Nerve Pain after Burn Injury: A Proposed Etiology-Based Classification

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Background: Understanding the mechanism of nerve injury may facilitate managing burn-related nerve pain. This proposed classification, based on cause of nerve injury, was developed to enhance the understanding and management of burn-related nerve pain.

Methods: This retrospective investigation included patients aged 15 years or older admitted to the burn center from 2014 to 2019. Burn-related nerve pain was patient-reported and clinically assessed as pain 6 months or more after burn injury, unrelated to preexisting illnesses/medications. The pain classification consisted of direct nerve injury, nerve compression, electrical injury, and nerve dysfunction secondary to systemic injury. The four categories were statistically analyzed between groups, using 52 variables.

Results: Of the 1880 consecutive burn patients, 113 developed burn-related nerve pain and were eligible for validation of the classification: direct nerve injury, $n = 47$; nerve compression, $n = 12$; electrical injury, $n = 7$; and nerve dysfunction secondary to systemic injury, $n = 47$. Factors, significantly increased, that distinguished one category from another were as follows: for direct nerve injury, continuous symptoms ($p < 0.001$), refractory nerve release response ($p < 0.001$), nerve repair ($p < 0.001$), and pruritus ($p < 0.001$); for nerve compression, Tinel signs ($p < 0.001$), shooting pain ($p < 0.001$), numbness ($p = 0.003$), intermittent symptoms ($p < 0.001$), increased percentage total body surface area burned ($p = 0.019$), surgical procedures ($p < 0.001$), and nerve release ($p < 0.001$); and for electrical injury, Tinel sign ($p < 0.001$), intermittent symptoms ($p = 0.002$), amputations ($p = 0.002$), fasciotomies ($p < 0.001$), and nerve release ($p < 0.001$). Nerve dysfunction secondary to systemic injury was distinguished by significantly less Tinel signs ($p < 0.001$), shooting pain ($p < 0.001$), numbness and tingling ($p < 0.001$), pruritus ($p < 0.001$), fascial excision ($p = 0.004$), skin grafts ($p < 0.001$), amputation ($p = 0.004$), nerve releases ($p < 0.001$), and third-degree burns ($p = 0.002$).

Conclusion: A classification consisting of direct nerve injury, nerve compression, electrical injury, and nerve dysfunction secondary to systemic injury is presented that may guide patient management and research methods, with the goal of improving pain outcomes in burn-related nerve pain. (*Plast. Reconstr. Surg.* 147: 635, 2021.)

It seems axiomatic that a patient with a burn will have acute pain related to the injury itself, acute pain related to the débridement and grafting, and perhaps pain during the healing phases. Burn physicians are well versed in the appropriate pharmacologic treatment of the acute forms of pain. Less well perceived, and less well understood, are the mechanisms involved with the burn patient who has chronic, neuropathic pain at the time of discharge from the burn unit. This chronic pain can affect the reconstruction process. Recently, chronic nerve compression and painful neuromas in burn patients have been described.[1,2]

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The prevalence of chronic pain after burn has been reported to range from a low of 7 percent to a high of 82 percent.[3–12] To understand the mechanisms that can involve the peripheral nerve as a source of pain in this group of patients, a classification of nerve injury in the burn patient must be created. The understanding derived from this classification will permit awareness during the inpatient care of the burn patient, and possibly create diagnostic and therapeutic approaches to manage these patients in the acute setting to prevent the creation of chronic pain. In the outpatient setting, after discharge from the burn unit, this classification has the potential to create diagnostic and therapeutic approaches to manage these patients to relieve their chronic pain.

PATIENTS AND METHODS

Study Design

We performed a retrospective, medical record review approved by The Johns Hopkins Medicine Institutional Review Board (IRB00213320) to collect a cohort of patients admitted to The Johns Hopkins Burn Center from January 1, 2014, through January 1, 2019. The Strengthening the Reporting of Observational Studies in Epidemiology guidelines were adhered to throughout the observational component of the review.[13] We were unable to identify an appropriate Enhancing the Quality and Transparency of Health Research network guideline to adhere to for reporting an evidence-based classification model.[14]

Study Population

Patients included were consecutive, older than 15 years, sustained a burn injury, and were admitted to the burn center. The burn center consisted of the burn wound unit and the burn intensive care unit. Patients were excluded if they had preexisting neuropathic pain caused by an underlying medical illness or medication, or less than a 6-month multidisciplinary coordinated follow-up.

