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Risk factors of costal pain of thoracic osteoporotic vertebral compression fractures: a multicenter retrospective analysis

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The phenomenon of costal pain of thoracic osteoporotic vertebral compression fractures (OVCFs) has been reported. However, to our knowledge, few reports with a larger sample size have analyzed the risk factors of costal pain of thoracic OVCFs. The aim of this study is to evaluate the risk factors of the costal pain in thoracic OVCFs patients. A total of 425 consecutive OVCFs patients were included in this retrospective study. Data on the clinical and radiological parameters were obtained and evaluated. Independent t-tests and chi-square tests were used in univariate analysis and multivariate logistic regression analysis was performed for statistically significant variables. $P < 0.05$ was considered to indicate statistical significance. Ultimately, 67 of 425 OVCFs patients with costal pain of were divided into Group A (costal pain group) and the rest into Group B (non-costal pain group). In the univariate analysis, the risk factors of costal pain of OVCFs included fracture level, TA, ratio of injured vertebral width, and reduction ratio of foraminal area ($P < 0.001$, $P = 0.031$, $P = 0.003$, $P < 0.001$, respectively). Multivariate logistic regression analysis revealed that independent risk factors of costal pain of thoracic OVCFs were middle thoracic vertebra [odds ratio (OR) = 5.520, $P < 0.001$], ratio of injured vertebral width [(OR = 76.138, $P = 0.025$)] and reduction ratio of foraminal area [(OR = 1.019, $P = 0.027$)]. The independent risk factors of costal pain of thoracic OVCFs were middle thoracic vertebra, ratio of injured vertebral width and reduction ratio of foraminal area.

Keywords Costal pain, Osteoporosis, Spinal fractures, Thoracic vertebra, Osteoporosis fracture, Intervertebral foramen, Multicenter, Risk factors

Abbreviations

OVCFs	Osteoporotic vertebral compression fractures
LK	Local kyphosis
TA	Thoracic Cobb angle (T4-12)
TLA	Thoracolumbar Cobb angle (T11-L2)
LA	Lumbar Cobb angle (L1-L5)
PVP	Percutaneous vertebroplasty
PKP	Percutaneous kyphoplasty

Osteoporotic vertebral compression fractures (OVCFs) are one of the most serious complications of osteoporosis,, with thoracic OVCFs being the most common[1–3]. Due to the special structure of thoracic OVCFs, in addition to the pain at the fracture site, it is often accompanied by costal pain[4–6]. The phenomenon of costal pain of thoracic OVCFs was first noticed by Gbison et al.[6], who referred to the pain in the hip, groin, chest and other non-fracture areas as non-midline pain. They retrospectively analyzed non-midline pain areas in 350 patients and found that costal pain of thoracic OVCFs was the most common. Costal pain of thoracic OVCFs refers to unilateral or bilateral costal pain associated with vertebral fractures and requires exclusion of costal pain due to rib fractures, intercostal neuritis, shingles, or other diseases, which often aggravated by deep breathing, sneezing,

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or postural changes[4–7]. Moreover, in some patients, the costal pain is more painful than the fracture site itself[8,9]. The pain at the fracture site of thoracic OVCFs patients can be significantly relieved after surgical treatment. However, unfortunately, there was no significant relief of the costal pain in some patients[4,5]. Therefore, in order to further understand the etiology and mechanism of costal pain of thoracic OVCFs, it is necessary to analyze the risk factors.

Previous studies have reported a variety of causes of thoracic OVCFs with costal pain, including sympathetic nerve damage, reduced vertebral height, foraminal stenosis, and facet imbalance[4–7]. However, to our knowledge, the relationship between costal pain and thoracic OVCFs remains elusive and few related studies with larger-scale sample have been reported. Therefore, this study was aimed at analyzing the risk factors of costal pain of thoracic OVCFs through multicenter data. In addition, we analyzed each risk factor to understand the pathogenesis of costal pain.

