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Geography of lumbar paravertebral muscle fatty infiltration: the influence of demographics, low back pain, and disability

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ABSTRACT

Study Design: Cross-sectional

Objective: We quantified fatty infiltration (FI) geography of the lumbar spine to identify whether demographics, temporal low back pain (LBP), and disability influence FI patterns.

Summary of Background Data: Lumbar paravertebral muscle FI has been associated with age, sex, LBP, and disability; yet, FI accumulation patterns are inadequately described to optimise interventions.

Methods: This cross-sectional study employed lumbar axial T1-weighted MRI in 107 Southern-Chinese adults (54 females, 53 males). Single-slices at the vertebral inferior end-plate per lumbar level were measured for quartiled-FI, and analysed against demographics, LBP, and disability (ODI: Oswestry Disability Index).

Results: Mean FI% was higher in females, on the right, increased per level caudally, and from medial to lateral in men ($p<0.05$). FI linearly increased with age for both sexes ($p<0.01$) and was notably higher at L4&5 than L1,2&3 for cases aged 40-65yrs. BMI and FI were unrelated in females and inversely in males ($p<0.001$). Females with LBP_{week} and males with LBP_{year} had 1.7% (each) less average FI ($p<0.05$) than those without pain at that time-point. Men locating their LBP in the back had less FI than those without pain ($p<0.001$). Disability was unrelated to FI for both sexes ($p>0.05$).

Conclusions: Lumbar paravertebral muscle FI predominates in the lower lumbar spine, notably for those aged 40-65, and depends more on sagittal than transverse distribution. Higher FI in females and differences of mean FI between sexes for BMI, LBP, and disabling ODI suggest sex-differential accumulation patterns. Our study contradicts pain models rationalising lumbar muscle FI and may reflect a normative sex-dependent feature of the natural history of lumbar paravertebral muscles.

Keywords: paravertebral; muscle; multifidus; low back pain; disability; disc degeneration; phenotypes; fatty infiltration

Level of Evidence: 2

KEY POINTS

- This is the first study to quantify the geography of lumbar paravertebral muscle fat infiltration (FI) in the transverse plane based on axial MRI.

- Fatty infiltration (FI) of the paravertebral muscles is predominantly noted in the lower lumbar spine, whereby spatial distribution of FI was dependent upon lumbar level rather than medial-lateral distribution in the axial profile.

- Although paravertebral FI increased with age, sex-differential fat accumulation patterns were noted, with variations with body mass index (BMI), low back pain (LBP) and disability profiles between males and females.

- Males were noted to have less paravertebral muscle FI with greater BMI and with LBP and/or sciatica but higher FI with greater disability profiles, whereas BMI and pain/disability profiles did not differ among the female population.

- This study contradicts previous models that relate pain and disability with FI of the paravertebral muscles.

INTRODUCTION

Low back pain (LBP) is one of the world's most disabling diseases,[1] and is forecast to increase in cost to society[2,3] alongside an ageing global population.[4] The condition is highly relevant, with a lifetime prevalence reportedly as high as 84%, and an annual prevalence between 22-65%.[5] However, the variety and uptake of treatments for LBP have increased[3,6,7] without an appreciable reduction in the problem.[1,2] There is an urgent need to develop different, effective, and resource-efficient management strategies to mitigate its economic, social, and personal impact.[8-11] Paravertebral muscles are receiving more attention as promising targets toward optimising spinal health in people with and without LBP.

Fatty infiltration (FI) of lumbar paravertebral muscles increases with age in healthy, asymptomatic adults,[12-16] and relates to spinal curvature[17] and posture.[18] Degenerative imaging features of the spinal column, such as facet joint osteoarthritis,[19] spondylolisthesis,[19] disc space narrowing,[19,20] and type 2 Modic changes,[19,20] have been associated with paravertebral muscle FI. Yet, despite a substantial body of literature associating back muscle FI with LBP[19-29] and spinal disorders,[30-36] inconsistent associations cast doubt not only on pain causation models but also measurement methods. Mechanistic/unloading[37] or skeletal muscle denervation theories[38] within the spinal degenerative cascade[39,40] may offer a viable rationale. Few longitudinal studies examine temporal changes to the lumbar muscle FI,[26,41,42] such that the influence of interventions on muscle composition remain unclear despite emerging evidence for the association of FI to altered function.[21] Understanding patterns of and measures for fat distribution in muscle tissues may help to determine where prevention and rehabilitation efforts could be best directed on a patient-by-patient basis.

