University of Alberta

Paraspinal muscle morphology, composition and asymmetries: determinants and relation to low back pain and pathology.

by

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DEDICATION

I dedicate this thesis to my loving fiancée Damianos, who accompanied me throughout this long journey and life-changing experience. Your love, partnership and constant support made me believe that this life project was achievable and worthy. To my parents, brother and sister who always encouraged me to pursue my dreams.

ABSTRACT

Background

The lumbar paraspinal muscles are critical to provide spine stability, maintain proper posture and assist trunk movement. Although considerable attention has been focused on the association between variations in paraspinal muscle morphology and low back pain (LBP), their role in the development and progression of LBP remains unclear.

Purpose

The purpose of this doctoral work was to identify potential determinants of paraspinal muscle asymmetry, characterize the natural progression of age-related changes in paraspinal muscle over a 15-year period and examine their association with LBP problems, and determine whether paraspinal muscle size, composition and asymmetry are risk indicators for the development of LBP.

Materials and Methods

Subjects were selected from the pre-existing database of the Twin Spine Study. Data were collected through a structured interview, physical examination and magnetic resonance imaging (MRI). Measurement of the multifidus and erector spinae muscle cross-sectional area (CSA), functional CSA (FCSA) (e.g. fat-free mass) and degree of asymmetry in size and composition was obtained from T2-weighted axial images for 202 men at baseline and 99 men at 15-year follow-up.

A novel and highly reliable thresholding technique, allowing for the separation of muscle and fat tissue, was developed to perform quantitative measurements of paraspinal muscle composition.

Results and Conclusions

Of the factors investigated, the few that were significantly associated with paraspinal muscle asymmetry in cross-sectional analyses included handedness, disc height narrowing, the amount of physical activity performed at work and leisure and familial aggregation. Yet, with the exception of handedness and familial aggregation, the associations were generally inconsistent across muscles and spinal levels and explained little of the variance in paraspinal muscle asymmetry. Over the 15-year follow-up period, the multifidus and erector spinae showed similar morphological changes including a decrease in size and an increase in fatty infiltration and asymmetry. However, no significant correlation was found between the long-term paraspinal muscle changes and LBP history. Moreover, multifidus and erector spinae muscle size, composition and degree of asymmetry do not appear to be major risk factors for the short-term (1-year) or long-term (15-year) development or prognosis of LBP, including sciatica.

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LIST OF SYMBOLS AND ABBREVIATIONS

BL	*Baseline*
BMI	*Body Mass Index*
CI	*Confidence Interval*
CSA	*Cross-Sectional Area*
CSA diff	*Side-to-side difference in Cross-Sectional Area*
FCSA	*Functional Cross-Sectional Area*
FCSA/CSA	*Ratio of Functional Cross-Sectional area to total Cross-Sectional Area*
FCSA diff	*Side-to-side difference in Functional Cross-Sectional Area*
ICC	*Intra-Class Correlation Coefficient*
LBP	*Low Back Pain*
MRI	*Magnetic Resonance Imaging*
MZ	*Monozygotic*
ROI	*Region Of Interest*
SD	*Standard Deviation*
SEM	*Standard Error of Measurement*
SI	*Signal Intensity*
SPSS	*Statistical Package for the Social Sciences*

CHAPTER 1

INTRODUCTION AND OBJECTIVES

1.1. INTRODUCTION

Low back pain (LBP) is one of the most common medical complaints and has become an endemic disorder in Western countries. [1,2] It is estimated that about two thirds of the adult population will have an episode of LBP at some point in their lifetime. [3] Despite the progress in diagnostic imaging techniques, the exact cause of LBP remains unknown in approximately 85% of the cases. [3] Moreover, the recurrence of LBP is extremely high; 60% to 84% of patients with an acute episode of LBP will have recurrent symptoms in the following year. [4-6]

In an effort to better understand the etiology and pathogenesis of LBP, epidemiological studies have focused on the intervertebral disc,[7-11] facet joints [12-14] and more recently the vertebral endplates [15-17] as potential sources of pain. Over the past decades some attention has also shifted towards paraspinal muscles, as variations in paraspinal muscle morphology (e.g. atrophy, fatty infiltration and asymmetry) have been observed in patients with LBP. [18-33] However, their role in spinal pathology and symptoms remains ambiguous.

Patients with chronic LBP have been reported to have smaller paraspinal muscles [33,34] and more fatty infiltration than healthy asymptomatic subjects, [23,24] yet other studies contradict these results. [21,35,36] The multifidus muscle, which plays an important role in spinal stability, [37] appears to be the most sensitive of the paraspinal muscle group to spinal pathology. Patients with unilateral LBP

have been found to have smaller multifidus cross-sectional area (CSA) and more fatty infiltration localized to the suspected pathological spinal level and symptomatic side; [18,20,26] although these findings have not been consistent in all studies. [29,38-40]

While paraspinal muscle CSA has been shown to be relatively symmetrical in individuals without LBP, [18,20,41] a recent MRI study demonstrated significant multifidus asymmetry in a group of asymptomatic men. [42] Paraspinal and trunk muscle asymmetry has also been commonly reported in elite athletes without LBP symptoms. [43-47]

Few studies have specifically investigated determinants of paraspinal muscle asymmetry [18,41] and composition (e.g. fatty infiltration), [24,36,48] other than back pain and pathology. Many physical therapists currently integrate specific multifidus strengthening and stabilization exercises in their rehabilitation protocols for LBP patients, attributing great clinical meaning to the atrophy and asymmetry observed in patients with LBP. However, findings reported in the scientific literature remain inconsistent, and one needs to be aware of other potential factors that may influence or lead to such paraspinal muscle variations before judging them as signifying risk or presence of pathology. Moreover, it is still unclear whether variations in muscle morphology, composition and asymmetry result from LBP and pathology, represent risk factors or possibly both.

Further research is needed to clarify determinants of multifidus asymmetry and other paraspinal muscle variations and their relation with the onset and progression of back pain problems and lumbar pathology. Longitudinal follow-up

studies of general population samples of persons with and without back pain problems are particularly needed in this field.

The aims of the studies included in this thesis were to: 1) identify possible determinants of paraspinal muscle asymmetry in size and composition (e.g. fatty infiltration), 2) describe the age-related changes in paraspinal muscle over a 15-year period in adulthood, and 3) clarify the relation of these muscle variations with LBP and pathology, through a series of cross-sectional and longitudinal studies using a general population sample of men.

1.2. OBJECTIVES

The overall purpose of this thesis was to investigate LBP and pathology and other factors as determinants of paraspinal muscle asymmetry in size and composition, describe the natural progression of changes in paraspinal muscle during adulthood, and clarify whether paraspinal muscle size, composition and asymmetries are risk factors for the development or prognosis of LBP. A novel quantitative method to measure paraspinal muscle composition was also developed. The next chapter (Chapter 2) will review the related literature, and the following chapters will each address one of the following objectives:

- To determine the inter-software agreement, intra-rater reliability and standard error of measurement (SEM) of paraspinal muscle CSA and composition measurements acquired while using two open source, readily available computer software programs, ImageJ and OsiriX. In addition, this chapter clearly describes the related image analysis protocols for both

software programs to allow standardized use and facilitate comparisons among studies (Chapter 3).

- To examine the association of a wide range of behavioral, environmental and constitutional factors (e.g. age, body mass index (BMI), lean body mass, handedness, physical demands at work and leisure, LBP history, disc height narrowing) with asymmetry in paraspinal muscle size and fatty infiltration in a general population sample of men (Chapter 4).
- To characterize the long-term changes in paraspinal muscle morphology and their association with lifestyle factors. More specific objectives were to: 1) define the natural progression of age-related changes in paraspinal muscle over a 15-year period during adulthood and 2) investigate the influence of the lifestyle and individual factors (e.g. physical activity at work and leisure, BMI and LBP history) (Chapter 5).
- To investigate paraspinal muscle morphology parameters as risk factors for the development or prognosis of LBP in the short and long-term. More explicitly, the objective was to investigate if paraspinal muscle size, composition and asymmetry at baseline are predictors of LBP problems (e.g. LBP frequency and intensity) at 1-year and 15-year follow-up, or predictors of the occurrence of sciatica at 15-year follow-up (Chapter 6).
- A final chapter will conclude this thesis with a summary and discussion of the main findings and recommendations for future research in this field (Chapter 7).

1.3. REFERENCES

1. Andersson GBJ. Epidemiological features of chronic low-back pain. *Lancet* 1999;354(9178):581-585.

2. Hart LG, Deyo RA, Cherkin DC. Physician office visits for low back pain: Frequency, clinical evaluation, and treatment patterns from a U.S. National survey. *Spine* 1995;20(1):11-19.

3. Deyo RA, Weinstein JN. Low back pain. *N Engl J Med* 2001;344(5):363-370.

4. Bergquist-Ullman M, Larsson U. Acute low back pain in industry. A controlled prospective study with special reference to therapy and confounding factors. *Acta Orthop Scand* 1977;48(suppl. 170):1-117.

5. Von Korff M, Deyo RA, Cherkin D, Barlow W. Back pain in primary care: Outcomes at 1 year. *Spine* 1993;18(7):855-862.

6. Hides JA, Jull GA, Richardson CA. Long-term effects of specific stabilizing exercises for first-episode low back pain. *Spine* 2001;26(11):E243-248.

7. Battié MC, Videman T, Gibbons LE, Fisher LD, Manninen H, Gill K. Determinants of lumbar disc degeneration: A study relating lifetime exposures and magnetic resonance imaging findings in identical twins. *Spine* 1995;20(24):2601-2612.

8. Videman T, Battié MC, Parent E, Gibbons LE, Vainio P, Kaprio J. Progression and determinants of quantitative magnetic resonance imaging measures of lumbar disc degeneration: A five-year follow-up of adult male monozygotic twins. *Spine* 2008;33(13):1484-1490.

9. Videman T, Battié MC, Ripatti S, Gill K, Manninen H, Kaprio J. Determinants of the progression in lumbar degeneration: A 5-year follow-up study of adult male monozygotic twins. *Spine* 2006;31(6):671-678.

10. Videman T, Battié MC, Gibbons LE, Maravilla K, Manninen H, Kaprio J. Associations between back pain history and lumbar MRI findings. *Spine* 2003;28(6):582-588.

11. Boos N, Dreier D, Hilfiker E, Schade V, Kreis R, Hora J, et al. Tissue characterization of symptomatic and asymptomatic disc herniations by quantitative magnetic resonance imaging. *J Orthop Res* 1997;15(1):141-149.

12. Bogduk N, Schwarzer A. Facet joint pain. *Aust Fam Physician* 1995;24(5):924.

13. Schwarzer AC, Aprill CN, Derby R, Fortin J, Kine G, Bogduk N. The relative contributions of the disc and zygapophyseal joint in chronic low back pain. *Spine* 1994;19(7):801-806.

14. Jackson RP. The facet syndrome: Myth or reality? *Clin Orthop Relat Res* 1992(279):110-121.

15. Wang Y, Videman T, Battié MC. Lumbar vertebral endplate lesions: Prevalence, classification, and association with age. *Spine* 2012;37(17):1432-1439.

16. Wang Y, Videman T, Battié MC. ISSLS prize winner: Lumbar vertebral endplate lesions: Associations with disc degeneration and back pain history. *Spine* 2012;37(17):1490-1496.

17. Wang Y, Battié MC, Boyd SK, Videman T. The osseous endplates in lumbar vertebrae: Thickness, bone mineral density and their associations with age and disk degeneration. *Bone* 2011;48(4):804-809.

18. Hides J, Gilmore C, Stanton W, Bohlscheid E. Multifidus size and symmetry among chronic LBP and healthy asymptomatic subjects. *Man Ther* 2008;13(1):43-49.

19. Hides JA, Richardson CA, Jull GA. Multifidus muscle recovery is not automatic after resolution of acute, first-episode low back pain. *Spine* 1996;21(23):2763-2769.

20. Hides JA, Stokes MJ, Saide M, Jull GA, Cooper DH. Evidence of lumbar multifidus muscle wasting ipsilateral to symptoms in patients with acute/subacute low back pain. *Spine* 1994;19(2):165-172.

21. Danneels LA, Vanderstraeten GG, Cambier DC, Witvrouw EE, De Cuyper HJ, Danneels L. CT imaging of trunk muscles in chronic low back pain patients and healthy control subjects. *Eur Spine J* 2000;9(4):266-272.

22. Kamaz M, Kiresi D, Oguz H, Emlik D, Levendoglu F. CT measurement of trunk muscle areas in patients with chronic low back pain. *Diagn Interve Radiol.* 2007;13(3):144-148.

23. Mengiardi B, Schmid MR, Boos N, Pfirrmann CWA, Brunner F, Elfering A, et al. Fat content of lumbar paraspinal muscles in patients with chronic low back pain and in asymptomatic volunteers: Quantification with MR spectroscopy. *Radiology* 2006;240(3):786-792.

24. Kjaer P, Bendix T, Sorensen JS, Korsholm L, Leboeuf-Yde C. Are MRI-defined fat infiltrations in the multifidus muscles associated with low back pain? *BMC Med* 2007;5.

25. Ploumis A, Michailidis N, Christodoulou P, Kalaitzoglou I, Gouvas G, Beris A. Ipsilateral atrophy of paraspinal and psoas muscle in unilateral back pain patients with monosegmental degenerative disc disease. *Br J Radiol* 2011;84(1004):709-713.

26. Barker KL, Shamley DR, Jackson D. Changes in the cross-sectional area of multifidus and psoas in patients with unilateral back pain: the relationship to pain and disability. *Spine* 2004;29(22):E515-519.

27. Kulig K, Scheid AR, Beauregard R, Popovich Jr. JM, Beneck GJ, Colletti PM. Multifidus morphology in persons scheduled for single-level lumbar microdiscectomy: Qualitative and quantitative assessment with anatomical correlates. *Am J Phys Med Rehabil* 2009;88(5):355-361.

28. Beneck GJ, Kulig K. Multifidus atrophy is localized and bilateral in active persons with chronic unilateral low back pain. *Arch Phys Med Rehabil* 2012;93(2):300-306.

29. Kader DF, Wardlaw D, Smith FW. Correlation between the MRI changes in the lumbar multifidus muscles and leg pain. *Clin Radiol* 2000;55(2):145-149.

30. Kang CH, Shin MJ, Kim SM, Lee SH, Lee CS. MRI of paraspinal muscles in lumbar degenerative kyphosis patients and control patients with chronic low back pain. *Clin Radiol* 2007;62(5):479-486.

31. Kim WH, Lee S-, Lee DY. Changes in the cross-sectional area of multifdus and psoas in unilateral sciatica caused by lumbar disc herniation. *J Korean Neurosurg Soc.* 2011;50(3):201-204.

32. Wallwork TL, Stanton WR, Freke M, Hides JA. The effect of chronic low back pain on size and contraction of the lumbar multifidus muscle. *Man Ther* 2009;14(5):496-500.

33. Chan S-, Fung P-, Ng N-, Ngan T-, Chong M-, Tang C-, et al. Dynamic changes of elasticity, cross-sectional area, and fat infiltration of multifidus at different postures in men with chronic low back pain. *Spine J* 2012;12(5):381-388.

34. Fortin M, Macedo L. Multifidus and Paraspinal muscle Group Cross-Sectional Areas of Patients with Low Back Pain and Control Patients: A

Systematic Review With a Focus on Blinding. *Phys Ther* 2013;93(7):873-888.

35. Lee S-, Chan CK-, Lam T-, Lam C, Lau N-, Lau RW-, et al. Relationship between low back pain and lumbar multifidus size at different postures. *Spine* 2006;31(19):2258-2262.

36. McLoughlin RF, D'Arcy EM, Brittain MM, Fitzgerald O, Masterson JB. The significance of fat and muscle areas in the lumbar paraspinal space: A CT study. *J Comput Assisted Tomogr* 1994;18(2):275-278.

37. Kay AG. An extensive literature review of the lumbar multifidus: Biomechanics. *J Man Manip Ther* 2001;9(1):17-39.

38. Hyun JK, Lee JY, Lee SJ, Jeon JY. Asymmetric atrophy of multifidus muscle in patients with unilateral lumbosacral radiculopathy. *Spine* 2007;32(21):E598-E602.

39. Battié MC, Niemelainen R, Gibbons LE, Dhillon S. Is level- and side-specific multifidus asymmetry a marker for lumbar disc pathology? *Spine J* 2012;12(10):932-939.

40. Stokes MJ, Cooper RG, Morris G, Jayson MIV. Selective changes in multifidus dimensions in patients with chronic low back pain. *Eur Spine J* 1992;1(1):38-42.

41. Stokes M, Rankin G, Newham DJ. Ultrasound imaging of lumbar multifidus muscle: Normal reference ranges for measurements and practical guidance on the technique. *Man Ther* 2005;10(2):116-126.

42. Niemeläinen R, Briand M, Battié MC. Substantial asymmetry in paraspinal muscle cross-sectional area in healthy adults questions its value as a marker of LBP and pathology. *Spine* 2011;36(25):2152-2157.

43. Engstrom CM, Walker DG, Kippers V, Mehnert AJH. Quadratus lumborum asymmetry and L4 pars injury in fast bowlers: A prospective MR study. *Med Sci Sports Exerc* 2007;39(6):910-917.

44. Hides J, Fan T, Stanton W, Stanton P, Mcmahon K, Wilson S. Psoas and quadratus lumborum muscle asymmetry among elite Australian Football League players. *Br J Sports Med* 2010;44(8):563-567.

45. Ranson C, Burnett A, O'Sullivan P, Batt M, Kerslake R. The lumbar paraspinal muscle morphometry of fast bowlers in cricket. *Clin J Sport Med* 2008;18(1):31-37.

46. Sanchis-Moysi J, Idoate F, Dorado C, Alayó S, Calbet JAL. Large asymmetric hypertrophy of rectus abdominis muscle in professional tennis players. *PLoS ONE* 2010;5(12).

47. Sanchis-Moysi J, Idoate F, Izquierdo M, Calbet JAL, Dorado C. Iliopsoas and gluteal muscles are asymmetric in tennis players but not in soccer players. *PLoS ONE* 2011;6(7).

48. Alaranta H, Tallroth K, Soukka A, Heliovaara M. Fat content of lumbar extensor muscles and low back disability: A radiographic and clinical comparison. *J Spinal Disord* 1993;6(2):137-140.

CHAPTER 2

LITERATURE REVIEW

2.1. PARASPINAL MUSCLES

2.1.1. ANATOMY, FUNCTION AND INNERVATION

The paraspinal muscles are deep back muscles that run in parallel on each side of the spine and attach directly onto the vertebrae, procuring individual segmental mobility and spine stability, [1,2] and also assisting with the larger motions of the trunk. The main lumbar paraspinal muscles include the erector spinae, which is composed of the illiocostalis and longissimus muscle, the multifidus, the psoas and the quadratus lumborum (Figure 2-1).

Erector spinae: Longissimus and iliocostalis

The thoracic and lumbar portions of the longissimus and iliocostalis muscles are architecturally [3] and functionally different. [4] The thoracic part of the erector spinae is composed of smaller muscle bellies, which originate from the thorax and caudal tendons shape the erector spinae aponeurosis. [5] The lumbar erector spinae attach on the accessory process and transverse process of L1 to L4, [5] and a large part has been claimed to either attach to the ilium via the erector spinae aponeurosis [6] or totally independently of the aponeurosis. [5] Acting together, the longissimus and iliocostalis extend the spine to maintain an erect position and also assist during side-flexion on the same muscle side. [7] The line of action of the

lumbar portion of the iliocostalis and longissimus has a posterior and caudal direction (almost perpendicular to the spinal compression axis), which cause posterior shear forces to be generated together with an extensor moment on the superior vertebrae.[8] These posterior shear forces stabilize the spine and compensate for any upper trunk forward flexion movement such as during a lifting motion. [8]

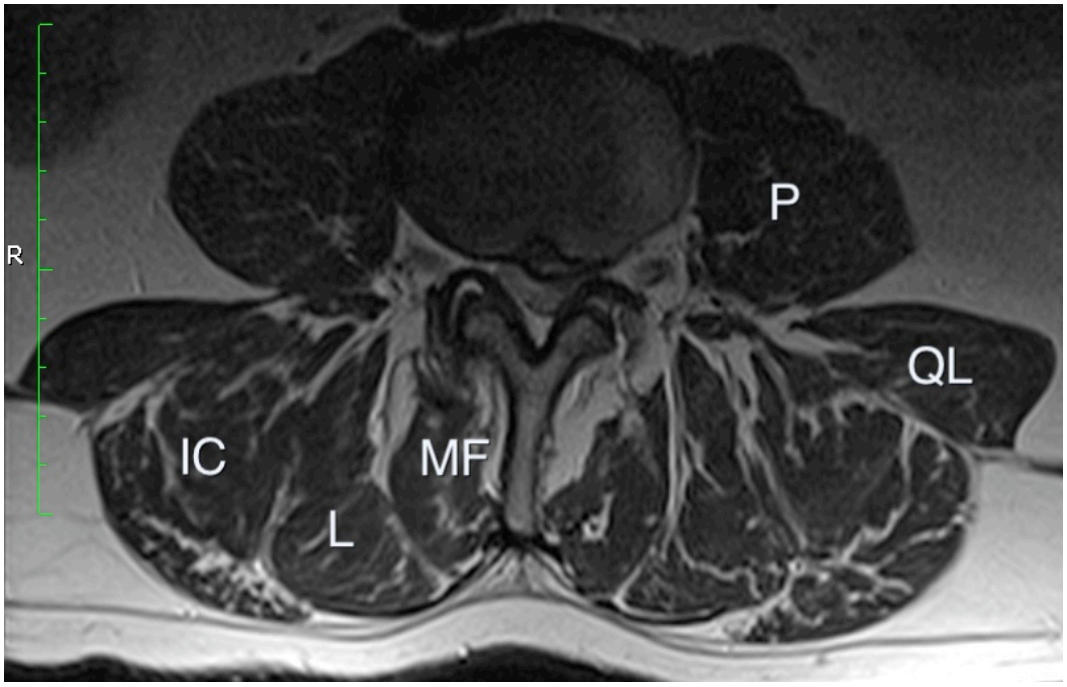


Figure 2-1: Axial T2-weighted MR image. The erector spinae is composed of the longissimus (L) and iliocostalis muscles (IC). The deep most medial layer is composed of the multifidus muscle (MF). The psoas (P) and quadratus lumborum (QL) are separated from the intrinsic muscles by the middle thoracolumbar fascia.

Multifidus

In addition to the longissimus and iliocostalis, the multifidus is also one of the primary extensors of the lumbar spine. [8] The multifidus is involved in the

arthrokinetic control of the lumbar vertebral segment [9] and also stiffening of the intervertebral discs. [10]

Because it inserts on the mammillary process and attaches to the spinous process of two to three lumbar vertebrae, the forces generated by the multifidus are applied to a local segment of the spine (Table 2-1). Thus, the multifidus has the ability to "correct" stresses by generating small amount of twisting and side-bending torque. [8] Conversely to the longissimus and ilicostalis, the multifidus line of action tends to be parallel to the compressive axis or occasionally run anteriorly and caudally. [8]

In 1986, Macintosh et al. [11] demonstrated through an anatomical study that the multifidus was innervated by a single nerve root (medial branch of the dorsal ramus). However, a number of authors have detected spontaneous activity in several levels caudally and cranially following a lumbar nerve root lesion, and suspect that the multifidus has a polysegmental innervation. [12-14] In another recent electrophysiological study, spontaneous activity in patients with L5 or S1 monoradicular nerve root compression showed pathological spontaneous activity one to three spinal levels cranial to the disc herniation. [15] Abnormal activity was also detected on the opposite side of the lesion. The latter findings revealed a discrepancy between the anatomic and electrophysiological studies, suggesting that delicate peripheral nerve branches might have been missed during postmortem investigation. [15]

Psoas

The psoas, which crosses the spine and hip, attach on T12 and every lumbar vertebrae to join the illiacus muscle and insert in the lesser trochanter of the femur. The psoas is primarily a hip flexor, however some argue that the psoas could also act as a spine stabilizer. In an experiment using an elastic metal strip model, Penning suggested that the psoas probably stabilizes the lumbar spine when positioned in an upright position by adapting the contraction of each fascicule to the degree of lordosis. [16] This hypothesis is supported by electromyographic studies showing continuous minimal activity of the psoas in a relaxed upright position. [17,18] On the other hand, McGill refuted this theory in a pilot study where he used intramuscular electrodes and showed that the psoas was only activated during hip flexion. Thus, it may be the case that the psoas acts as a spine stabilizer, providing shear stiffness, only in positions where a significant amount of hip torque is required. [8]

Quadratus lumborum

The quadratus lumborum originates from the iliac crest and inserts on the transverse processes of the each lumbar vertebrae. [19] The quadratus lumborum is an agonist of the extensor muscles and assists the erector spinae in extension. An intramuscular myoelectric activity study showed that this muscle is more active than the extensors during lateral bending. [20] The quadratus lumborum muscle activity was also increased when progressively greater axial spine compression was applied while holding a loaded bucket in each hand in a static upright

position. Stabilizing muscular activity was observed during flexion exercises and lifting tasks. [20] As a result, the quadratus lumborum is thought to be a powerful lumbar side flexor and provide frontal plane segmental stabilization during spinal movement and contralateral leg loading. [20] However, electromyographic access to this muscle is complicated and the actual position of the electrode within the muscle is difficult to determine. [8] Nevertheless, these findings suggest that the quadratus lumborum plays an important stabilizing role in a wide variety of tasks.

Table 2-1: Insertion, origins, action and innervation of major lumbar paraspinal muscles.

Muscle	***Origin***	***Insertion***	***Innervation***	***Main action(s)***
Erector spinae: Illiocostalis Longissimus	Arises by tendon from posterior part of iliac crest, posterior surface of sacrum, sacroiliac ligament, sacral and inferior lumbar spinous process, and supraspinous ligament. *	Iliocostalis: lumborum and thoracis fibers run superiorly to angles of lower ribs. Longissimus: thoracis and cervicis fibers run superiorly to ribs between tubercules and angles to transverse processes in thoracic and cervical regions. *	Posterior rami of spinal nerves. *	Acting bilaterally: extend vertebral column and head. Acting unilaterally: laterally flex vertebral column. *
Multifidus	Arises from posterior sacrum, posterior superior iliac spine of ilium, aponeurosis of erector spinae, sacroiliac ligaments, mammilary 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. *
Psoas major	T12-L5 vertebrae transverse processes and lateral surface of associated intervertebral discs. #	Lesser trochanter #	Branches of the lumbar ventral rami and the lumbar plexus ‡	Hip flexion and lateral rotation. Unilateral contraction: bends the trunk laterally to the same side. Bilateral contraction: raises the trunk from the supine position. #
Quadratus lumborum	Illiac crest and iliolumbar ligament #	12^{th} rib, L1-L4 vertebrae transverse processes #	T12, L1-L4 spinal nerves. Branches of the lumbar ventral rami and the lumbar plexus ‡	Unilateral contraction: Bends trunk to the same side. Bilateral contraction: Bearing down and expiration, stabilizes 12^{th} rib. #

*: Moore et al. 2007 (reference 7), #: Gilroy et al. 2008 (reference 21), ‡: Bogduk et al. 1983 (reference 22)

2.2. PARASPINAL MUSCLE PHYSIOLOGICAL CHANGES AND ADAPTATIONS

2.2.1. ASYMMETRY

Bilateral asymmetry of any body part (e.g. muscle, bone) or measure (e.g. girth, length) is defined as differences between the right and left sides taking into account the sign of the difference. [23] Directional asymmetry is defined as the dimensions of one side of the body being consistently greater than the opposite side, while fluctuation asymmetry is described as a random difference between the quantitative measurements of bilateral body parts. [24] The small random differences from perfectly symmetrical dimensions of a bilateral trait in fluctuating asymmetry is thought to reflect an individual's ability to adapt to genetic and environment stresses during development. [25,26] Bilateral asymmetry has been regarded as an indicator of occupational and environmental stresses, as well as a trait for inter-population and intra-individual variation. [23] When marked asymmetry is observed, it is often associated with a long history of rigorous unilateral activity, such as in sports and heavy physical labor, where the dominant and nondominant limb exhibit differences in strength. [27,28]

Trunk muscle asymmetry in athletes

Muscular asymmetry associated with sports involving repetitive arm or leg movements of the dominant limb is commonly observed. Sports that are asymmetrical in nature can lead to muscular imbalances and asymmetry, and are generally believed to be associated with a higher risk of injuries. [29-31] Therefore,

in sports favoring the usage of the dominant limb such as soccer, training of both limbs has been suggested to avoid developing side-to-side asymmetries. [32]

Studies looking at elite cricket fast bowlers have consistently reported asymmetrical hypertrophy of the quadratus lumborum on the side of the dominant bowling arm, which could be caused by the preferential and repetitive unilateral pattern of activation. [29,33,34] Australian Football League players have been shown to have a significantly larger psoas CSA on the side of the dominant kicking leg [35,36] and significantly greater quadratus lumborum CSA on the non-dominant side.[36] However, significant left-right muscular asymmetries were not associated with the number of injuries in Australian Football League players. [36] Although the physical demands of bowlers and football players are different, they both involve repeated dynamic asymmetrical motions of the trunk and limb, such as trunk side flexion and rotation, [37] which could explain the observed asymmetries.

Tennis players have been found to have significant asymmetrical hypertrophy of the illiopsoas muscle on the non-dominant side, [38] and significant rectus abdominis asymmetrical hypertrophy (35% greater volume) on the non-dominant side. [39] Whether the different patterns of hypertrophy of the illiopsoas were associated with injury was not determined. However, not every asymmetrical sport leads to paraspinal muscular asymmetry. McGregor et al. reported no significant right-left asymmetries of the multifidus, erector spinae or illiopsoas in a group oarsmen, [40] even if muscular activity during isometric trunk extension has been previously shown to be asymmetrical in rowers. [41]

Asymmetrical tasks and muscular asymmetry and physically demanding occupations

Epidemiological studies have shown that manual handling involving heavy lifting in awkward positions is a risk factor for LBP in industry workers. [42] Although no clear definition of asymmetrical movement has been adopted, it is generally accepted that asymmetrical tasks involve torso twisting and deviations from the sagittal plane. [43] Asymmetric work postures are generally considered to be more stressful, and sudden loading is expected to take place more often during non-sagittal postures. [44] To compensate for the external loading, internal forces are generated via the muscles to help stabilize the body. Since the back muscles have a short moment arm, they need to generate a great amount of force to overcome their mechanical disadvantage, which create compressive and shear spinal forces that are believed by some to be accountable for back injuries. [44] In addition, when tasks require a greater range of motion, the external moment arm is increased, augmenting external forces and spinal loading, which need to be counterbalanced by the muscles. During asymmetrical tasks, including twisted positions, the erector spinae has been found to have higher muscle activation on the contralateral side to the direction of the rotation. [45-47] Maximum voluntary contraction also decreases when the angle of the rotation (twist) increases. Marras et al. measured trunk strength in a sagittally symmetric position (0 degrees) and at 15 and 30 degrees deviation of the trunk from the sagittal plane toward the coronal plane (trunk asymmetry around L5-S1). Their results showed an 8-9% decrease in maximum trunk strength for every 15 degrees increase in trunk

asymmetry. [48] Whereas Van Dieën reported that in a 45-degree twisted position, maximum voluntary contraction of the trunk is 30% lower than in the neutral position. [47]

Paraspinal muscle asymmetry and LBP

The multifidus muscle appears to be the most sensitive of the lumbar paraspinal muscles to degenerative changes in the presence of spinal pathology and LBP. Multifidus muscle atrophy on the symptomatic side has been reported in patients with unilateral LBP, [49-55] yet findings in the scientific literature remain conflicting. The greatest multifidus asymmetry (in CSA or fat-free mass, functional CSA (FCSA)) in patients with a clinical presentation of unilateral LBP has been reported to be on the symptomatic side, at the level above, [51] the same level, [49] or the level below the pathology. [55] Conversely, some have reported greater multifidus muscle CSA on the symptomatic side, [56,57] or localized bilateral atrophy. [58] Similar contradictory findings have been reported with regards to the CSA of the psoas muscle in relation to unilateral LBP. [49,54,59]

On the other hand, oarsmen with LBP symptoms, were found to have no significant right-left asymmetry but instead, a hypertrophy of the multifidus, erector spinae and psoas muscles when compared to elite oarsmen without LBP. [40] It was suggested that the hypertrophy of the spinal muscles in rowers might be due to poor technique; rowers with LBP are believed to mainly use their back muscles instead of their legs to generate force during the stroke. [40] Similarly, elite

cricketers with LBP also have slightly greater paraspinal muscle CSA than cricketers without LBP. [29]

An experimental study using a porcine model showed rapid atrophy of the multifidus following spinal nerve or disc injury. [60] Denervation of the L3 nerve root (nerve injury) led to a reduction of the multifidus CSA over 3 vertebral segments. This pattern of atrophy correlates well with the anatomy of the multifidus muscle, given that a single nerve root innervates multiple fascicles. Conversely, after inflicting a lesion to the L3-L4 lumbar disc, CSA of the multifidus was reduced only at L4, the segment below the injury.

Spinal muscle asymmetry in individuals without LBP

Ultrasound studies investigating paraspinal muscle asymmetry in asymptomatic subjects (without LBP) reported mean multifidus side-to-side differences varying between 1.9%-5.2%, [50] 3±4% [53] and 7.2-9.2%. [61] According to the previous findings, Hides et al. suggested that multifidus asymmetry greater than 10% could be interpreted as a potential abnormality. [50] However, a recent MRI study using a sample size of 126 asymptomatic men (mean age 49.8 years), reported mean multifidus side-to-side asymmetry that varied between 10% to 13.2% according to lumbar level with 40% of the subjects having asymmetry above the 10% threshold. [62] Thus, multifidus asymmetry greater than 10% may not be an indicator of clinically relevant spinal abnormalities. It is noteworthy that the earlier studies had important limitations, such as the use of ultrasound, small sample size and relatively young subjects (which might not be comparable to the

older LBP population). [50,53,61] Also, the multifidus muscle has been reported to be one of the most difficult muscles to image using ultrasound. [61]

2.2.2. ATROPHY

Patients with chronic LBP have been reported to have smaller paraspinal muscles [50,58,63-66] than healthy asymptomatic controls. The erector spinae CSA at L5, as well as the proportion of the erector spinae CSA to the total lumbar muscle CSA (combined CSA of the paraspinal muscle group and psoas) at the same level have been suggested to be prognostic factors for the chronicity of LBP. [67] Although paraspinal muscle CSA measurement via imaging modalities may be influenced by changes in posture, it was demonstrated that the multifidus CSA remained smaller in patients with chronic LBP even when evaluated in four different postures (e.g. prone, standing, 25º stooping and 45º stooping). [63] However, the multifidus muscle was the only paraspinal muscle measured in the latter study.

Stabilization exercise programs targeting specific trunk muscles are widely used and prescribed to LBP patients to improve their spinal stability, control, stiffness and segmental motion. [68] A significant increase in paraspinal muscle CSA has been reported in patients with chronic LBP following the completion of a 10-weeks rehabilitation program including stabilization exercises and dynamic-static resistance training. [69] Hides et al. also reported a decrease in pain and an increase in CSA of the multifidus after 6-weeks of stabilization exercises in elite cricketers with LBP. [70] Conversely, a randomized control compared the effectiveness of a 12-weeks (12 sessions) conventional

physiotherapy exercises program (e.g. general active exercises) versus a conventional exercises program plus stabilization exercises for patients with recurrent LBP. [71] Although both groups had a reduction in pain and an improvement in physical functioning, there was no significant difference between the two groups at any time point (discharge, 6 months and 12 months follow-up), suggesting that stabilization exercises had no additional benefit.

2.2.3. FATTY INFILTRATION

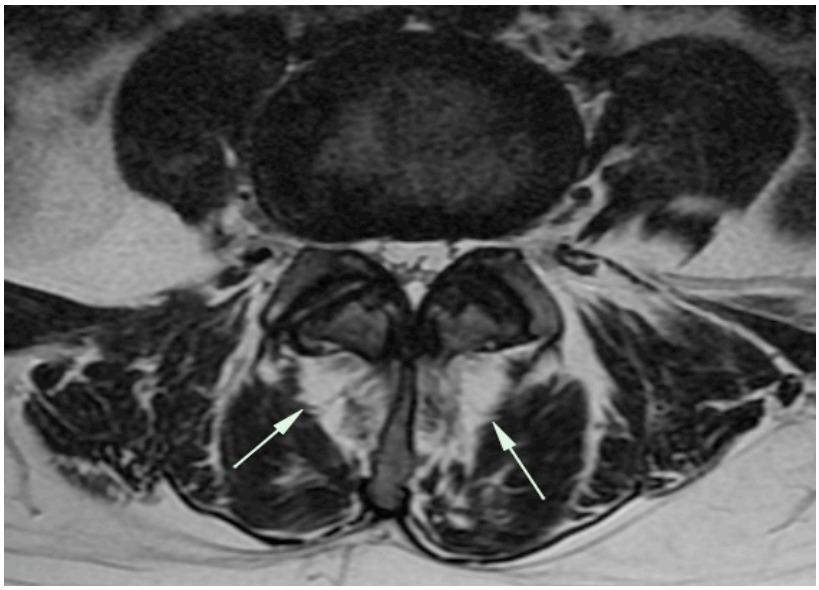
Skeletal intramuscular fatty infiltration is a deposit (accumulation) of fat that can be found intrafascicularly or intracellularly. [72] In the elderly, higher intramuscular fat content is associated with a loss of muscle strength [73] and a greater risk of mobility restriction. [74] Skeletal muscle fatty infiltration have been associated with neurological injury and denervation, [75-77] retraction of the musculotendinous unit in experimental animal models, [78,79] aging, [80,81] metabolic disorders, [82-84] genetic muscular disorders [85] and lamin A/C deficiency. [86] Lamin A/C is a protein of the inner nuclear envelope that regulates cell differentiation. [86]

Lumbar paraspinal muscle fatty infiltration and LBP

Greater fatty infiltration of paraspinal muscles has been reported with unilateral lumbar radiculopathy, [56,87] chronic LBP, [64,88-91] lumbar intervertebral disc and nerve injury, [60] lumbar spinal stenosis, [92] lumbar degenerative kyphosis, [93] degenerative lumbar scoliosis, [92] degenerative lumbar flat back [94] and sway-back posture. [95] While some have found that patients with chronic LBP have more fatty

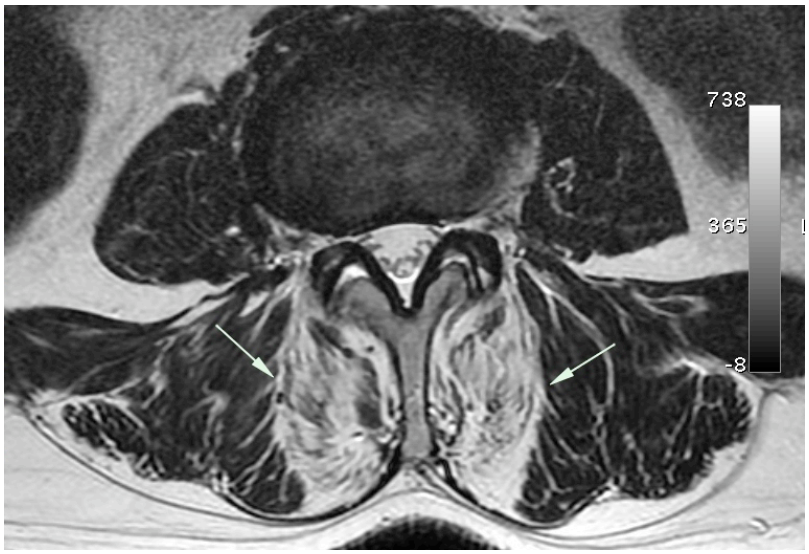
infiltration than healthy controls, [88,89] not all studies support this finding. [64] The difference in fatty infiltration seemed to be especially evident in the multifidus muscle where patients with chronic LBP have been reported to have 23.6% fat content in mean as opposed to 14.5% in control subjects. [89] It is noteworthy that this difference was not detectable using qualitative assessments. [89]

Fatty infiltration in patients with chronic LBP are generally bilateral (Figure 2-2) and at multiple spinal levels. [88,90] In general population samples with non-specific LBP, the highest amount of fatty infiltration tended to be located at the two lower lumbar levels (L4-L5 and L5-S1), [90,96] a trend that was similar in patients with chronic LBP. [91]



(a)

Figure 2-2: a) Fatty infiltration of the multifidus muscle.



