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Original Article

Associated Risk Factors for Vertebral Fractures in the Elderly: A Cross-Sectional Study Based on NHANES Database

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SUMMARY

Background: Vertebral fractures in elderly patients contribute to huge economic and social burden and seriously low quality of life. This study aims to identify the associated risk factors for vertebral fractures in the non-institutionalized old American population.

Methods: A total of 31034 people from National Health and Nutrition Examination Survey (NHANES) during 2005–2010 were included. Therein, 108 individuals with exact history of vertebral fractures were enrolled from a series of 4268 people (aged between 65 and 85 years old). The related demographic and laboratory examination data were collected. Further, univariate and multivariate analysis were applied to identify the related risk factors of vertebral fractures in the elderly. A nomogram risk prediction model was constructed and internally validated through the boot strapping method.

Results: Univariate analysis indicated these factors, age ($\chi^2 = 5.75$, $p = 0.017$), smoking ($\chi^2 = 4.46$, $p = 0.035$), and combined with osteoporosis ($\chi^2 = 41.26$, $p < 0.001$) were statistically different between the vertebral fracture group and no-vertebral fracture group. In multivariate analysis, the parameters of smoking (OR = 1.620, 95% CI: 1.080–2.440, $p = 0.021$), combined with osteoporosis (OR = 3.370, 95% CI: 2.220–5.110, $p < 0.001$), and the serum K (OR = 0.360, 95% CI: 0.230–0.560, $p < 0.001$) were screened as the independent risk factors for vertebral fractures in the elderly. The nomogram demonstrated a favorable level of discrimination with the area under the curve was 0.71. The calibration curves exhibited satisfactory agreement between the actual observation and nomogram prediction.

Conclusion: The nomogram (including osteoporosis, smoking, and serum K) was capable of predicting vertebral fracture and has certain auxiliary value in clinical applications.

1. Introduction

With the accelerating process of the population aging, the incidence rate of vertebral fractures worldwide is also increasing. Previous research figured out, the incidence of vertebral fractures in women over 60 years old is 2–3 times that in men in United States and Europe.[1,2] The incidence of thoracolumbar fracture patients hospitalized in Sweden is about 30/100000 per year, of which two-thirds are the people aged 65 years and over.[3] Adverse consequences of vertebral fractures in elderly patients, including persistent low back pain, kyphosis deformity, lung dysfunction, loss of activity ability and psychological disorders, still need to be fully valued because of its contributions to huge economic and social burden and seriously low quality of life.[4,5] Besides, previous literatures have reported that post menopausal women had significant bone loss due to the decline of estrogen, leading to a significantly higher risk of osteoporotic fractures of spine.[6] Meanwhile, age, smoking, drinking alcohol, high caffeine in-take, combined with hypertension, diabetes, and osteoporosis are all regarded as risk factors for vertebral fractures in the previous researches.[7–11]

However, the onset of vertebral fractures in the elderly is hidden, the early symptoms are also not obvious, their awareness of prevention is insufficient, and the treatment is often delayed.[12,13] In addition, the incidence of missed diagnosis of vertebral fractures in elderly from imaging examination is surprisingly reported to be approximately 40%.[14,15] Thus, in view of the severity and thorny nature of vertebral fractures in the elderly, it is essential to make a whole consideration on the prevention of vertebral fractures and related follow-up adverse events in the elderly, so as to create and provide an effective evaluation system for this group.

This study is aimed at examining the national condition of vertebral fractures as well as its risk factors in the elderly based on the representative population from the National Health and Nutrition Examination Survey (NHANES) 2005–2010. We constructed a practical nomogram to predict vertebral fracture in the elderly. Nomogram is a regression model-based graphical tool that quantifies the risk of an event through a variety of predictors and is used to build prediction models.[16] By transforming traditional statistical prediction models into visual graphs, nomogram can accurately predict relationships between multiple variables and outcome indicators such as incidence.[17]