Corresponding with degenerative features of the vertebra and discs,[43] there is an indication that FI predominates in the low lumbar levels[12,15,26,30] where paravertebral muscle volume is greatest.[12] Of the lumbar paravertebral muscles, the multifidus[12,13] or erector spinae[15,26,30] appear to be most susceptible, and where ethnicity, age, and sex-type seem influential.[44] As far as we are aware, no large-scale study has examined the spatial distribution of lumbar paravertebral muscle FI in the transverse plane. Such detail is necessary to better understand where fat has a propensity to accumulate, and therefore to identify where muscular interventions may be targeted. Our study therefore examined the distribution of paravertebral muscle FI throughout the lumbar spine using a method quantifying the geography of FI in the transverse plane. We analysed the results in relation to subject demographics, LBP and disability to identify differential characteristics.

METHODS

Study population and design

This was a cross-section study of 108 volunteers of Southern Chinese origin. Due to inability to assess axial imaging parameters in one participant, the study included 107 subjects. Individuals were recruited from an ongoing population-based cohort list, all of which were recruited by open invitation and whose details and protocol are reported elsewhere.[45-47] All subjects of the larger cohort were recruited to assess MRI changes of the spine and not based on the presence or not of pain. No subject was enrolled with known trauma, previous spine surgery, metabolic disorders, spinal deformities, and infections. These 107 subjects were randomly selected from this cohort list, irrespective of pain or disability profiles, and consecutively enrolled when invited and re-imaged to be part of a novel imaging study and spinal phenotype assessment. All 107 subjects underwent axial T1-weighted MRI. Participant demographics (e.g. sex, age, body mass index (BMI:kg/m^2)) were obtained at the time of clinical pain/disability assessment. Imaging was undertaken within three months of this clinical visit. Institutional review board approval was achieved to perform this study. Due to funding constraints, 108 subjects were recruited to be part of this imaging cohort.

Assessment of pain and disability

Subjects were asked to indicate the presence of LBP (localised LBP or sciatica (pain radiating into the lower extremity extending beyond the knee) for ≥two weeks; yes/no) at different time-points: (1) lifetime, (2) past year, (3) past month, (4) past week, and (5) today. Subjects were also asked the predominant location of their pain, which was categorised as LBP, sciatica, both, or none. Disability was examined using the Oswestry Disability Index (ODI) [48,49] where subjects with ODI ≥20% were assigned with disability, and those below the threshold without. Additional details regarding the assessment of pain and disability relevant to the parent study have been reported previously.[45,47]

MRI parameters and measurements

Lumbar MRIs were obtained using a 3-Tesla scanner (Siemens, Munich, Germany or Philips, Best, The Netherlands).[46] T1-weighted axial MRIs included the following parameters: central, supine body position within the bore; repetition time 500-800ms (body size dependent); echo time 9.5ms; FOV of 210x210mm; Matrix of 218x256; slice thickness 4mm with 0.4mm gap; flip angle 90°, and total acquisition duration 137 seconds. This scan included the caudal part of T12 to the cephalad portion of S3. Images were stored in DICOM format.

The reliability of our MRI method (intra-rater ICC=0.88, inter-rater ICC=0.82) for evaluating the spatial distribution of FI in this population by our rater has been previously described.[50] Briefly, images were evaluated in random order by a single observer (**ANM**) blinded to participants' clinical or demographic status. Single axial slices approximating the inferior vertebral end-plates of L1 through to L5 were selected (cross-referenced from the equivalent sagittal scans) and examined. Regions of interest (ROI) were manually traced (bilateral with randomly selected starting-side) over the lumbar paravertebral muscles encircling multifidus, longissimus thoracis lumborum, and iliocostalis lumborum (together)[51] using a semi-automated Matlab-based programme. The programme then automatically divided the ROI into equitable quarters based on pixel number, and then determined percent fat content (medial to lateral separately, and together) with reference to a rater-dependent selection of homogeneous subcutaneous fat[50] **(Figure 1)**.

