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Impact of paravertebral muscle in thoracolumbar and lower lumbar regions on outcomes following osteoporotic vertebral fracture: A multicenter cohort study

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Abstract

Purpose: Paravertebral muscle (PVM) is an important component of the spinal column. However, its role in the healing process after osteoporotic vertebral fracture (OVF) is unclear. This study aimed to clarify the effect of PVM in thoracolumbar and lower lumbar regions on OVF clinical and radiological outcomes.

Methods: This was a multicenter prospective cohort study from 2012 to 2015. Patients ≥65 years old who presented within 2 weeks after fracture onset were followed-up for 6-months. PVM was measured at the upper edge of the L1 and L5 vertebral body in the magnetic resonance imaging (MRI) T2-axial position at registration. The cross-sectional area (CSA), relative CSA (rCSA), and fat infiltration percentage (FI%) were measured. Severe vertebral compression, delayed-union, new OVF, and remaining low back pain (LBP) were analyzed.

Results: Among 153 patients who were followed-up for 6-months, 117 with measurable PVM were analyzed. Their average age was 79.1 ± 7.2 years, and 94 were women (80.3%). There were 48 cases of severe vertebral compression, 21 delayed union, 11 new OVF, and 27 remaining LBP. Among all poor prognoses, only the FI% of the PVM was significantly associated with new OVF ($p = 0.047$) in the thoracolumbar region and remaining LBP ($p = 0.042$) in the lumbar region.

Conclusion: The occurrence of additional OVF in the thoracolumbar region and remaining LBP in the lumbar region was significantly related to the FI% of the PVM. Physicians should be aware that patients with such fatty-degeneration shown in acute MRI may require stronger treatment.

Keywords: Fat infiltration, Paravertebral muscle, New osteoporotic facture, Remained low back pain.

Mini Abstract: We investigated the effect of paravertebral muscle (PVM) on poor prognosis in osteoporotic vertebral fracture (OVF) and remaining lower back pain (LBP) in the thoracolumbar and lower lumbar regions. Additional OVF occurrence in the thoracolumbar and remaining LBP in the lumbar region was significantly related to PVM fat infiltration percentage.

Declarations

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Conflict of interest/competing interests: Hasibullah Habibi, Shinji Takahashi, Masatoshi Hoshino, Kazushi Takayama, Ryuichi Sasaoka, Tadao Tsujio, Hiroyuki Yasuda, Takeharu Sasaki, Fumiaki Kanematsu, Hiroshi Kono, Hiromitsu Toyoda, and Hiroaki Nakamura declare that they have no conflict of interest.

Ethical approval: This study was approved by the Ethical Committee of Osaka City University. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Consent to participate: Informed consent was obtained from all participants included in the study.

Introduction

Paravertebral muscle (PVM) is an important component of the spinal column to consider in relation to a balanced spinal column, release from pain, and osteoporotic fractures [1–4]. Sarcopenia may be one the main causes of several pathologies in the spinal column. Previous studies revealed that the cross-sectional area (CSA) and fat infiltration percentage (FI%) of the paraspinal muscle correlate with spinal stability and alignment [5].

Larsson et al. demonstrated that sarcopenia is an age-associated pathology; with an increase in age, the muscle mass reduces [6]. In our previous study, we reported the importance of trunk muscle mass in spinal balance, lumbar dysfunction, increased Oswestry Disability Index, visual analog scale (VAS), and EuroQol 5 Dimension [7]. Furthermore, it has been reported that the FI% of the paraspinal muscle is associated with lower back pain (LBP) and disability [8].

With an increase in age, the incidence of the osteoporotic vertebral fracture (OVF) increases. In Japan, the USA, and Europe, 18% to 26% of post-menopausal women suffer from vertebral deformity [9]. Due to the life expectancy rate in Japan, women over the age of 65 years account for approximately 28% of the entire population, and this percentage is the highest in the world [10]. The negative impact of OVF causes patient to suffer from LBP, spinal deformity, altered daily life activity, and even mortality in developed counties [11–15]. Furthermore, it is important to diagnose delayed union, nonunion of vertebral fracture, various pathologies of the spine, and PVM appearance. Therefore, magnetic resonance imaging (MRI) is an important diagnostic tool for confirming the fracture scale [16, 17].

