Osteoporosis and Sarcopenia 10 (2024) 22–27

Contents lists available at ScienceDirect

Osteoporosis and Sarcopenia

journal homepage: www.elsevier.com/locate/afos

Original article

Development of a shape-based algorithm for identification of asymptomatic vertebral compression fractures: A proof-of-principle study

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ARTICLE INFO

Keywords:
Artificial intelligence
X-ray
Vertebra segmentation
Vertebral fracture
Shape-based algorithm

ABSTRACT

Objectives: Vertebral fracture is both common and serious among adults, yet it often goes undiagnosed. This study aimed to develop a shape-based algorithm (SBA) for the automatic identification of vertebral fractures.
Methods: The study included 144 participants (50 individuals with a fracture and 94 without a fracture) whose plain thoracolumbar spine X-rays were taken. Clinical diagnosis of vertebral fracture (grade 0 to 3) was made by rheumatologists using Genant's semiquantitative method. The SBA algorithm was developed to determine the ratio of vertebral body height loss. Based on the ratio, SBA classifies a vertebra into 4 classes: 0 = normal, 1 = mild fracture, 2 = moderate fracture, 3 = severe fracture). The concordance between clinical diagnosis and SBA-based classification was assessed at both person and vertebra levels.
Results: At the person level, the SBA achieved a sensitivity of 100% and specificity of 62% (95% CI, 51%–72%). At the vertebra level, the SBA achieved a sensitivity of 84% (95% CI, 72%–93%), and a specificity of 88% (95% CI, 85%–90%). On average, the SBA took 0.3 s to assess each X-ray.
Conclusions: The SBA developed here is a fast and efficient tool that can be used to systematically screen for asymptomatic vertebral fractures and reduce the workload of healthcare professionals.

1. Introduction

Vertebral fracture is a defining characteristic and a consequence of osteoporosis. The prevalence of vertebral fractures in Caucasian populations is approximately ~12% in women and ~14% in men [1], with an overall average being 12% for both sexes [2]. However, these figures are likely underestimated because the majority of vertebral fractures are asymptomatic [3] and only one-quarter to one-third are clinically recognized [4]. More importantly, vertebral fracture is a strong predictor of subsequent risk of non-vertebral fractures and premature mortality [5–7]. Collectively, previous data indicate that vertebral fracture is both common and serious among people aged 50 years and older, and this burden is expected to increase in the future as the global population is aging.

Currently, the common method for diagnosing vertebral fractures is to assess X-ray results using Genant's semiquantitative method [8]. This diagnosis can be time-consuming and subject to intra-subject reliability. In recent years, artificial intelligence (AI)-related algorithms are a promising approach for identifying vertebral fractures using computer tomography (CT) and to a lesser extent, X-rays [9–14]. However, the lack of transparency in these AI algorithms has hindered their widespread adoption in real-world scenarios, as clinicians seek to understand the underlying mechanisms behind their effectiveness in specific situations [15,16]. At least 2 AI models have been developed to detect vertebral fractures on X-rays. The first model lacked the ability to provide any insights into the functional prognostic of the machine. In the

Peer review under responsibility of The Korean Society of Osteoporosis.
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https://doi.org/10.1016/j.afos.2024.01.001
Received 26 October 2023; Received in revised form 25 November 2023; Accepted 14 January 2024
Available online 9 February 2024

second model, interpretability was added through a workflow that involved vertebra detection, segmentation, and classification of vertebral fractures. This AI model was capable of predicting vertebral height loss based on the vertebral masks generated by the segmentation module [17–21].

In this study, we used principles of segmentation AI which have been recently adopted in medical image analysis [22] to develop a shape-based algorithm (SBA) as an interpretable AI method for diagnosing asymptomatic vertebral fracture. Our SBA was designed as a rule-based AI to obtain the vertebral corners from a given vertebral mask for measuring the anterior and posterior heights of a vertebra, making the diagnosis of vertebral fracture objective and robust. The present study aimed at quantifying the predictive performance of the SBA in the diagnosis of vertebral fractures on plain X-rays.