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2. Methods

2.1. Study participants

We applied the NHANES 2005–2010 data to explore the associated risk factors for vertebral fractures in the elderly of the United States. NHANES is a database that aims to obtain nationally representative samples of the non-institutionalized US population to estimate the risk factors of common diseases and nutritional status of the US population. Moreover, NHANES collected detailed information on civilian non-institutionalized populations from the United States, and their health and laboratory examination data on the population were further collected. The cross-sectional surveys were conducted by the National Center for Health Statistics (NCHS), and the methodological details about NHANES database were available at www.cdc.gov/nchs/nhanes/.[18] Figure 1 shows the overall flow chart of the patient selection. Specifically, a total of 4268 participants aged 65 years and older with complete household interviews and medical examinations were included in this study. The specific study was approved by the ethics review board of National Center for Health Statistics, and written consent was obtained from each participant in NHANES, thereby there is no need to apply for an approval from our institution.

2.2. Associated risk factors

In NHANES 2005–2010, the overall individuals included in this study were divided into vertebral fracture group and no-vertebral fracture group in accordance with the exact history of vertebral fractures, and the condition of vertebral fractures was obtained by the self-reported methods. It was also worth noting that participants in the no-vertebral fracture group had no fracture. Specifically, the individuals with vertebral fracture were diagnosed in accordance with the exact chief complaint of back pain and the corresponding X-ray, computed tomography (CT), and magnetic resonance imaging (MRI) examination of vertebral body. The diagnosis of osteoporosis was mainly based on measurement of bone mineral density (BMD). BMD was measured by dual energy X-ray absorptiometry (DXA), and the specific diagnostic criteria of osteoporosis were defined as the T-score < -2.5 standard deviation (SD). The factors of age, gender, marriage, smoking, drinking alcohol, combined with hypertension, diabetes, and osteoporosis were enrolled into the statistical analysis. Moreover, the related laboratory examination (blood and urine specimens) of this study, such as the serum Ca, Fe, P, Cr, Na, K, uric acid (UA), and vitamin D (Vit D) were collected at the mobile examination centers and analyzed by the standardized laboratory test procedures. Moreover, it also needs to be further pointed out that the vertebral fracture of these individuals occurred after the laboratory exam, and the significance and value of prediction can be highlighted. Detailed data of this study can be searched at http://www.cdc.gov/nchs/nhanes.

2.3. Statistical analysis

We compared the demographic characteristics and laboratory examination between participants with and without vertebral fractures by Student's *t*-test for continuous variables and the Chi-square test for categorical variables, accounting for the complicated sample survey designs. The univariate analysis was applied to identify the related risk factors of vertebral fractures in the elderly, and the logistic regression model was constructed to perform the multivariate analysis. In logistic regression models, the relation between the vertebral fractures and risk factors was shown as an odds ratio (OR) with a 95% confidence interval (CI). p value < 0.05 was thought as statistically significant. Statistical analysis was conducted using R software (version 4.0.2, http://www.R-project.org). The package of rms was used to establish the nomogram, the bootstrapping method (resampling = 1000) was employed for internal verification to evaluate the modeling effect. Discrimination ability was assessed by the receiver-operating characteristics curve (ROC) analysis and predictive accuracy was measured by the area under the curve (AUC).

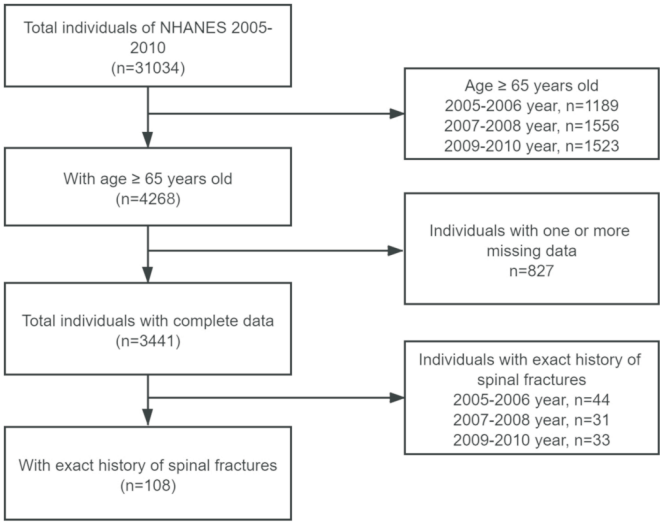

Figure 1. The flow chart of sample inclusion from NHANES 2005–2010. NHANES, National Health and Nutrition Examination Survey.

