pain conditions.

Patients and Methods

Approval to conduct this prospective, observational cohort study was granted by the Walter Reed National Military Medical Center and all participants who provided written informed consent. Enrollment and follow-ups occurred between December 2013 and February 2016.

Participants

All participants were treated in one of two pain treatment centers at Walter Reed National Military Medical Center by a board-certified pain medicine physician. Inclusion criteria for participation included age $\geq$ 18 years, a primary complaint of neck pain, duration $\geq$ 6 weeks, and either an initial visit for neck pain, or failure to respond to previously treatment. Exclusion criteria were previous neck surgery, response to prior treatment (e.g. a patient with neck pain radiating into the arm whose arm pain resolved with an injection or medication), duration > 10 years, and the presence of another pain condition(s) more predominant than neck pain (e.g. shoulder pain or headache).

Classification of Neck Pain

The principal means for neck pain classification was designation by the treating physician who performed a comprehensive history and physical exam, and was privy to the results of radiological studies and other relevant diagnostic tests (e.g. MRI, electrodiagnostic studies, pain drawings). This is considered to be the reference standard for pain categorization, with other instruments, including painDETECT and s-LANSS, using this as the standard for comparison.[3,13] At the time of designation, the treating

physician was blinded to the results of the pain classification questionnaires, though it could be used subsequently to inform therapy. This is consistent with other studies that have sought to validate instruments designed to categorize pain type, which are primarily utilized to supplement physician judgment, to assist non-pain specialists in cataloguing pain and guiding treatment decisions, and for research purposes.

In addition to physician labeling, two questionnaires validated for low back pain taxonomy and other conditions across multiple cultural and ethnic groups were administered in an effort to ensure and enhance diagnostic accuracy: painDETECT and s-LANSS. For the 7-question s-LANSS survey, a score > 11 has been found to denote pain of a predominately neuropathic nature. In order to provide consistency with the other 2 designators, based on the results of studies in which s-LANSS was used to categorize pain conditions that included mixed neuropathic-nociceptive pain[3,23] and discussions with the creator of the instrument (personal correspondence from Michael Bennett, January 2016), we designated a score of 1-11 as being nociceptive pain, 12-18 as mixed pain, and scores between 19 and 24 as indicating pain of predominantly neuropathic origin. painDETECT is a newer 12-item instrument which allows for the possibility of a "mixed pain" category. In painDETECT, a score < 13 indicates a predominately nociceptive origin of pain, a score between 19 and 38 suggests predominately neuropathic origin, and a score between 13 and 18 is categorized as "mixed" pain. Instrument scoring was performed by an investigator blinded to physician-rendered pain designation and clinical information.

The ultimate pain classification was based on both physician-designation and the results of the 2 self-administered questionnaires. A diagnosis of neuropathic pain was

rendered when the physician indicated the pain was predominantly neuropathic, and at least one of the 2 instruments concurred with the designation (i.e. neuropathic or mixed pain). Pain was considered to be nociceptive when a physician label of nociceptive pain was supported by s-LANSS and/or painDETECT (i.e. nociceptive or mixed pain). Neck pain was considered to be mixed when the physician designated it as such and one of the 2 instruments concurred with the classification, or in the case of a discrepancy between what the treating physician noted and both instruments indicated (e.g. the physician considered it to be nociceptive pain whereas both instruments were scored in the neuropathic or mixed range).

Treatment, Follow-up, Data Collection and Outcome

Therapeutic decisions were made by the participant's treating doctor, and were generally independent of survey results. Treatments considered included physical therapies, pharmacotherapy including adjuvants and opioids, alternative therapies, injections, and surgical referral, all of which could be utilized in combination. Baseline data collection included demographic information, pain duration, s-LANSS and painDETECT scores, baseline average neck and arm pain scores over the past week on a 0-10 numerical rating scale (NRS), neck disability index (NDI) score, military status, smoking and obesity status, opioid dose, co-existing psychiatric illnesses and etiology. Six months after enrollment, subjects were called by a disinterested investigator who inquired about additional treatments, and obtained final average neck pain, arm pain and NDI scores, along with a patient satisfaction score on a 1-5 scale (1=very unsatisfied with treatment and outcome results, 2= unsatisfied, 3=neutral, 4=satisfied, and 5=very

satisfied with treatment and outcome results). NDI is a validated, 10-point questionnaire graded on a 0-50 scale converted to a percentage, in which 10%-28% constitutes mild disability, 30%-48% percent indicates moderate disability, and scores above 48% suggest severe or complete disability.[30] A positive pre-defined successful outcome was considered to be a 2-point reduction in neck pain (or arm pain if worse than neck pain) coupled with a satisfaction score ≥ 4.

