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Article

Paraspinal Muscle Fat Infiltration as a Key Predictor of Symptomatic Intravertebral Vacuum Cleft: A Machine Learning Approach

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Abstract: Background/Objectives: Symptomatic intravertebral vacuum cleft (SIVC) is a complication of vertebral compression fractures (VCFs) that leads to persistent pain and deformity. Its prediction remains challenging due to multifactorial causes. Paraspinal muscle fat infiltration has been associated with spinal fracture outcomes but has not been extensively explored in SIVC prediction. To develop machine learning (ML) models for predicting SIVC and to evaluate the role of muscle-related variables in improving predictive performance. **Methods:** Demographic, radiological, and muscle-related variables were collected. ML models—including Logistic Regression, Random Forest, XGBoost, and Multi-Layer Perceptron—were trained and tested under two input conditions: baseline variables (SETTING_1) and baseline plus muscle-related variables (SETTING_2). Model performance was evaluated using accuracy, area under the receiver operating characteristic curve (AUC), and feature importance analysis. **Results:** The Random Forest model in SETTING_2, which incorporated muscle-related variables, achieved the highest accuracy (96.6%) and AUC (0.956). Multifidus fatty infiltration (MFfi), erector spinae fatty infiltration (ESfi), and endplate CSA were identified as the most significant predictors. The inclusion of muscle-related variables significantly improved the predictive performance of all ML models. **Conclusions:** ML models, particularly Random Forest, demonstrated high accuracy in predicting SIVC when muscle-related variables were included. Paraspinal muscle fat infiltration is a critical predictor of SIVC and should be integrated into risk assessment strategies to improve early diagnosis and management.

Keywords: machine learning; intravertebral vacuum cleft; vertebral compression fracture; risk factor

1. Introduction

Vertebral compression fracture (VCF) is a common spinal condition that has been increasing in prevalence in recent decades. If unresolved through conservative treatment due to various factors, it can lead to persistent back pain, kyphotic deformity, and neurological deterioration. [1–5] A hallmark of this condition is the intravertebral vacuum cleft (IVC), a distinctive radiological feature associated with non-union of VCF, some of which requires surgical intervention. [6,7] “Symptomatic” IVC (SIVC)

represents a distinct clinical entity where patients with VCF develop recurrent pain after initial improvement, accompanied by characteristic radiographic findings of IVC.

Unlike typical VCF cases that show spontaneous improvement, SIVC patients experience persistent or recurring pain (VAS >3) that correlates with specific radiological features. Early detection and accurate prediction of SIVC are clinically significant, yet this remains challenging due to the multifactorial nature of its pathogenesis. [8,9] SIVC has been reported to occur slightly more frequently in females, with other risk factors including renal disease, diabetes, chronic steroid use, osteoporosis, alcoholism, hypothyroidism, and radiation therapy. [6,8,10–14] Recent studies have also reported that fat infiltration of the paraspinal muscles may increase the risk of VCF or influence clinical and radiological outcomes following spinal fractures. [15–17]

In recent decades, the rapid development of machine learning (ML) algorithms has significantly impact on orthopedic surgery. ML enables high-accuracy analysis and prediction of complex patterns in medical imaging, electronic medical records (EMR), and other clinical datasets. [18] Previous studies have demonstrated the utility of ML in predicting osteoporotic VCF using magnetic resonance imaging (MRI) and demographic data alongside bone mineral density scores. [19,20] However, to our knowledge, no previous studies have employed ML approaches incorporating muscle-related variables to predict VCF and SIVC.

Therefore, the primary objective of this study was to determine whether muscle-related variables were significant risk factors in the prediction of SIVC using ML by comparing demographics and variables measured from plain radiography with and without muscle-related variables. The secondary objective was to investigate which ML algorithms could best predict SIVC and to what extent muscle-related variables had significant effects.