2. Methods

2.1. Vietnam Osteoporosis Study

This study was part of the Vietnam Osteoporosis Study (VOS) in which procedures and protocols have been described in detail elsewhere [23]. Briefly, 4157 participants were randomly recruited from the population via advertisement and computer-based selection. We collected the lateral digital X-rays of the spine using the digital X-ray imaging system FCR Capsula XLII (Fujifilm Corp., Tokyo, Japan). The study was approved by the Research and Ethics Committee of People's Hospital 115 and the Pham Ngoc Thach University of Medicine (Ethical approval number 297/BV-NCKH) and carried out according to the relevant guidelines and regulations in compliance with the Declaration of Helsinki. All participants gave their written informed consent.

The present study was designed as a proof-of-principle study. We assumed that the algorithm's sensitivity and specificity were approximately 90%. For a fracture prevalence of 30%, we estimated that the sample size was 116 individuals.

2.2. Clinical diagnosis by rheumatologists

For each participant, lateral spinal X-ray was taken with a 101.6 cm tube-to-film distance centered at L2, using the FCR Capsula XLII, a high-resolution all-in-one unit with a capacity of up to 50 μm reading (Fig. 1). Three rheumatologists read the films independently to diagnose vertebral fracture using the Harry Genant's criteria. Accordingly, a loss of vertebral height of 20%–25% was classified as grade 1 (mild); a loss of 25%–40% was classified as grade 2 (moderate); a loss greater than 40% was classified as grade 3 (severe). Two rheumatologists visually graded vertebrae from T4 to L4, and any discordance was resolved by a consensus reading with the third and more experienced rheumatologist.

2.3. Quantitative assessment by shape-based algorithm

To create the SBA, we began with image processing. A rheumatologist, unaware of the clinical diagnosis, utilized the GIMP 2 (GU Image Manipulation Program 2) to color each X-ray (Fig. 2a). The vertebral bodies were colored white and the background was colored black (Fig. 2b). Any protruding structures in X-ray film were considered part of the background.

The resulting information was stored in a binary image or spinal mask for each vertebra from L5 to T4. Because vertebral projections might overlap, which results in unusable segmentation, we stored the film in 2 spinal masks, each emphasized either superior projection or inferior projection (Supplement Fig. 1). These 2 masks were then merged for image processing.

Using computer vision techniques, we cropped a vertebral mask from the spinal mask, and subsequently utilized the SBA method to extract the vertebral corners for each cropped mask then measure the anterior height (Ha), posterior height (Hp), and height loss (ΔH) (Fig. 2c). We categorized vertebral fractures based on their ΔH values according to Genant's classifications (ie, mild, moderate, and severe), as mentioned earlier.

Fig. 1. Representative lateral view plain spine X-ray of a patient with moderate/grade 2 vertebral compression fracture at L1, and mild/grade 1 vertebral compression fracture at T12.

2.4. Design of shape-based algorithm

The SBA was designed to find the vertebral corners from the vertebral mask according to the 4-point morphometry of Smith-Bindman [24]. On a vertebral image (Fig. 3a), the 4 vertebral corners lie along the vertebral contour, which serves as the boundary separating the black and white regions of the vertebral mask (Fig. 3b and c). The SBA algorithm includes 2 processes: the first is extraction of the 4 potential points on the vertebral contour, and the second is assigning the correct corners.

To extract points, we assumed that the corners comprised a quadrilateral area that encompassed the majority of the white region. The four points possessed the following characteristics:

(1) The first point is the farthest from the centroid of the white region (Fig. 3d);
(2) The second point is the farthest from the first point (Fig. 3e);
(3) The third point maximized the triangular area formed with the first and second points (Fig. 3f);
(4) The fourth point maximized the quadrilateral area formed with the other points (Fig. 3g).

