Review Article

Double Crush Syndrome

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Abstract

Double crush syndrome is a distinct compression at two or more locations along the course of a peripheral nerve that can coexist and synergistically increase symptom intensity. In addition, dissatisfaction after treatment at one site may be the result of persistent pathology at another site along a peripheral nerve. Double crush syndrome is a controversial diagnosis; some scientists and surgeons believe it is an illness construction that may do more harm than good because it emphasizes an objective pathophysiologic explanation for unexplained symptoms, disability, and dissatisfaction that may be more psychosocially mediated. However, peripheral neuropathy may coexist with compressive neuropathy and contribute to suboptimal outcomes following nerve decompression. To better manage patients' expectations, treating practitioners should be aware of the possibility of concomitant cervical radiculopathy and carpal tunnel syndrome, as well as the presence of underlying systemic neuropathy.

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The classic description of double crush syndrome (DCS) describes a clinical entity of multiple sites of compression along a single peripheral nerve.[1] It was first described in 1973 by Upton and McComas,[1] who theorized that asymptomatic compression at one site predisposed a peripheral nerve to increased susceptibility to impairment at another anatomic location. This "double crush" eventually leads to disruption of axonal transport along the nerve, thus increasing the vulnerability of distal axons to compression syndromes and symptomatology. The clinicians developed their postulate after clinical observation of patients presenting with peripheral nerve neuropathy who also had associated cervicothoracic nerve root pathology. The value of the concept of DCS is debated because (1) there is no way to objectively verify that symptoms ascribed to so-called DCS are the result of pathophysiology at two levels of a peripheral nerve; (2) this speculative pathophysiology is typically applied when patients have more symptoms, disability, or dissatisfaction than expected; and (3) by emphasizing discrete pathophysiology (ie, biomedical model of illness), the concept of double crush may encourage additional surgery at another level when surgery may not be the most effective treatment option (ie, biopsychosocial model of illness).[2-4]

The etiology and pathophysiology of DCS is controversial. In 1987, Nemoto et al[4] studied a canine compression model and concluded that "a double lesion was greater than the sum of the deficits after each separate lesion." This idea of a summation injury was supported in another animal model by Dellon and Mackinnon;[3] the authors examined a rat sciatic nerve compression model and concluded that "the existence of two sites of simultaneous compression will result in significantly poorer neural function than will a single site of compression."

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However, other studies have challenged DCS as it was originally proposed. Wilbourn and Gilliatt[5] questioned the accuracy of DCS. In their critical analysis of DCS, the authors systematically illustrated anatomic, physiologic, and pathologic disease processes, which they argue did not justify the diagnosis of DCS as originally defined. Further supporting this dissenting opinion, multiple authors have produced electrophysiologic studies that fail to demonstrate an adequate neurophysiologic explanation to support the initial concept of DCS.[6,7] The original definition of DCS, although based on sound pathophysiologic processes, may be limited in scope because investigators have shown that compressive pathology is not the only contributor to nerve pathology. Despite the controversy surrounding the diagnosis, DCS is an important concept because it emphasizes the fact that patients' symptoms may not simply be related to one anatomic site of compression but may also be caused by a remote compressive lesion or a systemic process, such as peripheral neuropathy.

Epidemiology and Risk Factors

Little consensus exists about the epidemiology, characteristics, risk factors, and pathophysiology regarding DCS. The reported incidence of DCS is difficult to estimate accurately; estimates range from 6.7%[8] to as high as 73%.[1,9,10] However, if strict anatomic and electrodiagnostic criteria are applied to the original definition of DCS, in which two sites of compression along a peripheral nerve are required, the incidence is low. In a study of >12,000 limbs with either carpal tunnel syndrome (CTS) or ulnar neuropathy at the elbow, only 0.5% (69 of 12,736 cases) of patients demonstrated axon loss at the distal lesion site on electrodiagnostic examination;[11] the authors concluded that cervical nerve root pathology rarely serves as a proximal lesion with DCS entrapment pathologies. These findings again highlight the difficulty and inaccuracy of DCS.

