Cerebrovascular Diseases

Post Stroke Pain: Identification, Assessment, and Therapy

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Key Words

Abstract

Background: Pain is a common complication after stroke
and is associated with the presence of depression, cognitive
dysfunction, and impaired quality of life. It remains underdi-
agnosed and undertreated, despite evidence that effective
treatment of pain may improve function and quality of life.
Summary: We provide an overview of the means for clinical
assessment and risk factors for the development of post-
stroke pain, then review the newest available literature re-
garding the commonest post-stroke pain syndromes, in-
cluding central post-stroke pain, complex regional pain syn-
drome, musculoskeletal pain including shoulder subluxation,
spasticity-related pain, and post-stroke headache, as well as
the available epidemiology and current treatment options.
Key Messages: In the best interests of optimizing quality of
life and function after stroke, clinicians should be aware of
pain as a common complication after stroke, identify those
patients at highest risk, directly inquire as to the presence
and characteristics of pain, and should be aware of the op-
tions for treatment for the various pain syndromes.

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Introduction

Chronic pain syndromes are common after stroke and
are found in up to one-half of stroke patients [1]. As many
as 70% of affected patients experience pain on a daily ba-
sis [2].

The reported prevalence of post-stroke pain (PSP) var-
ies, reflecting differences in study design, definitions of
pain types, and sampled cohorts (table 1). Still, there is a
general consensus that PSP is an underreported phenom-
enon. PSP often goes undisclosed by patients unless ac-
tive inquiry is made by the physician [3]. Even when iden-
tified, PSP may not be sufficiently treated. In one retro-
spective study, it was found that two-thirds of those with
central pain had inadequate pain treatment, or were pre-
scribed no treatment at all [4].

Various non-motor complications of stroke common-
ly co-occur in those with PSP (table 2). Patients with pain
experience greater cognitive and functional decline [5],
lower quality of life [1], fatigue [6], and depression [7].
PSP is a predictor of suicidality after stroke [8]. Pain se-
verity correlates with severity of cognitive impairment
and depression [9]. The relationships between these vari-
ables continue to be explored [10–13].

Multiple factors contribute to post-stroke pain, in-
cluding central and peripheral mechanisms, psychologi-

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Table 1. Prevalence of post-stroke pain syndromes

Study	Design	Prevalence, n	Mean time from infarct to pain syndrome	Additional information
Langhorne, 2000 [3]	Prospective study recruiting patients at 3 centers with 30 months follow-up (n = 311)	43% (n = 134/311) over follow-up period (incidence)	N/A	9% had shoulder pain 34% had other types of pain over follow-up period
Widar, 2002 [4]	Inpatient registry at University Hospital Retrospective analysis with data gathered at 2 years post-stroke n = 972 patients on register, (n = 43) included in study	No overall prevalence measured (n = 43)	65% developed pain syndrome between 1–6 months post-stroke Syndromes developed at different times: <1 week: 28% 1 week–1 month: 23% 2–6 months: 44% 20–27 months: 5%	Types of pain syndromes: CPSP: 35% (n = 15/43) Nociceptive pain: 42% (18/43) Tension-type headache: 23% (n = 10/43)
Kong, 2004 [134]	Cross-sectional survey of an outpatient clinic at a tertiary rehab centre Screened for participants over a 3 months period (n = 107)	42% (n = 45/107)	N/A	71% of pain was MSK-type (n = 32); 29% central (n = 13) Pain was associated with a shorter amount of time post-stroke (mean 15.9 months versus pain-free patients in the registry who were mean 22.8 months post-stroke)
Jonsson, 2006 [9]	Population-based registry Prospective, assessed at 4 (n = 329) and 16 months (n = 297) post-stroke by interview	4 months: 32% of 329 had moderate to severe pain, 7% had mild pain At 16 months: 21% of 297 had moderate to severe pain, 4% had mild pain	Pain onset at 4 months visit: before stroke 38%, 0–2 weeks post-stroke 31%, 2 weeks–2 months post-stroke 14%, >2 months post-stroke 17% Pain onset at 16 month visit: before stroke 40%, 0–2 weeks after stroke 26%, 2 weeks–2 months after stroke 5%, >2 months after stroke 29%	Visual analogue scales (VAS) used to measure pain VAS significantly worse for those with moderate to severe pain at 16 months as opposed to those at 4 months Self perceived cause of pain at 16 months was stroke in 36%
Lundström, 2009 [7]	Cross-sectional survey performed on patients part of the Swedish National Quality Register for Stroke Care (n = 147)	49% (n = 68/147)	N/A	21% of patients had pain related to stroke 9% total related to shoulder pain 4% central post-stroke pain 11% total hip/leg/foot pain
Hansen, 2012 [33]	Prospective cohort of consecutive patients admitted to a university hospital over an 8 months period Follow up at 3 and 6 months after stroke onset (n = 275)	55.3% at 3 months (n = 156/282), 65.8% at 6 months (n = 181/275)	N/A	3 months: Headache in 15.3% (n = 42), shoulder pain on affected side in 10.2% (n = 28), CPSP not assessed at this visit 6 months: Headache in 13.1% (n = 36), shoulder pain in 12% (n = 33), possible CPSP in 10/6% (n = 29)
O'Donnell, 2013 [5]	Standard questionnaire administered as part of a randomized control trial. Patients enrolled 90–120 days after ischemic stroke (n = 15,754)	10.6% (n = 1,665/15,754)	Questionnaire administered at penultimate follow-up visit	Of those with identifiable sources/etiologies, 2.7% had CPSP, 1.5% with peripheral neuropathy, 1.3% with pain attributable to spasticity

