Diagnostic Technology for Spine Pathology

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Diagnostic techniques for spinal pathologies have been developed in accordance with advances in technology. Accurate diagnosis of spinal pathology is essential for appropriate management of spinal diseases. Since the development of X-rays in 1895 and computed tomography (CT) in 1967, several diagnostic imaging modalities have been utilized for detecting spinal pathologies, including radiography, CT, magnetic resonance imaging, and radionuclide imaging. In addition to diagnostic imaging technologies, electrodiagnostic tests, including electromyography and nerve conduction studies, play a significant role as diagnostic tools, as spinal diseases are mostly profoundly associated with pathologies of the neural structures, such as the spinal cord and nerve root, and extent of injury at the structure cannot be adequately detected by conventional imaging techniques. In patient-specific treatment strategies, usage of diagnostic modalities is of great importance; thus, we should be aware of the basic details and approaches of the different diagnostic modalities. In this review, the authors discuss the details of the technologies that aid in the diagnosis of spinal pathologies.

Keywords: Spinal diseases; Diagnosis; Images; Electrodiagnostic study

Introduction

The number of patients with spinal disease has gradually increased over time, and the burden related to spinal disease is challenging from economic, social, and others. Similar to other pathologies, the management and prognosis of spinal disease are profoundly linked to accurate diagnosis [1].

With advances in technology, diagnostic techniques have been improved for the accurate diagnosis of spinal pathologies. Since the development of X-rays in 1895, bony structures of the spine have been confirmed, leading to the development of diagnostic approaches using imaging modalities. Although radiography technology has further developed, much of the information about the spine, particularly disc, spinal cord, and root pathologies, cannot be identified due to the inherent limitations of radiography. In 1967, Sir Godfrey Hounsfield invented the first computed tomography (CT) scanner using X-ray technology [2]; in 1977, Raymond Damadian developed the first magnetic resonance imaging (MRI) machine for clinical use in human diseases [3]. The development of these novel technologies had a significant impact on the clinical diagnosis of all human diseases and the establish-

ment of therapeutic guidelines. However, despite these novel developments in diagnostic imaging technologies, there exists paucity in the field of spinal disease diagnosis, as the spinal pathologies are profoundly connected to neural structures, including the spinal cord, cauda equina, and nerve roots, and the extent of injury at the neural structure cannot be detected by conventional imaging techniques. Thus, electrodiagnostic modalities, including electromyography (EMG) and nerve conduction studies (NCSs), have been utilized as spinal diagnostic techniques [4]. In addition to these technologies, modalities, including bone scans, have been developed to better define spinal pathologies.

Owing to these novel techniques, more accurate diagnosis and patient-specific treatment can be offered for spinal diseases. In this review, we provided detailed information about the technologies that aid in the diagnosis of spinal pathologies.

Imaging Modalities

1. Plain radiography

Since the discovery and application of X-rays by Wilhelm Conrad Roentgen in 1895, they have been used as a first-line modality for diseases of human tissues based on osseous anatomy [5]. In spinal pathology, X-rays rapidly became widely used as an invaluable diagnostic tool in spinal imaging. With the development of modern radiographic technologies, advanced imaging modalities have been introduced. Nevertheless, plain radiograph remains the first and most widely used imaging modality for localizing suspected spinal symptoms, including pain, numbness, and weakness [6]. Radiography aids intuitive recognition of the patient's condition since it provides overall information about each spinal segment and the entire vertebral column in a few images [7]. Notably, imaging is relatively artifact-free compared with other modalities considering that it is achieved in a very short time.

Plain radiography has a comparative advantage over complex modern imaging techniques, as it is possible to acquire images while freely adjusting the patient's position. Beyond static imaging, it has the advantage of being able to obtain an image wherein the actual movement of the patient is performed while applying a dynamic factor, such as gravity (standing radiograph) and motion (flexion-extension and bending radiographs). Flexion-

extension lateral radiograph-based dynamic imaging can confirm the presence of instability and determine the dynamics of the spinal lesion [8-13]. In preoperative evaluation and surgical planning, dynamic radiography provides information, such as the effects of gravity, spinal mobility, and instability. Recently, imaging techniques, including bending X-rays [14,15] and prone-traction radiography [16], have been introduced to predict motion in an operative position before surgery. Although dynamic plain radiography is available, including gravity and dynamic elements, it does remain a static image. At the moment of filming, the patient must temporarily stop moving and remain stationary in one position.