After obtaining the 4 points in sequence, assuming a left-lateral view film, we utilized the following rules to identify the corners:

(1) The anterior column is identified by selecting the 2 points closest to the left border, with the anterior top above the anterior-bottom;

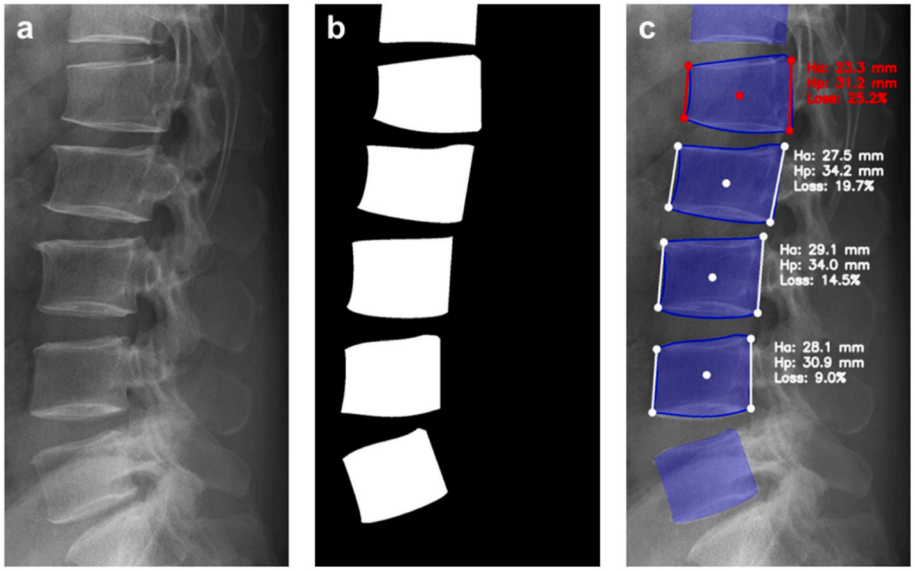

Fig. 2. (a) A cropped lumbar spine X-ray from L5 to L1 of a participant; (b) The mask provided by rheumatologists in which the white regions are vertebral bodies and the black region is the background; (c) The shape-based algorithm extracts the 4 vertices to calculate vertebral heights in millimeters (Ha: Anterior height; Hp: Posterior height) and height loss in percentage (loss), L1 is moderate/grade 2 vertebral compression fracture with a height loss more than 25%.