MSK = Musculoskeletal; CPSP = central post-stroke pain.

cal factors, and autonomic input. There are multiple treatment approaches that attempt to target these contributors (fig. 1). While the relationship between pain and these variables is complex, evidence from the non-stroke literature suggests that treatment of pain is associated with improvement of cognition and quality of life. Treatment of pain with opioids and amitriptyline has been shown to reverse pain-related cognitive impairment [14, 15]. Similarly, studies of osteoarthritis and post-herpetic neuralgia have shown that improved pain control, regardless of modality, is associated with improved perceived quality of life [16–19].

Currently, post-stroke pain is under-recognized and under-treated. Ensuring that clinicians are familiar with
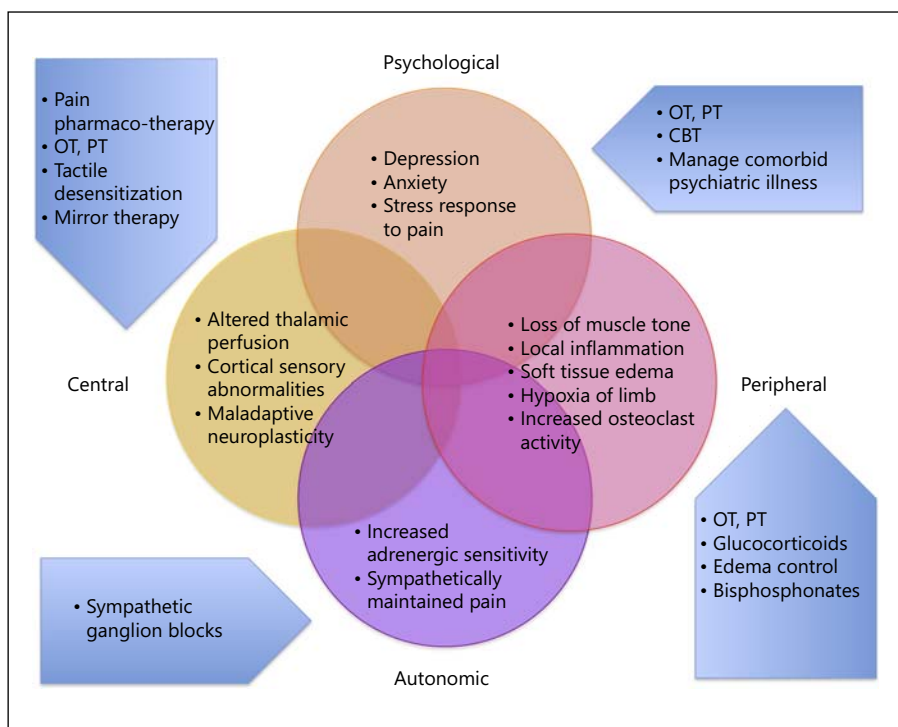
Fig. 1. Psychological, central, peripheral, and autonomic factors contributing synergistically to post-stroke pain and associated targeted therapeutic strategies (adapted from Gierthmulen et al. [111]). CBT = Cognitive-behavioral therapy; OT = Occupational therapy; PT = physiotherapy.