Statistical Analysis

We assessed the data distribution of each baseline characteristic and calculated means and standard deviation for continuous characteristics with normal distribution (e.g. age, NDI score), and percentages for categorical characteristics. Because data for pain DETECT scores and s-LANSS score were not normally distributed, they are presented as medians and median absolute deviations (MAD). Differences in population characteristics stratified by type of pain were evaluated using one-way analysis of variance (ANOVA) tests for continuous characteristics, Kruskal-Wallis test for pain detect and s-LANSS scores, and Fisher's exact tests for categorical variables. Pain treatment effects and patient satisfaction for the different pain classifications were compared using subgroup differences in mean pain scores at baseline and 6-month follow-up through ANOVA and Fisher's exact tests. To assess agreement between the various classification systems, the percentage of pain-type diagnoses are reported for each method, and simple kappa coefficient calculations were used to gauge concordance between doctors' designation, s-LANSS, and painDETECT questionnaires. Last, the percentage of treatments use for each pain category are reported descriptively, and

compared using Fisher's exact tests. All tests were two-sided, and all analyses were run using SAS V9.3.

Results

128 patients were screened for participation, with 100 being enrolled, and 97 being followed through their 6-month follow-up (see figure 1). The mean age of the participants was 42.17 years, with the average duration of pain being 2.9 years. 61% of participants were male, 75% were on active duty, and 43% reported a traumatic inciting event. Disease burden was in the moderate range, with participants reporting an average neck pain score of 5.28, an average arm pain score of 5.26 in those with extremity pain, and an NDI score of 36.23. 19% of participants were receiving opioid therapy, and 34% presented with a concomitant psychiatric diagnosis. 46 reported radiation of their pain distal to their elbow. Table 1 lists demographic and clinical characteristic of the study population.

Classification

Based on our designated reference standard combining physician classification and the 2 instruments, 7 of participants were considered to have neuropathic pain, 43 nociceptive pain, and 50 mixed pain. There were not significant differences between the 3 classification schemata with regard to the category assignments. PainDetect conferred a diagnosis of neuropathic pain in 20% of participants, which was followed by physician designation (18%) and s-LANSS (7%). Conversely, s-LANSS was the most likely diagnostic schema to assign the label nociceptive pain to a participant's condition (62% vs. 53% for painDetect and 51% for physician designation. Overall, there was strong concordance between the various classification systems, which was highest for

neuropathic pain. Figure 2 illustrates the concordance levels between different diagnostic methods.

Predictive Validity and Scoring Differences

In order to determine the predictive validity and scoring overlap between classification instruments and physician designation, the median s-LANSS and painDETECT scores of patients diagnosed with neuropathic, nociceptive and mixed pain via the survey instruments were compared to the median s-LANSS and painDETECT scores of those diagnosed with the 3 different pain types by physician designation. These results were similar ($\leq$ 3 points difference) for all categories except neuropathic pain. Specifically, the median s-LANSS score of neuropathic pain patients diagnosed via the instrument was 19 vs. 14 in those diagnosed with neuropathic pain by physician determination. For painDETECT scores, the median score in those participants diagnosed with neuropathic pain via the instrument was also higher than in the 18 individuals identified as having neuropathic pain via physician designation (22 vs. 17.5).

Statistical differences in mean s-LANSS and painDETECT scores were noted between those diagnosed with nociceptive pain via the instruments and by physician designation ($p < 0.0001$), but not for mixed or neuropathic pain, suggesting these instruments may not have good predictive validity for these pain types.

When the median s-LANSS and painDETECT scores of those diagnosed with the 3 different pain types by physician designation were compared, there was statistical significant with $p < 0.0001$. However, there is no statistical significant when comparing the neuropathic and mixed groups.

