SCINTIGRAPHIC TRIPHASIC BONE SCAN AS A DIAGNOSTIC TOOL IN COMPLEX REGIONAL PAIN SYNDROME (CRPS)

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Abstract. Traditionally, the use of scintigraphic triphasic bone scans (STBS) has been the most commonly applied test of choice for the diagnosis of complex regional pain syndrome (CRPS) in the past three decades. Whereas earlier, literature has described the STBS as highly sensitive and specific in establishing the diagnosis of CRPS (1).

Descriptors*. complex regional pain syndrome(CRPS), electromyography(EMG), infrared thermal imaging(ITI), laser evoked potential (LEP), nerve conduction velocity (NCV), quantitative sudomotor axon reflex test (QSART), quantitative thermal sensory evoked response test (QST), scintigraphic triphasic bone scan (STBS)*

INTRODUCTION

A meta-analysis by Lee and Weeks has shown that scintigraphic triphasic bone scans (STBS) to be positive in approximately 55% of the complex regional pain syndrome (CRPS) cases, which is quite close to a random statistical yield(2). The research of Chelimsky et al., found this test abnormal in no more than 25% of CRPS patients(3).

As CRPS becomes more chronic, the STBS yield becomes more variable(4). In the early stages, usually the test shows an increased flow and delayed periarticular uptake. Later, the flow normalizes but delayed views remain diffusely intense bilaterally. This lack of lateralization may be due to bilateral spinal cord representation of neurovascular functions in CRPS(5-7). In more chronic stages of CRPS, the flow becomes reduced and the STBS images return to normal(4). Realizing the fact that STBS shows symmetrical uptake in chronic stages, it misleads the clinician to conclude that the patient doesn't have CRPS. Subsequently, the patient is deprived of proper diagnosis and treatment. Malis et al., found that STBS changes to be nonspecific even in post-sympathectomy patients(8).

In CRPS, the temporal course of the disease is in constant flux. Even stages I through IV are usually meaningless because proper treatment and nerve blocks can reverse the stages of CRPS. As the disease becomes more chronic, the bone scan yield becomes more labile and variable (4). In early stages, usually the test shows an increased flow and delayed periarticular uptake. Later, the flow normalizes but the delayed views remain diffusely intense bilaterally. In more chronic stages, the flow becomes reduced and the STBS images return to normal(4).

COMPLEX REGIONAL PAIN SYNDROME (CRPS)

Complex Regional Pain Syndrome (CRPS) is one of the most misunderstood, over-diagnosed, under-diagnosed, and undiagnosed diseases in medicine. The basic medical school training of the autonomic nervous system, its physiology and its pathology, are too cursory and insufficient. The physicians approach to the diagnosis of CRPS, is the same principal of the blind trying to define an elephant.

The neurologists usually diagnose CRPS as “carpal tunnel syndrome,” or “somatoform disorder.” The rheumatologist has a tendency to diagnose it as “fibromyalgia.” The podiatrist as “tarsal tunnel syndrome and the pediatricians call it “Münchausen syndrome(9, 10).”

CRPS is a complex form of neuropathic pain associated with the four principal phenomena, which are exclusively seen in this disease (9). If any of the four is absent, the definitive diagnosis of CRPS cannot be made. The four principles consist of the following:

(i). Hyperpathic, allodynic, causalgic, or deep constant pain.

(ii). Vasomotor, sudomotor, or somatomotor reaction to the pain.

(iii). Neuroinflammation: (edema, entrapment neuropathy, plexopathy, usually mistaken for thoracic outlet syndrome), skin lesions, or interstitial cystitis(9-12).

(iv). The constant input of the neuropathic pain to the limbic system (Temporo-frontal lobes) results in insomnia, irritability, agitation, and depression(13). The Mayo Clinic uses the first three principles(3)**.** Adding the above-mentioned 4th principle makes the diagnosis practically certain. Of 824 CRPS patients studied in our clinic, every patient met the criteria(9). This method ruled out CRPS in 16% of previously over-diagnosed in other centers, and ruled in CRPS in 21% of patients under-diagnosed in other centers(9).

DIAGNOSTIC TESTS FOR CRPS

The above diagnostic principles confirm the diagnosis of the disease. Simply knowing the existence of CRPS in a region is not enough. The four principles do not accurately localize the area of nerve damage/dysfunction, and do not differentiate the original source of pain from the referred pain areas. This information is essential to help the clinician avoid causing more damage by performing surgery, or inserting a needle in the area containing already permanently damaged neurosensory nerves. Such iatrogenic damage is apt to aggravate, and even spread the disease(14-18)in a regional fashion. Further tests are needed to identify the areas of pathology.