Table 2. Non-motor complications of PSP

Complications Associated with Post-Stroke Pain
Cognitive decline
Functional decline
Fatigue
Depression
Suicidality
Lower quality of life

Table 3. Reported risk factors for the development of PSP

Demographic
Female sex
Older age at stroke onset
Premorbid
Alcohol use
Statin use
Peripheral vascular disease
Depression
Clinical
Spasticity
Reduced upper extremity movement
Sensory deficits
Stroke-related
Ischemic stroke
Thalamic localization
Brainstem localization

the pain syndromes after stroke, their identification, and their treatment can have a significant impact on pain outcomes, as well as on other variables that impact quality of life. Prognosis with regards to pain outcomes is improved when pain is treated early and aggressively [20]. Health providers should routinely assess for this common and important complication post-stroke, and have an understanding of its presentation and treatment to manage patients effectively. Patients are often inadequately educated about post-stroke pain, and may stop treatment too early if they are not properly informed [4].

Risk Factors

Various patient characteristics have been identified as independent risk factors for the development of PSP [5] (table 3). Incidence of PSP increases with age at stroke onset [21]. Clinical features associated with the development of PSP include increased muscle tone, reduced upper extremity movement, and sensory deficits [21]. Ischemic stroke is more frequently associated with pain than hemorrhagic stroke [2]. Stroke localization also has a role, with an overrepresentation of PSP after thalamic and brainstem strokes [2].

Identification of PSP

Challenges in Identifying Post-Stroke Pain

Several factors present challenges in the identification, assessment, and characterization of PSP, including the subjective nature of symptoms and patient-related factors, such as reluctance to disclose symptoms, language deficits, and neglect syndromes. There is significant variability in how pain is assessed for research purposes, with self-reported questionnaires, pain scales, and clinical assessment providing most of the data. Actively inquiring about pain is essential, as many patients do not volunteer these symptoms, particularly the elderly [22, 23].

The particular clinical deficits caused by strokes are associated with difficulties in reporting pain [24]. Although there are several rating scales for pain, no specific pain scale has been devised for the assessment of post-stroke pain. Options include visual analogue scales, faces pain scales, numeric rating scales, and verbal descriptor scales. In spite of these varied options, stroke patients are less likely than age-matched controls to be able to complete rating scales [25]. It is important to tailor the scale to the individual's deficits. For instance, the use of a faces pain scale has been found to be more reliable in left than right hemispheric strokes [26]. There is likely no single scale effective for all stroke patients given the heterogeneity of neurologic deficits in this population [26].

Common Post-Stroke Pain Subtypes

PSP occurs through both neuropathic and nociceptive mechanisms. Efforts to standardize descriptive terms for pain led to a publication by the International Association for the Study of Pain of pain terms and their definitions [27]. These are commonly used in studies of PSP to define pain subtypes [28–32]. The commonest types of PSP are central post-stroke pain (CPSP), pain secondary to spasticity, shoulder pain, complex regional pain syndrome (CRPS), and headache [5, 33]. Many patients report more than one pain subtype [2], with common combinations being CPSP and spasticity, or CPSP and shoulder pain [5]. By definition, CRPS has features of neuropathic pain, and as such, these syndromes co-occur as well.

Central PSP

Prevalence, Risk Factors, and Clinical Characteristics

CPSP is a common pain syndrome after stroke, estimated to account for over one-third of cases of post-stroke pain [4]. Latency to onset is variable. Most commonly, it develops within 3 to 6 months of stroke [34], though it may occur within a month after stroke [35]. Symptom onset is often gradual, coinciding with the improvement of perceived sensory loss and the appearance of dysesthesia [35]. The pain is frequently severe and unrelenting, with pain-free episodes not exceeding a few hours [35]. Risk factors for development of CPSP include young age, previous depression, current smoking and increased baseline stroke severity [5, 36]. Of note, a recent large cohort study confirmed that young stroke patients are twice as likely to develop CPSP (Helsinki Stroke Study) [36].