Methods

Participants

The study was approved by the Institutional Review Board and Ethics Committee of authors' hospital (KY2023056). This study was conducted in compliance with the Declaration of Helsinki and the Institutional Review Board (IRB) waived the requirement for informed consent due to the retrospective nature of the study. A multicenter retrospective case-control analysis was performed during the period from August 2019 to December 2022. We retrospectively reviewed all consecutive patients with thoracic OVCFs admitted to five tertiary hospitals (Affiliated Hospital of Southwest Medical University, Suining Central Hospital, the Second People's Hospital of Deyang, Jianyang City People's Hospital, and the First People's Hospital of Mianyang) in Sichuan, China. Inclusion criteria were as follows: (1) single new thoracic vertebral fracture; (2) low energy injuries, such as flat falls, sprains, etc.; (3) the bone mineral density was − 2.5 or lower. Exclusion criteria were as follows: (1) incomplete clinical and radiographic data; (2) vertebral fractures due to high-energy injury, such as traffic accident injury, high fall injury, etc.; (3) patients with costal pain caused by other reasons, such as rib fractures, intercostal neuritis, tumor or shingles, etc.; (4) previous thoracic spine surgery; (5) patients with severe scoliosis and axial rotation of the vertebral body.

Data Collection

Obtained from clinical records were patient demographics such as gender, age, as well as comorbidities including diabetes and hypertension. Vertebral fracture level, fracture type and fracture degree clarified by CT scan examination, meanwhile, we could also measure the local kyphosis (LK), thoracic Cobb angle (T4-12) (TA), thoracolumbar Cobb angle (T11-L2) (TLA) and lumbar Cobb angle (L1-L5) (LA) in each patient by CT scan examination. Reduction ratio of foraminal area and ratio of injured vertebral width were also measured by CT scan.

The fracture levels were categorized as the upper thoracic (T1-4), middle thoracic (T5-8), or lower thoracic (T9-12) according clinical significance and the needs of analysis[9]. The classification criteria of fracture types and degree in this study were used and modified based on the semi-quantitative OVCFs classification reported by Genant et al.[10]. Based on the vertebral shape observed in CT scans, along with the anterior, posterior, or intermediate vertebral heights, fracture types were categorized as wedge, biconcave, or crush types (Fig. 1). The degree of fracture was classified as mild (grade I, about 0–25% reduction in any height of the anterior, middle, or posterior vertebral body), moderate (grade II, about 25-40% reduction in any vertebral height), and severe (grade III, reduction at least 40% of any vertebral height) (Fig. 1).

The required parameters were measured using Picture Archiving and Communication Systems (PACS) on the lateral or coronal CT of the full spine. The sagittal plane of CT with the highest pedicle height in the injured vertebra was selected to measure the foraminal area. Reduction ratio of foraminal area was calculated as follow: reduction ratio of foraminal area $(\%) = \left\{ {[(\mathrm{A}+\mathrm{D})-(\mathrm{B}+\mathrm{C})]}/{(\mathrm{A}+D)} \right\}(\%)$, which was shown in Fig. 2. If the reduction ratio of foraminal area was zero or negative, it was denoted as "0".

For the measurement method of ratio of injured vertebral width, we refer to Xin et al.[5]. Firstly, the CT sagittal plane was selected and the injured vertebra was located. The lower edge of the injured pedicle was selected as a baseline to locate the coronal plane of the injured vertebra, and the maximum width of the injured vertebra was measured (Fig. 2). If the fracture involves only the upper or lower part of the vertebral body, the most appropriate coronal plane was chosen by two physicians to measure the width. Ratio of injured vertebral width was calculated as follow: ratio of injured vertebral width $= {2E}/{(F+G)}$ (E: fractured vertebral body width; F: width of adjacent vertebra above injured vertebra; G: width of adjacent vertebra below injured vertebra).

Several Cobb angle parameters were evaluated as follows: LK, Cobb's angle between the upper endplate of the superior vertebral body and the lower endplate of the inferior vertebral body of the injured vertebra; TA, Cobb's angle between the superior endplate of T4 and the inferior endplate of T12; TLA, Cobb's angle between the superior endplate of T11 and the inferior endplate of L2; LA, Cobb's angle between the superior endplate of L1 and the inferior endplate of L5 (Fig. 2).

Statistical analysis

Data were analyzed using SPSS 24.0 (SPSS Inc., Chicago, Illinois, USA). Independent t-test was used for continuous variables data and Chi-square test was used for categorical variables in univariate analysis. Multivariate logistic regression analysis was performed for variables with $P < 0.05$ in univariate analysis. If the P value was < 0.05, it was considered statistically significant in multivariate logistic regression analysis. Hosmer and Lemeshow tests were used to check the goodness-of-fit of the final models to ensure that they were well referential and fit.

