Relationship Between Paraspinal Muscle Morphology, Function, and Physical Status in Common Spinal Disorders

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ABSTRACT

Relationship Between Paraspinal Muscle Morphology, Function, and Physical Status in Common Spinal Disorders

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The deep paraspinal muscles are essential for providing physical support and stability to the spinal column. They play a vital role in maintaining fine postural control of the spine and are responsible for controlling all movements of the vertebral column. These muscles work in coordination to ensure proper alignment and movement of the spine, thereby contributing to overall spinal health and function. Dysfunction or weakness in paraspinal muscles can lead to instability, poor posture, and increased risk of spinal pain disorders. Therefore, understanding the role of deep paraspinal muscles is crucial in maintaining spinal health and preventing musculoskeletal disorders. This summary highlights the significance of assessing both morphology and function of paraspinal muscles in common spinal disorders including chronic low back pain (LBP) and degenerative cervical myelopathy (DCM). While previous studies have focused on either morphology or functional deficits separately, this dissertation aims to comprehensively investigate the structure-function relationship using advanced imaging techniques like magnetic resonance imaging (MRI) and ultrasound. Specifically, chapter three focuses on understanding the relationship between lumbar multifidus muscle (MF) muscle morphology and function in chronic LBP patients, utilizing measures such as fatty infiltration, contraction, stiffness, and elasticity. Similarly, chapter four and five aim to assess cervical muscle morphology as predictors of prognosis and functional recovery in patients with DCM, both pre- and post-operatively. Such comprehensive evaluations are crucial for improving

diagnosis, intervention, and therapeutic strategies in spinal disorders, ultimately enhancing patients' clinical outcomes and quality of life. Finally, chapter six discusses the findings from chapters three, four and five and offers a general conclusion and recommendations for future research.

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CONTRIBUTION OF AUTHORS

Manuscript 1:

Neda Naghdi participated in the research design, acquired the MRI cervical muscle measurements, completed the data analysis, and drafted the manuscript. James M. Elliott participated in the research design, interpretation of the results and critically reviewed the manuscript. Michael H. Weber and Michael G. Fehlings provided access to the data and critically reviewed the manuscript. Maryse Fortin contributed to the conception, design of the study, data analysis, interpretation of the data. All authors read and approved the final manuscript.

Manuscript 2:

Neda Naghdi participated in the research design, acquired the MRI cervical muscle measurements, completed the data analysis, and drafted the manuscript. Dr. Micheal Weber provided access to the data and critically reviewed the manuscript and Maryse Fortin contributed to the conception, design of the study, data analysis, interpretation of the data. All authors read and approved the final manuscript.

Manuscript 3:

Neda Naghdi participated in the research design, planned the statistical analyses, recruited the participants, collected the data, analyzed the results, and wrote the manuscript. Brent Rosenstein contributed to the recruitment, and data collection. Sara Messi and Cleo Bertrand participated in the MRI and ultrasound lumbar muscle measurements. Dr. Maryse Fortin, contributed significantly to the conception, design, data collection, analysis, revision, and editing of the manuscript. All authors read and approved the final manuscript.

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CHAPTER 1: INTRODUCTION

The deep paraspinal muscles play a crucial role in physical support and stability of the spinal column, fine postural control of the spine and control of all movements of the vertebral column (1). Accordingly, the association between paraspinal muscle morphological and functional deficits with spinal stability, posture, and the risk of injury has been a topic of interest in spinal biomechanics research. While some evidence suggest a link between weakened paraspinal muscles and adverse outcomes such as spinal instability and poor posture, (1-7) the level of certainty surrounding this relationship remains a subject of debate.

A large body of evidence suggest that patients with low back pain (LBP) have degenerative paraspinal muscle changes including reduced lumbar multifidus (MF) muscle size (1, 2), increase fat infiltration (3), asymmetry and muscle atrophy (4, 5) as compared to healthy controls. This may result from pain-related disuse, reflex inhibition, and/or muscle denervation (6, 7). Functional impairments of the MF are also associated with LBP and several studies have found the presence of muscular functional deficits in individuals with LBP (8, 9). Decrease muscle strength (10), delay contraction during postural perturbation (10) are some examples of reported functional changes in these patients.

On the other hand, recent studies have reported that the deep extensor neck muscles, especially the cervical MF and semispinalis cervicis (Scer), are often impaired in patients with cervical disorders (11, 12) and atrophied in patients with whiplash-type injury or chronic neck pain (13, 14). The deep extensor paraspinal muscles have shown to be associated with poor clinical symptoms and functional outcomes in degenerative cervical mylopathy (DCM) (15, 16).

As mentioned above, most previous studies have specifically examined either morphology alteration or functional deficit separately. Although the structure-function relationship of paraspinal muscles in LBP patients has been recently investigated in a few studies (16, 17), literature findings in non-specific chronic LBP remain conflicting; some studies found that lumbar fatty infiltration is accompanied by diminished muscle performance (1-3,10) . Whereas others could not find any relationship (18). Providing the evidence to support the theory that paraspinal muscle morphology has a significant impact on muscle function using the combination of two methods to assess the structure-function relationship, including magnetic resonance imaging (MRI) (to measure size, fat infiltration and asymmetry of muscle) and ultrasound (to assess thickness change during contraction, stiffness, elasticity) as comprehensive and contemporary standard imaging techniques is central to improve our insight and achieve more precise and inclusive assessment, diagnosis, intervention and therapeutic intervention in common spinal disorders. Moreover, using novel and non-invasive measures such as shear-wave elastrography (SWE) is key to further our understanding at a functional/physiological muscle level. Indeed, SWE can provide information about muscle function, as changes in shear modulus are linearly proportional to muscle force (19-22). Therefore, SWE can be used to evaluate the force production capability of individual muscles in motor tasks with muscle redundancy, which cannot be achieved with current clinical tests. The main objective of the third research project of this doctoral thesis was to determine the relationship between lumbar MF muscle morphology (e.g., fatty infiltration) and function (e.g., contraction, stiffness) in patients with chronic LBP.

Furthermore, while patients with chronic neck pain demonstrate alterations in cervical muscle morphology and delayed activation during postural perturbations (13), few studies have specifically examined how the cervical muscles may play a role in the development of symptoms and functional impairments in DCM (15). A recent study from Fortin et al. (16) was the first to establish an association between cervical muscle morphology, clinical symptoms, and functional status in patients with DCM. The same study also reported an increase in MF muscle fatty infiltration at the level below the spinal cord compression, most likely due to denervation (16). In another investigation, Fortin et al. (16) found a strong positive correlation between cervical muscle strength and lean muscle mass measured by MRI. Given these findings, it is probable that such variations in cervical muscle morphology and function may contribute to the variability in outcomes observed in patients with DCM undergoing surgical decompression (14). However, few studies have evaluated the deep extensor neck muscles of patients with DCM and their potential role as predictors of post-operative outcomes (15, 16). Therefore, the presence and extent of morphologic muscle changes in patients with DCM warrants further attention. As such, the objectives of the first project of this doctoral thesis was to assess preoperative cervical muscle size, composition, and asymmetry as possible predictors of prognosis and functional recovery following surgical treatment in patients with DCM. In the same vein, the second project described in this thesis evaluated the effect of decompression surgery on cervical muscle morphology and strength in patients with DCM.

The exploration of muscle morphology in the context of clinical outcomes for DCM and LBP offers a unique lens through which to understand the complexities of these conditions. DCM, characterized by progressive degeneration of cervical spinal cord and distinct imaging findings such as cord signal changes, presents a clear diagnostic pathway compared to the often elusive nature of LBP, where approximately 80% of cases are labeled as "non-specific." This marked contrast in diagnostic clarity and management approaches underscores the diverse challenges clinicians face in treating spinal conditions.

While the focus of this thesis lies primarily on the role of muscle morphology in shaping clinical outcomes, it is crucial to acknowledge the broader context within which these conditions manifest. DCM, with its well-defined clinical and radiological features, presents an opportunity for targeted intervention strategies aimed at halting disease progression and improving patient outcomes. Conversely, the multifactorial nature of LBP demands a more nuanced understanding of the interplay between biological, psychological, and social factors in its etiology and management.

Understanding the mechanical characteristics of muscles is essential for diagnosing and researching musculoskeletal disorders. Additionally, applying this knowledge in patient rehabilitation settings and targeted treatment strategies can yield significant benefits. The advancement of non-invasive techniques to assess the mechanical properties of muscles, both at rest and during contraction, offers clinicians valuable tools for diagnosing, treating, and investigating skeletal muscle conditions and adaptations across various populations. By incorporating this knowledge into clinical practice, rehabilitation outcomes can be enhanced, and our comprehension of musculoskeletal health can be further developed, leading to more effective treatment approaches and improved patient care.

1.1. Rationale for PhD thesis:

The introduction highlights the crucial role of deep paraspinal muscles in spinal stability and control, focusing on degenerative changes in patients with LBP and cervical disorders. Existing literature has explored either morphological alterations or functional deficits separately, leading to conflicting findings (1, 16, 17, 23). The overall goal of this thesis was to simultaneously examine the structure-function relationship of the paraspinal muscles in common spinal disorders and their possible implications with patients'clinical outcomes using advanced imaging techniques. While previous research has hinted at the importance of paraspinal muscle strength for spinal health, our investigations aimed to provide a more comprehensive understanding of this relationship and clarify areas of divergence within the current body of literature. Furthermore, by leveraging advanced imaging technologies utilizing a combination of MRI and ultrasound imaging techniques, we aspired to offer novel insights to inform future research directions, clinical interventions and therapeutic strategies to improve the prevention and management of spinal disorders.

In summary, this doctoral thesis builded upon existing knowledge by employing advanced imaging techniques to delve deeper into the relationship between paraspinal muscle structural deficits and its consequences for spinal health. To this end, we aimed to substantiate previous findings and generate new insights to inform future research directions and clinical interventions in the field of cervical and lumbar spinal disorders.

1.2. Study objectives and hypotheses

The purpose of this dissertation was to:

Objective 1: Cervical Muscle Morphometry and Composition Demonstrate Prognostic Value in Degenerative Cervical Myelopathy Outcomes (Manuscript 1, Chapter 3)

The purpose of this study was to examine whether preoperative cervical muscle size, composition and asymmetry are predictors of prognosis and functional recovery following surgical treatment in patients with DCM.

Hypotheses:

We hypothesized that smaller cervical muscle, greater pre-surgical asymmetry, and fatty infiltration on clinically warranted MRI scans will be associated with greater symptom severity and lower functional scores post-surgery.

Objective 2: Postoperative assessment of cervical muscle morphology, strength, and functional outcomes in patients with degenerative cervical myelopathy. (Manuscript 2, Chapter 4)

The purpose of this study was to investigate the effect of decompression surgery on cervical muscle morphology and strength in patients with DCM. The secondary objective was to examine the correlation between preoperative cervical muscle morphology, cervical muscle strength and postoperative functional outcomes in patients with DCM.

Hypotheses:

Based on previous findings (24), we hypothesized that cervical muscle strength will increase at 2-year post-surgery. Also, greater cervical muscle strength and lower fat infiltration pre-surgery would be associated with better functional outcome post-surgery.

Objective 3: Evaluation of structural alterations and mechanical properties of the MF muscle in chronic low back pain using contemporary images-based methods (Manuscript 3, Chapter, 5)

The aim of this study was to evaluate the relationship between MF muscle morphology (e.g., fatty infiltration) and function (e.g., contraction/thickness ratio, stiffness/elasticity) in individuals with and without LBP. Furthermore, a secondary objective was to identify and examine differences in MF muscle function between individuals with and without LBP.

Hypotheses:

We hypothesized that greater MF muscle fatty infiltration is associated with greater muscular contraction and greater muscle stiffness and subjects with LBP show a lower contraction and greater muscle stiffness as compared with subjects without LBP.

CHAPTER 2
REVIEW OF THE LITERATURE

Paraspinal muscle

2.1.1. Anatomy, function, and innervation

The paraspinal muscles are a group of deep muscles that run on both side of the vertebral column from the occipital bone to the sacrum and attaching directly into the spine (25, 26). Functionally, the posterior extensor muscles of the spine provide spinal stabilization, while maintaining the spinal alignment and segmental motion (Table 2.1) (25-27).

2.1.1.1. Cervical paraspinal muscle

Multifidus

The multifidus (MF) is the deepest and most medial muscle of the cervical spine, attaching directly on the spine and lying under the semispinalis muscles (28). The MF originates from the transverse process of one vertebra and insert on the spinous process of a vertebra located two to four segments above (Fig 2.1) (29). The cervical MF, as opposed to the thoracic and lumbar region, originates directly from the capsules of the zygapophyseal joints, which may partially explain its role in the development of neck pain and injury (29). Because the cervical MF muscle and semispinalis cervicis occupy the paravertebral groove between the spinous and transverse processes, it can be difficult to distinguish the two muscles and determine their respective muscle boundaries on magnetic resonance imaging (MRI) (28).

Figure 2.1. Origin and insertion of multifidus muscle

**https://www.kenhub.com/en/library/anatomy/multifidus-muscle*

Semispinalis cervicis:

Semispinalis cervicis (Scer) is located under the MF and erector spinae (longissimus cervicis, iliocostalis cervicis) (30). The fibers of the Scer attaches from the transverse processes of T1-T5 to spinous processes of C2-5 (Fig 2.2) (30, 31). This muscle acts as an extensor of vertebral column and also assist with rotation towards the opposite side, both in the upper thoracic and cervical areas (30, 31). Muscle fibers attaching to the prominent spinous process of C2 are exceptionally well developed, serving as important stabilizers for the suboccipital muscles (31). The boundaries of the Scer muscle and erector spinae are difficult to differentiate properly (28). The deep Scer muscle is also active predominately in extension with a small ipsilateral component (31). The Scer' preferred direction of activity, together with the splenius capitis and semispinalis capitis (Scap), attests its function as a main extensor (31, 32).

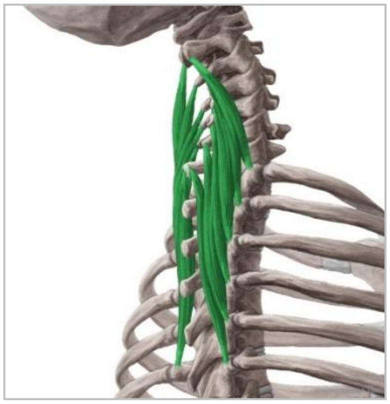

Figure 2.2. Origin and insertion of semispinalis cervicis muscle

**https://www.kenhub.com/en/library/anatomy/semispinalis-cervicis-muscle*

Semispinalis capitis

The Scap is a major muscle of the cervical spine, lying between Scer and splenius muscles, forming a large and distinct muscle layer (30, 31). The muscle originates primarily from the upper thoracic transverse processes (31). As it attaches to a very broad region on the occipital bone, the muscle is thicker superiorly, occupying most of the space between the superior and inferior nuchal lines (Fig 2.3) (28). Although the Scap is located between the occiput and T6/7, the cross-section of this muscle is most apparent between the occiput and C6/7 (28, 30). Below this level, the Scap becomes much thinner and less distinct (28).

Together, the Scap and Scer are the largest muscles composing the posterior side of the neck (31). Their large size and near-vertical fiber direction provide significant extension torque to the craniocervical region (31). The right and left Scap muscles, which feel like thick and circular cords on either side of the midline upper neck, are easily palpable (31, 32).

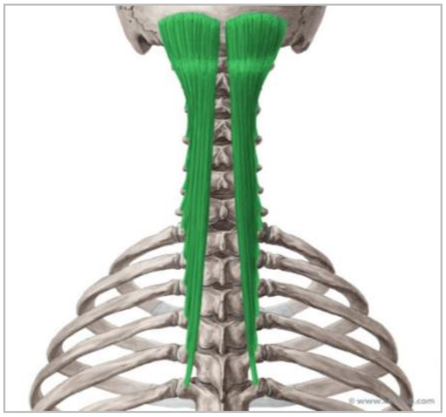

Figure 2.3. Origin and insertion of semispinalis capitis muscle

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Splenius capitis:

Splenius capitis arise from ligamentum nuchae, spinous process of seventh cervical vertebra and spinous process of first three or four thoracic vertebra (C7-T4) to the occipital bone and mastoid process of the temporal bone (30, 31) (Fig 2.4). This muscle as a distinct layer is located between the trapezius, sternocleidomastoid and the Scap (31). The splenius capitis acts on the head to produce extension, ipsilateral rotation, and ipsilateral side-bending of the cervical spine (30, 31).

Figure 2.4. Origin and insertion of splenius capitis muscle

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2.1.1.2. Lumbar paraspinal muscle

Lumbar MF muscle

The lumbar MF muscle is the most medial of the lumbar paraspinal muscles (33, 34). The muscle is innervated by the medial branch of the posterior root of the segmental nerve (33). Multiple fascicles of MF arise from a single segment and as these fibers transcend distally for 2 to 5 segments (Fig 2.1), it is expected that the effects of denervation or disuse would be apparent across several segments (35-37).

Among the deep paraspinal muscles, the MF muscle is the most important stabilizer (27, 38). The MF muscle also plays a crucial role in maintaining lumbar lordosis and control of vertebral segments, especially in the neutral zone (27, 39). MF size increases caudally down the spine, and thus is most developed in the lumbosacral region (31). Muscle fibers within the lumbar region comprise much of the concave space between the spinous and transverse processes (27, 31). The deep fibers of lumbar MF act as a vital segmental stabilizer that allows for lateral flexion, rotation, and extension, while the superficial fibers are thought to contribute to spinal compression and extension (5, 31). Moseley et al. (40) examined the timing of MF activation and found that the deep and superficial fibres were activated at distinct times. Based on previous findings, intersegmental deep muscle fibres have a significant role in neuromuscular function and motion segment control (27, 40, 41). They reinforce lumbar lordosis during rotation and antagonize lumbar flexion (27).

Table 2.1. Origin, insertion, innervation and action of paraspinal muscles.

Muscle Main		Origin	Insertion	Innervation	Action(s)
Cervical	Cervical Multifidus	Sacral region: Posterior surface of sacrum, medial surface of posterior iliac spine and postero-sacroiliac ligaments. Lumbar, thoracic, and cervical regions: Transverse processes of L5 through C4	Spanning two to four vertebrae, inserted into spinous process of one of vertebra above from last lumbar to axis (second cervical vertebra)	Medial branches of posterior rami of spinal nerves	Extension of vertebral column and rotation toward opposite side.
	Semispinalis Capitis	Tips of transverse processes of upper six or seven thoracic and seventh cervical vertebrae and articular processes of fourth through sixth cervical vertebrae.	Between superior and inferior nuchal lines of occipital bone	Greater occipital nerve	Extension of neck and rotation of head toward opposite side.
	Semispinalis Cervisis	Semispinalis cervicis/Spinal Transverse processes of upper five or six thoracic vertebrae	Cervical spinous processes of second through fifth cervical vertebrae	Medial branches of posterior rami of spinal nerves	Extension of vertebral column and rotation toward opposite side in upper thoracic and cervical areas.
	Splenius Capitis	Caudal 1/2 of ligamentum nuchae, spinous process of seventh cervical vertebrae, and spinous process of first three or four thoracic vertebrae	Occipital bone inferior to lateral 13 of superior nuchal line; mastoid process of temporal bone	Posterior ramus of spinal nerves C3 and C4	Extension, lateral flexion, and rotation of neck, turning face toward same side. Both sides acting together, extension of neck.
Lumbar	Lumbar Multifidus	Arises from posterior sacrum, posterior superior iliac spine of ilium, aponeurosis of erector spinae, sacroiliac ligaments, mammillary process of lumbar vertebrae.	Fibers pass obliquely superomedially to entire length of spinous processes of vertebrae, located 2-4 segments superior to origin.	Medial branches of lumbar dorsal rami.	Stabilizes vertebrae during local movements of vertebral column.

2.2. Paraspinal muscle morphology alterations

Alterations in morphometry of paraspinal muscles are known to occur in patients with common spinal disorders including changes in cross-sectional area (CSA) (7, 23, 42), functional cross-sectional area (FCSA) (8, 35, 43), asymmetry and muscle fat infiltration (MFI) (7, 18, 43-45).

MRI is the gold standard for examining the integrity, size, and quality of spinal muscles due to its higher resolution, greater soft tissue contrast, superior visualization of spinal landmarks, and potential for efficient semi-automated or automated segmentation (46, 47). Advances in MRI techniques have enabled skeletal muscle composition analysis to be more readily available, and as a result, different approaches are currently used to quantify MFI, which may have contributed to the conflicting literature findings (48). Nevertheless, MRI is an is effective and accurate method to quantifying paravertebral muscle fat for its capacity to distinguish fat and lean muscle tissue and measuring fat-signal fraction (FF) (49). The reliability and validity of determining the CSA and FCSA of the cervical and lumbar paraspinal muscles using MRI in terms of measuring muscle size and composition have reported in previous studies (28, 48-53). Although there are various MRI methodologies for measuring the water and fat of skeletal muscle, chemical-shift MRI, which produces water-and fat-only images from dual- and/or multi-echo acquisitions, is the current gold standard for assessing muscle size and structure (48, 54-57). Manual segmentation based on these imaging approaches has been demonstrated to be highly accurate when compared to spectroscopy (55) and histology (58), in a variety of neuromusculoskeletal disorders, including low back pain (LBP) (54, 55, 59). The chemical shift technique (DIXON in Siemens, IDEAL [iterative least squares solution] in GE, mDIXON (Philips), FatSepTM (Hitachi), or WFS (Toshiba)] captures data at echo times when fat and water are in phase and out-of-phase (48). Although this approach is not immune to field inhomogeneities, the data can be integrated to provide a co-registered fat and water picture (48). Chemical shift-based water–fat separation techniques divided the signal from water and fat into two distinct images by utilising discrepancies in water and fat resonant frequency, resulting in separate and high-quality water and fat alone images (60). The IDEAL technique, which has been successfully applied to the liver and musculoskeletal system, is currently being employed to improve fat and water image assessment (61, 62). Despite improvements in fat and water imaging, the great majority of population-based research use traditional T1-or T2-weighted MRI to investigate lumbar spine characteristics (e.g., muscle, intervertebral disc, and skeletal vertebral column), as they are the most used routine diagnostic sequences (48). As such T1- and T2-weigthed remain a reliable method and valuable resources to assess paraspinal muscle in large multi-centre studies (61).

2.2.1. Cross-sectional area

The physiologic CSA of a whole muscle represents the number of active proteins to create contraction force (31). Cutting through the muscular belly or dividing the muscle's volume by its length yields the physiologic CSA of the muscle expressing in square centimetres, reflecting the sum of the CSA of all muscle fibers inside the muscle (31). This value is used as a common indicator to assess muscle size in musculoskeletal disorders imaging studies (51).

Decreased CSA of deep neck extensors muscles have been reported in patients with neck pain as compared with healthy controls (63). While greater MF muscle CSA was reported in patients with whiplash associated disorders as compared to asymptomatic controls (17), others have reported reduced CSA in patients with chronic neck pain and degenerative cervical myelopathy (DCM) (16, 64-67). Fatty infiltration (e.g., composition) of muscle tissue might partly explain the inconsistent findings with regards to the CSA of the deep cervical extensors in patients with neck pain (14, 67). For example, the CSA of the MF was found to be smaller in a sample of patients with neck pain following a whiplash injury and in a group of patients with chronic nontraumatic neck pain as compared to healthy controls (64, 66). However, in a further study, the CSA of the MF was significantly larger in patients with whiplash-induced neck pain (17). Similarly, variable findings in patients with neck pain, including larger CSA of the Scap and splenius capitis, smaller CSA of Scap muscle and no change in CSA of the longissimus capitis were reported (60, 64, 68, 69). While 2.2 mm has been proposed as the least significant detectable change when measuring CSA of the Scap muscle with ultrasonography, literature results are contradictory, raising questions on the clinical use of cervical muscle CSA in patients with neck pain (69). Generalized disuse, persistent denervation, functional adaptation in response to changed activity in other muscles, facet joint injuries, and sympathetic nervous system involvement have all been linked to anatomical alterations in the deep cervical extensor muscles (14, 16, 69).