In general, there are thought to be three types of pain components with CPSP: (1) a constant pain, (2) a spontaneous intermittent component, and (3) hyperalgesia/allodynia [37]. The clinical features, diagnostic criteria and proposed pathophysiology and treatment of CPSP have been discussed in detail previously [31].

Localization and Proposed Pathophysiology

Thalamic lesions are commonly associated with pain, with Dejerine-Roussy syndrome being the best characterized CPSP syndrome. This syndrome accounts for approximately one-third of the cases of CPSP [35] and is characterized by severe and paroxysmal pain, accompanied by allodynia and hyperalgesia [38]. Lesions beyond the thalamus at any level of the neuroaxis, however, can produce neuropathic pain, particularly with the involvement of the spinothalamic tracts. Lateral medullary syndrome is the commonest brainstem syndrome associated with CPSP [29]. Approximately 80% of lesions causing CPSP are hemispheric [37]. Cortical strokes causing CPSP often involve the parietal lobe and possibly the underlying white matter [39]. Strokes affecting the right hemisphere are more commonly associated with pain, for both thalamic and non-thalamic strokes [35]. One explanation suggests the right hemisphere is more adept at monitoring the somatic state, and thus at pain processing; this leads to pain conditions being more intense in the left hemibody [40]. However, this lateralization is not consistently reproduced [41]. CPSP has also demonstrated a strong association with small vessel infarcts [5], likely because of the common association of this stroke mechanism with thalamic or pontine lesions [5, 42].

Identification in the Clinical Setting and Therapy

The presentation of CPSP is variable. Certain clinical characteristics, discussed in detail in previous reviews, can aid in its identification [31] (table 4). Adjectives such as lacerating, aching, burning, freezing, and squeezing are commonly used by patients [28]. Pain is often constant

Table 4. Clinical Features for identification of CPSP

Verbal Descriptors Used: lacerating, aching, burning, freezing, squeezing
Spontaneous dysesthesia
Allodynia to touch and mild temperatures
Variable pain quality
Abnormal sensitivity to pinprick and high temperatures
Raised thresholds for perception of touch and two-point discrimination

[28]. Based on these findings, diagnostic criteria for CPSP have been proposed [6].

CPSP is challenging to treat, and often involves a trial-and-error process with multiple different therapies. Various pharmacologic agents have been found to be effective in these patients, including tricyclic antidepressants, selective serotonin reuptake inhibitors, and antiepileptics, including lamotrigine, gabapentin, and pregabalin, and have been discussed in previous reviews [4, 6]. Intravenous lidocaine [43] and ketamine [44] have also been for acute relief in CPSP, but reports are limited to small case series. Currently, there is no evidence for pharmacologic prophylaxis for pain in stroke patients [45].

Newer studies have looked at the utility of methylprednisolone and levetiracetam in the treatment of CPSP. One small retrospective series found a reduction in pain scores and as-needed pain medications with a tapering oral course of methylprednisolone, though this has not been tested prospectively or in a randomized fashion [46]. Although other anti-seizure medications are helpful in CPSP, studies of levetiracetam have been disappointing. A 2013 Cochrane review found it ineffective for neuropathic pain [8], and a recent double-blind randomized control trial found it ineffective for CPSP specifically [9].

Neurostimulatory therapy has also been evaluated in central pain syndromes, including refractory cases of CPSP. The effectiveness of motor cortex stimulation was estimated to be around 50% in a systematic review [47], with effectiveness up to 77% when somatosensory evoked potentials were used to confirm stimulating electrode placement [48]. These success rates are lower than in patients with spinal cord injury and peripheral neuropathic pain [47, 49]. Deep brain stimulation has been utilized with electrodes being placed in the somatosensory thalamus and periventricular gray area; however, results have been disappointing for CPSP [50]. Noninvasive techniques for treatment of CPSP have also been explored. Repetitive transcranial magnetic stimulation (rTMS), with repetitive daily stimulation of the motor cortex, has been

shown to be effective in CPSP and may provide sustained pain relief [50]. One small case series of caloric stimulation in patients with CPSP found that this simple method provided lasting symptomatic relief [51].