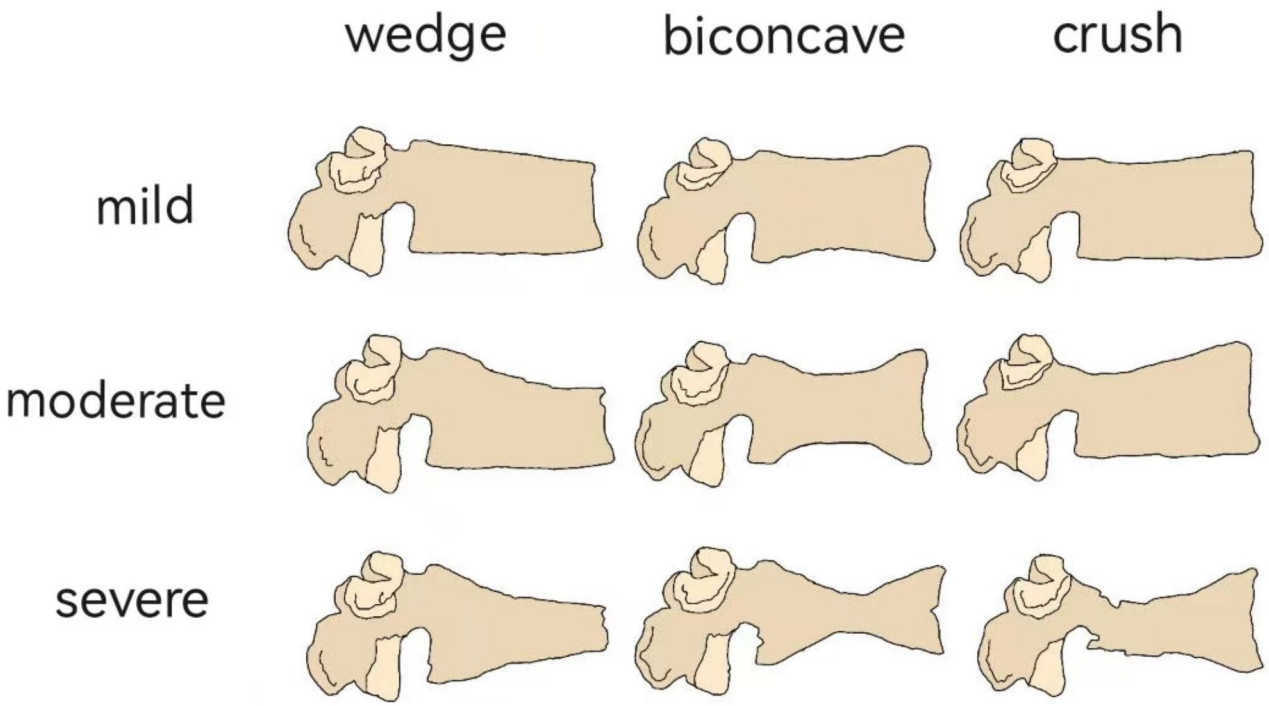

Fig. 1. Picture of Genant semi-quantitative OVCFs classification.

Results

A retrospective analysis of consecutive 427 cases with thoracic OVCFs were include in this study according to inclusion and exclusion criteria, of whom 68 patients had costal pain, and the incidence of costal pain was 15.93% (68/427). Of the 427 patients, there were 2 patients in the upper thoracic vertebra (2 cases of T4), one of whom had costal pain. Because the number of upper thoracic vertebrae was too small to be statistically significant, we eventually included 425 patients. Sixty-seven of 425 patients with costal pain of OVCFs were divided into costal pain group and the rest into non-costal pain group. The average ages of two groups were 73.82 ± 9.62 years and 72.65 ± 8.95 years and the percentages of females were 82.09% and 81.56%, respectively (Table 1).

In the present study, 5 cases of T5, 9 cases of T6, 28 cases of T7, 31 cases of T8, 18 cases of T9, 27 cases of T10, 60 cases of T11, and 247 cases of T12 were found. Proportion of costal pain in each vertebral segment: 2 cases in T5 (40%), 4 cases in T6 (44.44%), 14 cases in T7 (50%), 12 cases in T8 (38.71%), 5 cases in T9 (27.78%), 7 cases in T10 (25.93%), 7 cases in T11 (11.67%) and 16 cases in T12 (6.48%). It can be seen that the seventh thoracic vertebra has the highest proportion of costal pain among the fractured vertebral level (Fig. 3).