We stratified patients into four categories for comparison by type of nerve injury following their burn. Those categories were as follows: direct nerve injury, nerve compression, electrical injury, and nerve dysfunction secondary to systemic injury. All patients had neuropathic pain lasting greater than 6 months following burn. Pain was self-described clinically as shooting, stabbing, sharp, burning, tingling, pruritus, throbbing, numbness, and intermittent and/or continuous dysesthetic sensations. Although "pruritus" is not typically considered as neuropathic pain, we included it because patients verbalized this symptom. Neuropathic pain was evaluated by a minimum of two health care providers. A trial of one or more "neuropathic" medications was attempted for all patients, typically gabapentin (Neurontin; Pfizer, New York, N.Y.) or pregabalin (Lyrica; Pfizer). Patients were stratified into each nerve injury category based on the symptoms that contributed most to their morbidity on follow-up for simplicity and clarity. It is likely that patients had overlapping causes in different anatomical locations. All patients presented for follow-up visits after being discharged from the burn center.

Variables Analyzed

A total of 52 variables were measured for each of the four categories. These variables consisted of patient demographics, characteristics of pain rated on a 0- to 10-point scale, long-term medications, surgical and nonsurgical treatments, and complications. Variables were searched manually for each patient by notes from all health care providers/staff in electronic medical records. A variable was considered if evaluated and documented by a minimum of a physician and physical therapist or occupational therapist for each patient.

Statistical Analysis

Descriptive statistics were used to compare medians, interquartile ranges, odds ratios, 95 percent confidence intervals, areas under the curve, frequencies, and percentages between demographic and clinical variables based on the nonparametric distribution of population data and small sample sizes. Statistical analyses were performed to compare differences among the four nerve injury categories, followed by differences within each category. Dichotomous variables were assessed using Fisher's exact cross-tabulation tests. After a significant value for the Fisher's exact test was obtained, a post hoc test was run using a Bonferroni test with α of 0.006 from eight cells in a 2×4 contingency table to determine which groups were different.[15] Continuous variables were assessed using the Kruskal-Wallis test followed by the Dunn post hoc test. Univariate analyses were followed by multivariate stepwise logistic regressions adjusting for age, race, body mass index, and percentage total body surface area burned. Analyses outcomes were two-tailed, with a significance level set at α of 0.05. All analyses were performed with IBM SPSS Version 25.0 (IBM Corp., Armonk, N.Y.).

RESULTS

Of the 1880 consecutive burn patients, 113 developed chronic nerve pain (prevalence, 6 percent) after burn injury and were eligible for validation of the proposed classification model. There were statistically significant differences among all four categories of nerve injury ($p < 0.001$) (Table 1). Of the 113 patients with burn-related nerve injury, 47 were categorized as having direct nerve injury, 12 were categorized as having nerve compression, seven were categorized as having electrical injury, and 47 were categorized as having nerve dysfunction secondary to systemic injury (Table 2). Median overall follow-up was 26 months (range, 8 to 55 months).

Direct Nerve Injury

Direct nerve injury was significantly associated with characteristics of continuous pain symptoms ($p < 0.001$) and pruritus ($p < 0.001$) (Table 3). Attempts at treating direct nerve pain with nerve release were not significantly successful ($p < 0.001$); however, nerve repair was significantly associated with the resolution of chronic pain ($p < 0.001$) (Table 4). Median follow-up was 24 months (range, 8 to 52 months). Multivariate analyses resulted in decreased odds of direct nerve injury with the absence of pruritus (OR, <0.001; 95 percent CI, <0.001 to <0.001; area under the curve, 0.818; $p < 0.001$) and nerve repair (OR, <0.001; 95 percent CI to <0.001 to <0.001; area under the curve, 0.469; $p < 0.001$).

Table 1. Proposed Classification System

Diagnosis	Pathophysiology
DNI	Burn excision, graft donor-site harvest, wound healing by secondary intention
NC	Occult before injury, fibrosis during healing, compartment syndrome, compression related to dressing, patient positioning
EI	Nerve in the conduction pathway of the electrical injury
NDSSI	Neuromuscular weakness that develops in patients who are critically ill undergoing prolonged ventilation, acute primary axonal degeneration of sensory and motor nerve fibers, and an associated degeneration of skeletal muscles of unknown cause

DNI, direct nerve injury; NC, nerve compression; EI, electrical injury; NDSSI, nerve dysfunction secondary to systemic injury.

Table 2. Patient Demographics

Diagnosis	DNI (%)	NC (%)	EI (%)	NDSSI (%)	*p*
Sample size	47	12	7	47	
Age, yr					0.037
Median	49	49	34	54	
IQR	21–36	41–55	27–48	47–65	
Sex					0.430
Male	25 (53)	8 (67)	6 (86)	28 (60)	
Female	22 (47)	4 (33)	1 (14)	19 (40)	
Race					0.300
Caucasian	30 (64)	8 (67)	6 (86)	36 (77)	
African American	15 (32)	4 (33)	0 (0)	10(21)	
Other	2 (4)	0 (0)	1 (14)	1 (2)	
BMI, kg/m^2					0.589
Median	27	28	26	25	
IQR	23–30	18–26	23–26	14–23	
%TBSA burned					0.019
Median	7.5	32	9	4	
IQR	4–29	16–65*	5–10	2–15	
Third-degree burn	30 (64)	11 (92)	6 (86)	20 (43)*	0.003
Current everyday smoker	36 (77)	11 (92)	5 (71)	31 (66)	0.323
Recreational drug use	13 (28)	6 (50)	2 (29)	9 (19)	0.183
Prescription drug use	5 (11)	4 (33)	0 (0)	5 (11)	0.153
Substance abuse	14 (30)	8 (67)*	2 (29)	11 (23)	0.043
Alcohol use	19 (40)	3 (25)	0 (0)	11 (23)	0.094
Intubation on mechanical ventilation	15 (32)	8 (67)	2 (29)	13 (28)	0.068
ICU admission	15 (32)	8 (67)	4 (57)	13 (28)	0.883
No. of surgical procedures					<0.001
Median	2	10	6	1	
IQR	1–6	6–20*	6–10	0–2	
Hospital LOS, days					0.130
Median	12	23	15	9	
IQR	8–37	9–47	9–28	3–23	