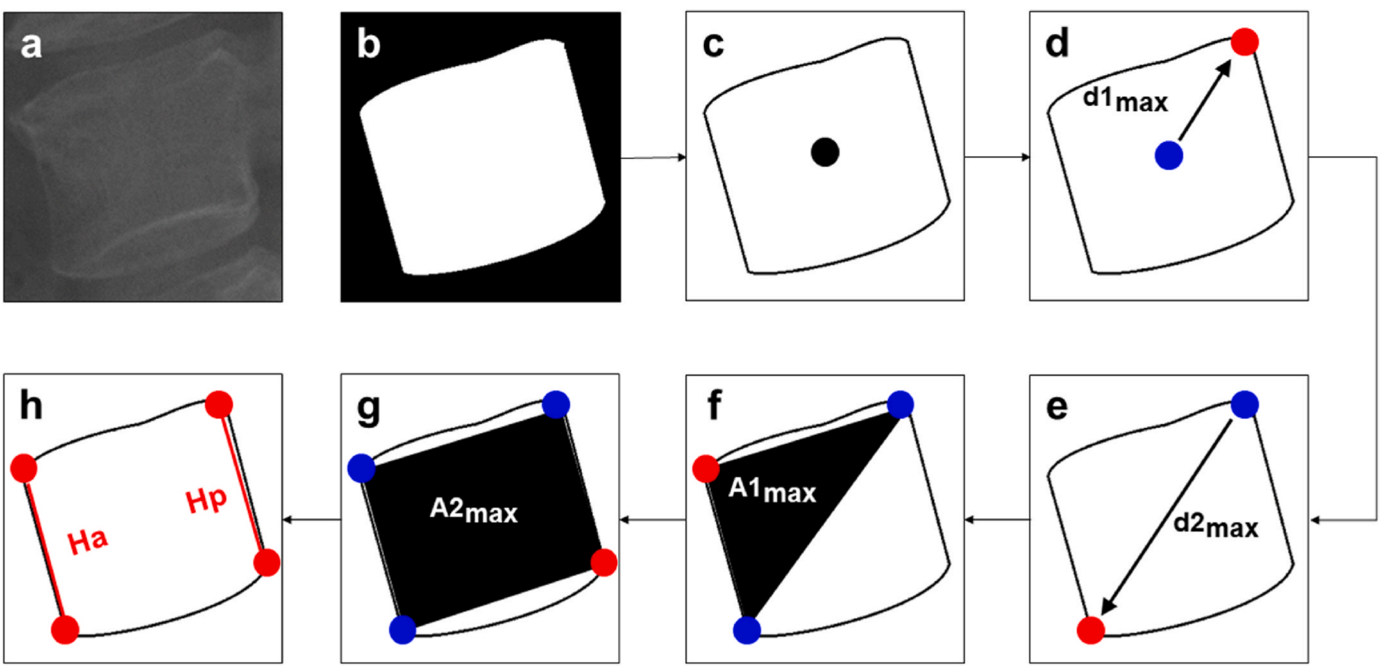

Fig. 3. The illustration of shape-based algorithm (SBA). (a) A cropped image of vertebra from a plain lateral spine X-ray; (b) The vertebral mask of the cropped image, black as background and white as vertebral body; (c) The vertebral contour as black line has centroid in black, the task is to identify the 4 corners with a known contour; (d) The arrow point to the first point in red which is the furthest from the blue centroid; (e) The arrow points to the second point in red which is the furthest point from the first point in blue; (f) The third point in red is chosen to maximize the area formed with found points in blue; (g) The fourth point in red is chosen to maximize the area formed with other points in blue; (h) SBA extracts morphometric properties, 2 examples are the anterior and posterior height.

(2) The posterior column is designed by the remaining points, with the posterior-top above the posterior-bottom.

The four corners extracted from the vertebral mask are used to calculate Ha, Hp then ΔH for the morphometric classification of the vertebral compression fracture (Fig. 3h). Height loss is calculated as:

$$\Delta H = \left(1\text{-}\frac{\mathrm{Min}(\mathrm{Ha},\mathrm{Hp})}{\mathrm{Max}(\mathrm{Ha},\mathrm{Hp})}\right) \times 100$$

Based on ΔH, a vertebra was classified as follows: (1) normal if $\Delta H < 20\%$; (2) mild fracture if $20\% \leq \Delta H < 25\%$; moderate fracture if $25\% \leq \Delta H < 40\%$; and severe fracture if $\Delta H \geq 40\%$.

3. Statistical analysis

We assessed the accuracy of the SBA both on an individual/person level and on a per-vertebra basis. At either person or vertebra level, we estimated the sensitivity (ie, the proportion of fractures clinically

Table 1
Baseline characteristics of 144 individuals stratified by fracture status.

	Vertebral fracture (N = 50)	No fracture (N = 94)	P-value
Number of women (N; %)	32 (64.0%)	74 (78.7%)	0.087
Age, yrs	61.6 (9.9)	51.3 (12.0)	< 0.001
Weight, kg	56.0 (8.7)	56.4 (10.9)	0.795
Height, cm	154 (7.9)	154 (7.1)	0.758
Body mass index, kg/m^2	23.5 (2.7)	23.8 (4.2)	0.545
Lumbar spine bone mineral density, g/cm^2	0.85 (0.17)	0.90 (0.14)	0.086

Values are mean (standard deviation) otherwise stated. All individuals did not have a prior known vertebral fracture. Vertebral fractures were clinically diagnosed using the Genant's criteria.

