ARTICLES

Neuropathic Pain in Patients with Upper-Extremity Nerve Injury

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ABSTRACT

Purpose: The purpose of this review was to present an analysis of the literature of the outcome studies reported in patients following traumatic upper-extremity (UE) nerve injuries (excluding amputation), to assess the presence of an association between neuropathic pain and outcome in patients following traumatic UE nerve injuries, and to provide recommendations for inclusion of more comprehensive outcome measures by clinicians who treat these patients.

Summary of Key Points: A Medline and CINAHL literature search retrieved 48 articles. This review identified very few studies of patients with peripheral nerve injury that reported neuropathic pain. When pain was reported, visual analogue or numeric rating scales were most frequently used; standardized questionnaires measuring pain or psychosocial function were rarely administered. Recent evidence shows substantial long-term disability and pain in patients following peripheral nerve injury.

Recommendation: To better understand neuropathic pain in patients following peripheral nerve injury, future outcome studies should include valid, reliable measures of physical impairment, pain, disability, health-related quality of life, and psychosocial functioning.

Key Words: literature review, nerve injury, neuropathic pain, outcome

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RÉSUMÉ

Objectif : L'objectif de cette revue était de présenter une analyse de la documentation portant sur les études répertoriées concernant les patients aux prises avec des lésions nerveuses traumatiques des membres supérieurs (excluant l'amputation), d'évaluer la présence d'un lien entre la douleur névropathique et les résultats attendus chez les patients à la suite de lésions nerveuses traumatiques des membres supérieurs et de formuler des recommandations en vue d'inclure le recours à des mesures de rendement plus complètes par les cliniciens traitant ces patients.

Résumé des principales étapes : Une recherche documentaire dans Medline et dans CINAHL a permis de répertorier 48 articles. Cette recherche a permis de constater que parmi les patients souffrant de lésions nerveuses périphériques étudiés, très peu avaient signalé des douleurs névropathiques. Lorsque de la douleur était signalée, des échelles de mesure numériques ou des échelles visuelles analogues étaient utilisées le plus fréquemment et l'on faisait rarement appel à des questionnaires normalisés pour évaluer la douleur ou la fonction psychosociale. Des faits récents démontrent qu'à la suite d'une lésion nerveuse périphérique, de nombreux patients ressentent de la douleur et souffrent d'une incapacité à long terme.

Recommandation : Pour mieux comprendre la douleur névropathique qui survient à la suite d'une lésion nerveuse périphérique, les prochaines études devraient inclure des mesures valables et fiables des déficiences physiques, de la douleur, des incapacités, de la qualité de vie liée à la santé et à la fonction psychosociale.

Mots clés : douleur névropathique, lésions nerveuses, résultats, revue documentaire

INTRODUCTION

The International Association for the Study of Pain (IASP) defines neuropathic pain as pain resulting from a lesion or disease in the peripheral or central nervous system.[1–3] Within this broad categorization, various etiologies may cause neuropathic pain; such pain may occur as a result of trauma, central nervous lesions, or diseases such as diabetic peripheral neuropathy, herpetic nerve lesions, or multiple sclerosis, and each etiology has different implications with regard to assessment and treatment. Many of the studies and reviews in the literature have evaluated neuropathic pain as it relates to disease states or limb amputation, but few have included other traumatic peripheral nerve injuries. Although it is commonly believed that traumatic upper-

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extremity nerve injury may be associated with poor outcomes that are often related to pain, most studies report only physical impairment related to motor and/or sensory recovery. Few studies report neuropathic pain following nerve injury or the impact of the resultant physical impairments on the patient.[4–6]

The purpose of this review was to present an overview of the literature of the outcome studies reported in patients following traumatic upper-extremity (UE) nerve injuries (excluding amputation). We were specifically interested in assessing the presence of an association between neuropathic pain and outcome in patients following traumatic UE nerve injuries and in providing recommendations for inclusion of more comprehensive outcome measures by clinicians.

METHODS

The following specific questions were investigated: In outcome studies of patients with traumatic nerve injury, is persistent pain systematically recorded? Is neuropathic pain reported when present? If it is reported, what types of assessments are used? Are valid measures of UE disability, such as the Disabilities of the Arm, Shoulder and Hand (DASH), used in outcome studies of patients with UE nerve injury?

Search Strategy

The literature for the present review was obtained via an electronic search of Ovid Medline databases (1950–2009), CINAHL (1979–2009), and the Cochrane Database of Systematic Reviews (2005–2009) and through subsequent review of the reference lists of retrieved articles. The search included both subject headings and keywords and included articles up to November 2009. It was limited to the English language and adults, and it excluded amputation injuries, case reports, and abstracts.