DNI, direct nerve injury; NC, nerve compression; EI, electrical injury; NDSSI, nerve dysfunction secondary to systemic injury; IQR, interquartile range; BMI, body mass index; %TBSA, percent total body surface area; ICU, intensive care unit; LOS, length of stay.
*Statistically significant value.

Table 3. Pain Characteristics

Characteristic	DNI (%)	NC (%)	EI (%)	NDSSI (%)	*p*
Tinel sign	6 (13)	11 (92)*	5 (71)*	0 (0)*	<0.001
Pain score at discharge					0.109
Median	7	7	7	4	
IQR	4–8	5–7	5–9	0–7	
Pain score long term					<0.001
Median	4	3.5	3	0*	
IQR	2–7	1–5	1–4	0–0*	
Pruritus	32 (68)*	2 (17)	0 (0)	0 (0)*	<0.001
Hyperesthesia	4 (9)	2 (17)	2 (29)	0 (0)	0.006
Burning	23 (49)	5 (42)	3 (43)	1 (2)	<0.001
Shooting	9 (19)	9 (75)*	4 (57)	0 (0)*	<0.001
Numbness	14 (30)	7 (58)*	3 (43)	3 (6)*	<0.001
Tingling	17 (36)	5 (42)	2 (29)	4 (9)*	0.003
Intermittent	12 (26)	9 (75)*	5 (71)*	0 (0)*	<0.001
Continuous	21 (45)*	2 (17)	1 (14)	2 (4)*	<0.001

DNI, direct nerve injury; NC, nerve compression; EI, electrical injury; NDSSI, nerve dysfunction secondary to systemic injury; IQR, interquartile range.
*Statistically significant value.

Table 4. Surgical and Nonsurgical Treatments for Nerve Pain

Treatment	DNI (%)	NC (%)	EI (%)	NDSSI (%)	*p*
Laser	11 (23)	5 (42)	4 (57)	3 (6)*	0.001
Nerve repair	11 (23)*	0 (0)	0 (0)	0 (0)	<0.001
Nerve release	0 (0)*	10 (83)*	4 (57)*	0 (0)*	<0.001
Fat grafting	0 (0)	1 (8)	0 (0)	0 (0)	0.168
PT/OT	35 (74)	11 (92)	7 (100)	22 (47)*	0.001

DNI, direct nerve injury; NC, nerve compression; EI, electrical injury; NDSSI, nerve dysfunction secondary to systemic injury; PT/OT, physical therapy/occupational therapy.
*Statistically significant value.

Nerve Compression

Nerve compression was significantly associated with an increased percentage total body surface area burned ($p = 0.019$), preburn substance abuse ($p = 0.005$), and more surgical procedures ($p < 0.001$) (Table 2). Pain characteristics associated with nerve compression were a positive Tinel sign ($p < 0.001$), shooting pain ($p < 0.001$), numbness ($p = 0.003$), and intermittent symptoms ($p < 0.001$) (Table 3). Fascial excision was significantly higher in those who developed nerve compression ($p = 0.002$) (Table 5). Serotonin-norepinephrine reuptake inhibitor use ($p < 0.001$), opioid use ($p < 0.001$), and treatment by nerve release ($p < 0.001$) were significantly higher in this category (Tables 4 and 6). Compression injury was significantly associated with these patients suffering from an overall complication ($p = 0.003$) (Table 7). Median follow-up was 35 months (range, 8 to 55 months). Multivariate analyses resulted in decreased odds of nerve compression with the absence of a Tinel sign (OR, 0.21; 95 percent CI, 0.002 to 0.22; area under the curve, 0.900; $p = 0.001$), shooting pain (OR, 0.06; 95 percent CI, 0.008 to 0.5; area under the curve, 0.807; $p = 0.007$), serotonin-norepinephrine reuptake inhibitor use (OR, 0.09; 95 percent CI, 0.01 to 0.6; area under the curve, 0.671; $p = 0.015$), opioid use (OR, 0.1; 95 percent CI, 0.02 to 0.6; area under the curve, 0.738; $p = 0.014$), nerve release (OR, <0.001; 95 percent CI, <0.001 to <0.001; area under the curve, 0.896; $p < 0.001$) and overall complications (OR, 0.19; 95 percent CI, 0.04 to 0.99; area under the curve, 0.707; $p = 0.049$).