Baseline Differences Between Pain Types

Several baseline differences were noted between pain categories. Females comprised a higher proportion of individuals with neuropathic pain (57%) than those with either nociceptive (40%) or mixed (36%) pain; p= 0.56). There was a trend for those with nociceptive pain to report a longer mean duration (3.49 years $\pm$ 3.05) compared to those with neuropathic (1.35 years $\pm$ 1.77) and mixed (2.59 years $\pm$ 3.14) pain conditions (p=0.14). Participants with neuropathic pain were more likely to have a co-prevalent psychiatric condition than those with other pain types (100% vs. 26% for nociceptive and 32% for mixed, p< 0.0001), and more likely to experience severe levels of disability related to their condition (mean NDI score 47.86 $\pm$ 12.81 SD vs. 31.23 $\pm$ 12.30 for nociceptive pain and 38.90 $\pm$ 16.25 for mixed pain (p= 0.005). Not surprisingly, arm pain scores were higher in the neuropathic vs. the nociceptive and mixed subgroups (6.07 vs. 1.22 and 3.68), but differences in pre-treatment neck pain scores did not approach statistical significance.

Treatments

Treatments differed considerably between pain categories. Compared to patients with nociceptive pain, those with neuropathic and mixed pain were more likely to undergo epidural steroid injections (71% and 60%, respectively vs. 19%, p<0.0001) and receive membrane stabilizers such as gabapentinoids (29%, and 34% vs. 7%, p=0.004). No significant differences were observed between treatment classifications for individuals who underwent facet blocks (14% for neuropathic vs. 37% for nociceptive and 22% for mixed pain; p= 0.22) and trigger point injections (29% for neuropathic vs. 33% for nociceptive and 14% for mixed pain; p=0.07). Neither were any differences were

noted in the prescribing rate of nonsteroidal anti-inflammatory drugs and opioids between the different pain subtypes. Those with neuropathic pain (29%) were more likely to be referred for surgery than those with nociceptive (2%) or mixed (12%) pain (p= 0.04; see figure 4).

Outcomes

For the most part, pain and disability reductions in the cohort with neuropathic pain were greater than those in the other 2 groups at 6-month follow-up, though most differences fell shy of statistical significance (see tables 3 and 4) The reduction in NDI (mean change in baseline for the neuropathic pain group -15.00, 95% CI.: -35.59, 5.59 vs. -10.81, 95% CI -14.65, -6.97 for the mixed pain and -6.63, 95% CI -10.69, -2.58 for the nociceptive pain group; p=0.20) and arm pain scores (mean change in baseline for the neuropathic pain group -3.50, 95% CI -6.95, -0.05 vs. -1.42, 95% CI -2.52, -0.33 for the mixed pain and 0.43, 95% C.I.: -1.24, 0.38 for the nociceptive pain group; p= 0.06) was greater for those with neuropathic pain than other pain categories. For neck pain, those with neuropathic pain (mean 3.93, 95% CI 2.03, 5.82) had similar pain scores at the conclusion of the study compared to those with mixed (mean 3.95, 95% CI 3.24, 4.66) and nociceptive pain (mean 3.69, 95% C.I.: 3.06, 4.31). The difference in the change from baseline for neck pain favoring neuropathic pain (-2.07, 95% CI: -5.03, 0.88 vs. -1.15, 95% CI: -1.89, -0.42 for nociceptive and -1.53, 95% CI: -2.13, -0.93 for mixed pain) did not approach statistical significance. Patients with mixed pain reported higher treatment satisfaction than those with neuropathic and nociceptive pain (p=0.04), but were not more likely to experience a positive outcome.