Paraspinal muscle CSA changes in relation to various lumbar spinal disorders have also been assessed in numerous reports (7, 42). There is considerable evidence of structural/morphological changes in lumbar paraspinal muscles, especially the MF muscle, in subjects with LBP (35, 70). In non-specific chronic LBP, studies established a reduction in MF muscle CSA (7, 42). Furthermore, according to Rahmani et al. (71), a decrease in MF muscle size was also observed in 15-18 years old male patients with LBP compared with their healthy counterparts. Wallwork et al. (42) carried out a study comparing MF muscle CSA and its capacity of creating voluntary isometric contraction at four vertebral levels in 34 healthy subjects and patients with LBP using sonography. The results demonstrated a decrease (e.g., atrophy) of the LM muscle at L5 in the patients with LBP as compared to the healthy group, which was also significantly correlated with the ability to produce a voluntary isometric contraction. As a result, the morphologic changes of MF muscle can be considered as an indirect index for alterations in muscle recruitment, leading to motor control dysfunction associated with LBP (42).

2.2.2. Functional cross-sectional area

Some reports have suggested that variations in paraspinal muscles, such as muscle atrophy related to LBP problems, might occur without observing an actual reduction in total muscle CSA (51). In fact, it has been suggested that muscle fibers may be replaced by fatty infiltration and fibrous connective tissue, resulting in a reduction of the overall contractile function of the muscle, but not necessarily a change in overall muscle size (9, 51). Thus, FCSA, the area containing only lean muscle fibers within fascial boundaries (excluding fat), is a better indicator of muscle atrophy and functional contractibility than total CSA, which has been widely used by investigators in this field (9, 51). Thresholding techniques on T1- or T2-weighted MR images, allowing for the separation of lean muscle from fat and fibrous tissue, are used to obtain FCSA measurements and were found to be highly reliable (51).

While decreased FCSA of the paraspinal muscle on the symptomatic side was reported in patients with unilateral neck pain and LBP (9, 14, 72), some studies have reported no significant MF FCSA asymmetry in patients with disc herniation, with or without radiculopathy (73). The percentage of muscle fatty infiltration was measured using different threshold procedures and measurement methodologies, which may have contributed to the disparate results (51). Furthermore, Fortin et al. (15) have revealed a significant correlation between the deep cervical extensor muscle morphology and strength in different positions in a group of patients with DCM, suggesting greater FCSA is correlated with higher muscle strength (15).

2.2.3. Fat infiltration

MFI is the pathological infiltration of muscle which can found intrafascicularly or intracellularly (74). Over the last decade, emphasis on the quantification of MFI in people with whiplash injury, neck pain and LBP lead to promising findings (16, 41, 48, 75). MFI is an indicator of muscle degeneration and its presence on MRI is considered as an emerging marker of injury and associated physiologic degenerative changes (48, 51). MFI is associated with poor outcomes in a variety of spinal pathologies, including chronic unilateral LBP (23, 76), disc herniation (76), disc disease (77), whiplash injury (54) and DCM (14). Chronic LBP changes the structural characteristics of paraspinal muscles, particularly the MF muscle, according to extensive studies (78, 79). Increased MFI has been reported in the lumbar paraspinal muscles in patients with acute (7) or chronic LBP (80) compares with healthy individual. The mean fat content of MF in healthy subjects and subjects with chronic LBP has been reported as low as 14.5% and as high as 23.6%, respectively (80, 81). MF with increased MFI between levels L2 and L5 is found in 80% of patients with chronic LBP (44). Hou et al. (69) examined the correlation between deep cervical paraspinal morphology alterations and the level of spinal cord compression in patients with C4-5 single level DCM. Their findings showed the degree of cervical paraspinal MFI and atrophy were greatest at the level of spinal cord compression. In patients with DCM, Fortin et al. (16) have also found a substantial increase in fatty infiltration and muscular CSA asymmetry in the cervical MF muscle below the most cranial level of compression. Increased MFI of the deep extensor cervical muscles in patients with DCM was also reported in a recent study using a deep learning automated segmentation algorithm (82).

This may occur because the deep neck extensor muscles play a critical role in postural biomechanics through their deep attachments to the cervical spine (13). Since the posterior paraspinal muscles are innervated by the dorsal branches that originate most proximally from the spinal nerves, denervation of these muscles is known to be a potential indicator of root avulsion (15, 69). Sensory innervation to the facet joint and motor innervation to MF and Scer muscles are provided by the dorsal ramus (69). It is hypothesized that when paraspinal muscle become denervated, efferent output to the respective muscle motor units is limited and the neural drive is reduced (83). Denervation causes morphological muscle changes (e.g., atrophy), resulting in the replacement of slow-twitch muscle fibres with fat and connective tissue over time (83, 84). There is preliminary evidence that suggests central mechanisms could drive morphological and compositional muscle changes secondary to the reduction in alpha-motoneuron drive (84).

Pain inhibition is the other possible reason to explain MFI in common spinal disorders (83). It is commonly considered that back muscular dysfunction causes pain inhibition resulting in fatty infiltration of the MF (83, 85). MF activity is inhibited by inhibition of alpha motor neuron in the anterior horn of the spinal cord. As a result, the lumbar muscles are unable to perform their functions, leading to a loss of postural control (37, 83, 85). Muscle degeneration may also be caused by disuse mechanism (83). Decreased muscle loading or neural muscular drive resulting from inactivity or rest leads to muscle degeneration (83).

2.2.4. Asymmetry

Muscular asymmetry is defined as a difference of the muscle dimensions from one side of the body as compared to opposite side, while considering the sign of the difference (86). Evidence suggests that paraspinal muscle asymmetry in size and composition (fatty infiltration) are associated with LBP problems (72, 76, 87). The MF muscle has attracted widespread attention, with findings indicating level and side-specific muscle atrophy in related to unilateral LBP (7) or radiculopathy (85), disc herniation (33) and disc degeneration (77). Decreased MF muscle size on the symptomatic side has been reported in patients with unilateral LBP (43, 70). Stokes et al. (88) have also found greater MF CSA ipsilateral to the side of radicular pain in patients with both more and less than 18 months of symptoms. However, the results of previous studies investigating paraspinal muscle asymmetry in relation to the symptomatic and asymptomatic side in patients with unilateral LBP remain inconsistent (77, 87-89). In a systematic review with a meta-analysis by Fortin et al. (90), the results showed a decreased in paraspinal muscle size in patients with chronic unilateral LBP but the results (e.g., pooled effect size) was not significant in patients with acute unilateral LBP.

Fortin et al. (91) investigated possible determinants of paraspinal muscle asymmetry in size and composition in a sample of monozygotic twins (n=202), including behavioral, environmental, and constitutional factors. Of the factors investigated, occupational physical demands, disk height narrowing, handedness, age and familial aggregation were significantly associated with paraspinal muscle asymmetry. However, associations were modest and inconsistent across spinal levels. The best predictor of asymmetry in paraspinal muscle composition was found to be familial aggregation.

In the neck region, previous studies have reported conflicting results regarding paraspinal muscle asymmetry in cervical spinal disorders (53, 54, 64). However, some studies showing nonspecific neck pain patients have more asymmetry in neck MF and Scap compare with healthy control group (8, 14, 82), others suggesting no significant CSA asymmetry of cervical MF muscles in women with bilateral chronic nonspecific neck pain (64). Asymmetrical cervical MF muscle size in MRI images was also observed in patients with cervical radiculopathy (92).

2.3. Paraspinal muscle functional deficits

In addition to structural changes, paraspinal muscle functional deficits and physical change are also reported in subjects with spinal disorders including motor control deficits (93, 94), altered recruitment patterns (95, 96), decreased in strength and contraction (15) and increase in muscle stiffness (97). Prior studies have also suggested that common spinal disorders have a negative impact on functional status and working ability in the young and adult population (46).

2.3.1. Thickness change and decrease in muscle activation.

Ultrasound imaging has been proved to be a reliable and valid approach for measuring changes in paraspinal muscle and trunk morphology and function, and it is increasingly being employed in research and clinical practice (98, 99). As compared to MRI and computed tomography (CT) scan, ultrasound imaging considerable advantages including, low examination costs, lack of exposure to ionizing radiation (non-invasive) and portability (99-101).

Ultrasound is a high frequency sound wave (20 kHz) which involves sending short pulses of ultrasound into the body and using reflections received from tissue interfaces to create images of internal structures (99). The application and usefulness of ultrasound in the field of musculoskeletal system has been demonstrated in many studies (89, 98-100). The characteristics (size) and function of the lumbar MF muscles have been visualised and measured using ultrasound imaging (33). CSA and muscle thickness (anterior to posterior linear thickness) are two ways for measuring lumbar MF muscle size using ultrasound imaging (100). Muscle thickness change has also been utilised to diagnose muscular and neuromuscular dysfunction associated with LBP using ultrasound imaging (89, 102). Changes in muscle thickness from rested to contracted state assess a person’s ability to modulate muscle thickness and estimate muscle activation (103). The reliability and validity of new diagnostic procedures are important issues which should be considered (100). In a systematic review intra-rater reliability for MF muscle CSA in healthy and LBP participant during rest has been reported between 0.74–0.97 and 0.93–0.97, respectively, while inter-rater reliability of MF muscle CSA in healthy and LBP participant during rest was 0.92 (100). Furthermore, the reported intra-rater reliability intraclass correlation coefficients (ICC) for MF muscle thickness in patients with LBP ranged from 0.95 to 1.00 and 0.86 to 1.00 during rest and contraction, respectively. (100). Also, inter-rater reliability of MF muscle thickness during rest and contraction in healthy participants were between 0.68–1.00 and 0.70–0.97 (100, 104). On the other hand, inter-rater reliability of 0.78–0.98 for MF muscle thickness during rest and 0.70–0.98 MF muscle thickness during contraction have been documented (100, 104). Good to high within-day (ICC = 0.80–0.97) and between-day reliability (ICC = 0.81–0.93) was reported for the assessment of MF muscle thickness via ultrasound (100). Surprisingly, the agreement between ultrasound and MRI for older adults with and without chronic LBP was high to measure lumbar MF muscle morphology (ICC= 0.90-0.97) (52).

It is well-known that muscle thickness changes when a muscle is activated (103). The amount of thickness change that occurs with muscle activation can be quantified with the use of ultrasonography by comparing resting muscle thickness values to those obtained during muscle activation (89, 103). Measurement of muscle thickness change compared to electromyography (EMG) activity has been performed on the gastrocnemius muscle, transverse abdominis and other trunk and peripheral muscles (105, 106). Detection of changes in MF muscle size and motor control in people with LBP in comparison with healthy subjects may provide useful information which can be used to guide rehabilitation approaches (100, 106). Evidence from an experimental study suggest that subjects with LBP have a decrease ability to contract the MF (107), nor voluntarily contract the MF muscle at the affected/atrophied vertebral level (42). Conversely, some studies have showed increased lumbar MF thickness change in patients with LBP (108), while EMG studies have reported both, increased and decreased muscle activation (73, 106, 107) in individuals with LBP.

2.3.2. Strength

Muscle morphological changes (e.g., decreased muscle size and fatty infiltration) (8, 23, 42, 49) and delayed muscle activation (107, 109) have been documented in individuals with common spinal disorders. Such degenerative muscle changes most likely impair muscle function to produce appropriate muscle force for the spine stability and movements (110). Previous studies have provided finding on the relationship of muscle strength and cervical muscle CSA (15). It is commonly believed that maximal muscle force and muscle CSA are strongly related (15). Reduced cervical muscle strength has been reported in patients with neck pain, whiplash disorders or insidious onset neck pain (24, 111, 112). However, some evidence reported positive association between muscle CSA and strength (15), others found no such correlation (113, 114).

2.3.3. Stiffness/Elasticity

The muscle contraction induced by active tension and the passive tension induced mostly by connective tissue cause normal skeletal muscle stiffness (115). Since tissue stiffness/elasticity can be altered in pathologic condition, muscle elasticity/stiffness measurements can be used as a useful non-invasive test for the diagnosis and management (116). However, only few studies have assessed the elasticity of various tissues related to musculoskeletal disorders (117). Different measurement techniques have been applied to estimate the stiffness of soft tissues including manual muscle test, modified Ashworth scale, force measurements using handheld and isokinetic dynamometers (118). While these measurements provide some information that clinicians can use to assess possible muscle dysfunction, some are subjective or unreliable (118).

Shear wave ultrasound elastography (SWE) is a revolutionary real-time diagnostic imaging technology with freehand capabilities that employs ultrasound to detect tissue stiffness variations quantitatively (118, 119). SWE was first used in differential diagnosis of cancer in the breast, but over the past few years, clinicians are now interested to use it for musculoskeletal pathologies (120, 121). The Young's (or elastic) modulus is one of the most important metrics for determining the stiffness (or elasticity) of soft tissues (97). The Young's (or elastic) modulus is defined as the slope of the stress–strain curve of a material in the elastic deformation zone as a mechanical property (121). Young's modulus measures tissue stiffness and is represented in Kilopascals (kPa) (121). The acoustic radiation force created by the ultrasonic push pulse generated by the ultrasound transducer is used in the recently developed SWE (Supersonic Imagine, Aix-en-Provence, France) (22). This force causes mechanical waves to propagate transversely through the tissue, including shear waves (22, 121). Ultrasound SWE can provide information about muscle function (97, 116), as changes in shear modulus are linearly proportional to the force produced by the muscle (19). Therefore, SWE can be used to evaluate the force production capability of individual muscles in motor tasks with muscle redundancy, which cannot be achieved with current clinical tests (19).

Reliability and validity in the assessment of lumbar spinal muscles stiffness /elasticity have been investigated in preliminary research (20, 21). A study by Moreau et al. (122) used SWE to evaluate lumbar spinal muscles and observed that the lumbar MF assessment was highly reliable. The inter- and intra-rater reliability were both deemed excellent (ICC=0.99 and ICC=0.95, respectively). However, this study had a limited sample size (n=10) and only looked at resting muscle conditions. Kopenhaver et al. (20) previously investigated the reliability of SWE to study the stiffness of the lumbar MF in asymptomatic individuals at rest and during contraction (contralateral arm lift), showing good to excellent reliability (ICC values of 0.77 to 0.94) (5, 23, 24). Factors were found to influence the reliability are muscle force during submaximal isometric contraction (20). In other words, more the muscle contracts or lengthens and more it becomes stiffer (121). Furthermore, the size of the region of interest (ROI) (i.e., the region of the muscle used to average the shear elastic modulus) should be considered when calculating the shear elastic modulus (122). Like many other tissues, muscle is heterogeneous, and the general recommendation is to take three to five measurements to obtain a valid average (97, 117).

Increased level of activity may cause the lumbar erector spinae muscle to become overloaded, resulting in a circulatory deficit, increased muscular stiffness, and the onset of LBP (97, 122). On the other hand, LBP may contribute to increased muscle stiffness (i.e., muscle spasm) of the lumbar back muscles, such as the lumbar erector spinae and lumbar MF muscles in LBP patients (97, 122). Recent studies have reported greater MF stiffness in patients with LBP as compared to healthy controls (97, 122). A study by Masaki et al. (97) in 2017 was the first to examine the association of LBP with muscle stiffness of the lumbar back muscles in prone position assessed using ultrasonic SWE in young and middle-aged medical workers. LBP was found to be associated with increased MF stiffness (e.g., increased shear elastic modulus) in comparison to a healthy asymptomatic group (97). Similarly, a recent study by Murillo et al. (122) was the first to investigate whether differences in passive muscular stiffness exist between the deep multifidus (DM) and superficial multifidus (SM), both in asymptomatic participants and in individuals with LBP. The findings illustrated a difference in muscular stiffness between the SM and DM, providing evidence to support possible differences in stiffness values between DM and SM (122). In addition, individuals with LBP exhibited increased muscular stiffness of the SM at rest, and a reduced ability to stiffen this muscle with isometric trunk extension compared to asymptomatic individuals (122).

2.4. Associations between paraspinal muscle morphology and muscle function/physical status

The structure-function relationship of paraspinal muscles in patients with LBP has been recently investigated in a few studies (123, 124). Results with regards to the relationship between morphology and function in non-specific chronic LBP remain conflicting, some studies found that lumbar fatty infiltration is accompanied by diminished muscle performance (125-127). Whereas others could not find any relationship between muscle structure/morphology and function (113). There are several potential explanations for these findings, including the characteristics of MF, issues related to the measures of MF morphology and function, and the nature of LBP (8, 9, 72, 125). Previous studies also reported an association between increased intra-muscular thigh fatty infiltration and decreased muscle power and performance (126, 128-130). Greater MF fatty infiltration is correlated with lower physical function among patients with lumbar stenosis, according to a study by Fortin et al. (8) and a recent report by Chen et al. (131). In older adults, the association between trunk MFI and functional activities was demonstrated in a study of older adults with and without back pain (10). Those with higher levels of trunk MFI (i.e., paraspinal muscle and lateral abdominals) were at greater risk of reduced mobility-related function over time. Similarly, smaller midthigh muscle CSA and greater fatty infiltration have been associated with poorer lower extremity performance in older men and woman (113).

On the other hand, the deep cervical extensor muscles have shown to be associated with poor clinical symptoms and functional outcomes in DCM (15, 16). Fortin et al. (16) reported an association between greater fatty infiltration and lower modified Japanese Orthopedic Association (mJOA) functional scores in patients with DCM. A significant correlation between the deep cervical extensor muscle morphology, clinical signs, and symptoms as well as cervical muscle strength was also observed (15, 16). This may occur because the deep extensor neck muscles of the cervical spine, including the MF and Scer, play a critical role in maintaining normal cervical curvature, cervical spinal stability, and activity through their deep attachments to the cervical spine (13, 15, 16, 69). The deep extensor neck muscles are innervated by the cervical plexus (C1-C4), cranial nerves, or dorsal rami of upper cervical nerves (69). Furthermore, previous evidence demonstrated the impact of DCM on muscles innervated by the brachial and lumbar plexus, suggesting that muscle denervation may progress at the same level, or level below the spinal cord compression in patients with DCM (15). Fortin et al. (16) also revealed that greater asymmetry in Scap muscle fatty infiltration was associated with higher Neck Disability Index (NDI) scores in patients with diagnosed DCM. On the contrary, Elliott et al. (66) reported no association between cervical MFI and NDI in subjects with persistent whiplash disorders, possibly due to the population sharing a clinical course of chronic pain and significant impairment. Similarly, no association between NDI score and the amount of relative fat infiltration in cervical extensor muscles was reported in Cloney et al.' study in 2018 (14).

CHAPTER 3: MANUSCRIPT 1

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Cervical Muscle Morphometry and Composition Demonstrate Prognostic Value in Degenerative Cervical Myelopathy Outcomes.

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Cervical muscle morphometry and composition demonstrate prognostic value in degenerative cervical myelopathy outcomes

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Objectives: This study aimed to examine whether preoperative cervical muscle size, composition, and asymmetry from magnetic resonance imaging (MRI) can predict post-operative outcomes in patients with degenerative cervical myelopathy (DCM).

Methods: A total of 171 patients with DCM were included. Relative total cross-sectional area (RCSA), functional CSA (fat-free area, FCSA), ratio of FCSA/CSA (fatty infiltration) and asymmetry of the multifidus (MF) and semispinalis cervicis (SCer) together (MF + SCer), and cervical muscle as a group (MF, SCer, semispinalis capitis, and splenius capitis) were obtained from T2-weighted axial MR images at the mid-disk, at the level of maximum cord compression and the level below. Univariate and multivariate linear regression analyses were used to assess the relationship between baseline cervical muscle measurements of interest with the modified Japanese Orthopedic Association (mJOA), Nurick Classification, Neck Disability Index (NDI), and SF-36 health survey at 6-month and 12-month post-surgery.

Results: Lower RCSA of MF + SCer, less CSA MF + SCer asymmetry and greater FCSA/CSA for the cervical muscle group (e.g., less fatty infiltration), and younger age were significant predictors of higher mJOA scores (e.g., less disability) at 6-month and 12-month post-surgery (all $p < 0.05$). Greater CSA asymmetry in MF + SCer and lower FCSA/CSA (e.g., more fatty infiltration) for the cervical muscle group were significant predictors of higher Nurick scores (e.g., more disability) at 6-month and 12-month post-surgery (all $p < 0.05$). Lower FCSA MF + Scer asymmetry, lower FCSA/CSA asymmetry of the muscle group, and greater RCSA MF + SCer were significant predictors of higher NDI scores at 6-month and 12-month post-surgery. Finally, greater FCSA/CSA asymmetry of the MF + SCer, greater FCSA asymmetry of the muscle group, greater RCSA of the muscle group, and greater CSA asymmetry of MF + SCer were significant predictors of lower post-operative SF-36 scores at 6- and 12-month post-surgery.

Conclusion: Our result suggested that cervical paraspinal muscle morphology, specifically greater asymmetry, and fatty infiltration may be important predictors of functional recovery and post-surgical outcomes in patients with DCM.

KEYWORDS

cervical extensor muscles morphology, cervical extensor muscles composition, degenerative cervical myelopathy, magnetic resonance imaging, post-operative outcome

1. Introduction

Degenerative cervical myelopathy (DCM) is the most prevalent cause of spinal cord dysfunction in adults worldwide (1–5). This age-related disorder of the cervical spine is associated with a progressive narrowing of the spinal canal, leading to pain and neurological impairment (2). In accordance with the World Health Organization, the number of people aged 60 years and over is expected to increase from 11% in 2010 to 22% in 2050 (2). Accordingly, health professionals globally will be expected to address a growing number of spinal disorders associated with advanced aging, particularly DCM (2, 4). Muscle hypotrophy occurs naturally and is proportional to aging, a possible confounding factor when assessing predictors of outcome (6). Common anatomical features of the aging spine include the degeneration of facet joints, intervertebral disks and/or vertebral bodies, hypertrophy of the ligamentum flavum, and ossification of the longitudinal ligament (OPLL) (5). While not mutually exclusive, all or any of these features can contribute to persistent compression of the spinal cord overtime (4, 7). Due to mechanical compression of the neural components, roughly 40% of individuals with features of and clinical indications for spinal degeneration will develop symptoms of neurological impairment (1, 2). The clinical presentation of DCM includes, but is not limited to, neck stiffness, gait impairment, numbness of the hands, and even tetraplegia (1, 8). While decompressive surgery is considered a practical option for patients with progressive DCM (1), nearly 40% of patients undergoing surgery report only partial recovery (e.g., <50% improvement) (1, 9). In such a setting, the prediction of who is likely to respond favorably to decompressive surgery is key to guide surgeons and manage patients' expectations. There is an urgent need to better understand the pathophysiological mechanisms leading to persistent (and worsening) clinical symptoms associated with DCM, which could ultimately improve the assessment and management of this condition.

Neck pain is increasingly recognized as a key clinical issue in patients with DCM and is associated with perceptions of post-operative quality of life (10). While patients with chronic neck pain demonstrate alterations in cervical muscle morphology (11, 12) and delayed activation during postural perturbations (13), few studies have specifically examined how the cervical muscles may play a role in the development of symptoms and functional impairments in DCM (8, 14). A recent innovation (8) established an association between cervical muscle morphology, clinical symptoms, and functional status in patients with DCM. The same study also reported an increase in multifidus (MF) muscle fatty infiltration at the level below the most cranial level of spinal cord compression, which is most likely related to denervation. A subsequent investigation (14) reported a strong positive correlation between cervical muscle strength and lean muscle mass measured by magnetic resonance imaging (MRI). Furthermore, recent evidence suggested cervical paraspinal muscle morphology and fatty infiltration are predictors of post-surgical outcomes in patients with adjacent segment degeneration undergoing anterior cervical discectomy and fusion (ACDF) (15) as well as in patients undergoing posterior cervical fusion (PCF) (16). Given these findings, it is probable that such variations in cervical muscle morphology and function may contribute to the variability in the surgical outcomes observed in patients with DCM. Therefore, the purpose of this study was to examine whether preoperative cervical muscle size, composition, and asymmetry are predictors of prognosis and functional recovery following surgical treatment in patients with DCM. We hypothesized that smaller cervical muscle, greater pre-surgical asymmetry, and fatty infiltration on clinically warranted MRI scans will be associated with greater symptom severity and lower functional scores post-surgery.