Electrical Injury

Electrical injury was significantly associated with a positive Tinel sign ($p < 0.001$) and

Table 5. Surgical Burn Treatments over Full Hospital Course

Diagnosis	DNI (%)	NC (%)	EI (%)	NDSSI (%)	*p*
Tangential excision	33 (70)	10 (83)	3 (43)	26 (55)	0.131
Fascial excision	9 (19)	5 (42)*	0 (0)	1 (2)*	0.001
Skin graft	37 (79)	12 (100)	7 (100)	24 (51)*	<0.001
Amputation	7 (15)	5 (42)	4 (57)*	0 (0)*	<0.001
Fasciotomy	1 (2)	1 (8)	5 (71)*	0 (0)	<0.001

DNI, direct nerve injury; NC, nerve compression; EI, electrical injury; NDSSI, nerve dysfunction secondary to systemic injury.
*Statistically significant value.

Table 6. Long-Term Patient Medications to Manage Pain

Medication	DNI	NC	EI	NDSSI	*p*
Gabapentin/pregabalin	32 (68)	10 (83)	3 (43)	33 (70)	0.374
SNRI	2 (4)	5 (42)*	1 (14)	4 (9)	0.006
TCA	2 (4)	2 (17)	0 (0)	5 (11)	0.331
Antiepileptic	0 (0)	0 (0)	0 (0)	2 (4)	0.651
Lidocaine	0 (0)	1 (8)	1 (14)	1 (2)	0.090
NSAID	13 (28)	4 (33)	3 (43)	13 (28)	0.793
Acetaminophen	16 (34)	0 (0)	0 (0)	17 (36)	0.014
Ascorbic acid	2 (4)	0 (0)	1 (14)	5 (11)	0.358
Opioid	16 (34)	9 (75)*	3 (43)	10 (21)	0.005
Tramadol	1 (2)	0 (0)	0 (0)	2 (4)	1.000

DNI, direct nerve injury; NC, nerve compression; EI, electrical injury; NDSSI, nerve dysfunction secondary to systemic injury; SNRI, serotonin-norepinephrine reuptake inhibitor; TCA, tricyclic antidepressant; NSAID, nonsteroidal antiinflammatory drug.
*Statistically significant value.

Table 7. Complications

Complication	DNI (%)	NC (%)	EI (%)	NDSSI (%)	*p*
Hospital infection	9 (19)	3 (38)	2 (29)	5 (11)	0.167
Ventilator-associated events	1 (2)	0 (0)	0 (0)	0 (0)	0.131
Pressure sores	0 (0)	0 (0)	0 (0)	0 (0)	0.168
VTE	1 (2)	1 (8)	1 (14)	0 (0)	0.073
Other complication	2 (15)	4 (38)	0 (0)	4 (44)	—
Overall complications	13 (28)	8 (67)*	3 (43)	9 (19)	0.011

DNI, direct nerve injury; NC, nerve compression; EI, electrical injury; NDSSI, nerve dysfunction secondary to systemic injury; VTE, venous thromboembolism.
*Statistically significant value.

intermittent symptoms (p = 0.002) compared with other categories (Table 3). Amputations (p = 0.002) and fasciotomies (p < 0.001) were significantly higher in patients suffering electrical injury. Compression, followed by nerve release, was significantly higher for treating pain (p < 0.001) in this category (Table 4). Median follow-up was 12 months (range, 8 to 36 months). Multivariate analyses resulted in decreased odds of electrical injury with the absence of amputation (OR, 0.02; 95 percent CI, 0.001 to 0.26; area under the curve, 0.716; p = 0.004) and fasciotomy (OR, <0.001; 95 percent CI, <0.001 to <0.001; area under the curve, 0.842; p < 0.001).

