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STUDY ON THE PREVALENCE, CHARACTERISTICS AND DEVELOPMENT OF A PROGNOSTIC NOMOGRAM FOR ASYMPTOMATIC VERTEBRAL FRACTURES IN INDIVIDUALS AGED 50 AND OLDER

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SUMMARY OF MEDICAL DOCTORAL DISSERTATION

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INTRODUCTION

1. THE URGENCY OF THE TOPIC

Vertebral fractures (VFs) are among the most common complications of osteoporosis and are the most frequently recorded type of osteoporotic fractures in the medical literature. Most vertebral fractures are asymptomatic, with up to 70% of cases remaining undetected. Current research on the prevalence and incidence of vertebral fractures shows significant variation globally. Many studies worldwide focus on strategies to assess and identify risk factors to predict vertebral fractures in high-risk patients. Several prediction tools for osteoporotic fractures have been developed, such as FRAX by the World Health Organization, the Qfracture algorithm, and the Garvan fracture risk calculator. However, these models primarily provide general predictions, focusing on hip fractures or overall fracture risk, without detailed consideration of vertebral fractures. In Vietnam, there is limited research reporting on the prevalence and incidence of vertebral fractures, especially in individuals over 50 years old. In this age group, bone loss accelerates, and primary osteoporosis begins to be recognized in both genders. Therefore, we conducted the study titled ***"Study on the prevalence, characteristics and development of a prognostic nomogram for asymptomatic vertebral fractures in individuals aged 50 and older***".

2. RESEARCH OBJECTIVES

1. Investigate the prevalence and characteristics of asymptomatic vertebral fractures in Vietnamese individuals aged 50 and older.

2. Determine the incidence and develop a prognostic nomogram for asymptomatic vertebral fractures in this study population.

3. SCIENTIFIC AND PRACTICAL SIGNIFICANCE

The study provides detailed characteristics of asymptomatic vertebral fractures in individuals aged 50 and older, contributing to a clearer understanding of the vertebral fracture situation in this population in Vietnam.

It also provides new incidence data and develops a prognostic model to help identify high-risk individuals early, facilitating timely diagnosis and management.

4. NEW CONTRIBUTIONS OF THE THESIS

The study demonstrates a high prevalence of asymptomatic vertebral fractures in the 50+ age group, highlighting the urgent need for early screening to diagnose and manage effectively.

It successfully develops a prognostic nomogram with high discrimination and accuracy, which is easy to apply for initial risk assessment to identify high-risk individuals for early diagnosis and effective management.

5. THESIS LAYOUT

The thesis consists of 120 pages: 3-page problem-setting, 31-page literature overview, 24-page research subjects and methods, 31-page research results, 28-page discussion, 2-page conclusion, 1-page recommendation. The thesis has 22 tables, 15 figures, 19

charts, 175 references (8 Vietnamese documents and 167 English documents).

Chapter 1: LITERATURE OVERVIEW

1.1. OVERVIEW OF VERTEBRAL FRACTURES

1.1.1. Definition and Causes of Vertebral Fractures

According to the European Society for Osteoporosis Research, a vertebra is considered fractured if there is evidence of a 20% (± 4 mm) or more reduction in vertebral height in the anterior, middle, or posterior areas compared to adjacent vertebrae on imaging, meeting the criteria for vertebral deformity on subsequent films (McCloskey-Kanis method). There are two main categories of causes: osteoporotic vertebral fractures and fractures due to other causes such as trauma, cancer, hyperthyroidism, chemotherapy, and infections.

1.1.2. Epidemiology

Studies on the prevalence of osteoporotic vertebral fractures worldwide show that the highest prevalence among European women is in Scandinavia (26%), and the lowest in Eastern Europe (18%). In Asia, the highest prevalence among women over 65 is in Japan (24%) and the lowest in Indonesia (9%). In Vietnam, a study in Ho Chi Minh City found the prevalence of vertebral fractures in individuals aged 50 and older to be 23.3% in men and 26.5% in women.

1.1.3. Imaging Diagnosis of Vertebral Fractures

Currently, spinal X-rays combined with quantitative and semi-quantitative reading methods are the most common for

screening and diagnosing vertebral fractures. Standard positions for detecting vertebral fractures include straight and lateral spinal X-rays. Various assessment methods include the Eastel quantitative method, Genant's semi-quantitative method, and qualitative diagnosis by stepwise exclusion.