Modelling

As our principle research question was to identify where FI accumulated in the transverse plane, in our initial modelling step, we estimated sex-specific models with FI as the dependent variable and level, quartile, the interaction between level and quartile, and right-left as covariates (Model 1). In order to control for potential confounders the initial model was subsequently adjusted for age, and BMI (Model 2). We also explored further models, adjusting for temporal pain, and disability. However, adjusting for the latter variables did not substantially change the association between FI and the covariates. Moreover, the great majority of temporal pain and disability covariates were not statistically significant. We therefore refrain from showing detailed results of our further model exploration and instead the results are reported in text.

Statistical Analyses

Stata Version 14.1 (StataCorp, College Station, TX, USA) was used for all statistical analyses. Mean and standard deviations (SD) noted as ± where applicable. We applied generalized estimation equation regression models for clustered data with robust standard errors based on the sandwich estimator and exchangeable correlation structure using Stata's xtgee command. We reported estimated regression coefficients with corresponding standard errors and 95% confidence intervals (CI). Statistical significance was established at $p<0.05$.

RESULTS

Descriptive statistics are presented in **Table 1**. The sample comprised 54 females and 53 males of similar mean age (females: 53.7±7 years; males: 51.3±8.1 years) and BMI (females: 23.6±4.0 kg/m^2; males: 25.5±2.5 kg/m^2). Females had higher mean FI (31.5±5.9%) than males (26.3±5.4%; $p<0.001$). Pain was present in diminishing proportions from life to today for both sexes (data not shown): Females: LBP_{life} 85.7%, LBP_{year} 77.1%, LBP_{month} 60.4%, LBP_{week} 46.8%, and LBP_{today} 33.3%; Males: LBP_{life} 81.8%, LBP_{year} 74.4%, LBP_{month} 58.1%, LBP_{week} 55.8%, and LBP_{today} 41.9%. Disability was present in 31.5% females and 34.0% males.

Results of the multivariate analyses (**Table S1**, http://links.lww.com/BRS/B426, Model 2) confirmed that females had higher mean FI than males, which was an observation shown for each lumbar level and quartile when adjusted for age and BMI (**Figure 2**). Fat content increased per level caudally ($p<0.001$), and per quartile from medial to lateral in males ($p<0.001$). However, this pattern of increasing lateral FI distribution differed at L5 for both sexes where the highest values were shown in the first and third quartiles. The pattern for transverse FI distribution observed in the upper levels (L1&L2) differed from the lower (L4&L5) (**Table S1**, http://links.lww.com/BRS/B426 and **Figure 2**). The right side showed more mean FI than the left for both sexes (by 0.79% in females (CI: 0.32-1.27%) and by 0.46% in males (CI: 0.03-0.88%; $p<0.05$)). A linear increase in FI with age was seen for both sexes (females: 2.2%/10 years, CI: 0.5-3.8%, $p<0.05$; males: 1.5%/10 years, CI: 0.4-2.4%, $p<0.01$) and was notably higher at L4&5 than L1,2&3 for cases aged ~40-65 years (**Table S1**, http://links.lww.com/BRS/B426 and **Figure 3**). BMI was unrelated to FI in females, yet showed an inverse relationship in males (-0.63% (per BMI_{unit}), CI: -0.90 to -0.36, $p<0.001$) (**Table S1**, http://links.lww.com/BRS/B426 and **Figure 4**).

Temporal pain was generally unrelated to FI for both sexes (data not shown), except in females with LBP_{week} who had 1.72% less mean FI (CI: -3.33 to -0.10%, $p<0.05$) than those without pain at that time-point, and males with LBP_{year} who had 1.68% less mean FI (CI: -3.20 to -0.15%, $p<0.05$) than those without pain at that time-point. Males describing localised LBP had less FI than those with no pain (-3.86%, CI: -5.40 to -2.33, $p<0.001$) and a trend for less FI in those with LBP and sciatica than those with no pain (-1.75%, CI: -3.76 to 0.26, $p<0.10$). Back disability (ODI≥20%) was unrelated to FI for both sexes but showed a trend for 1.57% higher FI in men with disability (females: $p=0.69$; males: $p=0.09$) (data not shown).

DISCUSSION

This study quantifies the geography of lumbar paravertebral muscle fat content in the transverse plane based on axial MRI. Our Asian representative population confirms higher proportions of FI in women and with age, and particular susceptibility at the lowest lumbar levels in both sexes. We reveal an increasing proportion of FI from medial to lateral particularly in the upper lumbar spine, and in men, and show differences in the spatial distribution of FI relating to age, sex, and BMI. Self-reported pain had only limited association to lumbar paravertebral fat content and its geography, and disability (ODI) was unrelated. The findings have mechanistic implications in explaining the presence of FI, and in targeting rehabilitation strategies where different requirements for each sex-type exist.

