REVIEW ARTICLE

Imaging Evaluation of Fat Infiltration in Paraspinal Muscles on MRI: A Systematic Review with a Focus on Methodology

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Purpose: Numerous studies have applied a variety of methods to assess paraspinal muscle degeneration. However, the methodological differences in imaging evaluation may lead to imprecise or inconsistent results. This article aimed to provide a pragmatic summary review of the current imaging modalities, measurement protocols, and imaging parameters in the evaluation of paraspinal muscle fat infiltration (FI) in MRI studies.

Methods: Web of Science, EMBASE, and PubMed were searched from January 2005 to March 2020 to identify studies that examined the FI of paraspinal muscles on MRI among patients with lumbar degenerative diseases.

Results: Intramyocellular lipids measured by magnetic resonance spectroscopy and FI measured by chemical-shift MRI were both correlated to low back pain and several degenerative lumbar diseases, whereas results on the relationship between FI and degenerative lumbar pathologies using conventional MRI were conflicting. Multi-segment measurement of FI at the lesion segment and adjacent segments could be a prognostic indicator for lumbar surgery. Most studies adopted the center of the intervertebral disc or endplate as the level of slice to evaluate the FI. Compared with visual semiquantitative assessment, quantitative parameters appeared to be precise for eliminating individual or modality differences. It has been demonstrated that fat CSA/total CSA (based on area) and muscle–fat index (based on signal intensity) as quantitative FI parameters are associated with multiple lumbar diseases and clinical outcomes after surgery.

Conclusion: Having a good command of the methodology of paraspinal muscle FI on MRI was effective for diagnosis and prognosis in clinical practice.

Key words: Degeneration; Fat infiltration; Imaging evaluation; Magnetic resonance imaging; Methodology; Introduction

Introduction

Fat infiltration (FI), a crucial indicator of composition change of paraspinal muscle degeneration, may contribute to the loss of muscle strength and endurance[1]. There has been increasing interest in imaging evaluation of FI as a potential diagnostic and prognostic tool in lumbar spine health in recent decades[2].

Systematic reviews have pointed out that the impact of FI on diseases has conflicting results[3–5]. These discrepancies might be due to methodological differences, such as imaging modality, measurement protocols, and parameter selection[1,4,6]. Several advanced MRI approaches have been proposed since 2006, including magnetic resonance spectroscopy (MRS) and chemical-shift MRI[7,8]. Heterogeneity of measurement protocols involves the level and

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slice selection (e.g. slice positioning) and the definition of the region of interest (ROI)[1]. Furthermore, numerous imaging parameters hitherto have been used to describe the degree of FI, including semiquantitative and quantitative parameters[1].

To our knowledge, no prior systematic reviews have examined these imaging methods. This review aimed to summarize the existing MRI methods of FI assessment from the methodological perspective of imaging modalities, measurement protocols, and parameter selection, and to discuss the diagnostic benefits for lumbar degenerative diseases of using various methods for measuring FI.

Literature Review

Three electronic databases (Web of Science, Embase, and PubMed) were searched from January 2005 to March 2020 to identify studies that examined the FI of the paraspinal muscles (psoas, multifidus, and erector spinae). All fields were searched for these terms: "paraspinal muscles," "multifidus," "transversospinales," "erector spinae," or "psoas major"; and "spinal degeneration" or "low back pain". Two independent reviewers determined whether studies were included based on the following inclusion criteria: (i) recruited participants who have reported lumbar degenerative diseases (i.e. radiculopathy, disk herniation, sciatica, spinal stenosis, spondylolysis, spondylolisthesis, osteoarthritis, or facet joint osteoarthritis) or nonspecific low back pain (LBP); and (ii) employed MRI (conventional MRI, MRS, and chemical-shift MRI) to measure the FI of paraspinal muscles. Exclusion criteria were: (i) patients without lumbar degenerative diseases or who were younger than 18 years of age to exclude some idiopathic spinal diseases; (iii) patients not involved in any FI assessments; (iii) patients evaluated only by kinematic MRI; (iv) case reports, editorials/letters, literature reviews, guidelines, and abstract-only publications; and (v) non-English literature.