As a diagnostic modality, the most serious limitation of plain radiography is the difficulty in identifying soft tissue structures. Occasionally, internal organ structures, such as the bowel gas, overlap bony structures, making it difficult to identify spinal osseous pathology, which can lead to finding false-positive lesions. When skeletal tissues, such as the rib, humeral head, and iliac crest, exist together around the spine, they can overlap and obscure the corresponding spinal column, making it difficult to identify lesions or cause underestimation.

Radiation hazards are an unavoidable risk in X-ray imaging, and although the cumulative amount is not large, it cannot be excluded from cancer risk [17]. Under specific conditions, such as the first trimester period of pregnancy, X-ray imaging is considered an absolute contraindication as it may directly harm the fetus [18]. Efforts are made to minimize radiation exposure when long-term, continuous, and repeated radiation is essential for several torso pathologies, such as in the evaluation of adolescent scoliosis [17].

2. Computed tomography

CT allows good visualization of spinal pathologies, including compression of neural structures and diseases of laterally situated structures (such as foraminal stenosis) [19-21]. Modern spiral CT with multidetector rows allows for fast and continuous data acquisition within a few seconds [22]. In the diagnosis of spinal diseases, CT is particularly valuable for evaluating osseous structures. Volumetric reconstruction of three-dimensional (3D) images and multiplanar post-image acquisition processing provides excellent visualization of the bony structure of the spinal column and intuitive information pre- and
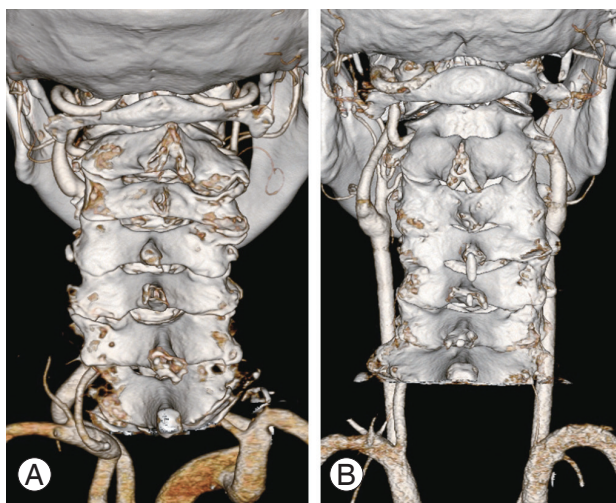
Fig. 1. Three-dimensional computed tomography images for preoperative planning. **(A)** Bilateral vertebral arteries with normal course were observed. **(B)** Right unilateral vertebral artery without left vertebral artery was detected.

postoperatively [23,24]. In particular, CT is appropriate to explore complex anatomical areas (such as occipito-cervical junctions and sacroiliac regions) or lesions wherein normal anatomy has largely been lost due to congenital anomalies, degenerative processes, or previous surgical treatments (Fig. 1) [25].

The intrinsic capability of CT in discriminating spinal osseous lesions arises from exceptional sensitivity and specificity to cortical bone abnormalities. Lesions, including cortical discontinuity, thinning, and margin irregularity, can be readily identified on CT. It is useful for identifying skeletal lesions that are very small or unclear on plain radiography [26]. CT provides higher sensitivity than MRI in distinguishing calcified hard disc lesions or ossification of ligamentous structures (such as the posterior longitudinal ligament or ligamentum flavum) [27-29]. Additionally, the evaluator can easily adjust the contrast and window level in the captured image. Subtle soft tissue abnormalities, such as intervertebral disc protrusion, can also be detected through adjustment to a density that can best visualize each soft tissue and bony structure. CT can accurately assess postoperative conditions, including achieving solid spinal fusion, positioning of implanted material, and hardware-related complications [30].