The results agree with literature spanning Asian and Caucasian ethnicities reporting higher proportions of FI in erector spinae than multifidus (Korean,[15] Finnish,[26] and Hungarian cohorts[30]). However, Crawford *et al.*[12] described higher fat content in multifidus at L1-4 in a

Swiss cohort, and higher proportions in erector spinae only at L5. Differences in imaging sequencing used between these studies, and their defined ROIs may explain these variations and highlight the need for standardised methodologies.[51] It is plausible that fat accumulates selectively secondary to variables not examined in our study, including genetic influences like spinal curvature and anatomical variations. **Figure 2** demonstrates an atypical FI distribution pattern at L5; this may be a result of morphological variabilities (e.g. fibre orientation)[52,53] and level-dependent influences on muscle fat accumulation and should be considered in further investigations. Emerging evidence points to differences between ethnicities in terms of yearly accumulation of fat in lumbar paravertebral muscles of asymptomatic cases, and where erector spinae composition appears to decline rapidly in Asians after middle age.[44]

In agreement with studies examining multiple lumbar levels,[12,15,17,26] our findings are clear that FI has a propensity for the lowest lumbar levels over the upper lumbar spine in both sexes, all ages, and within our cohort's range of BMI. Lee *et al.*[15] discuss a plausible mechanistic explanation for this caudal spatial distribution based on a cantilever phenomenon[54] where L5-S1 is rendered susceptible to degeneration as the motion hinge between the relatively fixed trunk (maintained by intraabdominal pressure[55]) and the fixed sacropelvic complex. Further, their results suggest a temporal pattern of fat distribution. Our findings presented in **Figure 3** suggest a distinct separation of the upper and lower lumbar spines for those aged late thirties to late sixties in both sexes. We speculate that this may reflect the normative degenerative cascade[56] where mid-adulthood aligns with the stage of instability[57] and probable modified loading and stress-shielding of tensile tissues. Another aligned speculation is that lordotic spinal curvature predisposes motion segments to the development of paravertebral muscle FI. In their MRI study of healthy Danish adults comparing FI proportion in several muscles including three regions of the spine, Dahlqvist *et* *al.*[16] noted higher fat content in the lumbar and cervical paravertebral muscles than those in the thoracic spine using Dixon methods. In addition, higher FI has been shown for Brazilians with sway back posture[18] indicating an influence of spinal curvature on fat accumulation. Further investigation regarding heritable features of the spine in relation to muscle composition remain important in refining our expectations on what and how muscle and other soft-tissues can be influenced.

Our results have also indicated a propensity for FI in right-sided lumbar paravertebral muscles compared to those on the left. The literature surrounding sided-asymmetry is conflicted with studies using similar methodologies based on quantifying FI from full muscle volumes in asymptomatic cohorts showing different results,[12,14] and with limited association to handedness.[12] As such, consensus regarding the meaningfulness of sided asymmetry has not been reached and may even be related to methodological limitations like body centring in the bore, starting side for manual segmentation[50], or phenotype variability in morphology.

An alternative explanation for the differences shown in the upper and lower lumbar levels may be that the method used has superiority for identifying FI in either the medial-lateral elongated muscle morphology of the upper lumbar levels or the rounded anterior-posterior nature in the lower lumbar spine (**Figure 1**).[51] However, in investigating our method's reliability, Mhuiris *et al.*[50] show higher repeatability for the lower lumbar levels than upper and for the first medial quartile compared with the two most lateral. This is encouraging given degenerative change and LBP predominate in the lower lumbar spine and therefore are where studies are more commonly undertaken; however, further investigation regarding method sensitivity and comparison to Dixon or other multi-echo sequencing is warranted. Furthermore, we consider there to be a need to better identify fat propensity within each quartile, particularly for those representing multifidus where the shorter fibres have a deeper position[52] and differential activity[58] than longer (superficial) fibres.