To assess the presence of the terms ''neuropathic pain'' and ''health-related quality of life outcome'' in studies of patients with traumatic nerve injury, the initial Medline search used the search string ''*neuropathic pain* AND *quality of life*.'' The term ''quality of life'' was used because it is a Medline subject heading and because, particularly in the surgical literature, this is the term commonly used to refer to disability- and health-related quality of life. We then performed a more extensive Medline search to include broader terms. The search strategy used the following search strings ''‘*brachial plexus* OR *radial nerve* OR *median nerve* OR *ulnar nerve*’ AND ‘*recovery of function* OR *treatment outcome*’ AND *pain*.'' To include all peripheral nerves, we used the following search string: ''*peripheral nerve* AND ‘*pain* OR *pain measurement*’ AND ‘*disability* OR *disability evaluation*’ AND ‘*arm* OR *arm injuries* OR *hand* OR *hand injuries* OR *upper extremity*.’'' The search in the Cochrane Database of Systematic Reviews used the following search string: ''*nerve injury* OR *brachial plexus* OR *median nerve* OR *ulnar nerve* OR *radial nerve*.''

RESULTS

The initial Medline search used the search string ''*neuropathic pain* AND *quality of life*''; this search found 79 citations. Based on the titles and abstracts, 59 articles described neuropathic pain resulting from spinal-cord injuries, amputations, low back, lower-extremity, or non-injury etiologies (e.g., cancer, diabetic neuropathy, herpes, multiple sclerosis); these articles were excluded. The other 20 articles were retrieved for closer examination. None of the 20 articles reported outcomes related only to patients with traumatic UE nerve injury; eight reported outcomes in patients with neuropathic pain resulting from various etiologies, including small samples of patients with nerve injury. The search was also performed in CINAHL, but no additional articles were retrieved.

A more extensive Medline search used broader terms: ''‘*brachial plexus* OR *radial nerve* OR *median nerve* OR *ulnar nerve*’ AND ‘*recovery of function* OR *treatment outcome*’ AND *pain*.'' This search retrieved 330 citations. Review of the titles and abstracts found 31 citations that appeared to be related to traumatic UE nerve injuries; these were retrieved for closer examination. Repeating the search in CINAHL retrieved no additional articles.

To include all peripheral nerves, the search string used was ''*peripheral nerve* AND ‘*pain* OR *pain measurement*’ AND ‘*disability* OR *disability evaluation*’ AND ‘*arm* OR *arm injuries* OR *hand* OR *hand injuries* OR *upper extremity*.’'' This search retrieved 387 citations, including 24 articles related to traumatic UE nerve injuries. Because the DASH[7–14] questionnaire is commonly used to measure UE outcomes, a separate search was conducted using the following search string: ''‘*arm injuries* OR *brachial plexus* OR *radial nerve* OR *median nerve* OR *ulnar nerve*’ AND ‘*recovery of function* OR *treatment outcome*’ AND ‘*disability* OR *DASH*.’'' This search retrieved 108 citations. A review of the titles and abstracts yielded 16 articles that evaluated outcome following nerve injury with consideration of disability and five articles that included evaluation with the DASH. The remaining five articles were not primarily reports of nerve injury outcome but reports of various orthopaedic surgical procedures in which nerve-related complications were reported. The same search was performed in CINAHL; no additional articles were retrieved.

The search in the Cochrane Database of Systematic Reviews retrieved 102 citations. There was one citation relevant to the treatment of radial nerve injuries, but only the protocol was published.

The relevant articles retrieved by these searches on outcomes following nerve injury are presented in Table 1.