Despite these advantages, CT has inherent limitations in the evaluation of spinal diseases. Since the introduction of CT, cancer risk due to high radiation exposure has been a fundamental challenge [31]. High-dose radiation

exposure to patients is required to obtain high-resolution images. Conversely, images of relatively low resolution are derived with low-dose radiation; therefore, there is a possibility that the diagnosis may be missed or misdiagnosed in the case of minute changes in the cortical bone. Distinguishing soft tissues (even with contrast agents) has limitations, particularly between muscles, ligaments, and neural structures around the spine. Spatial artifacts are a challenge, such that the size of the cortical bone appears larger than it is at soft tissue density. When cortical bone diameter/thickness is important, such as in surgical planning for screw placement, a change to bone density setting is recommended. CT images are vulnerable to the formation of metal artifacts from metal foreign bodies in the body, and specific image acquisition and reconstruction are required [32,33]. Particularly, detailed tissue examination may be hindered when previous implantation or foreign bodies containing steel are present around the lesion.

3. Magnetic resonance imaging

MRI is an imaging technology that detects and visualizes changes in the arrangement of hydrogen nuclei (protons) in cells within an artificial magnetic field. Similar to CT, MRI can achieve excellent anatomical and spatial resolution through multiplanar images [34]. Protons are temporarily aligned in one direction when an artificial magnetic field is generated; simultaneously applied radiofrequency pulses disrupt this uniform alignment. The protons attempt to return to their original arrangement when the magnetic field is removed. This shift-back timing varies according to the difference in the number of protons in the tissue, that is, the water content [35,36]. The MRI machine distinguishes shift-back timing (and water content) differences between tissues.

The strength of MRI is that it provides visualization and clear distinction through high-resolution images of individual tissues and organs, particularly soft tissue structures. Spinal diseases affect both the complex bony structure constituting the vertebral column and the diverse soft tissue structures, including ligaments and muscles surrounding the spine, intervertebral discs, and neural structures, including the spinal cord and nerve roots. Therefore, despite its relatively high cost and difficulty in accessibility, MRI, which can visualize both osseous and soft tissues, has become an essential element in the diagnosis of spinal diseases. With the advancement

of this technology, the field strength of the superconducting magnets of the MRI machine has gradually increased from 0.15 T initially to 9.4 T at some settings [37]. The standard protocol for spine MRI generally includes axial and sagittal images of T1- and T2-weighted sequences [34]. Depending on the characteristics and phase of the disease, fat suppression T2-weighted images, such as short tau inversion recovery or contrast-enhanced T1 images, are frequently added to sagittal images [34].

T1-weighted images are specialized in providing anatomical details of changes in the bone marrow, osseous structures, discs, and musculotendinous soft tissue [34]. The neural structure is expressed as intermediate signal intensity in the T2-weighted image; however, it provides well-visualized information through perfect contrast with the high signal intensity of the surrounding cerebrospinal fluid [38]. Fat suppression technology provides highly contrasted images for the visualization of pathological structures [39,40].

Similar to CT, intravenous contrast agents can be used in MRI. However, unlike CT, which provides detailed visualization of the vascular structure, gadolinium enhancement used in MRI reduces the relaxation time of molecules around the magnetic field and transmits an image with increased signal intensity of tissue showing hypervascularity. This enhancement appears most clearly at T1 and is used for the diagnosis of epidural fibrous scars, infections, tumors, vascular malformations, or leptomeningeal lesions [41-44].