Nerve Dysfunction Secondary to Systemic Injury

Nerve dysfunction secondary to systemic injury was significantly associated with fewer third-degree burns (p = 0.002) (Table 2). Pain characteristics included decreased long-term pain scores with treatment (p < 0.001), absence of signs and symptoms (Tinel sign) (p < 0.001), shooting pain (p < 0.001), numbness (p < 0.001), tingling (p < 0.001), and pruritus (p < 0.001) compared to other categories (Table 3). Significantly fewer surgical burn treatments were associated with systemic injury compared to other categories of pain [fascial excision (p = 0.004) and skin graft (p < 0.001)]. There were no amputations (p = 0.004) for patients with systemic injury compared to other categories of pain (Table 5). Significantly less surgical and nonsurgical treatments for nerve pain were required in systemic injury compared to other categories of pain [laser (p = 0.002) and physical therapy/occupational therapy (p < 0.001)]. There were no nerve releases (p < 0.001) for patients with systemic injury compared to other categories of pain (Table 4). Median follow-up was 26 months (range, 8 to 52 months). Multivariate analyses resulted in increased odds of nerve dysfunction secondary to systemic injury with the absence of symptoms [burning (OR, 42.7; 95 percent CI, 5.3 to 344.4; area under the curve, 0.281; p < 0.001), numbness (OR, 6.5; 95 percent CI, 1.7 to 25.7; area under the curve, 0.336; p = 0.007), tingling (OR, 5.6; 95 percent CI, 1.7 to 18.7; area under the curve, 0.347; p = 0.005), fascial excision (OR, 9.7; 95 percent CI, 1.1 to 84.3; area under the curve, 0.393; p = 0.039), skin grafting (OR, 3.7; 95 percent CI, 1.3 to 10.5; area under the curve, 0.324; p = 0.015), and less required physical therapy/occupational therapy (OR, 3.8; 95 percent CI, 1.3 to 10.9; area under the curve, 0.326; p = 0.012)].

DISCUSSION

By understanding the cause of chronic pain in the burn patient, it may be possible to formulate treatment algorithms to prevent this

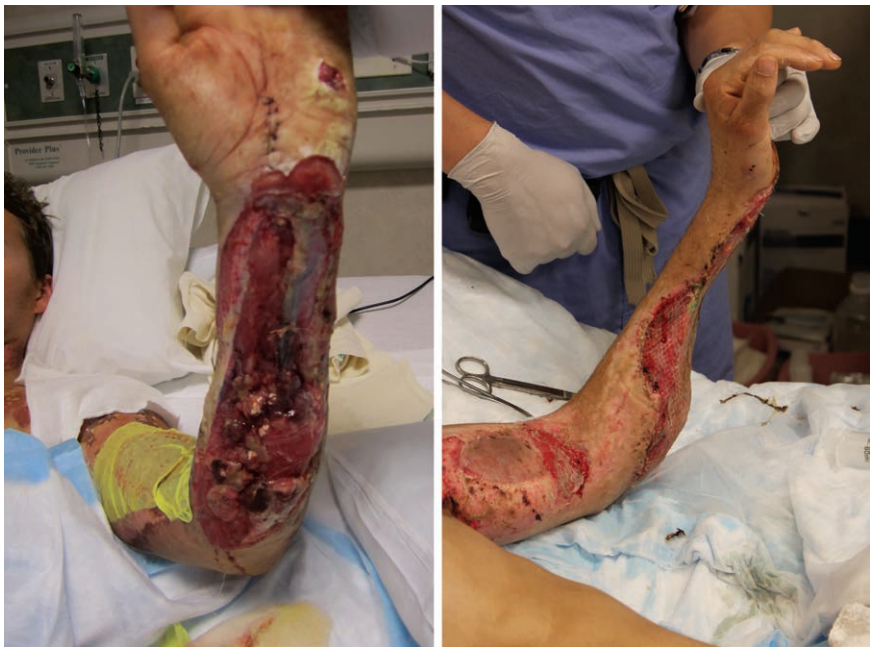

Fig. 1. (*Left*) Direct nerve injury to ulnar nerve and cutaneous sensory nerves after excision. (*Right*) Cutaneous sensory nerves are buried into remaining muscle to prevent neuroma formation. Autologous skin was meshed to provide skin coverage after addressing the nerve injuries.

complication. For example, with direct nerve injury, if during débridement of a wound a cutaneous nerve is divided, this should be recognized and the proximal end of that nerve implanted into a subjacent muscle proximal to the burn or repaired with a graft or allograft (Fig. 1).[16] If a tangential excision of a distal radial forearm wound required the division of the radial sensory and/or the lateral antebrachial cutaneous nerve, an incision could be made in the proximal forearm, away from the burn, and the proximal nerve ends implanted into the brachioradialis muscle.[17] If a proximal anterior thigh wound was débrided and branches of the lateral cutaneous nerve of the thigh were resected, this nerve could be identified at the inguinal ligament level and the proximal end of the damaged nerve divided and relocated into the pelvis.[18] This concept not only permits a proactive approach to prevention of chronic pain but also gives structure to a prospective analysis of this approach in the burn unit.[19]

Peripheral nerve injury, not repairable by physiologic remyelination, collateral sprouting, and axon regrowth can be surgically treated to reestablish continuity.[20] Nerve repair following direct injury was significantly associated with less chronic pain. This repair can be achieved by a direct repair or nerve connection or bridging with nerve transfers, conduits, or grafts.[21–23] In addition to surgery on the burn sites themselves, donor sites can sustain direct injury to free nerve endings during autologous skin grafting. Wound healing by secondary intention will form hypertrophic scar contractures. These scars have altered sensory function compared to uninjured tissues.[24] Direct injury to a peripheral nerve releases neurotransmitters as the wound heals, causing pain and pruritus.[25] Abnormal cutaneous innervation of injured nerve fibers can manifest in a chronic state of pain.[24,25] Forceful physical therapy during rehabilitation may also result in direct nerve injury from overstretching.[26]