2. Materials and Methods

2.1. Study Design and Patient Population

This study was a retrospective analysis of patients diagnosed with VCF who were enrolled between March 2013 and February 2023 (Figure 1). This study was approved by the Institutional Review Board (IRB) of the institution. The inclusion criteria were as follows: patients diagnosed with VCF at the thoracolumbar junction (TLJ, T10-L2) and patients diagnosed with SIVC at the TLJ. The exclusion criteria were patients with pathological VCF, such as tumors or infection, patients with multiple-location VCF, patients without MRI, and patients without adequate plain thoracolumbar anteroposterior and lateral radiographs.

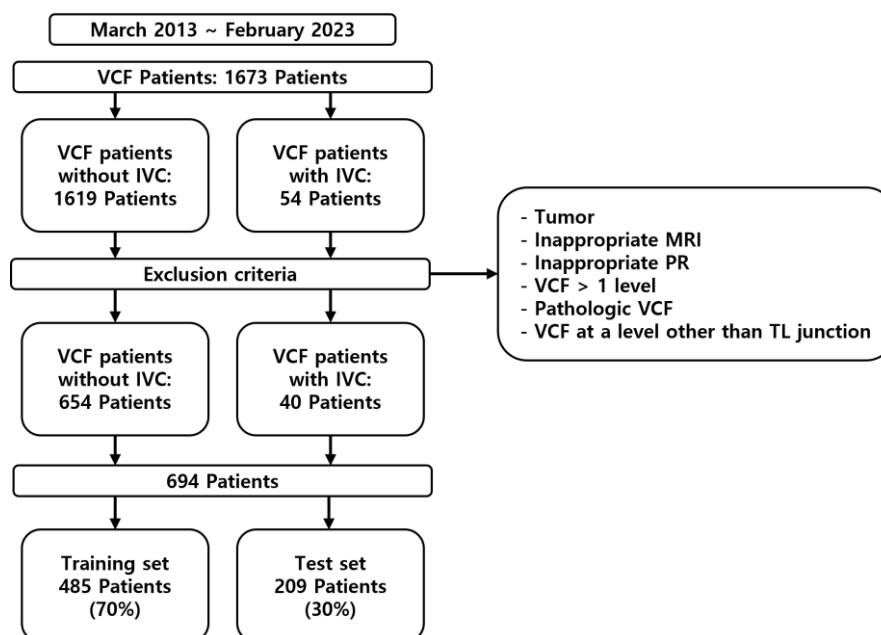


Figure 1. Diagram illustrating the data collection process and the segmentation process into training and test sets.

2.2. Definition and Diagnostic Criteria of SIVC

SIVC was defined by the following criteria:

- Clinical Criteria:
 - Initial acute pain following VCF
 - Period of initial improvement with conservative treatment
 - Development of recurrent pain (VAS >3)
 - Location-specific pain corresponding to the level of vacuum cleft
 - Radiographic Criteria:
 - Radiographic evidence of intravertebral vacuum cleft (IVC) on plain thoracolumbar radiographs
 - Absence of other significant pathology at the affected and adjacent levels, such as new fractures
- To address potential diagnostic subjectivity, two independent spine specialists (YHK, JA) confirmed the diagnosis of SIVC.

2.3. Data Collection

A clinical data warehouse (CDW) containing all medical records from the institution was used to select and study patients. Demographic and radiological data were collected from all enrolled patients. The demographic data included sex, age, diabetes, hypertension, adrenal insufficiency, hyperthyroidism, hypothyroidism, and steroid use. Radiological characteristics were measured using the following variables: the “angle” (local kyphotic angle) and compression ratio of the VCF were measured from the lateral view of the plane radiograph (PR) (Figure 2). From the axial view of MRI, the cross-sectional areas (CSA) of the VCF location and multifidus (MF) and erector spinae (ES) muscles were measured. Additionally, the percentage of fatty infiltration in MF (MFfi) and ES (ESfi) was measured using the imaging pre-processing ImageJ software (version 1.8.0) (Figure 3). In this study, relational multifidus (rMF) was defined as the MF/CSA of the endplate, and relational erector spinae (rES) was defined as the MF/CSA of the endplate.