MRI can identify small soft tissue structures in the spine, including the spinal cord, surrounding vessels, and nerve roots [45-47]. Spine MRI is an essential diagnostic tool for evaluating lesions in degenerative diseases, such as spinal stenosis, disc herniation, and myelopathy [47-49]; the vertebrae, ligaments, and spinal cord after trauma [50-52]; and the benign/malignant nature, size, and extent of tumorous lesions [45]. Similar to CT, in the case of acute traumatic osseous lesions, such as fractures, sensitivity, and specificity are high. However, the MRI identification point is different from CT in that it checks for fractures based on signal changes in the bone marrow and cancellous parts rather than direct visualization of the cortical bone. Using signal changes based on bone marrow edema, MRI identifies the presence and location of acute fracture or soft tissue injury and simultaneously distinguishes it from normal tissue without injury. T1-weighted imaging is useful for evaluating the integrity of ligament structures,
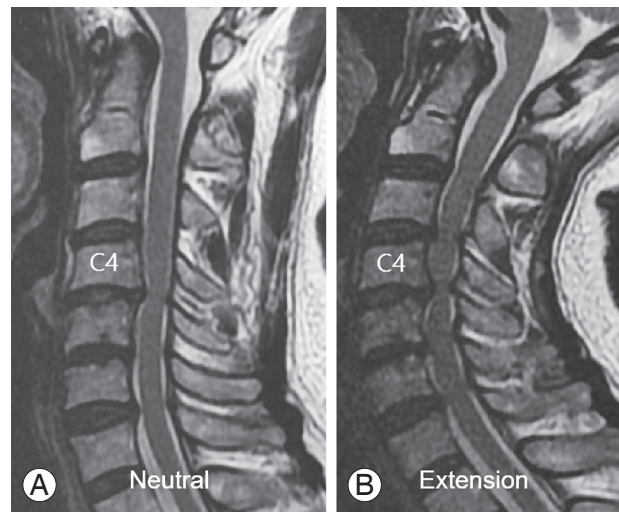

Fig. 2. A 63-year-old female patient with degenerative cervical myelopathy. **(A)** Neutral sagittal magnetic resonance (MR) imaging of the cervical spine showed a C4–5 canal stenosis with signal change of the spinal cord. **(B)** Extension sagittal MR of the cervical spine showed more aggravated cord compression of C4–5 segment, as well as the cranial and caudal extension of the cervical canal stenosis to C3–7 levels.

particularly anterior and posterior longitudinal ligaments and epidural hematomas [53-56]. MRI is also used to diagnose inflammatory conditions, such as multiple sclerosis, sarcoidosis, and transverse myelitis, because it can detect swelling of the spinal cord (acute inflammation) or demyelination (chronic inflammation) [57-59].

Dynamic or axial-loaded MRI was developed to perform MRI in locations that may best reveal pathology. In the diagnosis of cervical myelopathy, dynamic (neck extension) MRI usage is gradually increasing (Fig. 2) [60-63]. Recently, to obtain MRI with gravity added, weight-bearing MRI has been introduced in some facilities. It is promising that the pathologic status of the erect spine, including actual weight-bearing, can be reflected in the image [64-67]. However, it is unlikely to replace conventional MRI owing to technically limiting factors, such as lower image resolution [68,69] and longer examination time [67,70]; therefore, it is used as additional or auxiliary imaging technology. Given the cortical bone has sparse free-water content, most signals in MRI are generated by bound water; thus, signal decay is fast, and signal intensity is low [71]. To overcome these shortcomings, technologies, including ultrashort echo time sequences, have been developed to amplify weak cortical bone signals to enhance imaging [72,73].

Similar to other diagnostic imaging modalities, MRI

has drawbacks. Completing an MRI scan takes several minutes, which is longer than the period for completing a CT scan. The increase in magnetic field strength has dramatically improved the MRI resolution; however, this requires more imaging time, thereby causing patient inconvenience and increased possibility of motion artifacts. The possibility of artifact formation based on patient motion is inherent. Moreover, due to interference with magnetic fields, metal artifacts in MRI are formed more extensively than those in CT. In the case of ferrous metal-containing implants, including artificial discs, wires, or screws, extensive artifacts are formed in the area adjacent to the neural structure, thereby obscuring lesions in the adjacent area [74]. There is a possibility that imaging may be impossible or limited due to factors inherent to the patient, such as claustrophobia and the presence of ferromagnetic devices [74,75]. Furthermore, the imaging of tissues with very low water content or thickness, such as the cortical bone and calcified tendon/ligament or cartilage, is not as clearly distinguishable from other soft tissues [76]. For pregnant women, MRI is considered to be a relative contraindication, particularly in the first trimester [77].