With nerve compression, there will be some patients who have had a preexisting carpal tunnel syndrome or subclinical median nerve compression at the wrist. During the resuscitation phase of treatment, the swelling in the extremity makes that nerve compression symptomatic. In the overall treatment of the patient's burn, that relatively "unimportant" tingling in the fingers may not be recognized, leading to chronic pain in the extremity on discharge.[27] Compartment syndrome in an extremity can clearly cause nerve compression, which may persist if the fasciotomies alone do not release the nerve sufficiently. This recognition can lead the burn team to institute regular physical examinations for nerve compression at known sites of anatomical narrowing using the Tinel

sign, and using a noninvasive and nonpainful tuning fork for the evaluation of sensibility.[28,29] Tight dressings, compression garments, and incorrect splinting or positioning in their bed or on the operating room table can result in nerve compression unrelated to the burn itself.[26] Compression injuries should be recognized and prevented during the recovery period (Fig. 2).

Patients that did not undergo surgical nerve release were more likely to require opioids and serotonin-norepinephrine reuptake inhibitors to manage pain. Neuroma excision without proper management of the transected nerve is likely to result in the conversion of a nerve compression into a direct nerve injury. If the nerve is transected during neuroma excision, reestablishing continuity or burying the nerve in the muscle can reduce chronic pain symptoms. Improper initial diagnosis and management may increase long-term patient morbidity by overprescription of opioid and antidepressant medications to manage their pain instead of surgical treatment of the nerve injury.

Nerve compression was significantly associated with patients suffering from overall complications. For example, there were four patients with heterotopic ossification, two with cellulitis infections, one with necrotizing fasciitis infection, and one with a deep vein thrombosis. *Pseudomonas aeruginosa* was identified in blood cultures from two patients who had chronic pain related to nerve compression.

Electrical injury is known to cause the highest incidence of nerve injury among burn patients.[30] Electrical energy prefers to travel through nerve rather than tendon or bone, and creates a heat "sink" at a joint. The heat generated from electrical energy can directly injure a nerve; encase the nerve in fibrous tissue; or indirectly create damage through local inflammation, edema, and vascular damage.[31–38] Therefore, a peripheral nerve can be directly thermally injured and have to be reconstructed with a graft, or entrapped and decompressed. Acute and delayed timings of surgical decompression have both been shown to be efficacious in reducing pain symptoms in the upper and lower extremities.[5,8,19,32,39–41] Amputations and fasciotomies were more common after electrical energy (Fig. 3). These surgical procedures can directly injure peripheral nerves, creating a direct nerve injury. Symptoms may present with immediate onset, delayed onset, or a gradual progression.[32] These damaging effects often occur without noticeable cutaneous involvement and may lead to neuropsychiatric morbidity.[32,42]