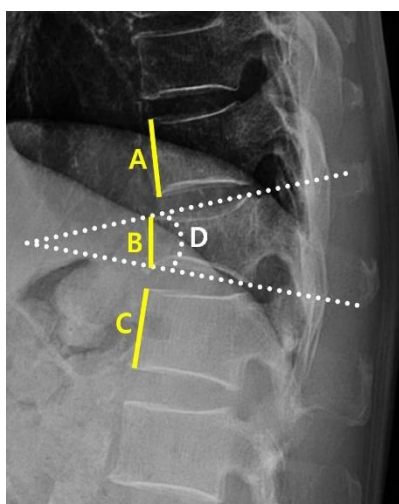


Figure 2. Measurement of kyphotic angular and compression value. The kyphotic angular and compression value are measured within the picture archiving and communication (PACS) system PR lateral view; D shows the kyphotic angle of the T11 fracture; the compression value is calculated as $((A+C)/2)-B) / ((A+2)/2)$.

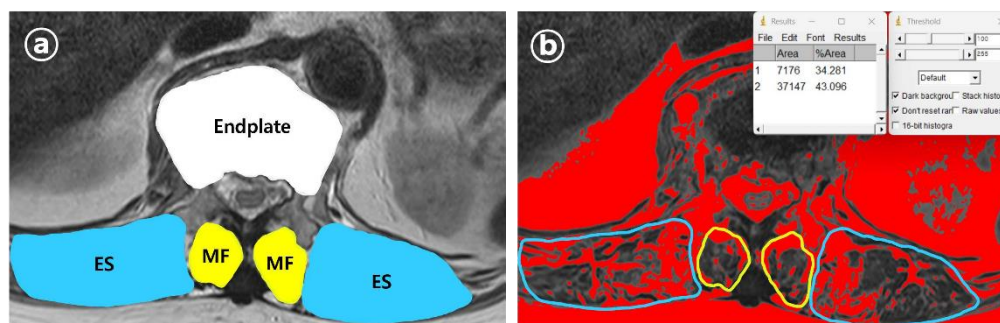


Figure 3. Measurement variables from axial view, (a) Measurement of CSA of endplate, MF and ES of VCF location, measured within PACS system MRI axial view. The CSA of MF, ES was calculated as the mean of the left and right CSA. (b) MFfi and ESfi measured within ImageJ program and calculated as the mean of the left and right fatty infiltration percentage.

2.4. Machine Learning Models

To confirm the known risk factors for VCF and SIVC, we conducted experiments using variables extracted from PR and EMR for SETTING_1 and variables extracted from PR, EMR, and MRI for SETTING_2. The patients were randomly divided into training (70%) and test (30%) datasets. A training set is used to develop the model. Supplementary 5-fold cross-validation was used to optimize the hyperparameters of the machine learning model in the training set, and the data of the training set were augmented using the SMOTE package to effectively learn fewer datasets. The test set was used to evaluate the performance of the learned models: Logistic Regression (LR) [21], random forest (RF) [22], extreme gradient boosting (XGBoost) [23], multilayer perceptron (MLP) [24]. Training and testing processes were conducted in Python 3.9.12 and PyCharm environments.

2.5. Evaluation Matrix

For objective performance evaluation, the areas under the accuracy, specificity, sensitivity, precision, F1-score, and area under the receiver operating characteristics curve (AUROC) of the models were measured and averaged ten times for each method in the test set.

3. Results

3.1. Patient Characteristics

Of the 1694 patients, data from 694 who met the inclusion criteria and did not violate the exclusion criteria were included in the study; of these, 485 were used for training the ML models and 209 were used for testing (Table 1).

Table 1. Patient demographics.