(b)

Figure 2-2: b) Severe bilateral muscle fatty infiltration of the multifidus muscle.

A rapid increase in the size of adipocytes was demonstrated after experimentally inflicting a lumbar disc or nerve root injury. [60] Interestingly, after the disc lesion at L3-L4, intramuscular fat increased at L3 through L5, but only on the injured side. Whereas, following an L3 nerve root lesion, adipocytes increased from L3 to L5, but mostly at the two lower levels, and this time, bilaterally. Similarly, after a surgical procedure leading to the denervation of the semimenbranosus proprius and semimenbranosus accessorius muscles in rabbits, large patches of fatty infiltration were observed one month after the surgery. [76] Denervation-induced fatty infiltration developed faster in the fast-twitch muscle (semimenbranosus accessorius), as compared to the slow-twitch (semimenbranosus proprius) muscle.

The origins of these fatty infiltrates are not fully understood. [76] Some have demonstrated that the degree of intramuscular fatty infiltration in humans is related to the amount of subcutaneous fat. [97] While others suggested that the

increase in fat cells could be from adipoblastic or myoblastic sources. [76] In response to inflammation due to an injury, fibroblasts and preadipocytes, which are found in muscle and connective tissue, might differentiate. [76] A second hypothesis may be that denervation leads to an increase in DNA synthesis, which in turn leads to the proliferation of satellite cells, macrophages and mast cells. [98,99] Macrophages and mast cells are known to secrete inflammatory mediators such as pro-inflammatory cytokines, growth factors and prostaglandins. [76] The presence of these inflammatory derivatives stimulates fibroblast and preadipocyte muscle precursors, [100,101] which can lead to the proliferation of adipocytes. [76]

2.2.4. MUSCLE FIBER ALTERATIONS

Paraspinal muscle fiber composition of patients with LBP has been shown to differ from asymptomatic control subjects. An important difference between paraspinal muscles and other skeletal muscles is the higher proportion of type I muscle fibers, which are slow-twitch and fatigue-resistant, two favorable characteristics for postural function. [102] Histochemical examination of biopsies obtained from patients with LBP revealed a significantly lower proportion of type I fibers accompanied with a higher proportion of type II fibers in comparison to control subjects. [103] Alternatively, patients with disc herniation were reported to have a higher proportion of type I fibers on the affected side. [104,105] Moreover, the size of the type I and type II muscle fibers has been shown to be significantly smaller on the affected size when compared with the non-affected side. [104,105] The

size of type I and type II muscle fibers in patients with LBP and healthy controls, however, was reported to be similar in other studies. [103,106]

Histological investigations of patients with LBP also demonstrated the presence of pathological fiber alterations such as small angular fibers, [104,105] fiber grouping, [104,105,107] moth-eaten fibers, [103,105-107] core-target fibers, [103,105-107] interstitial fibrosis, internal nuclei, group atrophy and fiber hypertrophy. [105] Core-targetoid, moth-eaten, and small angular fibers indicate denervation, [104,106] while fiber grouping is a sign of reinnervation. [104] Thus, possible causes of fiber size change and alterations in patients with lumbar disc herniation include denervation, reinnervation and nerve root impairment.

Although fiber alterations are generally more common and severe on the diseased side in patients with LBP, neurogenic and myogenic fiber changes were also observed on the non-affected muscle side. [104,105] Therefore, using the non-affected side as "normal" control may not be ideal in patients with LBP. [104] The presence of fiber alterations on the non-affected side also might be explained by the fact that histopathological abnormalities have been observed in healthy control subjects, as well. [103,108]

2.2.5. MUSCULAR ACTIVATION AND CONTROL DYSFUNCTION

Abnormal patterns in paraspinal muscle control and activation have been observed in individuals with chronic LBP. [109-115] Atypical motor activation patterns may remain after the resolution of back symptoms, which may explain the high rate of LBP reoccurrence. [116] Studies have looked at how clinical or

experimental pain influences paraspinal muscle timing, activation patterns and load sharing between the left and right muscle sides. However, results are conflicting and increased [111,112,114] and decreased [113] lumbar muscular activity has been reported in patients with chronic LBP while performing different dynamic or static tasks. Two models have been proposed in an attempt to explain the uncharacteristic paraspinal muscle activation patterns seen in individuals with chronic LBP.

Pain-spasm-pain model

This model was first proposed by Travell et al. [117] and suggested that pain leads to muscular hyperactivity in the form of muscle spasm, which in turn causes pain. In fact, the sustained muscular activity in patients with chronic LBP would cause hyperexcitability of the motorneurons, which eventually could create pain due to the accumulation of arachidonic acid, bradykinin, potassium and lactate, [118] causing the activation of muscle nociceptors. Following this model, Van Dieën et al. predicted that during rest and submaximal contraction, paraspinal muscle activation would be higher in patients with chronic LBP as compared to asymptomatic subjects. [118]

Pain-adaptation model

This model was proposed by Lund et al. to address the relationship between muscular motor activity findings and chronic musculoskeletal pain. [119] The model advocates that when pain is present, it decreases the activation of muscles that are

acting as agonists (muscles that are shortening) and increases muscular activity of muscle acting as antagonists (muscles that are lengthening), [119] regardless of the level of exercise. [118] This variation in muscular activation pattern is believed to prevent pain provocation. [118] Conversely to the pain-spasm-pain model, which predicts an increase in muscular activity during rest and submaximal concentric contraction, this model predicts no change in resting postures and a decrease in muscular activity when patients with LBP are performing submaximal tasks. [118]

Contradictory findings

A recent literature review revealed that neither of these two models is consistently supported. [118] Most studies demonstrated equal activity between patients with LBP and healthy controls during resting postures, although strong evidence also showed an increase in muscle activation in patients with chronic LBP. [118] As suggested by Van Dieën et al, the latter finding seems to be partly explained by the type of rest postures assumed. [118] While findings support an increase in muscular activity of patients with LBP, as compared with healthy controls during full trunk flexion, [120-122] no clear trend was demonstrated when performing concentric contraction tasks. [118] The absence of the flexion-relaxation phenomenon (cessation of muscular activity at ~90% of maximum trunk flexion) has also been reported in patients with LBP, [109,113] which contradicts the pain-adaptation model.

When experimentally inducing pain in healthy controls, Arendt-Nielsen et al. found an increase in EMG activity on the ipsilateral swing phase, a phase

where lumbar muscles are normally silent. [114] This altered muscular activity pattern mirrored the one observed in their group of patients with chronic LBP, hence supporting the pain-spasm-pain model. Zedka et al. observed bilateral EMG alterations with no relaxation of the erector spinae during trunk flexion, and no significant modification of the stretch reflexes in healthy subjects, following experimental pain induction. [124] When looking at muscle timing, Hemborg and Moritz reported a longer activation period of the lumbar erector spinae in patients with chronic LBP, when performing lifting and lowering tasks. [125] Again, this finding is more in line with the pain-spasm-pain model.

Patients with chronic LBP also demonstrated poorer postural control with delayed muscular response time during a sudden quick-release test [110] and sudden loading, [123] supporting the pain-adaptation model.

As none of the pain models are consistently supported and results are differing, it was suggested that the alterations in lumbar muscle recruitment patterns observed in patients with LBP are functional adaptations to provide stabilization to the spine and limit the range of motion, which in turn reduces the probability of harmful tissue stresses. [118]

2.3. POSSIBLE MECHANISMS OF PARASPINAL MUSCLE DEGENERATIVE CHANGES

Three main mechanisms have been suggested to explain paraspinal muscle atrophy, fatty infiltration and muscle fiber alterations.

2.3.1. DENERVATION

Muscle denervation can be caused by trauma, traction injury, neuropathies, neoplasia, entrapment syndrome, spinal cord pathology, as well as blood vessel pathologies, such as vasculitis, thrombosis and compression of the draining veins. [126,127] Denervation can occur in almost any voluntary muscle and clinical symptoms are often manifested as muscular weakness or pain. [127] Skeletal muscle denervation has been shown to cause muscle atrophy, [60,77] myopathology translated as muscular fiber changes, [104] myofiber atrophy, [77] and increased fatty infiltrates. [60,76,77] Moreover, denervation can lead to an increase in muscle blood volume caused by the enlargement of intramuscular capillary beds. [128] An increase in extracellular fluids has also been demonstrated. [129] The latter events are noticeable by MRI T2 signal abnormalities. [127] Occasionally, denervation can also cause pseudophypertrophy, where denervated muscle appears to enlarge, [127] a phenomenon that is normally accompanied with a significant amount of fatty infiltration. [130] However, this response to muscular denervation eventually subsides and noticeable muscle atrophy becomes visible. [131]

MRI and EMG can both be used to diagnose muscle denervation. MRI is helpful to detect muscle atrophy, fatty infiltration and abnormal signal intensity. [127] EMG detects abnormal muscle electrical activity, such as fibrillation potentials and positive sharp waves, [132] however it is an invasive procedure. In addition, caution should be taken when using EMG to diagnose lumbar radiculopathy, since electromyographic abnormalities in paraspinal muscle have been shown to occur

in 14.5% of asymptomatic individuals, [133] and the prevalence increases with age. [134]

2.3.2. DISUSE ATROPHY

Disuse has been suggested as another mechanism that could possibly lead to paraspinal muscle wasting in patients with LBP. However, this mechanism is questioned since localized patterns of muscle atrophy are frequently reported in patients with LBP and muscle disuse atrophy due to physical inactivity would be expected to have a more generalized effect. [53] Prolonged periods of immobilization, bed rest, spaceflight and physical inactivity, which reduce muscle activity and mechanical loading, can result in muscle disuse atrophy. [135] Microgravity experiments with rats showed a decrease in muscle volume up to 37% after only 1 week, [136] whereas after 14 days of rodent hind limb suspension, adductor longus showed a 60% reduction in fiber CSA accompanied by a 58% decrease in absolute muscle tension. [137] Following 17 weeks of bed rest, the ankle extensor and flexor muscle groups exhibited a 30% and 21% decrease in CSA, respectively. [138] While the quadriceps and hamstring showed 16-18% decreases, the lower intrinsic back muscles had a 9% decrease with no change observed in the psoas muscle. Thus, prolonged bed rest seems to predominantly affect the lower limb muscles. In addition to paraspinal muscle atrophy, consequences of prolonged bed rest include increased disc volume and decreased lumbar lordosis.[139]

An increase in muscle adipocytes has also been reported as a structural alteration in disuse atrophy. After 4 weeks of unilateral limb suspension in young adults (19-28 y), muscular atrophy was accompanied by a concomitant increase in intramuscular fat of 20% in the calf muscle and 14.5% in the thigh muscle. [140] Disuse also results in various imperative structural and functional adaptations, such as a loss of protein synthesis and increase in proteolysis, [141] neuronal changes, [142] modification of metabolic pathways, [143] and fiber type conversion from slow twitch to fast twitch. [142]

2.3.3. REFLEX INHIBITION

Since paraspinal muscle atrophy, more specifically of the multifidus muscle, is often localized on the pathological side and adjacent spinal levels, the hypothesis of reflex inhibition has been proposed as a possible cause of muscle atrophy. Reflex inhibition, which is a decrease of the excitability of the alpha motor neurons, has been associated with joint effusion related to injury, [144] surgery [145,146] or artificial injection of saline solution. [147] Experimental animal studies showed that stimulation of the lumbar disc annulus fibrosus [148] or the nerves within the posterolateral annulus [149] predominantly elicited ipsilateral multifidus activity at multiple spinal levels, although activity was also detected on the contralateral side. Whereas, stimulation of the facet joint capsule produced ipsilateral multifidus activation only at the same spinal level with a minimal contralateral response. [148] On the other hand, when injecting lidocaine in the facet joint and stimulating either the disc or facet joint, a marked decrease in muscle activation

was observed, [150] with no muscular activation on the contralateral side. [148] A similar reduction in motor unit activation was observed when injecting a saline solution in the facet joint. [149] The addition of saline solution may elicit a stretching reflex from the capsule, causing the excitation of inhibitory interneurons and generating a decrease in muscular activation. [149] Studies investigating artificially induced knee effusion also reported an inhibition of the quadriceps musculature. [147,151] One could expect that the same phenomenon would be observed after any joint sprain and effusion, where muscle inhibition would eventually cause muscle atrophy.

2.4. IMAGING OF PARASPINAL MUSCLE DEGENERATIVE CHANGES

2.4.1. MRI–THE METHOD OF CHOICE FOR SOFT TISSUE IMAGING

Paraspinal muscle morphology and intramuscular fat can be evaluated using various imaging techniques, including MRI, Computed Tomography (CT) scan and ultrasound. However, MRI technology provides higher resolution images as compared to ultrasound and CT scan, and allows better detection of soft tissues, such as fat and muscle. [152,153] MRI, as opposed to CT scan, has the benefit of being obtained without exposure to ionizing radiation. [152,153] MRI also allows greater precision of image repeatability than ultrasound, as the acquisition of different image sequences allow visualization of identifiable spinal landmarks to position scan slices, [152] which can be particularly important in longitudinal studies.

Can direct comparisons be made between paraspinal muscle measurements obtain from different imaging modalities?

Only two such validation studies have been conducted thus far. A study comparing multifidus muscle CSA measurement between MRI and ultrasound suggested that both modalities could be used interchangeably. [154] However, this study used a small sample of only ten healthy young females (21-31 years old), and such measures have not been validated in older individuals with LBP conditions. Atrophied muscles have more irregular boundaries and fatty infiltration, which greatly increase the level of difficulty when tracing the borders of the muscle of interest. [153] Moreover, ultrasound does not allow the differentiation of muscle and fat tissues, thus accurate distinction of muscle tissues from fat borders is challenging. [155,156] More interestingly, when comparing across studies the raw measurements of multifidus CSA (same spinal level and similar sample populations) obtained with ultrasound and MRI, there is a striking difference between studies using the two modalities. Mean muscle measurements obtained from ultrasound were consistently smaller than those obtained with MRI. When comparing measurements obtained with MRI and CT scans, the intra- and inter-rater reliability of lumbar paraspinal muscle FCSA and fatty infiltration measurements were acceptable with both modalities, but the MRI measurements were slightly better leading the authors to recommend using MRI over CT scan.[153] Given all of the aforementioned arguments, MRI appears to be the optimal imaging modality to evaluate paraspinal muscle morphology and composition.

Reliability of MRI paraspinal muscle measurements

Previous studies have shown that MRI provides reliable measurements of muscle CSA, [49,62,152,157] as well as fatty infiltration (higher signal intensity on T2 images). [157,158] Investigators looking at intra-observer reliability reported intra-class correlation coefficients (ICC) ranging from 0.89 to 0.99 for CSA [49,62,152,157,158] and from 0.96 to 0.99 for mean muscle signal intensity. [157,158]

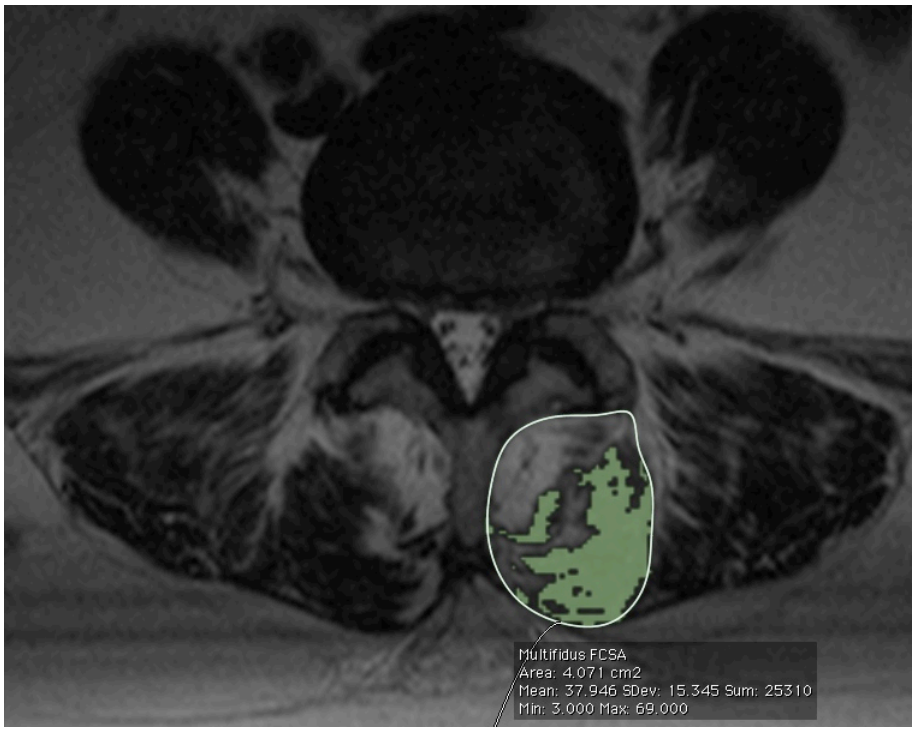
2.4.2. MEASUREMENT TECHNIQUES

Currently, several measurement techniques are used to examine paraspinal muscle morphology. Initially, investigators interested in examining paraspinal muscle morphology measured either muscle CSA via computer software or qualitatively graded the degree of muscle atrophy. Studies using a qualitative grading scheme to estimate muscle degeneration reported good inter-observer agreement of 0.85 and 0.86, [90,96] and inter-observer agreement of 0.58. [96] While using a qualitative grading method is quite simple and time-efficient, important information may be lost or not detected by the human eye. [89]

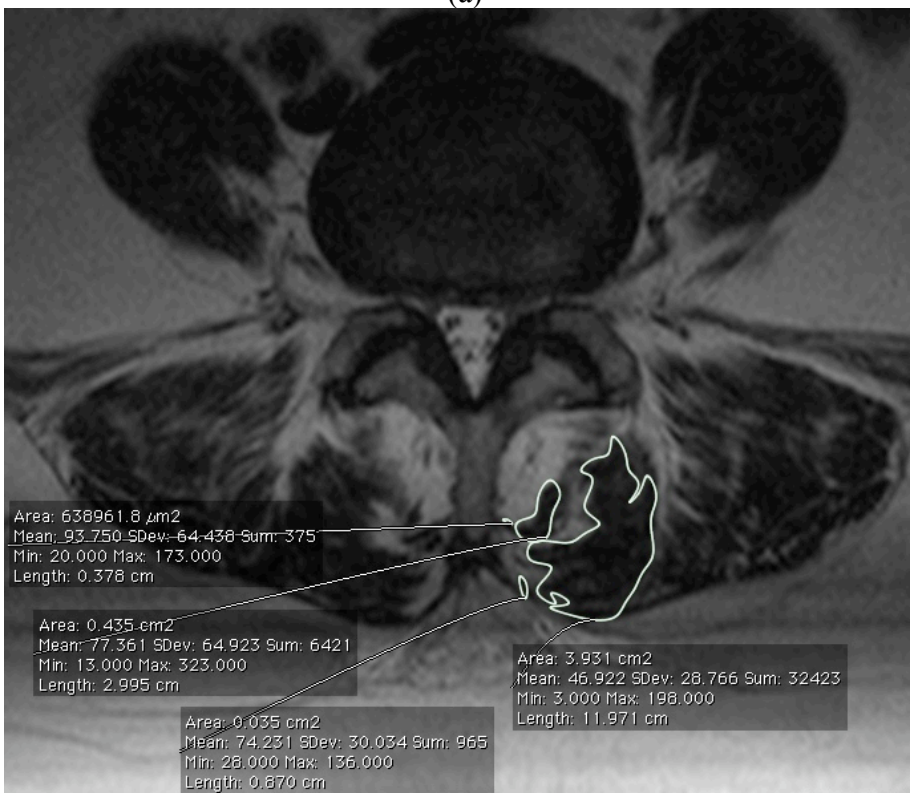
Controversies also exist regarding the best methodological approach to examine paraspinal muscle asymmetry. Some have suggested that variations in paraspinal muscles, such as muscle atrophy related to LBP problems, might occur without observing an actual reduction in total muscle CSA. [88,90] In fact, 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. [88,90] 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 mainly used by investigators in this field. [152] Consequently, new measurement techniques calculating FCSA, allowing the separation of lean muscle from fat and fibrous tissue, have been introduced.

Two general approaches are currently utilized to calculate FCSA. The threshold technique (Figure 2-3a) is a quantitative measure based on the difference in pixel intensity between muscle (low intensity) and fat tissue (high intensity) on T2-weighted axial images. After, a specific muscle CSA is traced, a signal intensity range is determined to reflect either fat or muscle fibers within the muscle. The difficulty of this technique is defining the signal intensity range to be used to differentiate the two types of tissues. The second technique consists of manually tracing one or more ROIs within a specific unilateral lumbar paraspinal muscle (Figure 2-3b), taking care to avoid any nearby fat deposits, bone or other soft tissues. [51,153,157,159] The sum of all the ROI areas within each muscle determines its FCSA. A challenge with this technique is that atrophied muscles have more irregular boundaries, increasing the difficulty of tracing the ROIs by the examiner and consequently amplifying the measurement error. [153] Yet, both techniques used to calculate FCSA have been shown to yield reliable measurements. [51,62,64,94,153,159]



(a)



(b)

Figure 2-3: a) Multifidus functional cross-sectional area (FCSA) (highlighted in green) using a thresholding technique and b) multifidus FCSA using the multiple region of interests (ROI) technique (FCSA=sum of all ROIs).

2.4.3. INTER-SOFTWARE AGREEMENT AND RELIABILITY

The literature on the error associated with different imaging analysis software while using the same or different measurement techniques to evaluate paraspinal muscle morphology is very scarce. In fact, we are not aware of any study that has evaluated this methodological issue. Part of this doctoral work was devoted to this question. We have compared the inter-software reliability and agreement of different paraspinal muscle measurements obtained with two commonly used open source analysis software, OsiriX and ImageJ (Chapter 3).

2.4.4. INTER-SCANNER RELIABILITY

Images obtained from different MRI scanners could be another source of systematic error. The inter-scanner reliability of paraspinal muscle measurement has not been investigated, however studies using similar techniques to measure brain volumes suggested that the error associated with the use of different scanners is negligible. A study evaluating inter-scanner reliability for brain volume measurements reported good agreement between scanners with a coefficient of variation of 2.4%. [160] Similar studies also reported good inter-scanner [161] and intra-scanner [161] agreement for volume determination or mapping of different brain structures, with minimal differences across field strength [162,163] or vendors. [160] A study investigating scanner effects for the segmentation of the grey matter in a group of 136 patients with Alzheimer's disease from MR images collected over 10 years, on 6 different scanners with multiple software upgrades,

also suggested that measurement variations attributable to individual scanner were negligible. [164]

2.5. PARASPINAL MUSCLE DEGENERATIVE CHANGES – ASSOCIATION WITH LBP AND PATHOLOGY

2.5.1. LUMBAR DISC HERNIATION AND UNILATERAL LBP

Several studies have used samples of patients with lumbar disc herniation to investigate the effect of this pathology on paraspinal muscle asymmetry. One advantage of unilateral and posterolateral disc protrusion is the ability to identify the level of pathology and the symptomatic side. Hence, allowing for the comparison of muscle size between the affected and non-affected side relative to the level of the known pathology of disc herniation.

Accordingly, some have reported that the maximum relative muscle atrophy was on the pathological side and at the level below for the multifidus, [55] and at the same level for psoas muscle. [59] Whereas, in a group of patients with unilateral LBP and monosegmental disc degeneration (including signal intensity and height loss, disc bulging or protrusion), psoas, quadratus lumborum, and erector spinae all showed maximum atrophy on the symptomatic side and at the level below the pathology, except for the multifidus muscle which showed the most atrophy at the level above. [51] Conversely, greater multifidus CSA has also been reported ipsilateral to the symptomatic side at the level of the disc herniation. [56] Similar findings were also found in patients with radicular unilateral

LBP. [57] Possible causes for the larger multifidus CSA on the symptomatic side include an increase in fatty infiltration [56,127,165] or an adaptative hypertrophy of type I muscle fibers due to increased muscular activity required to maintain spinal stability. [57] Finally, Hyun et al. [52] reported no significant multifidus asymmetry in a group of patients with localized lumbar disc herniation, with or without lumbosacral radiculopathy (according to electrodiagnostic findings). However, subjects with radicular pain were more likely to have a smaller multifidus muscle on the affected side as opposed to the subjects without radiculopathy. A decreased ability to regenerate multifidus fibers and myopathological alterations of the multifidus muscle at the level of nerve compression in patients with symptomatic lumbar disc herniation has been suggested from histological studies. [166]

In subjects with a clinical presentation of unilateral LBP, where the problematic spinal level was determined through manual [50,53] or MRI examination, [49] multifidus atrophy has been found to be bilateral, [58] side-[50] and level-specific [53] or side-specific at multiple levels (level above, below and same level). [49] The conflicting findings may be partly explained by the complexity of the anatomy and innervation of the multifidus muscle. Although the multifidus is believed to have a unisegmental innervation, a reduction in the increase in multifidus thickness during contraction was observed bilaterally, and at multiple spinal levels following unilateral pain induction in a group of 15 healthy subjects. [167]

While studies from patients with disc pathology and unilateral LBP suggest that the multifidus may be selectively responsive, or somewhat indicative

of localized disc or nerve root pathology, literature findings remain inconsistent. Thus, whether the multifidus muscle could be potentially used, as a marker of spinal pathology in clinical or research settings is still unclear. [56]

2.5.2. MECHANICAL LBP

The relationship between paraspinal muscle variations and LBP has also been studied in patients with "mechanical" or non-specific LBP, where the underlying cause of pain is unknown. In a sample of 90 patients with mechanical LBP, with or without leg pain, multifidus muscle degeneration (fatty infiltration) was noted in 80%. [90] Fatty infiltration was mostly present bilaterally, at L4-L5 and L5-S1, and a significant correlation was found between the degree of multifidus atrophy and leg pain (radicular and non-radicular pain) ($p<0.01$). Interestingly, a great proportion of patients with either root pain or leg pain had no other MRI abnormalities beside multifidus atrophy.

Differences in paraspinal muscle composition have also been observed between adults and adolescents with or without LBP. Using a sample of 412 adults and 442 adolescents, Kjaer et al. reported that 71% of adults had "slight" multifidus muscle fatty infiltration and 10% had "severe", while only 14% of adolescents were found to have "slight" multifidus muscle fatty infiltration and none had "severe". [96] In adults, "severe" fatty infiltration was significantly associated with ever having had LBP, but the amount of fatty infiltration in adolescents did not correlate with the presence of LBP symptoms. For the most part, multifidus muscle infiltration was present bilaterally, with no obvious

difference between sides, and at the two lower lumbar spinal levels. Similar results of no correlation between LBP symptoms severity and multifidus side-to-side differences in fat or CSA in a group of young adults with or without non-specific LBP were reported by Paalanne et al. [168]

2.5.3. SPINAL STENOSIS AND FACET JOINT OSTEOARTHRITIS

The literature on the association between paraspinal muscle degenerative changes with spinal stenosis and facet joint osteoarthritis is very scarce. Low muscle density (e.g. an expression of muscle degeneration) of the erector spinae and multifidus has been shown to be significantly associated with the presence of facet joint osteoarthritis after controlling for age. [169,170] Yet, no significant correlation for any paraspinal muscle at any spinal level was observed between muscle density and spinal stenosis evaluated by sagittal measure of spinal canal in a general population sample. [169] However, paraspinal muscle CSA has been reported to be smaller in patients with symptomatic lumbar spinal stenosis than in patients with non-specific LBP, without radicular symptoms. [171] While no significant side-to-side differences in multifidus and longissimus CSA and % of fatty infiltration were observed in patients with lumbar spinal stenosis and bilateral symptoms, [92] smaller multifidus CSA and greater % of fatty infiltration on the symptomatic side were reported in patients with spinal stenosis and unilateral symptoms. [92]

2.6. PARASPINAL MUSCLE DEGENERATIVE CHANGES – ASSOCIATION WITH LBP HISTORY

2.6.1. ASSOCIATION WITH PAIN DURATION

Studies have examined if pain duration is associated with the degree of paraspinal muscle atrophy and fatty infiltration, with mixed findings. Mengiardi and colleagues investigated a group of 25 patients with chronic LBP and found no significant correlation between pain duration and percentage of fat content of the multifidus or longissimus muscle (r= -0.37, p=0.061 and r=0.09, p=0.67, respectively). [89] While Barker et al. reported a positive correlation between symptom duration and percentage decrease in multifidus and psoas (rho: 0.872, p<0.01 and rho: 0.886, p=<0.01, respectively) of the affected and symptomatic level in 48 patients with a clinical presentation of unilateral LBP for a minimum of 12 weeks. [49] Evidence from another study suggests that only patients with disc herniation at L4-L5 or L5-S1 with concordant continuous sciatica symptoms (as opposed to intermittent symptoms) showed weak correlations between mean symptom duration (mean=29.3 months) and percentage atrophy of the psoas muscle at L4-L5 (rho=0.8, p=0.05) and at L5-S1 (rho=0.8, p=0.03). [59] Kim et al. compared a group of patients with acute sciatica (≤ 1 month) caused by a disc herniation at L4-L5 with a comparable group that had chronic symptoms (≥ 3months). [54] Significant multifidus CSA asymmetry (atrophy) (p<0.001) was only present in subject with symptoms duration of 3 months or more.

Yet, others have not found a significant correlation between symptom duration and paraspinal muscle CSA, challenging previous findings. No significant correlation was reported between pain duration and multifidus, psoas, erector spinae or quadratus lumborum CSA or relative muscle atrophy (muscle fat-free mass) in patients with chronic LBP [172] or unilateral LBP for at least 3 months. [51]

2.6.2. ASSOCIATION WITH PAIN SEVERITY

Some experiments also examined the possible correlation of pain intensity with paraspinal muscle morphology. Barker et al. reported that greater visual pain ratings were associated with more psoas muscle atrophy ($rho=0.608$, $p<0.01$) in patients with a history of unilateral LBP for at least 12 weeks. [49] Conversely, Mannion et al. found that visual analogue scale (VAS) scores had no significant association with psoas, erector spinae or quadratus lumborum CSA in patients with continuous or recurrent LBP (with or without referred pain) for more than 3 months. [172] The latter finding was also supported by Ploumis et al. in patients with unilateral LBP (≥3 months). [51] Furthermore, Lee et al. reported no association between paraspinal muscle isokinetic strength and pain intensity (or duration). [173]

The correlation between pain intensity and the degree of paraspinal muscle fatty infiltration was also considered. Mengiardi et al. showed no correlation of the percentage of fat content of the multifidus and longissimus muscle with VAS scores ($r=0,17$, $p=0.40$, $r= -0.20$, $p=0.33$). [89] While Kader et al. reported a non-

statistically significant trend toward greater multifidus fat content with higher ratings of pain intensity. [90]

A recent study looking at young adults (19-21 years old) with LBP evaluated whether pain severity, classified following cluster analysis as "always painful", "moderately painful", "recent onset of pain", "minor pain" or "no pain" predict the size and the degree of paraspinal muscle fatty infiltration. [168] The multifidus and erector spinae CSA or degree of fatty infiltration did not significantly vary across the different pain categories. However, these findings might not be representative of the older LBP population.

2.6.3. ASSOCIATION WITH DISABILITY

To measure the association between LBP-related disability and paraspinal muscle asymmetry and composition changes, most researchers used either the Owestry disability score [49,51,91] or the Roland and Morris disability questionnaire. [89,172] Three studies evaluated the correlation between disability scores and paraspinal muscle CSA or relative muscle asymmetry (FCSA) of the multifidus, psoas, erector spinae and quadratus lumborum, but all failed to find a significant correlation. [49,51,172]

Mengiardi et al. reported no significant correlation between disability scores and the degree of fatty infiltration of the multifidus or longissimus muscles in patients with chronic LBP. [89] While another study showed that fat content of the paraspinal muscle group at L5-S1 was significantly correlated with disability score in males (n=15, r=0.55, p=0.033) and the entire study group (n=38, r=0.33,

p=0.014). [91] Yet, this correlation was not seen in female participants (n=23, r=0.12, p=0.59) or at L3-L4 and L4-L5 spinal levels.

2.7. CONCLUSION

Considerable attention has been given to paraspinal muscle asymmetry and fatty infiltration in several studies focusing on the aetiology and prognosis of LBP. Despite the development of imaging procedures to quantify the size, degree of asymmetry and fatty infiltration of the paraspinal muscles, findings in the scientific literature regarding the association between LBP and paraspinal muscle morphology remain controversial. Whether LBP duration, severity and associated functional disability affect the degree of paraspinal muscle degenerative changes also remains unclear. Possible reasons underlying the discrepant findings include: 1) variations among the age and symptom duration of the studied populations, 2) small sample size, the lack of statistical power may be a cause of the conflicting results and weak associations, 3) variations among imaging modalities (MRI, CT scan and ultrasound), 4) differences in imaging protocols and measurement techniques (CSA versus FCSA). CSA is not the ideal measure to capture all the variations in muscle asymmetry and composition.

The cross-sectional nature of most studies in field is also a major limitation and longitudinal studies including general samples of individuals with and without LBP are needed to clarify whether paraspinal muscle morphological and composition variations are risk factors for the occurrence and progression of LBP. Furthermore, we are not aware of any study that specifically explored

potential determinants of paraspinal muscle asymmetry, other than low back pain problems and nerve root pathology. In order to judge the significance of paraspinal muscle asymmetry and fatty infiltration in patients with LBP problems, more information is needed about the extent of paraspinal muscle CSA and composition asymmetry present in the general population, the natural development of asymmetry over time with aging, and factors influencing asymmetry. Thus, this research project aims to: 1) identify potential determinants of paraspinal muscle asymmetry and fatty infiltration, 2) examine changes over time (15 years) in paraspinal muscle size and composition asymmetries in a general adult population sample, and 3) determine whether these variations are related to LBP and spinal pathology. The research results will help clinicians and researchers improve their interpretation of the significance of paraspinal muscle asymmetries and associated degenerative changes in patients with LBP and related spinal pathologies.

2.8. REFERENCES

1. Wilke H-, Wolf S, Claes LE, Arand M, Wiesend A, Bendix T. Stability increase of the lumbar spine with different muscle groups: A biomechanical in vitro study. *Spine* 1995;20(2):192-198.

2. Solomonow M, Zhou B-, Harris M, Lu Y, Baratta RV. The ligamento-muscular stabilizing system of the spine. *Spine* 1998;23(23):2552-2562.

3. Bogduk N. A reappraisal of the anatomy of the human lumbar erector spinae. *J Anat* 1980;131(3):525-540.

4. McGill SM, Norman RW. Effects of an anatomically detailed erector spinae model on L4/L5 disc compression and shear. *J Biomech* 1987;20(6):591-600.

5. Macintosh JE, Bogduk N. The morphology of the lumbar erector spinae. *Spine* 1987;12(7):658-668.

6. Daggfeldt K, Huang Q-, Thorstensson A. The Visible human anatomy of the lumbar erector spinae. *Spine* 2000;25(21):2719-2725.

7. Moore KL, Dalley AF, Agur AMR. Clinically oriented anatomy. 5th ed. Philadelphia: Lippincott Williams & Wilkins; 2006.

8. McGill S. Low back disorders : evidence-based prevention and rehabilitation. Champaign, IL: Human Kinetics; 2002.

9. Kay AG. An extensive literature review of the lumbar multifidus: Biomechanics. *J Man Manip Ther* 2001;9(1):17-39.

10. Wilke H-, Wolf S, Claes LE, Arand M, Wiesend A. Influence of varying muscle forces on lumbar intradiscal pressure: An in vitro study. *J Biomech* 1996;29(4):549-555.

11. Macintosh JE, Valencia F, Bogduk N, Munro RR. The morphology of the human lumbar multifidus. *Clin Biomech* 1986;1(4):196-204.

12. Gough JG, Koepke GH. Electromyographic determination of motor root levels in erector spinae muscles. *Arch Phys Med Rehabil* 1966;47(1):9-11.

13. Lalive PH, Truffert A, Magistris MR. Lombosacral radiculopathy (L3-S1) and specificity of multifidus EMG. *Neurophysiol Clin* 2004;34(1):41-47.

14. Wu PBJ, Kingery WS, Frazier ML, Date ES. An electrophysiological demonstration of polysegmental innervation in the lumbar medial paraspinal muscles. *Muscle and Nerve* 1997;20(1):113-115.

15. Kottlors M, Glocker FX. Polysegmental innervation of the medial paraspinal lumbar muscles. *Eur Spine J* 2008;17(2):300-306.

16. Penning L. Psoas muscle and lumbar spine stability: A concept uniting existing controversies. Critical review and hypothesis. *Eur Spine J* 2000;9(6):577-585.

17. Andersson GBJ, Ortengren R, Herberts P. Quantitative electromyographic studies of back muscle activity related to posture and loading. *Orthop Clin North Am* 1977;8(1):85-96.

18. Nachemson A. Electromyographic studies on the vertebral portion of the psoas muscle; with special reference to its stabilizing function of the lumbar spine. *Acta Orthop Scand* 1966;37(2):177-190.

19. Bergmark A. Stability of the lumbar spine. A study in mechanical engineering. *Acta Orthop Scand*, Supplement1989;60(230):5-54.

20. McGill S, Juker D, Kropf P. Quantitative intramuscular myoelectric activity of quadratus lumborum during a wide variety of tasks. *Clin Biomech* 1996;11(3):170-172.

21. Gilroy AM, MacPherson BR, Ross LM. Atlas of Anatomy. : Thieme Medical Publishers, Inc; 2008.

22. Bogduk N. The innervation of the lumbar spine. *Spine* 1983;8(3):286-293.

23. Krishan K. Marked limb bilateral asymmetry in an agricultural endogamous population of North India. *Am J Hum Biol* 2011;23(5):674-685.

24. Valen LV. A Study of Fluctuating Asymmetry. Evolution 1962;16(2):pp. 125-142.

25. Livshits G, Otremski I, Kobyliansky E. Biology of aging in an Israeli population. 2. Polymorphic blood markers and fluctuating asymmetry. *Anthropol Anz* 1994;52(2):97-117.

26. Otremski I, Katz M, Livshits G, Cohen Z. Biology of aging in an Israeli population. 1. Review of literature and morphological variation analysis. *Anthropol Anz* 1993;51(3):233-249.

27. Kannus P, Sievanen H, Vuori I. Physical loading, exercise, and bone. *Bone* 1996;18(1 SUPPL.):1S-3S.

28. Kannus P, Haapasalo H, Sankelo M, Sievänen H, Pasanen M, Heinonen A, et al. Effect of starting age of physical activity on bone mass in the dominant arm of tennis and squash players. *Ann Intern Med* 1995;123(1):27-31.

29. Hides J, Stanton W, Freke M, Wilson S, McMahon S, Richardson C. MRI study of the size, symmetry and function of the trunk muscles among elite cricketers with and without low back pain. *Br J Sports Med* 2008;42(10):509-513.

30. Elliott BC, Davis JW, Khangure MS, Hardcastle P, Foster D. Disc degeneration and the young fast bowler in cricket. *Clin Biomech* 1993;8(5):227-234.