Several studies have validated the impact of the PVM on OVF, and have revealed that PVM may play an important role in OVF incidence [18–22]. Our previous study demonstrated the natural course of PVM after the onset of OVF and showed that a reduction in PVM at the lumbar spine was significantly related to LBP and delayed union after OVF onset [23]. However, the impact of the PVM on OVF and remaining LBP in separate regions such as the thoracolumbar and lumbar regions has not been well studied. Therefore, this study aimed to clarify the impact of PVM on OVF and LBP in the thoracolumbar and lower lumbar regions.

Methods

This was a multicenter prospective cohort study involving 11 institutions in Japan (Osaka, Hyogo, and Nara). The details were described in our previous study [24], and 153 symptomatic consecutive patients completed a 6-month follow-up. The inclusion criteria of this study were symptomatic patients aged >65 years with fresh fragile vertebral fracture, which had occurred within 2 weeks prior to presentation. The exclusion criteria were multiple fractures, malignancies, pathologic fracture, fracture due to high energy trauma, infection, and direct trauma. Patient demographic data such as age, sex, body mass index (BMI), smoking history, old OVF, level of fracture, and VAS score were analyzed. BMI was calculated as body weight in kilograms divided by square of the body height in meters (kg/m^2). VAS was used to assess back pain severity, which the patient complained about after the injury in the first 2-weeks during the 6-month follow-up.

The four poor prognoses outcomes used to determine the impact of the PVM at the 6-month follow-up were as follows: 1; Severe vertebral compression (percentage of), defined as a decrease in vertebral body height of >40% [25]. 2; Delayed union (percentage of), defined by confirming the instability at fractured vertebra using dynamic X-ray at the 6-month follow-up. 3; New OVF, which comprised the detection of another fracture in addition to the previous fracture using MRI. 4; Remaining LBP, scored by patients as >40 mm on the VAS at the 6-month follow-up.

The patients' CSA, relative CSR (rCSA), and FI% in the thoracolumbar and lower lumbar regions were measured by MRI at enrollment and a the 6-month follow-up. X-ray was performed at enrollment and the 6-month follow-up.

Treatment by brace was continued for 2–3 months, and soft and hard braces were prescribed for 60% and 40% of the patients, respectively. The patients were allowed to be mobilized into an erect posture as the brace was applied. Additionally, patients were prescribed anti-osteoporotic and pain relieve medication.

Imaging assessment

All patients were examined by plain X-rays and MRIs of the spine at the time of enrollment (during the first 2 weeks after the onset of fracture) and at the 6-month follow-up, and two authors (S.T and M.H,

141 spine surgeons with 10 and 18 years of experience in spinal MRI, respectively) assessed the findings.
142 Plain X-rays were taken in sagittal view in both the supine and weight-bearing positions. The relative
143 height of the anterior wall (%) was calculated by the formula: {2×affected vertebral height / (lower
144 vertebral height + upper vertebral height)} × 100 [24].

145 When either the cranial or caudal adjacent vertebral body was deformed due to an old fracture, the
146 vertical height of the anterior wall of the fractured vertebral body was divided by the vertical height of
147 the anterior wall of the undeformed adjacent vertebral body. Delayed union was defined by a
148 recognizable intravertebral cleft on plain X-rays at the 6-month follow-up. Dual-energy X-ray
149 absorptiometry was used to measure the bone mineral density (BMD) of the mean femoral neck at the
150 time of enrollment in all patients. This detailed setup method was not unified due to the multicenter
151 study.

152 Our previous study demonstrated that MRI can provide better contrast compared to computed
153 tomography; however, standard spin echo T1-weighted sequences only provide a qualitative assessment
154 of fat, which appears white, compared with muscle, which in this sequence is dark. The extent of larger
155 agglomerations of adipose tissue can be measured, but the true fat content of muscle cannot be
156 determined from T1-weighted images because the gray values of the muscle voxels do not scale in a
157 known way with the fat content [26]. The reliability of MRI for measuring the CSA and FI% of the
158 PVM has been reported to be acceptable [27]. In the present study, two institutions used a 1.5-T MRI
159 scanner, while the remaining institutions used a 3.0-T MRI scanner. The following sequences were
160 obtained with the MRI scanners: T1-weighted turbo spin echo with a slice thickness of 3 mm (repetition
161 time [TR] 400–700 ms and time to echo [TE] minimum accessible, depending on the machine
162 capability), T2-weighted turbo spin echo with a slice thickness of 3 mm (TR 3,000–4,500 ms and TE
163 80–120 ms), and a fat saturation STIR sequence (TR 2,000–4,000 ms, TE 60–80 ms, and inversion
164 time 120–170 ms) [28]. Patients' CSA, rCSA, and FI% was measured at two different levels:
165 thoracolumbar level (T12/L1) and lower lumbar level (L4/5). The multifidus (MF) and erector spinae
166 (ES) were measured in the thoracolumbar and lower lumbar regions, which were chosen as the superior
167 endplate of the L1 and L5 vertebra (Figure). The CSA in cm^2 was calculated as the average of the right
168 and left PVM regions of interest of the axial T2-weighted MRI. The rCSA was the calculated as the