Data Source	Characteristics	Number of Patients (%)		Description	p Value	
		VCF Patients Without IVC	VCF Patients with IVC			
EMR	Age	72.44 ± 1.15	79.85 ± 3.35	Age at diagnosis	<0.05*	
	Sex	F: 464 (71%) M: 190 (29%)	F: 27 (67%) M: 13 (33%)	Sex of patients	0.7746	
	DM	P: 76 (12%) N: 578 (88%)	P: 4 (10%) N: 36 (90%)	Diabetes status	0.9549	
	HTN	P: 259 (40%) N: 395 (60%)	P: 13 (67%) N: 27 (33%)	Hypertension status	0.4676	
	Adrenal insufficiency	P: 7 (1%) N: 647 (99%)	P: 1 (3%) N: 39 (97%)	Adrenal insufficiency status	0.9527	
	Hyperthyroidism	P: 1 (1%) N: 653 (99%)	P: 0 (0%) N: 40 (100%)	Hyperthyroidism status	1.0	
	Hypothyroidism	P: 10 (2%) N: 644 (98%)	P: 0 (0%) N: 40 (100%)	Hypothyroidism status	0.9169	
	Steroid	P: 23 (4%) N: 631 (96%)	P: 1 (3%) N: 39 (97%)	Continuous taking oral steroids= for more than 3 months	1.0	
	PR (Lateral view)	Kyphotic angle (°)	19.89 ± 0.49	25.01 ± 4.21	Kyphotic angulation at VCF	<0.05*
		Compression Value	34.41 ± 1.27	48.31 ± 6.50	Compression ratio at VCF	<0.05*
MRI (Axial view)	Disc (cm/m2)	12.51 ± 0.21	15.14 ± 0.93	CSA of endplate at VCF	<0.05*	
	MF (cm/m2)	4.13 ± 0.14	2.95 ± 0.31	CSA of MF at VCF	<0.05*	
	MFfi (%)	16.39 ± 0.53	37.29 ± 4.58	Fatty infiltration percentage of MF	<0.05*	
	rMF	0.34 ± 0.01	0.20 ± 0.02	CSA of relative MF at VCF	<0.05*	
	ES (cm/m2)	20.37 ± 0.66	12.12 ± 1.43	CSA of ES at VCF	<0.05*	
	ESfi (%)	10.25 ± 0.51	29.03 ± 4.85	Fatty infiltration percentage of ES	<0.05*	
	rES	1.66 ± 0.05	0.83 ± 0.11	CSA of relative ES at VCF	<0.05*	

*, Statistically significant.

3.2. Machine Learning Models

The LR, RF, XGBoost, and MLP models showed that the AUC in SETTING_1 was 0.699, 0.698, 0.643, and 0.708, respectively, and the accuracies were 0.757, 0.871, 0.856, and 0.760, respectively (Figure 4, Table 2). The AUC in SETTING_2 was 0.947, 0.956, 0.951, and 0.904, respectively, and the accuracies were 0.951, 0.966, 0.962, and 0.961, respectively (Figure 5, Table 2). All ML models demonstrated superior performance in SETTING_2 compared to SETTING_1. Among them, the RF model achieved the highest accuracy in both settings. Notably, in SETTING_2, the RF model outperformed all other models, exhibiting the highest accuracy and AUC.

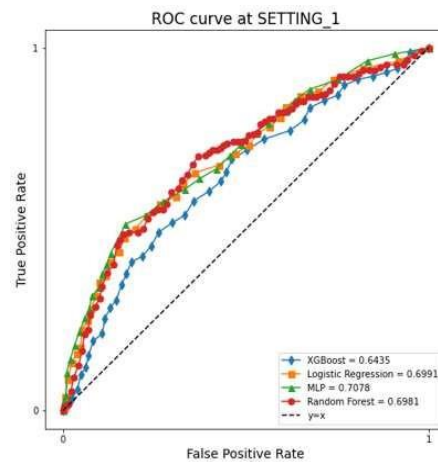


Figure 4. Receiver operating characteristic curve for each ML model on SETTING_1.