The positive relationship between age and FI was expected and is in agreement with several cohort- and population-based studies assessing either asymptomatic or LBP participants.[12,14,15,21,26,42] Our results revealing sex-differential relationships between FI and BMI agree with recent studies examining substantial asymptomatic Asian[15] and Caucasian[12] cohorts, and support the need for sexes to be analysed separately in studies determining parameters relating to paravertebral muscle composition. As depicted in **Figure 4,** females had no association between BMI and FI at any lumbar level; however, males showed an inverse relationship with less FI in participants with higher BMI. The latter observation is perhaps counterintuitive but may be indicative of males storing their fat elsewhere than the lumbar paravertebral muscles. This is plausible given body tissue composition differs substantially between sexes[59] with higher total and abdominal subcutaneous adipose tissue in women, and higher visceral adipose tissue in men.[60,61] Males are also known to have higher total lean muscle tissue but this attribution is typically based on studies examining larger muscles of the appendicular skeleton.[61]

Our findings appear inconsistent with various pain models explaining the presence of lumbar paravertebral muscle FI. Our statistical modelling with temporal self-reported pain as confounders revealed only two associations indicating slightly lower fat in those reporting pain at a week (females) or year (males). While this may agree with others reporting no or limited association between LBP and paravertebral muscle FI, we are hesitant to definitively negate any association between FI and pain given our statistical modelling emphasised description of the geography of lumbar paravertebral muscle FI. Further, the lack of definitive measure for pain as a highly individualised experience represents a limitation. Instead, examining pain as a dependent variable may reveal new insights. Our sample describes LBP lifetime (84%), annual (76%) and point (37%) prevalences toward the higher end of reported global ranges,[5] which appears to contradict the notion that people in Hong

Kong have less LBP.[62] Furthermore, our methods rely on self-reported recollection of historical pain, which is subject to bias and may not effectively represent the complex and changing state of LBP. Similarly, we reveal no association between FI and disability (as measured using the ODI at the time of clinical assessment). However, our finding indicating a trend for higher FI in men with disability is suggestive of a sex-specific relationship.

Our study has several strengths in examining a substantial sample of population-based (i.e. non-patient-based) Asians and employing a reliable quantitative MRI method for assessing lumbar paravertebral muscle composition. We provide novel contributions in describing the spatial distribution of FI in the lumbar spine, particularly in relation to accumulation patterns in the transverse plane, and according to lumbar level. The differences shown between sexes provide new insight that must be considered when planning future studies to allow for meaningful sub-group analyses. We acknowledge that our muscle composition data is represented by single slices of T1-weighted axial MRI at each lumbar level. While this method is reliable and has sound efficiency, we accept that a multi-slice approach may represent the whole level more effectively. Furthermore, we were limited to a clinical T1-weighed scan where a uniform frequency difference between fat and water species is assumed. Based on the differential precessional frequencies of fat and water protons, a multi-echo Dixon technique may provide a superior alternative.[51]

CONCLUSIONS

Our findings do not support previous pain models explaining lumbar paravertebral muscle FI and may better reflect a normative sex-dependent feature of the degenerative cascade. We confirm that lumbar paravertebral muscle FI predominates in the lower lumbar spine; its spatial distribution appears more dependent on lumbar level than on the medial-lateral distribution in the axial plane. Higher FI in females and differences of mean FI between sexes for BMI, LBP, and disabling ODI scores suggest sex-differential fat accumulation patterns, which should inform priori decisions in future studies. Whether paravertebral muscle fat content is modifiable with or without intervention requires further exploration in longitudinal studies.

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FIGURE LEGENDS

Figure 1: Axial T1-weighted MRI quantification method indicating each single slice location per lumbar level (left), and its application at L1 (right top) and L4 (right bottom) to demonstrate level differences. Regions of interest are manually defined and automatically quartiled from medial (Q1) to lateral (Q4) based on equal pixel numbers (demonstrated on the left side in blue). Subcutaneous fat reference areas are indicated in black circles. Multifidus (red) and erector spinae (longissimus and iliocostalis together) (green) are illustrated per lumbar level to represent their level-specific spatial differences.