Multiple retrospective studies have attempted to identify predictive risk factors for DCS. Lo et al[12] analyzed 765 patient medical records and electrodiagnostic reports of patients with suspected CTS and cervical radiculopathy; 151 patients (20%) had only CTS, 362 (47%) had only cervical radiculopathy, and 198 (26%) were diagnosed with both conditions. In this study, women were more susceptible to carpal tunnel compression and/or DCS than were men. However, men were more susceptible to cervical radiculopathy. This finding is consistent with other studies that suggest that men are more prone to cervical radiculopathy and women are more prone to CTS.[13] However, the evidence surrounding DCS is inconsistent; conflicting studies report a higher incidence of DCS in men compared with women.[9,14] This lack of consistency between studies highlights the complexity of the pathologic processes that contribute to DCS symptomatology.

DCS is not only a syndrome of anatomic compression; it can also result from various medical pathologic processes. Multiple studies have illustrated the increased susceptibility of nerves to compressive pathology secondary to systemic illness. Baba et al[15] reported an increased incidence of multiple compressive peripheral neuropathies in patients with diabetes, finding a 16% incidence of patients with both CTS and cubital tunnel syndrome. Various pharmacologic agents, infectious pathology, and many conditions, such as anatomic abnormalities, hypothyroidism, hereditary neuropathy, uremic neuropathy, vitamin deficiency, and chronic alcoholism, can alter neural physiology and consequently put peripheral nerves at similar risk[15] (Table 1).

Pathophysiology

The pathophysiology of peripheral neuropathy is complex, and controversy surrounds the exact underlying mechanisms of DCS. Multiple authors have proposed various explanations; the most accepted principle for DCS involves a primary nerve disorder that predisposes the nerve to further injury. The proposed pathophysiology of DCS is the disruption of nutrient flow in both antegrade and retrograde directions along the axon.

In a Delphi study, international experts concluded that four mechanisms were highly plausible: axonal transport, immune-response inflammation of the dorsal root ganglia, ion channel regulation, and neuroma-in-continuity.[16] As mentioned earlier, several animal studies have confirmed that increased pressure levels can impair axonal transport; however, debate still remains as to the exact resultant effect. Although animal studies can demonstrate impaired nerve function with prolonged compression, there is no evidence that compression at two points along a nerve creates a distinct pathophysiologic entity.

Presentation and Diagnosis

The diagnosis of DCS is typically made when patients are dissatisfied with the result of carpal tunnel release. Osterman[17] conducted a prospective study of patients with CTS and found that 90% of patients with concomitant cervical radiculopathy had proximal radiation of pain compared with 50% of patients with CTS alone. It was also noted that fewer than half the patients with concomitant cervical radiculopathy had median nerve paresthesias compared with 93% of patients with

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Table 1

Various Etiologies Contributing to Nerve Dysfunction

Anatomic	Metabolic/Systemic	Surgical/Pharmacologic
Structural Cervical ribs; meralgia paresthetica; cervical/lumbar spondylosis; Martin-Gruber anastomosis; enlarged bicipital bursa; thickened aponeurosis of the flexor carpi ulnaris; accessory head of the flexor pollicis longus; Guyon canal; carpal tunnel syndrome; tarsal tunnel syndrome **Vascular** Thrombosis; atherosclerosis; Sjogren syndrome; Behçet syndrome; deep vein thrombosis; inferior vena cava agenesis; polyarteritis nodosa	Diabetes mellitus; hypothyroidism; multiple sclerosis; meningitis; connective tissue diseases; autoimmune disease; HIV; sarcoidosis; scleroderma; rheumatoid arthritis; amyloid deposition; Lyme disease; Bell palsy; uremia; vitamin deficiency (B_6/B_{12})	Pneumatic tourniquet and epidural anesthesia; ethanol abuse; phenytoin; reverse transcriptase inhibitors (eg, zidovudine, stavudine); cisplatin; vincristine; nitrofurantoin

Adapted with permission from Childs S: Double crush syndrome. *Orthop Nurs* 2003;22(2):117-121.