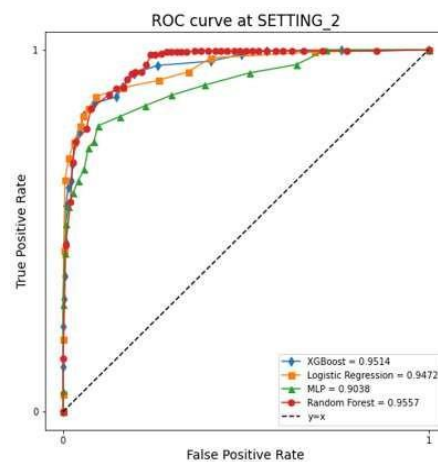


Figure 5. Receiver operating characteristic curve for each ML model on SETTING_2.

3.3. Feature Importance

Figure 6 illustrates the feature importance ranking of the RF model in SETTING_1, where ‘Angle’ (local kyphotic angle), age, and ‘Solondo’ (steroid use) were identified as the top three predictors. In contrast, the RF model in SETTING_2, which outperformed all other models (Figure 7), highlighted MFfi, ESfi, and ‘Disc’ (Endplate CSA) as the most influential predictors for SIVC, with feature importance values of 0.871, 0.702, and 0.575, respectively. Notably, feature importance values range from 0 to 1, indicating their relative contribution to the model’s predictive performance.

Table 2. Performance of each machine learning model on test set.

Datasets	Models	Accuracy	Specificity	Sensitivity	Precision	F1-score	AUROC
SETTING_1	Logistic Regression	0.757	0.957	0.143	0.527	0.223	0.699
	Random Forest	0.871	0.958	0.185	0.365	0.244	0.698
	XGBoost	0.856	0.949	0.154	0.296	0.192	0.643
	Multi-Layer Perceptron	0.76	0.961	0.151	0.553	0.232	0.708
SETTING_2	Logistic Regression	0.951	0.987	0.606	0.825	0.693	0.947
	Random Forest	0.966	0.982	0.737	0.731	0.731	0.956
	XGBoost	0.962	0.987	0.661	0.796	0.72	0.951
	Multi-Layer Perceptron	0.961	0.978	0.748	0.716	0.723	0.904

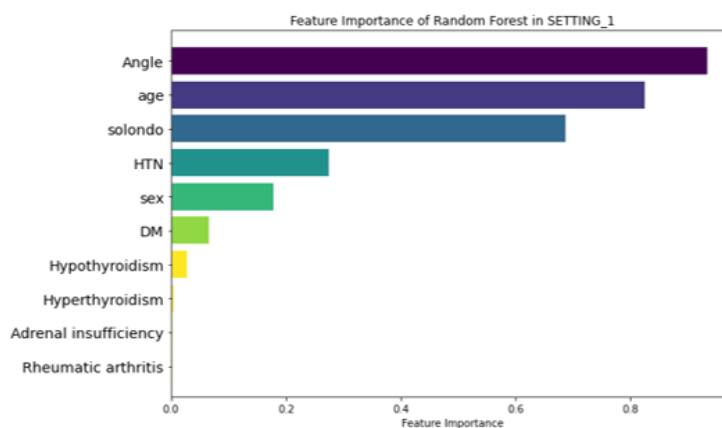


Figure 6. Feature importance of RF in SETTING_1.

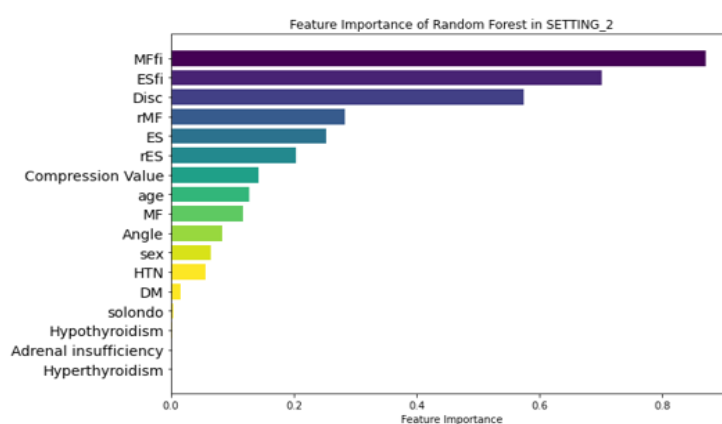


Figure 7. Feature importance of RF in SETTING_2.