31. Foster D, John D, Elliott B, Ackland T, Fitch K. Back injuries to fast bowlers in cricket: A prospective study. *Br J Sports Med* 1989;23(3):150-154.

32. McLean BD, Tumilty McA. D. Left-right asymmetry in two types of soccer kick. *Br J Sports Med* 1993;27(4):260-262.

33. Engstrom CM, Walker DG, Kippers V, Mehnert AJH. Quadratus lumborum asymmetry and L4 pars injury in fast bowlers: A prospective MR study. *Med Sci Sports Exerc* 2007;39(6):910-917.

34. Ranson C, Burnett A, O'Sullivan P, Batt M, Kerslake R. The lumbar paraspinal muscle morphometry of fast bowlers in cricket. *Clin J Sport Med* 2008;18(1):31-37.

35. Stewart S, Stanton W, Wilson S, Hides J. Consistency in size and asymmetry of the psoas major muscle among elite footballers. *Br J Sports Med* 2010;44(16):1173-1177.

36. Hides J, Fan T, Stanton W, Stanton P, Mcmahon K, Wilson S. Psoas and quadratus lumborum muscle asymmetry among elite Australian Football League players. *Br J Sports Med* 2010;44(8):563-567.

37. Burnett AF, Barrett CJ, Marshall RN, Elliott BC, Day RE. Three-dimensional measurement of lumbar spine kinematics for fast bowlers in cricket. *Clin Biomech* 1998;13(8):574-583.

38. Sanchis-Moysi J, Idoate F, Izquierdo M, Calbet JAL, Dorado C. Iliopsoas and gluteal muscles are asymmetric in tennis players but not in soccer players. *PLoS ONE* 2011;6(7).

39. Sanchis-Moysi J, Idoate F, Dorado C, Alayó S, Calbet JAL. Large asymmetric hypertrophy of rectus abdominis muscle in professional tennis players. *PLoS ONE* 2010;5(12).

40. McGregor AH, Anderton L, Gedroyc WMW. The trunk muscles of elite oarsmen. *Br J Sports Med* 2002;36(3):214-217.

41. Parkin S, Nowicky AV, Rutherford OM, McGregor AH. Do oarsmen have asymmetries in the strength of their back and leg muscles? *J Sports Sci* 2001;19(7):521-526.

42. Murtezani A, Ibraimi Z, Sllamniku S, Osmani T, Sherifi S. Prevalence and risk factors for low back pain in industrial workers. *Folia Med* 2011;53(3):68-74.

43. Gagnon M, Larrivé A, Desjardins P. Strategies of load tilts and shoulders positioning in asymmetrical lifting. A concomitant evaluation of the reference systems of axes. *Clin Biomech* 2000;15(7):478-488.

44. Lavender SA, Mirka GA, Schoenmarklin RW, Sommerich CM, Sudhakar LR, Marras WS. The effects of preview and task symmetry on trunk muscle response to sudden loading. *Hum Factors* 1989;31(1):101-115.

45. Lavender SA, Tsuang Y-, Andersson GBJ. Trunk muscle activation and cocontraction while resisting applied moments in a twisted posture. Ergonomics 1993;36(10):1145-1157.

46. Marras WS, Mirka GA. A comprehensive evaluation of trunk response to asymmetric trunk motion. *Spine* 1992;17(3):318-326.

47. Van Dieën JH. Asymmetry of erector spinae muscle activity in twisted postures and consistency of muscle activation patterns across subjects. *Spine* 1996;21(22):2651-2661.

48. Marras WS, Mirka GA. Trunk strength during asymmetric trunk motion. *Hum Factors* 1989;31(6):667-677.

49. Barker KL, Shamley DR, Jackson D. Changes in the cross-sectional area of multifidus and psoas in patients with unilateral back pain: the relationship to pain and disability. *Spine* 2004;29(22):E515-519.

50. Hides J, Gilmore C, Stanton W, Bohlscheid E. Multifidus size and symmetry among chronic LBP and healthy asymptomatic subjects. *Man Ther* 2008;13(1):43-49.

51. Ploumis A, Michailidis N, Christodoulou P, Kalaitzoglou I, Gouvas G, Beris A. Ipsilateral atrophy of paraspinal and psoas muscle in unilateral back pain patients with monosegmental degenerative disc disease. *Br J Radiol* 2011;84(1004):709-713.

52. Hyun JK, Lee JY, Lee SJ, Jeon JY. Asymmetric atrophy of multifidus muscle in patients with unilateral lumbosacral radiculopathy. *Spine* 2007;32(21):E598-E602.

53. Hides JA, Stokes MJ, Saide M, Jull GA, Cooper DH. Evidence of lumbar multifidus muscle wasting ipsilateral to symptoms in patients with acute/subacute low back pain. *Spine* 1994;19(2):165-172.

54. Kim WH, Lee S-, Lee DY. Changes in the cross-sectional area of multifdus and psoas in unilateral sciatica caused by lumbar disc herniation. *J Korean Neurosurg Soc* 2011;50(3):201-204.

55. Kulig K, Scheid AR, Beauregard R, Popovich Jr. JM, Beneck GJ, Colletti PM. Multifidus morphology in persons scheduled for single-level lumbar microdiscectomy: Qualitative and quantitative assessment with anatomical correlates. *Am J Phys Med Rehabil* 2009;88(5):355-361.

56. Battié MC, Niemelainen R, Gibbons LE, Dhillon S. Is level- and side-specific multifidus asymmetry a marker for lumbar disc pathology? *Spine J* 2012;12(10):932-939.

57. Stokes MJ, Cooper RG, Morris G, Jayson MIV. Selective changes in multifidus dimensions in patients with chronic low back pain. *Eur Spine J* 1992;1(1):38-42.

58. Beneck GJ, Kulig K. Multifidus atrophy is localized and bilateral in active persons with chronic unilateral low back pain. *Arch Phys Med Rehabil* 2012;93(2):300-306.

59. Dangaria TR, Naesh O. Changes in cross-sectional area of psoas major muscle in unilateral sciatica caused by disc herniation. *Spine* 1998;23(8):928-931.

60. Hodges P, Holm AK, Hansson T, Holm S. Rapid atrophy of the lumbar multifidus follows experimental disc or nerve root injury. *Spine* 2006;31(25):2926-2933.

61. Stokes M, Rankin G, Newham DJ. Ultrasound imaging of lumbar multifidus muscle: Normal reference ranges for measurements and practical guidance on the technique. *Man Ther* 2005;10(2):116-126.

62. Niemeläinen R, Briand M, Battié MC. Substantial asymmetry in paraspinal muscle cross-sectional area in healthy adults questions its value as a marker of LBP and pathology. *Spine* 2011;36(25):2152-2157.

63. Chan S-, Fung P-, Ng N-, Ngan T-, Chong M-, Tang C-, et al. Dynamic changes of elasticity, cross-sectional area, and fat infiltration of multifidus at different postures in men with chronic low back pain. *Spine J* 2012;12(5):381-388.

64. Danneels LA, Vanderstraeten GG, Cambier DC, Witvrouw EE, De Cuyper HJ. CT imaging of trunk muscles in chronic low back pain patients and healthy control subjects. *Eur Spine J* 2000;9(4):266-272.

65. Cooper RG, St Clair Forbes W, Jayson MIV. Radiographic demonstration of paraspinal muscle wasting in patients with chronic low back pain. *Br J Rheumatol* 1992;31(6):389-394.

66. Kamaz M, Kiresi D, Oguz H, Emlik D, Levendoglu F. CT measurement of trunk muscle areas in patients with chronic low back pain. *Diagn Interv Radiol* 2007;13(3):144-148.

67. Lee HI, Song J, Lee HS, Kang JY, Kim M, Ryu JS. Association between Cross-Sectional Areas of Lubar Muscles on Magnetic Resonance Imaging and Chronicity of Low Back Pain. *Ann Rehabil Med* 2011;35:852-859.

68. MacDonald DA, Lorimer Moseley G, Hodges PW. The lumbar multifidus: Does the evidence support clinical beliefs? *Man Ther* 2006;11(4):254-263.

69. Danneels LA, Vanderstraeten GG, Cambier DC, Witvrouw EE, Bourgois J, Dankaerts W, et al. Effects of three different training modalities on the cross sectional area of the lumbar multifidus muscle in patients with chronic low back pain. *Br J Sports Med* 2001;35(3):186-191.

70. Hides J, Stanton W, McMahon S, Sims K, Richardson C. Effect of stabilization training on multifidus muscle cross-sectional area among young elite cricketers with low back pain. *J Orthop Sports Phys Ther* 2008;38(3):101-108.

71. Cairns MC, Foster NE, Wright C. Randomized controlled trial of specific spinal stabilization exercises and conventional physiotherapy for recurrent low back pain. *Spine* 2006;31(19):E670-E681.

72. Trudel G, Ryan SE, Rakhra K, Uhthoff HK. Extra- and intramuscular fat accumulation early after rabbit supraspinatus tendon division: Depiction with CT. *Radiology* 2010;255(2):434-441.

73. Goodpaster BH, Carlson CL, Visser M, Kelley DE, Scherzinger A, Harris TB, et al. Attenuation of skeletal muscle and strength in the elderly: The health ABC study. *J Appl Physiol* 2001;90(6):2157-2165.

74. Visser M, Goodpaster BH, Kritchevsky SB, Newman AB, Nevitt M, Rubin SM, et al. Muscle mass, muscle strength, and muscle fat infiltration as predictors of incident mobility limitations in well-functioning older persons. *J Gerontol Ser A Biol Sci Med Sci* 2005;60(3):324-333.

75. Andary MT, Hallgren RC, Greenman PE, Rechtien JJ. Neurogenic atrophy of suboccipital muscles after a cervical injury. *Am J Phys Med Rehabil* 1998;77(6):545-549.

76. Dulor J-, Cambon B, Vigneron P, Reyne Y, Nouguès J, Casteilla L, et al. Expression of specific white adipose tissue genes in denervation-induced skeletal muscle fatty degeneration. *FEBS Lett* 1998;439(1-2):89-92.

77. Rowshan K, Hadley S, Pham K, Caiozzo V, Lee TQ, Gupta R. Development of fatty atrophy after neurologic and rotator cuff injuries in an animal model of rotator cuff pathology. *J Bone Jt Surg Ser A* 2010;92(13):2270-2278.

78. Gerber C, Meyer DC, Schneeberger AG, Hoppeler H, Von Rechenberg B. Effect of tendon release and delayed repair on the structure of the muscles of the rotator cuff: An experimental study in sheep. *J Bone Jt Surg Ser A* 2004;86(9):1973-1982.

79. Meyer DC, Hoppeler H, von Rechenberg B, Gerber C. A pathomechanical concept explains muscle loss and fatty muscular changes following surgical tendon release. *J Orthop Res* 2004;22(5):1004-1007.

80. Marcus RL, Addison O, Kidde JP, Dibble LE, Lastayo PC. Skeletal muscle fat infiltration: Impact of age, inactivity, and exercise. *J Nutr Health Aging* 2010;14(5):362-366.

81. Goodpaster BH, Chomentowski P, Ward BK, Rossi A, Glynn NW, Delmonico MJ, et al. Effects of physical activity on strength and skeletal muscle fat infiltration in older adults: A randomized controlled trial. *J Appl Physiol* 2008;105(5):1498-1503.

82. Ryan AS, Buscemi A, Forrester L, Hafer-Macko CE, Ivey FM. Atrophy and intramuscular fat in specific muscles of the thigh: Associated

weakness and hyperinsulinemia in stroke survivors. *Neurorehabil Neural Repair* 2011;25(9):865-872.

83. Ryan AS, Nicklas BJ. Age-related changes in fat deposition in mid-thigh muscle in women: Relationships with metabolic cardiovascular disease risk factors. *Int J Obes* 1999;23(2):126-132.

84. Krssak M, Falk Petersen K, Dresner A, DiPietro L, Vogel SM, Rothman DL, et al. Intramyocellular lipid concentrations are correlated with insulin sensitivity in humans: A 1H NMR spectroscopy study. *Diabetologia* 1999;42(1):113-116.

85. Marden FA, Connolly AM, Siegel MJ, Rubin DA. Compositional analysis of muscle in boys with Duchenne muscular dystrophy using MR imaging. *Skelet Radiol* 2005;34(3):140-148.

86. Tong J, Li W, Vidal C, Yeo LS, Fatkin D, Duque G. Lamin A/C deficiency is associated with fat infiltration of muscle and bone. *Mech Ageing Dev* 2011 0;132(11–12):552-559.

87. Campbell WW, Vasconcelos O, Laine FJ. Focal atrophy of the multifidus muscle in lumbosacral radiculopathy. *Muscle Nerve* 1998;21(10):1350-1353.

88. Parkkola R, Rytokoski U, Kormano M. Magnetic resonance imaging of the discs and trunk muscles in patients with chronic low back pain and healthy control subjects. *Spine* 1993;18(7):830-836.

89. Mengiardi B, Schmid MR, Boos N, Pfirrmann CWA, Brunner F, Elfering A, et al. Fat content of lumbar paraspinal muscles in patients with chronic low back pain and in asymptomatic volunteers: Quantification with MR spectroscopy. *Radiology* 2006;240(3):786-792.

90. Kader DF, Wardlaw D, Smith FW. Correlation between the MRI changes in the lumbar multifidus muscles and leg pain. *Clin Radiol* 2000;55(2):145-149.

91. Alaranta H, Tallroth K, Soukka A, Heliovaara M. Fat content of lumbar extensor muscles and low back disability: A radiographic and clinical comparison. *J Spinal Disord* 1993;6(2):137-140.

92. Shafaq N, Suzuki A, Matsumura A, Terai H, Toyoda H, Yasuda H, et al. Asymmetric degeneration of paravertebral muscles in patients with degenerative lumbar scoliosis. *Spine* 2012;37(16):1398-1406.

93. Kang CH, Shin MJ, Kim SM, Lee SH, Lee C-. MRI of paraspinal muscles in lumbar degenerative kyphosis patients and control patients with chronic low back pain. *Clin Radiol* 2007;62(5):479-486.

94. Lee JC, Cha J-, Kim Y, Kim Y-, Shin B-. Quantitative analysis of back muscle degeneration in the patients with the degenerative lumbar flat back using a digital image analysis: Comparison with the normal controls. *Spine* 2008;33(3):318-325.

95. Pezolato A, De Vasconcelos EE, Defino HLA, Defino A, Nogueira-Barbosa MH. Fat infiltration in the lumbar multifidus and erector spinae muscles in subjects with sway-back posture. *Eur Spine J* 2012;21(11):2158-2164.

96. Kjaer P, Bendix T, Sorensen JS, Korsholm L, Leboeuf-Yde C. Are MRI-defined fat infiltrations in the multifidus muscles associated with low back pain? *BMC Med* 2007;5.

97. McLoughlin RF, D'Arcy EM, Brittain MM, Fitzgerald O, Masterson JB. The significance of fat and muscle areas in the lumbar paraspinal space: A CT study. *J Comput Assisted Tomogr* 1994;18(2):275-278.

98. Murray MA, Robbins N. Cell proliferation in denervated muscle: Identity and origin of dividing cells. *Neuroscience* 1982;7(7):1823-1833.

99. Nahirney PC, Dow PR, Ovalle WK. Quantitative morphology of mast cells in skeletal muscle of normal and genetically dystrophic mice. *Anat Rec* 1997;247(3):341-349.

100. Lefaucheur J-, Gjata B, Lafont H, Sebille A. Angiogenic and inflammatory responses following skeletal muscle injury are altered by immune neutralization of endogenous basic fibroblast growth factor, insulin-like growth factor-1 and transforming growth factor-β1. *J Neuroimmunol* 1996;70(1):37-44.

101. Floss T, Arnold H-, Braun T. A role for FGF-6 in skeletal muscle regeneration. *Genes and Development* 1997;11(16):2040-2051.

102. Mannion AF, Dumas GA, Cooper RG, Espinosa FJ, Faris MW, Stevenson JM. Muscle fibre size and type distribution in thoracic and lumbar regions of erector spinae in healthy subjects without low back pain: Normal values and sex differences. *J Anat* 1997;190(4):505-513.

103. Mannion AF, Weber BR, Dvorak J, Grob D, Muntener M. Fibre type characteristics of the lumbar paraspinal muscles in normal healthy subjects and in patients with low back pain. *J Orthop Res* 1997;15(6):881-887.

104. Yoshihara K, Shirai Y, Nakayama Y, Uesaka S. Histochemical changes in the multifidus muscle in patients with lumbar intervertebral disc herniation. *Spine* 2001;26(6):622-626.

105. Zhao W-, Kawaguchi Y, Matsui H, Kanamori M, Kimura T.Histochemistry and morphology of the multifidus muscle in lumbar disc herniation: Comparative study between diseased and normal sides. *Spine* 2000;25(17):2191-2199.

106. Mattila M, Hurme M, Alaranta H. The multifidus muscle in patients with lumbar disc herniation. A histochemical and morphometric analysis of intraoperative biopsies. *Spine* 1986;11(7):732-738.

107. Zhu X-, Parnianpour M, Nordin M, Kahanovitz N. Histochemistry and morphology of erector spinae muscle in lumbar disc herniation. Spine 1989;14(4):391-397.

108. Meltzer HY, Rastogi S, Ellison J. Quantitative histochemical evaluation of normal human skeletal muscle. *Neurology* 1976;26(9):849-852.

109. Shirado O, Ito T, Kaneda K, Strax TE. Flexion-relaxation phenomenon in the back muscles: A comparative study between healthy subjects and patients with chronic low back pain. *Am J Phys Med Rehabil* 1995;74(2):139-144.

110. Radebold A, Cholewicki J, Polzhofer GK, Greene HS. Impaired postural control of the lumbar spine is associated with delayed muscle response times in patients with chronic idiopathic low back pain. *Spine* 2001;26(7):724-730.

111. Van Dieën JH, Cholewicki J, Radebold A. Trunk muscle recruitment patterns in patients with low back pain enhance the stability of the lumbar spine. *Spine* 2003;28(8):834-841.

112. Larivière C, Gagnon D, Loisel P. The comparison of trunk muscles EMG activation between subjects with and without chronic low back pain during flexion-extension and lateral bending tasks. *J Electromyogr Kinesiology* 2000;10(2):79-91.

113. Ahern DK, Follick MJ, Council JR, Laser-Wolston N, Litchman H. Comparison of lumbar paravertebral EMG patterns in chronic low back pain patients and non-patient controls. *Pain* 1988;34(2):153-160.

114. Arendt-Nielsen L, Graven-Nielsen T, Svarrer H, Svensson P. The influence of low back pain on muscle activity and coordination during gait: A clinical and experimental study. *Pain* 1996;64(2):231-240.

115. Fabian S, Hesse H, Grassme R, Bradl I, Bernsdorf A. Muscular activation patterns of healthy persons and low back pain patients performing a functional capacity evaluation test. *Pathophysiology* 2005;12(4):281-287.

116. MacDonald D, Moseley GL, Hodges PW. Why do some patients keep hurting their back? Evidence of ongoing back muscle dysfunction during remission from recurrent back pain. *Pain* 2009;142(3):183-188.

117. Travell J, Rinzter S, Herman M. Pain and disability of the shoulder and arm. *JAMA* 1942;120:417-422.

118. Van Dieën JH, Selen LPJ, Cholewicki J. Trunk muscle activation in low-back pain patients, an analysis of the literature. *J Electromyogr Kinesiology* 2003;13(4):333-351.

119. Lund JP, Donga R, Widmer CG, Stohler CS. The pain-adaptation model: A discussion of the relationship between chronic musculoskeletal pain and motor activity. *Can J Physiol Pharmacol* 1991;69(5):683-694.

120. Kaigle AM, Wessberg P, Hansson TH. Muscular and kinematic behavior of the lumbar spine during flexion- extension. J Spinal Disord 1998;11(2):163-174.

121. Paquet N, Malouin F, Richards CL. Hip-spine movement interaction and muscle activation patterns during sagittal trunk movements in low back pain patients. Spine 1994;19(5):596-603.

122. Ambroz C, Scott A, Ambroz A, Talbott EO. Chronic low back pain assessment using surface electromyography. *J Occupa Environ Med* 2000;42(6):660-669.

123. Magnusson ML, Aleksiev A, Wilder DG, Pope MH, Spratt K, Lee SH, et al. Unexpected load and asymmetric posture as etiologic factors in low back pain. *Eur Spine J* 1996;5(1):23-35.

124. Zedka M, Prochazka A, Knight B, Gillard D, Gauthier M. Voluntary and reflex control of human back muscles during induced pain. *J Physiol* 1999;520(2):591-604.

125. Hemborg B, Moritz U. Intra-abdominal pressure and trunk muscle activity during lifting. II. Chronic low-back patients. Scand J Rehabil Med 1985;17(1):5-13.

126. Aprile I, Padua L, Caliandro P, Pazzaglia C, Tonali P, Bendszus M, et al. Peroneal nerve palsy caused by thrombosis of crural veins. *Neurology* 2003;60(9):1559-1560.

127. Kamath S, Venkatanarasimha N, Walsh MA, Hughes PM. MRI appearance of muscle denervation. *Skelet Radiol* 2008;37(5):397-404.

128. Wessig C, Koltzenburg M, Reiners K, Solymosi L, Bendszus M. Muscle magnetic resonance imaging of denervation and reinnervation: Correlation with electrophysiology and histology. *Exp Neurol* 2004;185(2):254-261.

129. Kikuchi Y, Nakamura T, Takayama S, Horiuchi Y, Toyama Y. MR Imaging in the Diagnosis of Denervated and Reinnervated Skeletal Muscles: Experimental Study in Rats. *Radiology* 2003;229(3):861-867.

130. Petersilge CA, Pathria MN, Gentili A, Recht MP, Resnick D. Denervation hypertrophy of muscle: MR features. *J Comput Assist Tomogr* 1995;19(4):596-600.

131. Kato K, Tomura N, Takahashi S, Watarai J. Motor denervation of tumors of the head and neck: changes in MR appearance. *Magn Reson Med Sci* 2002;1(3):157-164.

132. Dumitru D, Diaz CA, King JC. Prevalence of denervation in paraspinal and foot intrinsic musculature. *Am J Phys Med Rehabil* 2001;80(7):482-490.

133. Date ES, Mar EY, Bugola MR, Teraoka JK. The prevalence of lumbar paraspinal spontaneous activity in asymptomatic subjects. *Muscle Nerve* 1996;19(3):350-354.

134. Tong HC, Haig AJ, Yamakawa KS, Miner JA. Paraspinal electromyography: age-correlated normative values in asymptomatic subjects. Spine 2005;30(17):E499-502.

135. Leblanc A. Muscle atrophy during long duration bed rest. *Int J Sports Med* 1997;18(Suppl. 4):S283-S285.

136. Fitts RH, Riley DR, Widrick JJ. Physiology of a microgravity environment invited review: Microgravity and skeletal muscle. *J Appl Physiol* 2000;89(2):823-839.

137. Riley DA, Bain JLW, Romatowski JG, Fitts RH. Skeletal muscle fiber atrophy: Altered thin filament density changes slow fiber force and shortening velocity. *Am J Physiol Cell Physiol* 2005;288(2):C360-C365.

138. LeBlanc AD, Schneider VS, Evans HJ, Pientok C, Rowe R, Spector E. Regional changes in muscle mass following 17 weeks of bed rest. *J Appl Physiol* 1992;73(5):2172-2178.

139. Belavý DL, Armbrecht G, Richardson CA, Felsenberg D, Hides JA. Muscle atrophy and changes in spinal morphology: Is the lumbar spine vulnerable after prolonged bed-rest? *Spine* 2011;36(2):137-145.

140. Manini TM, Clark BC, Nalls MA, Goodpaster BH, Ploutz-Snyder LL, Harris TB. Reduced physical activity increases intermuscular adipose tissue in healthy young adults. *Am J Clin Nutr* 2007;85(2):377-384.

141. Booth FW, Seider MJ. Early change in skeletal muscle protein synthesis after limb immobilization of rats. *J Appl Physiol* 1979;47(5):974-977.

142. Booth FW. Effect of limb immobilization on skeletal muscle. *J Appl Physiol Respir Environ Exercise Physiol* 1982;52(5):1113-1118.

143. Castro MJ, Apple Jr. DF, Staron RS, Campos GER, Dudley GA. Influence of complete spinal cord injury on skeletal muscle within 6 mo of injury. *J Appl Physiol* 1999;86(1):350-358.

144. Morrissey MC. Reflex inhibition of thigh muscles in knee injury. Causes and treatment. *Sports Med* 1989;7(4):263-276.

145. Stokes M, Young A. The contribution of reflex inhibition to arthrogenous muscle weakness. *Clin Sci* 1984;67(1):7-14.

146. Sherman KP, Young A, Stokes M. Joint injury and muscle weakness. *Lancet* 1984;2(8403):646.

147. Hopkins JT, Ingersoll CD, Andrew Krause B, Edwards JE, Cordova ML. Effect of knee joint effusion on quadriceps and soleus motoneuron pool excitability. *Med Sci Sports Exerc* 2001;33(1):123-126.

148. Indahl A, Kaigle A, Reikeras O, Holm S. Electromyographic response of the porcine multifidus musculature after nerve stimulation. *Spine* 1995;20(24):2652-2658.

149. Indahl A, Kaigle AM, Reikerås O, Holm SH. Interaction between the porcine lumbar intervertebral disc, zygapophysial joints, and paraspinal muscles. *Spine* 1997;22(24):2834-2840.

150. Kang YM, Choi WS, Pickar JG. Electrophysiologic evidence for an intersegmental reflex pathway between lumbar paraspinal tissues. *Spine* 2002;27(3):E56-63.

151. Spencer JD, Hayes KC, Alexander IJ. Knee joint effusion and quadriceps reflex inhibition in man. *Arch Phys Med Rehabil* 1984;65(4):171-177.

152. Ranson CA, Burnett AF, Kerslake R, Batt ME, O'Sullivan PB. An investigation into the use of MR imaging to determine the functional cross sectional area of lumbar paraspinal muscles. *Eur Spine J* 2006;15(6):764-773.

153. Hu Z-, He J, Zhao F-, Fang X-, Zhou L-, Fan S-. An assessment of the intra- and inter-reliability of the lumbar paraspinal muscle parameters using CT scan and magnetic resonance imaging. *Spine* 2011;36(13):E868-E874.

154. Hides JA, Richardson CA, Jull GA. Magnetic resonance imaging and ultrasonography of the lumbar multifidus muscle: Comparison of two different modalities. *Spine* 1995;20(1):54-58.

155. Wallwork TL, Stanton WR, Freke M, Hides JA. The effect of chronic low back pain on size and contraction of the lumbar multifidus muscle. *Man Ther* 2009;14(5):496-500.

156. Pressler JF, Heiss DG, Buford JA, Chidley JV. Between-day repeatability and symmetry of multifidus cross-sectional area measured using ultrasound imaging. *J Orthop Sports Phys Ther* 2006;36(1):10-18.

157. Ropponen A, Videman T, Battié MC. The reliability of paraspinal muscles composition measurements using routine spine MRI and their association with back function. *Man Ther* 2008;13(4):349-356.

158. Gibbons LE, Latikka P, Videman T, Manninen H, Battié MC. The association of trunk muscle cross-sectional area and magnetic resonance image parameters with isokinetic and psychophysical lifting strength and static back muscle endurance in men. *J Spinal Disord* 1997;10(5):398-403.

169. Fan S, Hu Z, Zhao F, Zhao X, Huang Y, Fang X. Multifidus muscle changes and clinical effects of one-level posterior lumbar interbody fusion: Minimally invasive procedure versus conventional open approach. *Eur Spine J* 2010;19(2):316-324.

160. Gasperini C, Rovaris M, Sormani MP, Bastianello S, Pozzilli C, Comi G, et al. Intra-observer, inter-observer and inter-scanner variations in brain MRI volume measurements in multiple sclerosis. *Mult Scler* 2001;7(1):27-31.

161. Gradin V, Gountouna V-, Waiter G, Ahearn TS, Brennan D, Condon B, et al. Between- and within-scanner variability in the CaliBrain study n-back

cognitive task. *Psychiatry Res Neuroimaging* 2010;184(2):86-95.

162. Briellmann RS, Syngeniotis A, Jackson GD. Comparison of hippocampal volumetry at 1.5 tesla and at 3 tesla. *Epilepsia* 2001;42(8):1021-1024.

163. Scorzin JE, Kaaden S, Quesada CM, Müller CA, Fimmers R, Urbach H, et al. Volume determination of amygdala and hippocampus at 1.5 and 3.0T MRI in temporal lobe epilepsy. *Epilepsy Res* 2008;82(1):29-37.

164. Stonnington CM, Tan G, Klöppel S, Chu C, Draganski B, Jack Jr. CR, et al. Interpreting scan data acquired from multiple scanners: A study with Alzheimer's disease. *Neuroimage* 2008;39(3):1180-1185.

165. D'Hooge R, Cagnie B, Crombez G, Vanderstraeten G, Dolphens M, Danneels L. Increased intramuscular fatty infiltration without differences in lumbar muscle cross-sectional area during remission of unilateral recurrent low back pain. *Man Ther* 2012;17(6):584-588.

166. Franke J, Hesse T, Tournier C, Schuberth W, Mawrin C, LeHuec JC, et al. Morphological changes of the multifidus muscle in patients with symptomatic lumbar disc herniation: Clinical article. *J Neurosurg Spine* 2009;11(6):710-714.

167. Dickx N, Cagnie B, Parlevliet T, Lavens A, Danneels L. The effect of unilateral muscle pain on recruitment of the lumbar multifidus during automatic contraction. An experimental pain study. *Man Ther* 2010;15(4):364-369.

168. Paalanne N, Niinimaki J, Karppinen J, Taimela S, Mutanen P, Takatalo J, et al. Assessment of association between low back pain and paraspinal muscle atrophy using opposed-phase magnetic resonance imaging: A population-based study among young adults. *Spine* 2011;36(23):1961-1968.

169. Kalichman L, Hodges P, Li L, Guermazi A, Hunter DJ. Changes in paraspinal muscles and their association with low back pain and spinal degeneration: CT study. *Eur Spine J* 2010;19(7):1136-1144.

170. Kalichman L, Kim DH, Li L, Guermazi A, Hunter DJ. Computed tomography-evaluated features of spinal degeneration: prevalence, intercorrelation, and association with self-reported low back pain. *Spine J* 2010;10(3):200-208.

171. Yarjanian JA, Fetzer A, Yamakawa KS, Tong HC, Smuck M, Haig A. Correlation of paraspinal atrophy and denervation in back pain and spinal stenosis relative to asymptomatic controls. *PM R* 2013;5(1):39-44.

172. Mannion AF, Käser L, Weber E, Rhyner A, Dvorak J, Müntener M. Influence of age and duration of symptoms on fibre type distribution and size of the back muscles chronic low back pain patients. *Eur Spine J* 2000;9(4):273-281.

173. Lee HJ, Lim WH, Park J-, Kwon BS, Ryu KH, Lee JH, et al. The relationship between cross sectional area and strength of back muscles in patients with chronic low back pain. *Ann Rehabil Med* 2012;36(2):173-181.

CHAPTER 3

QUANTITATIVE PARASPINAL MUSCLE MEASUREMENT: INTER-SOFTWARE RELIABILITY AND AGREEMENT USING OSIRIX AND IMAGEJ*

3.1. INTRODUCTION

Cross-sectional area (CSA) asymmetries of lumbar paraspinal muscles, [1-7] as well as fat infiltration, [8-9] have been associated with low back pain (LBP) and related pathologies using various imaging techniques. As a result, the measurement of paraspinal muscle asymmetry or composition has been emphasized in a number of studies related to the aetiology and prognosis of LBP. [1-15] There are inconsistencies, however, in study findings of the association between painful spinal conditions and paraspinal muscle morphology. For example, Ploumis et al. [6] used a manual segmenting technique to measure paraspinal muscle *functional* CSA (FCSA), defined as fat-free muscle mass, in a group of 40 patients with monosegmental disk disease and unilateral LBP, with or without radicular symptoms, and reported significant multifidus atrophy on the symptomatic side. Yet, in another magnetic resonance imaging (MRI) study, Hyun et al. [10] reported no significant asymmetry between involved and uninvolved sides in a group of 39 patients with disc herniation, again, with or without radiculopathy. They also measured multifidus FCSA, but used a technique to determine the proportion of

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muscle versus fat tissue based on a signal intensity threshold. Similarly, 2 studies that quantitatively compared the degree of paraspinal muscle fatty infiltration present in chronic LBP patients compared with a control group of individuals who were healthy showed conflicting results. [1,2] Different threshold techniques and measurement protocols were used to measure the proportion of muscle fatty infiltration, which may have contributed to the discrepant findings, but the effect of such differences on measurement is not known.

Variations in imaging modalities (MRI, computed tomography scan, and ultrasound), image analysis program, and measurement protocols contribute to conflicting results. Currently, several methods are used to investigate paraspinal muscle morphology, and too little attention has been given to whether they lead to roughly equivalent measurements. Some investigators have focused on total CSA, [3,4,7,12-14] whereas others contend that FCSA is a better indicator of muscle atrophy and contractibility. [16] Functional CSA is calculated by using either a manual technique or signal intensity threshold technique with the aid of computer software. Although the reliability of measurements of FCSA using the 2 different approaches has been investigated in several studies, [1,15-19] investigators interested in segmenting paraspinal muscles or fat tissues currently use a variety of computer software, including in-house custom software, [1,18] software that is part of a MRI scanner, [20] picture archiving and communications systems workstations, [17,19] commercial software, [10] computer aided drafting (auto-CAD) software, [3,21] and freeware. [15,16,22] Moreover, the use of proprietary software and insufficient descriptions of measurement protocols hinder replication of results by others, and

the comparability of measurements obtained using different software and measurement protocols has been neglected.

Although the measurement error related to the measurement methods used appears to be mostly associated with the observer, [23] the software used also might lead to measurement differences, and there is a need to determine whether direct comparisons can be made among different software packages (using comparable method). There is currently no standard protocol, and we found no investigations of reliability or agreement among measurements obtained with different software or protocols.

To clarify the measurement error related to use of 2 widely available, free image analysis programs and associated measurement techniques, the purpose of the present study was to determine the reliability and agreement, as well as the standard error of measurement (SEM), of paraspinal muscle CSA and composition measurements obtained using two open source, readily available computer software programs, ImageJ and OsiriX. In addition, the associated image analysis protocol is proposed for standardized use to facilitate comparisons among studies.

3.2. MATERIALS AND METHODS

3.2.1. MEASUREMENT STUDY DESIGN

Total CSA and FCSA measurements of multifidus muscle, erector spinae muscle, and the 2 muscles combined, bilaterally, were directly obtained for each subject

using 2 open source software packages. ImageJ (version 1.43, National Institute of Health, Bethesda, Maryland) is a free downloadable public domain image processing software (http://rsbweb.nih.gov/ij/download.html) that was developed by the National Institutes of Health. The 32 bit OsiriX (version 3.8.1, Pixmeo, Geneva, Switzerland) was downloaded from http://www.osirix-viewer.com/ and was previously assessed as a more user-friendly image analysis software package for the Apple Mac OS (Microsoft Corp, Redmond, Washington) than ImageJ. [24] One of OsiriX program's main advantages is its integrated PAC system, which allows patient data to be stored automatically. [24] Both software packages have been reported and utilized by clinicians and scientists in a wide variety of studies as functional tools for image analysis. [24-26]

To determine intrarater and intersoftware measurement reliability, each muscle measurement was acquired 4 times by the same rater, twice using each software program. In an effort to minimize bias from carryover or practice effects, the first complete set of measurements using each software program was obtained by alternating between programs after every block of ten participants' images, randomly selected and ordered. After all magnetic resonance images were assessed once using either ImageJ or OsiriX, the images were reordered and blinded to be similarly assessed again, a minimum of five days after the first measurements were completed.

3.2.2. SAMPLE OF LUMBAR MRI

A sample of 30 patients (11 female and 19 male) were randomly selected from an ongoing study of patients attending spine specialty clinics and having commonly diagnosed lumbar pathologies, including disk herniation, spinal stenosis and spondylolisthesis, and non-specific chronic low back pain. Patients were excluded if they were below 18 or over 60 years of age, had a contrast agent allergy, had reduced renal function, were not able to undergo MRI acquisition, or had a tumor, infection, spinal fracture, or rheumatoid arthritis, or were pregnant. This study was approved by the Health Research Ethics Board of the University of Alberta.

The MRI protocol included routine T2-weighted turbo spin echo sequences for both axial and sagittal images acquired with a Siemens Avanto 1.5T (Siemens AG, Erlangen, Germany) (axial T2 parameters included repetition time=4000, echo time=113, and slice thickness=3mm).

3.2.3 MUSCLE MEASUREMENTS

All muscle measurements were acquired by one of the investigators (M.F.) who, in preparation for the measurements, received training in spine MRI assessments focusing on lumbar intervertebral disk and paraspinal muscle morphology. For practice purposes, a sample of about 15 images was analyzed with each software application prior to the beginning of the measurement study.

Quantitative measurements of multifidus and erector spinae muscles individually, and as a group (multifidus and erector spinae together) were obtained from the T2-weighted axial images using ImageJ and OsiriX. ImageJ has

already been used in previous studies to measure total CSA and FCSA using a threshold method, with previously reported intraclass correlation coefficients for intrarater reliability of both area measurements ranging from .89 to .99. [15,16] We are not aware of any reports of reliability of paraspinal muscle morphology measurements using OsiriX. The same MRI slices were used for the ImageJ and OsiriX muscle measurements. Because the reliability of FCSA and total CSA measurements has been shown to be relatively equivalent across spinal levels, [16] measurements for this study were taken only at mid-disk for L4-L5 and mid-S1 for every participant. The 2 levels were selected because most lumbar pathologies and muscle morphological changes occur between L4-L5 and L5-S1. [27]

The paraspinal muscle measurements of interest in this study for multifidus, erector spinae muscles and the 2 muscles as a group included the following: total CSA, FCSA, ratio of FCSA to total CSA, side-to-side differences (muscle asymmetry) in total CSA and FCSA, and mean signal intensity of total CSA.

The FCSA was obtained by selecting a threshold signal within the total muscle CSA to include only pixels within the lean muscle tissue range (Figure 3-1A). The grey scale range for lean muscle tissue was established for every participant, on each scan slice. Four to 6 sample regions of interest (ROI) within the bilateral paraspinal muscle group (multifidus and erector spinae) were taken from areas of lean muscle tissue visible on each slice (Figure 3-1B). If atrophied paraspinal muscle with significant fatty infiltration was encountered, care was taken to avoid the inclusion of any visible pixel of fat. The maximum value

acquired from the sample ROIs was used as the highest threshold to distinguish muscle tissue from fat, in the same way the lower limit was determined by the minimum signal intensity value obtained from the different sample ROIs. However, because we observed that the lower limit was typically 0 or 1, it might be best to standardize the lower limit at 0. This standardization could potentially decrease related measurement error and simplify the protocol. When timing a sample of measurements obtained with each software program, the average time taken to complete the measurements of the 3 muscle regions bilaterally at one spinal level was approximately 9 minutes with OsiriX and 5 minutes for ImageJ.

3.2.4 DATA ANALYSIS

The statistical analysis was performed using Statistical Package for the Social Science version 18.0 (SPSS Inc, Chicago, Illinois). Means and standard deviations for each variable were obtained. The ICC (2,1) was calculated to determine the intrarater reliability of measurements using OsiriX and ImageJ for each measurement variable and every muscle of interest using a 2-way random-effects model and absolute agreement. The ICC reflects both the degree of correlation and agreement between the ratings and was interpreted using the following criteria as suggested by Portney and Watkins: .00-.49=poor, .50-.74=moderate, and .75-1.00=excellent. [28] The SEM was calculated to provide an estimate of the expected error related to a particular measurement. [28] The ICC defines the ability to discriminate among individuals, whereas the SEM defines the measurement error in the same units as the initial measurement. [29] Method agreement between

the measurements acquired from the different software programs was also evaluated using the 95% limits of agreement from Bland and Altman. [30-32] Reliability results were analyzed and reported according to spinal level, muscle investigated, and muscle side.