The literature review identified 4500 articles, of which 136 full-text articles were retrieved for full review. After the screening of titles and abstracts, the full text was retrieved and a total of 78 studies were deemed to meet the inclusion criteria. A search flow diagram is presented in Fig. 1.

Imaging Modality

Conventional MRI

Most studies[9–74] used conventional MRI for measuring FI. In the field of MRI sequence, our results showed that T2-weighted images[10,12–14,17,18,20,24,25,27,29,30,32–35,37,39–53,55,56,58–63,65,66,69,70] were used in quantitative assessments more often. It is expedient for orthopaedists to evaluate FI on frequently-used T2-weighted images. Suh *et al.* found that the intrarater and interrater reliability of parameters were generally excellent for both T1-weighted and T2-weighted images[53]. For predicting LBP using conventional MRI, cross-sectional studies found that greater FI was associated with LBP[50,68]. However, two longitudinal studies reported no association between FI and LBP[22,62].

Novel MRI Modalities

Because of the relatively limited accuracy of conventional MRI, several novel MRI modalities have emerged. We found some studies that applied MRS[7,75–81], chemical-shift MRI[51,69,82–85] and multi-echo MRI[75]. A comparison of different MRI modalities is included in Table 1.

MRI has facilitated detailed analyses of muscular fat masses by separating and recording the concentration of extramyocellular lipids (EMCL) and intramyocellular lipids (IMCL), which is not achievable with other technology (Fig. 2)[78]. EMCL and IMCL may play different roles in degenerative pathology. Studies have demonstrated that IMCL are significantly higher in those with chronic LBP and that there is a positive correlation between IMCL and VAS[78–80]. IMCL are also significantly correlated with sagittal alignment and anterior annulus fibrosus degeneration[76,77]. In contrast, EMCL have not been found to be significantly different between chronic LBP and normal groups[76]. Thus, IMCL of paraspinal muscles might be a useful indicator for diagnosis and rehabilitation strategies.

Chemical-shift MRI can produce water-only and fat-only images from dual-echo and/or multi-echo acquisitions that overmatch MRS when observing EMCL; thus, this is considered the contemporary standard for measuring FI. Excellent accuracy has been demonstrated for manual segmentation based on these imaging techniques compared to spectroscopy[75] and histology[81]. It is capable of quantifying proton density fat fractions (PDFF)[8,86], which has revealed favorable intra-reader and inter-reader reproducibility. Studies have demonstrated that FI based on chemical-shift MRI is associated with LBP[51,82,85] and herniated nucleus pulposus[69]. Moreover, using PDFF measurements could improve the prediction of paraspinal muscle strength beyond cross-sectional areas (CSA)[86]. Multi-echo MRI, another new approach based on exploiting chemical shift differences of water and fat resonances, produced a concurring result with the fat values derived by MRS[75]. Fischer *et al.* performed a quantification of fat content through multi-echo MRI in LBP patients[75].

Measurement Protocol

Single-Segment or Multi-Segment Measurement

Recent research has suggested that using a single-segment measurement to evaluate FI is insufficient for representing the whole lumbar area[32]. Surgeons should perform a multi-segment assessment instead of a single-segment assessment to evaluate the overall situation of paraspinal muscle degeneration. Considering that the MR slice has a certain thickness, volumetric measures based on a three-dimensional volume across L1–S1 (or the levels of interest) are more appropriate and realistic in representing the entire muscle volume variability[11].