Adverse Events

23 side effects or procedure-related complications were reported in 19 patients, which included 18% in mixed, 14% in nociceptive, and 57% in the 7 individuals with purely neuropathic pain. All were considered non-serious. In the mixed pain group, the most common cause was gabapentin (n=5), which included sedation/ cognitive effects (n=3) and one case each of weight gain and an allergic reaction. In the nociceptive group, there were 3 cases of procedure-related complications (1 case of post- facet denervation neuritis, and 2 cases of procedure-related discomfort after botulinum toxin and trigger point injections), and 4 instances of medication-related effects, including 2 associated with tramadol (vomiting and feeling "high"). Three of the 4 adverse events in the neuropathic pain group occurred after epidural steroid injections (2 cases of procedure-related pain and 1 of post-injection insomnia), and the other involved a 12-pound weight gain after initiation of gabapentin. In the mixed pain group, there was also one complication after an epidural steroid injection, which involved an emergency room visit for a participant who experienced procedure-related pain the day after the procedure.

Discussion

We conducted this longitudinal cohort study in order to categorize neck pain as neuropathic, nociceptive or mixed/indeterminate, to assess if patients with neuropathic neck pain in the study undergo different treatments compared to patients with mechanical neck pain, and to correlate between 2 validated questionnaires and the providers' accuracy to categorize pain. Our principal finding indicates that although the probability of having predominantly neuropathic pain was relatively low (7%) based on our conglomerated/ amalgamated/ combined system of classification, over half of the participants were likely to have a neuropathic component to their symptoms, defined as the product of neuropathic and mixed pain. The second major finding is that there was significant concordance between the different instruments and each other, the physician designation, and the final diagnosis, for all 3 pain subtypes. These ranged from a low of 52% for complete matching between painDetect and physician designation to a high of 94% between s-LANSS and the final, overarching designation for neuropathic pain. Based on the reference standard of physician-designation, our results suggest there is substantial agreement for both instruments for all pain categories. Our results differ from those of Fishbain et al,[12] who reported significant variations in the prevalence of neuropathic pain in low back pain patients (ranging from 18.2% for DN4 to 54.4% for s-LANSS) based on the method of diagnosis, though individual studies in this review did not utilize different instruments. Individuals with neuropathic pain, though few in number, reported higher levels of baseline disability and a higher co-prevalence rate of psychiatric illness than those with the other 2 pain types, confirming our hypothesis.

Comparison to Other Studies

Despite the burgeoning socioeconomic burden of chronic neck pain,[28] and the plethora of studies that have sought to quantify the proportion of low back sufferers with a neuropathic component,[1,10,13,15,16,24] there have been no similar studies conducted in individuals with cervical pain. In one study performed in 152 people with neck and upper limb pain associated with a suspected nerve lesion that sought to validate s-LANSS (using the bipartite classification system) and painDETECT, Tampin et al.[26] found that 72% had definite or probably neuropathic pain, and 18% had possible neuropathic pain according to the International Association for the Study of Pain Neuropathic Pain Special Interest Group clinical grading system.[29] The authors concluded that both instruments suffered from low sensitivities (painDETECT 64%, s-LANSS 22%) in this population. In a companion study by the same group of investigators evaluating quantitative sensory testing differences between individuals with cervical radiculopathy and those with nonspecific neck and arm pain, Tampin and colleagues[27] found that quantitative sensory testing, but not painDETECT, which had a sensitivity of 30%, was likely to detect neuropathic components in the subgroup with radicular pain.

Whereas the proportion of patients with predominantly neuropathic pain was relatively low in our study, our results are similar to other studies classifying low back pain. Beith and colleagues[1] used painDETECT to stratify 343 patients with chronic low back pain, and reported that 59% had likely nociceptive pain, 25% had mixed pain, and 16% were likely to have neuropathic pain. Freynhagen et al.[13] found that 64.7% of 7772 chronic low back pain patients had either mixed or likely neuropathic pain, which is slightly higher than the 52% in our study. Two other studies that collectively reported on over 2300 patients with chronic LBP used s-LANSS to classify pain into the binary

categories of neuropathic or nociceptive pain.[10,16] Both reported that 55% were predominantly neuropathic, defined as a score $\geq$ 12. Although this might seem higher at first glance than those we classified as having predominantly neuropathic neck pain, according to our scoring system for the s-LANSS instrument based on the work of Bennett et al.[3] and Schestasky et al.[23] that converted a binary system into a tripartite one that contained a mixed category, these 55% of patients had both mixed and neuropathic pain, which is statistically indistinguishable from the 52% in our study that classified chronic neck pain as either mixed or predominantly neuropathic.