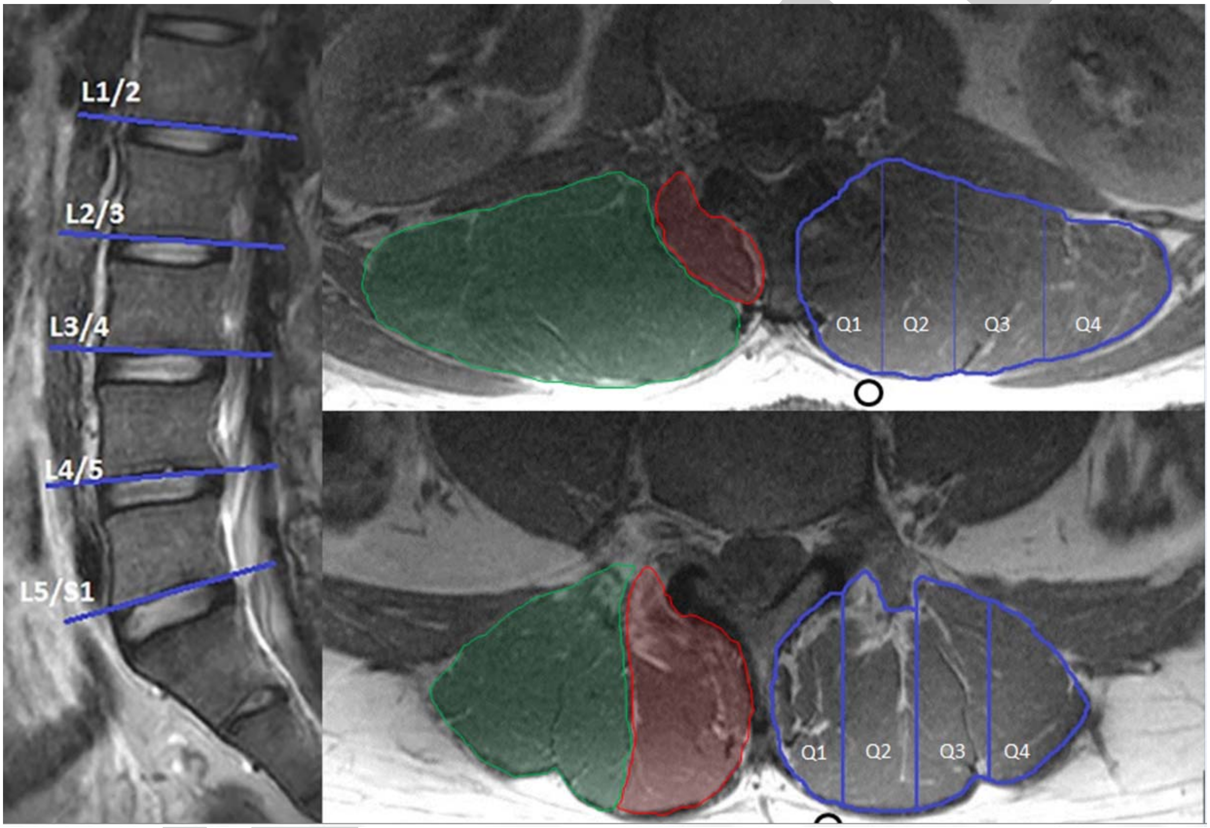


Figure 2: Adjusted predictions of FI (%) for females (left) and males (right) over quartiles by lumbar level (95% CI at means).