Radionuclide Imaging

Bone scans (bone scintigraphy) are one of the primary nuclear medicine tests. Bone scans have high sensitivity and can easily evaluate the bones of the whole body. Generally, this modality scans from the head to the toe using a gamma camera 2–6 hours after intravenous injection with ^{99m}Tc-labeled polyphosphonate. However, it includes obtaining a local planar image or a single-photon emission computed tomography (SPECT) image while the gamma camera is fixed. Bone scans are used to evaluate suspicion and extent of metastatic disease, differentiation of fractures and trauma from inflammatory diseases of the skeleton, and evaluation and observation of the prognosis of radiotherapy, benign tumors, arthritis, metabolic bone disease, infection, and other skeletal disorders [78,79].

Although their uptake mechanism is unclear, they are absorbed by chemisorption on the surface of hydroxyapatite by bone metabolism. The degree of accumulation of these drugs depends on biological factors, including bone blood flow and turnover. In the case of a whole-body bone scan, an intravenous injection of a phosphate compound is followed by imaging of the whole-body skeleton or a specific area 2–4 hours later according to the prescribed

protocol. The acquired images are 100% and 70% enhanced images; 100% images are used for shallow bone examination, and 70% images are used for thick bones, including the spine. When analyzing the bone condition and vascular distribution of soft tissues is necessary, such as in osteomyelitis, latent fractures, and joint diseases, the radiopharmaceutical is intravenously injected while a simultaneous flow image is obtained for 60 seconds, and a blood pool image is obtained within 10 minutes of injection. After 2–4 hours, a delayed image is obtained by statically capturing the image of the region of interest and evaluated. This image is known as a three-phase bone scan.

Bone scan is superior to X-ray in some circumstances, as it can show abnormal findings with only 3%–5% mineral change, whereas a 30%–50% change is required by other radiological examinations. Since the gamma-ray signal has a linear relationship with lesion severity, it is more useful than MRI in quantitative evaluation.

1. Bone scintigraphy (bone scan)

Radionuclide bone scintigraphy, also called bone scan, is a molecular imaging that is widely used in detecting spinal pathologies. Owing to its high sensitivity, bone scans can detect 3%–5% of bone mineral change; however, its specificity is relatively low. Due to this high sensitivity, it can be used for screening or confirming compression fractures that cannot be detected on plain radiographs. Vertebral compression fractures can be diagnosed using simple radiography, radionuclide bone imaging, and imaging modalities, including MRI. Occult fractures that are not visible on simple radiographs can be diagnosed by MRI or bone scan; however, Zhao et al. [80] found no difference in sensitivity between these two imaging modalities. In the case of MRI, the examination time is long, and the cost is high; therefore, it is considered cost effective to use bone scans for this diagnosis [81,82].

Osteomyelitis and pyogenic arthritis are accompanied by systemic symptoms related to inflammation, which can cause tissue destruction in the bones and joints. However, within 10 days of symptom onset, plain radiographs generally show normal or non-specific findings. Radionuclide imaging is a useful adjunct to MRI, which is the imaging test of choice for spinal infection. Although not useful for detecting soft tissue infections, it is a screening test for spondylodiscitis. Gallium-67 imaging with bone scan in-
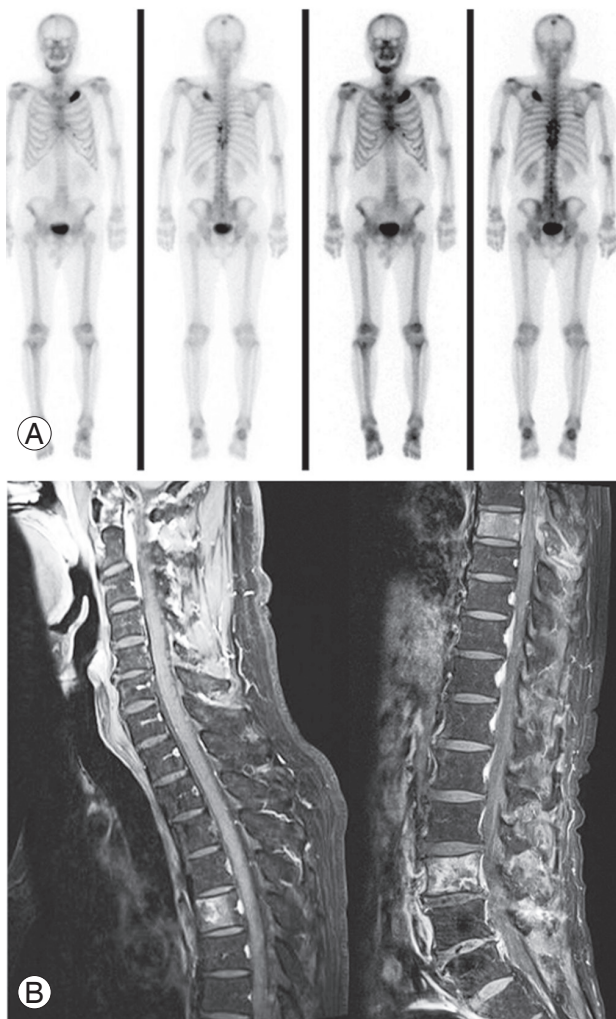
Fig. 3. A 75-year-old male patient was admitted to the emergency room with lower motor weakness and sensory change that gradually developed and was diagnosed with T7–9 epidural space mass lesion and prostate cancer multiple metastasis. **(A)** A preoperative whole-body bone scan showed hot-uptake of the skull, mandible, multiple ribs, T7–11, and L4–5, suggesting metastasis. **(B)** In the preoperative enhanced magnetic resonance image, metastasis was confirmed in the T5, T7, and L3 vertebral bodies, and T7–9 cord compression was seen.