Disease Burden

One of our hypotheses was that those individuals who had predominantly neuropathic pain would carry a greater disease burden than those with non-neuropathic pain. In our cohort, the neuropathic pain group presented with a higher co-prevalence rate of psychiatric morbidity, higher pain-related disability, and higher arm pain scores than those with mixed or nociceptive pain; however, neck pain scores and opioid use did not significantly differ between groups. Both Beith et al.[1] and Freynhagen et al.[13] found higher rates of depression and anxiety, higher baseline pain scores, and greater disability levels in patients with neuropathic pain than those with mixed or non-neuropathic pain. In the aforementioned instrument validation study by Tampin et al,[26] the authors reported higher worst neck pain scores in those with definite neuropathic pain, than those with non-neuropathic pain classifications.

The observed differences in treatments were not surprising, with those individuals who presented with neuropathic and mixed pain more likely to receive epidural steroid injections, anticonvulsants and surgery, than those with nociceptive pain. This reflects

standard of care, and is consistent with treatment guidelines based on clinical studies. Whereas those individuals who presented with mixed pain reported higher satisfaction scores, this did not translate into lower pain scores or better categorical treatment outcomes.

Explanation of Findings

One of the principal findings in this study is that fewer than 10% of participants had predominantly neuropathic pain. Nearly all cases of radicular pain, which manifests as arm pain with or without sensory or motor findings, are secondary to either a herniated disc, or central or foraminal stenosis. Yet, these etiologies are usually a result of degenerative conditions (e.g. facet joint arthritis, degenerative disc disease) that also result in mechanical neck pain.[7,14,22] Since neck pain was an inclusion criteria for study participation, it is likely that all of our subjects with neuropathic pain also had a component of nociceptive pain (i.e. we did not include those patients with arm pain in the absence of neck pain), which may have underestimated the epidemiological burden of neuropathic neck pain.

Regarding our mixed results on the question of pain-related disease burden, the difference between our findings and those of Beith et al.[1] and Freynhagen et al,[13] who reported greater levels of disease burden and poorer quality of life across all indices for low back pain, the difference may be explained by a relative lack of power in our study compared to the much larger studies by the other 2 groups. We found that those in the nociceptive pain group had a longer duration of pain than those in the mixed and neuropathic groups, which could reflect differences in the nature of the pathology in the different groups. For example, in the relatively young to middle-aged patients that

comprised a majority of our study population at an academic military treatment facility, herniated disc is the major cause of neuropathic pain. Radiological studies performed in individuals with cervical herniated discs have shown that between 40% and 76% undergo significant resorption,[18,19] which is consistent with large-scale studies that demonstrate that a large majority of individuals with acute cervical radicular pain will experience near-complete resolution of their symptoms.[21] In contrast, the facet joints and degenerated discs comprise the majority of etiologies for chronic cervical pain.[7,14,20] However, unlike pain emanating from a herniated disc, these conditions tend to be progressive in nature.

Limitations

There are several limitations to our study that should be considered when placing our results in context. First, for consistency sake, we converted what was originally a dichotomous system into one with 3 categories, based on the work of other investigators, to include the developer of the instrument.[3,23] Second, in contrast to the work of Tampin et al,[26] who used the IASP clinical grading system as the standard for comparison, and Bennett et al.[3] and Freynhagen et al.[13] who both used physician-designation, our final rendering was based on a combination of physician classification based on all available clinical and test results, and the 2 validated instruments, though physician-designation was given greater weight. This decision was made in acknowledgment that physicians consider not only patient "input" in their final classification, but also diagnostic test results (e.g. MRI); because both instruments have already been validated for spinal pain; and in recognition that no single system is infallible. Finally, our study was performed at a military treatment center, which treats a higher proportion of physically active, young

males than civilian institutions. These individuals may be subject to different physical and psychosocial stressors than their civilian counterparts, which can affect generalizability.

Conclusions

In summary, although only a relatively small percentage of individuals were categorized as having predominantly neuropathic neck pain, half had at least some component of neuropathic pain, and our results may have been excused by having neck pain (rather than only arm pain) as one of our inclusion criteria. There was significantly overlap between the various classification systems and each other, as well as final diagnosis. Individuals with neuropathic pain tended to report greater baseline disease burden, and were treated differently than those with nociceptive and mixed pain, though the differences in outcomes failed to reach statistical significance for most variables.