Studies that investigated nonspecific LBP were inclined to assess multiple segments in the lower lumbar region[21,23,24,26,28,34–36,48,49,52,54,55,57,60–65,83], especially

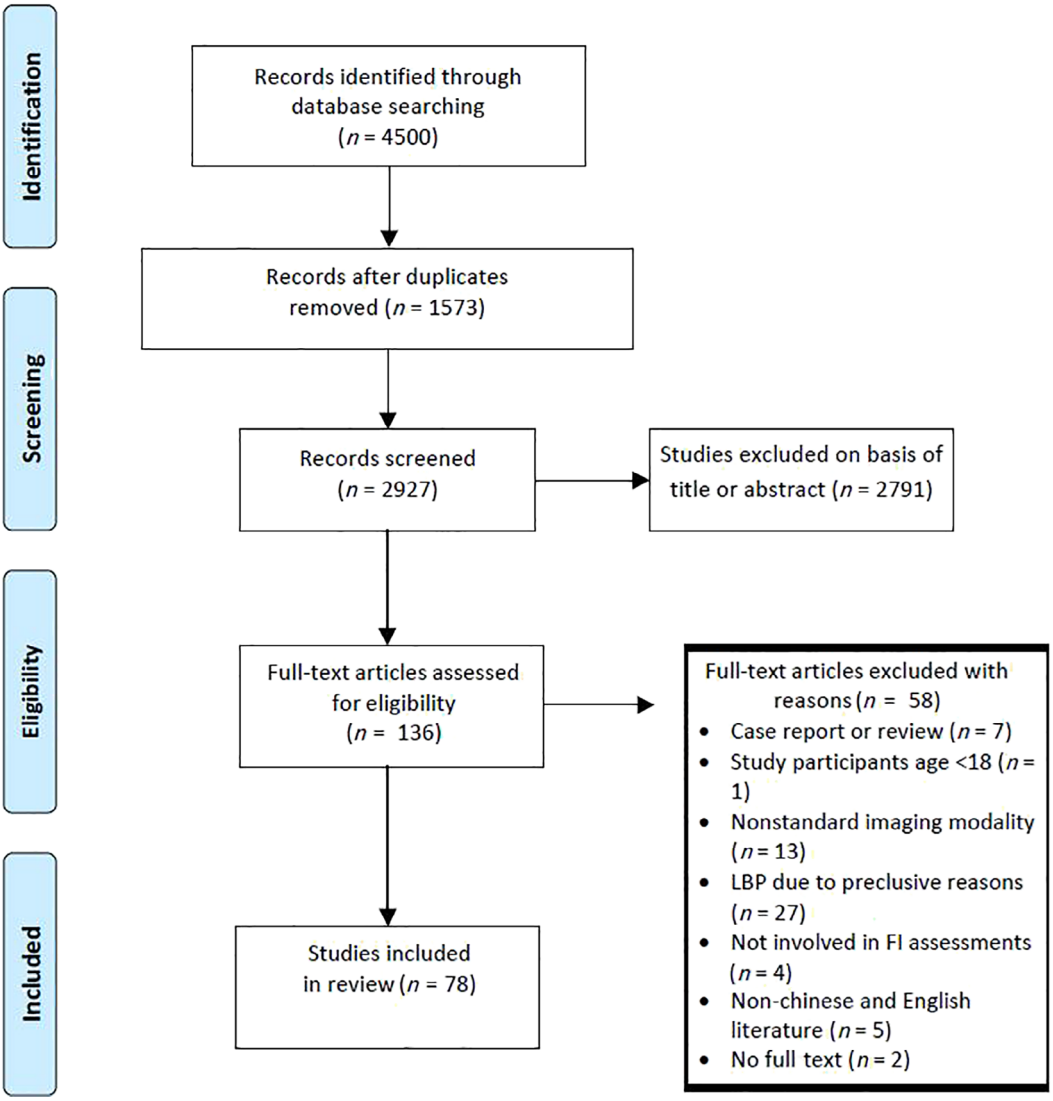

Fig 1 The selection flow for studies included in this review.

focusing on L4. According to Crawford *et al.*[87], the fat content at L4 best represented that of the entire lumbar region in healthy participants. Hebert *et al.*[22] also reported that pathological change appeared most often at L4. Storheim *et al.* revealed that higher FI at lower lumbar segments was associated with higher Oswestry disability index (ODI) scores and greater pain intensity in chronic LBP patients[49]. This indicated that the evaluation of FI in lower lumbar segments was useful and could reflect the morbid state of patients.