2. Materials and methods

2.1. Participants

Patients included in this study were selected from the multicentric Controlled Prospective AOSpine DCM-International cohort study database, which includes a total of 16 different international sites. Of the 479 symptomatic DCM patients comprised in this database and scheduled for surgical treatment, a total of 171 patients were included in the current study. The inclusion criteria included those as follows: (1) good quality pre-surgery MR T2-weighted axial images, (2) aged 18 years or older, (3) presenting with symptomatic DCM with at least one clinical sign of myelopathy, and (4) no previous cervical spine surgery. Patients were excluded if they were asymptomatic or diagnosed with active infection, neoplastic disease, rheumatoid arthritis, ankylosing spondylitis, or concomitant lumbar stenosis (Figure 1). All patients were followed for 2 years, and clinical outcomes were obtained at 6, 12, and 24 months following surgical treatment. Written informed consent was obtained from all patients acknowledging that their data would be used to improve the understanding of DCM. The Controlled Prospective AOSpine DCM-International study was approved by research ethics boards at each center. The Research Ethics Board at University Health Network (Toronto) approved the study at the principal coordinating site (Toronto Western Hospital: PI Michael Fehlings). The Ethics Research Board of McGill University also approved this study (#14-085-GEN).

2.2. Procedure

2.2.1. Cervical muscle measurements

Bilateral cervical muscle measurements included total CSA, functional CSA (FCSA), ratio of FCSA/CSA (fatty infiltration), and asymmetry of the multifidus and semispinalis cervicis (MF + SCer)

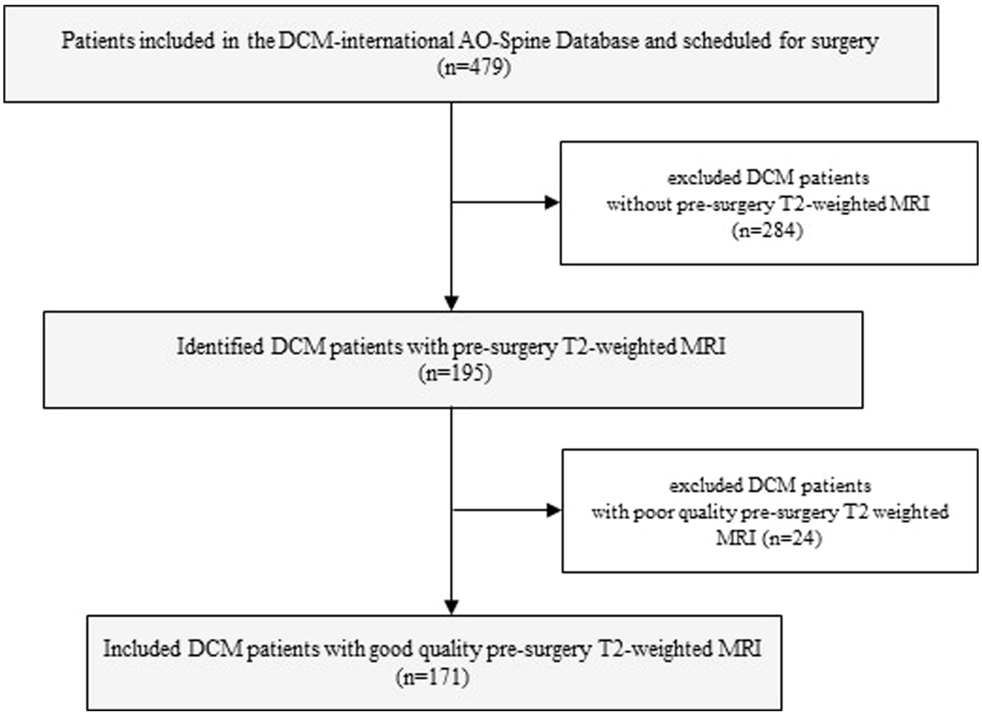

FIGURE 1
Flowchart depicting the stages and processes involved in including patients.

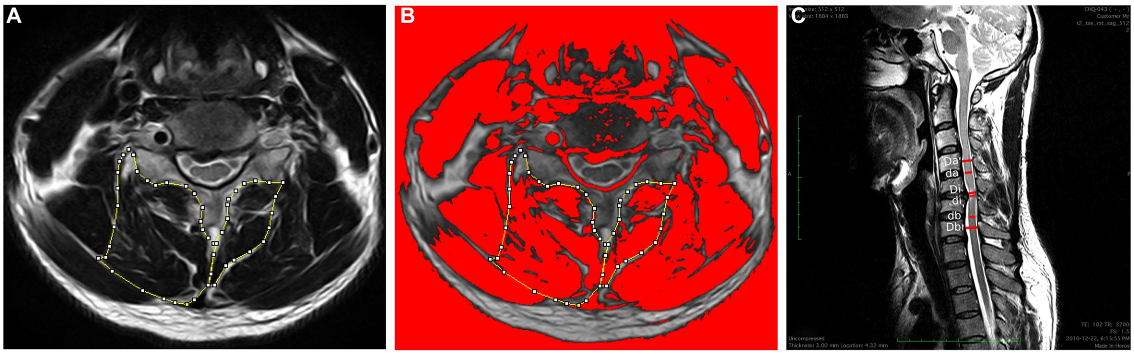

FIGURE 2
(A) Measurements of the total CSA of the MF + Scer muscles and extensor muscles group on axial T2-weighted images at the C4-C5 level. **(B)** The image shows the application of a signal threshold filter (ImageJ) to highlight the fat-free muscle area and obtain the FCSA muscle measurements. **(C)** Measurements required for MCC and MSCC calculation. Di, Da, and Db measure the diameter of the spinal canal at the site of maximum compression and at the nearest normal site above and below, respectively; Di, Da, and Db indicate the diameter of the spinal cord at the site of compression and at the normal site above and below, respectively.

together and the deep extensor muscles as a group were acquired at the level of maximum cord compression and level below at the mid-disk (Figures 2A,B). The cervical muscle measurements were described in detail elsewhere (17). The following formula defined by Fehlings et al. (18) was used to determine the level and degree of the maximum spinal cord compression (MSCC) and maximum canal compromise (MCC): $\text{MSCC} = [1 - \text{di}\quad(\text{da} + \text{db})/2] \times 100$, and $\text{MCC} = [1 - \text{Di}\quad(\text{Da} + \text{Db})/2] \times 100$ (Figure 2C). The FCSA was measured using a highly reliable thresholding technique described in detail elsewhere (19). The relative percent asymmetry of the paraspinal muscles on an axial view was calculated as follows: the relative asymmetry rate = $[(L - S)/L] \times 100$, where L is the larger side and S is the smaller side (17). To adjust for inter-individual anthropometric differences, total CSA was divided by the size of the disk at the level of interest and relative CSA (RCSA) was used in the analysis. The mean value of the sum of the muscle CSAs or FCSAs on the right and left side at each level and the means for the FCSA/CSA ratio were calculated for each level of interest (e.g., level of max compression, and level below, as well as both levels combined) and used in the analysis.

2.2.2. Self-reported questionnaires

Clinical signs of myelopathy and cervical functional test scores were collected at the time of recruitment (baseline) and followed by clinical and functional scores at 6, 12, and 24 months after surgical treatment. These were used to assess prognosis and functional recovery post-surgery at each time point: modified Japanese Orthopedic Association (mJOA), Nurick Classification, Neck Disability Index (NDI), and SF-36 health survey. The mJOA is an 18-point scale that quantitatively assesses upper and lower extremity motor and sensory function, which has been previously validated (20, 21); however, an additional study revealed that the inter-rater reliability is lower for the upper extremity sensory subscore (ICC = 0.63) (22). The NDI is a self-reported questionnaire used to measure related pain and disability; higher scores (out of 100) are indicative of greater disability. This questionnaire has previously demonstrated good levels of reliability and validity for neck pain (23, 24). The Nurick grade is another objective assessment of the severity of myelopathy but is more heavily weighted on the lower limb function. The score ranges from 0 (lowest disability) to 6 (greatest disability). This metric has been shown to be both reliable and valid regarding functional disability in patients with DCM (3, 25). The SF-36 health survey is a reliable and valid questionnaire, consisting of eight classified scores to measure health-related quality of life. Both physical and mental components of health are assessed in SF-36 health survey. The scores of all questions are summed together to calculate the final score, which is between 0 and 100, with a higher score reflecting a better quality of life (26, 27).

2.3. Statistical analysis

Means and standard deviations were calculated for the cervical paraspinal muscle measurements of interest. Univariate and multivariate linear regression analyses were used to assess the relationship between cervical muscle measurements of interest (e.g., independent variables) with post-surgical clinical symptoms and functional outcomes (e.g., dependent variables). Predictors with a univariate value of p of <0.20 were candidates for the multivariable analysis models. Only predictors with a value of p of <0.05 were considered to be statistically significant and retained in the multivariable analysis models. Age, BMI, and sex were considered as possible covariates. Separate models were performed for each level and each clinical outcome at every follow-up time point (e.g., 6-month and 12-month post-surgery). Diagnostic plots were used to assess model assumptions, and all assumptions were found to be tenable. All data analyses were performed with IBM SPSS (version 28.0).

3. Results

The average age of the subjects was 54.92 ± 11.85 years (range 28–87), and 112 (65.5%) were men (Table 1). Patients' characteristics, clinical signs and symptoms, and functional scores are presented in Table 1, and cervical muscle MRI measurements of interest are presented in Table 2. The mean value of the paraspinal muscle measurements of interest at both levels of maximum compression and level below was used as a value of combined level (Table 2).

TABLE 1 Demographic characteristics of patients ($n = 171$).

Characteristics of patients	Mean (SD) or frequency (%)		
Age (year)	54.92 (11.85)		
BMI (kg/m^2)	25.77 (5.43)		
Sex Male Female	112 (65.5%) 59 (34.5%)		
DCM duration (month)	30.23 (39.63)		
C3–C4 (max level of compression)	39 (22.8%)		
C4–C5 (max level of compression)	48 (28.07%)		
C5–C6 (max level of compression)	68 (39.76%)		
C6–C7 (max level of compression)	16 (9.35%)		
DCM symptoms			
Numb hands	89.8%		
Clumsy hands	71.7%		
Impairment of gait	80.7%		
Bilateral arm paresthesia	57.2%		
L'Hermitte's phenomena	19.9%		
Weakness	79.5%		
DCM signs			
Corticospinal distribution motor deficits	73.5%		
Atrophy of hand intrinsic muscles	36.1%		
Hyperreflexia	84.3%		
Positive Hoffman sign	66.9%		
Upgoing plantar responses	51.2%		
Lower limb spasticity	64.5%		
Broad-based unstable gait	65.7%		
DCM sources of stenosis			
Spondylosis	84.3%		
Disk	73.49%		
Ossified posterior longitudinal ligament	33.7%		
Hypertrophic ligamentum flavum	33.7%		
Subluxation	5.4%		
Other	0%		
Functional scores	Baseline	6 months	12 months
mJOA	12.05 (2.71)	14.24 (2.56)	14.7 (2.66)
NDI	39.31 (19.28)	26.89 (17.51)	24.59 (18.9)
SF-36	36.84 (12.13)	42.18 (11.32)	42.81 (12.09)
Nurick	3.45(1.21)	2.23 (1.54)	2.13 (1.52)

mJOA, modified Japanese orthopedic association; NDI, neck disability index; SF-36, short-form 36 health survey questionnaire; DCM, degenerative cervical myelopathy; BMI, body mass index; SD, standard deviation.

TABLE 2 Mean (standard deviation) of cervical paraspinal muscle measurements at the level of maximum compression, level below and both combined levels.

Paraspinal muscle measurements		Max level	Level below	Both levels combined
MF + SCer	RCSA	1.16 (0.37)	1.2 (0.34)	1.2 (0.3)
	FCSA/CSA	0.6 (0.16)	0.6 (0.11)	0.6 (0.13)
	CSA asy	10.48 (8.33)	9 (6.97)	9.84 (6.26)
	FCSA asy	13.31 (11.37)	13.13 (10.25)	13.26 (8.49)
	FCSA/CSA asy	11.07 (9.95)	11.09 (9.03)	11.2 (7.5)
Muscle group	RCSA	3.21 (1.1)	2.85 (0.9)	3.03 (0.92)
	FCSA/CSA	0.68 (0.09)	0.69 (0.09)	0.68 (0.07)
	CSA asy	7.16 (6.36)	6.65 (5.17)	6.83 (4.41)
	FCSA asy	7.6 (7.5)	7.21 (6.34)	7.32 (5)
	FCSA/CSA asv	5.8 (5.06)	6.52 (5.44)	6.2 (3.99)

CSA, cross-sectional area; FCSA, functional cross-sectional area; MF, multifidus muscle; SCer, semispinalis cervicis; Asy, asymmetry; RCSA, relative cross-sectional area.

3.1. Association between preoperative muscle parameters and functional scores at 6-month post-surgery

Univariate and multivariate regression analyses for cervical muscle parameters of interest and covariates (age, sex, gender, and BMI) with mJOA at 6-month post-surgery are presented in Table 3. FCSA/CSA MF + SCer, FCSA/CSA of the muscle group, CSA asymmetry of MF + SCer at both below and combined levels, RCSA for the muscle group at the level of maximum compression and combined level, and RCSA of the MF + SCer at the level of most compression and age were associated with mJOA in the univariate analysis and entered the multivariable model. Lower RCSA of the muscle group at the level of maximum compression (value of $p = 0.034$), less CSA MF + SCer asymmetry (value of p = <0.001), and greater FCSA/CSA of the muscle group (e.g., less fatty infiltration) (value of $p = 0.004$) at the level below and younger age (value of $p = 0.024$) were significant predictors of higher mJOA scores (e.g., less disability) at 6-month post-surgery (Table 3).

Univariate and multivariate regression analyses for Nurick scores at 6-month post-surgery are presented in Table 4. FCSA/CSA MF + SCer, CSA MF + SCer asymmetry at the level of maximum compression, level below and combined level, FCSA/CSA of the muscle group at both, the below and combined level, RCSA of the MF + SCer, FCSA asymmetry of the MF + SCer, and RCSA at the level of maximum compression and FCSA asymmetry of the muscle group at the level below were all associated with the Nurick score in the univariate analysis and entered the multivariable model. Less FCSA/CSA of the muscle group (e.g., greater fatty infiltration; value of $p = 0.002$) at the level below and greater CSA asymmetry MF + SCer (value of $p = 0.018$) at the combined level remained significant predictors of a higher Nurick score at 6-month post-surgery in the multivariable model. Lower FCSA asymmetry of MF + SCer was also associated with higher NDI scores at 6-month post-surgery. Finally, greater asymmetry in FCSA/CSA of the MF + SCer at the level of maximum compression and greater FCSA asymmetry of the muscle group at the level below were correlated with lower post-operative SF-36 scores ($p = 0.045$ and 0.018, respectively) in the multivariable model.

3.2. Association between preoperative muscle parameters and functional scores at 12-month post-surgery

Univariate and multivariate regression analyses for mJOA scores at 12-month post-surgery are presented in Table 5. Lower RCSA of both the MF + Scer and muscle group at all levels was associated with higher mJOA scores (e.g., lower disability) in the univariate analysis. Greater FCSA/CSA (e.g., less fatty infiltration) of the MF + SCer and muscle group at the level below and combined level and lower CSA asymmetry of the MF + SCer at the level below were all significantly associated with higher mJOA scores at 12-month post-surgery in the univariate analysis. Lower CSA asymmetry of MF + SCer ($p = 0.005$), greater FCSA/CSA of the muscle group at the level below ($p = 0.002$), and lower CSA asymmetry of the muscle group at both levels combined and younger age ($p = 0.032$) were significant predictors of higher mJOA (e.g., less disability) scores at 12-month post-surgery in the multivariable model.

Univariate and multivariate regression analyses with Nurick scores at 12-month post-surgery are presented in Table 6. Greater RCSA for MF + Scer and muscle group at almost all levels, lower FCSA/CSA for the MF + SCer at the level below and combined levels, and greater MF + Scer CSA asymmetry at the level below and muscle group FCSA/CSA asymmetry (combined levels) were all significantly associated with higher Nurick scores (e.g., more disability) at 12-month post-surgery in the univariate analyses. However, only greater RCSA for the muscle group at the maximum level and greater asymmetry for the MF + Scer at the level below and lower FCSA/CSA (e.g., more fatty infiltration) for the muscle group at the level below remained significant in the multivariable model.

Our results demonstrated that RCSA of the MF + SCer, FCSA asymmetry of MF + Scer, and FCSA/CSA asymmetry of the muscle group at all measured levels were associated with NDI in univariate analysis. Lower FCSA/CSA asymmetry of the muscle group (value of $p = 0.050$) and greater RCSA MF + SCer (value of $p = 0.034$) measured of the combined level remained significant in the multiple regression analysis with a higher NDI score at 12 weeks post-surgery. RCSA of the muscle group at the below level (value of $p = 0.003$) and CSA asymmetry of MF + SCer at the combined level (value of $p = 0.042$) had

TABLE 3 **Results of univariate and multivariate regression analyses and mJOA after 6-month post-surgery.**

Paraspinal muscle measurements		Univariate analysis(Coeff) [95% CI]	*p*-value	Multivariate analysis (Coeff) [95% CI]	*p*-value
Max level					
MF + SCer	RCSA	−0.7 [−1.758, 0.358]	0.193		
	FCSA/CSA	0.729 [−1.673, 3.132]	0.55		
	CSA asy	−0.024 [−0.071, 0.023]	0.32		
	FCSA asy	−0.018 [−0.053, 0.016]	0.301		
	FCSA/CSA asy	−0.006 [−0.046, 0.033]	0.745		
Muscle group	RCSA	−0.272 [−0.631, 0.088]	0.137	−0.158 [−0.710, −0.028]	0.034*
	FCSA/CSA	0.674 [−3.357, 4.704]	0.742		
	CSA asy	0.025 [−0.037, 0.086]	0.427		
	FCSA asy	0.021 [−0.032, 0.073]	0.44		
	FCSA/CSA asy	0.021 [−0.056, 0.099]	0.585		
Level below					
MF + SCer	RCSA	−0.457 [−1.618, 0.704]	0.438		
	FCSA/CSA	5.159 [1.685, 8.632]	0.004*		
	CSA asy	−0.081 [−0.136, −0.026]	0.004*	−0.249 [−0.144, −0.038]	<0.001*
	FCSA asy	−0.004 [−0.042, 0.035]	0.84		
	FCSA/CSA asy	−3.034E-5 [−0.044, 0.044]	0.999		
Muscle group	RCSA	−0.206 [−0.647, 0.235]	0.358		
	FCSA/CSA	6.749 [2.412, 11.086]	0.002*	0.211 [1.921, 10.269]	0.004*
	CSA asy	−0.046 [−0.122, 0.03]	0.233		
	FCSA asy	−0.035 [−0.097, 0.026]	0.259		
	FCSA/CSA asy	0.007 [−0.065, 0.079]	0.849		
Both levels combined					
MF + SCer	RCSA	−0.838 [−2.156, 0.479]	0.211		
	FCSA/CSA	3.218 [−0.224, 6.661]	0.067		
	CSA asy	−0.073 [−0.135, −0.010]	0.023*		
	FCSA asy	−0.02 [−0.066, 0.027]	0.411		
	FCSA/CSA asy	−0.006 [−0.059, 0.047]	0.826		
Muscle group	RCSA	−0.291 [−0.720, 0.138]	0.182		
	FCSA/CSA	4.778 [−0.178, 9.733]	0.059		
	CSA asy	−0.005 [−0.095, 0.084]	0.905		
	FCSA asy	−0.005 [−0.083, 0.072]	0.891		
	FCSA/CSA asy	0.025 [−0.075, 0.124]	0.629		
Patients' characteristics					
Age		−0.032 [−0.065, 0.001]	0.057	−0.168 [−0.068, −0.005]	0.024*
Gender		−0.501 [−1.353, 0.350]	0.247		
BMI		0.001 [−0.075, 0.077]	0.985		
DCM duration		−0.001 [−0.011, 0.009]	0.834		

CSA, cross-sectional area; FCSA, functional cross-sectional area; RCSA, ratio cross-sectional area; MF, multifidus muscle; SCer, semispinalis cervicis; Asy, asymmetry; mJOA, modified Japanese orthopedic association; BMI, body mass index; Coeff, coefficient; CI, confidence interval; DCM, degenerative cervical myelopathy, $^{*}p < 0.05$.

a negative significant relationship with SF-36 post-surgery in the multivariable analysis (results not presented).

4. Discussion

Our analysis revealed that several cervical muscle morphology characteristics were predictors of improved mJOA scores (indicating less disability) at 6 and 12 months after surgery, adding importance to the identification of preoperative factors that could potentially be optimized before surgery to enhance recovery after surgery (ERAS) (28). Our findings provide more evidence that clinical and imaging features of muscle composition and morphology can play a role in classifying those who will benefit from surgery (29–31) and should be considered for selecting patients that would be suitable for ERAS pathways versus those that might require a more extensive in-hospital stay after surgery (32).

TABLE 4 **Results of univariate and multivariate regression analyses and Nurick after 6-month post-surgery.**

Paraspinal muscle measurements		Univariate analysis (Coeff) [95% CI]	*p*-value	Multivariate analysis (Coeff) [95% CI]	*p*-value
Max level					
MF + SCer	RCSA	0.419 [−0.218, 1.056]	0.196		
	FCSA/CSA	−1.048 [−2.486, 0.391]	0.152		
	CSA asy	0.022 [−0.006, 0.051]	0.123		
	FCSA asy	0.015 [−0.005, 0.036]	0.146		
	FCSA/CSA asy	0.01 [−0.014, 0.034]	0.4		
Muscle group	RCSA	0.152 [−0.064, 0.369]	0.167		
	FCSA/CSA	−0.26 [−2.686, 2.167]	0.833		
	CSA asy	−0.008 [−0.045, 0.029]	0.672		
	FCSA asy	0.008 [−0.023, 0.04]	0.6		
	FCSA/CSA asy	0.005 [−0.042, 0.051]	0.84		
Level below					
MF + SCer	RCSA	0.053 [−0.647, 0.753]	0.882		
	FCSA/CSA	−3.017 [−5.111, −0.923]	0.005*		
	CSA asy	0.036 [0.003, 0.07]	0.034*		
	FCSA asy	0.004 [−0.019, 0.028]	0.702		
	FCSA/CSA asy	0.005 [−0.022, 0.031]	0.727		
Muscle group	RCSA	0.014 [−0.252, 0.28]	0.916		
	FCSA/CSA	−3.940 [−6.555, −1.325]	0.003*	−0.232 [−6.606, −1.447]	0.002*
	CSA asy	0.023 [−0.023, 0.069]	0.319		
	FCSA asy	0.027 [−0.011, 0.064]	0.159		
	FCSA/CSA asy	0.004 [−0.039, 0.048]	0.854		
Both levels combined					
MF + SCer	RCSA	0.359 [−0.436, 1.154]	0.374		
	FCSA/CSA	−2.532 [−4.589, −0.475]	0.016*		
	CSA asy	0.043 [0.005, 0.08]	0.026*	0.180 [0.008, 0.081]	0.018*
	FCSA asy	0.017 [−0.011, 0.045]	0.223		
	FCSA/CSA asy	0.013 [−0.019, 0.045]	0.434		
Muscle group	RCSA	0.115 [−0.144, 0.374]	0.382		
	FCSA/CSA	−2.692 [−5.686, 0.302]	0.078		
	CSA asy	0.007 [−0.046, 0.061]	0.784		
	FCSA asy	0.03 [−0.016, 0.077]	0.203		
	FCSA/CSA asy	0.008 [−0.052, 0.068]	0.796		
Patients' characteristics					
Age		0.008 [−0.012, 0.029]	0.407		
Gender		0.196 [−0.315, 0.707]	0.45		
BMI		−0.008 [−0.054, 0.038]	0.731		
DCM duration		−0.003 [−0.009, 0.003]	0.39		

CSA, cross-sectional area; FCSA, functional cross-sectional area; RCSA, ratio cross-sectional area; MF, multifidus muscle; SCer, semispinalis cervicis; Asy, asymmetry; mJOA, modified Japanese orthopedic association; BMI, body mass index; Coeff, coefficient; CI, confidence interval; DCM, degenerative cervical myelopathy, *$p < 0.05$.