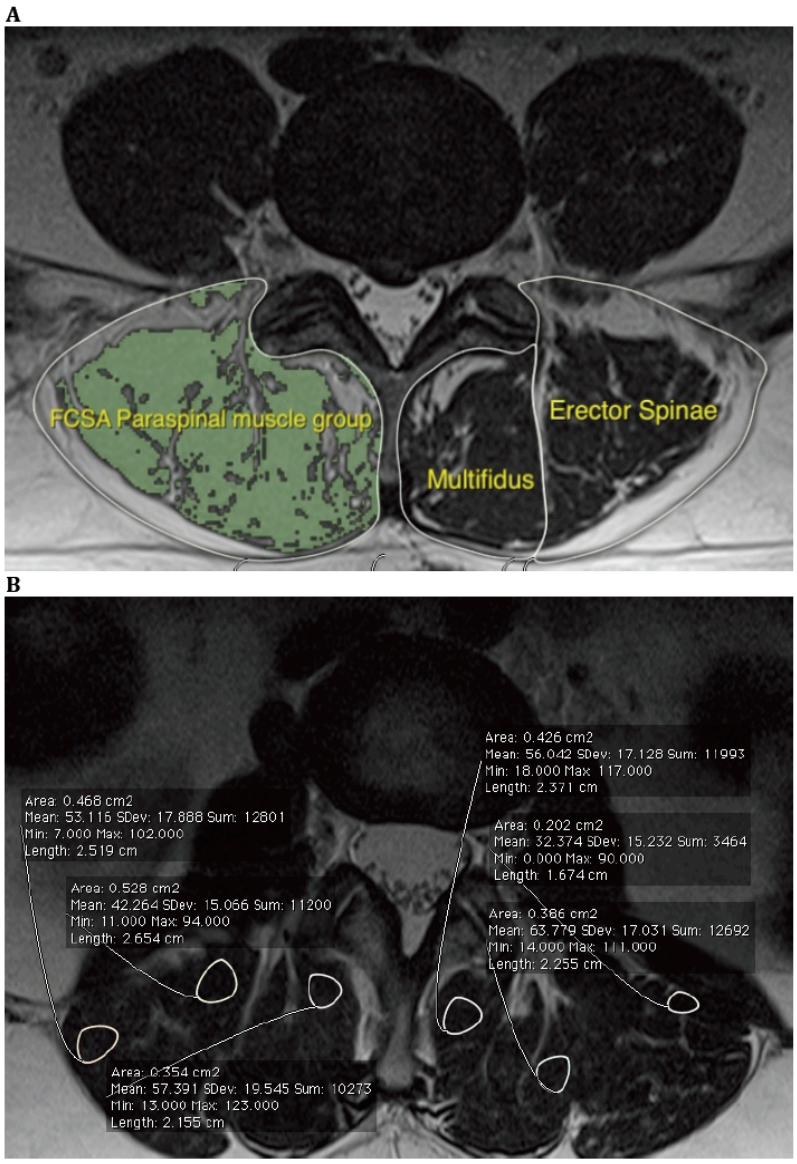

Figure 3-1: A) Measurement of total CSA of erector spinae and multifidus (right) at L4-L5. Lean muscle FCSA of the paraspinal muscle group using a thresholding method is represented by the area highlighted in green (left). B) Sample ROIs selection to define upper and lower signal intensity threshold limits.

3.3. RESULTS

3.3.1. INTER-SOFTWARE RELIABILITY OF MUSCLE MEASUREMENT USING OSIRIX AND IMAGEJ

The results for the inter-software reliability (ICC), SEM values, and descriptive statistics (mean ± SD) for the left side are presented in Table 3-1 for the L4-L5 spinal measurements and in Table 3-2 for the S1 measurements. The results for the right side were virtually equivalent and are not presented. The inter-software reliability was analyzed by comparing the first set of measurements collected with each software program. The ICCs for all the different muscle composition measurements, regardless of the muscle analyzed or spinal level, showed excellent agreement and varied between .81-.99. However, the SEM associated with the side-to-side difference measurements was of greater magnitude in comparison with the rest of the other muscle measurements.

3.3.2. INTER-SOFTWARE AGREEMENT

Figure 3-2 shows the combined Bland and Altman 95% limits of agreement plots for the different muscle composition measurements from the left multifidus muscle at L4-L5 using the first set of measurements collected with each software program. Two methods are considered to have good agreement when the measurement difference is small enough for both methods to be used interchangeably. [30] All the plots show good agreement between OsiriX and ImageJ and no systematic bias; the distribution of the scores around the mean

approximate zero and are spread evenly and randomly above and below the line. [28] As suggested by Bland and Altman, an initial histogram of the difference scores was performed for every measurement parameter and all followed a normal distribution. Because the error is normally distributed, we can observe that about 95% of the points are between the limits of agreement (noted by the dashed lines on the plots) for each measure. The width of the limits of agreement for the different measurements was also small (Figure 3-2).

Table 3-1: Inter-software reliability indexes for left paraspinal muscle measurements at L4-L5 [a]

Multifidus muscle

Parameters	Mean (SD)	ICC (95% CI)	SEM
CSA (cm^2)	10.07 (1.47)	0.96 (0.92-0.98)	0.29
SI	188.02 (40.89)	0.99 (0.99-1.00)	4.09
FCSA (cm^2)	5.92 (1.73)	0.96 (0.92-0.98)	0.35
FCSA/CSA	0.58 (0.12)	0.95 (0.91-0.98)	0.03
CSA diff (cm^2)	1.03 (0.77)	0.81 (0.63-0.90)	0.33
FCSA diff (cm^2)	0.72 (0.58)	0.87 (0.75-0.94)	0.21

Erector Spinae muscle

Parameters	Mean (SD)	ICC (95% CI)	SEM
CSA (cm^2)	18.49 (3.95)	0.99 (0.98-1.00)	0.39
SI	226.07 (47.96)	0.99 (0.96-1.00)	4.80
FCSA (cm^2)	9.71 (3.37)	0.97 (0.95-0.99)	0.58
FCSA/CSA	0.52 (0.13)	0.94 (0.88-0.97)	0.03
CSA diff (cm^2)	1.31 (1.35)	0.86 (0.68-0.94)	0.50
FCSA diff (cm^2)	1.22 (1.12)	0.98 (0.96-0.99)	0.16

Paraspinal muscle group

Parameters	Mean (SD)	ICC (95% CI)	SEM
CSA (cm^2)	28.49 (4.52)	0.99 (0.99-1.00)	0.45
SI	212.28 (43.21)	0.99 (0.99-1.00)	4.32
FCSA (cm^2)	15.63 (4.47)	0.97 (0.94-0.99)	0.77
FCSA/CSA	0.55 (0.12)	0.95 (0.91-0.98)	0.03
CSA diff (cm^2)	1.27 (1.18)	0.87 (0.75-0.94)	0.43
FCSA diff (cm^2)	1.23 (1.15)	0.96 (0.91-0.99)	0.23

[a] CSA= cross-sectional area, SI= signal intensity, FCSA = functional CSA, FCSA/CSA = ratio, CSA diff = side-to-side difference in CSA, FCSA diff = side-to-side difference in functional CSA.

Table 3-2: Inter-software reliability indexes for left paraspinal muscle measurements at S1 [a]

Multifidus muscle

Parameters	Mean (SD)	ICC (95% CI)	SEM
CSA (cm^2)	12.33 (1.74)	0.97 (0.93-0.99)	0.30
SI	233.13 (49.64)	0.99 (0.99-1.00)	4.96
FCSA (cm^2)	6.91 (2.11)	0.96 (0.93-0.98)	0.42
FCSA/CSA	0.56 (0.13)	0.94 (0.89-0.97)	0.03
CSA diff (cm^2)	1.00 (0.81)	0.88 (0.77-0.94)	0.28
FCSA diff (cm^2)	0.97 (1.03)	0.97 (0.94-0.99)	0.18

Erector Spinae muscle

Parameters	Mean (SD)	ICC (95% CI)	SEM
CSA (cm^2)	8.10 (4.10)	0.99 (0.98-1.00)	0.41
SI	304.52 (63.98)	0.99 (0.97-0.99)	6.40
FCSA (cm^2)	2.59 (1.85)	0.96 (0.93-0.98)	0.37
FCSA/CSA	0.31 (0.14)	0.93 (0.86-0.97)	0.04
CSA diff (cm^2)	1.45 (1.24)	0.87 (0.75-0.94)	0.45
FCSA diff (cm^2)	0.71 (0.65)	0.86 (0.73-0.93)	0.24

Paraspinal muscle group

Parameters	Mean (SD)	ICC (95% CI)	SEM
CSA (cm^2)	20.34 (4.72)	0.99 (0.99-1.00)	0.47
SI	259.12 (51.19)	0.99 (0.99-1.00)	5.12
FCSA (cm^2)	9.47 (2.98)	0.96 (0.92-0.98)	0.60
FCSA/CSA	0.47 (0.12)	0.92 (0.85-0.96)	0.03
CSA diff (cm^2)	1.62 (1.19)	0.89 (0.79-0.95)	0.40
FCSA diff (cm^2)	1.45 (1.16)	0.96 (0.93-0.99)	0.23

[a] CSA= cross-sectional area, SI= signal intensity, FCSA = functional CSA, FCSA/CSA = ratio, CSA diff = side-to-side difference in CSA, FCSA diff = side-to-side difference in functional CSA.

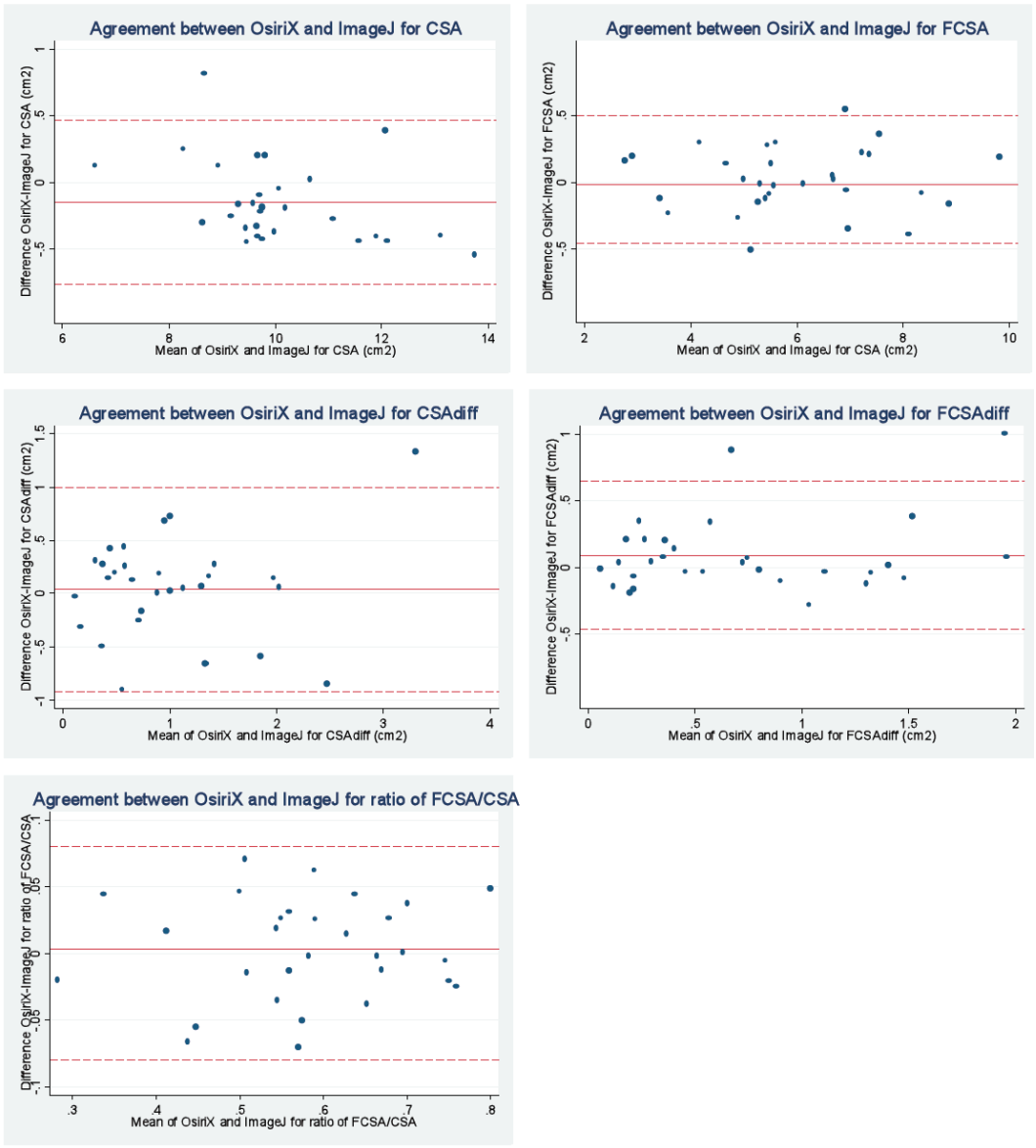

Figure 3-2: Bland-Altman 95% limits of agreement plots for the different muscle composition measurements of the left multifidus at L4-L5. CSA=cross-sectional area, FCSA=functional cross-sectional area, CSA diff=side-to-side difference in CSA, FCSA diff=side-to-side difference in CSA, FCSA/CSA=ratio.

3.3.3. INTRARATER RELIABITITY OF MUSCLE MEASUREMENTS USING OSIRIX AND IMAGEJ

The intrarater reliability (ICC), SEM and descriptive statistics (mean ± SD) related to OsiriX and ImageJ muscle measurements for the left side are presented in Table 3-3 for the L4-L5 level and in Table 3-4 for the S1 level. Again, the results for the right side were virtually equivalent and are not presented. The ICCs for intrarater reliability across both spinal levels for total CSA measurements of the paraspinal muscles, individually and as a group, ranged from .94-.99 for ImageJ and .97-.99 for OsiriX. The FCSA ICCs across both spinal levels for all the measured muscles tended to be slightly lower for ImageJ (ICC=.90-.96) compared with OsiriX (ICC=.97-.98), although all values were excellent.

The side-to-side difference measurements are of much smaller areas compared to the total CSA and FCSA measurements and had lower reliability values (ICC = .77-.97). The intrarater ICCs for the side-to-side difference in total CSA varied from .80-.90 for OsiriX and .78-.91 for ImageJ, and the side-to-side difference in FCSA varied from .77-.96 for OsiriX and .85-.97 for ImageJ. The reliability of the signal intensity of the total CSA and the ratio of FCSA/CSA also was measured because these data give a proportion estimate of a muscle fat content. The mean ICC for the signal intensity of the total CSA was .99 for measurements acquired with either software program, and the mean for the FCSA/CSA ratio was .96 for OsiriX and .91 for ImageJ (range = .88-.97). The SEM associated with each muscle composition measurement was generally

comparable between both software programs, except for the FCSA measurement where the SEM tended to be higher for ImageJ.

Table 3-3: Intra-rater reliability indices for OsiriX and ImageJ for left paraspinal muscle measurements at L4-L5 [a]

Multifidus muscle

	OsiriX			ImageJ		
Parameters	Mean (SD)	ICC (95% CI)	SEM	Mean (SD)	ICC (95% CI)	SEM
CSA (cm^2)	10.03 (1.47)	0.97 (0.93-0.98)	0.26	10.14 (1.49)	0.98 (0.96-0.99)	0.21
SI	188.49 (40.32)	0.99 (0.99-1.00)	4.03	187.30 (40.63)	0.99 (0.99-1.00)	4.06
FCSA (cm^2)	5.84 (1.71)	0.97 (0.93-0.98)	0.30	5.81 (1.73)	0.96 (0.88-0.99)	0.35
FCSA/CSA	0.58 (0.13)	0.97 (0.92-0.99)	0.02	0.57 (0.12)	0.93 (0.70-0.98)	0.03
CSA diff (cm^2)	1.01 (0.77)	0.80 (0.62-0.90)	0.34	1.03 (0.74)	0.87 (0.75-0.94)	0.27
FCSA diff (cm^2)	0.75 (0.59)	0.90 (0.78-0.95)	0.19	0.66 (0.52)	0.93 (0.85-0.96)	0.14

Erector Spinae muscle

	OsiriX			ImageJ		
Parameters	Mean (SD)	ICC (95% CI)	SEM	Mean (SD)	ICC (95% CI)	SEM
CSA (cm^2)	18.45 (3.95)	0.99 (0.99-1.00)	0.39	18.45 (3.96)	0.99 (0.98-1.00)	0.40
SI	227.45 (47.69)	0.99 (0.99-1.00)	4.77	224.50 (48.42)	0.99 (0.99-1.00)	4.84
FCSA (cm^2)	9.48 (3.50)	0.98 (0.94-0.99)	0.50	9.43 (3.19)	0.96 (0.71-0.99)	0.64
FCSA/CSA	0.51 (0.13)	0.97 (0.88-0.99)	0.02	0.51 (0.13)	0.92 (0.67-0.97)	0.04
CSA diff (cm^2)	1.12 (1.16)	0.86 (0.72-0.93)	0.42	1.34 (1.26)	0.86 (0.71-0.94)	0.47
FCSA diff (cm^2)	1.17 (1.12)	0.96 (0.92-0.98)	0.22	1.18 (1.09)	0.97 (0.92-0.99)	0.19

Paraspinal muscle group

	OsiriX			ImageJ		
Parameters	Mean (SD)	ICC (95% CI)	SEM	Mean (SD)	ICC (95% CI)	SEM
CSA (cm^2)	28.42 (4.57)	0.99 (0.99-1.00)	0.46	28.60 (4.60)	0.99 (0.99-1.00)	0.46
SI	214.31 (43.34)	0.99 (0.99-1.00)	4.34	211.42 (43.00)	0.99 (0.99-1.00)	4.30
FCSA (cm^2)	15.30 (4.60)	0.98 (0.92-0.99)	0.65	15.25 (4.35)	0.95 (0.76-0.98)	0.97
FCSA/CSA	0.53 (0.12)	0.96 (0.83-0.98)	0.02	0.53 (0.11)	0.92 (0.61-0.97)	0.03
CSA diff (cm^2)	1.26 (1.14)	0.87 (0.74-0.93)	0.41	1.27 (1.16)	0.87 (0.74-0.93)	0.42
FCSA diff (cm^2)	1.20 (1.15)	0.96 (0.92-0.98)	0.23	1.20 (1.16)	0.97 (0.94-0.99)	0.20

[a] CSA= cross-sectional area, SI= signal intensity, FCSA = functional CSA, FCSA/CSA = ratio, CSA diff = side-to-side difference in CSA, FCSA diff = side-to-side difference in functional CSA.

Table 3-4: Intra-rater reliability indices for OsiriX and ImageJ for left paraspinal muscle measurements at S1[a]

Multifidus muscle

	OsiriX			ImageJ		
Parameters	Mean (SD)	ICC (95% CI)	SEM	Mean (SD)	ICC (95% CI)	SEM
CSA (cm^2)	12.25 (1.67)	0.98 (0.97-0.99)	0.24	12.42 (1.75)	0.99 (0.97-0.99)	0.18
SI	234.09 (50.66)	0.99 (0.99-1.00)	5.07	232.61 (48.43)	0.99 (0.99-1.00)	4.84
FCSA (cm^2)	6.86 (2.18)	0.98 (0.97-0.99)	0.31	6.84 (2.05)	0.94 (0.88-0.97)	0.50
FCSA/CSA	0.55 (0.14)	0.97 (0.94-0.99)	0.02	0.55 (0.12)	0.92 (0.83-0.96)	0.03
CSA diff (cm^2)	0.99 (0.78)	0.88 (0.76-0.94)	0.27	1.05 (0.74)	0.91 (0.81-0.95)	0.22
FCSA diff (cm^2)	0.95 (1.03)	0.94 (0.88-0.97)	0.25	1.02 (1.04)	0.95 (0.91-0.98)	0.23

Erector Spinae muscle

	OsiriX			ImageJ		
Parameters	Mean (SD)	ICC (95% CI)	SEM	Mean (SD)	ICC (95% CI)	SEM
CSA (cm^2)	8.04 (4.19)	0.99 (0.99-1.00)	0.42	8.20 (4.12)	0.99 (0.98-1.00)	0.41
SI	305.10 (59.97)	0.99 (0.98-1.00)	6.00	305.00 (5.36)	0.99 (0.98-0.99)	6.54
FCSA (cm^2)	2.54 (1.89)	0.98 (0.96-0.99)	0.27	2.43 (1.60)	0.92 (0.80-0.96)	0.45
FCSA/CSA	0.30 (0.14)	0.95 (0.90-0.98)	0.03	0.29 (0.13)	0.89 (0.75-0.95)	0.04
CSA diff (cm^2)	1.40 (1.24)	0.80 (0.62-0.90)	0.55	1.46 (1.27)	0.86 (0.73-0.93)	0.47
FCSA diff (cm^2)	0.66 (0.62)	0.77 (0.57-0.88)	0.30	0.66 (0.58)	0.85 (0.72-0.93)	0.22

Paraspinal muscle group

	OsiriX			ImageJ		
Parameters	Mean (SD)	ICC (95% CI)	SEM	Mean (SD)	ICC (95% CI)	SEM
CSA (cm^2)	20.33 (4.71)	0.99 (0.99-1.00)	0.47	20.43 (4.82)	0.94 (0.97-0.99)	0.68
SI	260.20 (50.48)	0.99 (0.99-1.00)	5.05	258.30 (50.33)	0.99 (0.98-1.00)	5.03
FCSA (cm^2)	9.43 (3.12)	0.98 (0.96-0.99)	0.44	9.25 (2.74)	0.90 (0.77-0.95)	0.88
FCSA/CSA	0.47 (0.12)	0.96 (0.92-0.98)	0.02	0.46 (0.11)	0.88 (0.75-0.94)	0.04
CSA diff (cm^2)	1.55 (1.20)	0.90 (0.80-0.95)	0.38	1.59 (1.22)	0.78 (0.58-0.89)	0.56
FCSA diff (cm^2)	1.40 (1.16)	0.96 (0.91-0.98)	0.23	1.43 (1.17)	0.97 (0.95-0.98)	0.20

[a] CSA= cross-sectional area, SI= signal intensity, FCSA = functional CSA, FCSA/CSA = ratio, CSA diff = side-to-side difference in CSA, FCSA diff = side-to-side difference in functional CSA.

3.4. DISCUSSION

We have presented specific protocols for paraspinal muscle measurements using 2 readily available, free image analysis programs, OsiriX and ImageJ, in a level of detail to allow replication (Appendix 3.7). The reliability and agreement of related paraspinal muscle measurements were found to be reasonably comparable between software programs, with excellent reliability when applied to a clinically relevant population. These findings are supported by the Bland and Altman limits of agreement that indicate inter-software agreement is within an acceptable range to use either of the 2 methods. Furthermore, the similar intrarater and inter-

software reliability coefficients and SEMs suggest that the software used contributes little to the measurement error.

A threshold technique was utilized to calculate FCSA based on differences in pixel intensities between muscle (low intensity) and fat tissues (high intensity) on T2-weighted axial images. The application used in OsiriX is based on a region-growing algorithm, whereas ImageJ uses a signal intensity threshold algorithm. With OsiriX, once the lean muscle signal intensity is defined, the region-growing image segmentation involves the selection of seed points, which determine if other neighboring pixels will be included in the selection. This method is more time-consuming compared with a straight threshold algorithm where the only step needed is to indicate the upper and lower bounds of the threshold limit for muscle tissue. However, as suggested by Dello et al, [24] our impression was that OsiriX is a more user friendly software package in comparison to ImageJ. We are not aware of any other study that investigated the agreement of paraspinal muscle measurements between two different image analysis programs.

The results of this study related to intrarater reliability, however, are similar to those of other studies examining measurements of FCSA and total CSA that used a threshold technique. Danneels et al [1] reported ICCs for interarater reliability that varied between .81-.92 for FCSA, whereas others reported ICCs for intrarater reliability that were slightly higher (.90-.99). [15,16,18] Studies using a tracing technique to measure FCSA by manually segmenting muscle from fat tissues have shown somewhat lower ICCs for intrarater reliability varying between .81 and .96.[17,19] Other investigators measuring total CSA reported ICCs

for intrarater reliability that varied between .89- and .99. [3,15,22,33,34] In the present study, however, intrarater reliability indexes were computed primarily in order to better interpret the contribution of inter-software reliability to measurement error. The fact that inter-software reliability is similarly high as intrarater reliability further suggests that using one software program as opposed to the other contributes little to measurement error.

One of the strengths of this study is the report of reliability indexes related to both individual muscle measurements and side-to-side differences. After several investigations of individuals with chronic LBP and those who were asymptomatic, Hides et al. [4] suggested that total CSA side-to-side asymmetry of the multifidus muscle greater than 10% could potentially signify an abnormality. Other investigators are now referring to this guideline. [15] However, to our knowledge only 2 studies examined the reliability of side-to-side difference measurements, with ICCs varying between .77 and .97 for side-to-side difference measurements of total CSA and .82 to .94 for FCSA. [15,35] The ICCs for both side-to-side difference measurements reported in our study are similar. Despite both single muscle measurements and side-to-side difference measurements having high reliability coefficients, and similar SEMs, the error is relatively more important in the difference measurements, as they represent much smaller areas. For example, when using OsiriX, we found that the mean FCSA side-to-side difference of the multifidus muscle at L4-L5 was .75 cm^2 and the associated SEM was .19 cm^2, which is small in absolute terms but relatively large, as it represents approximately 25% of the mean measurement of multifidus asymmetry. The SEM

of .30 cm^2 represents only approximately 5% the mean multifidus muscle FCSA measurement of 5.84 cm^2. When changes over time are of interest, such as in preintervention and postintervention measurements, there may be a high probability that the differences observed are due to measurement error rather than true changes if they do not exceed two SEMs. [36] The greater measurement error related to side-to-side difference was confirmed by the Bland and Altman plots where the limits of agreement were relatively large in comparison to the other measurements.

Another strength of this study is that we studied patients with LBP conditions for whom the measurements are most likely to be of interest and who are expected to have more fatty infiltration [9,37] and muscle atrophy [1,4] compared with people who are healthy, increasing the difficulty of determining muscle boundaries during manual segmentation. Others authors reporting on the reliability of FCSA measurements primarily used samples of participants who were healthy. [15,16,18] Our results suggest that total muscle size, within the range studied, and spinal level (L4-L5, S1) do not influence intrarater reliability and inter-software agreement. Only the erector spinae muscle at S1 seems to have a proportionally higher SEM associated with the composition measurements with both software programs, in comparison with the other analyzed muscles. This finding could be explained by the high fatty infiltration and the smaller size of the erector spinae at S1, which increased the difficulty in determining the muscle borders.

A limitation of this study is the restriction of the measurement analysis to only 2 software packages. Even though inter-software reliability and agreement between OsiriX and ImageJ were excellent, even when measurements were obtained by an individual with modest experience, this finding might not be the case for other custom-made and commercial software used for image analysis. As determining inter-software reliability was the primary purpose of this study, replicate measures were obtained from the same image to introduce a potential extraneous source of measurement error. However, this represents a limitation when looking at intrarater reliability, where estimates might have been somewhat lower if the rater had repeated the entire procedure, including selecting the image from which to obtain the measurement.

3.5. CONCLUSION

In summary, a detailed protocol for paraspinal muscle CSA and composition measurements using two widely available, commonly used software programs was described, which yielded measurements with high inter-software and intrarater reliability. However, we found slightly lower reliability of side-to-side difference measurements as compared to measurements of single muscles, which may be an important consideration with the current interest in muscle asymmetry. Future related studies would benefit from using a standard muscle measurement protocol to facilitate replication and comparisons among studies.

3.5. REFERENCES

1. Danneels LA, Vanderstraeten GG, Cambier DC, Witvrouw EE, De Cuyper HJ. CT imaging of trunk muscles in chronic low back pain patients and healthy control subjects. *Eur Spine J* 2000;9(4):266-272.

2. Parkkola R. Rytökoski U. Kormano M. Magnetic resonance imaging of the discs and trunk muscles in patients with chronic low back pain and healthy controls subjects. *Spine* 1993;18(7):830-836.

3. Barker KL, Shamley DR, Jackson D. Changes in the cross-sectional area of multifidus and psoas in patients with unilateral back pain: the relationship to pain and disability. *Spine* 2004;29(22): E515-E519.

4. Hides J, Gilmore C, Stanton W, Bohlscheid E. Multifidus size and symmetry among chronic LBP and healthy asymptomatic subjects. *Man Ther* 2008;13(1):43-49.

5. Hodges P, Holm AK, Hansson T, Holm S. Rapid atrophy of the lumbar multifidus follows experimental disc or nerve root injury. *Spine* 2006; 31(25):2926-2933.

6. Ploumis A, Michailidis N, Christodoulou P, Kalaitzoglou I, Gouvas G, Beris A. Ipsilateral atrophy of paraspinal and psoas muscle in unilateral back pain patients with monosegmental degenerative disc disease. *Br J Radiol* 2011;84(1004);709-713.

7. Hides JA, Stokes MJ, Saide M, Jull GA, Cooper DH. Evidence of lumbar multifidus muscle wasting ipsilateral to symptoms in patients with acute/subacute low back pain. *Spine* 1994:19(2);165-172.

8. Mengiardi B, Schmid MR, Boos N, Pfirrmann CWA, Brunner F, Elfering A, et al. Fat content of lumbar paraspinal muscles in patients with chronic low back pain and in asymptomatic volunteers: quantification with MR spectroscopy. *Radiology* 2006;240(3):786-792.

9. Kjaer P, Bendix T, Sorensen JS, Korsholm L, Leboeuf-Yde C. Are MRI-defined fat infiltrations in the multifidus muscles associated with low back pain? *BMC Med* 2007;5:2.

10. Hyun JK, Lee JY, Lee SJ, Jeon JY. Asymmetric atrophy of multifidus muscle in patients with unilateral lumbosacral radiculopathy. *Spine* 2007;32(21):E598-E602.

11. Kader DF, Wardlaw D, Smith FW. Correlation between MRI changes in the lumbar multifidus muscles and leg pain. *Clin Radiol.* 2000;55:145-149.

12. Stokes MJ, Cooper RG, Morris G, Jayson MIV. Selective changes in multifidus dimensions in patients with chronic low back pain. *Eur Spine J* 1992;1(1):38-42.

13. Cooper RG, St Clair Forbers W, Jayson MI. Radiographic demonstration of paraspinal muscle wasting in patients with chronic low back pain. *Br J Rheumatol* 1992;31(6):389-394.

14. Hides JA, Richarson C, Jull GA. Multifidus muscle recovery is not automatic after resolution of acute, first episode low back pain. *Spine* 1996;21(23):2763-2769.

15. Niemeläinen R, Briand MM, Battie MC. Substantial asymmetry in paraspinal muscle cross-sectional areas in healthy adults questions its value as a marker of LBP and pathology. *Spine* 2011;36(25):2152-2157.

16. Ranson CA, Burnett AF, Kerslake R, Batt ME, O'Sullivan PB. An investigation into the use of MR imaging to determine the functional cross sectional area of lumbar paraspinal muscles. *Eur Spine J* 2006;15(6):764-773.

17. Fan S, Hu Z, Zhao F, Zhao X, Huang Y, Fang X. Multifidus muscle changes and clinical effects of one-level posterior lumbar interbody fusion: minimally invasive procedure versus conventional open approach. *Eur Spine J* 2009;19(2):316-324.

18. Gille O, Jolivet E, Dousset V, Degrise C, Obeid I, Vital JM, Skalli W. Erector spinae muscle changes on magnetic resonance imaging following lumbar surgery through a posterior approach. *Spine* 2007;32(11):1236-1241.

19. Hu JZ, He J, Zhao FD, Fang XQ, Zhou LN, Fan SW. An assessment of intra- and inter-reliability of the lumbar paraspinal muscle parameters using CT scan and magnetic resonance imaging. *Spine* 2011;36(13):E868-E874.

20. Marras WS, Jorgensen MJ, Granata KP, Wiand B. Female and male trunk geometry: size and prediction of the spine loading trunk muscles derived from MRI. *Clinic Biomech* 2001;16(1):38-46.

21. Kang CH, Shin MJ, Kim SM, Lee SH, Lee CS. MRI of paraspinal muscles in lumbar degenerative kyphosis patients and control patients with chronic low back pain. *Clin Radiol* 2007;62(5):479-486.

22. Hides JA, Belavy DL, Stanton W, Wilaon SJ, Rittweger J, Felsenberg D, Richardson CA. Magnetic resonance imaging assessment of trunk muscles during prolonged bed rest. *Spine* 2007; 32(15):1687-1692.

23. Keller A, Gunderson R, Reikeras O, Brox JI. Reliability of computed tomography measurements of paraspinal muscle cross-sectional area and density in patients with chronic low back pain. *Spine* 2003;28:1455-1460.

24. Dello SA, Stoot JH, van Stipout RS, Bloemen JG, Wigmore SJ, Dejong CH, Dam RM. Propspective volumetric assessment of the liver on a personal computer by nonradiologists prior to partial hepatectomy. *World J Surg* 2011;35(2):386-392.

25. Yamauchi T, Yamazaki M, Okawa A, Furuya T, Hayashi K, Sakuma T, Takahashi H, Yanagawa N, Koda M. Efficacy and reliability of highly functional open source DICOM software (OsiriX) in spine surgery. *J Clin Neurosci* 2010;17(6):756-759.

26. Albert S, Cristofari JP, Cox A, Bensimon JL, Guedon C, Barry B. Reconstruction mandibulaire par lambeau microanstomosé de fibula. Modélisation radiologique préorératoire par le logiciel OsiriX. *Ann Chir Plas Esthe* 2011;56(6):494-503.

27. Takatalo J. Karppinen J Niinimäki J, Taimela S, Näyhä S, Järvelin MR, Kyllonen E, Tervonen O. et al. Prevalence of degenerative imaging findings in lumbar magnetic resonance imaging among young adults. *Spine* 2009;34(16):1716-1721.

28. Portney LG, Watkins MP. *Fondations of Clinical Research: Applications to practice*. Second Edition, Prentice-Hall, 2000.

29. Stratford PW, Goldsmith CH. Use of the standard error as a reliability index of interest: an applied example using elbow flexor strength data. *Phys Ther* 1997;77(7):745-750.

30. Bland JM, Altman DG. Measuring agreement in method comparison studies. *Stat Methods Med Res* 1999;8(2):135-160.

31. Bland JM, Altman DG. Applying the right statistics:analyses of measurement studies. *Ultrasound Obstet Gynecol* 2003;22(1):85-93.

32. Bland JM, Altman DG. Statistical method for assessing agreement between two methods of clinical measurement. *Lancet* 1986;1(8476):307-310.

33. Ropponen A, Videman T, Battié MC. The reliability of paraspinal muscles composition measurements using routine spine MRI and their association with back function. *Man Ther* 2008;13(4):349-356.

34. Kim DY, Lee SH, Chung SK et al. Comparison of multifidus muscle atrophy and trunk extension muscle strength: percutaneous versus open pedicle screw fixation. *Spine* 2005;30(1):123-129.

35. Battié MC, Niemeläinen R, Gibbons LE, Dhillon S. Is level and side-specific multifidus asymmetry a marker for lumbar disc pathology? *Spine J* 2012;12(10):932-939.

36. Harvil LM. Standard error of measurement [NCME web site] Module 9, summer 1991. Available at: http//www.ncme.org/pubs/items.cfm. Accessed September 1st, 2011.

37. Lee JC, Cha JG, Kim Y, Kim YI, Shin BJ. Quantitative analysis of back muscle degeneration in the patients with the degenerative lumbar flat back using a digital image analysis: comparison with the normal controls. *Spine* 2008;33(3):318-325.

3.7. APPENDIX

3.7.1. MUSCLE TOTAL CSA MEASUREMENT PROTOCOL FOR OSIRIX AND IMAGEJ

1. Begin defining each Region of Interest (ROI) at the inferior-medial corner of the muscle.

2. Include fat between multifidus muscle and lamina within the multifidus ROI.

3. Include fat between erector spinae and multifidus muscles within the erector spinae muscle ROI.

4. Fat within the erector spinae muscle fascial boundary, lateral and posterior to iliocostalis lumborum, is included in the erector spinae muscle ROI for total CSA.

5. Fat within the erector spinae muscle fascial boundary posterior to the longissimus component is included in the erector spinae muscle ROI for total CSA.

6. Isolated deposits of intramuscular fat are included in the total CSA ROI for the muscle.

7. When a clear boundary between fat and muscle is not evident (ie, when a region of grey pixels is encountered), the ROI is defined through the middle of this region and in a manner that allows a reasonable approximation of the muscle's anticipated boundary.

3.7.2. DEFINING THE SIGNAL INTENSITY RANGE TO MEASUREMENT FCSA USING OSIRIX

1. Use the close polygon ROI tool (mouse button function) to select 4 to 6 ROIs of homogenous lean muscle tissue (excluding fat pixels) evenly and bilaterally (refer to Fig. 2-1B) within the paraspinal muscles (erector spinae and multifidus).

2. From the sample ROIs, use the lowest minimum value as the lower threshold bound and highest maximum value as the upper bound.

3. Use the close polygon ROI tool to trace the contour of the muscle of interest.

4. Double click on the muscle ROI results box and name the ROI (eg, right multifidus muscle). Close the ROI infomation window.

5. Make sure that muscle ROI (eg, right multifidus) is selected (results box should be highlighted in red). Open "ROI" pull-down menu in the main menu bar and choose *Set pixel Values to…* Select the option *outside ROIs* and then select the option *to this new value*. Change the new value to a negative number and click on OK. This step will "delete" the image background to apply the region-growing threshold only to the specific selected muscle ROI.

6. Open "ROI" pull-down menu in the main menu bar and choose *Grow region (2D/3D segmentation).* In the parameters section of the window, select the algorithm *threshold (lower/upper bounds)*. Make sure that *brush ROI* option is selected in the results section of the window and leave the window open. No other parameters/options need to be changed.

7. In the appropriate space of the parameters window section, enter the upper and lower threshold values previously defined in step 2 and leave the window open.

8. Click inside the paraspinal muscle ROI in a homogenous lean muscle tissue area.

9. To calculate the new FCSA ROI, click on *compute* button of the segmentation parameters window.

10. If needed, repeat steps 8 and 9 until lean muscle tissue of the entire muscle ROI is highlighted.

11. To combine all the brush ROIs together, open "ROI" pull-down menu in the main menu bar and choose *Brush ROIs* and then select *Merge selected brush ROIs.* Close the segmentation parameters window.

12. When completed, close the image slice and reopen from the main patients local database. The same image slice will appear with the initial image background and the newly created region-growing ROI representing the muscle FCSA.

13. Repeat steps 3 to 12 to measure the FCSA of another muscle. Give a different name to every muscle ROI (step 4).

3.7.3. DEFINING THE SIGNAL INTENSITY RANGE TO MEASURE MUSCLE FCSA USING IMAGEJ

1. Use the polygon selections ROI tool from the main menu bar to select 4 to 6 ROIs of sample homogenous lean muscle tissue (excluding fat pixels) evenly and bilaterally (refer to Fig. 2-1B) within the paraspinal muscle (erector spinae and multifidus). To obtain each ROI area, mean signal intensity and minimum/maximum values open "Analyze" pull-down menu and select *Measure* (or click control + M).

2. From sample ROIs, use lowest minimum value as lower threshold bound and highest maximum value as the upper bound.

3. Use the close polygon selections ROI tool from the main menu bar to trace the contour of the muscle of interest. To obtain muscle ROI area, mean signal intensity and minimum/maximun values open "Analyze" pull-down menu and select *Measure* (or click control + M).