1.1.4. Risk Factors for Osteoporotic Vertebral Fractures

1.1.4.1. Intrinsic Factors

Age

Older age is associated with a higher risk of vertebral fractures. Studies in women over 65 in the USA show that the risk of osteoporotic vertebral fractures increases by 28% for every additional 5 years of age.

Gender

Most studies indicate that the prevalence of vertebral fractures is higher in women compared to men aged 50 and older, especially post-menopausal women due to rapid ovarian function decline and estrogen deficiency.

History of Fractures

The CAIFOS randomized clinical trial showed that individuals with a history of one or more vertebral fractures have an increased risk of damage to other vertebrae.

Bone Density

Studies show that low bone density is associated with an increased risk of fractures.

Early Menopause

Women who experience early menopause have an increased risk of osteoporosis due to lower estrogen levels.

1.1.4.2. Extrinsic Factors

Corticosteroid Use

Glucocorticoid-induced osteoporosis is the most common form of secondary osteoporosis, resulting from reduced bone formation and increased bone resorption.

Smoking

Smoking increases the risk of many diseases, including osteoporosis and fractures. Some studies suggest that nicotine and cadmium affect bone metabolism through various factors such as body weight, sex hormone levels, and other hormones and enzymes related to bone metabolism regulation.

Body Biometrics

Larger muscle mass is independently associated with a lower risk of vertebral fractures, while a larger waist circumference is linked to a higher risk. These findings suggest that body fat distribution is an important predictor of vertebral fractures.

1.2. PROGNOSTIC MODELS FOR FRACTURES

1.2.1. Known Prognostic Models for Fractures

FRAX Model

FRAX has been highly valued for predicting hip fracture risk based on clinical indicators in several studies. However, in type 2 diabetes patients, FRAX underestimates the fracture risk compared to actual cases.

QFracture Model

In a cohort study of 1 million participants, QFracture showed an AUC of 82.7% for general fractures and 88.0% for hip fractures. However, in patients over 80 years, its prognostic accuracy is only moderate.

Garvan Model

The Garvan model provides good estimates for fracture cases (with or without bone density). However, it underestimates fracture risk in patients with stage 3 renal failure, osteoporosis, or osteopenia.

1.2.2. Steps to Develop a Prognostic Model for Fractures

The first step is to develop a good prognostic model. The essential components are the starting point and the specific outcome (end). The second step is to validate a prognostic model. The new model, once developed, needs to be internally appraised and externally appraised. The third step is to assess the impact of the prognostic model on clinical practice and outcomes. Evaluating the impact of a model on decision making and patient outcomes requires a comparative study. The fourth step is to update the prognostic model.

1.2.3. The Need for a Prognostic Nomogram for Osteoporotic Vertebral Fractures in Individuals Aged 50 and Older

A nomogram is a two-dimensional graphical tool that provides a graphical explanation for prognostication or diagnosis and can be used in settings without computer access. Osteoporotic vertebral fractures account for a large proportion of patients over 50, but only one-third of symptomatic patients are detected and treated promptly. This highlights the need for developing a prognostic nomogram for vertebral fractures in individuals aged 50 and older.

1.3. STUDIES IN VIETNAM AND ABROAD

1.3.1. Studies on the Prevalence and Incidence of Vertebral Fractures

Prevalence

In the Americas, the LAVOS study of 1922 women aged 50 and older from five countries (Argentina, Brazil, Colombia, Mexico, and Puerto Rico) recorded a prevalence of around 11%.

In Europe, the EVOS study, a population-based cross-sectional study with 15,570 participants aged 50-79 from 36 centers in 19 European countries, recorded a prevalence of 12% for both genders.

In Asia, a community-based epidemiological study by Shin C.S. et al. in South Korea found a prevalence of 11.9% in men and 14.8% in women. In Vietnam, a 2011 study by Ho Pham Thuc Lan et al. recorded a prevalence of 23.3% in men and 26.5% in women aged 50 and older.

Incidence

In Europe, the EPOS study recorded an incidence of 10.7/1000 person-years in women and 5.7/1000 person-years in men aged 50 and older.