CSA of the PVM divided by the whole vertebral body area. The FI% was calculated as the ratio of the fat signal divided by the CSA of the muscle, multiplied by 100 (fat/CSA × 100). The CSAs of the muscles were outlined by measuring the borders of the muscles at two different levels.

Data analysis

The χ 2 test or Fisher's exact test were used for categorical variables and the t-test was used for continuous variables. Analysis of covariance was used to compare the difference in PVM for each outcome. The models were adjusted for age, sex, and variables (severe vertebral compression, delayed union, new OVF, and remaining LBP) with a p-value of <0.10. Statistical test results were considered significant at $p < 0.05$. All p-values were two-sided and all analyses were performed using SAS version 9.4 (SAS Institute, Inc., Cary, NC, USA).

Results

Overall, 153 patients completed the 6-month follow-up, and 117 patients' data were eligible for this study. The mean patient age was 79.1 ± 7.2 years, and 94 were female (80.3%). Forty-one patients had old OVF among the 117 patients. OVFs were recorded in 10 patients at the thoracic level (T5–T9) (8.5%), 87 at the thoracolumbar level (T10–L2) (71.8%), and 24 at the lumbar level (19.7%). The average VAS at the first visit was 66.5 ± 12.5, and 23.1 ± 25.3 at the 6-month follow-up, and the patients' BMD score was -2.5 ± 0.4.

Severe vertebral compression was recorded in 63 patients (53.8%). There was no significant difference between the thoracolumbar region and lower lumbar region in terms of the CSA, rCSA, and FI% (Table 2). Delayed union occurred in 37 patients (32.5%). There was no significant difference in CSA, rCSA, and FI% of the PVM between the thoracolumbar (L1) and lumbar (L5) regions (Table 3). At the 6-month follow-up, 27 patients (23%) had remaining LBP. There were no significant differences in the CSA and rCSA between the thoracolumbar and lower lumbar regions. However, increased FI% of the PVM was significantly correlated with remaining LBP in the lumbar (L5) region (Table 4). Eleven patients (9.4%) had new OVF at the 6-month follow-up. The FI% of the PVM showed a significant correlation with new OVF in the thoracolumbar region (Table 5). Over 80% of both old and

new OVF occurred in the thoracolumbar region.

Discussion

To the best of our knowledge, this is the first study to show the impact of the FI% in the PVM in two different regions. In the thoracolumbar region, an increase in PVM FI% was significantly related to the occurrence of new OVF, and to remaining LBP in the lower lumbar region. However, PVM had no effect on severe compression fracture or delayed union.

Regarding the CSA of the PVM, there was no significant difference as the CSA is unlikely to reflect early change in the PVMs compared with the FI% [23]. Shahidi et al. [29] demonstrated that there was no change in the CSA with age in either sex ($p > 0.05$), although there was an increase in the fat signal fraction with age in the ES and MF muscles in both sexes ($p < 0.001$). Moreover, in a cross-sectional study of 72 patients with LBP, Teichtahl et al. demonstrated that paraspinal FI%, but not muscle CSA, was associated with disability and structural abnormalities in the lumbar spine [8]. Similarly, we found that the FI% of the PVM, unlike the CSA and rCSA, showed a significant relationship with the occurrence of new OVF in the thoracolumbar region and with remaining LBP in the lower lumbar region. A previous study reported that the FI% of the muscles can lead to the hip fractures rather than fall-induced vertebral fracture [26], and this may explain our findings. However, we did not have access to the data regarding which participants were prone to direct trauma or hip fracture due to a fall.