4. Open "Image" pull-down menu and select *Adjust,* and then click on *Threshold.* Click on the *Set* button from the threshold window. Write the lower and upper threshold value previously determined in step 2 in the Set Threshold Levels window and click OK. Leave the threshold window open.

5. The threshold color will be applied to the entire image. To calculate the FCSA of the selected ROI only, open the "Analyze" pull-down menu, then select *set measurement* and click on the option *limit to threshold.* This option modification only needs to be done once.

6. To obtain FCSA of the selected muscle ROI open "Analyze" pull-down menu and then select *Measure* (or click control + M).

7. To reset the image to the initial background, click on the *Reset* button from the Threshold window.

Repeat steps 3 to 7 (excluding step 5) to measure the FCSA of another muscle.

CHAPTER 4

FACTORS ASSOCIATED WITH PARASPINAL MUSCLE ASYMMETRY IN SIZE AND COMPOSITION IN A GENERAL POPULATION SAMPLE OF MEN*

4.1. INTRODUCTION

Paraspinal muscle asymmetry and fatty infiltration have received considerable attention related to the aetiology and prognosis of LBP. [1-5] More specifically, attention has been focused on the multifidus muscle, with reports suggesting level or side-specific atrophy in relation to symptoms and localized spinal pathology. [2,6-12] The paraspinal muscle asymmetry observed in subjects with LBP and pathology has been suggested to be a consequence of disuse, denervation or reflex inhibition, [12] although the mechanism is not fully understood. Despite the development of imaging procedures to quantify the size, degree of asymmetry and fatty infiltration of the paraspinal muscles, investigators use a wide variety of methodologies and there are inconsistencies regarding the association between LBP and paraspinal muscle morphology.

Ultrasound studies have shown that paraspinal muscles are relatively symmetrical in individuals without a history of LBP, with multifidus mean side-to-side differences varying between 2.9-9.2%. [2,8,13] Accordingly, Hides et al suggested that asymmetry greater than 10% could be interpreted as an

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abnormality. [2] However, a recent MRI study found that 40% of 126 asymptomatic men had multifidus asymmetry exceeding 10%. [14] Furthermore, evidence from a recent systematic review suggests that multifidus and the paraspinal muscle group are significantly smaller in patients with chronic LBP when compared to healthy controls, and on the symptomatic side of patients suffering from chronic, but not acute, unilateral LBP when compared to the asymptomatic side. [15] Accordingly, many physical therapists attribute clinical meaning to atrophy and asymmetry observed in patients with LBP, which influences rehabilitation protocols. However, one needs to be aware of other factors that may influence or lead to such muscle variations before judging them as signifying risk or presence of back pain and pathology.

A number of individual and environmental factors have been associated with paraspinal muscle cross-sectional area (CSA), including age, [16-18] gender, [2,13,17,19] anthropometric factors, such as body mass [16] and height, [16] lean-body mass, [16,17] maximum weight lifted at work, [16] and time spent in sports and physically demanding leisure activities [16,20] and familial aggregation. [16] However, with the exception of studies of athletes performing asymmetrical sports, [21-25] few studies have specifically investigated determinants of paraspinal muscle asymmetry [2,13] and composition (e.g. fatty infiltration) [18,26,27] other than LBP and nerve root pathology.

In order to better interpret findings of paraspinal muscle asymmetry in clinical and research contexts, it is important to be aware of the range of factors that could influence such findings. The purpose of the present study was to

examine the association of a wide range of behavioral, environmental and constitutional factors with asymmetry in paraspinal muscle size and fatty infiltration in a general population sample of men. We hypothesized that greater paraspinal muscle asymmetry in size and composition would be associated with a history of LBP, greater age, disc height narrowing (degeneration) and participation in asymmetrical sports or work activities. We also hypothesized that more of the suspected factors related to low back pain and pathology would be associated with asymmetry of multifidus than erector spinae, and that asymmetry would be greater at the L5-S1 than L3-4 level, due to a higher prevalence of spinal pathology at this level.

4.2. MATERIAL AND METHODS

4.2.1. STUDY DESIGN

A cross-sectional, observational study was conducted to investigate factors associated with asymmetry in paraspinal muscle size and composition, as measured from T2-weighted MR axial images, in a general population sample of men. Information concerning behavioral, environmental and constitutional factors was obtained from a comprehensive structured interview and clinical examination of study participants.

4.2.2. STUDY SAMPLE

All 116 male monozygotic (MZ) twin pairs (232 men) initially recruited into the Twin Spine Study were candidates for the present study. [28] The Twin Spine Study subjects came from the population-based Finnish Twin Cohort that included all same-sex twins born in Finland before 1958 and still alive in 1975. [29] The initial selection of MZ twins for the Twin Spine Study was based on co-twin discordance for one of a number of common exposures, including occupational or leisure physical activities. The MZ subjects in the Twin Spine Study have been shown to be highly representative of the Finnish Twin Cohort, which is representative of the Finnish population, on a variety of factors examined, including LBP histories. [30] Other factors examined where the sample of MZ twins was similar to the Finnish Twin Cohort included occupational category, outdoor versus indoor work, shift work, work monotony, level of leisure-time physical activity, smoking status, life-satisfaction, level of education and social class. [30] However, the MZ Twin Spine Study subjects were found to have slightly more physically demanding jobs as compared to the Finnish Cohort and were more likely to be employed.[30] Of the 116 MZ twin pairs considered, only those with a history of spinal surgery or traumatic spinal fractures were excluded.

Prior to their participation in the Twin Spine Study, all subjects were informed of study procedures and gave informed consent. Study protocols were approved by the Ethical Committee of the Department of Public Health at the University of Helsinki and the Human Subjects Committee at the University of Washington. This study was also approved by the Health Ethics Research Board of the University of Alberta.

4.2.3. DATA ACQUISITION

Occupational Physical Demands

A detailed lifetime job history was obtained where every job, with its associated tasks, was described and classified into one of 18 categories according to job type and degree of physical loading. [28] Following cluster analysis, each job held by a subject was placed in one of four categories: 1= sedentary work, 2-3= progressive degrees of materials handling and positional loading, and 4= very heavy loading. [28] In this study, two variables were used to examine occupational physical loading: the mean lifetime job code (4-point scale) and the mean job code during the past year, weighted by the number of months in the job. A previous study using the same population evaluated the response reliability of work history. The intraclass correlation coefficients were 0.75 for sitting, 0.77 for driving and 0.60 for total lifting per day. [28] In addition, for each identified job, subjects described the types of tasks performed and the time spent in different postures (e.g. sitting twisted, bent). A variable was then created based on the time spent working in various combinations of bent and twisted positions (mean minutes/day) during the past year. Associations of occupational physical loading variables with paraspinal muscle asymmetry were assessed as the amount of physical loading has been shown to associate with paraspinal muscle size [16] and composition, [26] and many manual handling jobs comprise asymmetrical tasks. [31]

Sports and Leisure Physical Activities

Each subject was questioned about his history of sport and exercise participation. All regularly performed exercise and competitive sports were reviewed from the age of 12 years up to the time of the interview. Subjects were asked to describe the type of activity, as well as the frequency, intensity, session duration and the number of months or years of participation. Using a 5-year test-retest reliability interval, an intra-class correlation coefficient (ICC) of 0.81 was found for the repeatability for lifetime history of "mean exercise hr/week" of the most commonly performed exercise mode. [32] For the present study, a variable was created to summarize the mean number of hours/week spent in any regularly performed sports or exercise during the past year. A second variable (mean hours/week) was created to specifically examine current participation in *asymmetrical* sports (e.g. volleyball, soccer, tennis, squash, other ball games, ice hockey, golf, bowling, field sports involving throwing). As subjects were also asked about participation in other leisure activities involving heavy physical loading in the current year, a third summary variable for the mean number of hours/week spent in such activities was created. Associations of these variables with paraspinal muscle asymmetry were investigated as the amount of time spent in sports and exercise has been shown to influence muscle size. [20,32] Moreover, athletes participating in asymmetrical sports have been found to have asymmetrical trunk and back muscles. [21-25]

Low Back Pain History

A detailed history of low back pain was obtained for each subject. The frequency of low back pain during the last 12 months was classified using a seven-point scale ranging from none to daily (1=daily, 7=none). [28] Subjects were also asked to rate their worst episode of LBP in the last 12 months on a scale of 0 to 100. To quantify disability associated with LBP, subjects were asked about the number of days they experienced difficulty doing daily work due to their LBP over the last 12 months. The back pain history questions were repeated in interviews conducted approximately one month apart in 48 subjects. The test-retest reliability was examined using weighted-kappa coefficients with the 95% confidence intervals obtained from 1000 bootstrap samples. A weighted kappa coefficient of 0.83 (0.67-0.93) was found for the low back pain frequency measurements, 0.79 (0.61-0.92) for the pain numeric scale measurements, and 0.68 (0.40-0.92) for the number of disability days, indicating good to moderate reliability.

Lumbar MR Imaging and Disc Height Narrowing (Degeneration)

T2-weighted sagittal and axial MR images of each subject's lumbar spine were obtained with a 1.5 Tesla scanner using a 256 X 256 matrix size, following a standardized protocol. All subjects were lying prone for 30-45 minutes immediately prior to imaging.

Each lumbar disc was assessed for disc height narrowing (degeneration) on the mid sagittal MR image using a four-point scale (0= Normal, disc thicker than the upper disc, 1= Slight, disc as thick as the upper disc, if normal, 2=

Moderate, disc thinner than the upper disc, if normal, 3= Severe, endplates almost in contact). Intra-rater reliability of the measurements was previously examined in the same sample, yielding an intra-class correlation coefficient of 0.84. [33] We used disc height narrowing as an indicator of possible disc pathology, with or without nerve root involvement, as disc and associated nerve root lesions have been associated with paraspinal muscle asymmetry at the involved level, as well as the levels below. [12] Thus, two variables were created from qualitative ratings of disc height narrowing. First, a rating of disc narrowing was obtained from of the same level of measurement as the paraspinal muscle measurement. Second, the rating for the greatest disc height narrowing at any of the three levels above the measurement level was obtained. Disc height narrowing has been reported to be a predictor of LBP, [34] and paraspinal muscle asymmetry has been observed in subjects with disc degeneration. [10]

Age, handedness, lean body mass and body mass index

Associations of age, handedness, lean body mass and body mass index with paraspinal muscle asymmetry were also of interest. Several studies have reported an association between paraspinal muscle asymmetry and LBP and spinal pathology; which vary by age, [35-37] as does fatty infiltration. [3,18]

Handedness was coded as a dichotomous variable, evaluating whether the larger side (in muscle CSA or FCSA/CSA ratio) corresponded with the subject's dominant hand.

Lean body mass was computed based on the percent body fat obtained via bioelectrical impedance [(1-body fat %) x weight] and BMI was calculated from weight and height measurements. Lean people (individuals with a greater lean body mass) have larger paraspinal muscles (high muscle density). In fact, lean body mass has been reported to account for 45-65% of the variance in paraspinal muscle CSA. [16] While greater BMI has been associated with larger paraspinal muscle CSA, [16] but lower muscle density (more fatty infiltration). [38]

4.2.4. PARASPINAL MUSCLE MEASUREMENTS

The paraspinal muscle measurements of multifidus and erector spinae (dependent variables) were obtained from T2-weighted, axial MR images oriented through the center of each L3-L4 and L5-S1 intervertebral disc, perpendicular to the paraspinal muscle mass. As most underlying spinal pathologies are believed to occur at the two lowest lumbar levels and fatty infiltration has been reported to be most notable at L5-S1, [26] this level was selected as a level likely to be affected if lumbar pathology is present. The L3-L4 level was selected as a level less likely to be affected by pathology. The rater (M.F.) was experienced in quantitative MRI muscle measurements and was blinded to subjects' clinical histories.

The following muscle measurements were obtained for multifidus and erector spinae separately: total CSA side-to-side difference (% asymmetry) and ratio of functional CSA (FCSA)/total CSA side-to-side difference.

The rater directly obtained total CSA by segmenting or tracing multifidus and erector spinae separately, bilaterally, at each of the lumbar spinal levels

investigated. Asymmetry in total CSA was calculated as a percentage with the following formula: [(larger side – smaller side)/larger side) x 100]. As a change in muscle composition can occur without a change in muscle size, FCSA is a better indicator of muscle atrophy and contractility. [39] FCSA was calculated using a highly reliable thresholding technique. [40] This technique is based on the difference in signal intensity between muscle (low signal) and fat tissue (high signal), allowing for the separation of both tissues. Thus the ratio of FCSA/CSA was used as an indicator of muscle degeneration (fatty infiltration) and the difference in FCSA/CSA ratio between sides was used to assess asymmetry in muscle composition.

The quantitative measurements of multifidus and erector spinae muscles were obtained from T2-weighted axial images using ImageJ software (Version 1.43, National Institutes of Health, Bethesda, Maryland, downloadable at http://rsbweb.nih.gov/ij/download.html). Details regarding the measurement protocol have been published elsewhere. [40]

4.2.5 STATISTICAL ANALYSIS

In order to account for the correlated observations in co-twins, we used random-effects models to determine the contribution of suspected independent predictors of asymmetry in paraspinal muscle and fatty infiltration. A twinship variable indicating the twin pairs was used as a random effect in the analyses. The normality assumption was assessed and a log-transformation was performed, wherever appropriate. Spinal levels were analyzed separately.

Associations were initially examined using univariate linear regression. Because of the multiple comparisons and the possibility for chance findings, particular attention was paid to the consistency of the findings. A multivariable random effect model was fitted using the purposeful selection model strategy. [41] Variables that had a $P<0.20$ in univariate analyses were candidates for the multivariable model. Variables with a $P>0.05$ were removed from the multivariable model, after being assessed as potential confounders (variables leading to a ±15% change of the beta coefficients of the significant variables included in the multivariable model). Potential two-way interactions were assessed for those variables remaining in the multivariable model. Diagnostic plots were used to evaluate model assumptions and possible influential observations. The assumptions were tenable for each model and no influential observations were detected. Model collinearity was also investigated and was not an issue. We estimated the relative contribution of, or variance explained by, familial aggregation (genetic influence and early shared environment) using intra-class correlation coefficients (ICC). All analyses were performed using STATA (version 9.2.; StataCorp LP, College Station, TX, USA).

4.3. RESULTS

Of the 116 pairs of MZ twins, fifteen pairs were excluded. Five pairs were excluded due to poor MR image quality, nine due to prior back surgery and the last pair because of spinal fracture. Therefore, our final sample population was composed of 101 MZ twin pairs (202 men). Subjects' mean age was 49.35±8.40

(range: 35-69) and LBP frequency during the past 12 months was 5.03±2.02 on a 7-point scale (5=2-3 times a year). Subject characteristics and possible determinants of paraspinal muscle asymmetry are presented in Tables 4-1 and 4-2 The percentage of subjects with multifidus asymmetry >10% was 34.2% at L3-L4 and 30.7% at L5-S1, while 13.4% of subjects had erector spinae asymmetry >10% at L3-L4 and 57.9% at L5-S1 (Table 4-3).

Table 4-1: Characteristics of Participants and Possible Determinants of Paraspinal Muscle Asymmetry

Factor	Mean (SD)
Age (years)	49.35 (8.40)
BMI (weight in kg/height meters^2)	25.96 (3.44)
Lean body mass [(1-body fat%) x weight].	59.69 (7.31)
Handedness (right)	94.0%
Occupational physical demands	
Mean lifetime job code (weighted 4-point scale)	2.50 (0.92)
Mean job code, past year (weighted 4-point scale)	1.83 (1.30)
Mean time working in twisted/bent postures (mean min/day)	97.19 (100.46)
Sport and leisure physical activities	
Sports and exercise (mean hr/wk)	3.87 (5.63)
Heavy leisure physical activities (mean hr/wk)	1.29 (6.86)
Asymmetrical sports (mean hr/wk)	0.33 (1.07)
Low back pain	
LBP frequency in past 12 months (7-point scale)	5.03 (2.02)
Pain severity in past 12 months (0-100)	28.54 (31.62)
Number of days experiencing difficulty doing daily work in past 12 months.	11.16 (52.47)

BMI= body mass index

Table 4-2: Disc height narrowing in participants investigated as possible determinants of paraspinal muscle asymmetry

Possible determinants	Rating (Points) on a scale 0-3	No. (%) participants
Disc height narrowing L3-L4 †	0	120 (59.70)
	1	58 (28.86)
	2	18 (8.96)
	3	5 (2.49)
Disc height narrowing L5-S1	0	92 (45.54)
	1	60 (29.70)
	2	27 (13.37)
	3	23 (11.39)
Greatest disc height narrowing at any of the 3 levels above L3-L4	0	100 (49.50)
	1	63 (31.19)
	2	31 (15.35)
	3	8 (3.96)
Greatest disc height narrowing at any of the 3 levels above L5-S1	0	31 (15.35
	1	91 (45.05)
	2	44 (21.78)
	3	36 (17.87)

†: Ratings for disc height narrowing were available for only 201 participants at L3-L4

Table 4-3: Muscle measurements, means (SD), by spinal level and percentage of asymmetry with exceeding 10%

Muscle Measurement	L3-L4		L5-S1	
	Multifidus	Erector Spinae	Multifidus	Erector Spinae
% asymmetry in total CSA	8.44 (5.92)	5.24 (4.03)	7.46 (5.72)	13.61 (9.39)
Side-to side difference in ratio of FCSA to CSA	0.07 (0.05)	0.12 (0.07)	0.07 (0.05)	0.16 (0.10)
% of participants with CSA asymmetry >10%	34.2	30.7	13.4	57.9

CSA=Cross-Sectional Area, FCSA=Functional Cross-Sectional Area

Crude analyses, followed by multivariable analyses, were conducted for asymmetry in total CSA and FCSA/CSA for each muscle and spinal level.

4.3.1. FACTORS ASSOCIATED WITH PARASPINAL MUSCLE CSA ASYMMETRY

Statistically significant associations with asymmetry in CSA were more often detected at the L3-L4 than L5-S1 spinal level (Table 4-4). Of the factors investigated, handedness (p=0.03) was associated with less CSA asymmetry, while greater age (p=0.02) and more disc height narrowing at the same level (p=0.001) were associated with more *erector spinae* CSA asymmetry at L3-L4. Less time spent in sports and exercise (p=0.04) and handedness (p=0.015) were associated with erector spinae CSA asymmetry at L5-S1. Age, disc height narrowing and handedness remained in the multivariable model, explaining 9% of the variance in erector spinae total CSA asymmetry at L3-L4. Whereas, sports and exercise participation, as well as disc height narrowing at any of the 3 levels above and handedness, entered the multivariable model of total CSA asymmetry of erector spinae at L5-S1, explaining 6% of the variance, with familial aggregation explaining an additional 18%.

With respect to *multifidus*, more CSA asymmetry at L3-L4 was associated with lower (less physically demanding) job codes, both over the past year (p=0.01) and lifetime (p=0.04), as well as less disc height narrowing at any of the 3 levels above (p=0.01). Both mean job code over the past year and disc height narrowing remained in the multivariable model and together explained 6% of the variance in multifidus CSA asymmetry at L3-L4. While handedness (p=0.001) was the only significant factor associated with greater multifidus CSA asymmetry at L5-S1 in the crude and multivariable analyses, explaining 5% of the variance.

Table 4-4: Univariable regression coefficients [and 95% CI] for associations of % asymmetry in multifidus and erector spinae CSA with factors of interest.

Factor	L3-L4		L5-S1	
	Multifidus^	Erector Spinae	Multifidus^	Erector Spinae^†
Anthropometrics				
Age (years)	.0081 [-.0065, .0228]	**.0773*** [.0120, .1425]	.0155 [-0.0014, .0325]	.0008 [-.0181, .0164]
BMI (weight in kg/height meters^2)	-.0195 [-.0553, .0162]	-.0042 [-.1657, .1572]	-.0018 [-.0437, .0400]	-.0072 [-.0485, .0340]
Lean body mass [(1-body fat%) x weight]	-.0013 [-.0176, .0174]	-.2453 [-.1041, .0550]	-.0048 [-.0250, .0153]	.0026 [-.0176, .0228]
Handedness	.0538 [-.2105, .3182]	**-1.2615*** [-2.4190, -.1040]	**.4760*** [.1853, .7668]	**-.3310*** [-.5981, -.6384]
Occupational physical loading				
Mean lifetime job code (weighted 4-point scale)	**-.1382*** [-.2706, -.0059]	.2562 [-.3435, 0.8561]	-.0010 [-.1568, .1547]	-.0364 [-.1818, .1088]
Mean job code, past year (weighted 4-point scale)	**-.1177*** [-.2112, -.0246]	-.0225 [-.4506, .4055]	-.0840 [-.1944, .0262]	.0455 [-.0602, .1512]
Mean time working in twisted/bent postures (mean min/day)	5.26e^{-06} [-.0012, .0012]	.0035 [-.0019, .0090]	-.0012 [-.0026, .0001]	.0002 [-.0011, .0016]
Other physical activities				
Sports and exercises (mean hr/wk)	.0004 [-.0213, .0223]	.0246 [-.0740, .1233]	-.0019 [-.0275, .0236]	**-.0251*** [-.0492, -.0010]
Leisure activity with heavy physical loading (mean hr/wk)	.0023 [-.0155, .0202]	-.0467 [-.1274, .0340]	-.0036 [-.0243, .0173]	-.0009 [-.0208, .0190]
Asymmetrical sports (mean hr/wk)	0.0100 [.1053, .1255]	-.1125 [-.6337, .4086]	-.1196 [-.2538, .0144]	-.0204 [-.1482, .1074]
Lower back Health				
LBP frequency past 12 months (7-point scale)	-.0154 [-.0767, .0457]	.0704 [-.2042, .3452]	.0041 [-.0671, .0753]	-.0332 [-.1021, .0356]
Pain severity past 12 months (0-100)	-.0007 [-.0046, .0031]	.0012 [-.0162, .0188]	-.0011 [-.0056, .0034]	2.96e^{-06} [-.0043, .0043]
Number of days experiencing difficulty doing daily work past 12 months.	-.0001 [-.0024, .0022]	-.0020 [-.0125, .0085]	.0016 [-.0010, .0044]	-.0002 [-.0028, .0023]
Disc height narrowing at the same level (0-3-point scale)	-.1095 [-.2711, .0519]	**1.1912*** [.4790, 1.9035]	-.0117 [-.1528, .1294]	.0394 [-.0980, .1770]
Disc height narrowing at any of 3 levels above (0-3-point scale)	**-.1805*** [-.3214, -.0397]	.1929 [-.4515, .8373]	-.0011 [-.1519, .1496]	.1309 [-.0145, .2763]

^ = Outcome measure was log-transformed.

† The morphology of the erector spinae is very different at L5-S1 as compared to L3-L4, which may explain the different distribution of the data between the two levels.

***** = P<0.05

4.3.2. FACTORS ASSOCIATED WITH SIDE-TO-SIDE DIFFERENCES IN FCSA/CSA

Unlike CSA asymmetry, associations with side-to-side differences in ratio of FCSA/CSA, representing asymmetry in fatty infiltration, were more often observed at L5-S1 (Table 4-5). In fact, handedness was the only significant factor associated with less side-to-side differences in FCSA/CSA at L3-L4 for the erector spinae ($p=0.026$) and multifidus ($p<0.001$) in the crude and multivariable analyses. Handedness explained 3% of the variance in erector spinae and 7% of the variance in the multifidus side-to-side differences in FCSA/CSA, with an additional 16% and 7% from familial aggregation, respectively.

At L5-S1, handedness ($p=0.001$), less sports and exercise participation ($p=0.04$) and more back pain severity over the past year ($p=0.009$) were associated with side-to-side differences in FCSA/CSA for *erector spinae*. Handedness and pain severity remained in the multivariable model, together explaining 7% of the variance at L5-S1, with familial aggregation explaining an additional 20%.

With respect to multifidus side-to-side differences in FCSA/CSA at L5-S1, handedness ($p<0.001$), more disc height narrowing ($p=0.03$) at any of the 3 levels above were crudely associated and the number of days experiencing difficulty doing daily work during the past 12 months due to low back pain approached significance ($p=0.06$). All three variables entered the multivariable model, together explaining 13% of the variance, with familial aggregation explaining an additional 10%.

Table 4-5: Univariable regression coefficients [and 95% CI] for associations of side-to-side difference in FCSA/CSA ratio in multifidus and erector spinae with factors of interest.

Factor	L3-L4		L5-S1	
	Multifidus^	Erector Spinae	Multifidus^	Erector Spinae
Anthropometrics				
Age (years)	.0028 [-.0106, .0164]	.0008 [-.0003, .0020]	.0020 [-.0115, .0162]	-.0006 [-.0022, .0010]
BMI (weight in kg/height meters^2)	-.0039 [-.0361, .0282]	.0007 [-.0021, .0036]	-.0073 [-.0397, .0250]	.0033 [-.0006, .0072]
Lean body mass [(1-body fat%) x weight].	0.0054 [-.0104, .0213]	.0001 [-.0013, .0015]	.0057 [-.0215, .0099]	.0011 [-.0007, .0030]
Handedness	**-.4459*** [-.6812, -.2107]	**-.0347*** [-.0653, -.0040]	**-.4457*** [-.6766, -.2147]	**-.0618*** [-.0993, -.0243]
Occupational physical loading				
Mean lifetime job code (weighted 4 point scale)	.0502 [-.0642, .1648]	.0063 [-.0037, .0164]	.0149 [-.1306, .1008]	.0084 [-.0056, .0225]
Mean job code, past year (weighted 4 point scale)	-.0167 [-.1011, .0676]	.00003 [-.0073, .0074]	-.0215 [-.1073, .0643]	.0017 [-.0085, .0120]
Mean time working in twisted/bent postures (mean min/day)	0.0001 [-.0009, .0011]	.00003 [-.00005, .0001]	-.0004 [-.0015, .0006]	.0001 [-.0001, .0001]
Other physical activities				
Sports and exercises (mean hr/wk)	.0125 [-.0065, .0316]	-.0013 [-.0029, .0003]	-.0013 [-.0214, .0186]	**-.0023*** [-.0047, -.00004]
Leisure activity with heavy physical loading (mean hr/wk)	.0128 [-.0281, .0025]	.0002 [-.0011, .0016]	.0011 [-.0141, .0164]	-.0005 [-.0024, .0014]
Asymmetrical sports (mean hr/wk)	.0028 [-.0970, .1026]	-.0005 [-.0094, .0083]	-.0430 [-.1422, .0560]	-.0013 [-.0137, .0110]
Lower back Health				
LBP frequency past 12 months (7 point scale)	.0294 [-.0236, .0826]	.0045 [-.0093, .0001]	-.0148 [-.0714, .0417]	-.0045 [-.0111, .0020]
Pain severity past 12 months (0-100)	-.0022 [-.0056, .0011]	.0002 [-.00007, .0005]	.0020 [-.0014, .0056]	**.0005*** [.0001, .0009]
Number of days experiencing difficulty doing daily work past 12 months.	-.0017 [-.0037, .0002]	.00006 [-.0001, .0002]	-.0019 [-.0039, .0005]	-.00004 [-.0002, .0002]
Disc height narrowing at the same level (4 point scale)	.0021 [-.1382, .1424]	.0117 [-.0008, .0243]	.0878 [-.0205, .1961]	-.0008 [-.0141, .0124]
Disc height narrowing at any of 3 levels above (4 point scale)	-.0366 [-.1638, .0905]	.0073 [-.0039, .0187]	**.1285*** [.0147, .2424]	.0042 [-.0099, .0183]

^ = Outcome measure was log-transformed.
***** = P<0.05

4.4. DISCUSSION

Few of the investigated factors were associated with paraspinal muscle asymmetry, and those identified explained little of the variance in muscle asymmetry. Furthermore, the associations identified, including age, handedness, physical activity levels at work or leisure, disc height narrowing, and back pain severity during the prior year were not only modest, but also inconsistent with the exception of handedness. Familial aggregation explained the greatest percentage of the variance in paraspinal muscle asymmetry, which may not be entirely surprising as familial aggregation and genetic influences have been previously shown to be substantial determinants of paraspinal muscle size. [16,42] BMI and lean body weight were not associated with any of the measures of paraspinal muscle asymmetry.

In our general population sample of men, the mean percentage of multifidus CSA asymmetry was similar to other related studies. [2,13] We found that 57.92% of subjects had erector spinae asymmetry greater than 10% at L5-S1, which is very similar to what has been previously reported. Ranson et al. [23] reported that 56% of young professional fast bowlers (mean age 26 years old) had erector spinae FCSA asymmetry greater than 10% at L5, as compared with 53% in a group of athletes involved in non-asymmetrical sports.

Our results suggest that individuals with higher physically demanding jobs or exercise and sports participation may have less asymmetry in paraspinal muscle size and fatty infiltration. A previous report found that individuals with greater participation in sports or heavy physical work had significantly less severe

multifidus fatty infiltration, but asymmetry was not examined. [26] Contrary to our original hypothesis, our results showed no significant association between paraspinal muscle asymmetry and mean hrs/week spent in asymmetrical sports at non-competitive levels. It should be noted, however, that only a small group of subjects in our sample participated in such sports and the time spent was far less than elite athletes. While some other imaging studies have reported significant paraspinal or trunk muscle asymmetry in the elite athletes performing "asymmetrical sports", [22-24,43] not all asymmetrical sports have been found to lead to significant paraspinal muscle asymmetry. [44] When hypertrophy was reported on the dominant side, the mean % difference between sides varied from 0.6% to 9.1%, [23,43] which is similar to what has been reported in non-athlete populations. [2,8,13]

Handedness was associated with greater multifidus CSA asymmetry at L5-S1, but the opposite was true for the erector spinae at both spinal levels. While the majority of subjects had a larger multifidus on the right side, 66.8% and 56.4% had a larger erector spinae muscle on the left side at L3-L4 and L5-S1, respectively. Although, both muscles are extensors, the multifidus is mainly a stabilizer providing support to local spinal segments, as the fibers only span over few vertebras. On the other hand, the activity of the erector spinae varies with different positions. For example, when holding a weight in one hand, the center of gravity is displaced sideways and the contralateral erector spinae must contract to avoid collapse and lateral flexion.[45] Our results also suggest that handedness was associated with less side-to-side differences in FCSA/CSA ratio. As most subjects

had a greater erector spinae on the left side, it is not surprising that the majority also had less fatty infiltration (higher FCSA/CSA) on the left side. Interestingly, subjects with a leaner multifidus or erector spinae muscle on the side of their dominant hand were also more active and had less asymmetry in muscle composition, which supports our finding suggesting that more active people have less paraspinal muscle asymmetry.

We found no significant association between LBP severity and disability in our univariable analysis, with the exception of the erector spinae difference in muscle composition at L5-S1. Other studies also failed to find a clear association between LBP intensity or disability and paraspinal muscle morphology. [3,4,6,10] Similarly to Kalichman et al., [38] reporting no significant association between paraspinal muscle density (an indicator of muscle degeneration) and the occurrence of LBP, our results showed no significant association between paraspinal muscle asymmetry and LBP frequency. Thus, our study does not support our initial hypothesis, as LBP history was not consistently associated with paraspinal muscle asymmetry. Moreover, contrary to our original hypothesis, back pain history and disc height narrowing were not found to be more highly associated with asymmetry in multifidus than erector spinae. However, it is important to note that we did not distinguish unilateral LBP and radicular symptoms from other back pain problems. Most studies reporting on the association between paraspinal muscle asymmetry and LBP examined patients with a clinical presentation of unilateral LBP. [2,6,8-10,46-48]

As all of the Twin Spine Study MZ twin pairs meeting the inclusion criteria were included in this study and this was a secondary data analysis, there was no possibility to add more subjects. However, the 95% CIs of the significant regression coefficients are quite narrow, suggesting that the precision of the estimates is good. Study strengths include the use and representativeness of a general population sample with extensive interview data, which allowed for the evaluation of several environmental and behavioral factors. Also, the selection of twins allowed us to investigate the portion of the variance in paraspinal muscle asymmetry explained by familial aggregation, representing shared early environmental and genetic influences. In a previous measurement study, we have also shown that our quantitative paraspinal muscle measurement technique is highly reliable in the hands of the same assessor who obtained measurements in the present study. [40] Furthermore, we estimated the standard error of measurement (SEM) for both outcomes and most asymmetry measurements in the current study were above 2 SEMs and likely to represent true asymmetries rather than measurement error. Thus, it is unclear what accounted for the large portion of unexplained variance in muscle asymmetry, but it may be that some degree of asymmetry is a naturally occurring phenomenon in human anatomy, including paraspinal muscle.

Limitations related to the study measurements include that the MR images were obtained in the 1990s when image quality was lower than typically seen today, and the low amount of fatty infiltration present at L3-L4 increased the difficulty of determining muscle borders. Another limitation was the reliance on

subjects' recall for LBP history and occupation and leisure physical loading factors. Although the reliability coefficients were generally good for these measurements, they certainly contain some degree of error, diluting associations. Finally, due to the broad number of investigated factors, many comparisons have been made in our analysis, which increase the probability of chance findings or making a type I error.

4.5. CONCLUSION

Our findings suggest that the behavioral, environmental and constitutional factors investigated, including age, BMI, handedness, physical activities, intervertebral disc height narrowing and back pain history, had little or no association with paraspinal muscle asymmetry, as observed in a population-based sample of men. The few associations identified were generally inconsistent across muscles and spinal levels, with the exception of handedness**,** and explained little of the variance in paraspinal muscle asymmetry in size and composition. Familial aggregation was found to be the strongest predictor of asymmetry in paraspinal muscle composition, although it, too, explained little of the asymmetry observed. Some degree of paraspinal muscle asymmetry may be a naturally occurring phenomenon and the particular factors studied, as found in a general population sample, may not be of major concern when considering paraspinal muscle asymmetry observed in clinical or research contexts. Finally, the modest and inconsistent association of paraspinal muscle asymmetry with LBP history,

questions its consideration as an important aspect of clinical assessment or as a target for rehabilitation.

4.6. REFERENCES

1. Danneels LA, Vanderstraeten GG, Cambier DC, Witvrouw EE, De Cuyper HJ. CT imaging of trunk muscles in chronic low back pain patients and healthy control subjects. *Eur Spine J* 2000;9(4):266-272.

2. Hides J, Gilmore C, Stanton W, Bohlscheid E. Multifidus size and symmetry among chronic LBP and healthy asymptomatic subjects. *Man Ther* 2008;13(1):43-49.

3. Kader DF, Wardlaw D, Smith FW. Correlation between the MRI changes in the lumbar multifidus muscles and leg pain. *Clin Radiol* 2000;55(2):145-149.

4. Mengiardi B, Schmid MR, Boos N, Pfirrmann CWA, Brunner F, Elfering A, et al. Fat content of lumbar paraspinal muscles in patients with chronic low back pain and in asymptomatic volunteers: Quantification with MR spectroscopy. *Radiology* 2006;240(3):786-792.

5. Parkkola R, Rytokoski U, Kormano M. Magnetic resonance imaging of the discs and trunk muscles in patients with chronic low back pain and healthy control subjects. *Spine* 1993;18(7):830-836.

6. Barker KL, Shamley DR, Jackson D. Changes in the cross-sectional area of multifidus and psoas in patients with unilateral back pain: the relationship to pain and disability. *Spine* 2004;29(22):E515-519.

7. Campbell WW, Vasconcelos O, Laine FJ. Focal atrophy of the multifidus muscle in lumbosacral radiculopathy. *Muscle Nerve* 1998;21(10):1350-1353.

8. Hides JA, Stokes MJ, Saide M, Jull GA, Cooper DH. Evidence of lumbar multifidus muscle wasting ipsilateral to symptoms in patients with acute/subacute low back pain. *Spine* 1994;19(2):165-172.

9. Hyun JK, Lee JY, Lee SJ, Jeon JY. Asymmetric atrophy of multifidus muscle in patients with unilateral lumbosacral radiculopathy. *Spine* 2007;32(21):E598-E602.

10. Ploumis A, Michailidis N, Christodoulou P, Kalaitzoglou I, Gouvas G, Beris A. Ipsilateral atrophy of paraspinal and psoas muscle in unilateral back pain patients with monosegmental degenerative disc disease. *Br J Radiol* 2011;84(1004):709-713.

11. Hayashi N, Masumoto T, Abe O, Aoki S, Ohtomo K, Tajiri Y. Accuracy of abnormal paraspinal muscle findings on contrast-enhanced MR images

as indirect signs of unilateral cervical root-avulsion injury. *Radiology* 2002;223(2):397-402.

12. Hodges P, Holm AK, Hansson T, Holm S. Rapid atrophy of the lumbar multifidus follows experimental disc or nerve root injury. *Spine* 2006;31(25):2926-2933.

13. Stokes M, Rankin G, Newham DJ. Ultrasound imaging of lumbar multifidus muscle: Normal reference ranges for measurements and practical guidance on the technique. *Man Ther* 2005;10(2):116-126.

14. Niemelainen R, Briand M-, Battie MC. Substantial asymmetry in paraspinal muscle cross-sectional area in healthy adults questions its value as a marker of low back pain and pathology. *Spine* 2011;36(25):2152-2157.

15. Fortin M, Macedo L. Multifidus and Paraspinal muscle Group Cross-Sectional Areas of Patients with Low Back Pain and Control Patients: A Systematic Review With a Focus on Blinding. *Phys Ther* 2013;93(7):873-888.

16. Gibbons LE, Videman T, Battié MC, Kaprio J. Determinants of paraspinal muscle cross-sectional area in male monozygotic twins. *Phys Ther* 1998;78(6):602-612.

17. Mannion AF, Kaser L, Weber E, Rhyner A, Dvorak J, Muntener M. Influence of age and duration of symptoms on fibre type distribution and size of the back muscles chronic low back pain patients. *Eur Spine J* 2000 2000;9(4):273-281.

18. McLoughlin RF, D'Arcy EM, Brittain MM, Fitzgerald O, Masterson JB. The significance of fat and muscle areas in the lumbar paraspinal space: A CT study. *J Comput Assisted Tomogr* 1994;18(2):275-278.

19. Cooper RG, St Clair Forbes W, Jayson MIV. Radiographic demonstration of paraspinal muscle wasting in patients with chronic low back pain. *Br J Rheumatol* 1992;31(6):389-394.

20. Peltonen JE, Taimela S, Erkintalo M, Salminen JJ, Oksanen A, Kujala UM. Back extensor and psoas muscle cross-sectional area, prior physical training, and trunk muscle strength - A longitudinal study in adolescent girls. *Eur J Appl Physiol Occup Physiol* 1998;77(1-2):66-71.

21. Engstrom CM, Walker DG, Kippers V, Mehnert AJH. Quadratus lumborum asymmetry and L4 pars injury in fast bowlers: A prospective MR study. *Med Sci Sports Exerc* 2007;39(6):910-917.

22. Hides J, Fan T, Stanton W, Stanton P, Mcmahon K, Wilson S. Psoas and quadratus lumborum muscle asymmetry among elite Australian Football League players. *Br J Sports Med* 2010;44(8):563-567.

23. Ranson C, Burnett A, O'Sullivan P, Batt M, Kerslake R. The lumbar paraspinal muscle morphometry of fast bowlers in cricket. *Clin J Sport Med* 2008;18(1):31-37.

24. Sanchis-Moysi J, Idoate F, Izquierdo M, Calbet JAL, Dorado C. Iliopsoas and gluteal muscles are asymmetric in tennis players but not in soccer players. *PLoS ONE* 2011;6(7).

25. Sanchis-Moysi J, Idoate F, Dorado C, Alayó S, Calbet JAL. Large asymmetric hypertrophy of rectus abdominis muscle in professional tennis players. *PLoS ONE* 2010;5(12).