For specific lumbar degenerative diseases, studies have tended to evaluate the lesion segment and adjacent segments[9,11–15,20,27,30,39,47,51,53,63,70]. Several studies have demonstrated that FI could be a risk factor for lumbar degenerative diseases[13–15,47]. We also found that FI of paraspinal muscles was associated with clinical outcomes. Higher FI of multifidus was correlated with lower functional status and less improvement in ODI in patients with LSS after surgery[63,70]. Thus, evaluating the FI at the lesion segment and adjacent segments could be a viable method for predicting the clinical outcomes of lumbar surgery.

Slice Selection

Most studies used the center of the intervertebral disc[10,21,27–30,39,43,45,50,52,53,56,59–62,65,71,74,79] or the superior/inferior endplate[9,15,19,20,26,31,34,35,41,44,47–49,57,63,64,66,68–70,82,83,85] as the level of slice. These slices are common and available in clinical practice. However, there is no research demonstrating the impact of different slice positioning on the FI results.

Defining the Novel Region of Interest

For manually defining the ROI, minute changes in muscle composition may not be clearly visible[88]. Semi-automatic

TABLE 1 Comparison of different MRI modalities

MRI modality	Characteristic	Application
Conventional MRI T2-weighted	Convenient in clinical practice; the accuracy is relatively low	The most commonly used tool in quantitative assessment
MRS	Can record the concentration of both IMCL and EMCL	IMCLs were correlated to several degenerative lumbar pathologies
Chemical-shift MRI	Overmatches MRS in terms of EMCL; the contemporary standard for measuring EMCL	PDFF were correlated to several degenerative lumbar pathologies; and predicted the paraspinal muscle strength better than CSA
Multi-echo MRI	Produces a concurring result compared with MRS	Have been performed in LBP patients

CSA, cross-sectional area; EMCL, extramyocellular lipids; IMCL, intramyocellular lipids; LBP, low back pain; MRS, magnetic resonance spectroscopy; PDFF, proton density fat fractions.

technologies emerging to define the border of paraspinal muscles have the potential to assist with this problem. Antony *et al.* implemented an interactive segmentation of the erector spinae and the multifidus muscles using the live-wire technique (Fig. 3A,B)[24].

Interestingly, two studies have proposed a method allowing for quantification of the spatial distribution of FI in each quartile of ROI (medial to lateral) and describing whether there is a geographical propensity for fat to accumulate (Fig. 4)[31,57]. They found that fat content increased per quartile from medial to lateral in males, whereas the increase of FI depended more on sagittal than transverse distribution[57]. Antony *et al.* proposed a new method to quantify the fat content in six regions with reference to the center of the spinal column, which represented the axis of spinal rotation[24]. These studies demonstrated that orthopaedists can keep a watchful eye on different muscle regions that might have various effects on pain levels.

Imaging Parameters

Visual Semiquantitative Parameters

Our review showed that several early studies used semiquantitative visual grading with distinct cut-off points (2-point scale[19,67], [19,67], 3-point scale[9,16,49,64,68,78], 4-point scale[7,15,18,29,34,37,48,50,59,80], and 5-point scale[17,28,35,51]). When muscles were graded, the interobserver and intraobserver agreements were both acceptable with or without cut-off points[7,34,51].

Semiquantitative evaluation is convenient and intuitive in clinical practice. Studies have reported that higher FI of paraspinal muscles based on semiquantitative evaluation was correlated to functional disability, pain level, and decreased range of motion of lumbar flexion in LBP patients[9,49,64,68]. Teichtahl *et al.* also reported that paraspinal FI, but not muscle area, was associated with high-intensity pain, disability, and structural abnormalities in community-based adults[50].