Infrared thermal imaging (ITI) is useful in diagnosis and management of neuropathic pain. It provides an overall picture of temperature changes in superficial and deep structures (27 mm) (19-21)(*Figure 1*).

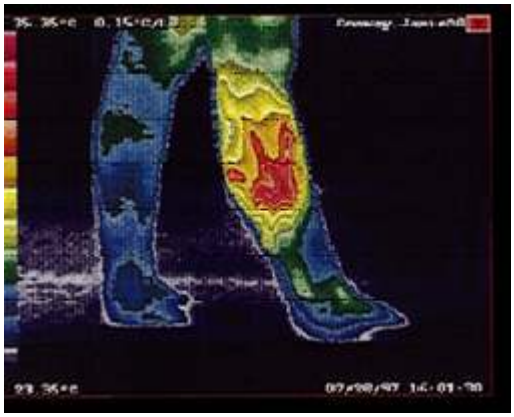

Figure 1. A previously undiagnosed right leg arteriovenous malformation over 27mm deep, complicated by complex regional pain syndrome (CRPS). ITI identified the deep lesion and spared the patient from the scheduled sympathectomy. Vascular surgery corrected the condition.

In approximately 1/3 of CRPS patients, the complex regional pain and inflammation can spread to other extremities(9,10,15-17). The spread through paravertebral chain of sympathetic ganglia may be vertical, horizontal, or both(9,10,15-17). The original source of CRPS may sensitize the patient to later develop CRPS in another remote part of the body triggered by a new albeit trivial injury(9,10,15,16,17,23). Surgical procedures such as amputation or sympathectomy can facilitate the spread of CRPS(9,22). ITI helps confirm the phenomenon of spread, helping the physician to treat the disease in target areas of spread (9,10,15,23).

In CRPS, the thermal regulatory responses are abnormal in a generalized fashion(2,24,25). This fact contributes to confusion and misunderstanding of ITI changes in CRPS. For example, spread of vasoconstriction to other extremities maybe mistaken for other diseases such as Raynaud's Phenomenon (26). The ITI, like any other test, cannot be expected to show 100% diagnostic sensitivity. Even with the cold water stress ITI testing (2,24,25), it is sensitive in 93% of the patients, specific in 89%, positive predictive value (PPV) of 90%. and negative predictive value in 94% (25). Recently, Herrick et al., have found cold stress ITI useful to diagnose patients suffering from fracture who are at risk for CRPS(26).

ITI provides useful clinical information when applied with proper technique. It provides diagnostic and therapeutic information limited to diseases involving autonomic, neurovascular, and neuroinflammatory changes. Conversely, it cannot be expected to help diagnose nerve injuries with no microvascular involvement such as somesthetic nerve injuries. Proper teaching and understanding of thermoregulation helps the clinician to obtain indispensable information from this test.

LABORATORY TESTS APPLIED IN THE DIAGNOSIS OF CRPS

In the early stages of CRPS, laboratory tests such as STBS or ITI show a spread of the disease from one side to the other. Usually, such tests as magnetic resonance imaging (MRI), computed tomography (CT) scans, electromyography (EMG), nerve conduction velocity (NCV) are not sensitive enough for the diagnosis of CRPS. The MRI and CT scan are anatomical tests which cannot identify the areas of microscopic sensory nerve supersensitization of C-Thermoreceptors unmyelinated nerve fibres in the wall of microvasculature (27-30).

Quantitative sudomotor axon reflex test (QSART) studies the post-ganglionic cholinergic sudomotor function of the sympathetic system, not the thermoregulatory function (3,31). Laser evoked potential (LEP)is a sensitive test for the study of capillary circulation (32-35). It studies a small area of the body thereby limiting its overall extent of information. Quantitative thermal sensory evoked response test (QST) is sensitive and useful in studying the functions of c-thermoreceptors and A-beta mechanoreceptors in CRPS (32,36,37). This test identifies the threshold of somatic(spinothalamic)cold or heat touch sensation-versus neuropathic (sympathetic) cold or heat pain sensation.

The EMG or NCV cannot identify an autonomic nerve dysfunction(38). These tests measure the function of large myelinated trunks of nerve fibres and nerve roots.

Realizing that CRPS type I (RSD) is due to the dysfunction of poorly myelinated or unmyelinated sensory nerve fibres, EMG and NCV cannot be expected to show any abnormality. NCV measures the velocity and function of the large myelinated fibres, which are not usually involved in CRPS type I(RSD). EMG and NCV cannot identify disturbance of small sensory or autonomic nerve fibres (38). Diagnosing CRPS with the help of EMG and NCV is similar to diagnosing a viral infection with a standard-rather than an electron microscope. The NCV usually yields either normal or confusing borderline delay of distal latency in CRPS (probably due too long standing vasoconstriction in the region). Multiple EMG needle insertions in the CRPS extremity may result in further sensitization of alpha-I receptors (9,39).