3. Results

As shown in Table 1, 108 individuals with vertebral fractures were identified from a total of 4268 participants. In terms of age, there was a significant statistical difference between the vertebral fracture group and the no-vertebral fracture group (χ^2 = 5.75, p = 0.017). As for smoking, individuals in the vertebral fractures group showed significant difference with the no-vertebral fractures group (χ^2=4.46, p = 0.035). Besides, individuals in the vertebral fractures group combined with osteoporosis also showed significant difference with the no-vertebral fractures group (χ^2 = 41.26, p < 0.001), while no significant difference between the two groups was screened in terms of gender, marriage, drinking alcohol, combined with hypertension, and combined with diabetes (p all > 0.05).

The univariate analysis of related laboratory examinations in the elderly with vertebral fractures included in NHANES 2005–2010 was shown in Table 2. Among the results, there was a significant statistical difference between individuals with and without vertebral fractures in the serum P (t = 2.021, p = 0.043), serum Na (t = -2.366, p = 0.020), serum K (t = 4.651, p < 0.001), and Vit D (t = 2.522, p = 0.012). Moreover, there was no significant difference between the two groups were screened in terms of serum Ca, serum Fe, UA, and serum Cr (p all > 0.05).

To identify the specific risk factors of vertebral fractures in our enrolled population, multivariate analysis was performed and results were presented in Table 3. In this multivariate analysis, the parameters of smoking (OR = 1.620, 95% CI: 1.080–2.440, p = 0.021), combined with osteoporosis (OR = 3.370, 95% CI: 2.220–5.110, p < 0.001), and serum K (OR = 0.360, 95% CI: 0.230–0.560, p < 0.001) were screened as the independent risk factors of elderly with vertebral fractures in non-institutionalized American population.

According to the predictors selected by multivariate analysis, a

Table 1
The univariate analysis of related risk factors in the elderly with vertebral fractures.

Factors	Vertebral fracture group (n = 108)	No-vertebral fracture group (n = 3333)	x^2/t	p value
Age, n (%)			5.75	0.017
65–80	63 (58.3)	2306 (69.2)		
≥ 80	45 (41.7)	1027 (30.8)		
Gender, n (%)			1.97	0.160
Male	48 (44.4)	1710 (51.3)		
Female	60 (55.6)	1623 (48.7)		
Marriage, n (%)			0.680	0.403
Not living alone (married, living with partner)	56 (51.9)	1862 (55.9)		
Living alone (widowed, divorced, separated, never married)	52 (48.1)	1471 (44.1)		
Smoking, n (%)			4.46	0.035
Yes	68 (63.0)	1755 (52.7)		
No	40 (37.0)	1578 (47.3)		
Drinking alcohol, n (%)			0.40	0.819
Yes	64 (59.3)	1923 (57.7)		
No	37 (34.3)	1226 (36.8)		
Combined with hypertension, n (%)			0.04	0.846
Yes	63 (58.3)	1913 (57.4)		
No	45 (41.7)	1420 (42.6)		
Combined with diabetes, n (%)			0.05	0.827
Yes	22 (20.4)	708 (21.2)		
No	86 (79.6)	2625 (78.8)		
Combined with osteoporosis, n (%)			41.26	< 0.001
Yes	40 (37.0)	483 (14.5)		
No	68 (63.0)	2850 (85.5)		

Values in the categorical variables were expressed as number (%).

Table 2
The univariate analysis of related laboratory examination in the elderly with vertebral fractures.