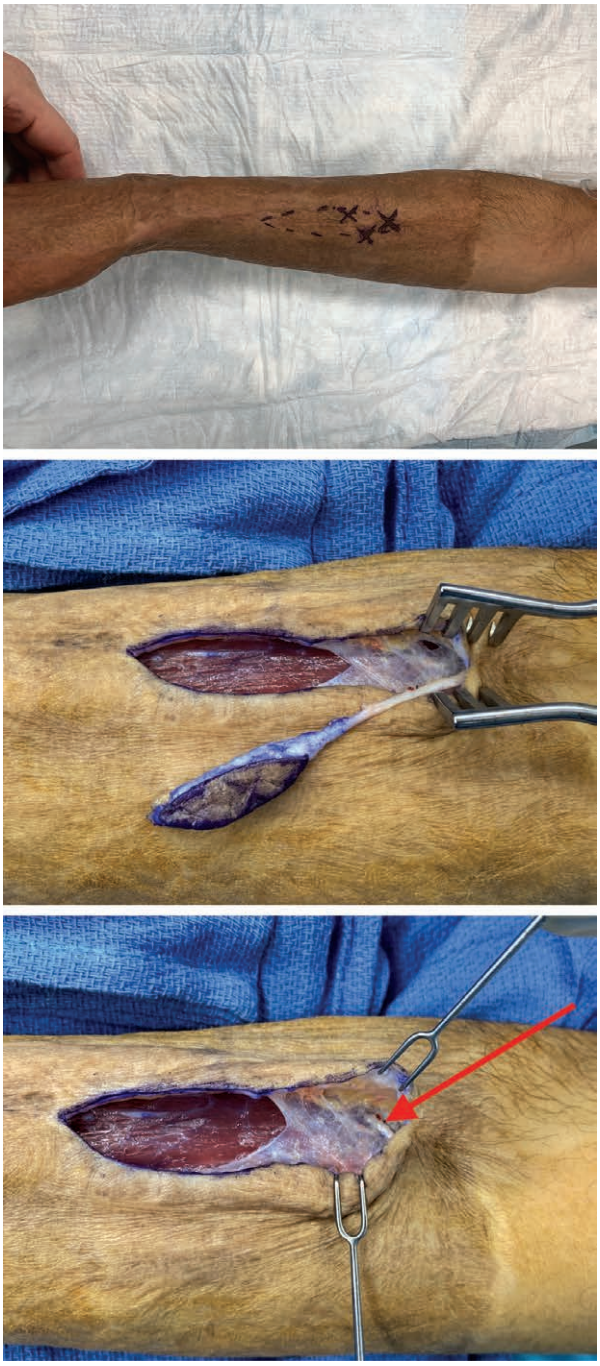

Fig. 2. (*Above*) A 26-year-old man with intermittent shooting right forearm pain (4 of 10) over previously grafted skin. Physical examination of the right upper extremity revealed three positive Tinel signs in the distribution of the lateral antebrachial cutaneous nerve. (*Center*) A neuroma was identified causing compression in the lateral antebrachial cutaneous nerve. (*Below*) The neuroma was excised and the proximal end of the lateral antebrachial cutaneous nerve was implanted into the brachioradialis muscle (*arrow*).

Nerve dysfunction secondary to systemic injury remains poorly understood etiologically but seems to be related to released inflammatory

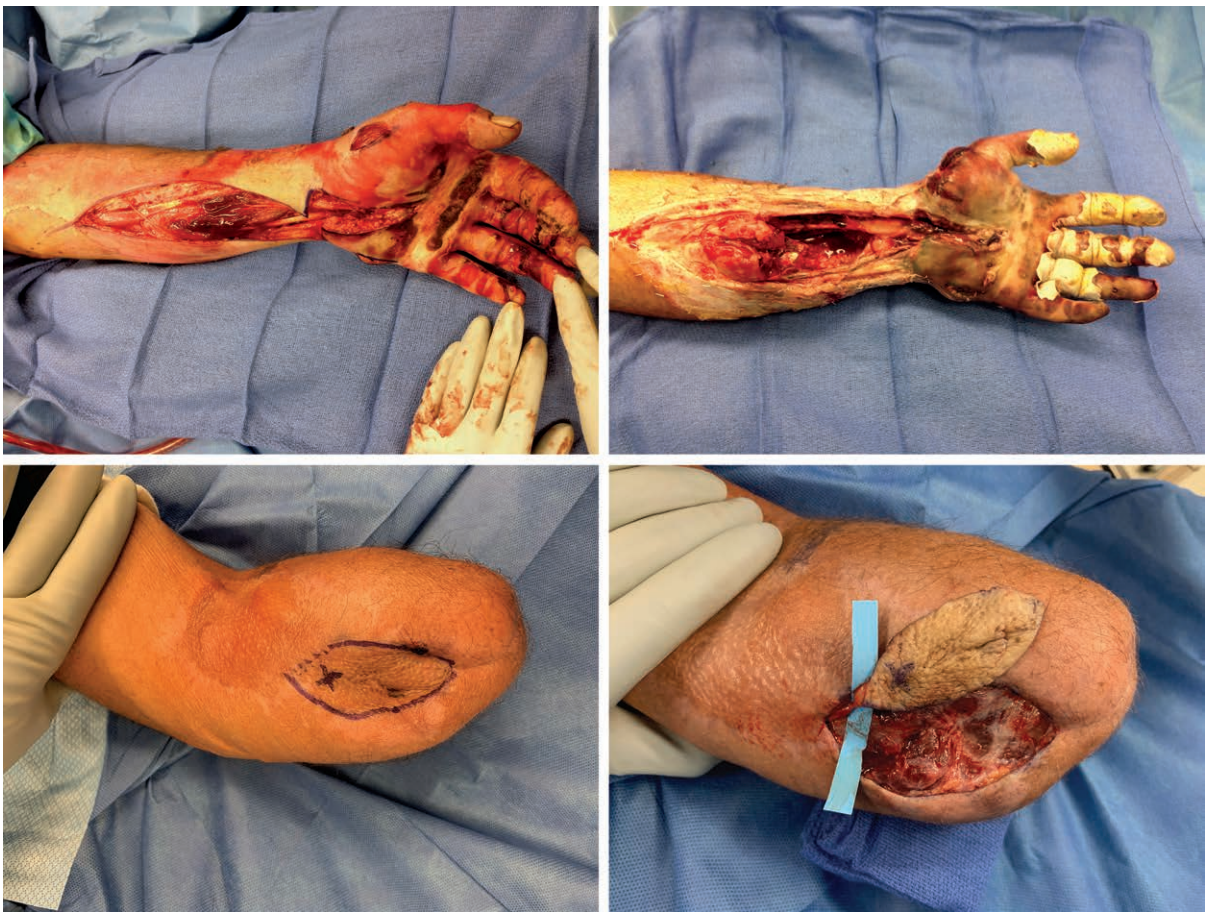

Fig. 3. (*Above*, *left*) A 45-year-old man with 30 percent total body surface area electrical injury from 7000 V, with a compartment syndrome of his left upper extremity, underwent fasciotomy. (*Above*, *right*) Subsequent necrosis resulted in amputation of the extremity. (*Below*, *left*) On follow-up, a positive Tinel sign was located at the amputation stump. (*Below*, *right*) An amputation revision and neuroma excision were performed to reduce pain.