creases the specificity of the scan [83,84].

In patients with malignant diseases, prompt diagnosis and appropriate treatment are significant factors for a healthy life. Since most bone metastases are asymptomatic, imaging modalities for early detection have been introduced, with bone scan being the modality of choice [85-88] (Fig. 3). Bone metastasis is often detected late, and serious effects, such as pathologic fracture and cord compression, are highly likely, significantly diminishing patient treatment outcomes and quality of life. Several studies have shown that bone scan sensitivities for bone and vertebral

body metastases are high (87% and 84%, respectively) [89,90]. However, when Park et al. [91] considered a bone scan performed on a patient with cervical spinal metastasis, the sensitivity and specificity were 59.1% and 94.6%, respectively. These dissimilar results were attributed to differences in bone metabolism related to the primary cancer type and anatomical characteristics of the cervical spine. Despite some controversial results, the value of a bone scan as a screening test for bone tumors and metastasis is considered high.

Imaging tests are significant for diagnosing rheumatoid arthritis and confirming the course of disease. Although simple imaging is widely used, plain radiographs have limitations in early diagnosis, whereas bone scans examine the whole body to identify early disease. Diagnosis of inflammatory diseases, such as rheumatoid arthritis, ankylosing spondylitis, and Reiter syndrome, is important as they accompany sacroiliac arthritis. To quantitatively evaluate sacroiliac joint inflammation, the sacroiliac joint/scrum ratio is computed based on the central portion of the sacrum in a bone scan. Sacroiliac arthritis is suspected if the value is 1.15 or more, and diagnosis is positive if it is 1.2 or more [78]. Gheita et al. [92] suggested that bone scans are useful for detecting disease activity and peripheral arthritis in patients with subclinical axial seronegative spondyloarthritis. Currently, bone scintigraphy of the spine is widely used.

2. Single-photon emission computed tomography/computed tomography

SPECT/CT is a fusion of CT imaging and SPECT, which acquires an image by rotating a gamma camera around the patient using radioactive isotopes to reconstruct a cross-sectional image. SPECT/CT complements SPECT, which has poor spatial resolution, to increase diagnostic specificity, and enable quantitative measurements [93,94]. Horger et al. [95] found that SPECT/CT was 85% more accurate than bone scan alone. Accuracy increases in areas with complex anatomical structures, such as axial skeletal structures, where planar evaluation is difficult. Arthritis causes back pain when it occurs in the facet joint of the spine; however, it is difficult to distinguish early due to slight changes using plain radiography. Using SPECT, osteoarthritis is diagnosed by confirming an increase in intake in the facet joint with a diagnostic sensitivity and specificity of 85%–100% and 71%, respectively; SPECT/

CT can be used to localize the uptake site, which results in more accurate diagnostic results [96-99].

