Identifying the Most Important Factors in Determining the Osteoporosis in Women Using Data Mining Techniques

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Abstract- Osteoporosis is one of the primary causes of disability and mortality in the elderly. If osteoporosis's significant features can be identified, the risk of developing this disease will be reduced. In recent years, data mining approaches have become a suitable tool for medical researchers. This study applied data mining methods to identify osteoporosis's significant features. This study applied data from women having osteoporosis or osteopenia in the period 2011-2019 in the Osteoporosis Diagnosis Center, Isfahan, Iran. Data mining methods such as linear regression, naïve bayes, decision tree, support vector machine, random forest, and neural network were implemented on the dataset. This study consisted of 8258 patients' information, of which 1482 had osteoporosis. The results showed that the support vector machine, decision tree, neural network are the best method based on accuracy, precision, and AUC measures. Six candidate features were age, weight, back pain, low activity, menopause date, and previous fracture. Support vector machine, decision tree, and neural network are the best candidate techniques for predicting osteoporosis. Thin older people are more at risk of osteoporosis than other people. Yet, people with middleweight and middle age are at lower risk of osteoporosis.

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Introduction

Today, with the change in people's lifestyles, people are more at risk of various diseases. Osteoporosis is a pervasive disease that is prevalent in people over 50 years of age. This disease can lead to bone fractures in the most severe form (1). People with an osteoporosis rate of 40% are more likely to be at risk for bone fractures (2). The World Health Organization estimates that more than 200 million women will get osteoporosis (3). This disease is one of the primary causes of disability and mortality in the elderly (4). It is predicted that Iran will become an elderly country in the next 50 years that will suffer from this disease (5). Osteoporosis is four times more common in women than in men. This subject shows that the number of female patients is much higher than male patients (6). Approximately one in three women over the age of 50 are at risk for the disease (7). So, predicting the disease is much more important in women than in men. The disease is usually asymptomatic and causes a sudden fracture of the bone. This subject will make it difficult to diagnose this disease (5). If important features affecting the disease can be identified, the risk of developing it will be reduced (8).

In recent years, data mining approaches have become a suitable tool for medical researchers, where they use different methods to diagnose the risk of various diseases (9-11). Many studies have been conducted in the field of data mining and osteoporosis. Moudani *et al.,* (12) used the random forest method to predict osteoporosis. Yoo *et al.*, identified bone mineral density

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in postmenopausal women using machine learning methods (13). The results showed the Support Vector Machine method performed better than others. Sharifkhani *et al*., used the decision tree approach to predict the risk of osteoporosis (14). Lee *et al*., used deep learning models to predict osteoporosis (15). Guannoni *et al*., used decision tree, support vector machines, and neural networks for predicting osteoporosis in Tunisia women (16). The results show that the support vector machine and the neural network performed better than the decision tree. De lira *et al*., used the j48 decision tree method to predict osteoporosis. The study derived several rules on the association of risk features with osteoporosis (17). Iliou *et al*., use a preprocessing method with the neural network method to predict osteoporosis (18). The results show that the method is more accurate than others in identifying the significant features. Langrizadeh *et al*., used the neural network to predict osteoporosis with approximately 86 percent accuracy (19). Mowafi *et al*., used regression methods for predicting the risk of osteoporosis in postmenopausal Egyptian women (20). The results showed that features such as old age, lack of exercise, and vitamin D deficiency cause getting osteoporosis. So, identifying the primary causes of osteoporosis can be impressive in preventing the disease in young people. Identifying significant features decrease the risk of getting osteoporosis in the future.

Materials and Methods

This study used six data mining methods for identifying important features of osteoporosis. It implements the methods on the data set by Rapid Miner software. There are three steps consisting of data collection, data preprocessing, and feature selection.

Data collection

This study applied data about women having osteoporosis or osteopenia in the period 2011-2019 in the Isfahan Osteoporosis Diagnosis Center. It selected 26 features by consulting with experts. This set contains information about 8258 women. The data is stored in a matrix so that each row is equal to patient information and each column is equal to a feature.