CTS alone. Osterman[17] also found distinctive differences between DCS and isolated CTS. In his prospective study evaluating patients presenting with upper extremity pain, patients with DCS reported more paresthesias and less numbness compared with those with CTS alone. Less than half the patients with DCS had distal median symptoms compared with 93% of those with CTS alone. Grip strength was subjectively weaker in patients with DCS compared with those with CTS.

Other investigators have attempted to further elucidate these subtle differences. Lo et al[12] found that the hallmark physical examination findings of CTS (ie, Tinel sign, Phalen test) were more frequently positive in patients with CTS only (36.4% and 33.8%, respectively), compared with those with DCS only (18.7% for each test) or sole cervical radiculopathy (12.7% and 10.2%, respectively). These studies illustrate the importance of the diagnosing physician having an astute understanding of classic presentations and understanding the subtle differences that may help distinguish DCS from a simpler single compression syndrome. Many patients have both cervical spondylosis (an expected part of aging) and CTS (a very common, genetically mediated narrowing of the carpal tunnel), but it is not currently possible to determine when these pathophysiologies are synergistic rather than just coexistent.

During evaluation for possible DCS, cervical radiographs are not recommended because 75% of patients in the seventh decade of life have degenerative radiographic changes; additionally, findings on radiographs are commonly similar between asymptomatic and symptomatic patients.[18] MRI is the test of choice for most patients who require cervical spine imaging; however, MRI must be interpreted with caution because of the high incidence of asymptomatic patients with cervical spine pathology.[19]

Ultrasonography has been proposed as a useful adjuvant tool to improve electrophysiologic testing for the diagnosis of peripheral nerve conditions. Given the inexpensive, noninvasive nature of ultrasonography, its use is likely to become more common in the future,[20-25] and further research into the utility of ultrasonography is warranted. However, at this time, there is no absolute confirmatory test, and an accurate diagnosis requires the summation of history, physical examination results, and diagnostic testing.

Double Crush Syndrome and the Lower Extremity

Compared with the upper extremity, less literature is available on lower extremity DCS. However, the concept and proposed pathophysiology is applicable to any nerve, and clear examples of DCS involving the lumbar roots and requisite peripheral nerves have been described. Giannoudis et al[26] reported an increased risk and poor prognosis for patients with acetabular fractures with proximal and distal nerve injury. Nine of 27 patients (33%) with initial neurologic injury who underwent fixation of an acetabular fracture had evidence of neuropathy involving the sciatic nerve proximally and the peroneal nerve distally at the neck of the fibula. In a study by Sunderland,[27] all patients with DCS pathology showed poor recovery.

Trauma may contribute to lower extremity DCS. Several reports note the high incidence of sciatic nerve injury, ranging from 10% to 25% in patients with posterior hip

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dislocation and acetabular fracture.[28,29] Golovchinsky[30] showed an overlap of distal peripheral entrapment in the lower extremities in patients with lumbar neural compression. Another clinical example of lower extremity DCS is represented by tarsal tunnel syndrome in which the posterior tibial nerve is compressed under the flexor retinaculum. In a case series of three patients, tarsal tunnel syndrome was diagnosed after an acute event proximal to and not involving the ankle, representing a DCS.[31]