The proportion of vertebral fractures in the middle thoracic vertebra was significantly higher than that in the lower thoracic vertebra in patients with costal pain of thoracic OVCFs ($P < 0.001$). Reduction ratio of foraminal area was significantly greater in patients with costal pain of thoracic OVCFs (18.69% vs. 9.52%; $P < 0.001$). Meanwhile, ratio of injured vertebral width was also significantly greater in patients with costal pain of thoracic OVCFs (1.057 vs. 1.024; $P = 0.003$). There was a statistically significant difference in TA between two groups ($P < 0.05$) (Table 1). Table 2 shows that the differences in diabetes and hypertension were no statistically significant between two groups. No significant differences in fracture type and fracture degree were noted between two groups. Meanwhile, there was also no statistical significance in LK, TLA and LA between two groups ($P > 0.05$).

Based on univariate analysis results, four indicators were used as independent variables, including fracture level, reduction ratio of foraminal area, TA and ratio of injured vertebral width. Multivariate logistic regression analysis identified three independent risk factors that is significantly correlated with costal pian of thoracic OVCFs: fracture level ($P < 0.001$), the ratio of injured vertebral width ($P = 0.025$) and reduction ratio of foraminal

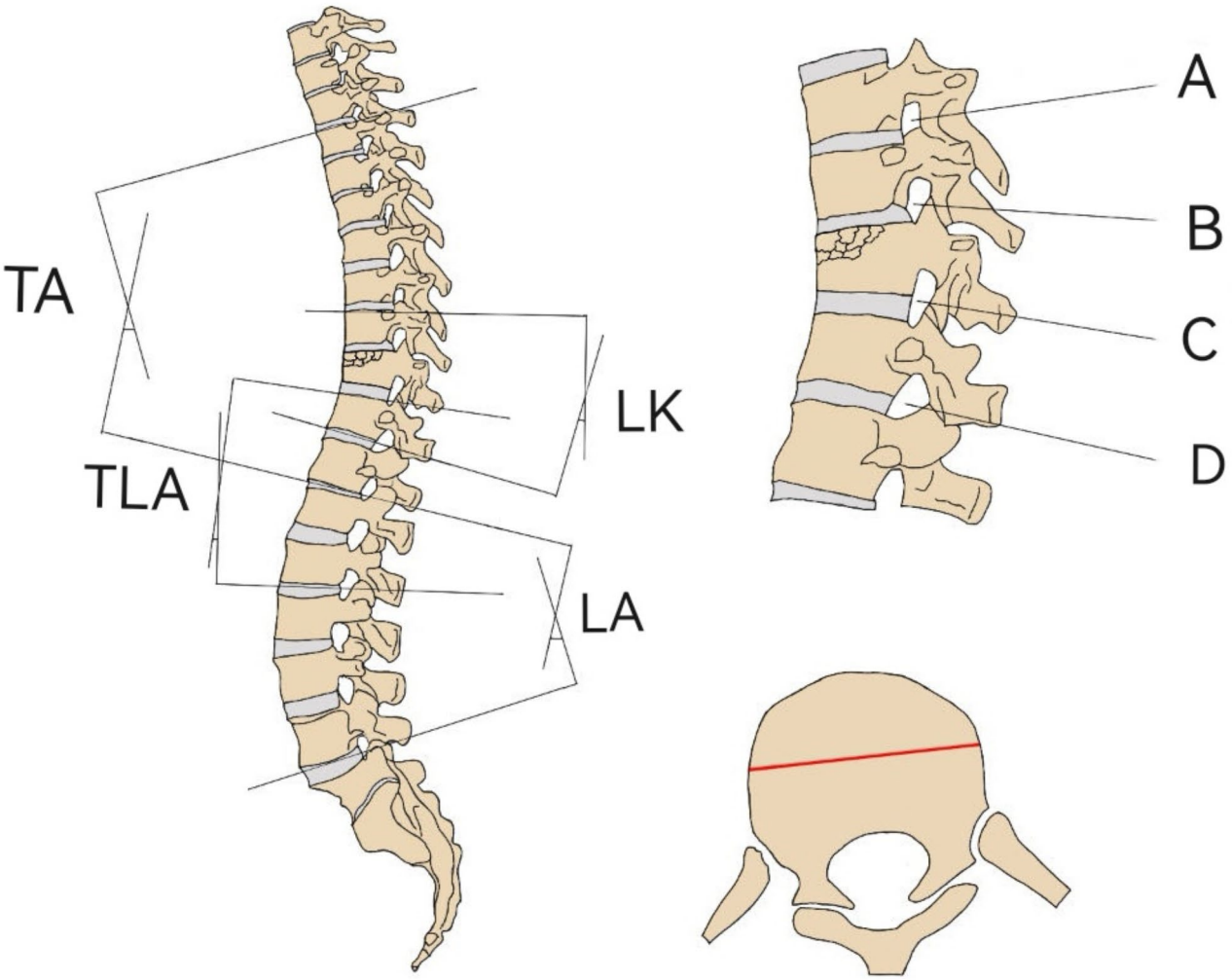