Data preprocessing

Data needs to be pre-processed before applying classification techniques. There are three stages in data preprocessing. The first stage is converting and choosing data features and the second stage is missing values. The final stage is goal selection.

Converting and choosing data features

The change involved placing the numerical values of age, weight, height, and menopause in a numerical interval. Among 26 features applied for osteoporosis prediction, only age, weight, and height point out the patient's personal information. The remaining 23 features are all clinical attributes collected from various medical examinations.

Missing values

Missing values for attributes are unknown values. The generation of the data is due to user error in data entry which can cause many problems in the accuracy of the methods. In this step, the missing values are deleted or corrected. If the number of missing attributes of the recorded is high, the record is deleted. In this data set, 1167 records were removed. In the remaining records, the number of missing attributes was very low, so the most frequent value was applied for missing attributes.

Goal selection

The target feature is the overall diagnosis consisting of two values of Osteoporosis and Osteopenia. This study considered the remaining 25 features as independent variables.

Feature selection

After collecting the required information, the data set was divided into two parts: the training data set and the test data set. 70% of the data set was used as a training data set and 30% was used as the test data set. The training data set was used to extract the significant features of osteoporosis disease. The data was categorized using RapidMiner software. This software uses various methods to classify information. The methods used in this study included Random Forest, Linear Regression Decision Tree, Naive Bayes, Neural Network, and Support Vector Machine. Each technique was then implemented on the test dataset. Among 25 features, all possible sets of 4 features were tested by different data mining techniques. We had 12,650 candidate sets. Among 12650 four-member sets, each method chose a set of four members having the highest accuracy, precision, and AUC.

Random forest operates randomly by creating several trees at random and making decisions (21), while the decision tree method is definite (22). The movement starts from the root node and then goes deep to the leaf node. The leaf node is the target variable and the other

nodes are independent variables. Linear regression predicts a dependent variable based on several independent variables (23). The independent variable here is the target variable, overall diagnosis, and the independent variables were age, weight, and height.

Naive Bayes measures the conditional probability of independent variables in relation to the dependent variables (24). In the neural network, there are three layers called the input layer, the processing layer, and the output layer (25). The dependent variable (target) corresponds to the output layer and the independent variables correspond to the input layer. The support vector machine (26) seeks a linear relationship with a high confidence margin between independent and dependent variables. The methods are among the most important classification methods, where they are implemented in the test data set.

Results

This section first examined the data set and then described the evaluation criteria. Then, it evaluated the performance of each method based on the measures. Then, each method extracted significant features. Finally, it selected the features with the most occurrence as significant features.

Dataset

Table 1 shows that most patients (48%) are between 56 and 65. Also, 85 percent of them are in the middle height (147-163) and the weights are mostly between 61 and 85. Table 2 shows the number of patients with osteoporosis and osteopenia. 6766 patients had osteopenia, and 1428 of them had osteoporosis.

Table 1. Features and values of osteoporosis dataset

Features	Values	Proportion
Age (years)	45-55	0.23
	56-65	0.48
	66-75	0.29
Height (cm)	130-146	0.06
	147-163	0.85
	164-178	0.09
Weight (kg)	34-60	0.25
	61-85	0.68
	86-110	0.07
Menopause Date	1990-1999	0.27
	2000-2009	0.44
	2010-2020	0.29
Blood pressure	Yes	0.33
	No	0.67
Low Activity	Yes	0.73
	No	0.27
Low Calcium	Yes	0..93
	No	0.07
Corticosteroids Use	Yes	0.01
	No	0.99
Early Menopause	Yes	0.16
	No	0.84
Hormone Replacement Therapy	Yes	0.01
	No	0.99
Diabetes (Type 2)	Yes	0.17
	No	0.83

Cont. table 1

Stomach Problem	Yes	0.004
	No	0.996
Ovaries Removal	Yes	0.06
	No	0.94
Kidney Problem	Yes	0.02
	No	0.98
LCA	Yes	0.2
	No	0.98
Thyroid Malfunction	Yes	0.14
	No	0.86
Previous Fracture	Yes	0.1
	No	0.9
Back Pain	Yes	0.34
	No	0.66
Diabetes Type 1	Yes	0.03
	No	0.97
Family History of Osteoporosis	Yes	0.03
	No	0.97
Irregular Periods	Yes	0.004
	No	0.996
Asthma	Yes	0.009
	No	0.991
Rheumatoid arthritis	Yes	0.03
	No	0.97