Quantitative Parameters

Quantitative evaluation is more accurate than semiquantitative evaluation. Numerous quantitative parameters based on area or signal intensity were applied to define FI (Table 2). In terms of area-based indicators, fat CSA/total CSA or fat signal fractions is a universal indicator

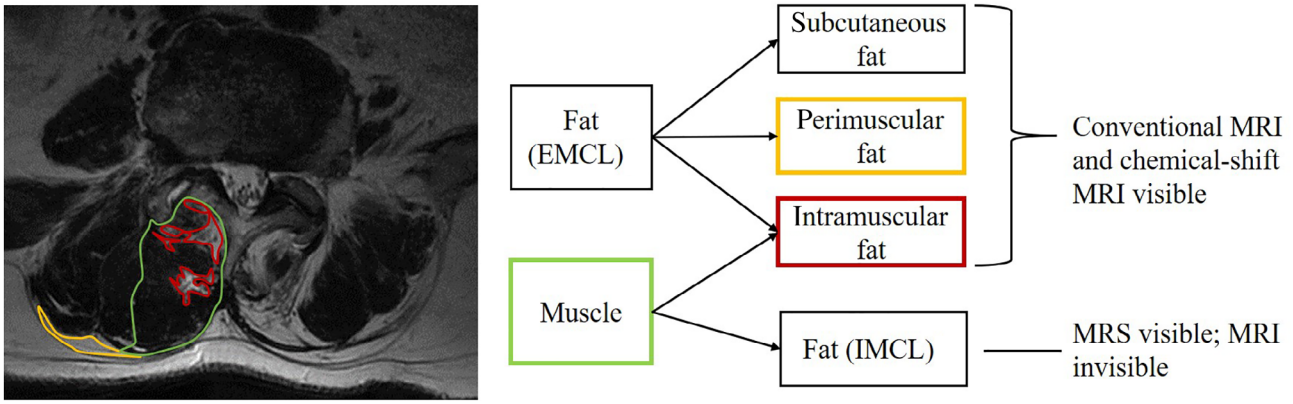

Fig 2 Distribution diagram of paraspinal muscle adipose tissue. Taking the T2-weighted image of the right multifidus muscle of the L4–5 segment as an example, the green contour represents the muscle mass, the yellow contour represents perimuscular fat, and the red contour represents intramuscular fat. The perimuscular fat is stored between muscle groups and intramuscular fat is inside muscles. The perimuscular fat and intramuscular fat pertaining to extramyocellular lipids (EMCL) can be visible on conventional MRI and chemical-shift MRI, while intramyocellular lipids (IMCL) stored in myocyte are shown only on magnetic resonance spectroscopy.