Smaller deep cervical extensors muscle size (e.g., reduced RCSA of the muscle group) at the maximum level of compression, less asymmetry in the CSA of MF + SCer, and greater FCSA/CSA for the group of muscles (indicating less fatty infiltration) below the maximum level of compression and less asymmetry of the muscle group at both combined levels were all associated with better post-surgery outcomes at both 6 and 12 months after surgery. The fact that reduced CSA is associated with better outcomes may be related to our measurement protocol. As we only assessed MF + Scer and the entire cervical extensor group, interstitial fat, if present, was included in the region of interest (ROI), which may have influenced our results. This hypothesis is further supported by the fact that we also found an association between greater muscle fat (lower FCSA/CSA) and worse post-operative outcomes. In addition, younger age was also a significant predictor of improved mJOA scores (all $p < 0.05$). Greater CSA asymmetry in MF + SCer and lower FCSA/CSA (e.g., more fatty infiltration) for the cervical muscle group at the below level of compression and greater RCSA of the cervical muscle group at most

TABLE 5 **Results of univariate and multivariate regression analyses and mJOA after 12-month post-surgery.**

Paraspinal muscle measurements		Univariate analysis (Coeff) [95% CI]	*p*-value	Multivariate analysis (Coeff) [95% CI]	*p*-value
Max level					
MF + SCer	RCSA	−1.236 [−2.323, −0.148]	0.026 *		
	FCSA/CSA	1.12 [−1.371, 3.61]	0.376		
	CSA asy	−0.002 [−0.052, 0.047]	0.929		
	FCSA asy	−0.004 [−0.04, 0.032]	0.82		
	FCSA/CSA asy	−0.005 [−0.046, 0.036]	0.799		
Muscle group	RCSA	−0.5 [−0.869, −0.13]	0.008*		
	FCSA/CSA	1.363 [−2.822, 5.547]	0.521		
	CSA asy	0.06 [−0.003, 0.123]	0.063		
	FCSA asy	0.023 [−0.032, 0.078]	0.407		
	FCSA/CSA asy	0.033 [−0.048, 0.113]	0.427		
Level below					
MF + SCer	RCSA	−1.493 [−2.68, −0.307]	0.014*		
	FCSA/CSA	5.396 [1.776, 9.015]	0.004*		
	CSA asy	−0.063 [−0.121, −0.005]	0.033*	−0.212 [−0.135, −0.025]	0.005*
	FCSA asy	−0.008 [−0.048, 0.032]	0.705		
	FCSA/CSA asy	0.009 [−0.036, 0.055]	0.684		
Muscle group	RCSA	−0.601 [−1.053, −0.149]	0.010*		
	FCSA/CSA	7.417 [2.922, 11.913]	0.001*	0.231 [2.583, 11.139]	0.002*
	CSA asy	−0.004 [−0.089, 0.08]	0.92		
	FCSA asy	−0.048 [−0.115, 0.02]	0.164		
	FCSA/CSA asy	0.004 [−0.072, 0.081]	0.915		
Both levels combined					
MF + SCer	RCSA	−1.922 [−3.264, −0.581]	0.005*		
	FCSA/CSA	3.722 [0.156, 7.288]	0.041*		
	CSA asy	−0.042 [−0.108, 0.024]	0.211		
	FCSA asy	−0.01 [−0.059, 0.039]	0.7		
	FCSA/CSA asy	0.002 [−0.053, 0.058]	0.939		
Muscle group	RCSA	−0.64 [−1.078, −0.201]	0.005*		
	FCSA/CSA	5.711 [0.584, 10.838]	0.029*		
	CSA asy	0.063 [−0.031, 0.157]	0.189	−0.265 [−1.181, −0.343]	<0.001*
	FCSA asy	−0.009 [−0.092, 0.074]	0.826		
	FCSA/CSA asy	0.031[−0.073, 0.135]	0.559		
Patients' characteristics					
Age		−0.03 [−0.065, 0.005]	0.088	−0.159 [−0.068, −0.003]	0.032*
Gender		−0.172 [−1.06, 0.716]	0.702		
BMI		0.03 [−0.049, 0.11]	0.456		
DCM duration		0.0 [−0.011, 0.01]	0.974		

CSA, cross-sectional area; FCSA, functional cross-sectional area; RCSA, ratio cross-sectional area; MF, multifidus muscle; SCer, semispinalis cervicis; Asy, asymmetry; mJOA, modified Japanese orthopedic association; BMI, body mass index; Coeff, coefficient; CI, confidence interval; DCM, degenerative cervical myelopathy, *$p < 0.05$.

compression level were significant predictors of higher Nurick scores (e.g., more disability) at both 6-month and 12-month post-surgery.

Therefore, muscle parameters, such as fatty infiltration and asymmetry, may have an impact on the prognosis and functional recovery of patients with DCM (8). Our results, suggesting an association between cervical muscle fat infiltration and clinical outcomes (e.g., mJOA score and Nurick scores), are in line with prior research in DCM and whiplash-associated disorders (11, 12). Patients with whiplash-associated disorders who nominated self-recovery at 12-month post-injury had significantly less neck muscle fat infiltration in the multifidus muscle (33). The presence of greater fatty infiltration and asymmetry in these muscles may be associated with worse functional scores, clinical signs, and symptoms (8, 14, 33).

Previous research reported that fatty infiltration of the semispinalis capitis (SCap) was linked to mJOA scores in DCM patients (8). In contrast, Cloney et al. (1) revealed that increased muscle fat infiltration of MF + Scer was correlated with decreased sensorimotor function as measured by the mJOA and Nurick scores,

TABLE 6 Results of univariate and multivariate regression analyses and Nurick after 12 months following surgery.

Paraspinal muscle measurements		Univariate analysis (Coeff) [95% CI]	*p*-value	Multivariate analysis (Coeff) [95% CI]	*p*-value
Max level					
MF + SCer	RCSA	0.942 [0.328, 1.556]	0.003*		
	FCSA/CSA	−1.285 [−2.698, 0.128]	0.074		
	CSA asy	0.011 [−0.018, 0.039]	0.456		
	FCSA asy	0.009 [−0.012, 0.029]	0.407		
	FCSA/CSA asy	0.002 [−0.021,0.025]	0.872		
Muscle group	RCSA	0.295 [0.084, 0.505]	0.006*	0.235 [0.126, 0.525]	0.002*
	FCSA/CSA	−1.584 [−3.966, 0.798]	0.191		
	CSA asy	−0.014 [−0.05, 0.023]	0.463		
	FCSA asy	0.005 [−0.026, 0.036]	0.743		
	FCSA/CSA asy	−0.001 [−0.047, 0.045]	0.958		
Level below					
MF + SCer	RCSA	0.696 [0.014, 1.379]	0.046*		
	FCSA/CSA	−3.058 [−5.128, −0.988]	0.004*		
	CSA asy	0.042 [0.008, 0.075]	0.014*	0.211 [0 0.014, 0.077]	0.005*
	FCSA asy	5.043E-5[−0.023,0.023]	0.997		
	FCSA/CSA asy	−0.006 [−0.032, 0.02]	0.665		
Muscle group	RCSA	0.26 [−0.001, 0.521]	0.051		
	FCSA/CSA	−4.734 [−7.283, −2.185]	<0.001*	−0.270 [−7.035, −2.154]	<0.001*
	CSA asy	0.008 [−0.041, 0.056]	0.757		
	FCSA asy	0.014 [−0.025, 0.053]	0.469		
	FCSA/CSA asy	0.007 [−0.037, 0.05]	0.766		
Both levels combined					
MF + SCer	RCSA	1.179 [0.416, 1.943]	0.003*		
	FCSA/CSA	−2.79 [−4.809, −0.772]	0.007*		
	CSA asy	0.036 [−0.002, 0.073]	0.061		
	FCSA asy	0.008 [−0.02, 0.036]	0.573		
	FCSA/CSA asy	−0.002 [−0.034, 0.029]	0.877		
Muscle group	RCSA	0.333 [0.081, 0.584]	0.01*		
	FCSA/CSA	−4.207 [−7.115, −1.299]	0.005*		
	CSA asy	−0.01 [−0.064, 0.044]	0.712		
	FCSA asy	0.017 [−0.031, 0.064]	0.489		
	FCSA/CSA asy	0.005 [−0.054, 0.065]	0.866		
Patients’ characteristics					
Age		0.004 [−0.016, 0.024]	0.675		
Gender		0.119 [−0.387, 0.626]	0.642		
BMI		−0.009 [−0.055, 0.036]	0.685		
DCM duration		0.002 [−0.003, 0.008]	0.412		

CSA, cross-sectional area; FCSA, functional cross-sectional area; RCSA, ratio cross-sectional area; MF, multifidus muscle; SCer, semispinalis cervicis; Asy, asymmetry; mJOA, modified Japanese orthopedic association; BMI, body mass index; Coeff, coefficient; CI, confidence interval; DCM, degenerative cervical myelopathy, *$p < 0.05$.

while Fortin et al. (8) reported no relationship between MF fat infiltration and mJOA scores. However, since both muscles are deep extensors that play a significant role in the stability of the cervical spine, their pathologies are probably reflected in overlapping clinical manifestations that are quantified by the mJOA score (1). Alternately, various other factors, including the level of measurement selected, might have had an impact on the findings and measurements of paraspinal muscles as Fortin et al. (8) only included symptomatic DCM patients with the most level of compression at C4-C5 and C5-C6 levels. Furthermore, in the current study and Cloney’s study, MF and Scer were segmented together (e.g., same ROI) as the boundary between these two muscles is not always clearly visible at all levels, while Fortin et al. (8) measured the MF by itself. In another study, however, Fortin et al. (14) observed an association between a greater mean FCSA/CSA ratio of the entire cervical extensor group (e.g., less fatty infiltration) with a higher mJOA score (e.g., lower disability). Similar to the current study, cervical muscle measurements were obtained bilaterally at the mid-disk from C2 to C7. In the lumbar spine, evidence clearly suggests that lower paraspinal muscle quality is associated with decreased strength, increased frailty, increased risks of fractures and falls, and worst post-operative outcomes (34–36). In addition to establishing the significance of preoperative muscle morphometry in predicting outcomes in DCM, our study has identified two novel predictors (deep extensor fat infiltration and asymmetry) of functional recovery after surgery. These findings demonstrate that deep extensor sarcopenia can likely be used as a predictive factor for poor Nurick grade and mJOA improvement post-surgery.

The effect of age on surgical outcomes in patients with DCM has been a topic of debate and research (4, 9, 37). Some studies suggest that younger age is a significant predictor of better outcomes, while others report that age is not a clear predictor (9, 37–39). Zileli et al. (37) found that age was a significant factor influencing outcomes in DCM patients, but no specific age cutoff value could predict the outcome. Tetreault et al. (38) hypothesized that reduced physiological reserves, poorer overall health status, and increased comorbidities may make older patients more susceptible to complications following DCM surgery. They found that age was a significant predictor of complications in their study. Overall, the effect of age on DCM surgical outcomes remains complex and requires further investigation.

While lower FCSA asymmetry of MF + Scer was associated with higher NDI scores at 6-month post-surgery, lower FCSA/CSA asymmetry of group muscle and greater RCSA MF + Scer were associated with higher NDI scores at 12-month post-surgery. This result is consistent with our previous study that has been recently published suggesting an association between lower asymmetry in cervical muscle morphology and increased NDI scores in baseline measurements (17). In contrast, Fortin et al. (8) reported an association between higher NDI scores and greater asymmetry in fatty infiltration of the semispinalis capitis muscle in patients with DCM. In the current study, however, the semispinalis capitis was not assessed individually but was included as part of the muscle group ROI, which may explain the different results. Furthermore, our study investigated the relationship between preoperative muscle morphology measurements and post-surgical outcome, while Fortin's study assessed the relationship between preoperative muscle characteristics and preoperative clinical outcomes. Lastly, Fortin et al. only included patients with spinal cord compression at C4-C5 and C5-C6 as their first level compression (e.g., most caudal level of compression). In the current study, all the levels were considered (e.g., from C2 to C7), and cervical muscle measurements were obtained in relation to the level of maximal cord compression. Finally, we found lower RCSA and lower FCSA asymmetry of the muscle group and lower asymmetry in FCSA/CSA and CSA of the MF + SCer had a significant relationship with higher SF-36 scores at 6-month and 12-month post-surgery. Fortin et al. reported no association between preoperative cervical muscle characteristics and preoperative SF-36 scores, (14) which is in accordance with our previous study (17). Therefore, SF-36 scores are likely not the best indicator of cervical muscle characteristics in this population.

While there is a growing body of evidence suggesting that surgery has a positive impact on patients with DCM (40), the role of non-operative treatment in this patient population is less clear (41–43). Rehabilitation plays a crucial role in the management of patients with neurological disabilities, including those with DCM and its importance should not be neglected (42, 43). Conservative rehabilitation can help patients with DCM achieve their maximum potential in terms of function and independence, as well as improve their overall wellbeing (42, 44). Our results suggest that exercise therapy including a range of motion and strengthening exercises to improve cervical muscle characteristics could likely enhance patients' outcomes. It has been demonstrated that timely and strategic rehabilitation is essential for maximizing functional outcomes in other neurological disorders such as stroke; therefore, it is crucial that appropriate perioperative rehabilitative interventions should be implemented, alongside surgical approaches to achieve the best possible outcomes (42, 44).

There are several limitations to our study that should be noted. First, as the paraspinal muscle morphology has been measured in different levels from C2 to C7, MF and Scer were regarded as a single group of muscles and the paraspinal muscle as another one as the precise border between each muscle was not always discernible. Second, we did not consider the impact of pre-surgery conservative treatment on the morphology of the deep extensor neck muscles. Third, T2-weighted images were used in the current study and acquired from different institutions, and therefore, the imaging scanner parameters were not standardized. Furthermore, only MRI assessment of muscle morphology/composition was performed, and additional measures of cervical muscle function should be considered in future study. Additionally, our analyses included numerous comparisons, which raised the possibility of chance finding or type I errors. It is also worth noting that deep learning automatic segmentation methods, such as convolutional neural networks, are advancing and have been used in a clinical population of patients with DCM (45) and whiplash (46) to rapidly and accurately evaluate the cervical muscles.

5. Conclusion

Our findings suggest that preoperative cervical muscle morphology/composition, specifically greater asymmetry, and fatty infiltration may be predictors of poor surgical outcomes. In other words, patients who have more severe changes in cervical muscle morphology may be less likely to experience and nominate good functional recovery post-surgery. This highlights the importance of considering muscle parameters in the assessment and treatment of patients with DCM. It would also be beneficial to examine whether variations in paraspinal muscle morphology and composition, as well as functional results, are influenced by changes in cervical lordosis and sagittal parameters (28, 47). Healthcare professionals may need to evaluate cervical muscle function and structure as part of their management plan for these patients to optimize their recovery and improve their outcomes. This study opens the possibility of targeting cervical muscle strengthening in ERAS protocols prior to undertaking surgery for DCM in individuals with compromised cervical muscle morphology (28).

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving humans were approved by The Research Ethics Board at University Health Network (Toronto) approved the study at the principal coordinating site (Toronto Western Hospital: PI MGF). The Ethics Research Board of McGill University also approved this study (#14-085-GEN). The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

Author contributions

NN participated in the research design, acquired the MRI cervical muscle measurements, completed the data analysis, and drafted the manuscript. JME participated in the research design, interpreted the results, and critically reviewed the manuscript. MHW and MGF provided access to the data and critically reviewed the manuscript. MF contributed to the conception, design of the study, data analysis, and interpretation of the data. All authors have read and approved the final manuscript.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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CHAPTER 4: MANUSCRIPT 2

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Postoperative assessment of cervical muscle morphology, strength, and functional outcomes in patients with degenerative cervical myolopathy

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Conflicts of interest

The authors have no conflicts of interest to declare.

4.1. Abstract

Objective: To examine the effect of decompression surgery on cervical muscle morphology and strength in patients with degenerative cervical myelopathy (DCM). The study also aimed to assess the relationship between preoperative cervical muscle morphology, strength, and postoperative functional outcomes in patients with DCM.

Method: A total of 10 patients with DCM underwent surgical treatment and were prospectively followed for 2 years. Among 10 patients, 7 (70%) underwent posterior fusion surgery while 3 (30%) underwent anterior cervical discectomy and fusion (ACDF) surgery. Cervical muscle strength and magnetic resonance imaging (MRI) muscle measurements were conducted both before and after surgery in a subgroup undergoing posterior fusion, as compared to the analysis involving ACDF. Cross-sectional area (CSA), functional CSA (fat free area, FCSA), ratio of FCSA/CSA (fatty infiltration) and asymmetry of the multifidus and semispinalis cervicis together (MF+Scer), and cervical muscle as a group (MF, SCer, semispinalis capitis, splenius capitis) were obtained from T2-weighted axial MR images at mid-disc, from various cervical levels, excluding instrumented areas. Functional scores including modified Japanese Orthopedic Association, Neck Disability Index and SF-12 health survey at 6-weeks, 12-months and 24 months post-surgery were used to assess prognosis and functional recovery.

Results: In our study comparing ACDF and posterior fusion approaches, no significant differences in isometric cervical muscle strength were observed at the two-year follow-up. Posterior fusion showed decreased in MF+Scer muscle CSA (p-value=0.01), MF+Scer muscle FCSA (p-value=0.027) and increased MF+Scer CSA asymmetry (p-value=0.003). The entire cervical extensor muscle CSA decreased (p-value<0.03) with a posterior approach. ACDF resulted in decreased CSA (p-value=0.001) and FCSA (p-value<0.001) of the entire cervical

muscle across all levels. Notably, no significant correlations were found between pre-surgery muscle measures and functional score changes in posterior fusion. These findings provide insights into the distinct impacts of surgical approaches on cervical muscle characteristics.

Conclusion: Among patients undergoing surgery for DCM, a posterior fusion surgery had a greater change in cervical musculature compared to an ACDF (anterior) approach. However, these changes in muscle morphology did not directly correlate with changes in functional scores. Further research with larger sample sizes, length of construct and longer follow-up periods is needed to fully understand the impact of these changes on patient outcomes and to develop more effective rehabilitation strategies.

4.2. Introduction

Degenerative cervical myelopathy (DCM) is a major cause of disability in the adult and elderly population (132). Approximately 25 percent of individuals with indications of spinal degeneration will develop symptoms of neurological impairment due to mechanical compression of the neural components (12, 133). Surgical hospitalizations for degenerative cervical spine diseases, including DCM, impose a significant economic burden amounting to a staggering $USD 2 billion annually. This estimation does not include additional expenses related to work absenteeism, rehabilitation, and non-surgical treatments (12). While surgery can help prevent the progression of DCM and improve neurological outcomes, functional status, and quality of life (132-134), whether surgical decompression is equally successful and safe in elderly individuals as it is in younger ones is a point of disagreement (132).

Recent studies have demonstrated that the deep extensor neck muscles, especially the cervical multifidus (MF) and semispinalis cervicis (Scer) are often impaired in patients with cervical disorders (66, 135, 136) and atrophied in patients with whiplash-type injury or chronic neck pain (66, 112). However, few studies have evaluated the deep extensor neck muscles of patients with DCM (15, 16, 137); the presence, extent, and clinical implications of morphologic muscle changes in patients with DCM warrants further attention. Fortin et al. (16) reported an association between greater fatty infiltration and lower functional scores in patients with DCM. A significant correlation between the deep cervical extensor muscle morphology, clinical signs, and symptoms as well as cervical muscle strength was also observed (15). Indeed, the MF and Scer play a critical role in maintaining normal cervical curvature, cervical spinal stability, and activity through their deep attachments to the cervical spine (15, 69). The deep cervical extensor muscles are innervated by the cervical plexus (C1-C4), cranial nerves, or dorsal rami of upper cervical nerves (16, 69), and previous evidence suggested that muscle denervation may progress at the same level, or level below the spinal cord compression in patients with DCM (15, 136). However, further research is needed to fully understand the relationship between cervical muscle morphology, muscular strength, clinical symptom, and functional status to truly comprehend the clinical significance of imaging-defined features of cervical muscle morphology and their impact on muscle function (e.g., strength). Improving our current knowledge regarding the characteristics and implications of cervical muscle morphology in DCM patients might provide useful insights for more effective surgical approaches (anterior vs. posterior) and comprehensive rehabilitation. Therefore, the purpose of this study was to investigate the effect of decompression surgery on cervical muscle morphology and strength in patients with DCM. The secondary purpose was to examine the correlation between preoperative cervical muscle morphology, cervical muscle strength and postoperative functional outcomes in patients with DCM. Based on previous findings (24), we hypothesized that cervical muscle strength will increase at 2-year post-surgery. Also, greater cervical muscle strength and lower fat infiltration pre-surgery would be associated with better functional outcome post-surgery.

4.3. Material and Method

4.3.1. Participants

The current study involved the enrollment of 20 patients diagnosed with symptomatic DCM, as confirmed by an orthopedic spine surgeon through MRI scans. All patients (n=20) underwent surgical decompression, but only 10 patients were subsequently monitored post-surgery, as the remaining expressed satisfaction with the surgery and did not feel the necessity to return for further follow-up appointments. This monitoring included 7 patients who underwent posterior fusion and 3 who underwent anterior cervical discectomy and fusion (ACDF) (Fig 4.1) and were recruited from the McGill University Orthopedic Clinic, based on the following inclusion criteria: 1) ≥ 18 years of age, 2) diagnosed with degenerative condition of the cervical spine, 3) present with symptom(s) of cervical myelopathy, 4) non-traumatic origin, 5) underwent MRI of the cervical spine (e.g. MRIs were obtained in different centers), 6) no previous cervical spine surgery. All patients signed informed consent forms agreeing that their information will be utilised for studies aimed at better understanding and describing DCM and this study was approved by the Ethics Research Board of McGill University Health Centre (Study Code: 13-436-GEN).

This cohort was followed for 2-years and outcomes were obtained post-surgery (e.g., 6 weeks, 12 months, and 24 months) following surgical treatment. Magnetic resonance imaging (MRI) and cervical strength measurements were collected at baseline and 2-years post-surgery. Clinical signs of myelopathy were collected at the time of recruitment and the following clinical and functional scores were used to assess prognosis and functional recovery post-surgery at each time point: modified Japanese Orthopedic Association (mJOA), Neck Disability Index (NDI) and SF-12 health survey. The mJOA is an 18-point scale which quantitatively assesses upper and lower extremity motor and sensory function and which has been previously validated (138, 139). The NDI is a self-reported questionnaire used to measure related pain and disability; higher scores (out of 100) are indicative of greater disability. This questionnaire has previously demonstrated good levels of reliability and validity for neck pain (140, 141). The SF-12 health survey is a reliable and valid questionnaire, consisting of 8 classified scores to measure health-related quality of life. Both physical and mental components of health are assessed in SF-12 health survey. The scores of all questions are finally summed together to calculate the final score, which is between 0 and 100, with higher score reflecting the best health of life (142, 143).

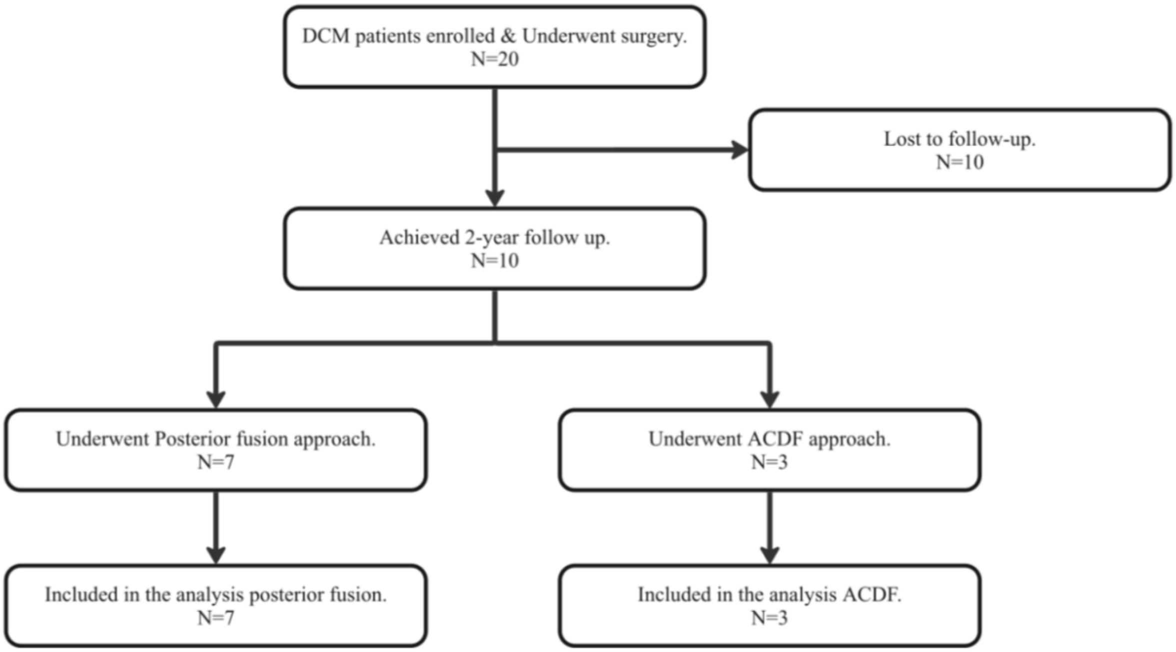

Figure 4.1. Flowchart depicting the stages and processes involved in including patients.