Fig. 2. Schematic diagram of measurement of foraminal area and in this study, we calculated reduction ratio of foraminal area using formula $\frac{\text{Reduction ratio of foraminal area}\,(\%)}{=\left\{[(\mathrm{A}+\mathrm{D})-(\mathrm{B}+\mathrm{C})]/(\mathrm{A}+D)\right\}(\%)}$. (**A**) Upper adjacent intervertebral foraminal area of injured vertebra; (**B**) Superior intervertebral foraminal area of injured vertebra; (**C**) Inferior intervertebral foraminal area of injured vertebra; (**D**) Lower adjacent intervertebral foraminal area of injured vertebra; TA, thoracic Cobb angle (T4-12); TLA, thoracolumbar Cobb angle (T11-L2); LK, local kyphosis; LA, lumbar Cobb angle (L1-L5); Measurement of width of injured vertebrae, the red line is the vertebral width.

Variables	Costal pain (*n* = 67)	Non-costal pain (*n* = 358)	*P* value
Age, y	73.82 ± 9.62	72.65 ± 8.94	0.331
LK (°)	15.15 ± 7.92	14.51 ± 8.48	0.568
Ratio of injured vertebral width	1.057 ± 0.07	1.024 ± 0.08	0.003*
TA (°)	32.14 ± 9.61	29.06 ± 10.91	0.031*
TLA (°)	11.96 ± 7.95	13.54 ± 10.97	0.262
LA (°)	32.52 ± 12.11	33.21 ± 12.71	0.683
Reduction ratio of foraminal area (%)	18.69 ± 15.70	9.52 ± 14.89	< 0.001*

Table 1. Independent t-test for factors between the two groups. LK, local kyphosis; TA, thoracic Cobb angle (T4-12); TLA, thoracolumbar Cobb angle (T11-L2); LA, lumbar Cobb angle (L1-L5).