Severe vertebral compression fracture and delayed union did not show any correlation with the CSA, rCSA, and FI% of the PVM in both regions. Severe vertebral compression fracture and delayed union might be affected by other causes rather than the CSA, rCSA and FI% of the PVM. Intravertebral cleft, AO types A2 and A4 (AO Spine Thoracolumbar Spine Injury Classification: predictive for progressive collapse in acute osteoporotic compression fractures), thoracolumbar level posterior wall injury, T1 or T2 diffuse low signal change, and T2 diffuse low or high signal change on MRI have been previously reported as risk factors for vertebral compression [28, 30]. Additionally, Kim et al. and Hoshino et al. clearly demonstrated that the type of conservative treatment has no impact on vertebral compression and nonunion. Therefore, the morphological characteristics at injury are as important as severe compression and nonunion [31, 32]. Furthermore, spinal compression results from the interaction of the

gravity force, ground reaction force, and force created by ligaments and muscles. Meanwhile, the thoracic compression force is greater due to body weight and kyphotic angle. Moreover, the gravity line falls anterior to the thoracic spine, causing flexion movement, which is counteracted by posterior extensor muscles and ligaments [33]. Harrison et al. reported that anterior translated posture, disc load, and stresses increase below the T9 level, and the posterior extensor muscle is required to maintain the static equilibrium balance [34].

Regarding the remaining LBP, previous studies have demonstrated the importance of the FI% of the PVM, which was related to the intensity of pain/disability and structural abnormality at the L3/L4 intervertebral disc level [8]. Furthermore, Paalanne et al. [35] previously reported the occurrence of back pain in patients with poor PVM mass due to an increase in the FI% regardless the CSA of the PVM. The results of the present study are somewhat consistent with the findings of previous studies; however, our study differs from others in that separate regions were investigate (thoracolumbar and lumbar regions), with remaining LBP showing a significant correlation with the FI% of the PVM in the lumbar region (L4/5). In support of our results, the difference in the biomechanics of the PVM in the lumbar region has been previously demonstrated; powerful muscle must be the result of the continuity of a thick tendon, in order to transmit huge forces [36]. Given their large volume, lumbar PVM are considered powerful muscles [37, 38].

The occurrence of new OVF in the current study showed a significant relationship with the FI% of the PVM in the thoracolumbar region. Katsu et al. [39] reported that the FI% of the ES and MF muscles was related to the union of OVF at the L3 level. Similarly, Kim et al. [4] demonstrated that the increase in the FI% and decrease in the CSA at the L3/L4 level was associated with post-menopausal OVF. Additionally, Hori et al. [7] emphasized the importance of trunk muscle mass. Pogrund et al. [40] reported the importance of the decrease in the psoas at the L3 level related to osteoporosis. The current study demonstrated that the FI% of the PVM was related to remaining LBP in the lower lumbar region, and the FI% of the MF and ES at the upper endplate of L1, and absence of the psoas muscle, might be responsible for the occurrence of both old and new OVF.

The present study demonstrates the importance of MRI for accurate assessment of the FI% of the PVM in elderly patients. It is recommended that the clinician pays close attention to the follow-up

of these patients and be aware of potentially new OVF, because the initiation of new treatment may decrease the risk of new OVF. The use of a brace or physical therapy may be beneficial, but requires further study.

There are several limitations of this study. First, the levels of vitamin D and parathyroid hormone were not checked in patients with low levels of anabolic hormones [8]. Second, the control patients without OVF were excluded from this study. It was unclear if the FI% of the PVM decreases due to age or other causes. Third, the prior cause of LBP was not assessed in the enrolled patients to ascertain whether the cause of the remaining LPB was due to sequels of OVF or other prior causes.

Regarding the clinical relevance of this study, the findings can serve as a guide for multi-field physicians to make earlier decisions regarding the treatment and prevention of OVF and LMP in elderly men and post-menopausal women upon detection of high FI% in axial-T2 weighted MRI scanning.

In conclusion, this study demonstrates that the FI% of the PVM in the thoracolumbar region is highly correlated with the occurrence of new OVF, and the FI% of the PVM in the lumbar region is related to remaining LBP.

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Figure legend

The area surrounded by a yellow circle is the cross sectional area of the multifidus and erector spinae at the superior endplate of the L1. The area which is not painted in red is the fat area.

Table 1: Patient demographics (n=117)

Characteristic	N (%) or Mean ± SD
Age (years)	79.1 ± 7.2
Sex (female)	94 (80.3%)
BMI (kg/m^2)	21.9 ± 3.4
BMD (g/cm^2)	0.63 ± 0.12
VAS 6	23.1 ± 25.3
Old OVF	41 (35.0%)
Level	
Thoracic (T5–T9)	10 (8.5%)
Thoracolumbar (T10–L2)	84 (71.8%)
Lumbar (L3–L5)	23 (19.7%)