4.3.2. Muscle strength

A micro FET2 dynamometer was used to manually measure the isometric neck muscular strength in flexion, extension, right- and left-side bending at the time of recruitment and two years after operation. Patients were asked for to exert a maximal force against the hand-held dynamometer and maintain the head and neck position for 3 second (144, 145). The patients' heads were maintained in a neutral position while they were lying down (prone or supine) to maximise patient stability and isolate the neck musculature (144-146). All patients had a practice round in each position before testing. The examiner's resistance was equal to the highest force exerted by the patients. Patients were positioned supine on a treatment table with the dynamometer on their foreheads, and resistance was given when they lifted their heads. The dynamometer was positioned centrally above the ear for side-bending. Patients were examined in a prone position on a treatment table with a pillow under their chest/shoulder area to assess extensor muscle strength. As they lifted their heads, the dynamometer was positioned over their backs and resistance was applied. Measurements were collected 3 times in each direction with 30- to 60-second rest periods in between, and the average will be used in the analysis. When compared to the gold standard isokinetic testing, hand-held dynamometry has been proved to be a viable instrument, and it has been suggested as a feasible standard for clinical settings (147). Previous studies have found that hand-held dynamometry is reliable for measuring neck muscle strength, with intra-rater reliability ICCs ranging from 0.80 to 0.97 (144, 146, 148, 149), inter-rater reliability ICCs ranging from 0.81 to 0.87 (149).

4.3.3. MRI cervical muscle measurements

Pre and post quantitative measurements of the deep extensor neck cervical muscles acquired from axial T2-weighted MR images at the C2 to C7 using ImageJ imaging software (version 1.43;National Institutes of Health, Bethesda, Maryland, downloadable at http://rsbweb.nih.gov/ij/download.html) after multiplanar reconstruction (3D MPR) using the 32-bitOsiriX software program (version 3.8.1; Pixmeo, Geneva, Switzerland) to position the image slices perpendicular to the muscle mass, when required. Cervical muscle measurements of interest, including CSA, FCSA (fat free area), ratio of FCSA/CSA (fatty infiltration) and CSA asymmetry for the MF+SCer together, and deep extensor muscles as a group (e.g., MF, SCer, semispinalis capitis, splenius capitis) were obtained bilaterally at mid-disc (Fig 4.2 A, B). Due to the instrumentation/surgery, muscle measurements were only acquired at the cervical level without instrumentation and thus from C2-C7 levels in 3 patients, C2-C5 levels in 1 patient, C2-C3 and C5-C7 in 1 patient, C2-C3 and C6-C7 in 1 patient, C2-C3 in 1 patient and C6-C7 in 1 patient. Muscle FCSA was measured using a highly reliable thresholding technique described in detail elsewhere (150) (Fig 4.2 B). The relative percent asymmetry of the paraspinal muscles on axial view was calculated as follows: the relative asymmetry rate = [(L−S)/L)] x 100, where L is the larger side and S is the smaller side (136). The mean value of the sum of the muscle CSAs or FCSAs on right and left side at each level, and the means for the FCSA/CSA ratio were calculated for each level of interest and used in the statistical analysis.

4.3.4. Statistical analysis

Statistical analysis was performed using IBM SPSS (version 29.0). Means and standard deviations was calculated for patients' characteristics. Kolmogorov-Smirnov test was applied to assess the normal distribution of data. An evaluation of the primary and secondary outcome measures, specifically examining the changes in cervical muscle strength and MRI muscle measurements from the pre-surgery to 2-year post-surgery phases were conducted. To analyze normally distributed variables, we employed paired samples t-tests. Similarly, Wilcoxon signed-rank test was used to make comparison between pre and post cervical muscle and strength measurements for those variables were not normally distributed. Of note, all participants had C2-C3 level available, the pre and post operation comparison was performed twice. The first analysis compared pre- to post-surgery "total" muscle measurements at levels available between C2-C7 , which was the sum of measurements at each level. While the second analysis compared pre- to post-surgery muscle measurements at C2-C3 only. All analyses were performed separately for patients that had a posterior fusion vs. ACDF to gain a comprehensive understanding of the outcomes associated with each surgical approach . Pearson correlations were used to assess the relationship between pre-surgical muscle measurements and post-op muscle strength, and pre-surgery muscle measurements with the changes in functional outcomes (mJOA, NDI, SF12-PCS and SF12-MCS) from baseline to 6 weeks, 12- and 24-months post-surgery in posterior fusion group of surgery. A p-value of < 0.05 was considered statistically significant in all analysis. Due to the limited number of participants (only 3) in the ACDF surgical approach group, correlation analysis was not conducted within this specific group.

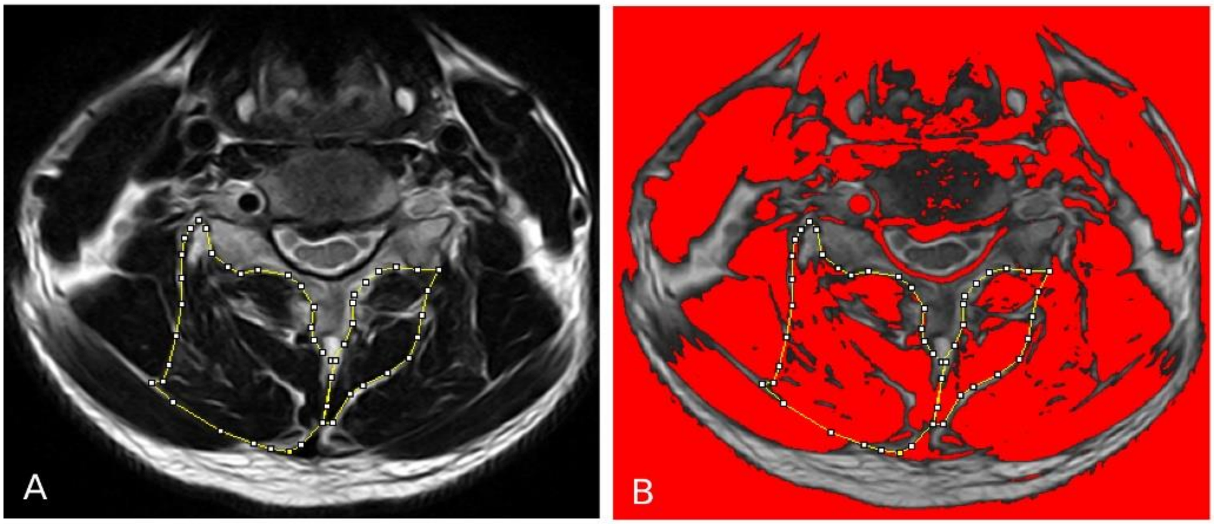

Figure 4.2. (A) Measurements of the total CSA of the MF+Scer muscles and extensor muscles group on axial T2-weighted images at the C4-C5 level. (B) The image shows the application of a signal threshold filter (ImageJ) to highlight the fat-free muscle area and obtain the FCSA muscle measurements.

4.4. Results

The mean age of patients that underwent a posterior fusion and ACDF was 66.86 ±8.03 years and 53.66 ± 9.07, respectively (Table 4.1). Only one participant had single level surgery (C3C4), while the remaining participants had multi-level surgery (Table 4.1).

Patients' clinical characteristics are presented in Table 4.1. Pre- and post-surgery measurements for cervical muscle strength and cervical muscle MRI measurements of interest are presented through Table 4.2 to Table 4.4.

Table 4.1. Demographic and characteristics of patients

Patients Characteristics	Mean (SD) or Frequency (%)	
Surgical approach	Posterior fusion (N=7)	ACDF (N=3)
Age (year)	66.86 (8.03)	53.66 (9.07)
BMI (kg/m2)	30.6 (5.63)	27.29 (3.19)
Sex Male Female	 2 (28.57%) 5 (71.42%)	 2 (66.66%) 1 (33.33%)
Symptoms duration (%)		
Less than 6 weeks	1 (14.28%)	--
3–6 months	1 (14.28%)	2 (66.66%)
6–12 months	1 (14.28%)	1 (33.33%)
1–2 years	2 (28.57%)	--
Over 2 years	2 (28.57%)	--
Levels treated		
Single level	1 (14.28%)	--
Multi levels 2 levels 3levels	 3 (42.85%) 3 (42.85%)	 2 (66.66%)) 1 (33.33%)

BMI: Body mass index, SD: Standard deviation, DCM: Degenerative cervical myelopathy, ACDF: Anterior cervical discectomy and fusion

Table 4.2. Cervical paraspinal strength measurements pre- and post- surgery

Cervical muscle strength (Newtons)	**Pre-surgery mean (SD)**	**2 years post-surgery mean (SD)**	**Mean difference [95% CI]**	**Change %**	**p-value**
Posterior Fusion (N=7)					
Neck flexion	15.53(6.39)	11.86 (4.14)	-3.26 [-1.19, 7.73]	-20.99%	0.11
Neck extension	26.2 (4.75)	15.13 (3.53)	-11.06 [-8.92, 31.05]	-42.21%	0.14
Right side-bending	14.1 (5.54)	10.58(2.11)	-3.51 [-0.83, 7.86]	-24.89%	0.09
Left side-bending	12.98 (6.49)	10.81(2.48)	-2.16 [-3.2, 7.53]	-16.64%	0.34
[b] ACDF (N=3)					
Neck flexion	16.4(10.93)	12.83(3.34)	-3.57	-21.76%	0.59
Neck extension	22.13(17.8)	15.23 (2.7)	-6.9	-31.17%	0.99
Right side-bending	14.53(7.5)	11.33(0.63)	-3.2	-22.02%	0.59
Left side-bending	15.4(9.93)	11.63(1.4)	-3.77	-24.48%	0.99

CI: Confidence interval, SD: Standard deviation, N: Number, %: percentage

[a]: Paired t-tests

[b]: Wilcoxon sign-ranked test

Table 4.3. MRI cervical paraspinal muscle measurements pre- and post-surgery for patients that underwent posterior fusion

Paraspinal muscle measurements		Pre-surgery mean (SD)	2 years post-surgery mean (SD)	Mean difference [95% CI]	Change %	p-value
All available levels between C2 and C7 (N=7)						
MF+SCer	CSA (mm^2)	367.59 (140)	306.09 (136.02)	-61.5 [-16.51, -106.49]	-16.82 %	**0.01***
	CSA asy	10.16 (8.16)	22.24 (14.55)	12.07 [19.41, 4.74]	118.79 %	**0.003***
	FCSA (mm^2)	215.12 (121.61)	177.64 (104.93)	-37.48[-4.78, -70.19]	-17.42 %	**0.027***
	FCSA/CSA	0.55 (0.17)	0.56 (0.18)	-0.005 [-0.07, -0.06]	-0.9 %	0.78
Cervical Extensors Muscle Group	CSA[a](mm^2)	1333.1 (540.56)	1256.03 (430.53)	-77.07	-5.78 %	**<0.03***
	CSA asy	5.45 (3.01)	5.26 (3.56)	-0.19 [-1.99, -2.37]	-3.48 %	0.87
	FCSA (mm^2)	865.59 (497.78)	803.67 (370.08)	-61.92 [-58, -181.84]	-7.15 %	0.29
	FCSA/CSA	0.62 (0.12)	0.62 (0.13)	-0.001 [-.05,0.59]	-0.16 %	0.94
C2-C3 Level Only (N=5)						
MF+SCer	CSA (mm^2)	354.7 (170.09)	316.74 (125.19)	-37.96 [-118.68, -194.61]	-10.7 %	0.53
	CSA asy	12.21 (12.45)	22.94 (10.44)	10.73 [15.87, 5.58]	87.87 %	**0.004***
	FCSA (mm^2)	237.83 (174.99)	209.57 (138.19)	-28.26[-112.67, -169.19]	-11.88 %	0.6
	FCSA/CSA	0.62 (0.27)	0.59 (0.25)	-0.02 [-0.18, 0.22]	-3.22 %	0.78
Cervical Extensors Muscle Group	CSA (mm^2)	1937.24 (597.79)	1774.45 (393.21)	-162.78[-180.73, -506.29]	-8.4 %	0.25
	CSA asy	7.77 (3.42)	6.91 (2.08)	-0.85 [-3.41, 5.133]	-10.93 %	0.6
	FCSA (mm^2)	1245.09 (723.2)	1129.04 (430.36)	-116.04 [-368.61, 600.7]	-9.31 %	0.54
	FCSA/CSA	0.6 (0.16)	0.61 (0.12)	0.01[-0.1, 0.13]	1.66 %	0.8

CSA: Cross-sectional area, FCSA: Functional cross-sectional area, MF: Multifidus muscle, SCer: Semispinalis Cervicis, Asy: Asymmetry, CI: Confidence interval, SD: Standard deviation. [a] Wilcoxon signed-rank test for nonparametric variables, N: Number, %: percentage.

Table 4.4. MRI cervical paraspinal muscle measurements pre- and post-surgery for patients that underwent ACDF.

Paraspinal muscle measurements		Pre-surgery mean (SD)	2 years post-surgery mean (SD)	Mean difference [95% CI]	Change %	p-value
All available levels between C2 and C7 (N=3)						
MF+SCer	CSA[a] (mm^2)	404.35 (212.2)	342.77 (184.88)	-61.58	-15.22 %	0.18
	CSA asy	10.77 (5.77)	10.92 (9.13)	0.14 [6.05, 5.75]	1.29 %	0.95
	FCSA[a] (mm^2)	258.59 (138.99)	221.98 (149.74)	-36.61	-14.15 %	0.08
	FCSA/CSA	0.63 (0.11)	0.62 (0.17)	-0.001[-0.06, .08]	-0.15 %	0.78
Cervical Extensors Muscle Group	CSA (mm^2)	1330.98 (554.66)	1121.72 (429.36)	-209.25[-102.62, -315.89]	-15.72 %	**0.001***
	CSA asy	6.8 (6.38)	4.14 (4.62)	-2.65 [-1.72, -7.03]	-38.97 %	0.2
	FCSA (mm^2)	962.55 (404.36)	819.66 (331.91)	-142.88 [-77.43, -208.34]	-14.84 %	**<0.001***
	FCSA/CSA	0.721 (0.1)	0.723(0.07)	0.002 [-0.04, .04]	0.27 %	0.92
C2-C3 Level Only (N=3)						

MF+SCer	CSA[a] (mm^2)	399.81 (344.04)	166.3 (90.95)	-233.51	-58.4 %	0.6
	CSA asy[a]	16.23 (2.02)	25.17 (12.49)	8.94	55.08 %	0.18
	FCSA[a] (mm^2)	210.6 (214.23)	49.82 (28.92)	-160.78	-76.34 %	0.1
	FCSA/CSA[a]	0.47 (0.13)	0.4 (0.39)	-0.07	-14.89 %	0.65
Cervical Extensors Muscle Group	CSA [a] (mm^2)	1769.8 (1133.9)	1338.79 (801.64)	-431.01	-24.35 %	0.18
	CSA asy[a]	5.7 (0.71)	1.42 (1.2)	-4.28	-75.08 %	0.18
	FCSA[a] (mm^2)	1112.17 (757.26)	878.87 (594.79)	-233.3	-20.97 %	0.18
	FCSA/CSA[a]	0.61 (0.03)	0.63 (0.06)	0.02	3.27 %	0.65

CSA: Cross-sectional area, FCSA: Functional cross-sectional area, MF: Multifidus muscle, SCer: Semispinalis Cervicis, Asy: Asymmetry, CI: Confidence interval, SD: Standard deviation. [a] Wilcoxon signed-rank test for nonparametric variables, N: Number, %: percentage.

Our findings revealed no significant difference in isometric cervical muscle strength in flexion, extension, right- and left-side bending at 2 years follow up after surgery for both ACDF and posterior fusion approach (Table 4.2). With regards to patients that underwent posterior fusion, our finding showed a significant decreased in MF+Scer CSA (*p*-value=0.01) and MF+Scer FCSA (*p*-value=0.027), with a significant increase in MF+Scer CSA asymmetry (*p*-value=0.003) (Table 3). Notably, the CSA of the entire cervical extensor muscle showed a significant decrease (*p*-value<0.03) at 2- year post-surgery (Table 4.3). Our analysis looking at C2C3 level only revealed a significant increase in MF+SCer CSA asymmetry (*p*-value= 0.004) post-surgery (Table 4.3). There were no significant correlations between pre-surgery muscle strength or pre-surgery cervical muscle morphology with changes in functional score including mJOA, NDI, SF12-PCS and SF12-MCS (Table 4.5) in patients that had a posterior fusion.

Our analysis for patients that underwent ACDF, revealed a significant decrease in the CSA of the entire muscle (*p*-value=0.001) and FCSA (*p*-value=<0.001) (Table 4.4) post-surgery when comparing cervical muscle morphology at all available levels (e.g., C2-C7). However, when examining the C2-C3 level only, no significant changes in muscle morphology were observed (Table 4.4).

Table 4.5. Associations between muscle strength and MRI muscle parameters
with functional outcomes for posterior fusion group.

Timepoint	**6-weeks post surgery**		**1-year post surgery**		**2-year post surgery**	
variables	**Correlation coefficient (r)**	**p-value**	**Correlation coefficient (r)**	**p-value**	**Correlation coefficient (r)**	**p-value**
Mean muscle strength						
mJOA	0.412	0.162	-	-	-	-
NDI	0.207	0.459	-0.039	0.905	0.127	0.694
SF12-PCS	-0.429	0.126	-0.351	0.32	-0.206	0.595
SF12-MCS	-0.064	0.828	-0.279	0.434	-0.304	0.426
C2-C7 mean CSA						
mJOA	0.305	0.361	-	-	-	-
NDI	-0.336	0.261	-0.246	0.494	0.09	0.792
SF12-PCS	-0.215	0.502	0.41	0.313	-0.337	0.415
SF12-MCS	0.007	0.983	-0.197	0.641	-0.122	0.773
C2-C7 mean FCSA						
mJOA	0.188	0.581	-	-	-	-
NDI	-0.212	0.487	-0.411	0.272	0.066	0.847
SF12-PCS	-0.328	0.298	-0.404	0.368	-0.27	0.517
SF12-MCS	0.082	0.801	-0.482	0.273	-0.23	0.584
C2-C7 mean FCSA/CSA						
mJOA			-	-	-	-
NDI	-0.162	0.564	-0.06	0.854	0.148	0.647
SF12-PCS	-0.119	0.698	0.123	0.734	-0.273	0.477
SF12-MCS	-0.058	0.843	-0.188	0.603	-0.286	0.456
C2-C7 mean CSA Asy						
mJOA[b]	0.470	0.144	-	-	-	-
NDI	-0.105	0.734	0.060	0.87	-0.091	0.791
SF12-PCS	0.069	0.832	0.071	0.868	-0.645	0.084
SF12-MCS	-0.171	0.596	-0.399	0.327	-0.242	0.563

CSA: Cross-sectional area, FCSA: Functional cross-sectional area, Asy: Asymmetry, CI: Confidence interval, mJOA: modified Japanese orthopedic association, NDI: Neck disability index, SF-12: Short form 12 health survey questionnaire, MCS: Mental component score, PCS: Physical component score, r: Pearson correlation coefficient, P: P-value. b the mJOA was only available at baseline and 6-week post-surgery.

4.5. Discussion:

DCM is a progressive spine disorder and the most common cause of spinal cord dysfunction in adults' population globally (14, 15, 133). The use of surgery as a preferred treatment approach for patients with DCM is growing, as it not only effectively stops the progression of the disease but also leads to substantial improvements in function and quality of life. Nevertheless, almost 40% of patients experience only partial recovery following surgical treatment, with less than 50% improvement reported (14, 136, 151, 152). As a result, identifying patients that are more likely to benefit from surgery is critical to help guide the clinical decision-making process and manage patients' expectations. Surgical decisions regarding whether to approach a procedure anteriorly or posteriorly are intricate and currently lack a thorough evaluation of the posterior cervical musculature (153). Additionally, both early and late complications, including post-operative neck pain, adjacent segment disease (ASD), and proximal junctional kyphosis (PJK), may be adversely influenced by the chosen surgical approach (154-156).

Patients with whiplash injury and chronic neck pain are frequently associated with abnormalities in the paraspinal muscles (17, 53, 68). Our study's findings, however, revealed no improvement in cervical muscle strength among patients with DCM 2-year post-surgery in both approach of surgery. Based on prior research, we had initially hypothesized that surgical treatment would lead to an increase in muscular strength (24). However, our findings do not corroborate with Fujibayashi et al.(24), who examined the progressive changes in neck muscular strength before and after cervical laminoplasty in a population with cervical spondylotic myelopathy. Indeed, Fujibayashi et al.'s study (24) examined cervical muscle strength based on Visual Analog Scale (VAS) scores at 3-month and 12-month post-surgery (e.g., non-pain group vs. pain group). They reported that cervical muscle strength was recovered by 3-month post-surgery, with a further increase up to 120% of the preoperative value at 12-month mark in the non-pain group (e.g., post-op VAS score <3). However, in the pain group (VAS score ≥3), neck muscle strength remained 60% below the preoperative baseline level at the 3-month mark and did not show any signs of recovery. These disparate findings may be attributed to the differences in surgical approaches between our study and Fujibayashi et al.'s study (24), as laminoplasty was used as a decompressive surgery in their study without fusion which generally leads to muscle atrophy across joints. Additionally, our study had a limited sample size in comparison to theirs, with only 7 DCM participants that underwent a posterior fusion and 3 participants that had an ACDF, whereas their study included 19 participants. Furthermore, previous reports have indicated that, in normal volunteers, men tend to exhibit approximately double the cervical muscle strength of women (154, 157). In their study, the non-pain group at the 3-month mark comprised 11 males and 2 females, and at the 12-month mark, it consisted of 11 males and 5 females. In our study, out of the 7 participants, 6 were females. These sex differences may also contribute to the variations observed in muscle strength outcomes between both studies.

Our findings reveal a significant decrease in MF+Scer CSA and a corresponding significant decrease in MF+Scer FCSA in patients who undertaken posterior fusion surgical approach. Furthermore, there was a noteworthy increase (118.79%) in MF+Scer CSA asymmetry two years after this surgical procedure. Also, when assessing changes in muscle morphology at C2C3 only, CSA asymmetry of the MF+Scer significantly increased post-surgery in patients who had a posterior fusion. Notable findings also emerged in our ACDF subgroup analyses, which meticulously compared cervical muscle morphology before and after surgery across all available levels from C2 to C7. Our results revealed a substantial decrease in the CSA and FCSA of the entire muscle post-surgery. This observation suggests that ACDF also had a notable impact on the overall cervical muscle structure, with a generalized reduction in muscle size. This is attributed to the fusion process, where muscles crossing a fused level no longer contribute to the motion segment, leading to atrophy. This observation emphasizes the intricate relationship between ACDF and its effect on cervical muscle morphology. Interestingly, when specifically examining the C2C3 level, a distinctive pattern emerged, as no significant changes in cervical muscle characteristics post-surgery were observed. Cervical muscle sparing morphology at the C2C3 level prompts further exploration and consideration of potential anatomical or biomechanical variations at this specific vertebral level. The absence of significant changes in this segment could signify unique characteristics or resilience within the C2C3 region in response to the ACDF surgical intervention, warranting additional investigation. These findings contribute valuable insights into the nuanced effects of ACDF cervical surgery on muscle morphology, emphasizing the importance of level-specific analyses to unveil differential impacts across the cervical spine.