Table 1 Characteristics of Included Studies

First Author (Year)	*Sample Size*	*Nerve-Injured Patients*	*Study*	*Outcomes Presented*
Gousheh (2009)[18]	19	19 brachial plexus	Outcome following free muscle transfer	MRC motor grading scale, overall result
Lefaucheur (2009)[61]	16	4 brachial plexus	Motor cortex stimulation for refractory peripheral neuropathic pain	VAS, brief pain inventory, MPQ, sickness impact profile, medication quantification scale
Novak (2009)[6]	84	84 upper extremity	Outcome following traumatic nerve injury	SF-36, DASH
Bertelli (2008)[16]	22	22 brachial plexus	Outcome following surgery	MRC motor grading scale
Bertelli (2008)[15]	36	36 brachial plexus	Outcome following surgery	MRC motor grading scale, pain intensity
Kanpolat (2008)[26]	55	14 brachial plexus	Outcome following DREZ procedure	Pain intensity, life quality, Karnofsky Performance Scale
Ruijs (2008)[88]	8	8 median or ulnar	Cold intolerance following nerve injury	Cold intolerance, thermography
Atherton (2008)[105]	33	33 upper-extremity neuromas	Outcome following surgery	Pain relief
Ahmed-Labib (2007)[4]	31	31 brachial plexus	Outcome following injury and surgery	SF-36, DASH
Ruijs (2007)[100]	107	107 median or ulnar	Cold intolerance after nerve injury	Cold Intolerance Severity Score
Kitajima (2006)[81]	30	30 brachial plexus	Outcome following surgery	SF-36, range of motion
Nath (2006)[20]	40	40 brachial plexus	Outcome following surgery	MRC motor grading scale, telephone interview quality of life questions
Wong (2006)[25]	28	28 median nerve	Outcome following injury	Sensory evaluation, pain intensity, pick-up test
Ricardo (2005)[21]	32	32 brachial plexus	Outcome following injury and surgery	Muscle strength, pain relief
Sindou (2005)[119]	44	44 brachial plexus	Outcome following DREZ procedure	Pain relief
Meiners (2005)[29]	125	125 digital, median, ulnar, or radial	Outcome following nerve injury	Questions regarding RTW, employment, pain, Groningen Activity Restriction Scale
Berman (2004)[107]	48	48 brachial plexus	Effect of cannabis-based extract on pain relief	Pain relief
Davidson (2004)[9]	274	18 brachial plexus	Outcome following injury	DASH
Hazari (2004)[112]	57	57 neuromas	Outcome following surgery	Pain intensity
Hsu (2004)[19]	8	7 adult, brachial plexus	Outcome following surgery	MRC motor grading scale, intra-operative findings, impairment scale
Lefaucheur (2004)[114]	60	12 brachial plexus lesion (radiation induced or traumatic)	Outcome following transcranial magnetic cortical stimulation	Pain relief
Saitoh (2003)[118]	9	6 brachial plexus	Outcome following motor cortex stimulation	Pain relief
Chen (2003)[108]	40	40 brachial plexus	Outcome following DREZ procedure	Pain relief
Bruyns (2003)[43]	96	96 median or ulnar	Outcome following injury	Strength, sensibility, RTW
Kim (2001)[113]	260	260 radial nerve	Outcome following surgery	Motor function recovery, pain relief
Eggers (2001)[28]	103	103 brachial plexus	Report new evaluation system	New classification system for flail upper limb
Samii (2001)[52]	47	47 brachial plexus	Outcome following DREZ procedure	Pain relief
Doi (2000)[17]	32	32 brachial plexus	Outcome following surgery	Motor recovery
Geertzen (2000)[54]	16	16 brachial plexus	Outcome following injury	Pain, muscle strength, Shoulder Disability Questionnaire
Rosen (2000)[46]	19	19 median and/or ulnar	Outcome following surgery	Strength, sensibility, function
Rosen (2000)[58]	70	70 median and/or ulnar	Validity and reliability of an evaluation tool	New assessment tool

First Author (Year)	*Sample Size*	*Nerve-Injured Patients*	*Study*	*Outcomes Presented*
Waikakul (1999)[27]	205	205 brachial plexus	Outcome following surgery	Motor function, pain relief, sensation
Terzis (1999)[22]	204	204 brachial plexus	Outcome following surgery	Motor recovery
Bentolila (1999)[53]	78	78 brachial plexus	Outcome following surgery	Motor recovery, pain relief, RTW, satisfaction
Polatkan (1998)[45]	28	28 median	Outcome following surgery	Sensibility, pick-up test
Sood (1998)[30]	13	13 neuromas	Outcome following surgery	Pain relief, hand function, RTW
Rath (1997)[116]	68	23 brachial plexus	Outcome following DREZ procedure	Pain relief
Emery (1997)[110]	37	37 brachial plexus	Outcome following surgery	Pain relief
Irwin (1997)[87]	389	389 hand and/or forearm	Cold intolerance following injury	Cold intolerance questionnaire
Choi (1997)[5]	32	32 brachial plexus	Outcome following surgery	Telephone questionnaire, satisfaction, employment, life domains
Berman (1996)[106]	19	19 brachial plexus	Outcome following surgery	Pain relief
Tonkin (1996)[24]	47	47 brachial plexus	Outcome following surgery	Motor recovery, MRC motor grading scale
Thomas (1994)[120]	44	44 brachial plexus	Outcome following surgery	Pain relief
Evans (1994)[111]	13	13 neuromas	Outcome following surgery	Pain relief, RTW
Mackinnon (1987)[115]	52	52 neuromas	Outcome following surgery	Pain relief
Dellon (1986)[109]	60	60 neuromas	Outcome following surgery	Pain relief
Mitz (1984)[44]	49	49 ulnar	Outcome following surgery	Strength, sensibility, vascular tests
Rorabeck (1980)[117]	23	23 brachial plexus	Outcome following surgery	RTW