393 BMI body mass index, BMD bone mass index, VAS visual analogue scale, OVF osteoporotic vertebral
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Table 2: Comparison of demographic data, osteoporosis, OVF level, and paravertebral muscle

between the presence and absence of severe vertebral compression fracture

Characteristic		Yes n = 63	No n = 54	p-value
Age (years)		79.5 ± 7.1	78.7 ± 7.3	0.595
Sex (female)		50 (82.0%)	44 (78.6%)	0.644
BMI (kg/m^2)		22.0 ± 3.4	21.9 ± 3.4	0.865
BMD (g/cm^2)		0.63 ± 0.09	0.64 ± 0.13	0..737
Old OVF (yes)		21 (34.4%)	20 (35.7%)	0.884
Level				
Thoracic (T5–T9)		8 (13.1%)	2 (3.6%)	<0.001
Thoracolumbar (T10–L2)		52 (85.3 %)	32 (57.1%)	
Lumbar (L3–L5)		1 (1.6%)	22 (39.3%)	
T12/L1	CSA	12.2 ± 2.8	13.1 ± 3.6	0.110*
	rCSA	1.2 ± 0.3	1.2 ± 0.4	0.311*
	FI%	39.6 ± 9.7	41.4 ± 9.7	0.536*
L4/5	CSA	16.3 ± 3.2	17.0 ± 3.0	0.587*
	rCSA	1.3 ± 0.3	1.2 ± 0.3	0.168*
	FI%	49.1 ± 10.1	50.5 ± 10.9	0.913*

405 BMI body mass index, BMD bone mineral density, CSA cross-sectional area, rCSA relative cross-
406 sectional area, FI% percentage of fat infiltration.
407 *When comparing clinical outcomes, analysis of covariance was used to adjust for covariates such as

age, sex, and level of fracture (thoracolumbar/non-thoracolumbar level)

Table 3: Comparison of demographic data, osteoporosis, OVF level, and paravertebral muscle

between the presence and absence of delayed union

Characteristic		Yes n = 21	No n = 96	p-value
Age (years)		81.0 ± 7.1	78.7 ± 7.3	0.178
Sex (female)		17 (80.1%)	77 (80.2%)	0.938
BMI (kg/m^2)		22.6 ± 4.3	21.8 ± 3.2	0.382
BMD (g/cm^2)		0.58 ± 0.14	0.64 ± 0.11	0.176
Old OVF (yes)		9 (42.8%)	32 (33.3%)	0.407
Level				0.003
Thoracic (T5–T9)		0	10 (10.4%)	
Thoracolumbar (T10–L2)		20 (95.2%)	64 (66.7%)	
Lumbar (L3–L5)		1(4.8%)	22 (22.9%)	
T12/L1	CSA	12.2 ± 3.6	12.9 ± 3.1	0.538*
	rCSA	1.1 ± 0.4	1.2 ± 0.3	0.577*
	FI%	40.7 ± 8.4	40.2 ± 10.0	0.683*
L4/5	CSA	17.3 ± 3.3	16.4 ± 3.1	0.680*
	rCSA	1.3 ± 0.3	1.2 ± 0.3	0.129*
	FI%	51.9 ± 8.0	49.1 ± 11.0	0.537*

BMI body mass index, BMD bone mineral density, CSA cross-sectional area, rCSA relative cross-sectional area, FI% percentage of fat infiltration.

*When comparing the clinical outcomes, analysis of covariance was used to adjust for covariates that included age, sex, and level of fracture (thoracolumbar/non-thoracolumbar level).

Table 4: Comparison of demographic data, osteoporosis, OVF level, and paravertebral muscle between the presence and absence of remaining lower back pain

Characteristic		Yes n = 27	No n = 90	p-value
Age (years)		79.6 ± 7.0	79.0 ± 7.3	0.730
Sex (female)		23 (85.2%)	71 (78.9%)	0.470
BMI (kg/m^2)		22.0 ± 4.3	21.9 ± 3.1	0.963
BMD (g/cm^2)		0.61 ± 0.12	0.64 ± 0.12	0.454
Old OVF (yes)		14 (51.9%)	27 (30.0%)	0.037
Level				0.950
Thoracic (T5–T9)		2 (7.4%)	8 (8.9%)	
Thoracolumbar (T10–L2)		20 (74.1%)	64 (71.1%)	
Lumbar (L3–L5)		5 (18.5%)	18 (20.0%)	
T12/L1	CSA	13.0 ± 2.8	12.6 ± 3.4	0.278*
	rCSA	1.2 ± 0.3	1.2 ± 0.4	0.413*
	FI%	42.7 ± 9.9	39.7 ± 9.6	0.258*
L4/5	CSA	17.2 ± 3.1	16.5 ± 3.1	0.609*
	rCSA	1.3 ± 0.3	1.2 ± 0.3	0.236*
	FI%	53.4 ± 10.0	48.9 ± 10.5	0.042*

BMI body mass index, BMD bone mineral density, CSA cross-sectional area, rCSA relative cross-sectional area, FI% percentage of fat infiltration.