Factors	Vertebral fracture group (n = 108)	No-vertebral fracture group (n = 3333)	x^2/t	p value
Serum Ca (mmol/L), mean (SD)	2.38 (0.11)	2.37 (0.10)	0.764	0.445
Serum Fe (mmol/L), mean (SD)	14.27 (6.21)	14.86 (5.70)	-1.053	0.292
Serum P (mmol/L), mean (SD)	1.23 (0.18)	1.20 (0.17)	2.021	0.043
UA (mmol/L), mean (SD)	342.34 (94.80)	342.96 (89.33)	-0.071	0.943
Serum Cr (mmol/L), mean (SD)	96.67 (36.58)	94.46 (48.13)	0.471	0.637
Serum Na (mmol/L), mean (SD)	138.52 (3.17)	139.25 (2.70)	-2.366	0.020
Serum K (mmol/L), mean (SD)	4.12 (0.41)	4.33 (0.46)	4.651	< 0.001
Vit D (mmol/L), mean (SD)	57.86 (20.65)	62.95 (21.25)	2.522	0.012

Values were expressed as mean (standard deviation). UA, uric acid; Vit D, vitamin D.

Table 3
The multivariate analysis of risk factors in the elderly with vertebral fractures.

Factors	β	Wald	p value	OR (95% CI)
Age	-0.270	1.680	0.195	0.770 (0.510, 1.150)
Combined with osteoporosis	1.220	32.670	< 0.001	3.370 (2.220, 5.110)
Smoking	0.480	5.320	0.021	1.620 (1.080, 2.440)
Serum P	-0.400	0.480	0.488	0.670 (0.220, 2.070)
Serum Na	0.06	3.290	0.070	1.060 (0.990, 1.130)
Serum K	-1.02	19.910	< 0.001	0.360 (0.230, 0.560)
Vit D	-0.01	2.590	0.108	0.990 (0.980, 1.000)

OR, odds ratio; Vit D, vitamin D; 95% CI, 95% confidence interval.

nomogram was constructed (Figure 2A). The predictor points on the upper most scale that corresponded to each patient variable are added up. The total points projected to the bottom scale indicate the risk of vertebral fracture. To determine the calibration accuracy of the nomogram, the authors performed internal validation with bootstrap sampling. The calibration curve was plotted for the analyses of vertebral fracture incident rate; the mean absolute error was 0.003, mean squared error was 0.00003, and 0.9 quantile of absolute error was 0.009 (Figure 2B). ROC was plotted to evaluate the predictive performance for vertebral fracture (Figure 2C). AUC of the nomogram was 0.71.

4. Discussion

Vertebral fractures in the elderly often result in intractable back pain, height loss of vertebral body and kyphosis deformity.[19] In severe cases, the loss of walking ability and the probability of re-fractures are significantly increased. Vertebral fracture not only seriously threatens the health and quality of life of the elderly, but also significantly increases the economic burden of the family and society.[20,21] We construct a nomogram model to predict the risk of vertebral fracture in the elderly. The nomogram model has the advantage that it can be used to predict the incidence of individuals