4. Discussion

In this study, we successfully predicted VCF and SIVC using muscle-related variables using ML models. The superior performance of SETTING_2 (incorporating muscle variables) over SETTING_1 (conventional variables only) suggests that muscle-related factors play a crucial role in SIVC development. The high feature importance of MFfi and ESfi (0.871 and 0.702 respectively) indicates that paravertebral muscle status may be more predictive of SIVC than traditional risk factors such as age and steroid use. This will also provide insight into the accurate diagnosis of SIVC in the future. To the best of our knowledge, this is the first study to explore SIVC using machine learning (ML) in conjunction with muscle-related variables. To date, SIVC has primarily been identified through radiological assessments. However, challenges in accurately distinguishing SIVC from VCF can result in inadequate treatment. Given that SIVC requires distinct treatments, such as bone cement augmentation, and has unique clinical features and prognoses compared with VCF, precise identification is essential [25].

In line with our hypothesis, both MFfi and ESfi were ranked among the top three predictors. Previous studies have reported that MF and ES play crucial roles in maintaining spinal balance [26,27]. This suggests that fat infiltration weakens the supportive capacity of the spine, potentially contributing to the development of SIVC. Consistent with this, previous studies have reported that fat infiltration in the ES and MF is associated with reduced spinal bone mineral density (BMD) [28,29], while fat infiltration in the MF has been linked to an increased risk of osteoporotic VCF [15]. In addition, it is noteworthy that high fat infiltration is associated with a low union rate following lumbar interbody fusion procedures [30,31]. This suggests that fat infiltration in the posterior muscles significantly affects the stability of the spinal column. In this study, the role of fat infiltration in the paravertebral muscles in the occurrence of SIVC was confirmed using feature importance analysis.

Enlargement of the endplate cross-sectional area (CSA), potentially resulting from the formation of intravertebral clefts, reflects biomechanical changes within the vertebral structure. These changes may represent a compensatory response to redistribute the mechanical load or indicate progressive instability associated with advanced spinal degeneration [32]. This finding emphasizes the complex nature of endplate pathology and its important role in SIVC development. Furthermore, structural changes in the endplate CSA could serve as valuable biomarkers for identifying patients at risk of SIVC [33]. However, further research is required to establish whether this predictor has a causal role or simply correlates with the condition and to determine how it can be integrated into diagnostic or therapeutic approaches.

The use of steroid has been identified as a contributing risk factor for the development of SIVC [6]. In this study, SETTING_2 demonstrated lower feature importance values for steroid use compared to other factors, while SETTING_1 highlighted its significance as one of the top three predictors. However, high-quality studies specifically investigating the relationship between steroid use and SIVC are limited. Notably, long-term improper use of steroids has been reported to increase the risk of new vertebral fractures, suggesting that inappropriate steroid use compromises vertebral stability [34,35].

Diabetes has been reported as a risk factor for SIVC and has been reported to be strongly associated with frailty index, which implies a significant impact on overall health and resilience [12]. Several mechanisms have been demonstrated to explain this relationship. Diabetes often contributes to muscle loss (or sarcopenia) and weakness, both essential components of frailty [36]. Nutritional challenges associated with diabetes, including altered dietary patterns and nutrient absorption, can further intensify frailty [37]. Additionally, diabetes is commonly accompanied by comorbidities such as cardiovascular disease, obesity, and kidney disease, all of which significantly affect the frailty burden [38]. While some studies suggest that diabetes does not always have a direct association with SIVC, its long-term complications and systemic effects contribute to its potential role in diminishing physical and structural resilience [39,40]. This, in turn, could indirectly impact outcomes such as vertebral stability and the risk of SIVC.