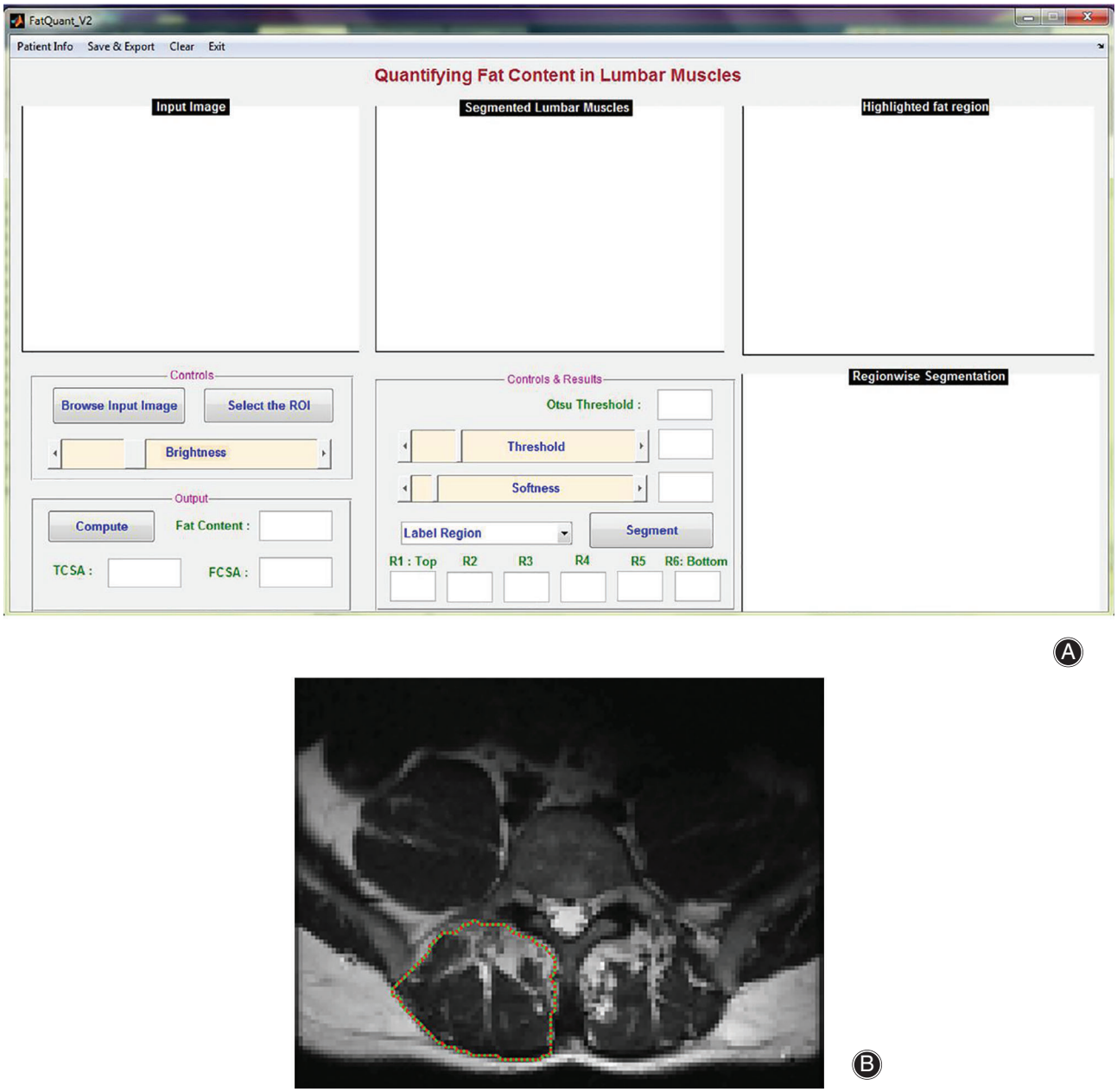

Fig 3 (A) A graphical user interface was developed based on interactive controls for selecting region of interest from the input image, threshold adjustment, and softness level adjustment. (B) MRI input image of the right erector spinae and the multifidus muscles, following a path that is as close as possible to image features detected as edges using Dijkstra's lowest cost path algorithm. However, the input image has to be down-sampled in the low-resolution image to ensure an effective running speed.

separating fat area through signal intensity difference with a threshold technology[13,24,25,28,32,33,40,46]. Studies have showed that LBP patients or those presenting with lumbar degenerative diseases have greater fat CSA/total CSA[13,25,40,46]. When multiplanar reconstruction was used, the ratio of fat volume to muscle volume outperformed fat CSA/total CSA, which was dependent upon specific slices. An MRI three-dimensional reconstruction study found that FI increased from L1–L2 to L5–S1 level in patients with lumbar spinal stenosis[11].