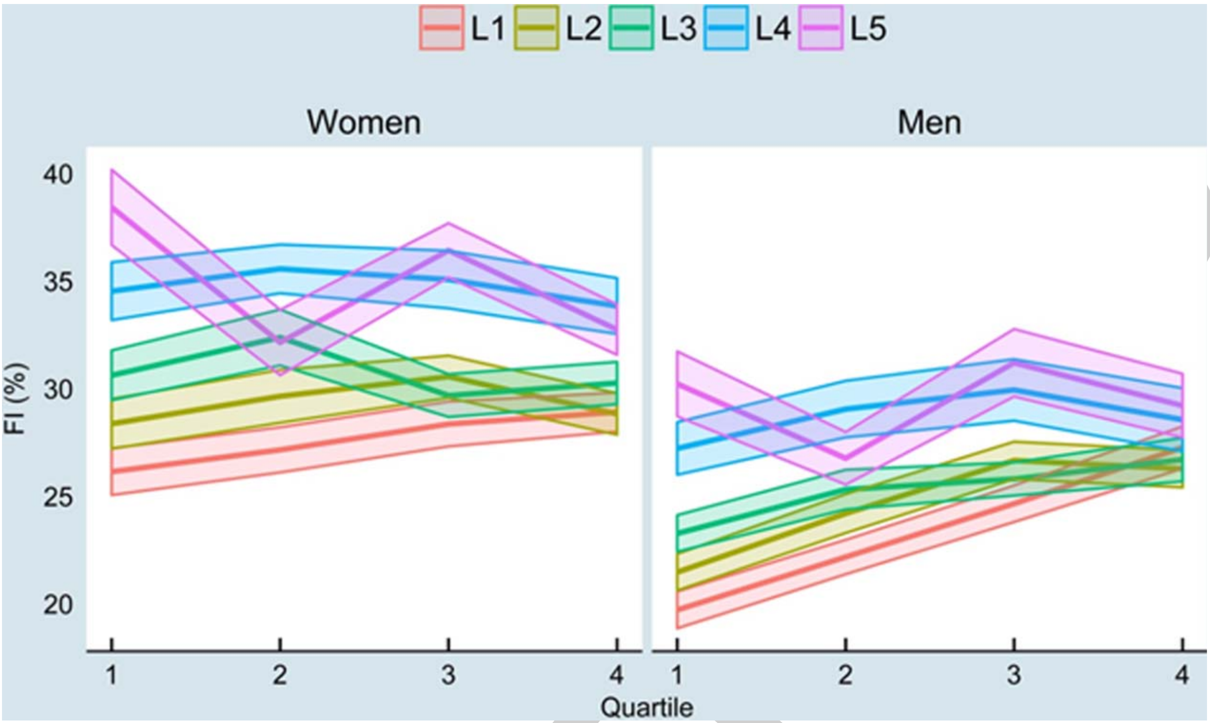


Figure 3: Adjusted predictions of FI (%) for females (left) and males (right) over age by lumbar level (95% CI at means).