The observed muscle atrophy (e.g., decrease in muscle size) suggests that the surgical procedures likely had an impact on the structural integrity of the cervical musculature (14, 151, 152, 158-160). In particular, we noticed that there were no significant alterations in the MF+Scer within the ACDF approach when compared to the posterior fusion approach. The results of our study provide valuable insights regarding the effect surgical treatment on overall cervical muscle morphology in patients with DCM. The lack of significant changes in MF+Scer in ACDF, in comparison to the posterior fusion, suggests that ACDF may not exert a pronounced impact on that muscle group. In contrast, patients that received a posterior fusion exhibited significant changes in MF+Scer, suggesting that the surgical approach from the posterior aspect may have more substantial effects on this specific muscle group. These findings underscore the importance of considering the differential impacts of surgical approaches on muscle structures, potentially influencing postoperative outcomes and rehabilitation strategies in patients undergoing cervical spine surgeries. Additionally, the significant increase in MF+Scer CSA asymmetry is a noteworthy finding in patients who had posterior fusion surgery as compared to ACDF. This asymmetry may indicate an uneven distribution of muscle size or changes in muscle composition between the left and right sides of the cervical spine. Such asymmetry can have implications for neck stability and function, potentially affecting patient outcomes. Furthermore, the observed significant decrease in CSA of the entire extensors muscle group in both surgical approaches emphasises the overall impact of this treatment on cervical muscle health. This decline in muscle size is likely related to a combination of muscle atrophy, scarring, and increased in fatty infiltration (13). These changes can have functional implications, including potential effects on neck mobility and strength (13, 24).

Previous literature on ACDF and posterior fusion cervical spine surgeries has provided valuable insights into their respective impacts on musculature. Studies focusing on ACDF have highlighted its efficacy in addressing cervical disc pathology, with favorable outcomes in terms of pain relief and functional improvement (154, 156). However, concerns have been raised regarding potential muscle-related complications, such as dysphagia and alterations in cervical spine biomechanics, specifically with fusion surgery (154, 156). In contrast, literature on posterior cervical spine surgeries, including laminectomy and fusion, has explored their effectiveness in decompressing neural structures and stabilizing the spine (161, 162). Some studies have emphasized the importance of preserving posterior musculature to mitigate postoperative muscle-related complications (161, 162). Cervical spine fusion may lead to two common post-operative complications: ASD and PJK. ASD involves degeneration in adjacent segments, managed conservatively or surgically, while PJK causes abnormal curvature above the fusion site, and likely requires additional interventions. Careful patient selection and monitoring are vital for optimal outcomes in cervical spine fusion (155). While both surgical approaches have demonstrated efficacy, the current findings suggesting greater changes in the MF+SCer muscle following posterior surgery add a nuanced layer to the existing literature, highlighting the need for further investigation into the differential impacts of these procedures on overall cervical muscle quality.

It is important to consider the clinical relevance of these findings. While the observed changes in muscle morphology were statistically significant, their clinical significance may vary among individuals. The functional implications of these morphological changes should be explored in future research, as they may provide insights into the long-term outcomes and quality of life of patients who undergo similar surgical procedures. Moreover, the timing of the assessments is critical. The two-year post-surgery period represents a specific point in the recovery process, and longer-term follow-up studies may be needed to fully understand the trajectory of muscle changes and their impact on patients' quality of life’s. The impact on the posterior musculature in cervical spine surgery is significantly influenced by the number of levels and the type of procedure (133, 145, 151, 152). Single-level surgeries generally result in less disruption to the posterior musculature, contributing to lower impact on muscle function and stability. In contrast, multi-level surgeries may necessitate more extensive manipulation of muscle tissue, potentially leading to increased trauma and affecting muscle strength (133, 145, 151, 152). Indeed, 70% (n=7) of the patients included in our study had a posterior fusion, and all except one patient, had a multi-level surgery. The latter likely explain the detrimental cervical muscle changes that we observed. Posterior-based surgeries, such as laminectomy or posterior cervical fusion, directly impact the posterior muscles, with the extent of dissection depending on the specific technique. Anterior-based surgeries, like ACDF or cervical disc replacement, typically involve less disruption to the posterior muscles, but indirect effects may occur due to changes in spinal alignment or biomechanics (133, 145) which corroborates with our findings.

Given the profound understanding that myelopathy significantly affects cervical musculature, coupled with the acknowledged atrophy of these muscles following fusion surgery—whether through an anterior or posterior approach—it is imperative to delve into the specific ramifications of disrupting posterior muscles with a posterior cervical approach as opposed to an anterior one. This nuanced exploration is crucial for comprehending the potential added impact on post-operative muscle morphology and function. Such insight is essential for anticipating and addressing surgical outcomes, both in the short term and over an extended period (beyond 2 years), encompassing factors like ASD, PJK, and neck pain. Moreover, recognizing the intricacies of how the disruption of posterior muscles influences post-operative recovery can inform the development of tailored rehabilitation programs and interventions. Different patient groups may benefit distinctively from specific rehabilitation approaches, such as isometric strengthening exercises, aimed at mitigating the impact on muscle structure and function. In the context of this project, it is paramount to acknowledge the inherent limitations stemming from its size. Subsequently, the next phase of investigation should delve into the correlation between the size and levels of fusion performed and their subsequent impact on musculature. As the pre- and postoperative rehabilitation process undoubtedly plays a pivotal role in ameliorating the negative consequences of surgery on musculature, it is incumbent upon surgeons and patients to engage in comprehensive discussions. These dialogues should encompass treatment options, considerations for overall health, and alignment of surgery goals with a keen focus on optimizing post-operative outcomes. Ongoing advancements in surgical techniques offer evolving options for minimizing musculature impact during cervical spine procedures (151, 152). Surgery posteriorly is clearly disrupting the normal muscles of the posterior cervical spine based on the quantification of these muscles volume pre- and post-operatively (152). The lack of functional change following posterior cervical spine surgery, despite disruption to normal muscles, may be attributed to pre-existing muscle dysfunction from spinal stenosis, adaptive changes in muscle function, incomplete recovery time, surgical technique, neurological adaptations, and the absence of targeted rehabilitation (162). A comprehensive exploration of these factors is crucial for understanding the complexities of post-operative outcomes in the posterior cervical spine.

The lack of correlation between pre-surgery neck muscle parameters and changes in functional scores, as observed in this study, aligns with some existing literature in the field (15, 137, 140). It is important to note that the relationship between cervical muscle morphology or strength and functional outcomes in patients undergoing cervical surgery is complex and multifactorial (15, 24). While several studies have explored the impact of cervical muscle characteristics on postoperative outcomes, findings remain contradictory (14, 16, 136, 137). Such inconsistency may be attributed to several factors; functional outcomes after cervical surgery are influenced by a myriad of variables, including surgical technique, disease severity, patient age, and comorbidities. These factors can often overshadow the influence of cervical muscle parameters in predicting functional changes. Variations in the methods used to measure muscle strength and morphology, as well as differences in functional score assessments, can also contribute to disparities in study results. Standardization of measurement techniques and functional assessments is crucial for meaningful comparisons. The timing of postoperative assessments can also play a significant role. Muscle recovery and functional improvement may occur at different rates, and a longer follow-up period might be necessary to detect potential associations. The absence of significant associations could be due to limitations in sample size or statistical power. A larger and more diverse sample may reveal subtle relationships that were not evident in the current study. Given these considerations, the fact that our findings revealed no significant correlations between pre-surgery neck muscle parameters and changes in functional scores does not necessarily imply that cervical muscle health is unrelated to postoperative outcomes. Our findings likely underscore the complexity of these relationships. More comprehensive analysis, possibly incorporating multiple variables and a longer follow-up, are needed to fully elucidate the role of cervical muscles health in post-surgery outcomes. Future research efforts should continue to explore this area to provide a clearer understanding of the intricate interplay between cervical muscle characteristics and patient outcomes.

Our study has certain limitations, including the small number of participants, which makes it difficult to ascertain how muscle strength, morphology and functional outcomes could be affected by surgical approach. Baseline T2-weighted images were acquired from different institutions, and therefore, the imaging scanner parameters were not standardized. Since degenerative muscle changes have primarily been observed in the extensor muscles compartment in previous studies examining the relationship between various cervical spine pathologies and cervical muscle morphology (133, 136, 137), we restricted our muscle quantitative MRI assessment to this compartment and did not consider the difference between upper versus lower cervical level flexion/extension. The accuracy of measuring muscle strength in the population may have been influenced by reduced physical activity, discomfort, and fear of movement. To address this, incorporating a load cell would have provided a more precise assessment of the overall strength of the cervical muscles. Furthermore, only MRI assessment of muscle morphology/composition was performed, additional measures of cervical muscle function should be considered in future work. Additionally, it is important to mention that there have been significant advancements in deep learning automatic segmentation techniques, like convolutional neural networks. These methods have been applied in clinical studies involving patients with DCM (82) and whiplash (163), enabling quick and precise assessment of the cervical muscles. To achieve a better understanding of the morphological and functional changes following surgery, a comprehensive longitudinal study with a substantial sample size of patients is needed. This could involve conducting a follow-up study to examine the specific alterations in morphology and function that occur after surgical treatment.

4.6. Conclusion

In conclusion, our study aimed to investigate the impact of cervical fusion surgery on both cervical muscle strength and morphology. Notably, while our findings did not reach statistical significant, there was a clear trend for a decrease in cervical muscle strength two years after surgery in all patients, irrespective if the surgical approach. However, the surgical intervention revealed significant alterations in cervical muscle morphology, resulting in reductions in CSA and FCSA, along with an increase in CSA asymmetry. While we found significant changes in both groups, our results do suggest that greater degenerative muscle changes occurred in patients that had a posterior surgical approach. Importantly, we did not find any significant bivariate associations between pre-surgery measurements of neck muscle strength and neck muscle MRI measurements. These findings suggest that, within the scope of this study, pre-surgery neck muscle characteristics do not appear to directly correlate with postoperative changes in functional scores. It is crucial to note that our study was conducted with a limited sample size and we did not control for the number of levels fused. As a result, our conclusions should be interpreted with caution, and we acknowledge the exploratory nature of this study.

Our findings highlight the importance of assessing and monitoring cervical muscle health in patients undergoing such procedures and suggest the need for further research with larger sample sizes, variable fusion construct length and longer follow-up periods to explore the functional consequences of these morphological and functional changes. As surgical treatment has a strong implication in the management of the DCM, a better understanding of the characteristics and implications of this treatment on the cervical muscle morphology and function in patients with DCM may provide valuable insight for more effective surgery and targeted pre- or post-surgery rehabilitation strategies.

CHAPTER 5: MANUSCRIPT 3

Will be submitted to The Spine Journal

Evaluation of structural alterations and mechanical properties of the multifidus muscle in chronic low back pain using contemporary images-based methods.

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Conflicts of interest

The authors have no conflicts of interest to declare.

5.1. Abstract

Introduction: Chronic low back pain (LBP) is a pervasive musculoskeletal disorder with a substantial impact on individuals and society. Despite advancements in diagnostic technologies, the etiology of LBP remains unknown in the majority of cases, hindering effective treatment and prevention strategies. Lumbar multifidus (MF) muscle alterations have been implicated in LBP, but a comprehensive understanding of the structure-function relationship is lacking. This observational case-control study aimed to explore the bivariate and multivariate relations between MF composition (e.g., fatty infiltration) and MF function among individuals with and without LBP. Morevere, a secondary objective was to determine differences in MF muscle function between individuals with and without LBP.

Methods: A total of 25 patients with chronic nonspecific LBP and an equal number of healthy controls, matched for age and sex were included. Inclusion criteria for LBP patients included 1) chronic nonspecific LBP, 2) moderate to severe disability on the Oswestry Disability Index, and 3) seeking current care for LBP. Participants underwent magnetic resonance imaging assessment for lumbar MF morphology and composition, utilizing iterative decomposition of water and fat with echo asymmetry and least-squares estimation (IDEAL) fat-water images. Ultrasound measures were used to evaluate lumbar MF function, including shear-wave elastography (SWE) for stiffness/elasticity and thickness change during rest and submaximal contraction task. All measurements were acquired at the L4/L5 and L5/S1 spinal levels, bilaterally. Bivariate and multivariate relations between morphology and function were explored with correlational and linear regression analyses, respectively. To quantify the increase in shear elastic modulus resulting from contraction, the contraction ratio, as outlined by Botanlioglu et al. (2013), was computed for the MF. This ratio was determined by dividing the shear modulus at rest by the

mean shear modulus observed during contraction (absolute values). Age, sex, body max index (BMI), physical activity levels and group status were explored as possible covariates in the regression models.

Results: Fifty participants were included (26 female) with overall mean age of 39.22 ±11.67. Age, BMI, sex, and physical activity levels was comparable between the individuals with LBP and healthy controls. Greater lumbar MF fat % was associated with greater resting MF SWE (p-value = 0.049) and MF SWE contraction ratio at L4/L5 level at (p=0.002). There were no other significant bivariate or multivariate relations between MF composition and MF function. Participants with LBP exhibited a significantly lower contraction ratio (p=0.041), reflected by a lower increase of muscular stiffness with contraction as compared to control group.

Discussion: This comprehensive study addresses the structure-function relationship of lumbar MF in chronic LBP, utilizing imaging techniques. The findings provide crucial insights into the prognostic value of imaging biomarkers, enhancing clinical assessment, and guiding targeted rehabilitation for individuals with LBP. Issues specific to MF measurement and recommendations for future research are discussed.

5.2. Introduction:

Low back pain (LBP) is a common musculoskeletal disorder with a reported lifetime prevalence of approximately 80% (1). Although 70 to 90% of patients with LBP will recover in 2 to 6 weeks, approximately 60 to 86% of patients with a first episode of LBP will relapse within a year, whereas 6 to 10% of patients develop chronic LBP (2, 102-104). The high prevalence of LBP is associated with an enormous socioeconomic burden (3) and disability (4). In spite of current diagnostic technology, the cause of LBP remains unknown in approximately 90% of patients (i.e., nonspecific LBP), which in turn hinders effective treatment and prevention of LBP (4).

Although the precise cause of LBP remains unknown in most cases (6), previous research has found that patients with LBP demonstrated degenerative changes in morphology (7, 42) and function of the lumbar multifidus (MF) muscle (96). Compared with asymptomatic individuals, patients with LBP displayed reduced MF thickness change during contraction (103), delayed feedforward (164, 165), fat infiltration and muscle atrophy (45, 127). Given the anatomic position of MF, this muscle plays an important role in maintaining intervertebral stiffness/stability and preventing LBP recurrence (33). The spine stabilizing system was further conceptualized by Panjabi (27) and defined as three subsystems: the spinal column, which provides intrinsic stability, the spinal muscles, surrounding the spinal column and providing dynamic stability, and the neural control unit evaluating and determining the requirements for stability and coordinating the require muscle response. Under normal conditions, the three subsystems work in harmony and provide the needed mechanical stability, but in patients with chronic LBP this system is impaired (166).

The muscle contraction induced by active tension and the passive tension induced mostly by connective tissue cause normal skeletal muscle stiffness (115). Since tissue stiffness/elasticity can be altered in pathologic condition, muscle elasticity/stiffness measurements can be used as a useful non-invasive test for the diagnosis and management (116). However, only few studies have assessed the elasticity of various tissues related to musculoskeletal disorders (117). Different measurement techniques have been applied to estimate the stiffness of soft tissues including manual muscle test, modified Ashworth scale, force measurements using handheld and isokinetic dynamometers (118). While these measurements provide some information that clinicians can use to assess possible muscle dysfunction, some are subjective or unreliable (118).

Shear wave ultrasound elastography (SWE) is a revolutionary real-time diagnostic imaging technology with freehand capabilities that employs ultrasound to detect tissue stiffness variations quantitatively (118, 119). SWE was first used in differential diagnosis of cancer in the breast, but over the past few years, clinicians are now interested to use it for musculoskeletal pathologies (120, 121). The Young's (or elastic) modulus is one of the most important metrics for determining the stiffness (or elasticity) of soft tissues (97). The Young’s (or elastic) modulus is defined as the slope of the stress–strain curve of a material in the elastic deformation zone as a mechanical property (121). Young's modulus measures tissue stiffness and is represented in pascals or Kilopascals (kPa) (121). The acoustic radiation force created by the ultrasonic push pulse generated by the ultrasound transducer is used in the recently developed SWE (Supersonic Imagine, Aix-en-Provence, France) (22). This force causes mechanical waves to propagate transversely through the tissue, including shear waves (22, 121). Ultrasound SWE can provide information about muscle function (97, 116). Changes in shear modulus are linearly proportional to the force produced by the muscle (19). Therefore, SWE can be used to evaluate the force production capability of individual muscles in motor tasks with muscle redundancy, which cannot be achieved with current clinical tests (19). Reliability, and validity in the assessment of lumbar spinal muscles have been investigated in preliminary research (20, 21).

While previous reports have assessed degenerative changes in morphology and function of the paraspinal muscles in LBP patients, most studies have examined each issue (e.g., morphology vs. function) separately. Only a few studies have assessed the structure-function relationship of the paraspinal muscle in patients with LBP (97), and most have failed to show a clear association (9, 124). We are aware of only two studies that have reported an association between muscle composition, strength, and postural control (125, 126). This comprehensive study combined two imaging modalities including magnetic resonance imaging (MRI) and ultrasound to provide a broad assessment of the structure-function relationship of the MF with MRI evaluating composition (e.g., morphology) and ultrasound examining stiffness/elasticity and thickness change related to functional deficit. The aim of the present study was to evaluate the relationship between MF muscle morphology (e.g., fatty infiltration) and function (e.g., contraction/thickness ratio, stiffness/ elasticity) in individuals with and without LBP. Furthermore, a secondary objective is to identify and examine differences in MF muscle function between individuals with and without LBP. We hypothesized that greater MF muscle fatty infiltration is associated with greater muscular contraction and greater muscle stiffness. Also, subjects with LBP show a lower contraction and greater muscle stiffness as compared with subjects without LBP.

5.3. Material and Method

5.3.1. Study Design and setting

This study was an observational, case-control study. This singularly centered investigation was carried out at the Concordia University's School of Health and approved by the Central Ethics Research Committee of the Quebec Minister of Health and Social Services (CCER-15-16-17). Each participant willingly contributed to the study by endorsing an informed consent form. The study's reporting adhered to the guidelines articulated in the CONSORT statement (34).

5.3.2. Participants recruitment

Participants in both groups were recruited from the local university community via email solicitations and from the Quebec LBP Consortium, a collective of experts spanning various disciplines dedicated to establishing a province-wide online database containing longitudinal data pertaining to individuals with LBP (34). Those individuals indicating interest in the study were subsequently contacted by a member of the research team to ascertain eligibility and facilitate enrollment. The recruitment of participants commenced in October 2020, with data collection concluding by February 2022.

5.3.3. Participants

Based on mean and standard deviation estimates of multifidus muscle stiffness from a relevant case-control study (published in 2019), with values for the LBP group (10.15 ± 4.21 kPa) and the control group (6.84 ± 1.69 kPa), the sample size was calculated at 20 participants per group, aiming to detect an effect size of 1.03, with a significance level of 0.05 and power of 0.90. To accommodate potential data collection challenges, 25 participants were recruited for each group. Participants in the LBP group (n=25) met all the following inclusion criteria: (1) chronic nonspecific LBP, defined as pain in the region between the lower ribs and gluteal folds, with or without leg pain, (2) symptoms duration ≥3 months between 20 and 65 years of age, (3) score of “moderate” or “severe” disability on the Oswestry Low Back Pain Disability Questionnaire, (4) do not engage in any sport or fitness training specifically for the lower back muscles up to 3 months prior to the enrollment in this study, (5) currently seeking care for LBP, (6) speak either French or English, and (7) no history of lumbar surgery. Participants were excluded if they had: (1) any evidence of nerve root compression or reflex motor sign deficits, (2) previous spinal surgery, or vertebral fractures, (2) major lumbar spine structural abnormalities (e.g., spondylosis, spondylolisthesis, scoliosis >10°) , (3) pregnancy, (4) any history of a sacroiliac joint dysfunction, (5) rheumatologic and neurologic disease, (6) metabolic diseases and malignancies or other major medical conditions, and (7) orthopedic device in the spinal column (34). An equal number of healthy control subjects (n=25) with no history of LBP (e.g., no prior LBP that lasted more than one week in the previous year) were recruited, and matched to the LBP group for age and sex.

5.3.4. Procedure

After confirming eligibility and obtaining consent, we collected demographic and clinical information, and participants completed self-report measures of physical activity. The international physical activity questionnaire (IPAQ) was used to determine the degree of physical activity of participants. The IPAQ is a 7-day self-reported questionnaire to determine the degree of physical activity of participants in minutes per week (METs based on intensity). The IPAQ assesses moderate and vigorous physical activity in 4 life domains: job-related work done outside the home, house and yard work, recreation, and transportation. This questionnaire also includes separate measures of time spent sitting at a desk, visiting friends, reading, or watching television. Physical activity levels are then classified as vigorous (8 MET), moderate (4 MET), walking (3.3 MET), or sitting/rest (1 MET). The total MET minutes are then divided by the number of minutes spent in each category, and the results are categorized as high, moderate, or low physical activity. Reliability and validity of this questionnaire have been previously reported (167).

5.3.4.1. MRI assessment of lumbar MF morphology

Sagittal and axial iterative decomposition of water and fat with echo asymmetry and least-squares estimation (IDEAL) images (Lava-fex, 2 echo sequence, TE:4.5, TE: minimum full, fip angle:5) were acquired to assessed MF muscle fat infiltration at the L4/L5 and L5/S1 (most common levels for spinal pathology) levels bilaterally for a total acquisition time of about 7 min. MRI images were collected using the PERFORM Centre's 3-tesla GE machine (Milwaukee, WI, USA), using a standard phased-array body coil with 4-mm slice thickness, 180-mm^2 field of view and 512x512 matrix. Multi-planar reconstruction was employed, when necessary, to correct the orientation of the MRI slice at the mid-disc position perpendicular to the muscle mass. For muscle composition analysis, we utilized water and fat axial images in the Horos DICOM viewer software (version 4.0.0). Initially, the region of interest for the MF CSA on each side and level delineated on the axial fat image manually. This delineation was then transferred onto the corresponding water image at each spinal level, as illustrated in Figure 5.1. Subsequent to outlining, signal intensities from both fat and water images were recorded. These values were then employed to determine the percentage fat signal fraction (%FSF) for each individual muscle, calculated using the formula: %FSF = (Signal_fat / [Signal_water + Signal_fat] × 100).

The intra- and inter-rater reliability of this measurement method has also been previously established (intraclass correlation coefficient (ICCs) =0.91-0.94) (60).

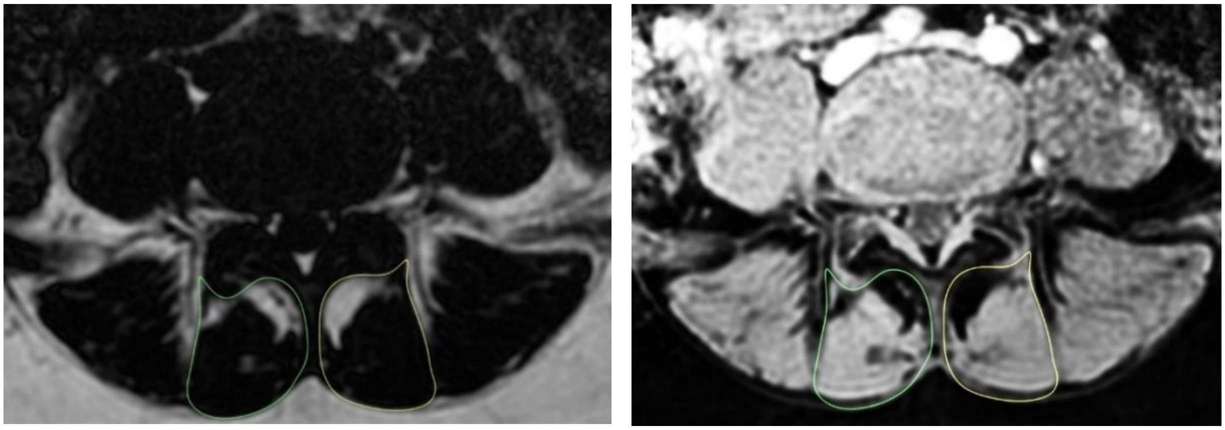

Figure 5.1. %FSF method. Example of region of intrest outlining the multifidus muscles using fat image (left) and water image (right)

5.3.4.2. Ultrasound measures of lumbar MF function

Ultrasound examination of the L4-L5 and L5-S1 level was acquired the same day. The PERFORM Centre's Aixplorer ultrasound unit (Supersonic Imagine, Aix-en-Provence, France) with SWE and SL10-2 curvilinear transducer with 5 MHz frequency was used to measure MF shear elastic modulus (e.g., index of muscle stiffness and elasticity) at rest and during submaximal contraction (Fig 5.2 and 5.3). The Aixplorer Multiwave generates two types of waves for each image: a compression wave that creates a high-quality B-mode image and a shear wave that propagates within the tissue (168). Together these two waves allow for the calculation of tissue shear modulus and render a quantitative, color-coded map of tissue elasticity (97, 168). MF thickness measurements at the same spinal levels was also acquired both at rest and during submaximal contraction. MF % thickness ratio (e.g., contraction) was computed using the following equation: %thickness ratio= (thickness contracted–thickness rest)/thickness rest) x100

(89, 169). Previous studies have shown that this method of measuring MF thickness using ultrasound is both reliable and valid (169, 170).