DASH = Disabilities of the Arm, Shoulder and Hand; DREZ = dorsal root entry zone; MPQ = McGill Pain Questionnaire; MRC = Medical Research Council; SF-36 = Short Form Medical Outcomes 36; RTW = return to work

DISCUSSION

Our literature search revealed very few articles that evaluated neuropathic pain and/or disability in patients following peripheral nerve injury. The term "neuropathic pain" is not typically used to refer to pain following a traumatic UE nerve injury. Many of the outcome studies following nerve injury or surgery included only measures of physical impairment and return to work as a measure of function,[15–30] and the studies that did include the DASH[4,6,9] were published more recently.

The IASP defines neuropathic pain as resulting from a lesion or disease in the peripheral or central nervous system, and pain following a traumatic peripheral nerve injury would therefore be classified as neuropathic pain. However, traumatic peripheral nerve injuries, excluding amputation injuries, are not frequently included in the neuropathic pain literature, and there have been few reports of patients with peripheral nerve injuries included among other more common etiologies.[31–35] In a literature review by Jensen et al.,[32] neuropathic pain was negatively associated with health-related quality of life, and stronger associations were demonstrated when pain-specific measures were compared to more generic measures. Numerous etiologies were included in Jensen et al.'s review, and there was no differentiation between types of lesions. An overview of neuropathic pain by Dworkin[31] identified nine common peripheral neuropathic pain syndromes; traumatic injury was not listed among them. Meyer-Rosberg et al. evaluated the burden of illness in patients with neuropathic pain, and their sample of patients included a small number with traumatic peripheral nerve injury.[33] The authors reported a high level of pain with significantly lower SF-36 scores in all domains compared to normative data, but information was not presented on the patients with traumatic peripheral nerve injury specifically.

In the surgical literature, studies that report outcomes following peripheral nerve injuries rarely report information about pain (e.g., pain quality, intensity, frequency of episodes, duration). In a survey of peripheral nerve surgeons, only 52% reported formally assessing pain in patients referred primarily for motor or sensory dysfunction following nerve injury, and in patients referred for pain, the most frequent method of assessing pain was a verbal patient response.[36] This lack of detailed assessment of neuropathic pain in patients with nerve injury parallels the under-representation of pain assessment in the surgical literature following traumatic peripheral nerve injury.

The paucity of material in the literature addressing neuropathic pain resulting from traumatic peripheral nerve injury may be related to the comparatively small number of cases of nerve injury relative to other causes of neuropathic pain and other types of trauma. An urban population survey from the United Kingdom reported a 45% prevalence of chronic pain, 8% of which was of neuropathic origin.[37] The causes of neuropathic pain were not reported in this study. A 3.3% prevalence of neuropathic pain was reported in a study from Austria, in which the majority of subjects identified non-traumatic etiologies as the cause of the pain.[38] The exact prevalence of traumatic nerve injuries is difficult to determine.[39–41] Midha reported that 4,538 trauma patients were seen from January 1986 to December 1994 at a level 1 trauma centre in Ontario, Canada, including 60 patients with brachial plexus injuries.[40] Noble et al. reported the prevalence of upper- and lower-extremity peripheral nerve injuries from the same institution.[41] From January 1986 to November 1996, 5,777 trauma patients were seen; 200 nerve injuries were identified in 162 patients (2.8%). An epidemiological study of humeral fractures from Sweden reported that only 8.5% of injuries involved a radial nerve palsy.[42] These studies reveal a low prevalence of peripheral nerve injuries compared to the overall prevalence of traumatic injuries; however, the morbidity associated with these injuries may be severe, and early comprehensive assessment and intervention are essential for optimal outcomes.