Spasticity-Related Pain

Prevalence, Risk Factors and Clinical Characteristics

Spasticity is an abnormal pattern of muscle activation with externally imposed perturbation [52]. It is common after stroke, with nearly one-quarter of patients developing some increase in muscle tone within one week [53]. Spasticity itself can take on various forms. In its simplest form, it is velocity-dependent increased tone. Other features of an upper motor neuron syndrome include spastic dystonia, spastic co-contraction, and exaggerated reflexes [54]. The majority of patients with spasticity after stroke experience pain [21]. A prospective observational study demonstrated a strong association between the development of spasticity and pain, with 72% of patients with spasticity developing pain, while only 1.5% of non-spastic patients experienced pain syndromes [53].

Proposed Pathophysiology

The nature of the relationship between spasticity and pain is not fully understood. There are potential neuropathic and nociceptive mechanisms by which they are related [7]. The neuronal networks that mediate pain and spasticity at the spinal and cerebral levels may overlap, supported by the finding that pain is be reduced by stimulation of cortical motor areas [50, 55]. Nociceptive pain may be produced by the abnormal loading on muscles and ligaments caused by spasticity [7]. Spasticity can cause changes in rheologic muscle properties, leading to fibrosis, and atrophy [56]. Patients often report pain independent of exacerbations of spasticity, suggesting that the pain may be related to prolonged abnormal muscle contraction [57]. Patients with a higher degree of spasticity have been found to have lower Barthel Index scores, lower quality of life, and more pain [53].

Identification in the Clinical Setting and Therapy

A thorough clinical assessment is essential in the identification of spasticity. Low Barthel Index Score at day 7, hemiplegia at admission, left-sided weakness, and smoking history have been identified as independent risk factors for the development of spasticity [58]. On physical exam, spasticity is detected by an increased response to passive movement. Other more quantitative scales as well as electromyography have also been used to characterize spasticity, though primarily in the research setting [52, 59].

Pain can be considered an indication for treatment of spasticity using local neuromuscular blockade or pharmacological treatment, but must be weighed against the disadvantage of removing the potential functional benefits of increased muscle tone. In general, the goal of treatment is to reduce reflex activity, thus reducing muscle tone. Mechanical muscle fiber properties may propagate spasticity, and can also be targeted [56]. There is little evidence regarding the treatment of spasticity specifically after stroke [60]; much of the evidence is derived from the literature on other neurologic conditions, such as multiple sclerosis and cerebral palsy and is well summarized elsewhere [61–66].

Musculoskeletal Pain: Glenohumeral Subluxation and Contractures

Prevalence, Risk Factors and Clinical Characteristics

Shoulder pain is a common nociceptive pain syndrome post-stroke [67]. Musculoskeletal shoulder pain can be divided into two main types: shoulder subluxation (inferior glenohumeral joint displacement) and contractures.

It is reported that hemiplegic shoulder pain is prevalent in 16–72% of stroke patients [67–71]. Prevalence is commonly estimated between one-quarter and one-half of stroke patients [67, 71, 72]. Pain onset is often within 3 weeks of the stroke [71]. Risk factors associated with the development of shoulder pain include upper extremity weakness and stroke severity [69, 73]. Other high-risk features for shoulder pain include sensory abnormalities [69], an abnormal rheumatologic exam [69], spasticity [74], right hemispheric lesions [75] and a low Barthel Index Score [68]. In comparing groups of patients with and without shoulder pain in a rehabilitation facility, those without shoulder pain were significantly more likely to be functionally independent [72].

Pathophysiology

The development of shoulder pain is likely multifactorial and can involve glenohumeral subluxation, impingement, rotator cuff tears, bicipital tendinitis, and CRPS. The shoulder joint is unique compared to most joints in the body, as it is loosely constrained by a thin articular capsule, relying on muscles and ligaments for stability (fig. 2). Weakness can thus lead to instability and immobility of the glenohumeral joint. Glenohumeral subluxation, can result from the weakness of these surrounding muscles. Subluxation can occur immediately after stroke, when the upper extremity has flaccid tone and is most vulnerable to instability [76]. However, pain most often

becomes apparent when spasticity develops [69]. The evolution of subluxation is associated with the development of shoulder pain, and reduced functional outcomes of the affected upper extremity [77]. Potential complications of subluxation also include CRPS [18] and secondary brachial plexus injury [78].