SPECT/CT is a highly recommended diagnostic tool for specific spinal pathologies, including spondylolysis, occult fracture, infection, and malignancy. While bone scans have high diagnostic sensitivity, SPECT/CT can evaluate the spine as a 3D tomography image; therefore, it can have a higher diagnostic accuracy than bone scans [100,101]. Studies have shown that SPECT/CT can be a useful diagnostic method for detecting spinal diseases, including malignant tumors, active phases of arthritis, minor trauma, infections, pseudoarthrosis, and postoperative pain caused by minor factors [102,103].

Electrodiagnostic Studies

1. Central motor conduction time study

Central motor conduction time (CMCT) studies evaluate the state of the corticospinal tract in the brain or spinal cord based on motor evoked potentials (MEPs) (Fig. 4A). Generally, the values for CMCTs are recorded from the bilateral biceps brachii (BB), abductor pollicis brevis (APB), and tibialis anterior (TA) muscles. Electrodes are attached to the selected muscles to induce an MEP. Magnetic stimulation is initiated over the primary motor cortex and delivered to the muscles on the contralateral side of the stimulated cortex by inducing muscle contraction. Muscle contractions are recorded as MEPs, and the latency is calculated; CMCT is estimated by subtracting the latency of nerve conduction between the spinal nerve root around the intervertebral foramen and the muscle, where an electrode was attached, from the latency of nerve conduction from the cerebral cortex to the muscle via the corticospinal tract. The cut-off values are 8.5, 9.2, and 18.1 ms for BB-CMCT, APB-CMCT, and TA-CMCT, respectively [104].

2. Sensory evoked potential study

Sensory evoked potential (SEP) studies evaluate the state of the sensory tract in the brain or spinal cord. The SEPs of the bilateral median and posterior tibial (PT) nerves are generally assessed (Fig. 4B); SEPs of median nerve stimulation at the wrist (N19, P23) and PT nerve at the ankle (N37, N45) are recorded on the scalp overlying the primary sensory area (median nerve: C3' and C4', PT nerve:

Fig. 4. Assessment of central motor conduction time **(A)** and sensory evoked potential **(B)**.

Cz') in the parietal lobe contralateral to the stimulated side. The cut-off values are 21.0 (N19) and 24.6 ms (P23) for median-SEP and 43.4 (P37) and 51.1 ms (N45) for PT-SEP [104].

3. Nerve conduction study and electromyography

NCS and EMG evaluate the state of peripheral nerves and muscles [105,106]; the information on the degree and site of nerve injury can be obtained. Using EMG, the presence of muscle pathology can be investigated. In NCS, electrical stimulation is delivered to the nerves by the stimulating electrode, while the recording electrode attached to specific sites on the nerves receives electrical activity [105]. Subsequently, the latency for the muscles to contract in response to the nerve electrical stimulation, conduction velocity, and amplitude are assessed. EMG evaluates the electro-physiological condition of a muscle by the insertion of a thin needle electrode directly into the muscle tissue [107]. Electrophysiological alterations occur in a muscle if nerve or muscle damage is present. In spinal disorders, NCS/EMG can be used to evaluate the presence and level of radiculopathy. Before spinal surgery, NCS/EMG is used for the differentiation of other possible unexpected disorders, including motor neuron disease, Guillain–Barré syndrome, and peripheral demyelinating disease [108,109]. Therefore, NCS/EMG can prevent un-

necessary spinal surgery by accurately diagnosing the lesions causing neurological symptoms.

Conclusions

Accurate diagnosis and patient-specific treatment strategies for spinal diseases are of paramount importance although remain challenging despite the advancement of diagnostic technologies. In recent years, these technologies have significantly improved, allowing for greater accuracy and reliability to be achieved in diagnosing spinal pathologies. Diagnostic technologies, such as X-rays, CT, MRI, and electrodiagnostic tests, can aid in appropriate patient management and accurately determine prognosis. Therefore, to determine the best approach for each patient, clinicians should be aware of the essential diagnostic modalities for the spine.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Conceptualization: GWL; data curation: GUK, GWL; formal analysis: GWL; funding acquisition: GWL; methodology: GUK, GWL; project administration: GWL; visualization: WTP, MCC; writing–original draft: GUK, WTP, MCC, GWL; and writing–review & editing: GWL.

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