In Asia, a cohort study of 2356 elderly individuals in Japan recorded an incidence of 5.2/1000 person-years in women and 2.5/1000 person-years in men aged 50, increasing to 56.1/1000 person-years in women and 25.9/1000 person-years in men aged 80.

1.3.2. Studies on Prognostic Models for Major Osteoporotic Fractures

A meta-analysis by Beaudoin C. et al. found that QFracture provides better discrimination for hip fracture risk (AUC = 0.88) compared to FRAX and Garvan, but after adjusting for covariates, FRAX with bone density (BMD) and Garvan with

BMD showed the highest discrimination for hip fracture risk (AUC = 0.81 and 0.79, respectively). For osteoporotic fractures at other major sites (wrist, shoulder, spine), QFracture had the best discrimination (AUC = 0.77).

Using health records of over 1 million people, the AUC values for predicting hip fractures were 0.83 for FRAX, 0.82 for QFracture, and 0.78 for Garvan.

Chapter 2: RESEARCH SUBJECTS AND METHODS

2.1. RESEARCH SUBJECTS

This study is part of the Vietnam Osteoporosis Study (VOS), a cohort study involving men and women aged 18 and older living in Ho Chi Minh City and neighboring provinces. The subjects for this study were selected from VOS participants who met the following criteria:

2.1.1. Inclusion Criteria

- Vietnamese citizens working and living in Vietnam.
- Aged 50 and older and willing to participate in the study.
- Participants in VOS who had follow-up examinations every 2 years from June 2019 to December 2020.

2.1.2. Exclusion Criteria

- Individuals with mental illnesses or unable to answer interview questions and cooperate with clinical examinations.
- Currently using medications affecting bone metabolism (e.g., corticosteroids, diabetes medications, antiepileptics, anticoagulants, cancer drugs, antidepressants).

- History of diseases affecting bone density (e.g., renal failure, hyperthyroidism, hypothyroidism, parathyroid disorders, bone cancer).

- Incomplete records of at least one biometric characteristic, spinal X-ray history, and bone density measurement from June 2019 to December 2020.

2.2. RESEARCH METHODS

2.2.1. Study Design

Objective 1: Cross-sectional descriptive study.

Objective 2: Cohort study with retrospective and prospective elements.

2.2.2. Sample Size

Objective 1: Calculated using the formula:

$$n \geq \frac{Z^2_{1-\alpha/2} \times p(1-p)}{d^2}$$

With $Z1\text{-}\alpha/2 = 1{,}96$ ($\alpha = 0{,}05$), d=0,05, p=0,125 and 0,2, resulting in a minimum sample size of $n \geq 168$ for men and 246 for women.

Objective 2:

To develop a prognostic nomogram, the Peduzzi method was used to estimate the sample size based on the number of events for each prognostic factor, with a minimum ratio of 10 events per prognostic factor. Based on the study by Mai Duy Linh, the incidence of new vertebral fractures was 14.4% in women and 29.0% in men, estimating a minimum of 104 men and 209 women.

The actual sample size was 168 men and 287 women.

2.2.3. Research Procedures

- List subjects aged 50 and older from VOS for follow-up examinations from June 2021 to December 2022.

- Contact subjects by phone for follow-up appointments, interviews, and measurements.

- Record information on age, gender, and medical history.

- Select subjects meeting inclusion criteria and not falling under exclusion criteria.

- Conduct physical examinations, including biometric measurements and muscle strength assessments of the back and legs.

- Measure bone density and perform thoracic and lumbar spinal X-rays.

- Assess the prevalence and characteristics of current vertebral fractures.

- Compare current spinal X-ray results with those from June 2019 to December 2020 to assess new vertebral fracture incidence.

- Develop a nomogram to predict the risk of new vertebral fractures over 2 years.

2.2.4. Research Variables

Defined and listed in detail.

2.2.5. Research Procedures and Techniques

Detailed descriptions of procedures and techniques used in the study.