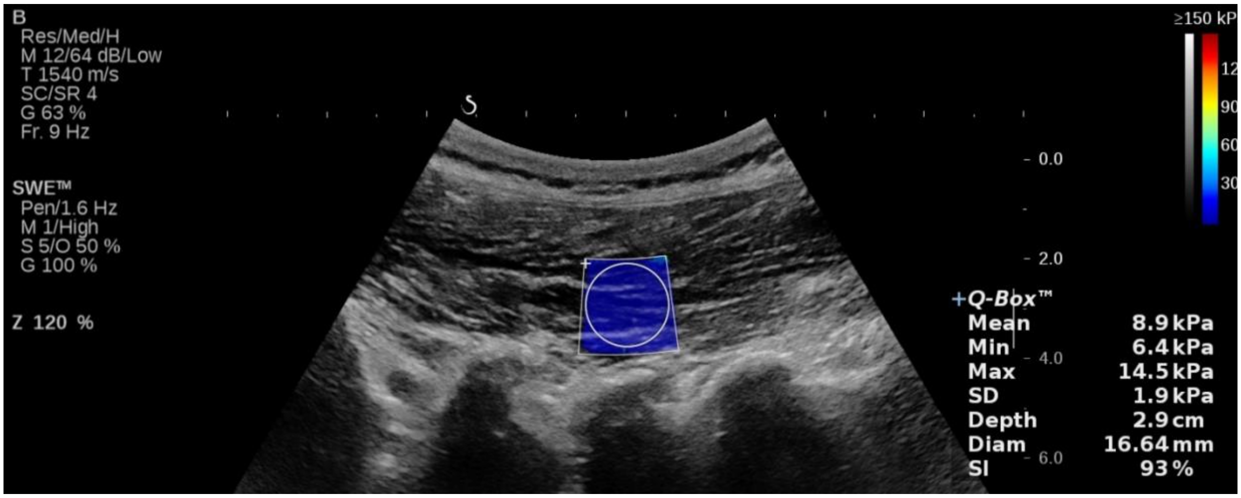

Figure 5.2. Representative elastograms recorded from an LBP participant: muscular stiffness of the MF at rest.

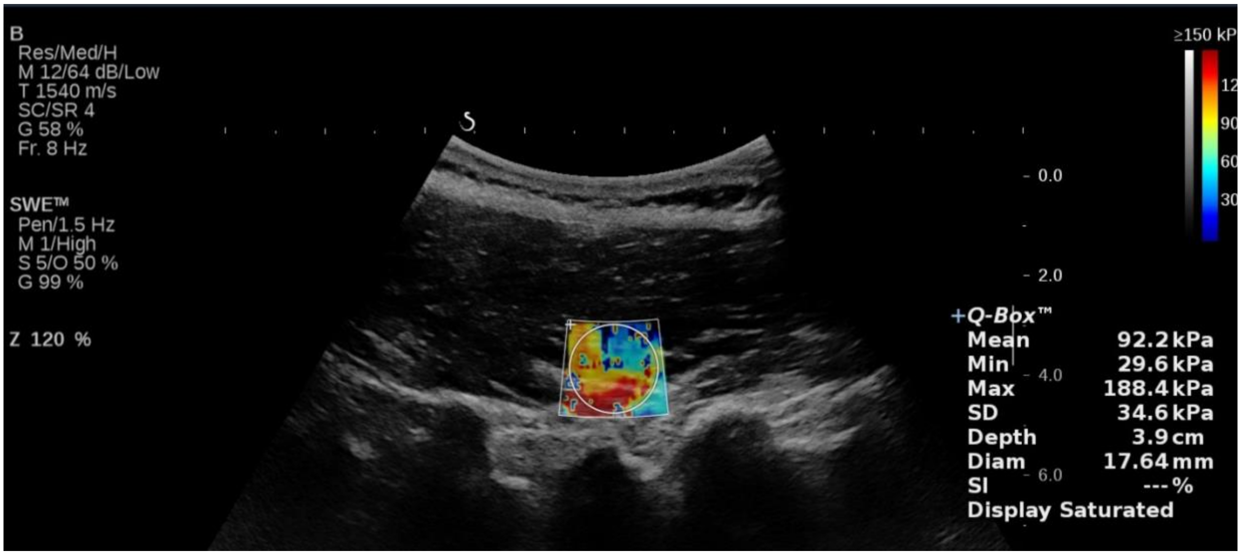

Figure 5.3. Representative elastograms recorded from an LBP participant: muscular stiffness of the MF at contraction.

5.3.4.2.1. Ultrasound MF muscle measurements at rest

Participants were positioned prone on a therapy table with a pillow placed under the participants' pelvis to reduce lumbar lordosis and maximize transducer contact (102). The spinous process was identified through palpation and marked as a reference point. The ultrasound probe was placed approximately 2cm lateral to the level of the lumbar spinous process in sagittal plane (33). The ultrasound probe was then rotated approximately 10° counter clockwise in the frontal plane and tilted approximately 10° from the sagittal plane to ensure that the ultrasound beam is directed medially towards the facet joint, ensuring that it is approximately parallel to the lumbar MF muscle fibres (122). Minimal pressure was applied to the probe. Both SWE and thickness measurements were acquired 3 times per side and spinal level (103) and the average was used in the analysis to reduce measurement error.

5.3.4.2.2. Ultrasound MF muscle measurements during submaximal contraction

Participants were positioned prone on a therapy table, as describe above with the elbows flexed to 90°, and shoulders abducted to 120° and externally rotated to 90° (103). The probe was placed and oriented in the same way as describe above for the resting position. Participants were instructed to perform a contralateral arm lift approximately 5 cm off the table using a small hand-held based on the participant's body mass (e.g., subjects weighing less than 68 kg used a 0.45 kg weight, those between 68 and 90 kg used a 0.68 kg weight, and subjects weighing over 90 kg used a 0.91 kg weight) (103). Each contraction was held for three to five seconds followed by at least 30 s of rest between each contraction (33). Again, SWE and thickness measurements during submaximal contraction were acquired 3 times per side and spinal level and the average was used in the analysis. To quantify the increase in shear elastic modulus resulting from contraction, the contraction ratio, as outlined by Botanlioglu et al. (2013) (171), was computed for the lumbar MF. This ratio was determined by dividing the shear modulus at rest by the mean shear modulus observed during contraction (absolute values).

The ultrasound images were then transferred to a desktop computer and analysed offline using the HOROS imaging analysis software. The examiner was blinded to the participant's demographic identification and MRI analysis.

5.3.5. Statistical Analysis

Descriptive statistics for demographic characteristics and outcomes were calculated. The correlation between MF muscle fat infiltration and MF function (thickness ratio and stiffness/elasticity) variables measurement was examined using bivariate and multivariate analyses. To determine multivariate relationships between MF muscle morphology and function variables, separate linear regression models were used for each muscle sites. Furthermore, the impact of the following potential covariates was examined including age, sex, body mass index (BMI), group assignment (LBP vs. healthy controls) and physical activity level on MF muscle fat infiltration and MF function. Initially, variables displaying noteworthy ($p<0.10$) bivariate associations with either muscle function or the percentage of intramuscular fat infiltration were included as covariates (9). Subsequently, in the second step, the percentage of intramuscular fat in within the lumbar MF was introduced (9). This purposeful selection strategy was employed to ascertain whether the muscle function of the lumbar MF was linked to the percentage of FSF after accounting for the variance associated with the included covariates. The adjusted r-squared values were computed iteratively at each step, accounting for the portion of variance in the dependent variable explained by the independent variables and adjusting for the number of independent variables included into the regression model. Model assumptions were verified and tenable. Differences in muscle morphology and function between LBP and control subjects were further examined using independent sample test to evaluate the between-subject factor of group (LBP and controls) and within group factors (morphology and function). A p-value of <0.05 was considered statistically significant.

5.4. Results

Age, BMI, sex, and physical activity levels was comparable between the individuals with LBP and healthy controls. The demographic and clinical characteristics of the study participants are presented in Table 5.1. The mean values and standard deviations (SD) of age and sex was 39.22 ±11.67 years, 26 female (62%), respectively. MF function and %FSF outcomes are reported in Table 5.2 and bivariate and multivariate results are reported in Tables 5.3 through 5.5. Figures 5.2 and 5.3 display illustrative elastograms used to assess MF muscular stiffness at rest and during contraction for an asymptomatic individual and an individual with LBP.

Table 5.1. Demographic and clinical characteristics of participants

Characteristic	All (n = 50) Mean (SD) or Frequency (%)	Controls (n = 25) Mean (SD) or Frequency (%)	LBP (n = 25) Mean (SD) or Frequency (%)	P-value
Age (year)	39.22 (11.67)	38.56 (11.43)	39.88 (12.11)	0.694
BMI (kg/m2)	24.18 (3.88)	23.64 (3.63)	24.74 (4.13)	0.323
Sex Male Female	24 (48%) 26 (62%)	12 (%) 13 (%)	12 (%) 13 (%)	1.000
IPAQ score Low Moderate Hight	38 % 30 % 32 %	40 % 28 % 32 %	36 % 32 % 32 %	0.753
ODI (%)	---	---	26.68 (9.23)	---
Group status LBP Healthy	25 (50%) 25 (50%)	25 --	-- 25	

BMI: Body mass index, SD: standard deviation, IPAQ: international physical activity questionnaire, ODI: oswestry disability index, LBP: Low back pain.

Bivariate regression analysis for lumbar MF muscle parameters of interest and covariates (age, sex, BMI, group status, and physical activity) are presented in Table 5.3. Notably, there were no significant bivariate associations observed between MF function including thickness ratio, SWE at rest and SWE contraction ratio and intramuscular fat infiltration. Multivariate analyses revealed no significant relationship between MF thickness ratio and intramuscular fat infiltration after adjusting for age, gender, BMI, group status and IPAQ level (Table 5.4). However, MF SWE at rest and MF SWE contraction ratio at the level of L4/L5 were positively significant correlated with intramuscular fat infiltration after adjusting for covariates (age, gender, BMI, group status and IPAQ level) with the *p*-value of 0.049 and 0.002, respectively (Table 5.5).

Table 5.2. MF% FSF measurements,
thickness ratio and shear elastic modulus.

Variables	Mean (SD)
MF % FSF	
L4/L5	19.92(6.99)
L5/S1	22.2 (9.3)
MF Th ratio	
L4/L5	20.07(8.09)
L5/S1	12.68(7.67)
MF SWE rest (kPa)	
L4/L5	12.94(4.21)
L5/S1	13.21(3.85)
MF SWE contraction ratio	
L4/L5	0.31(0.18)
L5/S1	0.35(0.35)

MF: Multifidus, FSF: fat signal fraction, Th: thickness, SWE: shear wave elastography, kPa: Kilo pascal

Table 5.3. Bivariate correlations between lumbar multifidus infiltration and function with age, sex, body mass index, group status, and physical activity.

Variables	Age		Sex		BMI		LBP status		Physical activity	
	Coeff (95%CI)	**P**	**Coeff (95%CI)**	**P**	**Coeff (95%CI)**	**P**	**Coeff (95%CI)**	**P**	**Coeff (95%CI)**	**P**
MF % FSF										
L4/L5	0.37[0.23,0.5]	<0.001*	5.73[2.07, 9.4]	0.003*	-0.01[0.54,0.5]	0.94	1.86[2.12, 5.84]	0.35	2.05[0.33, 4.44]	0.09
L5/S1	0.36[0.16,0.56]	<0.00*	8.26[3.4,12.98]	<0.001*	-0.37 [1.05,0.29]	0.26	1.08[4.19, 6.37]	0.68	2.35[-.85, 5.56]	0.14
MF Th ratio										
L4/L5	-0.06 [0.26,0.13]	0.49	0.65 [3.98, 5.28]	0.77	-0.814 [1.36, 0.26]	0.005*	-5.344[9.711,0.97]	0.01*	0.09[2.79, 2.98]	0.94
L5/S1	0.02[0.16, 0.21]	0.78	0.291[4.07, 4.65]	0.89	-0.48 [1.03,0.062]	0.08	-0.51[4.88,3.84]	0.81	-1 [3.72,1.71]	0.46
MF SWE rest (kPa)										
L4/L5	-0.05[0.16,0.04]	0.27	1.705[-0.66,4.07]	0.15	0.07[0.23, 0.39]	0.61	-0.87[3.28,1.52]	0.46	0.04[1.44, 1.53]	0.95
L5/S1	-0.05[0.15,0.03]	0.21	0.23[-1.98, 2.45]	0.83	0.15[0.12,0.44]	0.26	0.04[2.17, 2.26]	0.96	0.61[1.96,0.74]	0.36
MF SWE contraction ratio										
L4/L5	0.00[0.005,0.004]	0.93	-0.023[0.12,0.08]	0.66	0.017[0004,0.029]	0.01*	0.1[0.03, -0.005]	0.04*	0.008[0.05,0.07]	0.81
L5/S1	0.003[0.005,0.01]	0.43	-0.08[0.28,0.12]	0.42	0.03[0.005,0.05]	0.01*	-0.18[0.37,0.01]	0.07	0.03[0.09,016]	0.58

MF: Multifidus, FSF: fat signal fraction, Th: thickness, SWE: shear wave elastography, BMI: body mass index, Coeff: coefficient, CI: confidence interval, kPa: kilo pascal

Table 5.4. Results of multivariate regression analyses between MF %FSF and function (MF Th ratio) after controlling for covariates identified in the bivariate analyses.

Analysis	**Variables**	**Adjusted R2**	**R2 Change significance**	**Coeff (95%CI)**	**P-value**
Outcome variable	MF Th ratio at L4/L5				
Model 1 (covariates)	L4/L5 MF % FSF	0.161	0.266	0.261 [-0.201, 0.723]	0.261
	Age			-0.052 [-0.307,0.203]	0.683
	Sex			-3.682 [-9.1, 1.736]	0.178
	BMI			-0.859 [-1.504, -0.213]	0.01*
	LBP status			-4.616 [-8.992, -.024]	0.039*
	IPAQ level			0.032 [-2.698, 2.761]	0.981
Outcome variable	MF Th ratio at L5/S1				
Model 2 (covariates)	L5/S1 % MF FSF	0.032	0.133	0.182 [-0.131,0.495]	0.247
	Age			0.053 [-0.18,0.286]	0.649

	Sex	-3.3 [-8.66, 2.061]	0.221
	BMI	-0.618 [-1.273,0.036]	0.063
	IPAQ level	-1.479 [-4.237,1.278]	0.285

MF: Multifidus, FSF: fat signal fraction, Th: thickness, SWE: shear wave elastography, BMI: body mass index, Coeff: coefficient, CI: confidence interval.

Table 5.5. Results of multivariate regression analyses between MF %FSF and function (SWE contraction ratio and SWE rest) after controlling for covariates identified in the bivariate analyses.

Analysis	Variables	Adjusted R2	R2 Change significance	Coeff (95% CI)	P-value
Outcome variable	LM SWE cont. ratio at L4/L5				
Model 1 (covariates)	L4/L5 MF % FSF	0.242	0.321	0.016 [0.006, 0.025]	0.002*
	Age			-0.007 [-0.012, 0.001]	0.014*
	Sex			-0.048 [-0.163, 0.067]	0.405
	BMI			0.021 [0.007, 0.034]	0.004*
	IPAQ			-0.006 [-0.064, 0.052]	0.833
Outcome variable	LM SWE cont. ratio at L5/S1				
Model 2 (covariates)	L5/S1 % MF FSF	0.12	0.23	0.007 [-0.007,0.021]	0.335
	Age			-0.002 [-0.012, 0.009]	0.76
	Sex			-0.027 [-0.266,0.213]	0.824
	BMI			0.037 [0.008, 0.067]	0.015*
	IPAQ			0.032 [-0.091, 0.155]	0.604
	LBP status			-0.223 [-0.42, -0.026]	0.027*
Outcome variable	LM SWE rest L4/L5(kPa)				
Model 3 (covariates)	L4/L5 % MF FSF	0.047	0.126	0.242 [0.01, 0.494]	0.049*
	Age			-0.129 [-0.263, 0.005]	0.058
	Sex			0.286 [-2.454, 3.027]	0.834
	IPAQ			-0.111 [-1.606, 1.384]	0.882
Outcome variable	LM SWE rest L5/S1(kPa)				
Model 4 (covariates)	L5/S1% MF FSF	-0.046	0.041	-0.058 [-0.218, 0.102]	0.471
	Age			-0.021 [-0.134, 0.092]	0.713
	Sex			0.593 [-2.016, 3.202]	0.649
	IPAQ			-0.431 [-1.858, 0.996]	0.546

MF: Multifidus, FSF: fat signal fraction, Th: thickness, SWE: shear wave elastography, BMI: body mass index, Coeff: coefficient, CI: confidence interval, kpa: kilo pascal.

With regards to between-group comparisons, there was a statistically significant difference in lumbar MF thickness ratio (*p-value*=0.017), SWE during contraction (*p-value*=0.03), and SWE contraction ratio (*p-value*=0.041), with a notably smaller ratio observed in patient groups with LBP compared to healthy control participants at L4/L5 level (Table 5.6). Moreover, shear elastic modulus of the MF at contraction were greater for the LBP group relative to the control group at L5/S1 level (*p-value*=0.041). There was no other statistically significant difference between the LBP group and control group (Table 5.6).

Table 5.6. Between groups comparison for lumbar MF function

Variables	**Controls mean (SD)**	**LBP mean (SD)**	**p-value**
MF Th ratio			
L4L5	22.62 (8.52)	17.28 (6.72)	0.017*
L5S1	12.93 (8.52)	12.41 (6.69)	0.812
MF SWE rest (kPa)			
L4L5	13.38 (4.07)	12.5 (4.37)	0.467
L5S1	13.19 (3.74)	13.23 (4.04)	0.967
MF SWE contraction (kPa)			
L4L5	43.28 (13.94)	52.11 (13.89)	0.03*
L5S1	42.78 (16.17)	53.91 (15.65)	0.017*
MF SWE contraction ratio			
L4L5	0.36 (0.22)	0.25 (0.1)	0.041*
L5S1	0.44 (0.47)	0.26 (0.1)	0.073

MF: Multifidus, Th: thickness, SWE: shear wave elastography, SD: standard deviation, kPa: kilo pascal.

5.5. Discussion:

Lumbar MF muscle is a deep muscle of the spine that plays a crucial role in providing stability and support to the lumbar spine (9). Changes in MF muscle morphology, such as fat infiltration, can be associated with various spinal conditions and may impact muscle function (9, 33, 43, 98). SWE is an imaging technique that measures tissue stiffness (122). It is commonly used to assess the mechanical properties of muscles, including the lumbar MF (122). Stiffness of the muscle may be influenced by factors such as muscle composition and fat infiltration (21, 172). Delving into the mechanical characteristics of muscles, such as muscular stiffness, could provide a more comprehensive understanding of the variations within MF muscle fibers and the connection between muscle structure and both normal and altered function (44, 122). The aim of this study was to examine the correlation between lumbar MF morphology, as indicated by fat infiltration observed through MRI, and functional aspects assessed through thickness change and SWE using ultrasound.

5.5.1. Relationship between MF fat infiltration and muscle function (MF SWE)

In accordance with our initial hypothesis, our results revealed a positive correlation between MF fat infiltration and both the resting MF muscle SWE and SWE contraction ratio at the L4-L5 level, suggesting greater fat infiltration is associated with more passive and active MF muscle stiffness. In simpler terms, more fat in the MF muscle was linked to increased stiffness of the muscle, both at rest and during contraction. From a clinical perspective, this suggests that the presence of higher fat levels and related connective tissue in the MF muscle may be associated with issues related to muscle stiffness, especially in the lower back area (L4-L5 level). Muscle stiffness can have implications for overall musculoskeletal health, potentially affecting factors such as movement, flexibility, and stability (172).

According to recent studies, the development of LBP is connected to the fatty degeneration of the MF muscle (36, 124). When compared to asymptomatic individuals, LBP patients have MF atrophy and intramuscular adipose tissue invasion (101). Electromyography (EMG) research has confirmed that individuals with LBP also have reduced function of this muscle (173). It has been theorized that both, the differences in function and the functional impairment observed in people with LBP, may be related to the muscle structure, but research in this vein is limited. To our knowledge, only a few studies investigated the lumbar MF muscle structure-function relationship (8, 9). Fortin et al. (89) reported that the echo-intensity (e.g., indicator of fatty infiltration) of the LM muscle was not associated with certain aspects of muscle function, such as percentage thickness change. Similarly, La Cara et al. (9) reported no relationship between MF fat infiltration and muscle function measured by thickness change from rest to contraction. In Fortin's and La Cara's studies (9, 89), one aspect of lumbar MF function was measured, specifically the change in thickness during submaximal contraction. However, other functional measures, such as stiffness, strength, endurance, and electrical activity during maximal or submaximal contractions, might exhibit more robust correlations with fatty degeneration (9). For example, previous research has reported fatty degeneration to be associated with decreased thigh muscle performance (174, 175). This discrepancy may be explained in part by the unique attributes of the MF(175). The implication is that the chosen measure may not fully capture the relationship between fatty degeneration and various aspects of MF function, and exploring additional functional measures could provide a more comprehensive understanding of this relationship. Previous studies have shown that LBP may contribute to increased muscle stiffness (i.e., muscle spasm) of the lumbar back muscles, such as the lumbar MF muscles in LBP patients (176). Furthermore, Ateş et al. (19) in 2015 also reported a positive linear relationship between shear elastic modulus, contraction and the level of muscular activity and muscle force measured via EMG while performing isometric fingers abductions.

Ultrasound SWE can provide information about muscle function (89), as changes in shear modulus are linearly proportional to the force produced by the muscle (172, 177, 178). Therefore, SWE can be used to evaluate the force production capability of individual muscles in motor tasks with muscle redundancy, which cannot be achieved with current clinical tests (179). Muscle stiffness measured using ultrasonic SWE is influenced by muscle elongation or muscle activity (180). The observed increased stiffness in the LBP group could be attributed to muscle spasm induced by pain, often stemming from stress on intervertebral disks or intervertebral joints, which may affect the lumbar MF muscle (181). Muscle stiffness of the lumbar MF muscle is assumed to increase with muscle contraction (122). In this case, the overuse caused by muscle spasm of the lumbar MF muscle may lead to circulatory difficulty within the muscle, which contributes to secondary LBP occurrence in the future (21, 122). The observed variations in shear elastic modulus between individuals with LBP and those without may indicate distinctions in muscle composition (97). This is noteworthy because passive stiffness of skeletal muscles is not solely determined by the contractile muscle tissue (182). A relevant animal model study by Brown et al. (2011) (183) induced lumbar disc degeneration in rabbits, which led to an increase in paravertebral muscle stiffness. Interestingly, the stiffness increase was more prominent in fiber bundles, comprising both muscle fibers and connective tissue (122). This insight suggests that fat proliferation combined with a concommittant increase in connective tissue likely contribute to higher shear elastic modulus values in individuals with LBP, providing a potential explanation for the current study’s findings (184).

Our finding will assist clinicians and researchers to advance further investigations into the relationship between muscle composition, fat infiltration, and functional outcomes to develop more targeted interventions or treatment strategies, especially for individuals experiencing issues related to muscle stiffness in the lower back.