mediators that can affect peripheral nerve function.[10,26,43,44] Greater percentage total body surface area burns result in greater systemic responses by releasing larger quantities inflammatory mediators into systemic circulation. Several inflammatory mediators identified that can cause nerve damage are cyclic adenosine monophosphate, cyclic guanosine monophosphate, prostaglandin E2, insulin-like growth factor–binding protein 3, and tumor necrosis factor-alpha.[45] When released systemically, these mediators can cause damage to nerves at locations distal from the sites of injury.[45,46] In addition, nociceptive fibers may upregulate and increase fiber density in both burned and unburned tissues with concurrent central plasticity.[25] This reemphasizes that local burns can manifest systemically in unaffected areas from central and peripheral nerve changes in chronic, neuropathic pain.[46,47]

Surgical interventions were categorized into those performed for the primary burn and those performed to treat the nerve pain that followed. Fascial excision was associated with more nerve compression and less nerve dysfunction secondary to systemic injury. Skin grafting was associated with less nerve dysfunction secondary to systemic injury. Amputation was associated with more electrical injury and less nerve dysfunction secondary to systemic injury. Fasciotomy was associated with more electrical injury. Surgical interventions to treat nerve pain were used once pharmacologic interventions were optimized or unsuccessful for treating the symptoms of pain. Less laser was used for nerve dysfunction secondary to systemic injury. More nerve repairs were performed for direct nerve injury with successful results. More nerve releases were performed for nerve compression and electrical injury, and less nerve releases were performed for direct nerve injury and nerve dysfunction secondary to systemic injury. Fewer patients required physical therapy/occupational therapy for nerve dysfunction secondary

to systemic injury. Nerve dysfunction secondary to systemic injury had the greatest reductions in pain scores at final follow-up. This category of nerve pain was self-limiting for many, and did not require long-term pharmacologic therapy or surgical interventions. Reductions in pain scores at final follow-up were achieved through combinations of surgical and pharmacologic therapies. With prospective studies, we hope to further clarify specific responses to interventions and corresponding reductions in pain scores.

Limitations of our study relate to the disproportionate sizes of categories and retrospective design. The sample size did not allow for a normal distribution; therefore, we used the Fisher's exact test and Kruskal-Wallis test, and implemented posttest analyses to prevent overestimating our results and a type II error. Although we were able to compare different categories of burn nerve injury, the small, unequal sizes of our samples require prospective validation. Patients were stratified into each nerve injury category based on the symptoms that contributed most to their morbidity on follow-up for simplicity and clarity. It is likely patients have overlapping causes in different anatomical locations, which we plan to investigate. Long-term follow-up care information was difficult to obtain in international patients, homeless patients, and patients with substance abuse or advanced psychiatric illness. Of the 2024 possible consecutive burned patients evaluated over the 5 years, 1880 met eligibility criteria and were included. All 113 of the 1880 patients included in the study had multidisciplinary coordinated follow-up to confirm a clinical diagnosis of chronic pain beyond 6 months. The 144 burned patients that were excluded consisted of the difficult long-term follow-up population and those with preexisting neuropathic pain caused by an underlying medical illness or medication. We analyzed data from a single burn center. Although categories of nerve injury would remain the same, our findings should be generalized with caution until further validation is performed through a multicenter study, and in the pediatric population.

Strengths of our study relate to the rigidity of our methods in the largest known study performed to date assessing a proposed evidence-based classification model for nerve pain after burn injury. We performed multidisciplinary evaluations by different clinicians and used consistent definitions for nerve pain and chronicity. Patients with neuropathic pain attributed to an underlying medical illness and/or medication, and signs and symptoms of neurologic impairment before burn injury, were removed from our study. The rigidity of our methodology may explain the lower prevalence of 6 percent observed in our population compared to the literature. A misconception that has reoccurred in the literature is the use of electrodiagnostic studies to diagnose pain. Pain is subjective, and electrodiagnostic studies are not capable of differentiating pain from no pain. This has resulted in higher reported rates of chronic pain in other studies. We diagnosed nerve pain clinically in our patient population.

CONCLUSION

In burn patients, direct nerve injury, nerve compression, electrical injury, and nerve dysfunction secondary to systemic illness were categorized into a comprehensive etiology-based classification to guide patient management and research methods to improve patient pain outcomes.

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