2.2.6. Data Analysis

Data is processed and analyzed using R 4.3.2 software. Formulate a prognostic diagram: apply Bayesian averaging (BMA) to select the optimal model. BMA can produce many

possible models; Choose 5 optimal models with the highest probability of determination. The posterior probability of a model is determined by the method of re-sampling with return. The prognostic value of the model is evaluated through two indicators: discrimination reflected by AUC, and calibration reflected by the Brier index. The best model chosen is used to draw the diagram.

2.2.7. Research Ethics

Approved by the Biomedical Research Ethics Committee of the University of Medicine and Pharmacy, Hue University (Approval Code: H2021/391).

Chapter 3: RESEARCH RESULTS

3.1. GENERAL CHARACTERISTICS OF THE RESEARCH SAMPLE

3.1.1. Biometric Characteristics

The average age of participants was 62.38 ± 6.27 years. The 60-69 age group accounted for about half of the sample. The female/male ratio was 1.7/1. The prevalence of overweight and obesity was 53.8%. Men had higher leg and back muscle strength compared to women ($p<0.001$).

3.1.2. Medical History Characteristics

The prevalence of smoking and alcohol consumption was 11.9% and 9.7%, respectively, with significantly higher rates in men than women ($p<0.001$). 8.1% of participants had a history of falls.

3.1.3. Muscle Strength Characteristics

Leg and back muscle strength was generally higher in men across all age groups. Muscle strength decreased with age in both genders, with a greater decline in men..

3.1.4. T-score Characteristics of Bone Density

The prevalence of osteopenia and osteoporosis accounted for more than half of the study population when considering both measurement sites (lumbar spine and femoral neck). Women had higher rates of osteopenia and osteoporosis than men at both sites, with significant differences. As age increased, the T-score of bone density in the lumbar spine and femoral neck decreased more rapidly in women compared to men. Lower leg and back muscle strength were associated with lower T-scores of bone density in men more than in women.

3.2. CHARACTERISTICS OF CURRENT VERTEBRAL FRACTURES

3.2.1. Prevalence of Current Vertebral Fractures

Among 455 subjects, 57 had vertebral fractures, corresponding to a prevalence of 12.5%.

3.2.2. Number of Fractured Vertebrae

Among 57 subjects with vertebral fractures, most had a single fractured vertebra (86.0%).

3.2.3. Severity of Current Vertebral Fractures

Among 57 subjects with vertebral fractures, 67 vertebrae were fractured. Grade 1 fractures were the most common (36 vertebrae), followed by Grade 2 and Grade 3 (3 vertebrae).

3.2.4. Type of Current Vertebral Fractures

Among 57 subjects with vertebral fractures, 67 vertebrae were fractured. Edge fractures were the most common (52 out of 67).

3.2.5. Location of Current Vertebral Fractures

Among 67 fractured vertebrae, 42 were at the thoracolumbar junction (T12-L1), with 23 at L1 and 19 at T12.

3.2.6. Biometric Characteristics of Subjects with Current Vertebral Fractures

The prevalence of VF increases gradually by age group, in the 50-59 age group is 7.7%; The 60-69 group was 10.6% and the 70-year-old ≥ group was 37.3%, a statistically significant difference.

There is no difference between VF and body mass index, waist circumference, hip circumference, waist-to-hip ratio.

3.2.7. Muscle Strength Characteristics of Subjects with Current Vertebral Fractures

Subjects with vertebral fractures had lower leg and back muscle strength than those without fractures, with significant differences.

3.2.8. Medical History Characteristics of Subjects with Current Vertebral Fractures

The prevalence of vertebral fractures was three times higher in subjects with a history of falls compared to those without ($p<0.001$).

The prevalence of vertebral fractures was nearly twice as high in smokers compared to non-smokers (22.2% vs. 11.2%; $p=0.038$).

No significant differences were found between vertebral fractures and alcohol consumption.

3.2.8. Bone Density T-scores in Subjects with Current Vertebral Fractures

The prevalence of vertebral fractures varied according to bone density T-scores at the lumbar spine and femoral neck, with higher rates in the osteoporosis group compared to the osteopenia and normal groups, with significant differences.