Outcome Measures

Studies that have evaluated outcome following peripheral nerve injury have routinely focused on physical impairment, including sensory and motor dysfunction.[15–22,24,25,43–46] Outcome measures following motor nerve injury usually include manual muscle testing with the Medical Research Council (MRC) grading system, amount of weight that can be lifted, or subjective grading by the researchers on scales ranging from "excellent" to "poor."[47] Patient functional assessment and/or pain evaluation are rarely included in outcome studies. The few studies that have reported pain predominantly included patients following brachial plexus nerve injuries.[15,26,27,48–54] In these studies, traumatic injuries, root avulsions, and injuries proximal to the dorsal root ganglion were associated with more pain; surgical intervention and the timing of surgery relative to injury were identified as important factors in alleviating pain. These outcome studies reported pain intensity and frequency but did not include validated patient-report questionnaires to assess the impact of the pain or impairment on the patient.

Riess et al. reported significant short- and long-term disability following scapulothoracic dissociation relative to patients with brachial plexus nerve injuries.[55] Outcome was evaluated via telephone interviews that included basic questions about UE strength and work. No validated outcome measures were used in this study, and participants were not asked about pain. In another telephone survey, Choi et al. contacted 32 patients with brachial plexus injury and administered quality-of-life questions from the US General Social Survey.[5] Moderately high general life satisfaction and quality of life were reported; 75% of patients reported "significant pain," and 38% were using pain medications.

Rating scales and composite scores have been introduced for the assessment of sensibility, motor function, and impairment following nerve injury. In general, these rating scales and composite scores place very little emphasis on pain, including pain associated with cold sensitivity. The MRC scale is a six-point scale (0–5) based on the function of the muscle against gravity or with manual resistance; modifications of this scale have been described.[56] Highet and Zachary introduced a scale to categorize recovery of sensibility that was later modified by Mackinnon and Dellon.[57] This scale includes a range from "no sensibility" to "complete recovery" and considers touch, two-point discrimination, and pain response. The composite score introduced by Rosen and Lundborg includes three domains (sensory, motor, pain/discomfort);[58] cold intolerance and hyperaesthesia are ranked on a numeric scale, and these two parameters make up the pain/discomfort domain. Aberg et al. presented a method for clinical evaluation following peripheral nerve injury.[59] They investigated the applicability of a battery of clinical tests in a small sample consisting of 15 patients with median nerve injuries and 15 control subjects. The tests in this clinical assessment were sensory recovery (two-point discrimination, cutaneous pressure thresholds, pin prick, thermal thresholds, sensory nerve conduction velocity and amplitude), motor recovery (manual muscle testing, grip and pinch strength, motor nerve conduction velocity and amplitude, needle electromyography), and functional recovery (four questions about function, pain, cold intolerance and dysaesthesia; DASH; motor performance test; Sollerman hand function test; sensorimotor test). Only one question addressed pain (present or absent) and one question addressed cold intolerance (present or absent); the study included no quantification of intensity, frequency, or impact on functional outcome.

Measurement of Neuropathic Pain

Pain is a subjective experience that is best evaluated by subjective patient report. Various approaches have been described for assessing neuropathic pain, ranging from simple verbal rating scales (VRS), numeric rating scales (NRS), and visual analogue scales (VAS) to multi-item, multidimensional questionnaires that measure the quality and intensity of pain. The VAS, NRS, and VRS, which usually provide a unidimensional measure of pain intensity (or pain affect, depending on the scale anchors), are commonly used to measure pain in the clinical setting. Introduced by Melzack in 1975, the McGill Pain Questionnaire (MPQ) is the most frequently used and cited pain questionnaire.[60] However, only one outcome study used the MPQ to assess pain following treatment for neuropathic pain.[61]

The MPQ, developed by Melzack to obtain quantitative and qualitative measures of the experience of pain,[60] yields two global scores: the pain rating index (PRI) and the present pain intensity (PPI). The PRI is the sum of the rank values of the 75 words chosen from 20 sets of qualitative words, each containing two to six adjectives that describe the sensory, affective, and evaluative properties of pain. The lists of pain descriptors are read to patients, who are asked to choose the word in each category that best describes their pain at the moment. The PPI is rated on a scale of 0 (none) to 5 (excruciating). The short-form MPQ (SF-MPQ) was developed by Melzack[62] for use when time is limited and when more information is required than is provided by unidimensional measures such as the VAS. The SF-MPQ consists of 15 adjectives from the sensory ($n = 11$) and affective ($n = 4$) categories of the original MPQ. Each adjective is rated on a four-point scale.