Identification, Prevention and Treatment

A thorough clinical exam is essential to identify post-stroke shoulder pain. Patients' self-report of pain far underestimates the extent of pain found on physical exam: In one study, nearly 40% of post-stroke patients who denied shoulder pain would subsequently show pain on physical examination, even in those without evidence of visual or somatosensory neglect [71]. The most common physical signs of post-stroke shoulder pain were bicipital tendon tenderness, supraspinatus tenderness, and a positive Neer sign (pain with placement of fully pronated arm in forced flexion) [71].

Prevention is key to the management of post-stroke shoulder pain [79] (table 5). After the onset of severe upper extremity motor weakness, and prior to the development of spasticity, the shoulder has significant laxity and thus is particularly vulnerable to injury. Attention to stabilization during this flaccid stage, as well as a physiotherapy regimen that starts with passive range of motion, should commence as soon as the patient is medically stable [80].

Once the full pain syndrome has developed, treatment should commence. Subluxation rarely resolves spontaneously [81]. Treatment options include mechanical stabilization with shoulder slings, lap boards and arm troughs in wheelchairs, and shoulder strapping. Medications should be started conservatively, with simple analgesics and non-steroidal anti-inflammatories being used first line [79]. Anti-spasmodic agents may also be helpful if hypertonicity is contributing to pain; they can be used in conjunction with the physiotherapy regimen [74].

Transcutaneous neuromuscular electrical stimulation (TENS) is a treatment option. TENS is proposed to be effective through the gate-control theory of pain, activating myelinated sensory fibers and disrupting the pain signals of unmyelinated C-fibers [82]. Functional electrical stimulation (FES) may be used to maintain isometric electrical strength of the shoulder girdle, and has been shown to improve pain, range of motion, and arm function [76]. FES has been targeted at the supraspinatus and posterior deltoid muscles, as these are critical for maintaining shoulder stability [83]. Botulinum toxin injections have been associated with improvement, and in some cases resolu-
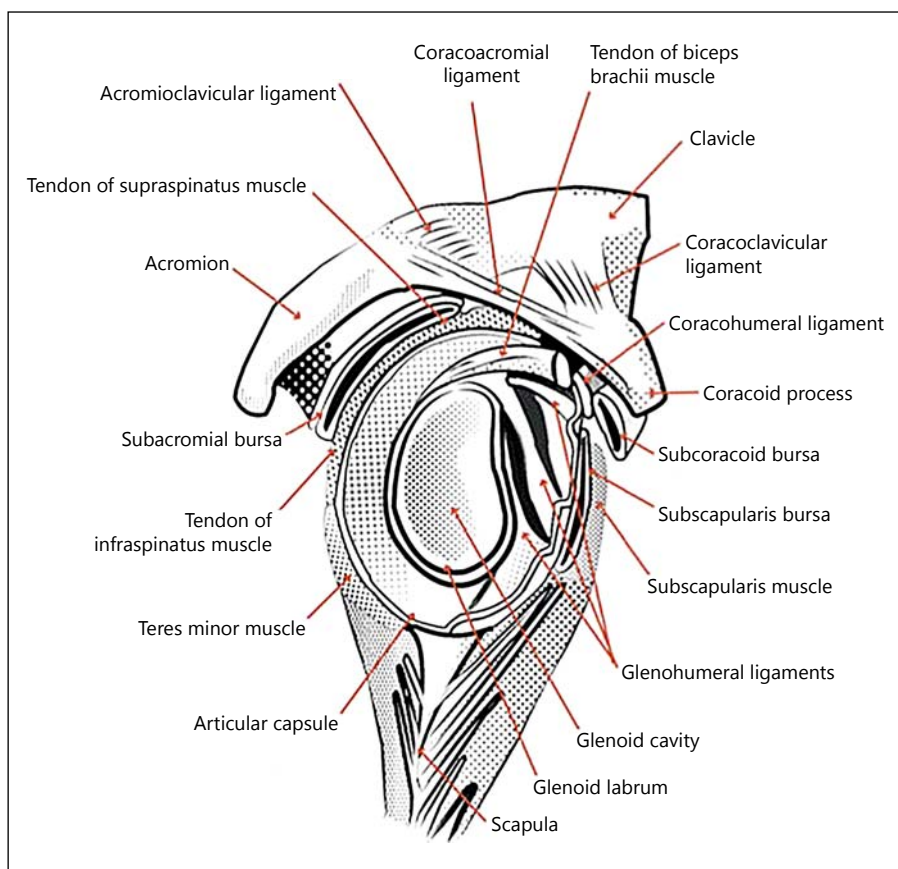
Fig. 2. Shoulder anatomy (lateral view). Diagram adapted from Netter's anatomy and amicus visual solutions.