3.3. INCIDENCE OF NEW VERTEBRAL FRACTURES AND DEVELOPMENT OF A PROGNOSTIC MODEL

3.3.1. *Characteristics of New Vertebral Fractures*

3.3.1.1. Incidence of New Vertebral Fractures

Following 455 participants for a median of 2.38 years (Q1 = 2.15; Q3 = 2.5): 29 subjects had new vertebral fractures (6.4%). The incidence of new vertebral fractures was 28/1000 person-years (95% CI: 19-40) in both genders, with higher rates in men and increasing with age.

3.3.1.2. Type of New Vertebral Fractures

Among 29 subjects with new vertebral fractures, 30 vertebrae were affected. New complete fractures accounted for 11 vertebrae (36.7%), and increased severity fractures for 19 vertebrae (63.3%).

3.3.1.3. Severity of New Vertebral Fractures

Grade 2 fractures were the most common among new vertebral fractures (17 vertebrae), with Grade 3 being the least common (2 vertebrae).

3.3.1.4. Type of New Vertebral Fractures

Most new vertebral fractures were edge fractures (22 vertebrae).

3.3.1.5. Location of New Vertebral Fractures

Most new vertebral fractures were at the thoracolumbar junction (T12-L1), with 9 vertebrae at T12 and 12 at L1.

3.3.1.6. Biometric Characteristics of Subjects with New Vertebral Fractures

The incidence of VF increases with age. In the 50-59 age group, it is 2.4%; the 60-69 age group is 7.5%; The 70-year-old ≥ group is up to 33.3%.

There was no statistically significant difference between waist circumference, hip circumference, waist/hip circumference, gender, BMI and newly acquired VF.

3.3.1.7. Medical History Characteristics of Subjects with New Vertebral Fractures

The incidence of new vertebral fractures was higher in subjects with a history of falls compared to those without (17.2% vs. 5.6%; p=0.030).

No significant differences were found between new vertebral fractures and smoking or alcohol consumption.

3.3.1.8. Bone Density T-scores in Subjects with New Vertebral Fractures:

The incidence of new vertebral fractures was higher in the osteoporosis group compared to the osteopenia and normal groups at the lumbar spine (31.3%, 7.2%, and 1.5%, respectively; significant differences). Similarly, at the femoral neck, the incidence was higher in the osteoporosis group compared to the osteopenia group (44.0% vs. 7.6%, p<0.001).

3.3.1.9. Muscle Strength in Subjects with New Vertebral Fractures

No significant differences were found between leg and back muscle strength and new vertebral fractures.

3.3.2. Development of a Prognostic Nomogram for Vertebral Fractures

3.3.2.1. Selection of Prognostic Models

Prognostic models were developed based on available factors, including age, gender, BMI, history of falls, smoking, and femoral neck bone density T-scores using the BMA method, resulting in 5 possible models. Three models with the highest posterior probability (Models 1, 2, and 3) were selected for further analysis.

3.3.2.2. Multivariate Analysis of Models 1, 2, and 3

Model 1: Includes gender, age, and femoral neck bone density T-scores, with a posterior probability of 0.61.

Model 2: Includes age, smoking, and femoral neck bone density T-scores, with a posterior probability of 0.16.

Model 3: Includes gender, age, BMI, and femoral neck bone density T-scores, with a posterior probability of 0.07.

3.3.2.3. Discrimination of Models

The area under the curve (AUC) for Model 1 was 0.910 (95% CI: 0.864-0.956); Model 2 was 0.894 (95% CI: 0.831-0.957); Model 3 was 0.913 (95% CI: 0.871-0.956).

3.3.2.4. Calibration of Models

The Brier scores for Models 1, 2, and 3 were 0.042, 0.041, and 0.041, respectively, indicating similar calibration.