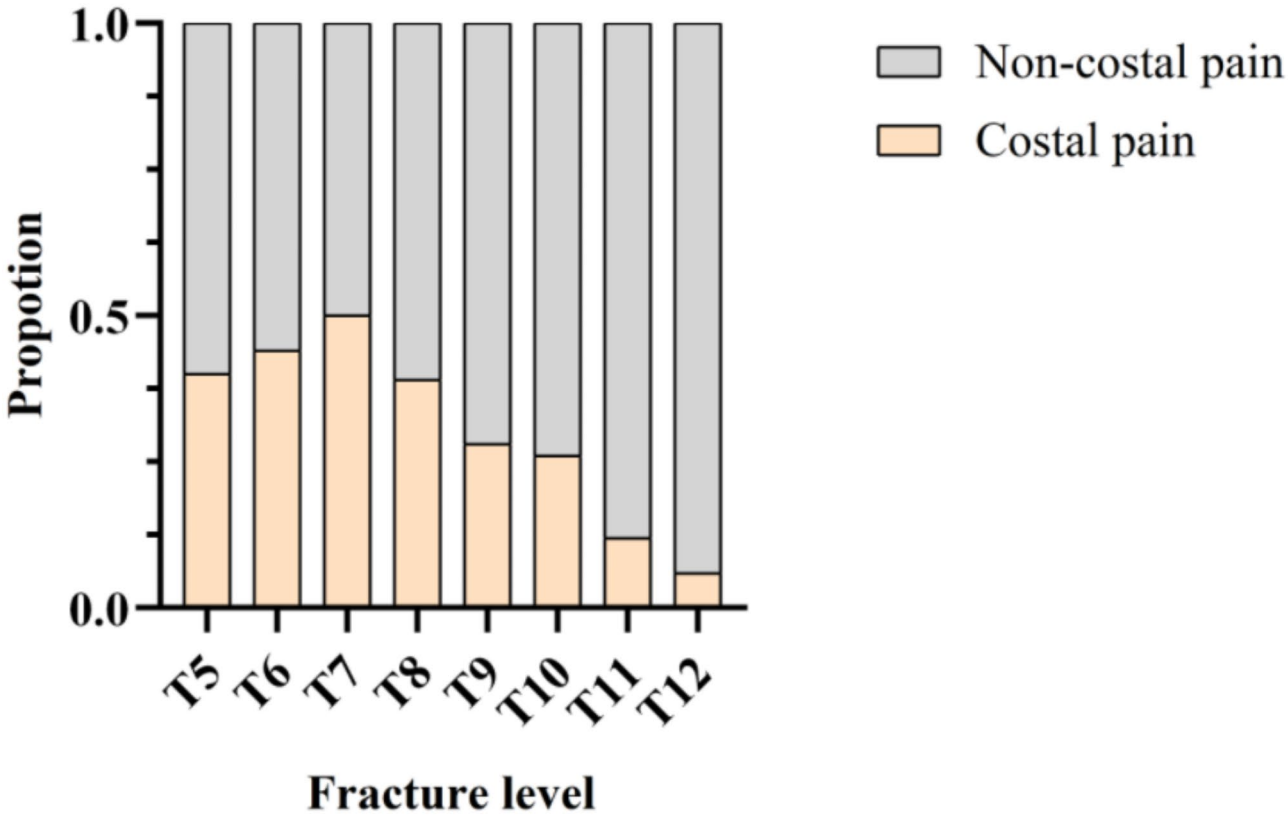

Fig. 3. Proportion of costal and non-costal pain in each vertebral level.

Variables	Costal pain ($n=67$)	Non-costal pain ($n=358$)	*P* value
Gender			
Male	12	66	0.919
Female	55	292	
Fracture segment			
Middle thoracic spine	32	41	< 0.001*
Lower thoracic spine	35	317	
Diabetes			
Yes	9	37	0.454
No	58	321	
Hypertension			
Yes	24	111	0.437
No	43	247	
Fracture type			
Wedge	19	142	0.142
Biconcave	43	183	
Crush	5	33	
Fracture degree			
Mild	18	137	
Moderate	26	113	0.199
Severe	23	108	

Table 2. Chi-square test between the two groups.

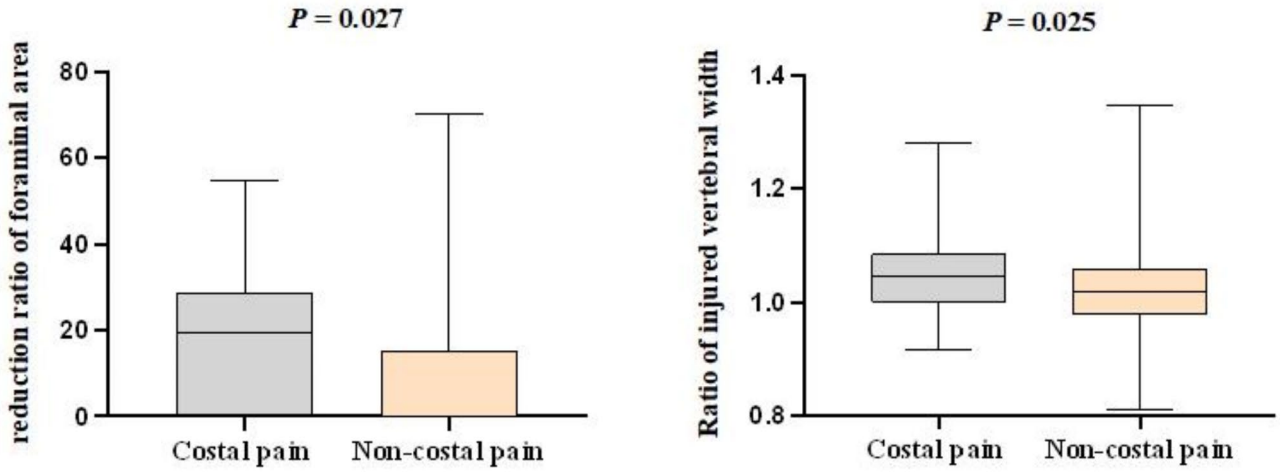

Fig. 4. Box diagram of two groups of reduction ratio of foraminal area and ratio of injured vertebral width.