26. Kjaer P, Bendix T, Sorensen JS, Korsholm L, Leboeuf-Yde C. Are MRI-defined fat infiltrations in the multifidus muscles associated with low back pain? *BMC Med* 2007;5.

27. Alaranta H, Tallroth K, Soukka A, Heliovaara M. Fat content of lumbar extensor muscles and low back disability: A radiographic and clinical comparison. *J Spinal Disord* 1993;6(2):137-140.

28. Battie MC, Videman T, Gibbons LE, Fisher LD, Manninen H, Gill K. Determinants of lumbar disc degeneration: A study relating lifetime exposures and magnetic resonance imaging findings in identical twins. *Spine* 1995;20(24):2601-2612.

29. Kaprio J, Koskenvuo M. Genetic and environmental factors in complex diseases: The older Finnish Twin Cohort. *Twin Research* 2002;5(5):358-365.

30. Simonen RL, Videman T, Kaprio J, Levälahti E, Battié MC. Factors associated with exercise lifestyle - A study of monozygotic twins. *Int J Sports Med* 2003;24(7):499-505.

31. Gagnon M, Larrivé A, Desjardins P. Strategies of load tilts and shoulders positioning in asymmetrical lifting. A concomitant evaluation of the reference systems of axes. *Clin Biomech* 2000;15(7):478-488.

32. Ropponen A, Levälahti E, Simonen R, Videman T, Battié MC. Repeatability of lifetime exercise reporting. *Scand J Med and Sci Sports* 2001;11(3):185-192.

33. Videman T, Battié MC, Ripatti S, Gill K, Manninen H, Kaprio J. Determinants of the progression in lumbar degeneration: A 5-year follow-up study of adult male monozygotic twins. *Spine* 2006;31(6):671-678.

34. Videman T, Battié MC, Gibbons LE, Maravilla K, Manninen H, Kaprio J. Associations between back pain history and lumbar MRI findings. *Spine* 2003;28(6):582-588.

35. Hoy D, Brooks P, Blyth F, Buchbinder R. The Epidemiology of low back pain. *Best Pract Res Clin Rheumatol* 2010;24(6):769-781.

36. Gourmelen J, Chastang J-, Ozguler A, Lanoë J-, Ravaud J-, Leclerc A. Frequency of low back pain among men and women aged 30 to 64 years in France. Results of two national surveys. *Ann Readapt Med Phys* 2007;50(8):640-644.

37. Horváth G, Koroknai G, Ács B, Than P, Illés T. Prevalence of low back pain and lumbar spine degenerative disorders. Questionnaire survey and clinical-radiological analysis of a representative Hungarian population. *Int Orthop* 2010;34(8):1245-1249.

38. Kalichman L, Hodges P, Li L, Guermazi A, Hunter DJ. Changes in paraspinal muscles and their association with low back pain and spinal degeneration: CT study. *Eur Spine J* 2010;19(7):1136-1144.

39. Ranson CA, Burnett AF, Kerslake R, Batt ME, O'Sullivan PB. An investigation into the use of MR imaging to determine the functional cross sectional area of lumbar paraspinal muscles. *Eur Spine J* 2006;15(6):764-773.

40. Fortin M, Battie MC. Quantitative Paraspinal Muscle Measurements: Inter-Software Reliability and Agreement Using OsiriX and ImageJ. *Phys Ther* 2012;92(6):853-864.

41. Hosmer DW, Lemeshow S, May S. Model Development. Applied Survival Analysis: Regression Modeling of Time to Event Data. 2nd Edition ed.: Wiley-Interscience;2008. p. 132-168.

42. Ropponen A, Levälahti E, Videman T, Kaprio J, Battié MC. The role of genetics and environment in lifting force and isometric trunk extensor endurance. *Phys Ther* 2004;84(7):608-621.

43. Stewart S, Stanton W, Wilson S, Hides J. Consistency in size and asymmetry of the psoas major muscle among elite footballers. *Br J Sports Med* 2010;44(16):1173-1177.

44. McGregor AH, Anderton L, Gedroyc WMW. The trunk muscles of elite oarsmen. *Br J Sports Med* 2002;36(3):214-217.

45. Middleditch A, Olivier J. Muscles of the vertebral column. Functional Anatomy of the Spine. Second edition ed.: Elsevier Butterworth-Heinemann; 2005. p. 87-152.

46. Kulig K, Scheid AR, Beauregard R, Popovich Jr. JM, Beneck GJ, Colletti PM. Multifidus morphology in persons scheduled for single-level lumbar microdiscectomy: Qualitative and quantitative assessment with anatomical correlates. *Am J Phys Med Rehabil* 2009;88(5):355-361.

47. Kim WH, Lee S-, Lee DY. Changes in the cross-sectional area of multifdus and psoas in unilateral sciatica caused by lumbar disc herniation. *J Korean Neurosurg Soc* 2011 2011;50(3):201-204.

48. Dangaria TR, Naesh O. Changes in cross-sectional area of psoas major muscle in unilateral sciatica caused by disc herniation. *Spine* 1998;23(8):928-931.

CHAPTER 5

PARASPINAL MUSCLE MORPHOLOGY AND COMPOSITION IN A GENERAL POPULATION SAMPLE OF MEN: A 15-YEAR LONGITUDINAL MRI STUDY*

5.1. INTRODUCTION

The lumbar paraspinal muscles help stabilize the spine, maintain proper posture and assist in trunk movement. The multifidus muscle, in particular, plays a critical role in spinal stability. Paraspinal muscle size has been associated with gender, [1,2] body weight, [3] physical activity levels [3,4] and familial aggregation. [3] Paraspinal muscle atrophy, [5] asymmetry [5] and fatty infiltration [6,7] have been observed in relation to low back pain (LBP) problems, yet these associations have not been consistently found. [8,9]

Several longitudinal studies have reported age-related changes of skeletal muscle in adulthood, including a decrease in size, [10] loss of strength [10] and increased fatty infiltration. [11,12] While such longitudinal studies are not available specifically for lumbar paraspinal muscle, cross-sectional studies have revealed lesser functional cross-sectional area (FCSA, fat-free area) of paraspinal muscle associated with greater age, [13] but associations of total cross-sectional area (CSA) and degree of fatty infiltration in paraspinal muscle with age are conflicting.

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[2,3,13,14] Age has not been associated with paraspinal muscle asymmetry when examined in asymptomatic and symptomatic subjects. [2,15]

Longitudinal studies are needed to clarify age-related changes in paraspinal muscle size, composition and asymmetry in adulthood. While some short-term follow-up studies have evaluated paraspinal muscle changes in elite athletes (with or without LBP) [16] and LBP patients following an exercise program, [17] we are aware of no studies examining changes in lumbar paraspinal muscles in the general population. The purpose of this study was to 1) define the natural progression of age-related changes in paraspinal muscle over a 15-year period during adulthood and 2) investigate the influence of the lifestyle and individual factors (e.g. physical activity levels at work and leisure, body mass index (BMI), and LBP history).

5.2. MATERIAL AND METHODS

5.2.1. STUDY SAMPLE

Participants for this study came from the 116 monozygotic (MZ) twin pairs initially recruited in the Twin Spine Study, which were drawn from the population-based Finnish Twin Cohort that included all same-sex twins born in Finland before 1958 and still alive in 1975. [18] The initial selection of male MZ twins, which has been described in detail previously, [18] was based on co-twin discordance for one of a number of common environmental exposures, including occupational or leisure physical activities. The MZ subjects in the Twin Spine

Study have been shown to be highly representative of men in the Finnish Twin Cohort [19] in terms of level of leisure activity, outdoor vs. indoor work, level of education, LBP history, smoking and social class. [19] However, due to the selection criteria, the MZ pairs were more likely to be working and had slightly higher levels of physical loading at work compared to the entire cohort. [19] The Finnish Cohort has been shown to be representative of the Finnish population. [20] Of the 116 pairs of twins, 75 pairs were later selected for participation in a 5-year follow-up based only on age to represent the age distribution of the original group. Of these 75 twin pairs, 114 twins were still living and able to travel to the study center to be re-examined again approximately 15 years after their baseline evaluations. Of these twins who were considered for the present study, 8 were excluded due to a history of spinal surgery, 1 due to a spinal fracture and 6 due to poor MR images quality. Thus, the final group for the present study was composed of 99 MZ twins, including 40 pairs. All subjects were informed of study procedures and gave informed consent. Study protocols were approved by the Ethical Committee of the University of Kuopio and the Health Ethics Research Board of the University of Alberta.

5.2.2. DATA ACQUISITION

All subjects travelled to a central location in Finland for baseline and follow-up imaging, height and weight measurements and a structured interview. The baseline data were acquired in 1992-1993 and follow-up in 2007-2008.

Magnetic resonance imaging

Baseline MR images were obtained with a 1.5 Tesla Magnetom SP 4000 scanner (Siemens AG, Erlangen, Germany) with surface coil using a 256 X 256 matrix size. All T2-weighted lumbar axial images were acquired from L2-L3 to L5-S1 with the slices oriented through the center of each intervertebral disc. All subjects lay prone for 30-45 minutes before imaging. The 15-year follow-up images were obtained with a 1.5 Tesla Siemens Zebra scanner ("Avanto" with software MR B15). The same examination protocol was used at baseline and follow-up, with MRI sequences set to result in similar image parameters.

Paraspinal muscle measurements

Quantitative measurements of multifidus and erector spinae muscles were taken from T2-weighted axial images using ImageJ software (Version 1.43, National Institutes of Health, Bethesda, Maryland, downloadable at http://rsbweb.nih.gov/ij/download.html). The paraspinal muscle measurements of interest for the multifidus and erector spinae included the following: total CSA, FCSA representing fat-free area (lean muscle mass), FCSA/total CSA ratio as an indicator of muscle composition or fatty infiltration, CSA asymmetry, FCSA asymmetry and side-to-side difference in ratio FCSA/total CSA. We also examined the percentage of subjects with muscle CSA asymmetry >10%, as this threshold has been previously suggested to represent a potential abnormality. [2]

All muscle measurements were obtained at L3-L4 and L5-S1 levels, mid intervertebral disc, perpendicular to the muscle mass for both baseline and follow-

up images. As most underlying spinal pathologies are believed to occur at the two lowest lumbar levels and fatty infiltration has been reported to be most notable for paraspinal muscle measurements at L5-S1, [6] this level was selected as a level likely to be affected if lumbar pathology is present. The L3-L4 level was selected as a level less likely to be affected by pathology. Asymmetry in total CSA or FCSA was calculated as a percentage with the following formula: [(larger side – smaller side)/larger side) x 100]. [2] The FCSA measurements were obtained using a highly reliable thresholding technique, which is based on the difference in signal intensity between muscle and fat tissue. The reliability and standard error of measurements (SEM) of the different multifidus and erector spinae muscle measurements (using the same protocol and imaging software) has been previously examined and intra-class correlation coefficients varied between 0.89-0.99 for CSA (SEM=0.18-0.41 cm^2), FCSA (SEM=0.35-0.64 cm^2) and FCSA/CSA (SEM=0.03-0.04) measurements and 0.85-0.97 for CSA and FCSA side-to-side differences (SEM=0.14-0.47 cm^2). [21] Furthermore, the reliability of the paraspinal muscle measurements was assessed using the baseline images of 10 study subjects, yielding similar results (ICC=0.80-0.99). Details regarding the measurement protocol and reliability have been published elsewhere. [21] The rater (MF) was experienced in obtaining quantitative MRI muscle measurements and was blinded to subjects' identities and backgrounds.

Interview data

A structured interview was conducted at baseline and the same questions were repeated at the time of follow-up. A detailed lifetime job history was obtained where every job, with its detailed description of associated tasks, was classified into one of five categories according to job type and degree of physical loading: 0=retired or unemployed, 1= sedentary work, 2-3= progressive degrees of materials handling and positional loading, and 4= very heavy loading. [18] A previous study using the original Twin Spine Study sample evaluated the response reliability of work history. The intraclass correlation coefficients were 0.75 for mean sitting hours per day, 0.77 for driving hours per day and 0.60 for total lifting per day. [18] History of prior and current sports participation, exercise types, and frequency and duration of participation were obtained at both baseline and follow-up. A summary variable for the total mean hours per week in which the subject participated in regularly performed sport and exercise was created. Using a 5-year test-retest reliability interval, an intra-class correlation coefficient (ICC) of 0.81 was found for the repeatability for lifetime history of "mean exercise hr/week" of the most commonly performed exercise mode. [22]

A detailed history of low back pain was obtained for each subject. The frequency of low back pain during the last 12 months was classified using a seven-point scale ranging from none to daily (1=daily, 7=none). [18] Subjects were also asked to rate their worst episode of LBP in the last 12 months on a scale of 0 to 100. In addition, subjects were questioned at baseline about whether they had experienced sciatica (e.g. radiating leg pain) during their worst episode ever, and whether they had ever had sciatica during the 15-year follow-up. The back pain

history questions were repeated in interviews conducted approximately one month apart in 48 subjects to examine test-retest reliability. Weighted-kappa coefficients with 95% confidence intervals were obtained from 1000 bootstrap samples. A weighted kappa coefficient of 0.83 (0.67-0.93) was found for the low back pain frequency measurements, 0.79 (0.61-0.92) for the pain numeric scale measurements.

5.2.3. STATISTICAL ANALYSIS

Descriptive statistics, including means and standard deviations of the muscle measurements, were used to investigate the progression of age-related changes from baseline to 15-year follow-up (*objective 1*). Linear regression, clustering for the twinship pair, was used to examine the difference between the baseline and follow-up data of the muscle measurements.

In order to account for the correlated observations in co-twins, we used linear mixed-effects models to examine the association between changes in paraspinal muscle measurements and age crudely. A twinship variable was created for each twin pair, which was used as a random effect in all analyses. Linear mixed effect models were also used to examine the association between changes in paraspinal muscle measurements and changes in lifestyle and individual factors *(objective 2)*. A separate multivariable model was fit for each muscle and each outcomes of interest: % change in CSA, change in FCSA/CSA, change in CSA asymmetry and change in side-to-side difference in ratio FCSA/CSA. In addition to age and spinal level (L3-L4 and L5-S1), the covariates

included the change in physical activity levels (mean hr/wk), job codes, BMI, LBP frequency and LBP intensity (past 12 months) from baseline to follow-up, and the presence of sciatica at baseline or follow-up (e.g. sciatica ever). As we initially hypothesized that physical loading and activity levels (sports and work) or LBP at baseline may influence the association of the change in muscle morphology and change in physical demands or LBP, we also tested the baseline parameters as potential predictors. Any factor with a univariate significance of <0.20 was a candidate for the multivariable model. The significance of plausible interactions and confounders was assessed. Variables leading to a ±15% change of the beta coefficients of the significant variables were included in the multivariable model. Diagnostic plots and statistics were used to evaluate model assumptions and the effect of influential outliers. The assumptions were respected for each model and the fit of each model was reasonable. Collinearity was assessed and was not an issue. We estimated the relative contribution of, or variance explained by, familial aggregation (genetic influence and early shared environment) for the 40 twin pairs using intra-class correlation coefficients (ICC). All statistical analyses were performed using Stata (version 12.0; StataCorp LP, College Station, TX, USA).

5.3. RESULTS

The mean age of the subjects was 47.3±7.4 years old at baseline and 62.3±8.0 at follow-up. Subject characteristics including BMI, job code and average time spent in sports and physical activities and LBP histories are presented in Table 5-1.

Table 5-1: Baseline and follow-up characteristics of subjects (N=99).

	Baseline	Follow-up
Age	47.3±7.4	63.2±8
BMI	26±3.1	26.7±3.2
Weighted job code, prior year* (5-point scale)	2.3±1.1 *Unemployed/retired N=10*	2.6±1 *Unemployed/retired N=53*
Physical activity, prior year (mean hr/wk)	*Working:* 3.7±4.9 *Unemployed/retired:* 2.5±3.2	*Working:* 5.9±5.9 *Unemployed/retired:* 6.5±5.9
LBP frequency (7-point scale)	5.1±2	5.7±1.9
LBP severity (0-100 scale)	29.9±33.5	22.1±30.9
Sciatica (# of subjects)	28	31

BMI=Body Mass Index, LBP= Low Back Pain

*Only subjects working at the time of the interview were included in the mean and standard deviation

5.3.1. CHANGES IN MUSCLE OBSERVED OVER 15 YEARS DURING ADULTHOOD

Our results showed a decrease in multifidus and erector spinae CSA over the 15-year period, which was statistically significant only at L5-S1 (Tables 5-2 and 5-3). Greater age ($p=0.012$) was crudely associated with a greater % decrease in CSA at L5-S1 in mutifidus, with a similar trend for older individuals to have a greater decrease in CSA in erector spinae at L3-L4 ($p=0.06$). A significant decrease in lean muscle mass, as indicated by a decrease in FCSA, was observed at both spinal levels in the multifidus and erector spinae muscles ($p<0.001$). Greater age was associated with a greater % decrease in FCSA at L3-L4 and L5-S1 ($p<0.001$, $p=0.007$, respectively) in multifidus in the crude analysis, and in erector spinae at L3-L4 ($p=0.005$). A clear change in muscle composition was demonstrated in both muscles by a significant decrease in FCSA/CSA (e.g. increase in fatty infiltration) at both spinal levels (Figure 5-1), which also correlated with age at L3-L4 in multifidus only ($p=0.001$).

Table 5-2: Longitudinal changes (means and standard deviations) of the multifidus (n=99).

	Baseline	Follow-up	*P* value‡	% Change or Change
L3-L4				
CSA (cm^2)	7.21±1.32	7.09±1.18	0.186	-0.71±10.98%
FCSA (cm^2)	5.38±1.17	3.82±1.22	<0.001	-28.84±18.42%
FCSA/CSA	0.75±0.1	0.54±0.14	<0.001	-0.21±0.11
CSA asymmetry (%)	8.33±6.34	10.19±7.65	0.023	1.86±7.54
FCSA asymmetry (%)	10.12±6.66	14.85±12	<0.001	4.73±10.6
FCSA/CSA diff	0.07±0.05	0.08±0.06	0.032	0.02±0.07
L5-S1				
CSA (cm^2)	12.24±1.68	10.94±1.56	<0.001	-10.24±9.53%
FCSA (cm^2)	8.47±1.57	5.27±1.39	<0.001	-37.47±12.98%
FCSA/CSA	0.69±0.08	0.48±0.1	<0.001	-0.21±0.09
CSA asymmetry (%)	7.03±5.96	8.21±6.21	0.064	1.18±6.77
FCSA asymmetry (%)	9.03±6.16	13.51±11.68	0.002	4.48±12.91
FCSA/CSA diff	0.06±0.05	0.07±0.05	0.206	0.01±0.06

‡ Linear regression, clustering for twinship pair, was used to obtain p-values
CSA=Cross-Sectional Area, FCSA= Functional Cross-sectional Area, FCSA/CSA diff= side-to-side difference in ratio of FCSA/CSA

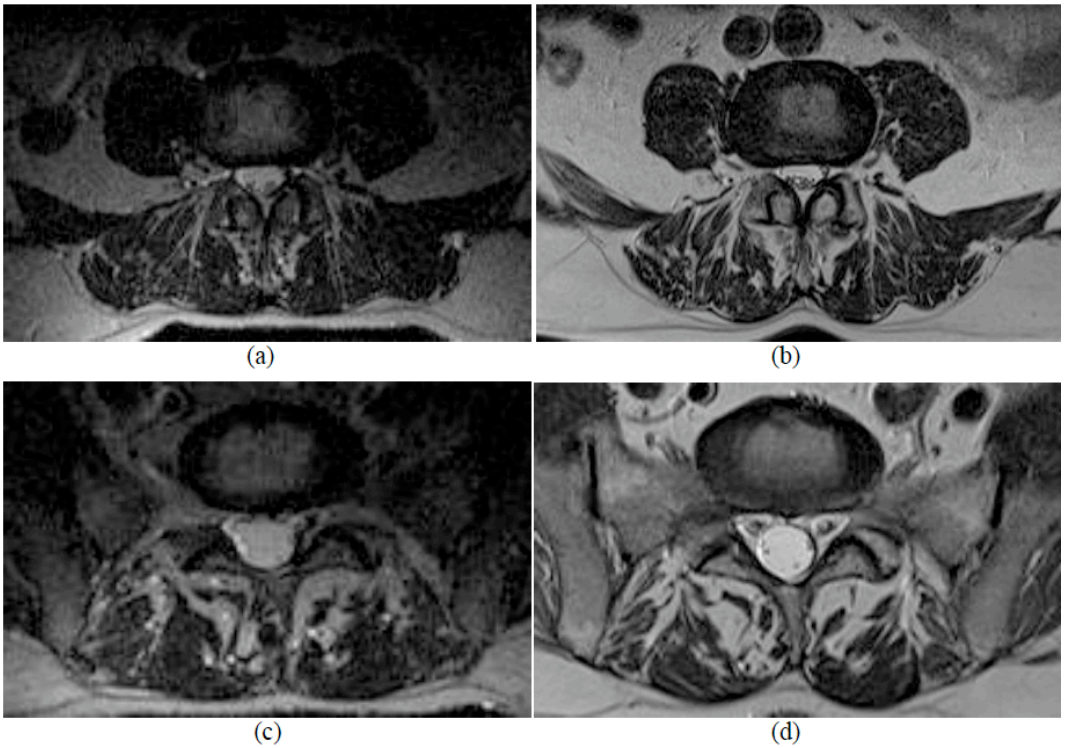

Figure 5-1: T2-weighted axial images showing the longitudinal paraspinal muscle changes of a 43-year-old man. a) Baseline paraspinal muscles at L3-L4, b) 15-year follow-up paraspinal muscles at L3-L4, c) baseline paraspinal muscles at L5-S1, d) 15-year follow-up paraspinal muscle at L5-S1.

In general, the multifidus and erector spinae asymmetry in CSA, FCSA and side-to-side difference in FCSA/CSA increased over time at both spinal levels, though not all the changes were statistically significant. However, none of the asymmetry parameters were crudely associated with age, with the exception of erector spinae CSA asymmetry at L5-S1 (p=0.025). When examining the overall change of the asymmetry parameters, there was great variability among individuals, which led to large standard deviations (Tables 5-2 and 5-3). At the L3-L4 spinal level, 33.3% of subjects had multifidus CSA asymmetry >10% at baseline and 45.5% at follow-up, compared to 10.1% and 19.2% for the erector spinae. Whereas, at L5-S1 spinal level, CSA asymmetry >10% was found in 29.3% of subjects at baseline and 35.3% at follow-up, compared to 58.6% and 55.6% for the erector spinae.

Table 5-3: Longitudinal changes (means and standard deviations) of the erector spinae muscle (n=99).

	Baseline	**Follow-up**	***P* value‡**	**% Change or Change**
L3-L4				
CSA (cm^2)	20.45±3.04	20.15±3.15	0.141	-1.21±9.54%
FCSA (cm^2)	15.82±2.67	9.17±2.65	<0.001	-41.76±14.62%
FCSA/CSA	0.77±0.08	0.47±0.13	<0.001	-0.30±0.1
CSA asymmetry (%)	4.88±3.63	5.92±4.96	0.026	1.05±4.73
FCSA asymmetry (%)	17.40±9.53	22.74±14.93	0.002	5.34±15.1
FCSA/CSA diff	0.14±0.07	0.12±0.1	0.259	0.01±0.1
L5-S1				
CSA (cm^2)	11.57±4.27	6.91±2.63	<0.001	-38.87±14.81%
FCSA (cm^2)	7.46±3.55	1.62±1.02	<0.001	-78.46±9.19%
FCSA/CSA	0.63±0.1	0.23±0.1	<0.001	-0.40±0.09
CSA asymmetry (%)	13.65±9.42	13.75±11.25	0.943	1.00±13.12
FCSA asymmetry (%)	27.98±17.66	33.60±19.92	0.021	5.61±22.45
FCSA/CSA diff	0.18±0.1	0.08±0.06	<0.001	-0.10±0.01

‡ Linear regression, clustering for twinship pair, was used to obtain p-values.
CSA=Cross-Sectional Area, FCSA= Functional Cross-Sectional Area, FCSA/CSA diff= side-to-side difference in ratio of FCSA/CSA.

5.3.2. LIFESTYLE FACTORS ASSOCIATED WITH LONGITUDINAL PARASPINAL MUSCLE CHANGES

Paraspinal muscle size and composition

We used multivariable analyses to investigate the possible correlations between the changes in paraspinal muscle size and composition with changes in individual and lifestyle factors over the 15-year period. The level of physical demands (work or leisure) at baseline and the change in physical demands from baseline to follow-up were not associated with changes in multifidus or erector spinae CSA or FCSA/CSA, except for change in FCSA/CSA of multifidus, which was crudely associated with the change in job codes (Table 5-4). Similarly, no association with changes in LBP frequency, or LBP intensity or history of sciatica was found. Of the factors investigated, only age ($p=0.019$) and disc level ($p<0.001$) entered the multivariable model for % change in *multifidus* CSA (adjusted-$R^2=0.20$), with greater age and the L5-S1 disc level associated with greater % change in multifidus CSA over time. Greater age and BMI at baseline were crudely associated with an increase in multifidus fatty infiltration, expressed by a decrease in FCSA/CSA, but only age ($p=0.01$) remained statistically significant in the multivariable model (adjusted-$R^2=0.06$).

With respect to *erector spinae*, disc level (L5-S1) and lesser change in BMI (less weight gain) from baseline to follow-up was associated with a greater decrease in CSA (Table 5-4). Both variables ($p<0.001$) entered the multivariable model (adjusted-$R^2=0.73$), and their interaction was also found to be significant

(p=0.002), meaning that slope for % change in CSA was different at each spinal level and that subjects with more weight gain had a lesser decrease in CSA at L3-L4 than L4-L5. Greater BMI at baseline and disc level (L5-S1) were crudely associated with a greater increase in erector spinae fatty infiltration (smaller FCSA/CSA), but only disc level ($p<0.001$) remained statistically significant in the multivariable model (adjusted-R^2=0.21).

Paraspinal asymmetry in size and composition

Similar to the other paraspinal muscle measures, the level of physical demands (work and leisure) or LBP at baseline, and the change in physical loading from baseline to follow-up were not significantly associated with multifidus or erector spinae muscle changes in CSA asymmetry or FCSA/CSA side-to-side differences (Table 5-5). Only greater BMI at baseline was associated with less asymmetry in multifidus FCSA/CSA over time (p=0.009, adjusted-R^2=0.03).

With respect to *erector spinae*, none of the factors investigated were significantly associated with the change in CSA asymmetry (Table 5-5). Yet, greater age, greater BMI at baseline and change in BMI from baseline to follow, and disc level (L5-S1) were all crudely associated with less erector spinae side-to-side difference in FCSA/CSA (composition), with all factors entering the multivariable model (adjusted-R^2=0.23), in addition to change in LBP frequency which reached significance in the multivariable analysis.

Table 5-4: Crude and multivariable regression coefficients [and 95% CI] for association of paraspinal muscle change in CSA and FCSA/CSA with individual and lifestyle factors.

	Multifidus		**Erector Spinae**	
	% Change CSA	*Change FCSA/CSA*	*% Change CSA*	*Change FCSA/CSA*
	Coefficient [95% CI]	Coefficient [95% CI]	Coefficient [95% CI]	Coefficient [95% CI]
Age (years)	**-.254 [-.4668, -.0412]***	**-.0031 [-.0052, -.0009)***	-.2398 [.6487, .169]	.0002 [-.0025, .002]
Adjusted†	**-.2554 [-.4696, -.0413]***	**-.0022 [-.0045, -.00002]***	-	-
Spinal level (L5-S1)	**-9.52 [-11.97, -7.08]***	-.0017 [-.0189, .0223]	**-37.65 [-41.02, 34.29]***	**-.1000 [-.1222, -.0777]***
Adjusted†	**-9.52 [-11.97, -7.08]***	-	**-36.28 [-39.60, -34.29]***	**-.1000 [-.1222, -.0777]***
Change scores				
Change PA (mean hr/wk)	-.0742 [-.3318, .1832]	-.0017 [-.0042, .0008]	-.2117 [-.7021, .2785]	-.0003 [-.0028, .0022]
Adjusted†	-	-	-	-
Change job codes (5-point scale)	-.2014 [-1.22, .8128]	**.0123 [.0028, .0218]**	.2243 [-1.73, 2.18]	.0076 [-.0022, .0175]
Adjusted†	-	.0082 [-.0015, .0179]	-	-
Change BMI (kg/height m^2)	.7467 [.0773, 1.42]	.0010 [-.0055, .0075]	**1.47 [.1703, 2.77]***	-.0020 [-.0086, .0045]
Adjusted†	-	-	**4.64 [2.52, 6.76]***	-
Change LBP frequency (7-point scale)	-.4989 [-1.18, .1821]	-.0041 [-.0107, .0024]	-.3017 [-1.63, 1.02]	-.0015 [-.0081, .0051]
Adjusted†	-	-	-	-
Change LBP intensity (0-100 scale)	.0376 [-.0047, .0800]	.0001 [-.0002, .0005]	.0434 [-.0392, .126]	.00002 [-.0003, .00004]
Adjusted†	-	-	-	-
Sciatica ever (dichotomous variable)	.2811 [-3.02, 3.56]	.0072 [-.0251, .0396]	-1.21 [-7.49, 5.07]	.0033 [-.0290, .0358]
Adjusted†	-	-	-	-
Baseline Variables				
PA (mean hr/wk)	.2704 [-.0699, .6107]	.0015 [-.0017, .0048]	.306 [-.3549, .9669]	.0011 [-.0021, .0045]
Adjusted†	-	-	-	-
Job codes (5-point scale)	.2303 [-1.09, 1.56]	-.0014 [.0141, .0112]	.8568 [-1.71, 3.42]	-.0091 [-.0220, .0037]
Adjusted†	-	-	-	-
BMI (kg/height m^2)	-.4626 [-.9873, .062]	**-.0057 [-.0109, -.0005]***	-.0910 [-1.0944, .914]	**-.0043 [-.0095, .0009]***
Adjusted†	-	-.0043 [-.0093, .0008]	-	-.0042 [-.0091, .0008]
LBP frequency (7-point scale)	.1712 [-.6343, .9769]	.0023 [-.0055, .0101]	.2586 [-1.29, 1.81]	-.002 [-.0099, .0058]
Adjusted†	-	-	-	-
LBP intensity (0-100 scale)	-.0189 [-.0677, .0298]	.00008 [-.0003, .0005]	-.0357 [-.1298, .0582]	.0001 [-.0003, .0006]
Adjusted†	-	-	-	-
Sciatica (dichotomous variable)	-.4458 [-4.13, 3.24]	.0017 [-.035, .0386]	-3.48 [-10.47, 3.49]	.004 [-.0322, .0404]
Adjusted†	-	-	-	-
Total variance explained	20%	6%	73%	21%

CSA=cross-sectional area, FCSA=Functional Cross-Sectional Area, CI=Confidence Interval, PA=Physical Activity, BMI=Body Mass Index, LBP=Low Back Pain

†= Adjusted multivariable model regression coefficient and [95% CI]

*=P<0.05

Table 5-5: Crude and multivariable regression coefficients [and 95% CI] for association of paraspinal muscle change in size and composition asymmetry with lifestyle factors.

	Multifidus		**Erector Spinae**	
	Change CSA asymmetry	*Change FCSA/CSA side-to-side difference*	*Change CSA asymmetry*	*Change FCSA/CSA side-to-side difference*
	Coefficient [95% CI]	Coefficient [95% CI]	Coefficient [95% CI]	Coefficient [95% CI]
Age (years)	-.0002 [-.0017, .0012]	-.0004 [-.0017, .0007]	.0018 [-.0002, .0039]	**-.0019 [-.0044, -.0006]***
Adjusted†	-	-	-	-.0022 [-.0048, -.0003]‡
Spinal level (L5-S1)	-.0086 [-.0306, .0132]	-.0071 [-.0221, .0078]	-.008 [-.0405, .0243]	**-.0891 [-.1124, -.0659]***
Adjusted†	-	-	-	**-.0874 [-.1107, -.0642]***
Change Scores				
Change PA (mean hr/wk)	.0016 [-.0001, .0033]	.0011 [-.0003, .0026]	-.001 [-.0036, -.0014]	-.0005 [-.0034, .0024]
Adjusted†	-	-	-	-
Change job codes (5-point scale)	-.0006 [-.0077, .0063]	.0018 [-.0040, .0078]	-.0031 [-.0132, .0069]	.0018 [-.0040, .0078]
Adjusted†	-	-	-	-
Change BMI (kg/height m^2)	-.0014 [-.0032, .0062]	.0008 [-.0031, .0048]	-.0029 [-.0097, .0038]	**-.0031[-.0108, -.0046]***
Adjusted†	-	-	-	**-.0125 [-.0206, -.0043]***
Change LBP frequency (7-point scale)	.0009 [-.0038, .0057]	.0005 [-.0035, .0046]	.0031 [-.0036, .0099]	-.0065 [-.0143, .0011
Adjusted†	-	-	-	**-.0086 [-.0159, -.0014]***
Change LBP intensity (0-100 scale)	-.00001 [-.0003,.0002]	.0001 [-.00006, .0004]	-.0002 [-.0006, .0002]	.0004 [-.00002, .0009]
Adjusted†	-	-	-	-
Sciatica ever (dichotomous variable)	.005 [-.0176, .0277]	.0022 [-.0170, .0214]	-.0036 [-.0361, .0288]	.0365 [-.0007, .0738]
Adjusted†	-	-	-	-
Baseline Variables				
PA (mean hr/wk)	-.0001 [-.0025, .0022]	-.0084 [-.0028, .0011]	.0012 [-.0021, .0046]	-.006 [-.0033, .0045]
Adjusted†	-	-	-	-
Job codes (5-point scale)	.001 [-.0082, .0102]	-.0006 [-.0084, .0071]	-.008 [-.0212, .0052]	.0064 [-.0085, .0214]
Adjusted†	-	-	-	-
BMI (kg/height m^2)	.0003 [-.0032, .0039]	**-.0039 [-.0069, .0009]***	.0013 [-.0038, .0065]	**-.0087 [-.0145, -.0028]***
Adjusted†	-	**-.0039 [-.0069, -.0009]***	-	**-.0123 [-.0183 -.0063]***
LBP frequency (7-point scale)	.0013 [-.0042, .0069]	-.0024 [-.0071, .0022]	-.0035 [-.0115, .0044]	.0087 [-.0003, .0178]
Adjusted†	-	-	-	-
LBP intensity (0-100 scale)	-.00004 [-.0003,.0002]	-.0001, [-.0004, .0001]	.0002 [-.0002, .0007]	-.0005 [-.0010, .00004]
Adjusted†	-	-	-	-
Sciatica (dichotomous variable)	-.0011 [-.0262, .024]	-.0088 [-.0302, .0125]	-.0097 [-.046, .0265]	-.0088 [-.0512, .0336]
Adjusted†	-	-	-	-
Total variance explained	-	3%	-	23%

CSA=cross-sectional area, FCSA=Functional Cross-Sectional Area, CI=Confidence Interval, PA=Physical Activity, BMI=Body Mass Index, LBP=Low Back Pain

†= Adjusted multivariable model regression coefficient and [95% CI]

‡= Confounder

*=P<0.05

In addition to the individual and lifestyle factors investigated, in the 40 twin pairs included in the sample, familial aggregation explained an additional 23-25% of the variance in paraspinal muscle change in size or composition, and 9-19% of change in paraspinal muscle asymmetry.

5.4. DISCUSSION

Although a number of cross-sectional studies have examined the relationship between age and other lifestyle factors with lumbar paraspinal muscle morphology, we are not aware of any prior longitudinal studies on the age-related changes of lumbar paraspinal muscle in adulthood. In general, the present 15-year follow-up study revealed a decrease in multifidus and erector spinae total CSA and lean muscle mass and an increase in fatty infiltration (mean increase varied between 28.7-64.7% increase), as well as greater side-to-side differences in size and composition in multifidus and erector spinae. Both muscles displayed greater changes at L5-S1 than L3-L4 for most measures. While age and BMI were often significantly associated with the degree of paraspinal muscle changes, the level of physical demands at work and leisure and LBP history (e.g. frequency, intensity, sciatica) were generally not.

Paraspinal muscle size and lean muscle mass

Longitudinal studies have shown minimal changes in distribution of muscle fiber type and fiber size over 9-12 years, [10] suggesting that atrophy related to ageing may result from a decline in the number of muscle fibers. [10,23] Evidence suggests

that skeletal muscle atrophy accelerates after the age of 50 yr [24] to reach an estimated reduction in CSA of 1%/yr. [10] In the present study, the reduction in CSA was 0.68%/yr for multifidus and 2.60%/yr for erector spinae at L5-S1. However the reduction rates were much smaller at L3-L4, suggesting that the decrease in muscle CSA varies across muscle groups and spinal level, and the presence of regional pathologies may contribute to greater muscle atrophy. Although age was statistically significantly associated with the degree of change in multifidus fatty infiltration at L5-S1, the r-squared value was quite small, suggesting the effects of age were of little consequence**.** One striking finding was the 73% of variance in % change in CSA of erector spinae explained by the final multivariable model, with 69% explained by spinal level alone. No overly influential outliers were detected, suggesting a major influence of spinal level on changes in this muscle attribute over time (Table 5.3.). In a recent 10-year longitudinal study of the cervical region using a group of 62 asymptomatic subjects (mean age 37.3±12.6), Okada et al. reported an increase in CSA of posterior extensor muscles in subjects into their forties, and a decrease thereafter. [25] However, muscle composition was not assessed and caution should be taken when interpreting these results, as muscle size does not equate muscle mass. In our general-population sample of men, despite an increase in physical activity levels over time, we observed a decrease in multifidus and erector spinae total CSA and lean muscle mass at both spinal levels with ageing. An earlier case-control study found that 70 year-old men with a history of regular swimming or running (average of 3 times/wk for 12-17 years) had similar arm and leg muscle

CSAs as age-matched sedentary controls. [26] Conversely, the men who had been weight training regularly had muscle CSAs comparable to a group of sedentary 28-year old subjects, [26] suggesting that weight training is key to maintaining muscle mass. Accordingly, we initially planned to perform a separate analysis to see whether subjects that were weight training had less atrophy and fatty infiltration over time. However, only five subjects were weight training at baseline and four at follow-up, which were too few to draw trustworthy conclusions. Most subjects in our sample were involved in endurance type activities (e.g. running) and ball games. Thus, it may be that the activities the subjects were engaged in were not of the type and intensity to influence the muscle measurements.

Paraspinal muscle composition

Similar to studies of other skeletal muscles, [12,27] we found a clear increase in fatty infiltration over the 15-year period, which was greater in the oldest subjects and at L5-S1 as compared to L3-L4. Greater muscle fatty infiltration has been shown to be associated with muscle weakness, [11] poorer function [28] and mobility limitations. [29] While we are aware of no longitudinal studies investigating the effect of ageing on paraspinal muscle composition, a randomized control trial of exercise training in the elderly (70-89 years old) reported an 18% increase in intramuscular fatty infiltration of the mid-thigh muscles at one-year follow-up. [12] Interestingly, the same authors reported that regular physical activity consisting of a combination of aerobic, strength, flexibility and balance training was effective

to prevent the age-related increase in fatty infiltration. Again, evidence suggests that weight training is key to improve overall muscle quality, as a significant decrease in skeletal muscle fatty infiltration, including the paraspinal muscles, [30] has been reported following the participation in a resistance-training program. [27] In addition to ageing, possible causes for the increased muscle fatty infiltration in older adults include insulin resistance, [31] metabolic syndrome [32] and deconditioning. [29] Degeneration of nerve structures, including motor neurons has also been reported with ageing, [33] and denervation is recognized to cause an increase in muscle fatty infiltration. [34]

The greater paraspinal muscle atrophy in CSA, FCSA and FCSA/CSA at L5-S1 than L3-L4 might be related to the higher prevalence of spinal pathology and degeneration occurring at that spinal level. The L5-S1 level is also the spinal level that bears the most weight. The center of gravity is located through this spinal level, and the transition from a mobile vertebra (L5) to a fixed segment (S1) greatly increases the stress on the vertebral unit. [35] Moreover, the angle between the L5 and S1 level is greater than at any other lumbar segment, which allows for more movement and greater stress as compared to other lumbar levels. [35] The latter factors are likely to be related to the greater paraspinal muscle changes observed at this level.