References

1. Beith ID, Kemp A, Kenyon J, Prout M, Chestnut TJ. Identifying neuropathic back and leg pain: a cross-sectional study. Pain 2011; 152: 1511-6.
2. Bennett M. The LANSS Pain Scale: The Leeds assessment of neuropathic symptoms and signs. Pain 2001; 92: 147-57.
3. Bennett MI, Smith BH, Torrance N, Potter J. The S-LANSS score for identifying pain of predominantly neuropathic origin: validation for use in clinical and postal research. J Pain 2005; 6: 149-58
4. Bogduk N: On cervical zygapophysial joint pain after whiplash. Spine (Phila Pa 1976). 2011; 36
5. Bouhassira D, Attal N, Alchaar H, Boureau F, Brochet B, Bruxelle J, Cunin G, Fermanian J, Ginies P, Grun-Overdyking A, Jafari-Schluep H, Lantéri-Minet M, Laurent B, Mick G, Serrie A, Valade D, Vicaut E. Comparison of pain syndromes associated with nervous or somatic lesions and development of a new neuropathic pain diagnostic questionnaire (DN4). Pain. 2005; 114: 29-36
6. Carroll LJ, Holm LW, Hogg-Johnson S, Côté P, Cassidy JD, Haldeman S, Nordin M, Hurwitz EL, Carragee EJ, van der Velde G, Peloso PM, Guzman J. Bone and Joint Decade 2000-2010 Task Force on Neck Pain and Its Associated Disorders. Course and prognostic factors for neck pain in whiplash-associated disorders (WAD): Results of the Bone and Joint Decade 2000-2010 Task Force on Neck Pain and Its Associated Disorders. Spine (Phila Pa 1976). 2008; 15: 33(4 Suppl): S83-92.

7. Cohen SP: Epidemiology, diagnosis, and treatment of neck pain. Mayo Clin Proc 2015; 90: 284-99
8. Cohen SP, Brown C, Kurihara C, Plunkett A, Nguyen C, Strassels SA. Diagnoses and factors associated with medical evacuation and return to duty for service members participating in Operation Iraqi Freedom or Operation Enduring Freedom. A prospective cohort study. Lancet 2010; 375: 301-9.
9. Cohen SP, Kapoor SG, Nguyen C, Anderson-Barnes V, Brown C, Schiffer D, Turabi A, Plunkett A. Neck pain during combat operations: an epidemiological study analyzing clinical and prognostic factors. Spine 2010; 35: 758-63.
10. El Sissi W, Arnaout A, Chaarani MW, Fouad M, El Assuity W, Zalzala M, Dershaby YE, Youseif E. Prevalence of neuropathic pain among patients with chronic low-back pain in the Arabian Gulf Region assessed using the Leeds assessment of neuropathic symptoms and signs pain scale. J Int Med Res 2010; 38: 2135-45.
11. Fejer R, Kyvik KO, Hartvigsen J. The prevalence of neck pain in the world population: A systematic critical review of the literature. Eur Spine J 2006; 15:834-48.
12. Fishbain DA, Cole B, Lewis JE, Gao J. What is the evidence that neuropathic pain is present in chronic low back pain and soft tissue syndromes? An evidence-based structured review. Pain Med 2014; 15: 4-15.
13. Freynhagen R, Baron R, Gockel U, Tolle TR. painDETECT: A new screening questionnaire to identify neuropathic components in patients with back pain. Curr Med Res Opin 2006; 22:1911-20.

14. Gellhorn AC, Katz JN, Suri P. Osteoarthritis of the spine: the facet joints. Nat Rev Rheumatol 2013; 9: 216-24.

15. Hassan A, Saleh H, Baroudy Y, Abdul-Rahman KI, Najjar MW, Kazi MS, El-Gazar MA, Hafez MA, Abdullah MA, Abdul-Rahman YA, Youseif EA. Prevalence of neuropathic pain among patients suffering from chronic low back pain in Saudi Arabia. Saudi Med J 2004; 25: 1986-90.