Table 2
Concordance of the shape-based algorithm in the grading of vertebral compression fracture compared to rheumatologist-based grading on 144 individuals or 1026 vertebrae.

At the person level				
SBA classification	Clinical classification			
	Normal (N = 94)	Mild (N = 30)	Moderate (N = 16)	Severe (N = 4)
Normal (N = 58)	58 (61.7%)	0 (0%)	0 (0%)	0 (0%)
Mild (N = 37)	29 (30.9%)	6 (20.0%)	2 (12.5%)	0 (0%)
Moderate (N = 40)	7 (7.4%)	23 (76.7%)	9 (56.3%)	1 (25.0%)
Severe (N = 9)	0 (0%)	1 (3.3%)	5 (31.3%)	3 (75.0%)
At the vertebra level				
SBA classification	Clinical classification			
	Normal (N = 969)	Mild (N = 35)	Moderate (N = 18)	Severe (N = 4)
Normal (N = 857)	848 (87.5%)	5 (14.3%)	4 (22.2%)	0 (0%)
Mild (N = 96)	89 (9.2%)	6 (17.1%)	1 (5.6%)	0 (0%)
Moderate (N = 64)	30 (3.1%)	23 (65.7%)	10 (55.6%)	1 (25.0%)
Severe (N = 9)	2 (0.2%)	1 (2.9%)	3 (16.7%)	3 (75.0%)

At the person level. Percent of concordance: 52.8%. Cohen's kappa coefficient: 0.275.
SBA, shape-based algorithm.
At the vertebra level. Percent of concordance: 84.5%. Cohen's kappa coefficient: 0.251.
SBA, shape-based algorithm.

diagnosed that were correctly identified as fractures by the SBA) and specificity (ie, the proportion of non-fractures clinically diagnosed that were correctly identified as non-fractures by the SBA). We also assessed the area under the operating characteristic curve (AUC) and its 95% confidence intervals. The R statistical environment (Version 4.2.1) was utilized for all data management and statistical analyses [25].

Table 3
Concordance between clinically diagnosed vertebral fractures and shape-based algorithm classifications.

At the person level		
SBA Classification	Clinical classification	
	Vertebral fracture (N = 50)	No fracture (N = 94)
Fracture	50	36
No fracture	0	58
At the vertebra level		
SBA Classification	Clinical classification	
	Vertebral fracture (N = 57)	No fracture (N = 969)
Fracture	48	121
No fracture	9	848

At the person level. Percent of concordance = 75%. Sensitivity = 100% (95% CI, 92.9 to 100). Specificity = 61.7% (95% CI, 51.1 to 71.5). Area under the ROC curve: 0.95 (95% CI, 0.92 to 0.98). Cohen's kappa coefficient: 0.528.
SBA, shape-based algorithm.
At the vertebra level. Percent of concordance = 87.3%. Sensitivity = 84.2% (95% CI, 72.1 to 92.5). Specificity = 87.5% (95% CI, 85.3 to 89.5). Area under the ROC curve: 0.92 (95% CI, 0.89 to 0.94). Cohen's kappa coefficient: 0.373.
SBA, shape-based algorithm.

4. Results

The study included 144 participants (106 women) whose average was 55 (standard deviation [SD] 12 years). As expected, individuals with a clinically diagnosed fracture (N = 50) were older than those without a fracture. However, there were no statistically significant differences in weight and height between the 2 groups (Table 1).

There were 50 individuals who were clinically diagnosed to have a vertebral fracture (Table 2). Among those with a fracture, the distribution according to severity was as follows: 60% grade 1, 32% grade 2, and 8% grade 3. The SBA demonstrated a concordance of 84.5% at the vertebra level and 52.8% at the person level for grading vertebral compression fractures. For fracture classification at the person level, the sensitivity was 100% (lower 95% CI was 93%) and the specificity was ~62% (95% CI, 51%–72%) (Table 3). The AUC value was 0.95 (95% CI, 0.92 to 0.98) (Fig. 4).