Variables	Odds ratio (95% confidence intervals)	*P* value
Fracture level	5.520 (3.006–10.135)	< 0.001*
Reduction ratio of foraminal area (%)	1.019 (1.002–1.037)	0.027*
Ratio of injured vertebral width	76.138 (1.714-3381.606)	0.025*
TA (°)	1.017 (0.990-1.045)	0.219

Table 3. Multivariate logistic regression of related factors. TA, thoracic Cobb angle (T4-12). Hosmer and Lemeshow goodness of fit chi-squared $P = 0.762$ (8 degrees of freedom).

area ($P = 0.027$) (Fig. 4). The model had good predictive ability, with the Hosmer and Lemeshow goodness of fit chi-squared $P = 0.762$ (8 degrees of freedom) (Table 3).

Discussion

Currently, there is limited literature examining the incidence of ratio of costal pain of thoracic OVCFs. In 2012, Choi et al.[11] retrospectively observed 35 patients with thoracic OVCFs who underwent percutaneous vertebroplasty (PVP) or percutaneous kyphoplasty (PKP); the incidence of costal pain was first reported as 28.6% (10/35). Tang et al.[4] in 2017, through a retrospective analysis of 188 patients, reported that the incidence of costal pain was 20.2% (38/188). In this study, the incidence of costal pain was 15.93% (68/427), which was lower than that reported by Tang et al. (4) and Choi et al.[11] It can be clearly seen that costal pain of thoracic OVCFs is common. However, few studies have been reported on its risk factors. To our knowledge, this is the first multicenter retrospective study to analyze independent risk factors of costal pain of thoracic OVCFs. The aim of this study is to identify risk factors for costal pain in thoracic OVCFs, which could potentially inform evidence-based recommendations for clinical diagnosis and treatment.

The results of this present study showed that the fracture segment located in the middle thoracic vertebra, the greater the reduction ratio of foraminal area, the wider the ratio of injured vertebral width, the more prone to costal pain.

Radiating pain of intercostal nerve caused by thoracic nerve root stimulation is considered by many scholars as a mechanism of costal pain of thoracic OVCFs[4,5,12]. The posterior ventral branch of the thoracic nerve root exits the foramen anteriorly and runs outwards through the costal space to innervate the chest and abdominal wall. This kind of neuralgia radiates to the chest and abdomen in a band, corresponding to the dermatome innervated by the somatosensory nerve, and has the characteristics of clear sensation and clear localization[4,12]. After the occurrence of thoracic OVCFs, the collapse of the vertebral body leads to the reduction of the height and the narrowing of the intervertebral foramen, which directly stimulates the thoracic nerve root to produce intercostal nerve radiating pain[4,5]. Doo et al.[13] analyzed the pain pattern of OVCFs and explained that the distant non-fracture pain may be caused by the narrowing of the foramina due to the reduction of the vertebral height, which stimulates the posterior branch of the spinal nerve corresponding to the nerve root. In our study, the greater the reduction ratio of foraminal area, the higher the incidence of costal pain also supports this view to some extent. However, there were some radiographic findings showing that patients without foraminal collapse have costal pain and the pain site was blurred, suggesting that there were other mechanisms other than radiative pain caused by stenosis of the foramen.

Jinkin et al.[14] described a type of referred pain associated with afferent sympathetic fibers distributed in specific regions of the spinal column. These fibers are present in the anterior longitudinal ligament, the vertebral body itself, the periosteum surrounding the vertebral body, and potentially the entire vertebral column. This

extensive network of fibers is called the paravertebral autonomic neural plexus[14]. Some afferent nerve fibers pass through the sympathetic ganglion and through the white ramus communicans, eventually entering the dorsal root ganglion. By stimulating afferent nerve fibers, pain is generated in other somatic distribution areas originating from the same ganglion[7,14]. This pain is dull, diffuse, and inaccurately localized. Xin et al.[5] found a statistically significant correlation between the increase in injured vertebral width and costal pain in thoracic OVCFs, which is consistent with our analysis showing a similar relationship. This suggests that referred pain due to sympathetic nerve stimulation caused by peripheral bulging of the vertebral body after vertebral compression fracture may be one of the mechanisms of costal pain of thoracic OVCFs. This finding could explain why the location of the patient's intercostal pain did not match the injured vertebral segment, and the pain was diffuse and poorly localized in some patients. Choi et al.[11] reported that the incidence of costal pain in vertebral fracture type of biconcave and crush was higher than that in wedge fracture. They explain that the presence of middle column injury in non-wedge fractures is an important factor in costal pain of thoracic OVCFs. After the injury of the middle column, the extraforaminal ligament appears edema and deformation, and the thoracic nerve roots attached to the external foraminal ligament could be pulled or compressed[15]. However, in our study, we did not find a significant correlation between the presence of costal pain and the type of vertebral fracture.