Paraspinal muscle asymmetry

The presence of side and level-specific asymmetry of the multifidus muscle has been observed in relation to chronic unilateral LBP, with or without radiculopathy

in some studies. [2,15,36] Our results do not support such findings, but it is noteworthy that very few subjects were suffering from chronic LBP problems in our general population sample. No cross-sectional studies reported a significant relationship between age and paraspinal muscle asymmetry in symptomatic or asymptomatic subjects. [2,15] Our results revealed that over time, there was a general increase in paraspinal muscle asymmetry in size and composition. Also, unlike cross-sectional study results, [2,15] greater age was significantly associated with increased CSA asymmetry of the erector spinae muscle at follow-up. The percentage of subjects with multifidus or erector spinae CSA asymmetry >10% also increased over time.

Lifestyle and individual factors

Our findings suggest no association between the amount of physical loading at work and leisure and paraspinal muscle changes over time. Although previous cross-sectional studies have reported an association between occupational, sports or leisure physical activities and paraspinal muscle CSA, [3,4] the variance explained was negligible (2-3%). [3] Similar to our findings, familial aggregation (combined effects of genes and shared early environment) has been reported to be the strongest predictor of paraspinal muscle parameters, explaining between 71-83% of the variance in paraspinal muscle CSA in an earlier study. [3] However, one should keep in mind that although no relationships were observed between physical activity levels and paraspinal muscle changes, it is possible that little variation in physical activity changes occurred between subjects over time. For

example, active subjects practicing activities that stress the lumbar extensor muscles possibly have more muscle mass, but muscle atrophy may occur at similar rate than subjects with less muscle mass if the change in physical activity were similar over time. This study could not address this point. Our findings of an association between BMI and paraspinal muscle changes are also in accordance with previous cross-sectional studies reporting that greater BMI and body weight are associated with larger muscle CSA, [3] and lower muscle density (more fatty infiltration). [37] Although there r-squared value was quite small and may not be of clear importance, greater BMI was also statistically significantly associated with less asymmetry in multifidus FCSA/CSA over time, suggesting that fatty infiltration is more evenly distributed (more symmetrical) in heavier subjects. Our results also suggest that paraspinal muscle changes were not influenced by LBP frequency or severity over the prior year. Previous cross-sectional studies also reported no significant association between LBP severity and paraspinal muscle size [36] or composition. [7] Although one cross-sectional study reported a clear trend towards greater fatty infiltration of the paraspinal muscle, rectus abdominis and lateral abdominals (all combined together) with increased LBP severity in the past year, but no association was found for muscle CSA. [28] While Matsumoto et al. reported no association between the change in cervical muscle CSA over 10-years and clinical symptoms. [38]

The present study has some limitations that should be acknowledged. First, the two MRI scanners employed to obtain the baseline and follow-up images were different, which had an impact on images quality and slightly

increased the level of difficulty when performing the baseline muscle measurements. Yet, imaging studies evaluating inter-scanner difference suggest minimal effects. For example, a study evaluating inter-scanner reliability for brain volume measurements reported good agreement between scanners with a coefficient of variation of 2.4%. [39] Similar studies have also reported good inter-scanner agreement for volume determination of different brain structures, [40] vendors [39] and software updates. [40] Second, our sample was composed of men only, and our results may not be representative of the paraspinal muscle changes that occur in the female population over 15-year during adulthood. Also, a study of different age range, such as the elderly, may result in a different progression of paraspinal muscle changes. While the twins included in this study were representative of the Finish population, their level of physical activity and BMI may not be typical of men living in Western countries. Finally, we relied on subject recall to estimate subject's occupational and physical activity participation. Although the reliability coefficients were generally good for these measurements, they certainly contain some degree of error, diluting possible associations.

5.5. CONCLUSION

In summary, the present 15-year longitudinal study suggests that over time the multifidus and erector spinae lumbar muscles have similar morphological changes, which include a decrease in size and muscle mass, and an increase in muscle fatty infiltration and asymmetry, which appeared greater in older

individuals and at the L5-S1 level as compared to L3-L4. The level of physical activity at work and leisure and LBP problems were not associated with the changes in paraspinal muscle morphology, but a significant correlation between BMI and the degree of multifidus and erector spinae muscle changes was identified.

5.6. REFERENCES

1. Cooper RG, St Clair Forbes W, Jayson MIV. Radiographic demonstration of paraspinal muscle wasting in patients with chronic low back pain. *Br J Rheumatol* 1992;31(6):389-394.

2. Hides J, Gilmore C, Stanton W, Bohlscheid E. Multifidus size and symmetry among chronic LBP and healthy asymptomatic subjects. *Man Ther* 2008;13(1):43-49.

3. Gibbons LE, Videman T, Battie MC, Kaprio J. Determinants of paraspinal muscle cross-sectional area in male monozygotic twins. *Phys Ther* 1998 1998;78(6):602-612.

4. Peltonen JE, Taimela S, Erkintalo M, Salminen JJ, Oksanen A, Kujala UM. Back extensor and psoas muscle cross-sectional area, prior physical training, and trunk muscle strength - A longitudinal study in adolescent girls. *Eur J Appl Physiol Occup Physiol* 1998;77(1-2):66-71.

5. Fortin M, Macedo L. Multifidus and Paraspinal muscle Group Cross-Sectional Areas of Patients with Low Back Pain and Control Patients: A Systematic Review With a Focus on Blinding. *Phys Ther* 2013;93(7):873-888.

6. Kjaer P, Bendix T, Sorensen JS, Korsholm L, Leboeuf-Yde C. Are MRI-defined fat infiltrations in the multifidus muscles associated with low back pain? *BMC Med* 2007;5.

7. Mengiardi B, Schmid MR, Boos N, Pfirrmann CWA, Brunner F, Elfering A, et al. Fat content of lumbar paraspinal muscles in patients with chronic low back pain and in asymptomatic volunteers: Quantification with MR spectroscopy. *Radiology* 2006;240(3):786-792.

8. Battié MC, Niemelainen R, Gibbons LE, Dhillon S. Is level- and side-specific multifidus asymmetry a marker for lumbar disc pathology? *Spine J* 2012;12(10):932-939.

9. Danneels LA, Vanderstraeten GG, Cambier DC, Witvrouw EE, De Cuyper HJ, Danneels L. CT imaging of trunk muscles in chronic low back pain patients and healthy control subjects. *Eur Spine J* 2000;9(4):266-272.

10. Frontera WR, Hughes VA, Fielding RA, Fiatarone MA, Evans WJ, Roubenoff R. Aging of skeletal muscle: A 12-yr longitudinal study. *J Appl Physiol* 2000;88(4):1321-1326.

11. Goodpaster BH, Carlson CL, Visser M, Kelley DE, Scherzinger A, Harris TB, et al. Attenuation of skeletal muscle and strength in the elderly: The health ABC study. *J Appl Physiol* 2001;90(6):2157-2165.

12. Goodpaster BH, Chomentowski P, Ward BK, Rossi A, Glynn NW, Delmonico MJ, et al. Effects of physical activity on strength and skeletal muscle fat infiltration in older adults: A randomized controlled trial. *J Appl Physiol* 2008;105(5):1498-1503.

13. McLoughlin RF, D'Arcy EM, Brittain MM, Fitzgerald O, Masterson JB. The significance of fat and muscle areas in the lumbar paraspinal space: A CT study. *J Comput Assissted Tomogr* 1994;18(2):275-278.

14. Alaranta H, Tallroth K, Soukka A, Heliovaara M. Fat content of lumbar extensor muscles and low back disability: A radiographic and clinical comparison. *J Spinal Disord* 1993;6(2):137-140.

15. Barker KL, Shamley DR, Jackson D. Changes in the cross-sectional area of multifidus and psoas in patients with unilateral back pain: the relationship to pain and disability. *Spine* 2004;29(22):E515-519.

16. Hides J, Stanton W, McMahon S, Sims K, Richardson C. Effect of stabilization training on multifidus muscle cross-sectional area among young elite cricketers with low back pain. *J Orthop Sports Phys Ther* 2008;38(3):101-108.

17. Hides JA, Jull GA, Richardson CA. Long-term effects of specific stabilizing exercises for first-episode low back pain. *Spine* 2001;26(11):E243-248.

18. Battie MC, Videman T, Gibbons LE, Fisher LD, Manninen H, Gill K. Determinants of lumbar disc degeneration: A study relating lifetime exposures and magnetic resonance imaging findings in identical twins. *Spine* 1995;20(24):2601-2612.

19. Simonen RL, Videman T, Kaprio J, Levälahti E, Battié MC. Factors associated with exercise lifestyle - A study of monozygotic twins. *Int J Sports Med* 2003;24(7):499-505.

20. Kaprio J. Koskenvuo M. Artimo M. et al. The Finnish Twin Registy: Baseline Characteristics. Section I: Materials, Methods, Representativeness and Results for Variables Special to Twins Studies; 1979.

21. Fortin M, Battie MC. Quantitative Paraspinal Muscle Measurements: Inter-Software Reliability and Agreement Using OsiriX and ImageJ. *Phys Ther* 2012;92(6):853-864.

22. Ropponen A, Levälahti E, Simonen R, Videman T, Battié MC. Repeatability of lifetime exercise reporting. *Scand J Med Sci Sports* 2001;11(3):185-192.

23. Lexell J, Downham D, Sjostrom M. Distribution of different fibre types in human skeletal muscles. Fibre type arrangement in m. vastus lateralis from three groups of healthy men between 15 and 83 years. *J Neurol Sci* 1986;72(2-3):211-222.

24. Lexell J, Taylor CC, Sjostrom M. What is the cause of the ageing atrophy? Total number, size and proportion of different fiber types studied in whole vastus lateralis muscle from 15- to 83-year-old men. *J Neurol Sci* 1988;84(2-3):275-294.

25. Okada E, Matsumoto M, Ichihara D, Chiba K, Toyama Y, Fujiwara H, et al. Cross-sectional area of posterior extensor muscles of the cervical spine in asymptomatic subjects: A 10-year longitudinal magnetic resonance imaging study. *Eur Spine J* 2011;20(9):1567-1573.

26. Klitgaard H, Mantoni M, Schiaffino S, Ausoni S, Gorza L, Laurent-Winter C, et al. Function, morphology and protein expression of ageing skeletal muscle: A cross-sectional study of elderly men with different training backgrounds. *Acta Physiol Scand 1990*;140(1):41-54.

27. Marcus RL, Addison O, Kidde JP, Dibble LE, Lastayo PC. Skeletal muscle fat infiltration: Impact of age, inactivity, and exercise. *J Nutr Health Aging* 2010;14(5):362-366.

28. Hicks GE, Simonsick EM, Harris TB, Newman AB, Weiner DK, Nevitt MA, et al. Cross-sectional associations between trunk muscle composition, back pain, and physical function in the health, aging and body composition study. *J Gerontol Ser A Biol Sci Med Sci* 2005;60(7):882-887.

29. Visser M, Goodpaster BH, Kritchevsky SB, Newman AB, Nevitt M, Rubin SM, et al. Muscle mass, muscle strength, and muscle fat infiltration as predictors of incident mobility limitations in well-functioning older persons. *J Gerontol Ser A Biol Sci Med Sci 2*005;60(3):324-333.

30. Mooney V, Gulick J, Perlman M, Levy D, Pozos R, Leggett S, et al. Relationships between myoelectric activity, strength, and MRI of lumbar extensor muscles in back pain patients and normal subjects. *J Spinal Disord* 1997;10(4):348-356.

31. Goodpaster BH, Krishnaswami S, Resnick H, Kelley DE, Haggerty C, Harris TB, et al. Association between regional adipose tissue distribution and both type 2 diabetes and impaired glucose tolerance in elderly men and women. *Diabetes Care* 2003;26(2):372-379.

32. Goodpaster BH, Krishnaswami S, Harris TB, Katsiaras A, Kritchevsky SB, Simonsick EM, et al. Obesity, regional body fat distribution, and the metabolic syndrome in older men and women. *Arch Intern Med* 2005;165(7):777-783.

33. Porter MM, Vandervoort AA, Lexell J. Aging of human muscle: structure, function and adaptability. *Scand J Med Sci Sports* 1995;5(3):129-142.

34. Hodges P, Holm AK, Hansson T, Holm S. Rapid atrophy of the lumbar multifidus follows experimental disc or nerve root injury. *Spine* 2006;31(25):2926-2933.

35. Magee DJ. Orthopedic physical assessment. 5th ed. ed.; 2008.

36. Ploumis A, Michailidis N, Christodoulou P, Kalaitzoglou I, Gouvas G, Beris A. Ipsilateral atrophy of paraspinal and psoas muscle in unilateral back pain patients with monosegmental degenerative disc disease. *Br J Radiol 2011*;84(1004):709-713.

37. Kalichman L, Hodges P, Li L, Guermazi A, Hunter DJ. Changes in paraspinal muscles and their association with low back pain and spinal degeneration: CT study. *Eur Spine J* 2010;19(7):1136-1144.

38. Matsumoto M, Ichihara D, Okada E, Chiba K, Toyama Y, Fujiwara H, et al. Cross-sectional area of the posterior extensor muscles of the cervical spine in whiplash injury patients versus healthy volunteers - 10 year follow-up MR study. *Injury* 2012;43(6):912-916.

39. Gasperini C, Rovaris M, Sormani MP, Bastianello S, Pozzilli C, Comi G, et al. Intra-observer, inter-observer and inter-scanner variations in brain MRI volume measurements in multiple sclerosis. *Mult Scler* 2001;7(1):27-31.

40. Stonnington CM, Tan G, Klöppel S, Chu C, Draganski B, Jack Jr. CR, et al. Interpreting scan data acquired from multiple scanners: A study with Alzheimer's disease. *Neuroimage* 2008;39(3):1180-1185.

CHAPTER 6

ARE VARIATIONS IN PARASPINAL MUSCLE MORPHOLOGY AND COMPOSITION PREDICTORS OF LBP?

6.1. INTRODUCTION

The paraspinal muscles are comprised of two layers, extrinsic and intrinsic muscles. The extrinsic muscles are the superficial large back muscles, mostly responsible for spine and limb motion. [1] The intrinsic muscles are deep spinal muscles, such as the multifidus, which control the intersegmental motion of individual vertebrae and provide stability to the spine. [2,3] Studies have shown an association of paraspinal muscle structural changes or dysfunction compromising muscle function and spinal stability, including muscle atrophy, [4-6] fatty infiltration, [7,8] fiber alterations [9-11] and motor control deficits, [12] with low back pain (LBP).

According to the scientific literature, the multifidus muscle seems to be predominantly associated with degenerative changes (e.g. atrophy) in patients with LBP. [4,13] Patients with chronic LBP have been found to have smaller multifidus muscles [5,6] and a higher percentage of muscle fatty infiltration [7,8] as compared to healthy controls. However, not all investigators have reported significant differences in paraspinal muscle size [4,14] or fat content [4,15] between patients with LBP and asymptomatic controls. Paraspinal muscle asymmetry also has been reported in patients with unilateral LBP, with atrophy generally present

ipsilateral to the painful side and localized at the suspectedpathological spinal level or adjacent level. [5,16-19] Yet, this association, too, has not been consistently found. [13,20,21]

When specifically studying paraspinal muscle in individuals with LBP, in cross-sectional studies, some investigators have found correlations of paraspinal muscle size with pain duration [16,22] and pain intensity, [16] while other studies have failed to find such associations. [18,23] With respect to fatty infiltration, Mengiardi and colleagues found no correlation between the fat content of the multifidus or longissimus muscle and pain duration or intensity. [7] While Kader et al. reported a tendency for increased multifidus fat content with higher ratings of pain intensity, the association did not reach statistical significance. [36]

Despite the inconsistencies in the scientific literature, the weight of current evidence suppored the view that paraspinal muscles are smaller in patients with chronic LBP than in asymptomatic control and on the symptomatic side of patients with chronic unilateral LBP compared with the asymptomatic side. [24] Although variations in paraspinal muscle morphology, composition and asymmetry have been observed in patients with LBP, one fundamental question remains. Are these paraspinal muscle variations a result of LBP and pathology, risk factors, or possibly both? Longitudinal follow-up studies of general population samples of persons with and without LBP problems are needed to clarify whether paraspinal muscle atrophy, fatty infiltration or asymmetry precede LBP or vise-versa. The aim of the present longitudinal study was to clarify this longstanding controversy by investigating if paraspinal muscle size, composition

and asymmetry at baseline are predictors of LBP problems (frequency and intensity) at 1-year and 15-year follow-up.

6.2. MATERIAL AND METHODS

6.2.1. STUDY SAMPLE

Participants for this study were selected from the 116 monozygotic (MZ) twin pairs initially recruited in the Twin Spine Study, which were drawn from the population-based Finnish Twin Cohort that included all same-sex twins born in Finland before 1958 and still alive in 1975. [25] The initial selection of MZ twins, which has been described in detail previously,[25] was based on co-twin discordance for one of a number of common environmental exposures (e.g. occupational or leisure physical activities). The MZ subjects in the Twin Spine Study have been shown to be highly representative of the Finnish Twin Cohort in terms of level of leisure activity, outdoor vs indoor work, level of education, LBP history, smoking and social class, [26] and the Cohort is representative of the Finnish population. [27] However, due to the selection criteria, the MZ pairs were more likely to be working and had slightly higher levels of physical demands at work compared to the entire Finnish Twin Cohort. [26]

Five years later, 75 of the twin pairs were re-examined and of these 114 twins were still living and able to travel to the study center to be re-examined again approximately 15 years after their baseline evaluations. The mean age of the subjects was 47.3±7.4 years at baseline and 62.3±8.0 at 15-year follow-up. Eight

of the twins were excluded due to a history of spinal surgery, 1 due to spinal fracture and 6 due to poor MR image quality. Thus, the final group for the present study was composed of 99 MZ twins, including 40 pairs. All subjects were informed of study procedures and gave informed consent. Study protocols were approved by the Ethical Committee at the University of Kuopio and the Health Ethics Research Board of the University of Alberta.

6.2.2. DATA ACQUISITION

Magnetic resonance imaging

Baseline MR images were obtained with a 1.5 Tesla scanner with surface coil (Magnetom SP 4000, Siemens AG Erlangen, Germany) using a 256 X 256 matrix size (0.98 pixels/mm). All T2-weighted lumbar axial images were acquired from L2-L3 to L5-S1 with the slices oriented through the center of each intervertebral disc. All subjects lay prone for 30-45 minutes before imaging.

Quantitative measurements of multifidus and erector spinae muscles were taken from T2-weighted axial images using ImageJ imaging software (Version 1.43, National Institutes of Health, Bethesda, Maryland, downloadable at http://rsbweb.nih.gov/ij/download.html). The paraspinal muscle measurements of interest for the multifidus and erector spinae included the following: total CSA (Figure 6-1), the ratio of functional CSA (FCSA) (e.g. fat-free mass) to total CSA (FCSA/CSA), CSA asymmetry and side-to-side difference in ratio of FCSA/total CSA. All muscle measurements were obtained at L3-L4 and L5-S1 levels,

through the center of each intervertebral disc, perpendicular to the muscle mass for the baseline and follow-up images. Asymmetry in total CSA was calculated as a percentage with the following formula: [(lager side – smaller side)/larger side) x 100]. The FCSA measurement was obtained using a highly reliable thresholding technique. This technique is based on the difference in signal intensity between muscle (low signal) and fat tissue (high signal), allowing for the separation of both tissues. The reliability of the different multifidus and erector spinae muscle measurements (using the same rater, measurement protocol and imaging software) has been previously examined and intra-class correlation coefficients varied between 0.92-0.99 for CSA and FCSA/CSA measurements and 0.85-0.97 for CSA and FCSA side-to-side differences. [28] Further details regarding the measurement protocol and reliability have been published elsewhere. [28] The rater (MF) was experienced in quantitative MRI muscle measurements and was blinded to subjects' identity and clinical history. The height and weight of each study participant were also measured and BMI (kg/ht^2) was calculated.

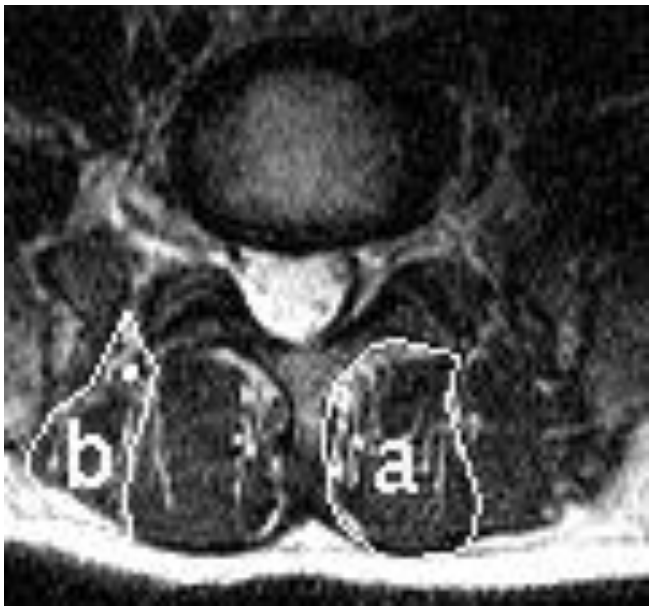

Figure 6-1: a) Multifidus and b) erector spinae cross-sectional area (CSA).

Interview

A structured interview was conducted at baseline and the same questions were repeated at 1-year and 15-year follow-ups. A detailed history of LBP was obtained for each subject. The frequency of LBP during the last 12 months was initially classified using a seven-point scale ranging from none to daily (1=daily, 7=none). [29] The coding was reversed (1=none, 7=daily) for the purpose of this study in order to facilitate the interpretation of the results. Subjects were also asked to rate their worst episode of LBP in the last 12 months on a numerical scale of 0 to 100. In addition, subjects were questioned about whether they ever had sciatica. The test-retest reliability was examined using weighted-kappa coefficients with bootstrap 95% confidence intervals, using 1000 replications on a sample of 48 subjects whose interviews were repeated several weeks later. A weighted kappa coefficient of 0.83 (0.67-0.93) was found for the low back pain

frequency measurements and 0.79 (0.61-0.92) for the pain numeric scale measurements.

A detailed lifetime job history was obtained where every job and associated tasks were described and classified into one of four categories according to job type and degree of physical loading: 1=sedentary work, 2-3=progressive degrees of materials handling and positional loading, and 4=very heavy loading. [25] A previous study using the same population evaluated the response reliability of work history. The intraclass correlation coefficients were 0.75 for time spent sitting, 0.77 for driving hours and 0.60 for total lifting per day. [25] Data on sports participation and exercise types and the frequency and duration of participation were collected at both time points. A summary variable for the total mean hours per week (past year) in which the subject participated in regularly performed sport and exercise was created. Using a 5-year test-retest interval, an intra-class correlation coefficient (ICC) of 0.81 was found for the repeatability for lifetime history of "mean exercise hours/week" of the most commonly performed exercise mode. [29]

6.2.3. STATISTICAL ANALYSIS

In order to account for the correlated observations in co-twins, we used linear mixed-effects models to examine the association between baseline paraspinal muscle morphology parameters and the progression of LBP over time. A twinship variable was created for each twin pair, which was used as a random effect in all analyses.

First, we tested the hypothesis that greater atrophy or asymmetry in paraspinal muscle CSA and fatty infiltration at baseline was associated with increased LBP problems (frequency and intensity) from baseline to 1-year and 15-year follow-up. A change score for LBP frequency was calculated by subtracting the follow-up scores from the baseline score. Similarly, the change score for LBP intensity was calculated by subtracting the follow-up scores from the baseline score and both change scores were used as outcome variables. Separate analyses were performed for each muscle and spinal level. Possible confounding effects of age, BMI, mean job code at baseline and mean time spent in sports and physical activity were tested. Any variables with univariate significance of <0.20 was a candidate for the multivariable linear mixed-effects model. Variables with a $P>0.05$ were removed from the multivariable model after being assessed as potential confounders (variables leading to a ±15% change of the beta coefficients of the significant variables included in the multivariable model).

As the change scores for LBP frequency do not take into account where on the scale the change is occurring, a separate analysis was conducted to further investigate the relationship of baseline muscle measurements with changes in LBP outcomes at 1-year follow-up. Subjects were classifieds into 5 groups according to the change in LBP frequency from baseline to 1-year: 1) No LBP at baseline or 1-year follow-up, 2) LBP frequency decreased over time (change ≥2 categories), 3) Mild or no change in LBP frequency over time (no change or change of ±1 category), 4) LBP frequency increased over time (change ≥2

categories, 5) Frequent LBP at baseline and follow-up (daily or weakly). In this case, multinomial logistic regression, adjusting for the twinship, was used.

Second, we tested the hypothesis that greater paraspinal muscle asymmetry and atrophy at baseline will be associated with a greater prevalence of sciatica from baseline to 15-year follow-up. Subjects were classified into 4 categories according to their history of sciatica over the 15-year period (0= no sciatica, 1= history of unilateral sciatica at baseline, 2= during follow-up, and 3= at baseline and follow-up. Again, multinomial logistic regression, adjusting for twinship, was used. Models were built as described above. All statistical analyses were performed using Stata (version 12.0; StataCorp LP, College Station, TX, USA).

6.3. RESULTS

The mean LBP frequency in the sample was 2.9 at baseline to 2.6 at 1-year follow-up and 2.4 at 15-year follow-up, with 3=2-3 times a year on the 7-point scale (Table 6-1). Daily LBP symptoms were reported by 9% of the subjects at baseline, 10.1% at 1-year follow-up and 6.1% at 15-year follow-up. In addition, 28.2% of the subjects reported having had a history of sciatica at baseline, and 31.3% at 15-year follow-up. Subject characteristics including BMI, job code and average time spent in sports and physical activities, as well as back pain history, are presented in Table 6-1, and baseline paraspinal muscle measurements in Table 6-2.

Table 6-1: Subject characteristics at baseline, 1-year and 15-year follow-up (N=99).

	Baseline	***1-year follow-up***	***15-year follow-up***
Age *(years)*	47.3±7.4	48.4±7.7	63.2±8.0
BMI *(kg/height m^2)*	26.0±3.1	-	26.7±3.2
Job code, past 12 months *(weighted 4-point scale)*	2.3±1.1 *n=89*	-	2.6±1.0 *n=46*
Physical activity *(mean hr/wk)*	3.6±4.8	-	6.2± .9
LBP frequency *(7-point scale)*	2.9±2.0	2.6±2.2†	2.4±1.9
LBP groups (based on change in LBP frequency from baseline to 1-year follow-up) *(5 groups, n (%))*		1=30 (30.6%)† 2=22 (22.5%) 3=27 (27.6%) 4=11 (11.2%) 5=8 (8.16%)	-
LBP severity *(0-100 scale)*	29.9±33.5	22.8±31.1	22.1±30.9
Sciatica symptoms *(% of subjects)*	28.3%†	-	31.3%
Sciatica groups (based on presence of history of sciatica at baseline and 15-year follow)*(4 groups, n(%))*	-	-	0=50 (51.0%)† 1=17 (17.4%) 2=20 (20.4%) 3=11 (11.2%)

BMI=Body Mass Index, LBP=Low Back Pain
†=N=98, one subject had a missing value.

Table 6-2: Mean and standard deviation of baseline multifidus and erector spinae measurements at L3-L4 and L5-S1.

	Multifidus		**Erector spinae**	
	L3-L4	***L5-S1***	***L3-L4***	***L5-S1***
CSA (cm^2)	7.21±1.32	12.24±1.68	20.45±3.04	11.57±4.27
FCSA/CSA	0.75±0.10	0.69±0.08	0.77±0.08	0.63±0.10
CSA asymmetry (%)	8.33±6.34	7.03±5.96	17.40±9.53	13.65±9.42
FCSA/CSA side diff	0.07±0.05	0.06±0.05	0.14±0.07	0.18±0.10

CSA= cross-sectional area, FCSA=functional cross-sectional area, FCSA/CSA side diff= side-to-side difference in ratio of FCSA/CSA

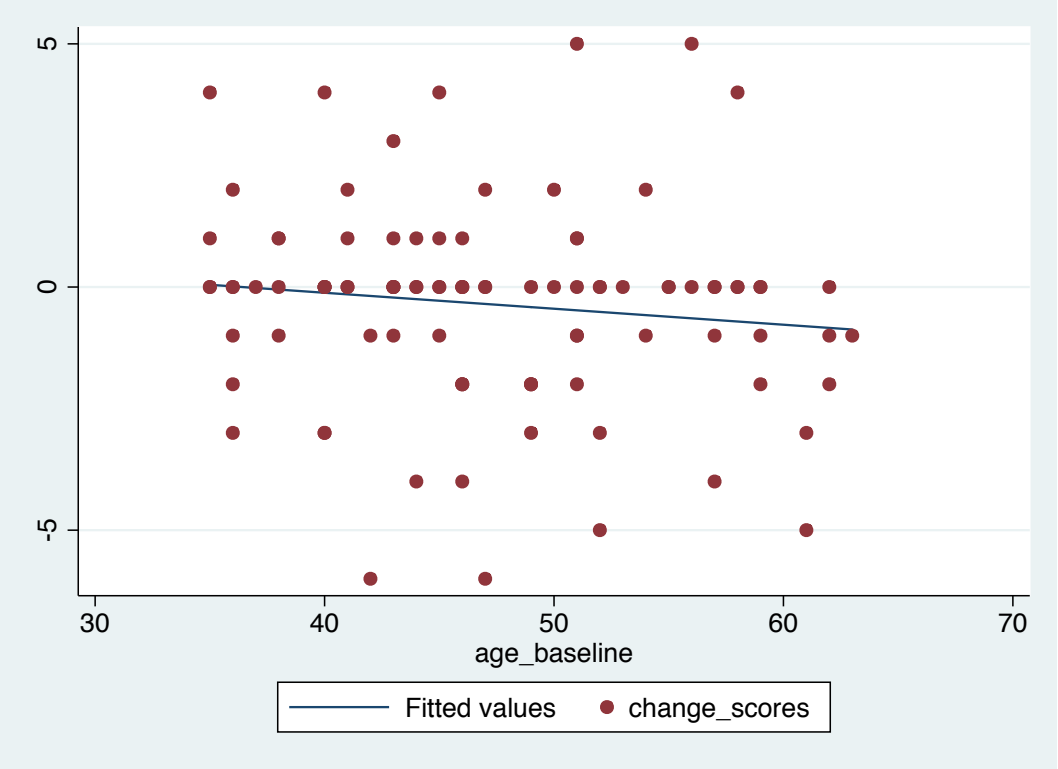

Figure 6-2: Change scores in LBP frequency from baseline to 1-year follow-up by age. Change scores were obtained from subtracting follow-up scores from baseline scores. Maximum change scores are ±6, where positive change scores indicate an increase in LBP frequency overtime.

With respect to muscle morphology measurements at baseline as predictors of LBP outcomes at 1-year follow-up, only the mean multifidus CSA at baseline at the L5-S1 spinal level was significantly associated with greater change in LBP intensity (greater pain intensity) (Table 6-3). Age was not significantly associated with the change in LBP frequency or intensity (Figure 6-2), nor were BMI or the amount of physical activity at work or leisure. Beside mean multifidus CSA at L5-S1 for the change in LBP intensity, no other factors (e.g. other muscle measures, age BMI, physical activity) entered any of the multivariable models as either predictors or confounders. The additional analysis using the LBP groups (as

described in the statistical analysis section) gave a different perspective (Table 6-4). Subjects with greater multifidus CSA at L3-L4 were less likely (relative risk ratio 0.58 [0.34-0.99]) to be in the "frequent LBP group" as compared with the "no LBP group", and greater multifidus or erector spinae FCSA/CSA ratio (less fatty infiltration) at L5-S1 was associated with a decreased risk of being in the "frequent LBP group" versus the "no LBP group". Subjects with greater erector spinae CSA asymmetry at L3-L4 were also found to be less likely (relative risk ratio 0.71 [0.52-0.98]) to be in the "frequent LBP group". Conversely, greater erector spinae side-to-side difference in FCSA/CSA at L3-L4 was associated with an increased risk of being in the "frequent LBP group" (relative risk ratio 1.11 [1.01-1.22]) and at L5-S1 in the "LBP less frequent over time group" (relative risk ratio 1.05 [1.00-1.10]) versus the "no LBP group". All associations remained significant in the multivariable models.

Table 6-3: Crude regression coefficients [and 95% CI] for the association between the change in LBP frequency and intensity *from baseline to 1-year follow-up* and baseline paraspinal muscle parameters at L3-L4 and L5-S1.

Predictor	**Multifidus**		**Erector spinae**	
	Change in LBP frequency	*Change in LBP intensity*	*Change in LBP frequency*	*Change in LBP intensity*
L3-L4				
CSA (cm^2)	.046 [-.274, .365]	-3.51 [-1.46, 8.49]	-.059 [-.199, .080,]	1.24 [-.902, 3.38]
FCSA/CSA (%)	.035 [-.007, .078]	.024 [-.833, .881]	.034 [-.019, .087]	.852 [-.297, 2.00]
CSA asymmetry (%)	.039 [-.102, .025]	-.626 [-1.67, .410]	.080 [-.029, .191]	.449 [-1.35, 2.25]
FCSA/CSA side diff (%)	.075 [-.012, .161]	.325 [-1.10, 1.75]	-.056 [-.113, .001]	-.686 [-1.63, .260]
L5-S1				
CSA (cm^2)	.205 [-.041, .045]	**5.02 [1.12, 8.79]***	-.009 [-107, .089]	.966 [-.558, 2.49]
FCSA/CSA (%)	.037 [-.017, .092]	.662 [-.469, 1.79]	.013 [-.027, .054]	.517 [-.253, 1.29]
CSA asymmetry (%)	-.027 [-.095, .040]	-.299 [-1.40, .797]	-.002 [-.046, .041]	.393 [-.302, 1.08]
FCSA/CSA side diff (%)	-.029 [-.117, .059]	-.817 [-2.22, .589]	-.016 [-.055, .022]	-.439 [-1.02, .139]

LBP=Low back pain, CSA= cross-sectional area, FCSA=functional cross-sectional area, FCSA/CSA side diff= side-to-side difference in ratio of FCSA/CSA * = p<0.05.

Table 6-4: Multinomial crude relative risk ratios [and 95% CI] for the association between low back pain groups (based on the change in LBP frequency from baseline to 1-year follow-up) and baseline paraspinal muscle parameters at L3-L4 and L5-S1.

Predictor	*LBP less frequent over time ¶*	*Mild or no change in LBP frequency ¶*	*LBP more frequent over time ¶*	*Frequent LBP at BL and FU ¶*
Multifidus				
L3-L4				
CSA (cm^2)	.97 (.62, 1.50)	1.03 (.70, 1.51)	.86 (.52, 1.42)	**.58 (.34, .99)***
FCSA/CSA (%)	.94 (.86, 1.03)	.96 (.89, 1.04)	1.03 (.95, 1.12)	.95 (.87, 1.03)
CSA asymmetry (%)	1.01 (.92, 1.11)	1.01 (.93, 1.10)	.97 (.87, 1.08)	.98 (.87, 1.11)
FCSA/CSA side diff (%)	1.03 (.93, 1.14)	1.01 (.89, 1.15)	1.09 (.94, 1.27)	.99 (.85, 1.15)
L5-S1				
CSA (cm^2)	.88 (.59, 1.29)	.95 (.70, 1.28)	1.01 (.67, 1.52)	.76 (.48, 1.22)
FCSA/CSA (%)	.93 (.85, 1.03)	.95 (.88, 1.02)	1.04 (.95, 1.15)	**.85 (.75, .97)***
CSA asymmetry (%)	1.06 (.97, 1.16)	.97 (.88, 1.07)	1.01 (.89, 1.14)	1.11 (.99, 1.25)
FCSA/CSA side diff (%)	1.05 (.91, 1.21)	1.02 (.91, 1.14)	1.05 (.91, 1.21)	1.08 (.92, 1.28)
Erector Spinae				
L3-L4				
CSA (cm^2)	1.05 (.90, 1.22)	1.00 (.85, 1.17)	.86 (.67, 1.10)	.79 (.60, 1.03)
FCSA/CSA (%)	.95 (.87, 1.05)	1.00 (.92, 1.09)	1.05 (.95, 1.16)	.97 (.87, 1.07)
CSA asymmetry (%)	.99 (.84, 1.17)	1.04 (.92, 1.17)	1.07 (.89, 1.29)	**.71 (.52, .98)***
FCSA/CSA side diff (%)	1.09 (.99, 1.18)	1.03 (.94, 1.12)	1.00 (.93, 1.08)	**1.11 (1.01, 1.22)***
L5-S1				
CSA (cm^2)	1.02 (.92, 1.13)	.89 (.78, 1.00)	.92 (.76, 1.10)	.89 (.74, 1.07)
FCSA/CSA (%)	.94 (.89, 1.00)	.94 (.89, 1.00)	.95 (.89, 1.02)	**.90 (.85, .96)***
CSA asymmetry (%)	.99 (.92, 1.06)	.98 (.92, 1.04)	.99 (.93, 1.05)	.93 (.86, 1.01)
FCSA/CSA side diff (%)	**1.05 (1.00, 1.10)***	1.05 (.99, 1.11)	1.03 (.98, 1.09)	1.04 (.98, 1.10)

**P*<0.05

¶ Comparison group is "No LBP at baseline or follow-up"

LBP=Low Back Pain, CSA=Cross-sectional Area, FCSA=Functional Cross-Sectional Area, FCSA/CSA side diff= side-to-side difference in ratio of FCSA/CSA, BL=Baseline, FU=Follow-up

With respect to muscle morphology measurements at baseline as predictors of LBP outcomes at 15-year follow-up, in the crude analyses a 10% side-to-side difference in erector spinae FCSA/CSA at L3-L4 was associated with a 0.8 mean change decrease in LBP frequency (about 1-category change) from baseline to 15-year follow-up (Table 6-5), while 10% greater erector spinae FCSA/CSA (less fatty infiltration) at L5-S1 at baseline was associated with a mean increase of 8.5 points on the 0-100 LBP intensity scale from baseline to 15-year follow-up. Greater age (p=0.04) at baseline was found to be associated with a decrease in LBP frequency at 15-year follow-up, but did not enter the multivariable model as an independent predictor or confounder. Again, BMI and the amount of physical activity at work or leisure were not associated with change in LBP frequency or intensity. Beside the side-to-side difference in FCSA/CSA for erector spinae at L3-L4, none of the factors investigated entered any of the multivariable models.

Table 6-5: Crude regression coefficients [and 95% CI] for the association between the change in LBP frequency and intensity *from baseline to 15-year follow-up* and baseline paraspinal muscle parameters at L3-L4 and L5-S1.