5.5.2. Relationship between MF fat infiltration and muscle function (MF Thickness ratio)

Contrary to our initial hypothesis, we did not observe any correlations between the percentage of MF intramuscular fat infiltration and MF thickness ratio. The lack of a clear relationship between measures of muscle function (specifically related to the lumbar MF) and fat infiltration has been observed in the current literature (8, 9). Similarly, no association between lumbar MF fat infiltration and MF muscle function measuring MF thickness change was reported in Le Cara et al.' study in 2014 (9). Several potential explanations for these findings include the characteristics of the cohort studied, possible issues related to the measures of morphology and function, and the inherent nature of LBP (9).

Function of the lumbar MF can vary between its deep and superficial layers. Specifically, a study by MacDonald et al. (181) reported that patients with recurrent LBP demonstrated activation impairments in the deep fibers of the MF compared to individuals without LBP. This finding suggests that there may be specific functional differences between the deep and superficial layers of the MF, particularly in the context of recurrent LBP (122, 181). Furthermore, while ultrasound imaging is claimed to be a valid measure of MF function, it is unknown whether this technique adequately assesses both deep and superficial muscle layers (9, 71, 98). This highlight a potential limitation or uncertainty in the application of ultrasound imaging for comprehensively evaluating the function of different layers of the lumbar MF muscle. It also underscores the importance of considering the specific characteristics of the muscle layers when assessing their function, as well as the need for further research to validate the effectiveness of imaging techniques in capturing these nuances.

Moreover, the task used in the current study to asses muscle function aimed to contract the MF muscle at approximately 30% of the maximum voluntary isometric contraction (104). Given that this task was a submaximal contraction and that MF intramuscular fatty infiltration is more proeminent in the deep portion of the muscle, the asymmetrical accumulation of fat may have been compensated for by additional activation of muscle in less-affected (superficial) regions (42). An alternative measure involving higher-intensity contraction strategies may be preferable to capture the full scope of MF function, especially in the presence of fatty infiltration (22). There is the possibility that the relationship between MF morphology and function in patients with LBP might exist along different pathways. This raises the question of whether some patients could be categorized as experiencing a muscle impairment primarily related to morphological changes or functional issues. The concept of subgrouping patients with LBP based on muscle-related variables (e.g., muscle composition, strength, endurance, activation) is suggested as an avenue for future study, aiming to improve clinical decision-making, concluding by emphasizing the need for future research efforts in the area. It is recommended to explore alternative measures of MF function, specifically direct measures of deep MF activation, as well as measures of muscle strength and endurance. Additionally, the exploration of muscle-related variables that may identify patients whose LBP is associated with morphologic changes or functional impairment is encouraged.

5.5.3. Differences in MF SWE between group

Participants with LBP exhibited a significantly lower contraction ratio, reflected by a lower increase of muscular stiffness with contraction (176). As the contraction ratio provides a more precise assessment of stiffness variations during muscle contraction and force generation (122), it can be used as a metric to compare the extent of muscular stiffness increase during contraction across various conditions, such as those with and without pain or between different muscles. This finding aligns with previous research that has also identified segment-specific changes in lumbar MF associated with LBP (122).

Our findings corroborate with a recent study by Murillo et al. (122) which was the first study to investigate whether differences in passive muscular stiffness exist between the deep and superficial MF muscles, both in asymptomatic participants and in individuals with LBP. Participants with LBP exhibited increased muscular stiffness of the superficial MF muscle at rest, and a reduced ability to stiffen the muscle with isometric trunk extension compared to asymptomatic individuals (122). The differences in shear elastic modulus between LBP and asymptomatic individuals may reflect differences in muscle composition since passive stiffness is not only attributed to the contractile tissue within the muscle (179). Interestingly, Brown et al. (2011) (184) induced lumbar disc degeneration in rabbits and found that, though the individual paravertebral muscle fibers became stiffer, the fiber bundles (composed of both muscle fibers and connective tissue) displayed a greater increase in stiffness. Thus, the increase of connective tissue due to a fibrotic proliferation may increase the shear elastic modulus values in LBP individuals (183). Consistent with our results, a study found reduced normalized active muscular stiffness in the deeper posterior neck muscles during isometric neck extension in individuals experiencing neck pain (185). In accordance with our findings, previous studies have also reported decreased activation of the MF during trunk extension in a prone position among individuals with acute and experimental LBP (176, 186). The observed deficit in contraction in individuals with LBP, indicated by a lower increase in muscular stiffness, which may be attributed in part by the fibrotic proliferation of collagen content and connective tissue (122).

These alterations within the muscle could lead to a reduction in contractile tissue, resulting in a diminished capacity for efficient muscle contraction (122).

While the current study adds to this body of evidence, it is noteworthy that no significant difference was observed in SWE at rest between participants with and without LBP. Further exploration is warranted to reconcile these findings, and future studies could build on existing knowledge by investigating potential contributing factors and refining clinical implications. In contrast, Masaki et al. (97) previously reported significantly greater shear elastic modulus of MF at rest (measured at the level of L4) in individuals with LBP; however, Chan et al, (49) did not observe group differences even if MF was examined at the same spinal level. In Masaki et al.'s study (97), only young and middle-aged medical workers were included, while our study was comprise of individuals aged between 21 to 61 years old with various work. Furthermore, contrary to our study, Masaki et al. (97) did not match healthy controls and participants with LBP for age and sex.

This study has certain limitations. Firstly, the assessment of lumbar MF muscles was limited to the two lower spinal levels. Future investigations should expand the analysis to include paraspinal muscle composition at additional spinal levels, and also explore other muscles associated with LBP, such as the erector spinae muscle. Secondly, this study did not extensively delve into biomechanical factors that could influence lumbar MF function, such as posture, movement patterns, or occupational factors. Incorporating these variables could provide a more comprehensive understanding of muscle function in individuals with LBP. Additionally, the evaluation of physical activity relied solely on self-report measures; employing direct measures would have offered more accurate estimates of physical activity levels.

5.6. Conclusion

Our investigation into the relationship between lumbar MF morphology, fat infiltration, and muscle function reveals nuanced associations. Multivariate analyses did not find a significant relationship between MF thickness ratio and intramuscular fat, while MF SWE measures at the L4/L5 level showed a significant positive association with fat infiltration, highlighting the sensitivity of SWE in assessing altered muscle composition. When comparing individuals with LBP to healthy controls, the observed lower increase in muscular stiffness during contraction in those with LBP may suggest a deficiency in the activation of the MF muscle. Notably, no differences in SWE resting values were found between both groups. Patients with LBP displayed notably smaller contraction ratio, emphasizing the potential role of these parameters as indicators of altered lumbar MF health in the context of LBP. Our findings underscore the need for a comprehensive assessment considering both morphological and functional aspects when evaluating lumbar MF in individuals with LBP, paving the way for future research into clinical implications and targeted interventions.

Understanding the biomechanics of a healthy MF muscle and how its function changes due to various pathologies is vital for the development of effective rehabilitation strategies and protocols. Shear wave elastography holds the potential to improve the clinical assessment of paraspinal muscles, allowing for the evaluation of changes in MF muscle function in response to treatments like exercise-based therapy and electrical stimulation.

CHAPTER 6: GENERAL DISCUSSION

The purpose of this dissertation was to examine relationship between paraspinal muscle morphology, function, and physical status in common spinal disorders. The question was tackled by using an holistic view of cervical muscle morphometry and composition to demonstrate prognostic value in degenerative cervical myelopathy (DCM) outcomes (Chapter 3: Manuscript 1), to examining postoperative assessment of cervical muscle morphology, strength, and functional outcomes in patients with DCM (Chapter 4: Manuscript 2), to the evaluation of structural alterations and mechanical properties of the multifidus (MF) muscle in chronic low back pain (LBP) using contemporary images-based methods (Chapter 5: Manuscript 3). The literature review performed for the purpose of this dissertation has provided a framework to support the importance of understanding the structure-function relationship of the paraspinal muscle in the context of spinal pathologies. However, this review has also revealed numerous gaps in our current knowledge; gaps that were further illustrated in the review of the literature presented in Chapter 2. Despite some limitations, the 3 manuscripts included in this doctoral thesis (chapters 3, 4 and 5) provided novel insights and new directions for future studies in this field.

6.1. Manuscript 1: Cervical Muscle Morphometry and Composition Demonstrate Prognostic Value in Degenerative Cervical Myelopathy Outcomes.

The exploration of the complex interplay between cervical muscle morphology and surgical outcomes in DCM reveals multifaceted insights with profound implications for preoperative strategies, patient selection, and postoperative recovery. Our study suggests a nuanced understanding of predictors, associations, and considerations that shape the landscape of DCM treatment, both pre- and post-surgery.

6.1.1. Predictors of Improved modified Japanese Orthopedc Association Scores

Our findings accentuate the pivotal role of preoperative factors in shaping post-surgery outcomes. The identification of smaller deep cervical extensor muscle size as a predictor for improved modified Japenes Orthopedic Association (mJOA) scores at 6 and 12 months post-surgery underscores the importance of understanding and optimizing these factors before a surgical intervention. This revelation provides clinicians with valuable insights into potential markers for patient selection and further emphasizes the need for tailored preoperative assessments.

Additionally, the inverse relationship between fatty infiltration and post-surgery success adds another layer of complexity to the predictive landscape. Notably, the recognition that less fatty infiltration correlates with better clinical outcomes emphasizes the potential modifiability of these factors, opening avenues for novel and more targeted interventions. This highlights the importance of considering muscle composition in patient stratification and further underscores the need for a comprehensive understanding of individual patient characteristics.

6.1.2. Muscle Composition and Morphology Impact on Surgery Benefits

This study underscores the crucial role played by both clinical and imaging features of muscle composition and morphology in classifying patients who would benefit from surgery. Smaller deep cervical extensor muscle size, indicative of reduced muscle cross-sectional area (CSA) at the maximum level of compression, emerges as a predictor for improved post-surgery outcomes. This brings attention to the potential utility of this metric in refining patient selection criteria for enhanced recovery after surgery (ERAS) pathways (187).

Furthermore, the identification of novel predictors such as deep extensor fat infiltration and asymmetry adds granularity to our understanding of DCM. These markers offer potential insights into the individualized nature of DCM, suggesting that tailoring interventions based on these morphological characteristics could likely optimize postoperative recovery. As the field progresses, these findings may pave the way for targeted therapeutic strategies focused on modifying these predictors to enhance outcomes.

6.1.3. Association Between Muscle Fat Infiltration and Clinical Outcomes:

Our study not only validates previous research (15) (16) linking cervical muscle fat infiltration to clinical outcomes in DCM but also introduces two novel predictors—deep extensor fat infiltration and asymmetry. This expands the scope of prognostic considerations, offering a more comprehensive view of factors influencing functional recovery post-surgery. The association between greater muscle fat infiltration (lower FCSA/CSA) and worse outcomes aligns with prior research in DCM and whiplash-associated disorders, highlighting the robustness of our findings (14, 53, 82).

The observed relationship between greater fatty infiltration and asymmetry in cervical muscles and worse Nurick scores at both 6- and 12-months post-surgery underscores the clinical relevance of these morphological characteristics. This association supports the notion that specific muscle parameters, such as fatty infiltration and asymmetry, play a pivotal role in the prognosis and functional recovery of patients with DCM (112). Understanding these associations can guide clinicians in refining patients' selection and tailoring interventions based on individualized risk profiles.

6.1.4. Complex Role of Age in Surgical Outcomes

The impact of age on surgical outcomes in patients with DCM remains a topic of debate and research. While our findings align with the general trend of younger age correlating with better outcomes, the nuanced nature of this relationship necessitates further investigation. The absence of a definitive age cutoff value emphasizes the need for a more nuanced approach to patient stratification. Future research endeavors should delve into the intricate interplay between age, physiological reserves, health status, and comorbidities to unravel the complexities associated with age and DCM surgical results.

Despite the complexity surrounding the role of age, our study contributes to the ongoing discourse, providing valuable insights into the age-related nuances that influence surgical outcomes in patients with DCM. The exploration of age as a multifaceted factor offers a foundation for future investigations, aiming to untangle the intricate web of variables contributing to the relationship between age and surgical results.

6.1.5. Role of Rehabilitation in DCM Management

The integration of rehabilitation into the broader context of DCM management emerges as a central theme in our study. The endorsement of exercise therapy, including range of motion and strengthening exercises, as a crucial component in improving cervical muscle characteristics aligns with the evolving paradigm of holistic patient care (111). Recognizing rehabilitation as an essential adjunct to surgical interventions emphasizes the need for a comprehensive, patient-centered approach to maximize functional outcomes.

Our results suggest that timely and strategic rehabilitation is not only essential for maximizing functional outcomes but also crucial for achieving the best possible results in neurological disorders. The positive correlation between exercise therapy and improved outcomes underscores the importance of implementing appropriate perioperative rehabilitative interventions. The holistic integration of rehabilitation strategies alongside surgical approaches represents a promising avenue for enhancing overall patient well-being and independence.

6.1.6. Study Limitations and Future Directions

While our study provides valuable insights, it is imperative to acknowledge its limitations to ensure a nuanced interpretation of the results. The measurements of paraspinal muscle morphology at different levels introduces variability, and the lack of consideration for the impact of pre-surgery conservative treatment represents a potential confounding factor. Standardizing imaging parameters and incorporating additional measures of cervical muscle function can enhance the robustness and generalizability of findings in future research.

Future investigations should consider leveraging advanced technologies, such as deep learning automatic segmentation methods, to evaluate cervical muscles rapidly and accurately. The incorporation of these technologies, like convolutional neural networks, has shown promise in clinical populations and may offer a more efficient and standardized approach to evaluating muscle morphology. Additionally, the consideration of alternative imaging modalities beyond T2-weighted images, along with the inclusion of diverse patient populations, can contribute to a more comprehensive understanding of cervical muscle characteristics in DCM.

In conclusion, our study provides a thorough examination of cervical muscle morphology in the context of surgical outcomes for DCM. The identified predictors, associations, and considerations offer a foundation for refining patient selection criteria, tailoring interventions, and optimizing postoperative recovery strategies. As we navigate the intricate landscape of DCM research, our findings contribute vital knowledge towards personalized, comprehensive, and effective treatment strategies, ultimately improving patient outcomes and quality of life.

6.2. Manuscript 2: Postoperative assessment of cervical muscle morphology, strength, and functional outcomes in patients with degenerative cervical myolopathy

6.2.1. Implications of Cervical Muscle Morphology on Surgical Outcomes:

DCM stands as a prevalent spinal disorder globally, emphasizing the necessity for effective treatment strategies. Surgical intervention has emerged as a crucial approach, halting disease progression, and improving functionality. However, the observed variability in post-surgical outcomes underscores the need for a nuanced understanding of factors influencing recovery. Nearly 40% of patients experiencing only partial recovery emphasizes the complexity of DCM and the imperative need for tailored approaches (14-16).

Our study addresses a critical gap in the evaluation of posterior cervical musculature, shedding light on its potential influence on surgical outcomes. The absence of a comprehensive assessment of posterior cervical muscles in surgical decision-making highlights the need for refined clinical guidelines. Moreover, the recognition that complications like post-operative neck pain, adjacent segment disease (ASD), and proximal junctional kyphosis (PJK) may be influenced by surgical approach further emphasizes the importance of optimizing the selection of surgical techniques (161, 162).

6.2.2. Muscle Strength Changes Following Surgery

Contrary to initial hypotheses and existing literature (24), our study did not observe an improvement in cervical muscle strength two years post-surgery in either surgical approach. The anticipated increase in muscle strength, as reported by Fujibayashi et al. (24) did not align with our findings. Discrepancies may arise from differences in surgical approaches, with laminoplasty inducing muscle atrophy across joints in Fujibayashi's study (24). The limited sample size in our study, particularly in the anterior cervical discectomy and fusion (ACDF) subgroup, could contribute to variations in outcomes. Additionally, sex differences in muscle strength, observed in both studies, underline the importance of considering demographic factors when interpreting results.

6.2.3. Impact of Surgical Approach on Muscle Morphology:

Distinctive patterns emerged when evaluating the impact of surgical approaches on muscle morphology. Posterior fusion surgery resulted in significant decreases in mudtifidus and semispinalis cervisis (MF+Scer) CSA and functional cross sectional area (FCSA), accompanied by increased CSA asymmetry. In contrast, ACDF demonstrated a generalized reduction in the CSA and FCSA of the entire muscle group. Level-specific analyses revealed intriguing findings, particularly at the C2C3 level, suggesting unique characteristics or resilience within this region. These results contribute valuable insights into the nuanced effects of surgical approaches on cervical muscle morphology, emphasizing the need for personalized strategies based on anatomical considerations.

The observed muscle atrophy post-surgery, evident in both approaches, underscores the structural impact of these procedures on cervical musculature. The distinction in changes between surgical approaches, specifically the significant alterations in MF+Scer following posterior fusion, highlights the need for a tailored understanding of the differential impacts on muscle structures. The increased CSA asymmetry in the posterior fusion group carries clinical significance, indicating potential implications for neck stability and function.

6.2.4. Complex Relationship Between Cervical Muscle Health and Postoperative Outcomes

The complex relationship between cervical muscle health and postoperative outcomes is evident in the absence of significant correlations between pre-surgery neck muscle parameters and changes in functional scores. This aligns with existing literature complexities, emphasizing the multifactorial nature of postoperative outcomes (15, 16). Standardization of measurement techniques, functional assessments, and longer follow-up periods are crucial for comprehensive analyses, ensuring a clearer understanding of the role of cervical muscle health in post-surgery outcomes.

6.2.5. Study Limitations and Future Directions

Acknowledging study limitations, including a small sample size and non-standardized imaging parameters, prompts considerations for future research. The incorporation of deep learning automatic segmentation techniques, standardized imaging, and additional measures of cervical muscle function could enhance future investigations. A longitudinal study with a larger, diverse sample, assessing alterations in morphology and function post-surgery, will contribute to a more comprehensive understanding.

In conclusion, our extended discussion underscores the intricacies surrounding cervical muscle morphology, surgical outcomes, and the need for personalized approaches in DCM treatment. The interplay between surgical techniques, muscle changes, and functional outcomes requires ongoing exploration. As we navigate this complex landscape, our study contributes valuable insights, fostering a foundation for future research endeavors aimed at refining surgical strategies, optimizing patient outcomes, and enhancing the overall quality of life for individuals with DCM.

6.3. Manuscript 3: Evaluation of structural alterations and mechanical properties of the multifidus muscle in chronic low back pain using contemporary images-based methods

6.3.1. Significance of Lumbar MF Muscle

The lumbar MF muscle is a crucial component of the spine, providing essential stability and support to the lumbar region (27, 71, 102, 106). Lumbar MF morphology, particularly changes such as fat infiltration, has been linked to various spinal conditions, prompting the exploration of its impact on muscle function (78). In this context, shear wave elastrography (SWE), a non-invasive method used in medical imaging , provides quantitative information about tissue stiffness, which is crucial for assessing muscle health and guiding clinical decisions in various medical specialties (21, 22, 97, 122, 172).

6.3.2. Correlation Between Fat Infiltration and Muscle Stiffness

Our results revealed a positive correlation between fat infiltration in the lumbar MF muscle, as observed through magnetic resonance imaging (MRI), and muscle stiffness measured by both resting MF muscle SWE and SWE contraction ratio at the L4-L5 level. This suggests that increased fat levels within the MF muscle are associated with increased stiffness, both during rest and contraction. Clinically, these findings suggest that higher fat content may contribute to issues related to muscle stiffness, particularly in the lower back area (L4-L5 level).

The implications of muscle stiffness extend to factors such as movement, flexibility, and stability, highlighting the broader musculoskeletal consequences of fat infiltration.

These results align with existing literature linking fatty degeneration of the lumbar MF muscle to LBP (8, 34, 87). Individuals with LBP often exhibit MF atrophy and intramuscular adipose tissue invasion, accompanied by reduced muscle function confirmed through electromyography (EMG) research (94, 130, 173). The study's focus on SWE adds a nuanced layer to this understanding, providing a direct correlation between fat infiltration and muscle stiffness.

6.3.3. Complex Relationship Between Muscle Morphology and Function

The complex relationship between lumbar MF muscle morphology and function is highlighted by inconsistent findings in previous studies (9, 87, 94, 186). While some research (9) suggests no association between muscle fat infiltration and certain aspects of muscle function, such as percentage thickness change, this study uncovers significant correlations with stiffness measures. The discrepancies may be attributed to variations in the chosen measures of lumbar MF function and the multifaceted nature of lower back pain.

Our results emphasize the need for exploring additional functional measures beyond thickness change during submaximal contraction to comprehensively understand the relationship between fatty degeneration and various aspects of MF function. This includes assessments of stiffness, strength, endurance, and electrical activity during both maximal and submaximal contractions. The intricate nature of lumbar MF function, with variations between deep and superficial layers, prompts a revaluation of how different layers contribute to the overall functionality of the muscle.

6.3.4. SWE as a Tool for Muscle Function Assessment

The use of SWE is justified by its ability to provide information about muscle function. Changes in shear modulus, linearly proportional to muscle force, offer a means to evaluate the force production capability of individual muscles. SWE's sensitivity to muscle elongation or activity adds valuable dimensions to the assessment of muscle function. In the context of LBP, the observed variations in shear elastic modulus between individuals with and without LBP suggest distinctions in muscle composition, potentially involving factors beyond contractile tissue.

Our findings with regards to a decreased contraction ratio and stiffness increase during muscle contraction in individuals with LBP aligns with previous research (122), and suggest a deficiency in the activation of the lumbar MF muscle, possibly due to increased collagen content and connective tissue, leading to alterations within the muscle. This study underscores the importance of SWE in detecting subtle variations in muscle function associated with LBP, contributing to the growing body of evidence in this field.

6.3.5. Study Limitation and Future Direction:

The study's limitations, such as the focus on the two lower spinal levels and the absence of an extensive exploration of biomechanical factors, prompt avenues for future investigations. Expanding the analysis to include paraspinal muscle composition at additional spinal levels and incorporating variables like posture, movement patterns, and occupational factors could enhance the understanding of muscle function in individuals with LBP.

Clinicians and researchers can leverage these findings to guide further investigations into the intricate relationship between muscle composition, fat infiltration, and functional outcomes. The study encourages a shift toward more targeted interventions or treatment strategies for individuals experiencing issues related to lumbar MF muscle stiffness in the lower back. Future research endeavors are recommended to explore alternative measures of MF function, considering direct measures of deep MF activation, muscle strength, and endurance.

In conclusion, this study provided valuable insights into the nuanced relationship between lumbar MF muscle morphology, fat infiltration, and functional aspects assessed through SWE. The positive correlation between fat infiltration and muscle stiffness underscores the clinical relevance of assessing muscle composition in the context of LBP. This study calls for a comprehensive approach to evaluating lumbar MF function, considering both morphological and functional aspects. SWE emerges as a promising tool for this purpose, providing clinicians with a nuanced understanding of muscle health and paving the way for targeted interventions and rehabilitation strategies.

6.5. General Conclusion

In the comprehensive exploration of cervical spine disorders and lumbar MF muscle dynamics, the discussions reveal intricate relationships that significantly contribute to the understanding of musculoskeletal health. The investigation into DCM surgeries highlights the complexity of surgical decisions, emphasizing the need for a nuanced evaluation of posterior cervical musculature to minimize complications. The findings, contrasting with prior expectations, underscore the impact of surgical approach on cervical muscle morphology, necessitating consideration for sex differences and level-specific analyses.

Transitioning to lumbar MF muscles, the discussions shed light on the multifaceted interplay between muscle morphology, fat infiltration, and functional outcomes. SWE has become increasingly recognized as an valuable tool, revealing positive correlations between fat infiltration and muscle stiffness in the lumbar region. The nuanced associations uncovered suggest that higher fat content may contribute to issues related to muscle stiffness, particularly in the context of LBP. However, the complex relationship between LM muscle morphology and function, including variations between deep and superficial layers, prompts further exploration of functional measures for a comprehensive understanding.

In conclusion, our findings collectively highlight the importance of considering individualized approaches in the assessment and treatment of spinal disorders. Surgical decisions and interventions must be tailored to account for variations in anatomy, sex differences, and the unique characteristics of different spinal regions. The utilization of advanced imaging techniques, such as SWE, offers a more nuanced understanding of muscle health, opening avenues for targeted interventions and rehabilitation strategies. These insights not only contribute to the existing body of knowledge but also emphasize the imperative need for continued research to refine clinical practices and optimize patient outcomes in the realms of cervical spine and lumbar MF health.

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Note: These references are for chapters one, two, four, five and six. The references for chapter three can be found at the end of the chapter to keep the integrity of the published versions.

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