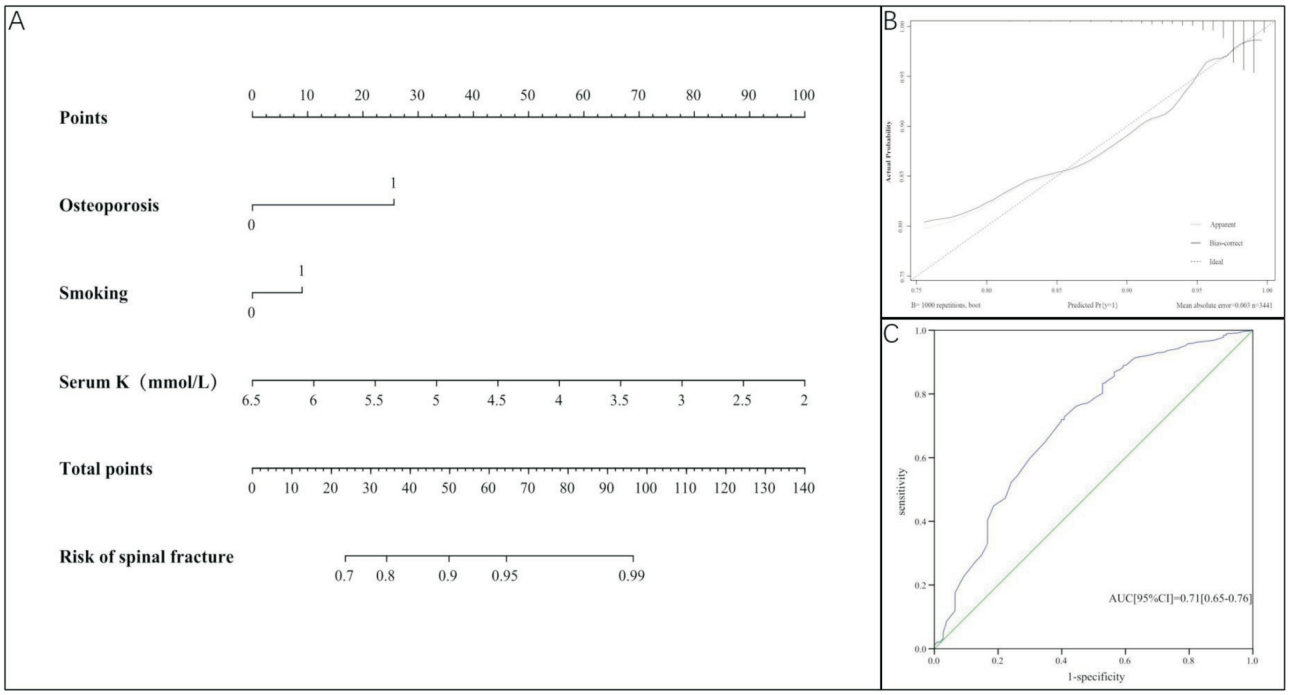

Figure 2. A nomogram prediction model for risk of vertebral fracture in the elderly. AUC, area under the curve; 95% CI, 95% confidence interval.

through the scoring system without complex formula calculation. Therefore, the nomogram model is easily accepted by medical personnel and can be effectively applied to the general population.

Our analysis using NHANES 2005–2010 showed a significant statistical difference in age between the vertebral fracture group and no-vertebral fracture group ($\chi^2 = 5.75$, $p = 0.017$), which emphasizes that age is a significant risk factor of the elderly with vertebral fractures in the non-institutionalized American population. With regard to this, a previous study has shown that age-related low BMD and falls are the important risk factors for osteoporotic vertebral fractures.[22] With the growth of age, the rate of bone loss and the incidence of low BMD gradually increased. Additionally, the risk of falls increased significantly due to the decline of neuromuscular function and body coordination function in elderly individuals.[23,24] Accordingly, this result is also verified in the risk factor of osteoporosis, and the individuals combined with osteoporosis in the vertebral fractures group also showed significant difference with the no-vertebral fractures group ($\chi^2 = 41.26$, $p < 0.001$).

In addition, similar to the previous reports by Nelson et al.[25] and Center et al.[26] smoking (OR = 1.620, 95% CI: 1.080–2.440, $p = 0.021$) was regarded as another important risk factor for the elderly with vertebral fractures. A previous study reported the mean BMD of smokers was 5% to 10% lower than that of non-smokers, they further described in detail that BMD of lumbar spine, femoral neck and femoral shaft of smokers were 2%, 2% and 1.4% lower than that of non-smokers.[27] Another study proved that for each 10% decrease in BMD, the bone strength will decrease by 30% accordingly. As long as the BMD decreases by 10% within 10 years, the incidence of subsequent vertebral fractures will increase by 44%. Moreover, it is also estimated that about 250000 elderly individuals around the world were hospitalized for vertebral fractures caused by osteoporosis every year, among which women were 6–8 times as many as men.[28,29]