Our study showed that the incidence of costal pain in patients with middle thoracic fracture was higher than that in patients with lower vertebral fracture, especially in the 7th thoracic vertebra. We hypothesized that the physiological curvature of the middle thoracic vertebra exerts a unique biomechanical force, making the vertebra or small joints more prone to instability after thoracic OVCFs. The biomechanical effects of the secondary deformity to spinal fractures reported by Wilson et al.[16] lead to sagittal imbalance and overload of facet joints and paravertebral muscles, resulting in pain at nonfracture sites. They explained the instability of the facet joint and the sagittal imbalance were the reasons of pain in the area far from the fracture. Similarly, it may be due to the collapse of the vertebral body after thoracic OVCFs, the physiological curvature of the middle thoracic spine increases the likelihood of coronal and sagittal plane imbalance, leading to instability in the vertebral body, intervertebral disc, and facet joints, which in turn stimulates the costal nerves[5,16,17]. This mechanism could reasonably explain the aggravation of costal pain in patients with thoracic OVCFs after changing their postures.

Currently, the efficacy of percutaneous vertebroplasty (PVP) or percutaneous kyphoplasty (PKP) on thoracic OVCFs has been widely recognized by clinicians[18,19]. A large number of prospective and retrospective studies have shown that compared with conservative treatment, PVP and PKP can rapidly relieve pain, decrease the incidence of complications associated with prolonged bed rest, and improve quality of life[18,19]. PKP is developed on the basis of PVP. The latter uses balloon expansion to create space in the vertebral body, reducing the thrust required for bone cement injection and significantly reducing the risk of bone cement leakage. Meanwhile, PKP can provide better correction of local kyphosis and greater recovery of injured vertebra height than the PVP by injecting bone cement through balloon expansion[19,20]. In this study, we found that middle thoracic vertebra, ratio of injured vertebral width and reduction ratio of foraminal area are independent risk factors of costal pain of OVCFs. Therefore, for OVCFs patients with costal pain, we recommend using PKP to restore the vertebral height and restore the fractured vertebral body to its original shape as much as possible, effectively reduce the entrapment of nerve roots by the foramen and reduce the stimulation of the peripheral sympathetic nerve by the fractured vertebral body. The PKP may be effective in relieving the costal pain in OVCFs patients[7]. In addition, the costal pain was not relieved in time after surgical treatment for some patients, which may be related to local nerve edema, inflammatory exudation of nerve root outlet and repeated stimulation exudation. For these patients, local nerve blocks, taking non-steroidal anti-inflammatory drugs, or other combination treatments may be necessary to relieve pain[21–23].

However, some limitations of our study should be mentioned. This study is still a retrospective analysis. Some potentially relevant factors, such as bone mineral density (BMD) and body mass index (BMI), as well as the production and release of inflammatory mediators like interleukin (IL) and tumor necrosis factor (TNF) by injured vertebrae, were not considered in our study. These inflammatory mediators may stimulate the corresponding nerve roots, leading to costal pain, which was not examined in our current study[2]. We expect prospective studies with larger samples to confirm or modify the findings of this study.

Conclusion

In the multivariate analysis, middle thoracic vertebra, ratio of injured vertebral width and reduction ratio of foraminal area were identified as independent risk factors. Therefore, for OVCFs patients with costal pain, it is necessary to restore the height of the injured vertebra as much as possible and correct the deformity of the injured vertebra, reducing the risk of postoperative residual costal pain.

Data availability

Te dataset generated and analysed during the current study is available from the corresponding author on reasonable request.

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Author contributions
RC, PZ, and GL worked through the whole study from designing the study, acquisition of data, analysis and interpretation of data, and drafting the manuscript. KL and QL contributed in designing the study, collecting data, and editing and revising the manuscript.GL made substantial contributions to conception to this paper and contributed in critically revising the manuscript.

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Declarations

Ethics approval and consent to participate
This study project was approved by the institutional research and ethics committee of Affiliated Hospital of Southwest Medical University (KY2023056).

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Additional information
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