Table 5. Prevention of hemiplegic shoulder pain [91]

1	Joint protection strategies Positioning and supporting the arm during rest Protecting and supporting the arm during functional mobility Protecting and supporting the arm during wheelchair use by using a hemi-tray or arm trough During the flaccid stage slings can be used to prevent injury, however beyond the flaccid stage the use of slings remains controversial
2	Overhead pulleys should not be used
3	The arm should not be moved beyond 90 degrees of shoulder flexion or abduction, unless the scapula is upwardly rotated and the humerus is laterally rotated
4	Patients and staff should be educated to correctly handle the involved arm

tion, of shoulder pain [84]. Surgery is also an option for refractory cases, with operations on contractures in muscle tendons, surgical repair of rotation cuff tears, and scapular mobilization.

A contracture is a permanent shortening of a muscle or joint, usually in response to prolonged hypertonic spasticity in a concentrated muscle area. In one registry, contractures were found in half of patients at 6 months post-stroke [85]. The commonest sites for contractures were the hip, shoulder, and elbow [86]. Shoulder contractures were most common in those with the most severe disability [86].

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Therapies for contractures remain controversial. Regular stretch therapy has not been shown to have a long-term impact on joint mobility, pain, or quality of life [87]. Surface neuromuscular electrical stimulation may reduce the progression of contractures in elderly stroke patients, quantified by a change in the passive range of motion [88].

Complex Regional Pain Syndrome
Prevalence, Risk Factors and Clinical Characteristics
Complex regional pain syndrome (CRPS) involves pain, edema, vasomotor changes, and patchy bone demineralization of an extremity. It is also referred to as reflex sympathetic dystrophy, causalgia, and Sudeck's atrophy; or shoulder-hand syndrome when seen after stroke. There are two types: Type I, where there is no definable nerve lesion, and Type II, where a definable nerve lesion is present. Most stroke patients are categorized as Type I CRPS, although it is impossible to rule out microtrauma to nerves [89].

The reported incidence of CRPS after stroke is variable, with estimates between 2 and 49% [90, 91]. This variation is at least in part due to the lack of consensus on diagnostic criteria in previous studies. In an effort to standardize the diagnosis of CRPS, the International Association for the Study of Pain (IASP) have adopted a set of clinical diagnostic criteria, classifying both sensory and sudomotor/vasomotor components [92, 93].

Proposed Pathophysiology
Impaired biomechanics of the glenohumeral joint have been implicated in the development of CRPS after stroke. This is supported by findings that subluxation is more common in these patients [94] and that the degree of weakness and immobility in the shoulder is related to the probability of developing CRPS [95]. It is postulated that trauma to the affected shoulder is associated with the development of CRPS [96]; however, how this translates into the constellation of symptoms associated with this particular pain syndrome is not known. Historically, hyperactivity of the sympathetic nervous system and changes in the peripheral nervous system were implicated; contemporary imaging studies also demonstrate the role of the central nervous system and local inflammation in this process. Alterations in thalamic perfusion have been found in CRPS patients [97]. These patients also display cortical sensory abnormalities [98]. Local inflammation of the affected extremity has been demonstrated by increased migration of immunoglobulins and other inflammatory mediators toward the area affected by CRPS [99, 100]. Relative hypoxia has been demonstrated in the af-

fected limb, with evidence of reduced capillary oxygenation when employing skin spectrophotometry [101] and local muscle acidosis on nuclear magnetic resonance spectroscopy [102].