Age has been reported as a significant risk factor for the occurrence of past VCF [41,42]. In this study, the age parameter showed significant results in SETTING_1, but the age parameter in SETTING_2 did not show significant results compared to other variables. This means that muscle-related variables representing an individual's health status are more important than chronological age in the fracture-healing process. Of course, age should not be overlooked in the occurrence of SIVC because there have been reports that age, osteoporosis, and sarcopenia are correlated [43]. However, it can be seen that it should be interpreted differently from the meaning of risk factors mentioned in previous studies [36].

This study provides data-driven insights and valuable medical perspectives. With the development of computer and data science, grafting into the medical field is taking place. This provides an accurate identification and diagnosis of SIVC and can lead to the discovery of risk factors through data analysis.

Nevertheless, several limitations should be considered when interpreting our results. First, the retrospective nature of the study meant that standardized pain scores were not available throughout the follow-up period, potentially affecting our ability to fully characterize pain progression patterns. Second, while we carefully defined SIVC criteria, the distinction between SIVC-related pain and other sources of chronic pain relies partly on clinical judgment. Third, potential contributing factors such as frailty index [44], BMI, and BMD were excluded due to missing data. Fourth, our focus on single-level fractures, while improving study homogeneity, limits generalizability to multilevel cases. Finally, the relatively small number of SIVC cases ($n=40$) suggests the need for larger validation studies. Given these limitations, future studies should investigate the potential clinical application of muscle-related predictors in the early diagnosis and treatment of SIVC, further validating their role in improving patient outcomes.

5. Conclusions

This study identified paravertebral muscle variables as novel risk factors for SIVC, and highlighted effective prediction methods. Among these, the RF model demonstrated the best performance, suggesting that it is a reliable strategy for SIVC prediction.

Author Contributions:: Conceptualization, JCL.; methodology, YS, JA.; formal analysis, YS, JA; investigation, JA, JL; data curation, JL; writing—original draft preparation, JA; writing—review and editing, JS, JA; statistical analysis, YS; visualization, JL; critical revision, JS, JA, YHK, YS, JSL, HYP; supervision, YHK; funding acquisition, JA. All authors have read, reviewed and approved the final version of the manuscript. JA and JS contributed equally to this work.

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Institutional Review Board Statement: This study was conducted in accordance with the Declaration of Helsinki, and approved by the Institutional Review Board of Bucheon St. Mary's Hospital, The Catholic University of Korea. (IRB No.: HC24WASI0020, 09/04/2024).

Informed Consent Statement: Written informed consent was waived due to the retrospective nature of the study and the use of fully anonymized medical records and imaging data, which precluded any personal identification of patients.

Data Availability Statement: The patients' data were collected in Bucheon St. Mary's Hospital, The Catholic University of Korea. The datasets generated and/or analysed during the current study are available from the corresponding author (YS) on reasonable request.

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Conflicts of Interest: The authors declare no personal competing interests in any of the materials, or devices described in this article. No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article. (JA: nothing to disclose, JS: nothing to disclose, YHK: nothing to disclose, JCL: nothing to disclose, JSL: nothing to disclose, HYP: nothing to disclose, JL: nothing to disclose, YS: nothing to disclose).

Abbreviations

The following abbreviations are used in this manuscript:

SIVC	Symptomatic intravertebral vacuum cleft
VCF	Vertebral compression fracture
EMR	Electronic medical records
ML	Machine learning
TLJ	Thoracolumbar junction
MF	Multifidus
ES	Erector spinae
MFfi	MF fat infiltration
ESfi	ES fat infiltration
CSA	Cross-sectional area
rMF	Relative CSA of multifidus per CSA of endplate
rES	Relative CSA of erector spinae per CSA of endplate
LR	Logistic regression
RF	Random forest
XGBoost	Extreme gradient boosting
MLP	Multi-layer perceptron
AUROC	Area under the receiver operating characteristic curve
BMD	Bone mineral density

BMI	Body mass index
PR	Plain radiograph

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