16. Kaki A, El-Yaski A, Youseif E. Identifying neuropathic pain among patients with chronic low-back pain: use of the Leeds Assessment of Neuropathic Symptoms and Signs pain scale. Reg Anesth Pain Med 2005; 30: 422-8.

17. Landis JR, Koch GG. The measurement of observer agreement for categorical data. Biometrics 1977; 33: 159–74.

18. Maigne JY, Deligne L. Computed tomographic follow-up study of 21 cases of nonoperatively treated cervical soft disc herniation. Spine (Phila PA 1976) 1994; 19: 189–91.

19. Mochida K, Komori H, Okawa A, Muneta T, Haro H, Shinomiya K. Regression of cervical disc herniation observed on magnetic resonance images. Spine (Phila Pa 1976) 1998; 23: 990-5

20. Onyewu O, Manchikanti L, Falco FJ, Singh V, Geffert S, Helm S 2nd, Cohen SP, Hirsch JA. An update of the appraisal of the accuracy and utility of cervical discography in chronic neck pain. Pain Physician 2012; 15: E777-806.

21. Radhakrishnan K, Litchy WJ, O'Fallon WM, Kurland LT. Epidemiology of cervical radiculopathy. A population-based study from Rochester, Minnesota, 1976 through 1990. Brain 1994; 117: 325-35.

22. Raj PP. Intervertebral disc: anatomy-physiology-pathophysiology-treatment. Pain Pract 2008; 8: 18-44.
23. Schestatsky P, Félix-Torres V, Chaves ML, Câmara-Ehlers B, Mucenic T, Caumo W, Nascimento O, Bennett MI. Brazilian Portuguese validation of the Leeds Assessment of Neuropathic Symptoms and Signs for patients with chronic pain. Pain Med 2011; 12: 1544-50.
24. Selimoglu E, Murat S, Turgut ST, Gurek SY, Icagasioglu A. The prevalence of neuropathic pain in patients with chronic low back pain and its relationships with quality of life, disability and depression. The Turkish Journal of Physical Medicine and Rehabilitation 2013; 59: 293.
25. Smith BH, Torrance N, Bennett MI, Lee AJ. Health and quality of life associated with chronic pain of predominantly neuropathic origin in the community. Clin J Pain 2007; 23: 143-9.
26. Tampin B, Briffa NK, Goucke R, Slater H. Identification of neuropathic pain in patients with neck/upper limb pain: application of a grading system and screening tools. Pain 2013; 154:2813-22.
27. Tampin B, Slater H, Briffa NK. Neuropathic pain components are common in patients with painful cervical radiculopathy, but not in patients with nonspecific neck-arm pain. Clin J Pain 2013; 29: 846-56.
28. The state of US health, 1990-2010. Burden of diseases, injuries, and risk factors. JAMA 2013; 14: 591-608.

29. Treede RD, Jensen TS, Campbell JN, Cruccu G, Dostrovsky JO, Griffin JW, Hansson P, Hughes R, Numikko T, Serra J. Neuropathic pain. Redefinition and a grading system for clinical and research purposes. Neurology 2008; 70:1630–5.
30. Vernon H, Mior S. The neck disability index: A study of reliability and validity. J Manipulative Physiol Ther 1991; 14: 409-15.

Figure Legends

Figure 1: Flow Chart Demonstrating Progression Throughout the Study

Contributions

SPC designed study, participated in data collection, helped consent patients, helped draft protocol and consent, drafted manuscript

RL wrote protocol, helped consent patients, participated in data collection, helped draft manuscript

CK consented most patients and performed most data collection, helped draft figure 1

HT performed statistical analysis, helped draft tables and figures

PS wrote consent form, helped consent patients and participated in data collection

MB helped interpret data and assisted with analysis

PP helped with study design and obtained funding

Declaration of Interests: The authors report no conflicts of interest. SPC has served on the Advisory Boards of Semnur Pharmaceuticals, Halyard, Regenesis, Zynerba, SPR and St. Jude Medical in the past 2 years.

The corresponding author had full access to the data and assumes responsibility for submission of this manuscript (guarantor).

Protocol and statistical code available upon request from corresponding author.