CRPS type II (causalgia) is frequently due to ectopic, ephaptic (non-synaptic) electrical transmission between damaged myelinated and unmyelinated fibres(40-44). EMG and NCV findings may be abnormal in a minority of these patients, but such test results do not yield an exclusive diagnostic value for CRPS.

The dysfunction of thermal sensory nerves in the wall of arterioles cannot be detected by EMG or NCV. Ignoring this fact may mislead the clinician to diagnose the condition as "psychogenic" or "functional." Our results were compatible with the review of current medical literature.

Relying on tests that yield no information regarding the autonomic nervous system (such as MRI, CT, EMG, and NCV) can mislead the physician either to arrive at the diagnosis of a "malingerer," "Münchausen syndrome," or to decide to perform surgery for a "disc herniation," or a "carpal tunnel syndrome" when the true diagnosis may be sympathetic neuroinflammation mimicking the above mentioned somatic syndromes(10).

Obviously the neurovascular dysfunction cannot be studied by EMG or NCV, but can be evaluated by doppler fluxmetry or ITI (45). Other tests directly or indirectly measure different functions of the autonomic sympathetic system (Table I).

Table I. Commonly used tests for neuropathic pain and somatic pain.

	Nerve Function					Anatomy	
Tests	**Somatic**	**Sympathetic**	**Para-Sympathetic**	**Nerve Fiber Type**	**Clinical Application**	**Advantages**	**Disadvantages**
Scintigraphic Triphasic Bone Scan (STBS)	–	+	–	Deep chemo-receptors fibres	Informative in early stages	Harmless	Only diagnostic in 25-55% of patients (2,3)
EMG; NCV	+	–	–	Somatic, myelinated nerves	Study of efferent spino-thalamic nerves	Neuro-muscular and myelinated somatic nerve study	It cannot study the thermo-receptor or vasomotor function
Infrared Thermal Imaging (ITI)	–	+	–	Micro- vascular and C-thermo-receptors	Sympathetic function	A total body regional study	Shows old and new pathologies indiscrim-inately
Laser Evoked Potential (LEP)	+	+	–	Poorly myelinated C-fibres; A δ	Study of peripheral and central neuropathic pain	Study of C, Aβ, and Aδ fibres	Mainly research
MRI and CT	+	–	–	Large myelinated	–	–	–
Quantitative Sensory Test (QST)	+	+	–	C- thermo-receptors vs spino-thalamic tactile nerves	Accurate test for thermo-receptors vs tactile somato-sensory nerves	Sensitive study of C- thermo-receptors vs somatic fibres	Studies a limited area of the body
Quantitative Sudomotor Axon Reflex Test (QSART)	–	–	+	Para-sympathetic; cholinergic, sudomotor nerves	Sweat function	Sudomotor function	Studies a limited area. It cannot study the thermal function
Somato-Sensory Evoked Potential (SSEP)	+	–	–	Somato-sensory nerve fibres	Identifies sensory nerve tracks	Harmless	Not an autonomic test

SUMMARY AND CONCLUSION

In our study of 824 CRPS patients revealed the fact that no specific test (STBS, ITI or quantitative sudomotor axon test **(**QSART**)**) can "diagnose" CRPS (9). The diagnosis is a clinical one, on the basis of the four principles of: *(I).* Hyperpathic and allodynic pain; *(ii).* Vasomotor and somatomotor dysfunction; *(iii).* Neuroinflammation; and *(iv).* Limbic system dysfunction(9). In this disease, MRI, CT scan, and EMG/NCV are non-diagnostic. The use of STBS is diagnostic in no more than 25-55% of CRPS patients(2,3). ITI shows bilateral thermal changes when the disease involves a single extremity. The ITI identifies the area of permanent neurovascular damage as focal hyperthermia, usually surrounded by hypothermia due too dysfunctional (but not damaged) sympathetic system.

The use of ITI can help facilitate early diagnosis of CRPS, and can achieve a higher recovery rate among CRPS patients by virtue of early diagnosis of the disease (10,25,46,47). It also helps spare the patient from unnecessary sympathetic ganglion blocks by revealing pathologic hyperthermia in the extremity-evidence of "virtual sympathectomy." The phenomenon proves further sympathetic ganglion nerve blocks to be unnecessary and harmful (9,15,19,48).

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