In terms of the levels of laboratory examination, there was a significant statistical difference between the elderly individuals with and without vertebral fractures in serum P ($t = 2.021$, $p = 0.043$), serum Na ($t = -2.366$, $p = 0.020$), serum K ($t = 4.651$, $p < 0.001$), and Vit D ($t = 2.522$, $p = 0.012$). Therein, hyponatremia is positively correlated with the incidence of vertebral fractures, which is consistent with the previous study by Renneboog et al.[30] They have performed a study on related hazards of persistent hyponatremia, and the results showed that persistent hyponatremia may affect the nervous system function of the elderly and cause gait instability, thereby increasing the incidence of fractures. In our study, we also found a lower level of serum K in the vertebral fracture group (OR = 0.360, 95% CI: 0.230–0.560, $p < 0.001$). Hypokalemia can also cause confusion and muscle strength decline in the elderly to a certain extent, leading to falls-related fractures. However, although we have obtained a positive correlation between serum P and vertebral fractures in the univariate analysis ($t = 2.021$, $p = 0.043$), there is still no clear explanation for its relationship in previous reports, which still needs further consideration.[31]

Furthermore, Cairns et al.[32] have designed and prepared the animal model of hyponatremia, and by further studying the changes of the nerve conduction and muscle strength activity of experimental animals with serum Na level and exercise time, it was found that serum Na level had a certain effect on muscle strength. Moreover, muscle fatigue was more likely to occur in a low sodium state, leading to the decline of muscle strength, and thus affecting the occurrence and the maintenance of activity. On the basic level, Barsony et al.[33] designed an experimental study at the cell level, and the results showed that osteoclasts cultured in low sodium level had larger volume and stronger cell activity. However, there are also different sounds. Hoorn et al.[34] designed a prospective study with a high level of evidence, and the results showed that the BMD of the patients with hyponatremia was exactly lower than that with normal blood sodium. However, through multivariate correlation analysis, after adjusting for age, gender and other factors, the level of BMD in the hyponatremia group was even higher than that in the normal blood sodium group, thus it was considered that there may not be a direct correlation. Thus, it is still essential to further focus on the relationship between hyponatremia and the risk of fractures in the elderly in the future.

Additionally, the elderly are universally at high risk of Vit D

deficiency, and this deficiency is mainly due to the reduction of sunlight exposure and the limited dietary intake.[35,36] Moreover, the Vit D deficiency can also reduce the intestinal absorption and the renal tubular reabsorption of calcium, resulting in the decrease of blood calcium concentration and the increase of parathyroid hormone secretion. Parathyroid hormone is able to promote the formation of osteoclasts, and osteoclasts can also release alkaline phosphatase and proteolytic enzyme, which will accelerate the dissolution of calcium salt and bone matrix on the wall of bone tubules.[37] Thus, a large amount of calcium salt is transported from bone tissue into blood and extracellular fluid, which increases the concentration of blood calcium and maintains the blood calcium in the normal range. This process will accelerate the bone turnover and destroy the bone microstructure, thus increasing the risk of associated fractures.[38–40] With regard to this, increasing the time of sunlight exposure and dietary intake or exogenous supplement to improve the level of Vit D will contribute to the situation of vertebral fractures in the elderly to a certain extent.

5. Limitations

Finally, further supplements and explanations are still needed for the short comings of this current study. Firstly, considering the self-reported nature of this current study, the variables such as the history of vertebral fractures, smoking and drinking alcohol are uncertain, and the possible self-report and recall biases also exist. In spite of this, the process of data setting and extraction in NHANES 2005–2010 is stable and reliable, which wholly ensures the feasibility of this current study and the authenticity of data. Secondly, the overall sample size of self-reported vertebral fractures was relatively small in this study, and only 108 individuals aged 65 years and older were finally enrolled. Thus, further studies with more year cycles and more sample size for continued analysis and validation is still needed in the future. Thirdly, our study is a cross-sectional study based on NHANES database. All the data are from NHANES, which makes it impossible for us to obtain the data outside NHANES, such as physical condition, medication, visual acuity, physical activity, body mass index, calcium and/or vitamin D intake and so on, thereby causing certain inevitable limitations, which also needs further improvement in future research.

6. Conclusions

In conclusion, based on the NHANES 2005–2010, authors developed a nomogram to predict the risk of vertebral fracture in the elderly. With advantages such as simplicity, intuitiveness, and practicality, the nomogram (including osteoporosis, smoking and serum K) was capable of predicting vertebral fracture and has certain auxiliary value in clinical applications.

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Potential financial and non-financial conflicts of interest

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