The individuals contributed 1026 vertebrae; of which 57 were clinically diagnosed to have a fracture (Table 2), with the majority located in the vicinity of the thoracolumbar spine junction (Supplement Fig. 2a and b). Of the 57 clinically diagnosed fractures, the SBA identified 48 fractures (sensitivity of 84%) (Table 3). On the other hand, among the 969 non-fracture vertebrae, the SBA algorithm correctly identified 848 (or 88%) as non-fracture. The AUC value for the SBA classification was 0.92 (95% CI, 0.89 to 0.94) (Fig. 4).

5. Discussion

Despite the significant morbidity and mortality associated with a vertebral fracture, a large proportion of cases remain undiagnosed, primarily due to its asymptomatic feature. Moreover, the diagnostic process for vertebral fractures is both labor-intensive and time-

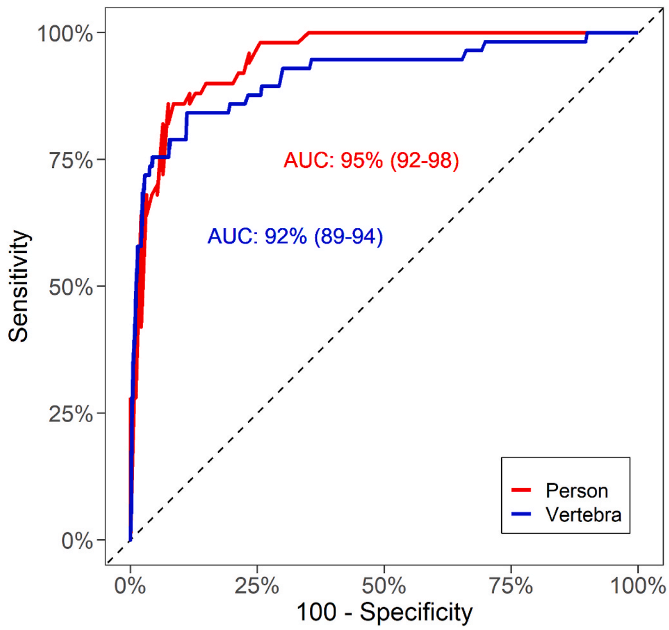

Fig. 4. The area under the receiver operating characteristic curve; The vertebra level is blue and the person level is red; AUCs were presented in percentage and 95% confidence interval.

consuming, and has the potential for bias. In this study, we have created and evaluated a novel AI-based algorithm, known as the 'shape-based algorithm,' for the identification of vertebral fractures. Our findings suggest that the Algorithm can accurately differentiate between individuals with and without fractures, indicating its potential for reducing the workload in daily clinical practice.

Our findings of the performance of SBA are comparable to previous studies' using X-rays. For instance, a study trained a deep convolutional neural network (Visual Recognition V3) on lateral and anteroposterior thoracolumbar spine X-ray to identify vertebral fractures (defined as Genant grades 2 and 3), and this algorithm achieved a sensitivity of 85%, specificity of 87%, and an AUC of 0.91 [12]. Another study utilized a multistage model with Random Forest classifier achieved a sensitivity of 74% [13]. Collectively, few algorithms had the same prognostic performance as ours. However, our algorithm was faster, taking an average of 35 ms (SD 8) to analyze each vertebra or 312 ms (SD 41) per film compared to the classifier's reported time of 1000–2000 ms on a higher-spec CPU (AMD Ryzen 5 3600 CPU, ours: Intel Xeon Gold 6132 CPU).