Identification in the Clinical Setting, Prevention and Treatment
The clinical findings of CRPS are outlined in the diagnostic criteria provided by the IASP [19]. These include a constellation of symptoms and signs including neuropathic pain, motor limitations, vasomotor and sudomotor changes, and trophic changes affecting hair, nails, and skin in the affected limb. Plain films or CT of affected areas often demonstrate patchy bone loss in late CPRS [103, 104]. MRI of the affected area may demonstrate skin thickening, tissue enhancement with contrast material, and soft tissue edema to support a diagnosis of CRPS [105].

CRPS treatments target the proposed causative mechanisms. There is no definitive treatment for post-stroke CRPS at this time. Goals of treatment are to reduce pain, maintain joint mobility, and restore function [106]. An interdisciplinary approach involving occupational and physical therapists to provide mobilization and strengthening of the affected limb, edema control, and desensitization techniques is considered a cornerstone of care in these patients [106].

Given that early joint injury can contribute to the development of CRPS, a preventative approach to joint injury may also reduce incidence [107]. To target sympathetic mediated effects, nerve blocks can be given at the level of the stellate ganglion [108]. Desensitization is a gradual process in which increasingly painful sensory stimulus is applied to the affected area. It is thought that this gradual increase in normalized sensation may reset the altered central processing in the nervous system [109]. Other non-pharmacological therapies such as motor imagery and mirror therapy have been studied in the treatment of CRPS. With mirror therapy, participants watch their unaffected limb in the mirror as though it is the affected limb, and perceive it moving with ease. Mirror therapy is associated with decreased CRPS-related pain and improved motor recovery after stroke [110]. Proposed mechanisms include cortical change and reorganization. Psychological factors, such as depression and anxiety, may be premorbid or occur in response to pain; addressing these components is an important part of managing the disorder [111, 112].

Pharmacologic agents used for neuropathic pain, including memantine [113], gabapentin [114], carbamazepine [115], and heterocyclic antidepressants [116] have all

had suggested benefit in CRPS, though their efficacy has not been directly studied in the stroke population. Bisphosphonates, which are thought to counteract osteoclast hyperactivity, have demonstrated pain reduction in CRPS in a non-stroke cohort [117]. As inflammation likely plays a role in the pathogenesis and continuance of CRPS, it is also a potential therapeutic target. Corticosteroids have been tested in non-stroke and post-stroke CRPS populations [116, 118]. Data from two small randomized placebo-controlled trials in post-traumatic [119] and post-stroke [120] CRPS demonstrate significant pain relief with a short course of oral glucocorticoids.

Post Stroke Headache

While common in our own clinical experience, post-stroke headache remains poorly characterized in the literature. Chronic headache has been estimated to occur in 10% of patients after stroke [6, 20].

Some features of chronic post-stroke headache disorder have been identified. Headache at stroke onset is shown to be predictive of headache at 6 months post-stroke [33]. Those with a history of tension-type or vascular headache are more likely to develop headache with or after stroke [121]. In general, post-stroke headache has been characterized as a tension-type headache that has a pressing quality, and is not aggravated by movement [33, 122].

The pathophysiology of post-stroke headache is not well understood. It has been proposed that the predominant underlying mechanism is stimulation of the trigeminovascular system [21]. This may be due to various factors including brain injury, damage or alterations to the blood vessels, subsequent inflammation or disruption and/or reinnervation of pain pathways, or even medications (dipyridamole, for example, has been commonly associated with headache [5, 123]). Further study is needed regarding the prevalence, risk factors, and therapy for this condition.

Conclusion

Pain is a common phenomenon in stroke patients. There are multiple contributing mechanisms for post-stroke pain and several well-characterized, post-stroke pain syndromes. Nonetheless, the identification of pain in the post-stroke population often proves challenging. Careful inquiry, use of rating scales, and physical examination may lead to improved identification and effective treatment of post-stroke pain. This may improve patient comfort, mood, rehabilitation, and quality of life.

Acknowledgment

Conflicts of Interest

None to declare.

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