Selection of the optimal treatment approach and/or medication may be optimized by differentiating between nociceptive and neuropathic pain.[63] A modification of the SF-MPQ was recently published that is reliable and valid for patients with both neuropathic and non-neuropathic pain.[64] The two main differences between the SF-MPQ and the revised SF-MPQ-2 are the addition of seven adjectives relevant to neuropathic pain and the inclusion of a 10-point NRS to rate the intensity of each descriptor. Each version of the MPQ has been shown to have at least adequate psychometric properties, and all are reliable and valid measures of acute and chronic pain.[65] Other questionnaires that have been described for assessment of neuropathic pain include the Neuropathic Pain Scale,[66] the Pain Quality Assessment Scale,[67] and the PainDetect.[68] The Neuropathic Pain Scale is a 10-item scale that asks patients to rank various dimensions (intensity, quality, allodynia) of pain on an 11-point NRS. This scale was validated with a diverse group of patients that included those with peripheral nerve injury, and it has been shown to be sensitive to alterations in the quality and intensity of neuropathic pain.[66,69,70] However, the validation of the scale was limited to those patients who attended a chronic pain clinic, and, as outlined by the authors, it may not represent all of the pain qualities that patients with neuropathic pain experience. The Pain Quality Assessment Scale is a 20-item questionnaire modified from the Neuropathic Pain Scale to include more descriptors to differentiate neuropathic and non-neuropathic pain. This scale was validated in 40 patients with carpal tunnel syndrome; the group did not include other etiologies of neuropathic pain.[67] The PainDetect is a 20-item questionnaire developed to evaluate the qualities associated with neuropathic pain.[68] Patients are asked to rank the degree of their symptoms on a scale of 0 to 10 for different qualities of pain; a higher score indicates more pain. This questionnaire was validated in a sample of patients with chronic low back pain; the group did not include patients with a traumatic nerve injury. The authors reported sensitivity of 85% and specificity of 80% in classifying patients with neuropathic pain.[68] Although these findings indicate moderate sensitivity and specificity, this measure has not been validated for use in patients with neuropathic pain following traumatic nerve injury. None of these neuropathic pain questionnaires has been universally accepted, and none has been used exclusively in patients with traumatic peripheral nerve injury.

Assessment of Disability and Health Status

Biopsychosocial models of disablement and health linking the biomedical, social, and personal perspectives have been developed by the World Health Organization (WHO)[71] and by others including Nagi[72] and Verbrugge and Jette.[73] Based on Nagi's model, Verbrugge and Jette described the disablement process as a pathway between active pathology, impairment, functional limitations, and disability, with consideration of other individual and risk factors.[73,74] Within the framework of the International Classification of Function, Disability and Health (ICF) model developed by the WHO, body structures and functions (physiological function), activity, and participation are considered in the context of life domains with interaction between the contextual environmental and personal factors.[71,75] In terms of nerve injury, this model takes into consideration the interaction between the condition after injury (physical impairment and activity performance, including participation) and contextual (personal and environmental) factors.

Generic health measures such as the Short Form Medical Outcomes 36 (SF-36) were designed to assess health status. Responses to the SF-36 may be calculated in eight domains and/or summarized in physical and mental component scores.[76–80] Meyer-Rosberg et al. compared scores on the SF-36 and the Nottingham Health Profile for a diverse group of patients with neuropathic pain.[34] They found that these patients had poorer scores relative to normative values and that patients with high levels of pain scored worse on both measures. In a retrospective chart review, patients with traumatic UE nerve injuries had a significantly lower health status in all SF-36 domains and component scores.[6,78] Ahmed-Labib et al. reported significantly worse health status in all SF-36 scores except general health, vitality, and the mental component score, as well as a higher level of disability, in patients following brachial plexus injury and reconstructive surgery.[4] Based on correlational analysis, the authors concluded that root-avulsion injuries and delayed surgical repair were associated with poorer functional outcome. Kitajima et al. evaluated 30 patients with brachial plexus nerve injuries with a minimum follow-up of 12 months.[81] Compared to the Japanese normative data, the nerve-injured patients had significantly lower health status (physical function, bodily pain, role physical and physical composite score). Generic questionnaires are useful for assessing general health status, but they may be limited in the assessment of UE outcome. Disease-specific questionnaires such as the DASH may be more sensitive to diagnoses and pathologies affecting the upper extremity.