Our novel method adds to the modest but growing collection of AI tools for vertebral fracture prediction. However, our method was different from previous methods mainly in its interpretability. Indeed, in line with recent trends in interpretable AI, our method promotes partnership with clinicians [16]. We consider that the workflow of our method is transparent, which is often demanded by clinicians.

Our method and findings have important implications in clinical settings. As many vertebral fractures are opportunistic findings, our method can be used for opportunistic screening a large number of X-rays and lessening the burden of clinicians. Moreover, our method, like other AI based methods, can also be used to quickly provide a second opinion to improve the quality of X-ray reports.

However, our findings should be viewed within the context of strengths and potential limitations. The study was designed as a case-control investigation with participants being recruited from the general community, not from clinics where biases could be introduced. As a result, most participants had normal vertebral shapes, and there was a small number of compression fractures. The modest sample size of this study is a potential weakness because estimates of sensitivity and specificity might have been overestimated. The lack of an independent and external validation of this new algorithm is a potential weakness. An advantage is that the algorithm invented here is not a black box, and clinicians know exactly how the diagnosis is made based on morphometric properties, thereby promoting interaction between doctors and AI methods. Moreover, our method extracts vertebral corners, which extends its application to other morphometric definitions.

Currently, the algorithm demonstrates effective identification of vertebral fractures, though its performance is moderate in grading severity. The agreement between SBA grading and clinical grading for categorizing vertebral conditions as "normal", "mild", "moderate", or "severe" stands at 84% at the vertebral level and 53% at the individual level. However, this performance can be enhanced through fine-tuning with a larger sample size and an optimized threshold. At the current development, SBA exclusively focuses on the prevalent crush and wedge-shaped fractures, overlooking bi-concave fractures, a limitation we aim to address in future studies. Another weakness was that the development and testing in an ideal scenario where the segmentation model achieves doctors' performance. Nevertheless, the difference in practice might be negligible because segmentation models were excellent at drawing out the vertebral body [13,17–20].

6. Conclusions

We have developed and validated a novel shape-based algorithm that is interpretable and can accurately identify asymptomatic vertebral fractures. The algorithm will lessen the workload of clinicians in the assessment of vertebral fractures in high volume settings.

Credit author statement

Huy G. Nguyen: Conceptualization, Methodology, Formal analysis, Visualization, Writing-original draft. **Hoa T. Nguyen**: Data curation. **Linh T.T. Nguyen**: Data curation. **Thach S. Tran**: Conceptualization, Methodology, Writing-review & editing. **Lan T. Ho-Pham**: Data curation, Funding acquisition. **Sai H. Ling**: Supervision, Formal analysis. **Tuan V. Nguyen**: Supervision, Methodology, Writing-review & editing, Funding acquisition.

Availability of data and materials

The shape-based algorithm and a tutorial are available in the 12542344/sba repository [https://github.com/12542344/sba].

This manuscript corresponds to a preprint available on Research Square with the original title, 'Identification of asymptomatic vertebral compression fracture using a novel shape-based algorithm' (Link: https://www.researchsquare.com/article/rs-2742621/v1). Subsequently, the manuscript has been updated, and the title has been revised to 'Development of a shape-based algorithm for the identification of asymptomatic vertebral compression fractures: a proof-of-principle study.' Please note that it is not possible to remove the preprint from Research Square as per their policy.

Conflicts of interest

The authors declare no competing interests.

Acknowledgments

This study was funded by a grant to Prof. Tuan Van Nguyen from the National Health and Medical Research Council of Australia (Grant Number APP1195305). **ORCID** Huy Gia Nguyen: 0000-0002-6545-7242. Hoa Thai Nguyen: 0000-0002-6062-9228. Linh Thi-Thuy Nguyen: 0009-0003-1190-1437. Thach Son Tran: 0000-0002-6454-124X. Lan Thuc Ho-Pham: 0000-0001-8382-5080. Sai Ho Ling: 0000-0003-0849-5098. Tuan Van Nguyen: 0000-0002-3246-6281.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.afos.2024.01.001.

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