3.3.2.4. Prognostic Nomogram for Vertebral Fractures

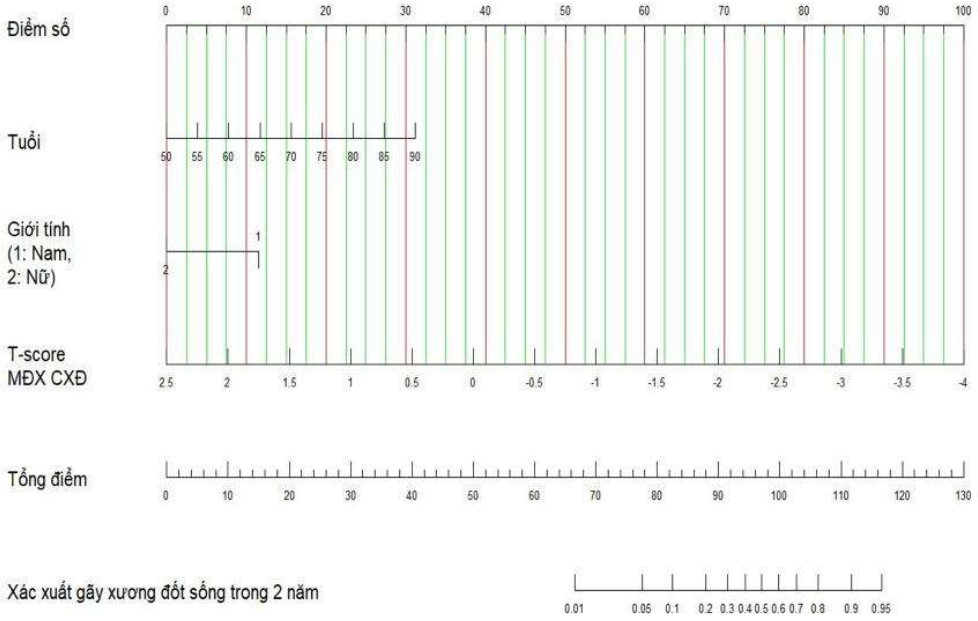

Chart 3.1. Nomogram chart prognosticating the risk of new vertebral fracture

Chapter 4: DISCUSSION

4.1. GENERAL CHARACTERISTICS OF THE RESEARCH SAMPLE

4.1.1. Biometric Characteristics

The average age of the research sample was 62.38 ± 6.27 years, with a male/female ratio of 1:1.7. Reports from Europe, using EVOS data, recorded the average age of participants as 64.1 ± 8.6 years, with 54% being female. In Asia, reports from India, South Korea, and Thailand show similar age distributions to our current study, while Japan has an age pattern similar to Europe.

4.1.2. Medical History Characteristics

The medical history factors in our study are consistent with other global populations, with males consuming more alcohol and tobacco than females.

4.1.3. Muscle Strength Characteristics

We observed an age-related decline in muscle strength, with males having significantly higher muscle strength than females. An osteoporosis study in individuals aged 60 and older indicated an average annual muscle strength decline of 1.5% in males and 1.6% in females.

4.1.4. Bone Density T-score Characteristics

Regarding the distribution of bone density T-scores, our results are similar to those reported by Yakemchuk V.

4.2. PREVALENCE AND CHARACTERISTICS OF VERTEBRAL FRACTURES IN THE STUDY GROUP

4.2.1. Prevalence of Vertebral Fractures g

The current study used Genant's semi-quantitative method to determine the prevalence of asymptomatic vertebral fractures, which was 12.5%, similar for both genders. Additionally, this prevalence increased with age. Data on the global prevalence of vertebral fractures is varied. Among Caucasians, a population study in Norway reported a prevalence ranging from 3% in those < 60 years to 19% in those ≥ 70 years for females and from 7.5% to approximately 20% for males, with an overall prevalence of 11.8% in females and 13.8% in males ($p = 0.07$). In Latin America, specifically Brazil, the observed prevalence of vertebral fractures was three times our results at 29.4%. The gender-specific prevalence was 27.5% for females and 31.8% for

males, increasing with age in both genders. In Asia, data from Taiwan indicated an overall prevalence of vertebral fractures in women over 65 at 20% and in men at 12.5%. In South Korea, the prevalence was 11.9% in men and 14.8% in women.

4.2.2. Number of Fractured Vertebrae

Our current data show that most cases involved the fracture of a single vertebra. An Indian study reported that approximately 40% of vertebral fractures involved a single vertebra, similar to findings in Norway.

4.2.3. Severity of Current Vertebral Fractures

Regarding severity, we found that Grade 1 (mild) fractures were the most common, consistent with previous studies where Grade 1 fractures accounted for around 50% or more of cases.

4.2.4. Type of Current Vertebral Fractures

We recorded that edge fractures were the most common type, consistent with reports from Canada and the Netherlands.