Signal intensity-based indicators include the muscle–fat index (MFI)[20,21,26,38,47,53,54,57] and mean MRI signal intensity[14,25,27,31]. MFI was calculated by dividing the mean signal intensity of the total muscle by the intramuscular fat to reduce individual differences, and it has been proven to be highly reliable[65,72]. Greater MFI was correlated to poor

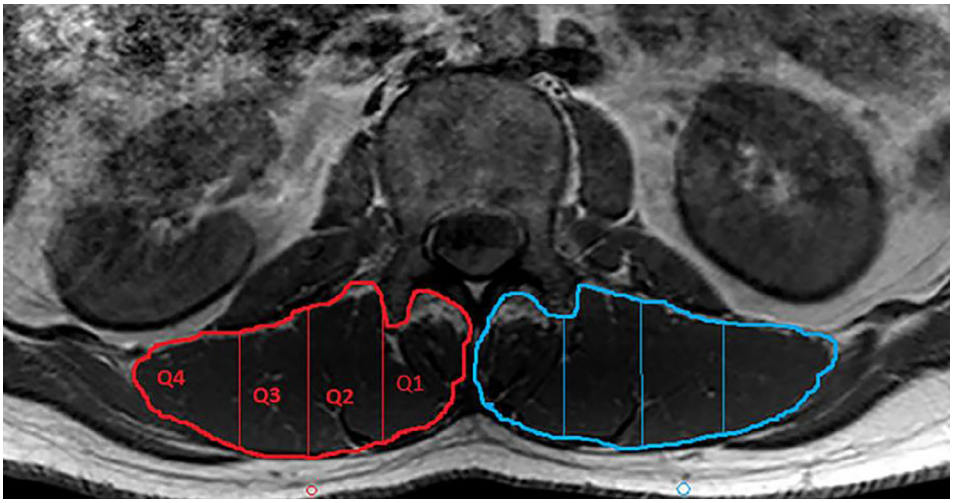

Fig 4 Paraspinal muscles were quartiled from medial (Q1) to lateral (Q4) with equal-area division (demonstrated on the right side in red).

TABLE 2 Comparison of different imaging parameters of FI

Indicator	Suggested application	Disadvantage
Semiquantitative grading	Intuitive and suitable for clinical evaluation among elderly patients; correlated with functional status and clinical outcomes	The cut-off value is uncertain and the measurement error of people with slight FI is relatively large
Fat CSA/total CSA	Quantitative parameters based on area; correlated with multiple lumbar degenerative diseases	Requires threshold method
Fat volume/ muscle volume	Quantitative parameters based on volume; reflects the overall situation of muscles	Requires three-dimensional reconstruction
MFI	Quantitative parameters based on signal intensity; correlated with clinical outcomes	The reference of fatty signal intensity in MFI was diverse
Mean MRI signal intensity		Can be influenced by individuals and measurement tools

CSA, cross-sectional area; FI, fat infiltration; MFI, muscle–fat index.

physical function[38] and high incidence of proximal junctional kyphosis[20]. However, the reference of fatty signal intensity was used in a variety of ways. Some studies used a homogenous region of perimuscular fat[21,38,54] or subcutaneous fat[20,47,57] as fat region when identifying intramuscular fat was impracticable. Applying cerebrospinal fluid from the same axial level of each MRI scan as the reference of signal intensity could also lessen variations in MRI background intensity[66,71,72]. Like CT attenuation, the mean MRI signal intensity was also considered to reflect FI in some studies but might be affected by individual differences and MRI operation differences[14,25,27,31]. We recommend combining parameters based on area and signal intensity for use as an indicator of FI.

Conclusion

Novel technologies like MRS and chemical-shift MRI have emerged to provide details on intramyocellular or extracellular fatty concentration and could be used in distinguishing degeneration of the lumbar spine. Studies might perform a multi-segment assessment including at least L4 instead of a single-segment assessment. Adopting the center of the intervertebral disc or endplate as the level of slice is expedient. The spatial distribution of FI might have a particularity in degenerative lumbar spines. Numerous quantitative parameters based on area or signal intensity were applied to define the FI, among which fat CSA/total CSA and MFI seem to be the better choices in diagnosing and predicting clinical outcomes.

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