The DASH is a 30-item patient-report measure to assess UE disability that has established psychometric properties.[7,8,11–14,82] Although the DASH is the most validated measure of UE disability, it was not commonly used in the outcome studies found in our literature search. Studies that did evaluate disability with nerve injury reported high DASH scores,[4,6,9,39,83,84] indicating a high level of disability. Novak et al.'s evaluation of patients following UE nerve injury found substantial disability, and this was predicted by pain, older age, and brachial plexus injury.[6] Davidson used the DASH to evaluate 274 patients following UE traumatic injuries, including amputations and brachial plexus injuries; high levels of disability were reported, and these were significantly higher in patients with brachial plexus injuries.[9] Ahmed-Labib et al. evaluated 31 patients following surgery for a brachial plexus injury; assessment included the DASH and SF-36.[4] These patients reported high levels of disability, and their scores for six of the eight SF-36 domains were significantly worse than the normative data. Topel et al. evaluated 33 patients following UE arterial trauma[84] and found that patients with concomitant nerve injury (81%) had more functional deficits, with a significantly higher DASH score and lower SF-36 physical composite score. Patients with a radial nerve palsy following humeral fractures were evaluated by Ekholm et al. using patient-reported outcome, including the DASH and the SF-36;[39] most patients reported low disability levels and good health status. Following digital nerve repair, Bushnell et al. reported low levels of disability as assessed by the QuickDASH.[83] Wong et al. evaluated 146 patients following traumatic hand injuries, both before participation in a rehabilitation program and at discharge.[85] Both DASH scores and QuickDASH scores were included in the data analysis, which showed a high correlation ($r = 0.96$) between these scores at admission and at discharge. There was a significant improvement in DASH scores at discharge; patients who did not return to work reported significantly more disability at both admission and discharge ($p < 0.05$).

Considerations of Cold Sensitivity and Contextual (Psychosocial) Factors

Cold Sensitivity

Cold sensitivity, described as pain or discomfort, stiffness, sensory disturbance, and colour changes with exposure to cold, is frequently reported following traumatic UE injuries.[36,86–89] The terms "cold sensitivity" and ''cold intolerance'' have been used interchangeably in the literature; in this review, the term ''cold sensitivity'' is used, except in cases where reference is made to published studies whose authors have used the term ''cold intolerance.'' The symptoms of cold sensitivity are often attributed to poor outcome following traumatic peripheral nerve injuries and have been reported more frequently in patients with digital amputations and replantations.[86,87,89–100] Several studies have supported the continuation of cold-sensitivity symptoms in patients with hand injuries and nerve injuries and following replantation.[89,91,92,97,101,102] Campbell and Kay evaluated 176 patients following hand injuries, 73% of whom reported cold-related symptoms; most of these were related to pain.[91] Graham and Schofield evaluated patients more than 2 years after hand injury;[86] most of these patients (90% of trauma cases) reported cold intolerance, and only 9% reported an improvement over time. Long-term cold intolerance in patients with hand injuries was evaluated by Nancarrow et al.;[97] 69% of patients reported cold intolerance, and 97% of these patients continued to have symptoms 5 years after injury. Collins et al. reported long-term follow-up of patients after UE nerve injury.[92] Among patients who were at least 5 years post injury, 76% reported cold intolerance, and 87% of these patients reported moderate or severe symptoms. Dabernig et al. evaluated patients after digital replantation, with a mean follow-up time of 5 years.[94] The mean DASH score was 11 (of a possible 100), and cold intolerance was reported by 87% of patients. In a diverse group of patients with neuropathic pain that included traumatic nerve injuries, cold-evoked pain was rated as the most intense pain.[33]

Evaluation of cold sensitivity in the literature is variable and includes verbal scales, patient-report questionnaires, and physical assessment.[86,87,92,93,96,99,103,104] Traynor and MacDermid compared cold immersion and a patient-report questionnaire in healthy control subjects;[104] while both physical and subjective assessments were reliable, they were not significantly correlated with each other. Objective tests such as cold immersion, measurement of rewarming, or arterial pressures may adequately assess vascular status, but these types of assessments provide no indication of the pain and cold symptoms perceived by the patient.[90,98,101,102,104] Patient-report questionnaires such as the Cold Sensitivity Severity Scale, introduced by McCabe et al.,[96] and the Cold Intolerance Symptom Scale,[87,99,100] introduced by Irwin et al.,[87] provide an opportunity for patients to rank their symptoms on a numeric scale. On both scales, a higher score indicates a greater degree of cold sensitivity.