Predictor	**Multifidus**		**Erector spinae**	
	Change in LBP frequency	*Change in LBP intensity*	*Change in LBP frequency*	*Change in LBP intensity*
L3-L4				
CSA (cm^2)	.214 [-.146, .574]	1.60 [-4.26, 7.45]	.044 [-.115, .203]	.267 [-2.33, 2.86]
FCSA/CSA (%)	.016 [-.035, .066]	-.165 [-.976, .646]	-.023 [-.084, .039]	.036 [-.96, 1.03]
CSA asymmetry (%)	.049 [-.025, .123]	.616 [-.554, 1.79]	.105 [-.023, .233]	.351 [-1.69, 2.39]
FCSA/CSA side diff (%)	-.007 [-.109, .095]	.006 [-1.60, 1.62]	**-.080 [-.141, -.019]***	-.847 [-1.89, .198]
L5-S1				
CSA (cm^2)	.259 [-.023, .542]	2.52 [-2.09, 7.13]	.021 [.092, -.134]	1.54 [-.657, 2.96]
FCSA/CSA (%)	.023 [-.039, .086]	.342 [-.677, 1.36]	.014 [-.032, .060]	**.85 [.128, 1.59]***
CSA asymmetry (%)	-.022 [-.101, .057]	-.099 [-1.34, 1.14]	-.002 [-.052, .049]	.125 [-.678, .927]
FCSA/CSA side diff (%)	-.022 [-.124, .079]	-.708 [-2.31, .899]	-.038 [-.082, .007]	-.426 [-1.13, .277]

LBP=Low back pain, CSA= cross-sectional area, FCSA=functional cross-sectional area, FCSA/CSA side diff= side-to-side difference in ratio of FCSA/CSA * = p<0.05.

Few of the factors investigated were significantly associated with the occurrence of sciatica from baseline to 15-year follow-up and results were discrepant (Table 6-6). While greater multifidus CSA asymmetry at L3-L4 was associated with a decrease in the relative risk of having sciatica at baseline and follow-up, greater multifidus side-to-side difference in FCSA/CSA at L5-S1 was associated with an increase in the relative risk of having sciatica at baseline and follow-up. Conversely, greater erector spinae side-to-side difference in FCSA/CSA at L3-L4 was associated with a decrease in the relative risk of having sciatica at follow-up. All 3 significant crude associations remained significant in the multivariable analyses, and age also entered the multivariable models.

Table 6-6: Multinomial crude relative risk ratios [and 95% CI] for the association of sciatica at *baseline and during 15-year follow-up* with baseline paraspinal muscle parameters at L3-L4 and L5-S1.

Predictor	*Sciatica BL* ¶	*Sciatica FU* ¶	*Sciatica BL and FU* ¶
Multifidus			
L3-L4			
CSA (cm^2)	.91 [.54, 1.53]	.97 [.68, 1.39]	.74 [.44, 1.24]
FCSA/CSA (%)	.99 [.93, 1.05]	.99 [.94, 1.04[	1.01 [.95, 1.08]
CSA asymmetry (%)	.99 [.91, 1.07]	1.0 [.92, .1.09]	**.88 [.81, .96]***
FCSA/CSA side diff (%)	.97 [.86, 1.10]	.96 [.85, 1.08]	.91 [.81, 1.03]
L5-S1			
CSA (cm^2)	.93 [.62, 1.39]	1.00 [.75, 1.34]	.74 [.52, 1.05]
FCSA/CSA (%)	1.03 [.95, 1.12]	1.03 [.97, 1.09]	.96 [.88, 1.05]
CSA asymmetry (%)	.98 [.91, 1.07]	.98 [.89, 1.07]	1.09 [.96, 1.25]
FCSA/CSA side diff (%)	.96 [.85, 1.09]	.94 [.84, 1.06]	**1.16 [1.03, 1.30]***
Erector Spinae			
L3-L4			
CSA (cm^2)	.91 [.77, 1.08]	1.07 [.88, 1.29]	.77 [.58, 1.03]
FCSA/CSA (%)	.96 [.90, 1.03]	.99 [.93, 1.07]	.98 [.90, 1.07]
CSA asymmetry (%)	1.05 [.91, 1.20]	.96 [.80, 1.15]	.81 [.64, 1.03]
FCSA/CSA side diff (%)	1.00 [.92, 1.09]	**.89 [.81, .97]***	.98 [.92, 1.05]
L5-S1			
CSA (cm^2)	.90 [.74, 1.09]	.94 [.84, 1.05]	.80 [.60, 1.09]
FCSA/CSA (%)	.99 [.94, 1.06]	1.04 [.97, 1.10]	.95 [.89, 1.01]
CSA asymmetry (%)	.97 [.91, 1.04]	.96 [.91, 1.01]	1.00 [.93, 1.07]
FCSA/CSA side diff (%)	1.02 [.97, 1.08]	.95 [.90, 1.01]	.98 [.93, 1.03]

**P*<0.05

¶ Comparison group is "No history of sciatica at baseline or during follow-up"

CSA=Cross-sectional Area, FCSA=Functional Cross-Sectional Area, FCSA/CSA side diff=side-to-side difference in ratio of FCSA/CSA, BL=Baseline, FU=Follow-up

6.4. DISCUSSION

This longitudinal study aimed to clarify whether paraspinal muscle size (e.g. CSA), composition (e.g. FCSA/CSA) and degree of asymmetry (e.g. % CSA asymmetry and FCSA/CSA side-to-side difference) are associated with developing LBP problems. Although some paraspinal muscle parameters were associated with the change in LBP frequency and intensity over time, results were generally inconsistent across muscles and spinal levels and may have been due to chance. Consequently, variations in multifidus and erector spinae morphology do not appear to be clear or major risk factors for the short-term or long-term development or prognosis of LBP problems, including sciatica.

The significant association between larger multifidus CSA at L5-S1 and greater pain intensity from baseline to 1-year follow-up may be due to an increase in fatty infiltration. Patients with persistent whiplash-associated disorders (3 months to 3 years post injury) have been reported to have larger cervical muscle CSAs [30] in one study and more fatty infiltration in another [31] than healthy control subjects. Similarly, larger paraspinal muscles have been reported in elite athletes with LBP when compared with their asymptomatic counterparts. [31,32] The significant crude associations of larger multifidus CSA at L5-S1 with increased LBP intensity at one-year follow-up, and greater FCSA/CSA (greater percentage of muscle tissue) and less erector spinae FCSA/CSA asymmetry with LBP frequency and intensity from baseline to 15-year follow-up may reflect a higher risk for physically active individuals (e.g. heavy lifting) to have an episode of LBP. We found in a previous study that higher levels of physical activity at work or leisure were associated with less paraspinal muscle asymmetry, [33] and it is generally the case that physically active people have greater muscle mass. [8,34,35] However, no significant relationship was found between the amount of physical activity (work or leisure) at baseline and the change in LBP frequency or intensity over time, making this explanation unlikely. As multiple comparisons were made, it is also possible that these were chance findings.

The multinomial logistic regression analysis using the 5 LBP groups also yielded few significant associations, which were generally inconsistent across muscles and spinal levels. One possible exception was greater multifidus and erector spinae FCSA/CSA (less fatty infiltration) at L5-S1, which was associated

with a decrease in the likelihood of having frequent LBP at baseline and 1-year follow-up. This finding suggests that poor muscle composition may be associated with persistent, frequent LBP. However, as discussed before, greater erector spinae FCSA/CSA was also found to be associated with an increase in LBP intensity at 15-year follow-up. In addition to LBP frequency and intensity being different constructs, the association of such a finding with symptoms as far in the future as 15 years may be suspect as FCSA/CSA may have varied substantially over the years.

Results were also inconsistent for the association between the occurrence of sciatica during the 15-year follow-up and baseline paraspinal muscle asymmetry parameters. While the analyses using the LBP and sciatica groups were performed in an attempt to further investigate the relationship between variations in paraspinal muscle morphology and LBP history, few subjects in our general population sample had severe LBP problems.

We are not aware of any other prospective studies investigating variations in paraspinal muscle morphology as risk factors for the development or prognosis of LBP in a population-based sample. Although, several cross-sectional studies have examined the association between paraspinal muscle morphology and LBP symptoms and pathology, [5-8,16,17,18,19,36,] results remain inconsistent [4,13,14,20,21] and conclusions from cross-sectional studies are limited. A randomized clinical trial suggested that subjects with first episode of unilateral LBP, who received medical management and followed a specific exercise therapy program that restored paraspinal muscle and reduced CSA asymmetry after 4-weeks, reported a lower

LBP recurrence rate at 1-year and 3-year follow-up when compared to a control group (medical management only). [37] Yet, this finding awaits replication.

Our inconsistent findings may be due to the small sample size, although our sample was larger than most previous cross-sectional studies in this field. While the twins included in this study appeared highly representative of the Finnish men, their level of physical activity and BMI may not be typical of men living in others countries. As our sample was composed of middle-age men only, the association between muscle measurements and the development of LBP in woman and other age groups may vary. Limitations related to the study measurements include that the baseline MR images were obtained in the 1990s when image quality was lower than typically seen today, and the low amount of fatty infiltration present at L3-L4 increased the difficulty of determining muscle borders. Although the muscle measurement reliability coefficients were generally good, the measurements certainly contain some degree of error, diluting associations. Another limitation was the reliance on subjects' recall for LBP history and occupational and leisure physical demands.

6.5. CONCLUSION

This longitudinal study provided evidence that variations in paraspinal muscle size, composition and asymmetry observed on MRI in a general population of men appear to have a limited, if not uncertain, role in the short- (1-year) and long-term (15-year) changes in LBP frequency and intensity and the occurrence of

sciatica. Greater multifidus and erector spinae fatty infiltration at L5-S1 appears to be associated with having frequent, persistent LBP.

6.6. REFERENCES

1. Bierry G, Kremer S, Kellner F, Abu Eid M, Bogorin A, Dietemann JL. Disorders of paravertebral lumbar muscles: from pathology to cross-sectional imaging. *Skeletal Radiol* 2008;37(11):967-977.

2. Solomonow M, Zhou B-, Harris M, Lu Y, Baratta RV. The ligamento-muscular stabilizing system of the spine. *Spine* 1998;23(23):2552-2562.

3. Panjabi MM. Clinical spinal instability and low back pain. *J Electromyogr Kinesiology* 2003;13(4):371-379.

4. Danneels LA, Vanderstraeten GG, Cambier DC, Witvrouw EE, De Cuyper HJ. CT imaging of trunk muscles in chronic low back pain patients and healthy control subjects. *Eur Spine J* 2000;9(4):266-272.

5. Hides J, Gilmore C, Stanton W, Bohlscheid E. Multifidus size and symmetry among chronic LBP and healthy asymptomatic subjects. *Man Ther* 2008;13(1):43-49.

6. Kamaz M, Kiresi D, Oguz H, Emlik D, Levendoglu F. CT measurement of trunk muscle areas in patients with chronic low back pain. *Diagn Interv Radiol* 2007;13(3):144-148.

7. Mengiardi B, Schmid MR, Boos N, Pfirrmann CWA, Brunner F, Elfering A, et al. Fat content of lumbar paraspinal muscles in patients with chronic low back pain and in asymptomatic volunteers: Quantification with MR spectroscopy. *Radiology* 2006;240(3):786-792.

8. Kjaer P, Bendix T, Sorensen JS, Korsholm L, Leboeuf-Yde C. Are MRI-defined fat infiltrations in the multifidus muscles associated with low back pain? *BMC Med* 2007;5.

9. Mannion AF, Dvorak J, Taimela S, Muntener M. Increase in strength after active therapy in chronic low back pain (CLBP) patients: Muscular adaptations and clinical relevance. *Schmerz* 2001;15(6):468-473.

10. Yoshihara K, Shirai Y, Nakayama Y, Uesaka S. Histochemical changes in the multifidus muscle in patients with lumbar intervertebral disc herniation. *Spine* 2001;26(6):622-626.

11. Zhao W-, Kawaguchi Y, Matsui H, Kanamori M, Kimura T. Histochemistry and morphology of the multifidus muscle in lumbar disc herniation: Comparative study between diseased and normal sides. *Spine* 2000;25(17):2191-2199.

12. Van Dieën JH, Selen LPJ, Cholewicki J. Trunk muscle activation in low-back pain patients, an analysis of the literature. *J Electromyogr Kinesiology* 2003;13(4):333-351.

13. Beneck GJ, Kulig K. Multifidus atrophy is localized and bilateral in active persons with chronic unilateral low back pain. *Arch Phys Med Rehabil* 2012;93(2):300-306.

14. Lee HJ, Lim WH, Park J-, Kwon BS, Ryu KH, Lee JH, et al. The relationship between cross sectional area and strength of back muscles in patients with chronic low back pain. *Ann Rehabil Med* 2012;36(2):173-181.

15. McLoughlin RF, D'Arcy EM, Brittain MM, Fitzgerald O, Masterson JB. The significance of fat and muscle areas in the lumbar paraspinal space: A CT study. *J Comput Assisted Tomogr* 1994;18(2):275-278.

16. Barker KL, Shamley DR, Jackson D. Changes in the cross-sectional area of multifidus and psoas in patients with unilateral back pain: the relationship to pain and disability. *Spine* 2004;29(22):E515-519.

17. Hides JA, Stokes MJ, Saide M, Jull GA, Cooper DH. Evidence of lumbar multifidus muscle wasting ipsilateral to symptoms in patients with acute/subacute low back pain. *Spine* 1994;19(2):165-172.

18. Ploumis A, Michailidis N, Christodoulou P, Kalaitzoglou I, Gouvas G, Beris A. Ipsilateral atrophy of paraspinal and psoas muscle in unilateral back pain patients with monosegmental degenerative disc disease. *Br J Radiol* 2011;84(1004):709-713.

19. Kim WH, Lee S-, Lee DY. Changes in the cross-sectional area of multifdus and psoas in unilateral sciatica caused by lumbar disc herniation. *J Korean Neurosurg Soc* 2011 2011;50(3):201-204.

20. Battié MC, Niemelainen R, Gibbons LE, Dhillon S. Is level- and side-specific multifidus asymmetry a marker for lumbar disc pathology? *Spine J* 2012;12(10):932-939.

21. Stokes MJ, Cooper RG, Morris G, Jayson MIV. Selective changes in multifidus dimensions in patients with chronic low back pain. *Eur Spine J* 1992 1992;1(1):38-42.

22. Dangaria TR, Naesh O. Changes in cross-sectional area of psoas major muscle in unilateral sciatica caused by disc herniation. *Spine* 1998;23(8):928-931.

23. Mannion AF, Kaser L, Weber E, Rhyner A, Dvorak J, Muntener M. Influence of age and duration of symptoms on fibre type distribution and size of the back muscles chronic low back pain patients. *Eur Spine J* 2000 2000;9(4):273-281.

24. Fortin M, Macedo L. Multifidus and Paraspinal muscle Group Cross-Sectional Areas of Patients with Low Back Pain and Control Patients: A Systematic Review With a Focus on Blinding. *Phys Ther* 2013;93(7):873-888.

25. Battié MC, Videman T, Gibbons LE, Fisher LD, Manninen H, Gill K. Determinants of lumbar disc degeneration: A study relating lifetime exposures and magnetic resonance imaging findings in identical twins. *Spine* 1995;20(24):2601-2612.

26. Simonen RL, Videman T, Kaprio J, Levälahti E, Battié MC. Factors associated with exercise lifestyle - A study of monozygotic twins. *Int J Sports Med* 2003;24(7):499-505.

27. Kaprio J. Koskenvuo M. Artimo M. et al. The Finnish Twin Registy: Baseline Characteristics. Section I: Materials, Methods, Representativeness and Results for Variables Special to Twins Studies.; 1979.

28. Fortin M, Battié MC. Quantitative Paraspinal Muscle Measurements: Inter-Software Reliability and Agreement Using OsiriX and ImageJ. *Phys Ther* 2012;92(6):853-864.

29. Ropponen A, Levälahti E, Simonen R, Videman T, Battié MC. Repeatability of lifetime exercise reporting. *Scand J Med Sci Sports* 2001;11(3):185-192.

30. Elliott J, Jull G, Noteboom JT, Galloway G. MRI study of the cross-sectional area for the cervical extensor musculature in patients with persistent whiplash associated disorders (WAD). *Man Ther* 2008;13(3):258-265.

31. McGregor AH, Anderton L, Gedroyc WM. The trunk muscles of elite oarsmen. *Br J Sports Med* 2002;36(3):214-217.

32. Hides J, Stanton W, Freke M, Wilson S, McMahon S, Richardson C. MRI study of the size, symmetry and function of the trunk muscles among elite cricketers with and without low back pain. *Br J Sports Med* 2008;42(10):509-513.

33. Fortin M, Yuan Y, Battié MC. Factors associated with paraspinal muscle asymmetry in size and composition in a general population sample of men. *Phys Ther* 2013;[Epub ahead of print].

34. Gibbons LE, Videman T, Battie MC, Kaprio J. Determinants of paraspinal muscle cross-sectional area in male monozygotic twins. *Phys Ther* 1998 1998;78(6):602-612.

35. Peltonen JE, Taimela S, Erkintalo M, Salminen JJ, Oksanen A, Kujala UM. Back extensor and psoas muscle cross-sectional area, prior physical training, and trunk muscle strength - A longitudinal study in adolescent girls. *Eur J Appl Physiol Occup Physiol* 1998;77(1-2):66-71.

36. Kader DF, Wardlaw D, Smith FW. Correlation between the MRI changes in the lumbar multifidus muscles and leg pain. *Clin Radiol* 2000;55(2):145-149.

37. Hides JA, Jull GA, Richardson CA. Long-term effects of specific stabilizing exercises for first-episode low back pain. *Spine* 2001;26(11):E243-248.

CHAPTER 7

GENERAL DISCUSSION AND CONCLUSIONS

7.1. OVERVIEW

Although there is a growing body of evidence suggesting an association linking paraspinal muscle morphological changes with low back pain (LBP) and spinal pathology, the mechanisms leading to such changes and the role of paraspinal muscles in the development of LBP and spinal pathology is far from explicit. For example, it remains unclear whether variations in paraspinal muscle morphology, including atrophy, asymmetry and fatty infiltration, precede LBP or are a consequence of LBP and spinal pathology. The importance of paraspinal muscles in spinal stability is irrefutable, [1] and such degenerative changes are expected to compromise spinal stability and increase the risk of LBP reoccurrence. However, the cross-sectional nature of most studies does not address the cause and effect relationship, and longitudinal studies are urgently needed in this field. Using a general population sample of men with various histories of LBP, this doctoral work aimed to clarify this longstanding controversy. More specifically, this series of cross-sectional and longitudinal studies intended to identify potential determinants of paraspinal muscle asymmetry, illustrate the natural progression of paraspinal muscle changes over a 15-year period, and clarify whether variations in paraspinal muscle cross-sectional area (CSA), composition and asymmetry precede or follow the occurrence or progression of common LBP as experienced in men.

7.2. DETERMINANTS OF, AND CHANGES IN, PARASPINAL MUSCLE SIZE, COMPOSITION AND ASYMMETRY OVER ADULTHOOD

7.2.1. DETERMINANTS OF PARASPINAL MUSCLE ASYMMETRY

Paraspinal muscle asymmetry in size and composition (e.g. fatty infiltration) has been reported in patients with a clinical presentation of unilateral low back pain (LBP), with or without radiculopathy. [2-6] Specifically, selective changes of the multifidus muscle suggesting level or side-specific atrophy in relation to symptoms and spinal pathology have been reported. Subsequently, numerous studies have been conducted to replicate and better understand this phenomenon and determine whether it is consistently present in different patient populations. [2-8] Yet, findings remain conflicting. [9,10] Furthermore, multifidus asymmetry has also been demonstrated to be common in asymptomatic healthy subjects. [11]

Possible causes for the discrepant results include variations in imaging modalities and measurement methodologies, as well as the case definition of subjects studied. As an example, some studies investigating similar patient populations but using different imaging modalities have conflicting results. [2,11] Similarly, other studies using the same imaging modality but different measurement methodologies also have conflicting results. [3,12] Lastly, differences also exist between studies using sample populations of patients with specific inclusion criteria (e.g. monosegmental posterolateral disc herniation with concordant radicular leg pain), [9] as opposed to more general case definitions (e.g. first episode of unilateral LBP). [13]

With the exception of studies of athletes performing asymmetrical sports,[14-17] few studies have specifically investigated determinants of paraspinal muscle asymmetry [2,18] and composition [19-21] other than LBP and nerve root pathology. Using a general population sample of 202 men, magnetic resonance imaging (MRI) and more accurate quantitative measures as compared to previous studies, the research within this thesis revealed that few of the factors studied are of importance to paraspinal muscle asymmetry. Contrary to our original hypothesis, greater asymmetry in paraspinal muscle size and composition was not associated with having had a history of LBP or participation in asymmetrical sports or work activities. Moreover, back pain history and disc height narrowing were not found to be more highly associated with asymmetry in multifidus than erector spinae. Of the factors investigated, handedness and familial aggregation were found to be the greatest predictors of paraspinal muscle asymmetry in size and composition. BMI and lean body mass were not associated with any of the measures of paraspinal muscle asymmetry. However, subjects that were more physically active (at work or leisure) were found to have less multifidus and erector spinae asymmetry in size and composition, while greater disc height narrowing was associated with more paraspinal muscle asymmetry. Yet, the associations identified between the behavioral, environmental and constitutional factors investigated, were generally inconsistent across muscles and spinal levels, explaining little of the variance in paraspinal muscle asymmetry.

In summary, this study does not support the hypothesis that subjects with a history of LBP have greater paraspinal muscle asymmetry. Yet, it is important to

consider that most studies reporting such an association examined patients with unilateral LBP and that we did not distinguished unilateral LBP and radicular symptoms from other back pain problems. Thus, it remains unclear what is accounting for the large portion of unexplained variance in muscle asymmetry, but it may be that some degree of asymmetry is a naturally occurring phenomenon in human anatomy, including paraspinal muscles. Although we found no association between paraspinal muscle asymmetry and participation in asymmetrical sports or work activities, few subjects were involved in such activities in our general population sample and further investigation with larger sample sizes is needed to confirm our results. Nonetheless, our data suggest that the particular factors studied may not be of major concern when examining paraspinal muscle asymmetry in clinical or research settings.

7.2.2. LONG-TERM PARASPINAL MUSCLE CHANGES

The paraspinal muscles, including the multifidus, erector spinae (e.g. longissimus and iliocostalis muscles), quadratus lumborum and psoas, play a critical role in spine stabilization and mobility. [22-24] The multifidus muscle has been reported to contribute as much as two thirds of the segmental stiffness of the spine when compared to other paraspinal muscles. [1] Given the essential role of this muscle in spinal stability and the many reports suggesting an association between multifidus degenerative changes and LBP, its morphology is generally thought to influence its optimal function and thus, play a role in the development or recurrence of LBP. However, due to the cross-sectional nature of most studies in this field, the

age-related changes in paraspinal muscle size, composition and asymmetry during adulthood remains undetermined. Whether lifestyle factors, such as the amount of physical activity at work or leisure, and body mass index (BMI) influence the long-term changes in paraspinal muscle morphology also remain unclear.

This longitudinal study revealed that over the 15-year period, the multifidus and erector spinae muscles exhibited a decrease in CSA and functional cross-sectional area (FCSA) (e.g. fat free-mass), and an increase in fatty infiltration and side-to-side difference in size and composition at both spinal levels. However, the changes were generally larger at L5-S1 than L3-L4. In fact, our data showed that 69% of the variance in % change in CSA of the erector spinae was explained by spinal level only. This finding may be due to the higher prevalence of spinal pathology and degeneration, or greater stress occurring at that spinal level. [25]

Greater age was associated with a greater % decrease in paraspinal muscle CSA and FCSA, and a significant increase in fatty infiltration. However, none of the asymmetry parameters were associated with age, with the exception of CSA asymmetry of the erector spinae at L5-S1. However, greater BMI was associated with an increase in multifidus and erector spinae fatty infiltration (FCSA/CSA) and a decrease in the side-to-side difference in FCSA/CSA, suggesting that fatty infiltration is more evenly distributed (more symmetrical) in heavier subjects. This study also provided some evidence that heredity influences long-term change in paraspinal muscles, as 9-25% of the variance in paraspinal muscle changes in size, composition and asymmetry was explained by familial aggregation.

Despite an increase in physical activity over time, our general-population sample of men exhibited a decrease in muscle size and lean muscle mass, and an increase in fatty infiltration of the multifidus and erector spinae at both spinal levels with ageing. Taking into account that weight training appears to be a key component to maintain muscle mass and improve overall muscle quality, [26-28] it may be that the activities the subjects were engaged in were not of the type and intensity to influence muscle measurements. Additional prospective studies including woman, other age groups and subjects with diverse physical activity backgrounds and levels are needed to further investigate the relationship between age and long-term paraspinal muscle changes.

7.3. THE ROLE OF PARASPINAL MUSCLE IN COMMON SPINAL DISORDERS

Despite the numerous reports demonstrating an association between degenerative paraspinal muscle changes and LBP, the role of paraspinal muscle in LBP and spinal pathology is uncertain. While an experimental study confirmed that variations in paraspinal muscle morphology do occur following disc or nerve injury, [7] this does not exclude the possibility that preexisting muscle changes could be present in humans, and perhaps represent risk factors for the development of LBP. Although it is often hypothesized that paraspinal muscle atrophy and fatty infiltration may contribute to recurrent LBP, this theory still remains to be proven. Moreover, it remains unclear how much of an influence, if

any, LBP severity and associated disability have on the observed variations in paraspinal muscle morphology.

Whether paraspinal muscle atrophy, asymmetry and fatty infiltration predict the development of LBP or worsen LBP symptoms requires further examination using a longitudinal design. When such a design was used in the current thesis research, contrary to our hypothesis, few of the investigated paraspinal muscle parameters were significantly associated with changes in LBP frequency and intensity over the short-term (1 year) or long-term (15 years). Moreover, significant associations were generally inconsistent across muscle and spinal level (e.g. L3-L4 and L5-S1). Age, BMI and the amount of physical activity at work or leisure reported by the general population sample of Finnish men were not significantly associated with changes in LBP frequency or intensity. Similar results were also true for the associations between paraspinal muscle parameters at baseline and the occurrence of sciatica at 15-year follow-up. However, this study provided some evidence to suggest that poor muscle composition (more fatty infiltration) may be a risk indicator for development of LBP at 1-year follow-up. Although most cross-sectional studies reported no significant correlation between pain severity and paraspinal muscle size [5,29,30] or fatty infiltration, [30,31] Hicks and colleagues also found an association between greater paraspinal muscle and abdominal muscle fatty infiltration with increased LBP severity in the past year. [32]

Taking into account the weak and inconsistent associations, it appears that paraspinal muscle size, composition and asymmetry play a limited role for the

short-term and long-term development of LBP and sciatica. However, the associations identified between greater fatty infiltration and frequent LBP suggest that poor muscle quality may be associated with having more persistent LBP.

7.4. STUDY LIMITATIONS

As mentioned in previous chapters, this doctoral work has some limitations that should be acknowledged. 1) Our measurement study was limited to only 2 imaging analysis software packages. Thus, our findings may not be representative of the inter-software reliability and agreement for other custom-made and commercial software used for image analysis. 2) Our general population sample was composed of middle-age men only. The long-term age-related changes and their associations with LBP in woman or other age groups remain unknown. 3) The twins included in this study were found to be representative of the Finnish adult male population, but their level of physical activity and BMI may not be typical of men living in other countries. 4) We relied on subject recall to estimate subjects' LBP history and occupational and physical activity participation. Although it was previously established, using the same population, that the reliability coefficients of these measurements were generally good, they certainly contain some degree of error that may have influenced our results or diluted possible associations. 4) The MR images used for the baseline measurements were obtained in the 1990s and the image resolution and quality was lower than scanners typically used today. This made the measurements of paraspinal muscles at L3-L4 more challenging as there is usually less fatty infiltration at this spinal

level, thus determining muscle borders was more difficult. 5) Two different MRI scanners were used to acquire the baseline and 15-year follow-up images. However, such a difference may have minimally biased our findings as other imaging studies reported good agreement between scanners while taking similar measurements, [33] despite multiple software updates. [34] Performing measurements with only one scanner would have been ideal, but it is often not feasible in real-life clinical or research settings, especially in the case of long-term prospective studies.

7.5. FUTURE RESEARCH

The longitudinal studies in this thesis substantially contributed to current knowledge by clarifying age-related changes of the paraspinal muscles and their association with LBP history. While it appears that variations in paraspinal muscle morphology play a limited role in the development or prognosis of LBP, additional longitudinal studies using samples of woman, clinical populations, and possibly larger sample sizes, are needed to confirm and extend our findings.

Our longitudinal study provided some evidence for a correlation between the degree of fatty infiltration and frequent, persistent LBP over time. Recent cross-sectional studies also reported an association between paraspinal muscle fatty infiltration and LBP frequency [35] or intensity. [32] As nociceptive stimuli have been shown to induce generalized inhibition of the multifidus, erector spinae and psoas muscle, [36] the frequency and intensity of pain may play a role in the development of muscle fatty infiltration. Further experimental studies are needed

to establish whether peripheral nociception is involved in the development of fatty infiltration via reflex inhibition. Furthermore, it remains unclear whether paraspinal muscle fatty infiltration is reversible as studies are very scarce and findings are conflicting. [27,37] It would be valuable to further examine whether reversibility is possible, and if so, whether it correlates with improvement in LBP symptoms. Lastly, comprehensive studies correlating paraspinal muscle morphological changes observed on MRI and biomechanical (functional) muscle dysfunctions are also needed to confirm their clinical relevance.

Currently, various imaging modalities and measurement protocols are used to examine paraspinal muscle morphology, which likely contributed to the conflicting literature findings. Because MRI has the highest image resolution to study soft tissues, allows for the separation of muscle and fat tissues, and offers greater reliability indexes, [38] investigators should favor this imaging modality over CT scan and ultrasound. While we showed high agreements between paraspinal muscle measurements obtained with two open source, readily available imaging software (OsiriX and ImageJ), our measurement reliability cannot be generalized to other software or measurement techniques. Therefore, more reliability and validation studies are needed to better judge the extent of the measurement difference between modalities and associated protocols. Future related studies would benefit from using a standard protocol and readily available software to facilitate replication and comparison among studies.

7.6. CONCLUSIONS

In summary, a general population sample of men with diverse histories of LBP was used to determine possible determinants of paraspinal muscle asymmetry, illustrate the paraspinal muscle changes occurring over a 15-year period in adulthood, and clarify whether paraspinal muscle size, composition and asymmetry are associated with the development of LBP. Handedness, disc height narrowing, familial aggregation, and physical demands at work and leisure were associated with the degree of erector spinae and multifidus asymmetry in size and composition. Yet, with the exception of handedness and familial aggregation, the associations identified were generally weak and inconsistent across muscle and spinal level and thus, the behavioral, environmental and constitutional factors investigated appears to have a modest influence on paraspinal muscle asymmetry. Our longitudinal study revealed that multifidus and erector spinae displayed similar morphological changes over the 15-year follow-up period, including a decrease in size and lean muscle mass, and an increase in fatty infiltration and asymmetry. However, the changes in paraspinal muscle morphology over 15 years were not associated with subjects' LBP history or physical demands at work or leisure. Finally, while there was some evidence of greater fatty infiltration in subjects with more frequent, persistent LBP, the associations between paraspinal muscle size, composition and asymmetry at baseline and LBP history at 1-year and 15-year follow-up were generally modest and inconsistent. Thus it appears that variations in paraspinal muscle morphology have a limited role in the

development or prognosis of LBP, as well as sciatica as experienced in Finnish men.

7.7. REFERENCES

1. Wilke H-, Wolf S, Claes LE, Arand M, Wiesend A, Bendix T. Stability increase of the lumbar spine with different muscle groups: A biomechanical in vitro study. *Spine* 1995;20(2):192-198.

2. Hides J, Gilmore C, Stanton W, Bohlscheid E. Multifidus size and symmetry among chronic LBP and healthy asymptomatic subjects. *Man Ther* 2008;13(1):43-49.

3. Barker KL, Shamley DR, Jackson D. Changes in the cross-sectional area of multifidus and psoas in patients with unilateral back pain: the relationship to pain and disability. *Spine* 2004;29(22):E515-519.

4. Campbell WW, Vasconcelos O, Laine FJ. Focal atrophy of the multifidus muscle in lumbosacral radiculopathy. *Muscle Nerve* 1998;21(10):1350-1353.

5. Ploumis A, Michailidis N, Christodoulou P, Kalaitzoglou I, Gouvas G, Beris A. Ipsilateral atrophy of paraspinal and psoas muscle in unilateral back pain patients with monosegmental degenerative disc disease. *Br J Radiol* 2011;84(1004):709-713.

6. Hayashi N, Masumoto T, Abe O, Aoki S, Ohtomo K, Tajiri Y. Accuracy of abnormal paraspinal muscle findings on contrast-enhanced MR images as indirect signs of unilateral cervical root-avulsion injury. *Radiology* 2002;223(2):397-402.

7. Hodges P, Holm AK, Hansson T, Holm S. Rapid atrophy of the lumbar multifidus follows experimental disc or nerve root injury. *Spine* 2006;31(25):2926-2933.

8. Shafaq N, Suzuki A, Matsumura A, Terai H, Toyoda H, Yasuda H, et al. Asymmetric degeneration of paravertebral muscles in patients with degenerative lumbar scoliosis. *Spine* 2012;37(16):1398-1406.

9. Battié MC, Niemelainen R, Gibbons LE, Dhillon S. Is level- and side-specific multifidus asymmetry a marker for lumbar disc pathology? *Spine J* 2012;12(10):932-939.

10. Stokes MJ, Cooper RG, Morris G, Jayson MIV. Selective changes in multifidus dimensions in patients with chronic low back pain. *Eur Spine J* 1992;1(1):38-42.

11. Niemelainen R, Briand M-, Battie MC. Substantial asymmetry in paraspinal muscle cross-sectional area in healthy adults questions its value

as a marker of low back pain and pathology. *Spine* 2011;36(25):2152-2157.

12. Hyun JK, Lee JY, Lee SJ, Jeon JY. Asymmetric atrophy of multifidus muscle in patients with unilateral lumbosacral radiculopathy. *Spine* 2007;32(21):E598-E602.

13. Hides JA, Stokes MJ, Saide M, Jull GA, Cooper DH. Evidence of lumbar multifidus muscle wasting ipsilateral to symptoms in patients with acute/subacute low back pain. *Spine* 1994;19(2):165-172.

14. Engstrom CM, Walker DG, Kippers V, Mehnert AJH. Quadratus lumborum asymmetry and L4 pars injury in fast bowlers: A prospective MR study. *Med Sci Sports Exerc* 2007;39(6):910-917.

15. Hides J, Fan T, Stanton W, Stanton P, Mcmahon K, Wilson S. Psoas and quadratus lumborum muscle asymmetry among elite Australian Football League players. *Br J Sports Med* 2010;44(8):563-567.

16. Ranson C, Burnett A, O'Sullivan P, Batt M, Kerslake R. The lumbar paraspinal muscle morphometry of fast bowlers in cricket. *Clin J Sport Med* 2008;18(1):31-37.

17. Sanchis-Moysi J, Idoate F, Izquierdo M, Calbet JAL, Dorado C. Iliopsoas and gluteal muscles are asymmetric in tennis players but not in soccer players. *PLoS ONE* 2011;6(7).

18. Stokes M, Rankin G, Newham DJ. Ultrasound imaging of lumbar multifidus muscle: Normal reference ranges for measurements and practical guidance on the technique. *Man Ther* 2005;10(2):116-126.

19. Kjaer P, Bendix T, Sorensen JS, Korsholm L, Leboeuf-Yde C. Are MRI-defined fat infiltrations in the multifidus muscles associated with low back pain? *BMC* Med 2007;5.

20. McLoughlin RF, D'Arcy EM, Brittain MM, Fitzgerald O, Masterson JB. The significance of fat and muscle areas in the lumbar paraspinal space: A CT study. *J Comput Assisted Tomogr* 1994;18(2):275-278.

21. Alaranta H, Tallroth K, Soukka A, Heliovaara M. Fat content of lumbar extensor muscles and low back disability: A radiographic and clinical comparison. *J Spinal Disord* 1993;6(2):137-140.

22. Bierry G, Kremer S, Kellner F, Abu Eid M, Bogorin A, Dietemann JL. Disorders of paravertebral lumbar muscles: from pathology to cross-sectional imaging. *Skeletal Radiol* 2008;37(11):967-977.

23. Solomonow M, Zhou B-, Harris M, Lu Y, Baratta RV. The ligamento-muscular stabilizing system of the spine. *Spine* 1998;23(23):2552-2562.

24. Panjabi MM. Clinical spinal instability and low back pain. *J Electromyogr Kinesiology* 2003;13(4):371-379.

25. Magee DJ. Orthopedic physical assessment. 5th ed. ed.; 2008.

26. Klitgaard H, Mantoni M, Schiaffino S, Ausoni S, Gorza L, Laurent-Winter C, et al. Function, morphology and protein expression of ageing skeletal muscle: A cross-sectional study of elderly men with different training backgrounds. *Acta Physiol Scand* 1990;140(1):41-54.

27. Mooney V, Gulick J, Perlman M, Levy D, Pozos R, Leggett S, et al. Relationships between myoelectric activity, strength, and MRI of lumbar extensor muscles in back pain patients and normal subjects. *J Spinal Disord* 1997;10(4):348-356.

28. Marcus RL, Addison O, Kidde JP, Dibble LE, Lastayo PC. Skeletal muscle fat infiltration: Impact of age, inactivity, and exercise. *J Nutr Health Aging* 2010;14(5):362-366.

29. Mannion AF, Kaser L, Weber E, Rhyner A, Dvorak J, Muntener M. Influence of age and duration of symptoms on fibre type distribution and size of the back muscles chronic low back pain patients. *Eur Spine J* 2000 2000;9(4):273-281.

30. Paalanne N, Niinimaki J, Karppinen J, Taimela S, Mutanen P, Takatalo J, et al. Assessment of association between low back pain and paraspinal muscle atrophy using opposed-phase magnetic resonance imaging: A population-based study among young adults. *Spine* 2011;36(23):1961-1968.

31. Mengiardi B, Schmid MR, Boos N, Pfirrmann CWA, Brunner F, Elfering A, et al. Fat content of lumbar paraspinal muscles in patients with chronic low back pain and in asymptomatic volunteers: Quantification with MR spectroscopy. *Radiology* 2006;240(3):786-792.

32. Hicks GE, Simonsick EM, Harris TB, Newman AB, Weiner DK, Nevitt MA, et al. Cross-sectional associations between trunk muscle composition, back pain, and physical function in the health, aging and body composition study. *J Gerontol Ser A Biol Sci Med Sci* 2005;60(7):882-887.

33. Gasperini C, Rovaris M, Sormani MP, Bastianello S, Pozzilli C, Comi G, et al. Intra-observer, inter-observer and inter-scanner variations in brain

MRI volume measurements in multiple sclerosis. *Mult Scler* 2001;7(1):27-31.

34. Stonnington CM, Tan G, Klöppel S, Chu C, Draganski B, Jack Jr. CR, et al. Interpreting scan data acquired from multiple scanners: A study with Alzheimer's disease. *Neuroimage* 2008;39(3):1180-1185.

35. D'Hooge R, Cagnie B, Crombez G, Vanderstraeten G, Dolphens M, Danneels L. Increased intramuscular fatty infiltration without differences in lumbar muscle cross-sectional area during remission of unilateral recurrent low back pain. *Man Ther* 2012;17(6):584-588.

36. Dickx N, Cagnie B, Achten E, Vandemaele P, Parlevliet T, Danneels L. Changes in lumbar muscle activity because of induced muscle pain evaluated by muscle functional magnetic resonance imaging. *Spine* 2008;33(26):E983-989.

37. Willemink MJ, Van Es HW, Helmhout PH, Diederik AL, Kelder JC, Van Heesewijk JPM. The effects of dynamic isolated lumbar extensor training on lumbar multifidus functional cross-sectional area and functional status of patients with chronic nonspecific low back pain. *Spine* 2012;37(26):E1651-E1658.

38. Hu ZJ, He J, Zhao FD, Fang XQ, Zhou LN, Fan SW. An assessment of the intra- and inter-reliability of the lumbar paraspinal muscle parameters using CT scan and magnetic resonance imaging. *Spine* 2011;36(13):E868-74.