4.2.5. Site of Current Vertebral Fracture

The most common locations for vertebral fractures were T12 and L1, consistent with published literature.

4.2.6. Prevalence of Vertebral Fractures by BMI, Waist Circumference, and Hip Circumference

The prevalence in our study was higher in the overweight and obese group compared to the normal weight group (14.7% vs. 9.6%). There were no significant differences in waist circumference, hip circumference, or waist-to-hip ratio between those with and without vertebral fractures. Paik JM reported that waist circumference ranging from 71-108 cm generally increased the risk of vertebral fractures, although this impact was not clear.

4.2.7. Prevalence of Vertebral Fractures by Muscle Strength

In the group with current vertebral fractures, leg and back muscle strength were lower than in the non-fracture group ($p < 0.05$). Weak muscle strength, indicated by reduced muscle mass, increased fall frequency, decreased bone density, and sex hormone deficiency, could lead to higher fracture risk.

4.2.8. Prevalence of Vertebral Fractures by Fall History, Smoking, and Alcohol Consumption

The prevalence of vertebral fractures was higher in individuals with a history of falls and smoking, with no significant difference for alcohol consumption. Australian data showed that falls increased the risk of vertebral fractures in men (HR = 1.34; 95% CI: 0.87-2.05). Smoking has long been considered a risk factor for osteoporosis and related fractures. Brazilian studies reported no significant difference between alcohol consumption and vertebral fractures.

4.2.9. Prevalence of Vertebral Fractures by Bone Density

Our study found that the prevalence of vertebral fractures increased with decreasing bone density, similar to studies in Vietnam, Thailand, and Brazil.

4.3. INCIDENCE AND PROGNOSTIC MODEL FOR VERTEBRAL FRACTURES IN THE STUDY GROUP

4.3.1. Characteristics of New Vertebral Fractures

4.3.1.1. Incidence of New Vertebral Fractures

The incidence of new vertebral fractures in our study was 28 per 1000 person-years (95% CI: 19-40) in individuals aged 50 and older, higher in men than in women, and increased with age. Generally, vertebral fracture incidence data in Europe are lower

than our findings in the Vietnamese population, similar to data from Thailand.

4.3.1.2. Characteristics of New Vertebral Fractures by Severity, Type, and Location

In our study, most new vertebral fractures were Grade 2 (moderate) at 56.7%. This can be explained by the definition that fractures appearing on the first X-ray are considered old fractures (current vertebral fractures), while new fractures are defined as new or increased severity fractures. Similar to old fractures, edge fractures were the most common type in new fractures. The most common locations for new fractures were T12 and L1, consistent with published literature.

4.3.1.3. Medical History Characteristics of New Vertebral Fractures

We found that the incidence of new vertebral fractures was higher in individuals with a history of falls but not significantly related to smoking or alcohol consumption. Recent studies in Vietnam reported that falls increased the risk of vertebral fractures. Canadian reports indicated higher vertebral fracture risk in smokers. South Korean studies reported higher fracture risk in men who consumed alcohol, but no significant findings for women or current alcohol users.

4.3.1.4. Bone Density T-score in New Vertebral Fractures

Similar to current vertebral fractures, decreased bone density at the lumbar spine and femoral neck was associated with increased new vertebral fracture incidence. A decrease of 0.1-0.12 g/cm2 in femoral neck bone density increased vertebral

fracture risk by 1.4-1.8 times, higher than lumbar spine bone density.

4.3.1.5. Muscle Strength in New Vertebral Fractures c

Our study did not find significant differences in leg and back muscle strength between groups with and without new vertebral fractures. However, muscle strength measured near the time of fracture may better predict fracture risk than measurements taken years before the fracture.

4.3.2. Development of a Prognostic Model for Vertebral Fractures

We used Bayesian analysis principles to identify significant variables and select the optimal prognostic model for vertebral fractures. This method's advantage is excluding non-significant variables, selecting fewer variables than the stepwise method, and reflecting model selection uncertainty. Among the five analyzed models, Models I, II, and III met the criteria. These models had posterior probabilities of 0.61, 0.16, and 0.07, and good AUC values (0.910, 0.894, and 0.913, respectively). The calibration of all three models was good, with similar Brier scores close to 0 (0.042, 0.041, and 0.041, respectively). Model I had excellent discrimination (AUC = 0.910; 95% CI: 0.864-0.956). Kong SH et al. developed models with 20 variables, achieving a maximum AUC of 0.688. Similarly, Lin YC et al.'s model had a maximum AUC of 0.671.