*When comparing with clinical outcomes, analysis of covariance was used to adjust for covariates that included age, sex, and old OVF.

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Table 5: Comparison of demographic data, osteoporosis, OVF level. and paravertebral muscle between the presence and absence of new osteoporotic vertebral fracture

Characteristic		Yes n = 11	No n = 106	p-value
Age (years)		79.8 ± 5.9	79.1 ± 7.3	0.741
Sex (female)		10 (90.9%)	84 (79.3%)	0.690
BMI (kg/m^2)		24.4 ± 4.3	21.7 ± 3.2	0.015
BMD (g/cm^2)		0.59 ± 0.08	0.63 ± 0.12	0.384
Old OVF (yes)		5 (45.5%)	36 (34.0%)	0.513
Level				0.873
Thoracic (T5–T9)		0	10 (9.4%)	
Thoracolumbar (T10–L2)		9 (81.8%)	75 (70.8%)	
Lumbar (L3–L5)		2 (18.2%)	21 (19.8%)	
T12/L1	CSA	12.5 ± 2.7	13.5 ± 3.3	0.053*
	rCSA	1.2 ± 0.3	1.2 ± 0.4	0.299*
	FI%	46.1 ± 8.5	39.8 ± 9.7	0.047*
L4/5	CSA	17.5 ± 3.1	16.5 ± 3.1	0.866*
	rCSA	1.3 ± 0.3	1.3 ± 0.3	0.632*
	FI%	52.5 ± 8.6	49.7 ± 10.7	0.545*

BMI body mass index, BMD bone mineral density, CSA cross-sectional area, rCSA relative cross-sectional area, FI% percentage of fat infiltration.

*When comparing the clinical outcomes, analysis of covariance was used to adjust for covariates such as age, sex, and BMI.

474 Figure

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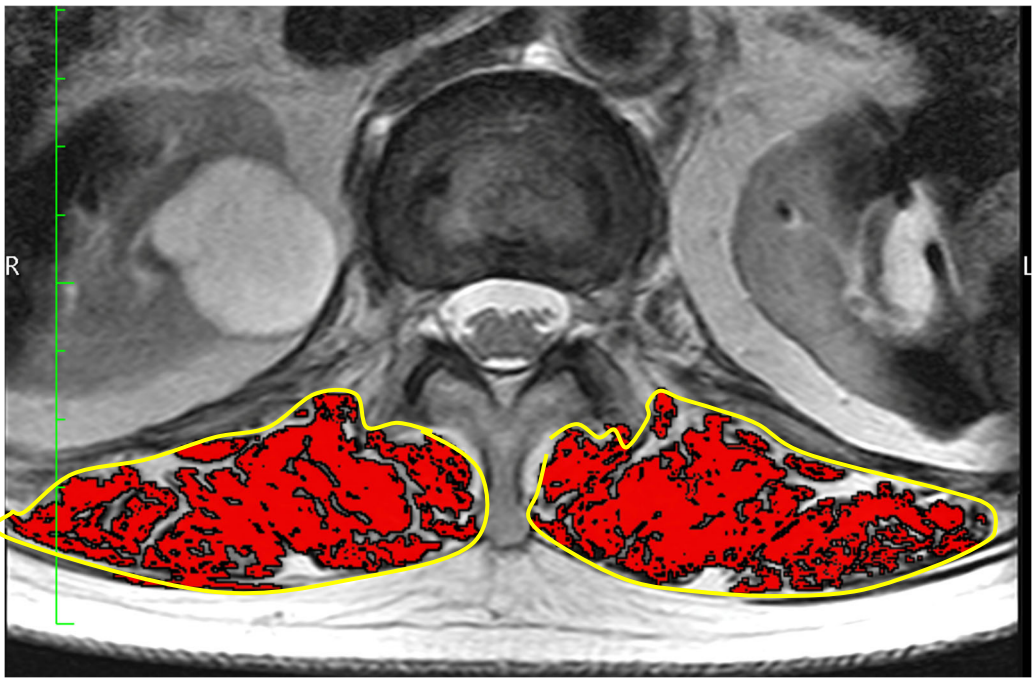

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