Table 2

Common Proximal and Distal Sites of Compression

Proximal Nerve	Distal Nerve
Upper Extremity	
C5, C6 myelopathy	Axillary nerve
Cervical root	Brachial plexus/thoracic outlet Median nerve at elbow/AIN/wrist Ulnar nerve at elbow/wrist Radial nerve at elbow/radial tunnel
Brachial plexus/thoracic outlet	Median nerve at elbow Median nerve at wrist/carpal tunnel Ulnar nerve at elbow Ulnar nerve at wrist Radial nerve at elbow/radial tunnel
Median nerve at elbow/pronator syndrome	Median nerve at wrist/carpal tunnel
Ulnar nerve at elbow	Ulnar nerve at wrist
Lower Extremity	
Lumbosacral root	Femoral nerve Tibial nerve at popliteal fossa Peroneal nerve at fibular head Tibial nerve at foot/tarsal tunnel
Tibial nerve in leg	Tibial nerve at foot/tarsal tunnel

AIN = anterior interosseous nerve

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Treatment

Initially, conservative treatment should be trialed with distinct management that focuses on the unique pathology and symptomatology of each lesion (Table 2). Cervical nerve root compression may be initially treated with oral steroids, avoidance of irritating movements, a short period of immobilization with a soft collar, and physical therapy. Common palliative treatments of distal lesions of compressive neuropathies include splinting, NSAIDs, and steroid injections. The surgeon who makes the diagnosis of DCS initially provides standard nonsurgical management of each suspected level of nerve compression.

It is important for the physician to consider the benefits versus the adverse effects with each patient and plan on having the patient take an active role in his or her treatment plan. Interestingly, lack of clinical improvement with carpal tunnel injection may be used as a predictor for poor surgical improvement with carpal tunnel release alone because patients with DCS may have a suboptimal response to injection.[17] Osterman[17] found that 33% of patients with both CTS and cervical radiculopathy viewed release of the carpal tunnel as a failure, compared with 7% in those with CTS alone. Nonsurgical management of thoracic outlet syndrome may include exercise and bracing to widen the thoracic outlet;[32] surgical treatment would involve excision of any anomalous offending anatomy.

Most surgical treatments of dual compression in the upper extremity focus on cervical spine decompression and surgical release of the compressive site distally. Determining the need for one or both surgeries and the order in which to pursue the surgeries can be challenging; the decision should be based on the severity of compression and symptomatology at each site. Surgical treatment options for cervical neuroforaminal stenosis include anterior cervical diskectomy and fusion, total disk replacement, and posterior laminoforaminotomy. Surgical options for thoracic outlet syndrome include first rib resection or resection of an offending muscle.[32] Surgical treatment of distal compression is performed by releasing the compressing structure to relieve pressure on the nerve. In patients with dual compression, surgical treatment may be less effective than that performed for those with only one site of compression if both sites are compressed.

Surgical outcomes for the treatment of DCS are difficult to study. Although a sham-surgery, placebo-controlled study would be optimal to investigate the effectiveness of intervention for DCS, this would be impossible to perform because of the relative rarity of the condition and the ethical ramifications of retaining neural compression in symptomatic patients.

Summary

DCS was initially described as two compressive lesions along the course of a single peripheral nerve leading to symptomatic pathology; however,

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this narrow definition is controversial and incomplete. A complete understanding of the disease process remains elusive, although continuing research has broadened our knowledge of this intriguing pathologic process. Current understanding of this phenomenon takes into account systemic and vascular pathologic factors as contributing components to compressive pathology. DCS is a clinical entity that physicians should be aware of when evaluating patients with combined symptoms of not only proximal and distal nerve compression but also systemic disease and polyneuropathy. A combination of patient history, physical examination findings, selective radiographic imaging, and electromyography should be used to diagnosis DCS. Management should focus on accurate diagnosis and treatment of all contributing pathology.

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Evidence-based Medicine: Levels of evidence are described in the table of contents. In this article, references 5-7, 10, 12, 14, 23, and 24 are level III studies. References 9, 11, 13, 22, 26, and 29-31 are level IV studies. References 16, 20, 21, 25, and 32 are level V expert opinion and case reports.

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