LIMITATIONS OF THE STUDY

Although the study developed a high-performing prognostic nomogram for vertebral fractures, it has limitations, including lack of external cohort validation, a sample primarily from Ho Chi Minh City and neighboring provinces, and not being representative of the national population.

CONCLUSION

1. Prevalence and Characteristics of Current Vertebral Fractures

- Prevalence of vertebral fractures in men and women: 12.5%.

- Characteristics: 86.0% had a single vertebra fracture, over 50% were Grade 1 fractures (53.7%), edge fractures were the most common type (77.6%), and T12 and L1 were the most common locations (62.6%). Prevalence increased with age: 7.7% (50-59 years), 10.6% (60-69 years), and 37.3% (≥ 70 years), $p < 0.001$. Higher prevalence in those with a history of falls (35.1% vs. 10.5%; $p < 0.001$) and smokers (22.2% vs. 11.2%; $p = 0.038$). Higher prevalence in osteoporosis compared to osteopenia and normal at both lumbar spine and femoral neck ($p < 0.05$). Lower leg and back muscle strength in those with current vertebral fractures ($p = 0.001$ and < 0.001).

2. Incidence and Development of a Prognostic Model for Vertebral Fractures

- Incidence: 28 per 1000 person-years (95% CI: 19-40). Higher in men (33 per 1000 person-years; 95% CI: 23-46) than women (24 per 1000 person-years; 95% CI: 16-35). Incidence

increased with age: 8 per 1000 person-years (50-59 years; 95% CI: 4-15), 20 per 1000 person-years (60-69 years; 95% CI: 12-30), and 126 per 1000 person-years (≥ 70 years; 95% CI: 105-149). Higher incidence in those with a history of falls (17.2% vs. 5.6%; $p = 0.03$). Higher incidence in osteoporosis compared to osteopenia at the femoral neck (44.0% vs. 7.6%; $p < 0.001$) and higher in osteoporosis compared to osteopenia and normal at the lumbar spine (1.5%, 7.2%, and 31.3%, respectively; $p \leq 0.001$).

- Model I had the highest posterior probability (0.55) and the best AIC value. It included gender, age, and femoral neck bone density. Male gender increased the risk by 5.67 times (95% CI: 2.0-16.11), every 5-year increase in age by 1.8 times (95% CI: 1.29-2.5), and a 0.5 SD decrease in femoral neck bone density by 3.19 times (95% CI: 2.09-4.86).

RECOMMENDATIONS

The study highlights the high prevalence of asymptomatic vertebral fractures in individuals aged 50 and older, emphasizing the urgent need for early screening, diagnosis, and effective management to limit complications.

The successfully developed prognostic nomogram for vertebral fractures in Vietnamese individuals, including three simple factors (age, gender, and femoral neck bone density T-score), shows high discrimination and accuracy. The nomogram is easy to apply for initial risk assessment to identify high-risk individuals for early diagnosis and management.

External validation is needed to evaluate the model's accuracy.

THE PUBLISHED ARTICLES
RELATED TO THE STUDY

1. Hoa T. Nguyen, Bao T. Nguyen, Thi H. Nhung Thai, An V. Tran, Tan T. Nguyen, Tam Vo, Linh D. Mai, Thach S.Tran, Tuan V. Nguyen, Lan T. Ho Pham (2024), Prevalence, incidence of and risk factors for vertebral fracture in the community: the Vietnam Osteoporosis Study, Sci Rep, 14, 32. pp. 1-7. https://doi.org/10.1038/s41598-023-50145-w.

2. Nguyen Thai Hoa, Thai Thi Hong Nhung, Chan Viet An, Nguyen The Bao, Phu Tri Nghia, Ho Pham Thuc Lan, Vo Tam **"**Prevalence and risk factors of asymptomatic vertebral fractures in individuals 50 years or older", *Hue Journal of Medicine and Pharmacy – Hue University of Medicine and Pharmacy*, 3(13), pp.139-145.

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