Contextual (Psychosocial) Factors

While pain questionnaires and rating scales (verbal and numeric) can assess the intensity, quality, and frequency of pain and are often used in the surgical literature,[105–120] these types of measures do not evaluate the psychosocial factors that are often associated with neuropathic pain. The European Federation of Neurological Societies has presented guidelines for the assessment of neuropathic pain;[1] a baseline assessment can be achieved with NRS, VRS, or VAS, and more in-depth assessment can include pain descriptors, temporal factors, and functional impact.[1,121] In a recent survey of peripheral nerve surgeons, 75% of surgeons reported that they quantitatively assess pain in patients referred for pain following nerve injury, but very few used a validated questionnaire to assess pain in these patients.[36] Although it is recognized that psychosocial factors may contribute to poor outcomes and ongoing neuropathic pain, these factors are rarely reported in the surgical literature following traumatic peripheral nerve injuries.[6,122–125]

Associated contextual (psychosocial) factors have been shown to play an important role in the experience of chronic pain in other populations. In particular, the role of depression,[126] fear-avoidance,[127] pain catastrophizing,[128] and post traumatic stress disorder (PTSD) symptoms[129] in other chronic pain populations warrants serious consideration and study in patients with traumatic peripheral nerve injuries. Given the traumatic nature of the injuries that these patients have sustained, we believe that it is essential to thoroughly evaluate not only pain but also PTSD symptoms.

PTSD typically develops after exposure to an event or situation that is perceived to be threatening to the physical or emotional integrity of an individual. DSM-IV-TR diagnostic criteria[130] for PTSD cover three symptom clusters: (1) re-experiencing the traumatic event (e.g., nightmares and ''flashbacks''); (2) emotional numbing (e.g., feeling detached from others) and avoidance of thoughts, feelings, and activities associated with the trauma; and (3) increased arousal (e.g., insomnia, exaggerated startle reflex, hyper-vigilance). Recent data show that chronic pain and PTSD are strongly associated.[129,131] One possible reason for the high comorbidity of PTSD and chronic pain may be the substantial symptom overlap common to both disorders, including anxiety and hyper-arousal, attentional biases, avoidant behaviours, emotional lability, and elevated somatic focus. The overlap in symptoms suggests that the two disorders may be mutually maintaining or may share an underlying psychological vulnerability that makes certain individuals more likely to develop one or both disorders. Anxiety sensitivity has been identified as one of the trait vulnerability factors that predispose individuals to developing chronic pain, PTSD, or both.[129] The intractability of the two disorders is not surprising when viewed in the context of mutual maintenance and shared vulnerability models. This underscores the importance of screening for both disorders when either one is present, especially in patients who have sustained a traumatic nerve injury, given the painful and traumatic nature of the precipitating event.

Limitations

The major limitation of this review is the paucity of literature reporting outcomes following nerve injury beyond physical impairment. Assessment following nerve injury should include measures of physical impairment such as range of motion, strength, and sensibility. Pain assessment with questionnaires such as the modified MPQ to assess both neuropathic and nociceptive pain will provide valuable information beyond pain intensity. Additional patient-report questionnaires such as the DASH will provide information about UE disability, and questionnaires to evaluate for symptoms of depression, fear-avoidance, pain catastrophizing, and PTSD symptoms will be useful in identifying concomitant psychosocial factors that may affect outcome.

Future Directions

Assessment of pain in patients with neuropathic pain secondary to traumatic peripheral nerve injuries has lagged behind that of patients with neuropathic pain of other etiologies. The relative lack of information extends beyond measures of pain per se; as described in this review, there is very little information on the associated UE disability, pain disability, or health status of patients with traumatic peripheral nerve injuries. Assessment in future studies should include measures of physical impairment, pain, associated contextual (personal and environmental) factors, and functional outcomes, such as disability, to provide a more comprehensive patient evaluation and the opportunity to maximize patient outcome and minimize morbidity following nerve injury.

KEY MESSAGES

What Is Already Known on This Subject

Neuropathic pain may occur as a result of a number of different causes, and each etiology has different implications with respect to assessment and treatment. Although it is commonly believed that pain as a result of traumatic upper-extremity nerve injury may be associated with poor outcome, most studies report only physical impairment related to motor and/or sensory recovery. Few studies report neuropathic pain following nerve injury or the impact of the resultant physical impairments on the patient.

What This Study Adds

This study highlights the need for assessment in future studies to include measures of physical impairment, pain, associated contextual factors, and functional outcomes, such as disability, to provide a more comprehensive patient evaluation and the opportunity to maximize patient outcome following nerve injury.

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