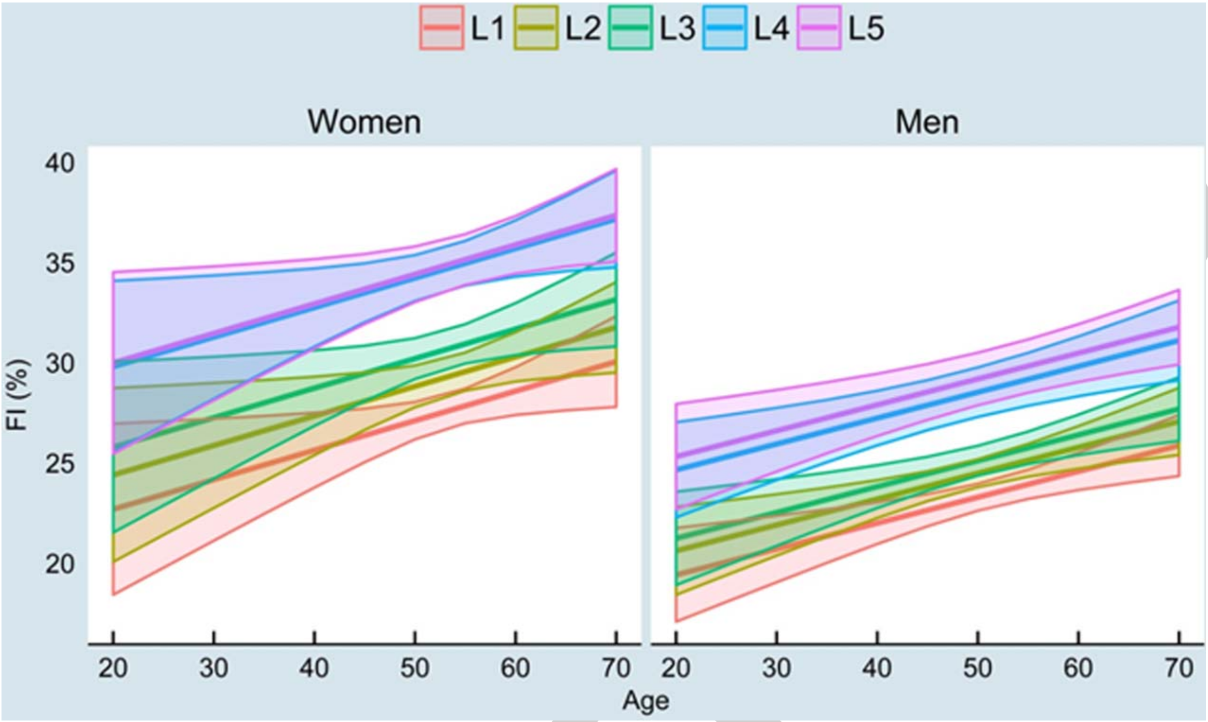
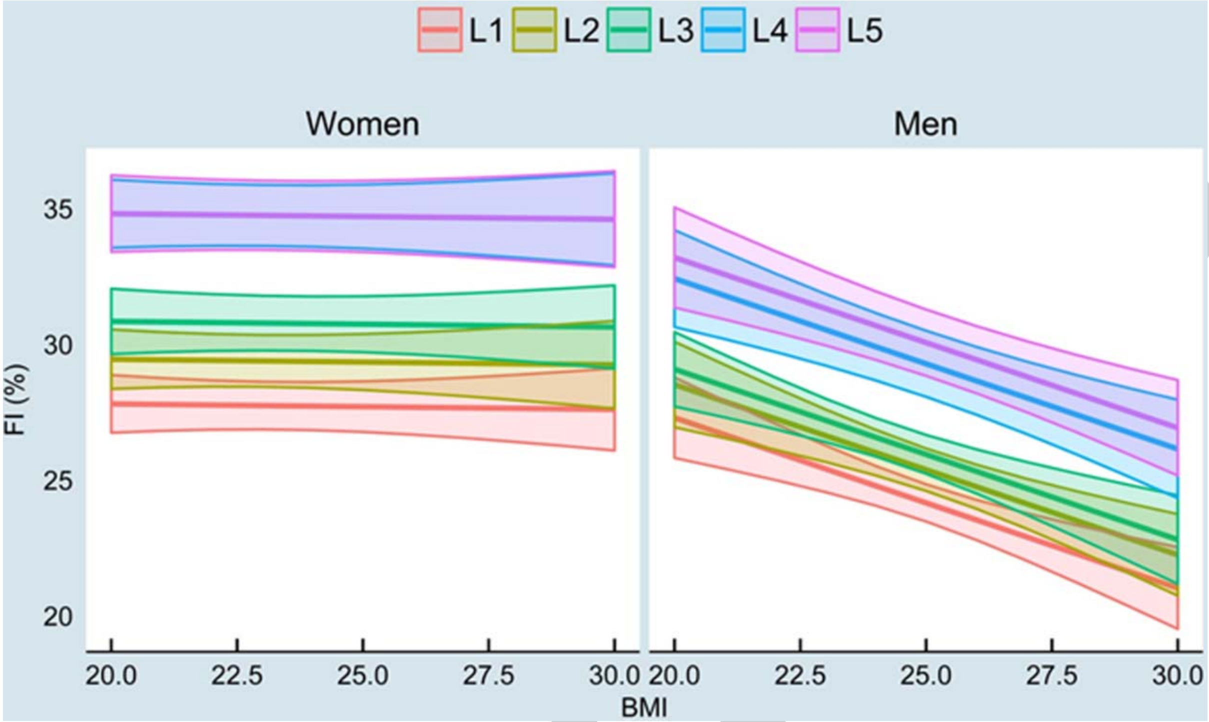


Figure 4: Adjusted predictions of FI (%) for females (left) and males (right) over BMI by lumbar level (95% CI at means).



TABLE

Table 1: Descriptive statistics of continuous variables according to sex (females=53; males=54) and total sample.

	Females				**Males**				**Total**			
Variables	Mean	SD	Min	Max	Mean	SD	Min	Max	Mean	SD	Min	Max
FI total (%)	31.5	5.9	16.8	56.1	26.3	5.4	12.8	50.4	28.9	6.2	12.8	56.1
Age (years)	53.6	6.9	22.3	67.2	51.3	8.1	25.6	65.5	52.5	7.6	22.3	67.2
BMI (kg/m^2)	23.6	4.0	18.1	39.5	25.6	2.5	20.8	29.8	24.5	3.5	18.1	39.5
ODI (%)	12.7	13.0	0	48.0	11.9	12.5	0	60.0	12.4	12.8	0	60.0

SD: standard deviation; Min: minimum; Max: maximum; FI: fatty infiltration; kg: kilograms; m: meters; %: percentage; BMI: body mass index; ODI: Oswestry Disability Index