Table 2. The set achieved by each data mining method

Method	Accuracy	Set
Support Vector Machine	83%	Menopause Date, Weight, Low Calcium Age
Random Forest	81%	Weight, Previous Fracture, Low Activity, Age
Neural Net	78%	Low Activity, Blood pressure, Age, LCA
Decision Tree	76%	Weight, Age, Menopause Date, Previous Fracture
Naive Bayes	77%	Menopause Date, Low Calcium, Low Activity, Weight
Linear regression	70%	Blood pressure, Diabetes Type 1, Irregular Periods, Family History Of Osteoporosis

Evaluation criteria

This study used the test data set to check the methods. First, it determined the confusion matrix. it consists of various criteria such as True Positive (TP), True Negative (TN), False Positive (FP), and False Negative (FN). The target class was osteoporosis. TP specifies the number of records that the category has correctly placed in the target class. TN identifies records that have not been categorized correctly as part of the final class. FP identifies the records that the category has placed in the target class. FN identifies records that mistakenly have not been categorized into the target class. Then, based on this matrix, the criteria for the efficiency of the data mining method are calculated. One

of these criteria is accuracy (27) that the closer the accuracy of this criterion, the better the result. This criterion is calculated based on the following formula:

$$Accuracy = \frac{TP+TN}{TP+TN+FP+FN} \quad (1)$$

Other criteria are precision (28) and AUC (29) which the closer to one, the better performance.

Analysis

In the test data set, out of 2479 patients, 2058 people suffer from osteopenia and 421 people get osteoporosis. This study implements six methods on the osteoporosis dataset. Table 3 lists the set extracted by each data mining method based on the accuracy measure. Table 2 shows that the support vector machine has the highest accuracy among other techniques. Moreover, the set consisting of age, weight, menopause date, and low calcium was more accurate than the other sets. The feature age is in the three top sets extracted by the three top accurate techniques. The linear regression set accuracy was less than the other sets.

Table 3 shows that the decision tree, random forest, and naïve bayes achieve the highest precision. Set consisted of weight, age, low activity, and thyroid malfunction to achieve the highest precision. The features age and weight were in the three top sets extracted by the three top accurate techniques.

Table 3. The set achieved by each data mining method

Method	precision	Set
Decision Tree	90%	Weight, Age, Low Activity Thyroid Malfunction
Random Forest	88%	Weight, Previous Fracture, Age Family History Of Osteoporosis
Naive Bayes	87%	Menopause Date, Weight, Age Back Pain
Support Vector Machine	85%	Menopause Date, Low Calcium, Early Menopause, Back Pain,
Neural Net	85%	Hormone Replacement Therapy, Blood pressure, Back Pain, Age
Linear regression	83%	Blood pressure, Family History Of Osteoporosis, Stomach Problem Kidney Problem

Table 4 shows that the AUC of the neural net is more than other techniques. Random Forest is the second-best technique based on this measure. The set consisted of back pain, age, and low activity, LCA achieved the highest AUC among other techniques. The feature back pain was in three top sets extracted by the three top accurate techniques.

According to table 5, the age feature has the highest occurrence (8 sets). This feature is in the selected set of three top-accurate techniques. The weight is the second most frequent feature with 7 occurrences. This feature and age are chosen by all three highest precision techniques. Back pain is the third feature selected by all three highest AUC techniques. Low activity is the fourth technique in 4 of 7 occurrences. Previous fracture, menopause date, and low calcium were considered the fifth, sixth, and seventh-most frequent features influencing the diagnosis of osteoporosis. 3 of 7 methods considered the features as significant features. The seven first features include age, weight, back pain, low activity, previous fracture, menopause date, and low calcium. So, these features can be considered as a selected set for identifying osteoporosis patients. It is noteworthy that the information of the features consist of rheumatoid arthritis, kidney problem, stomach problem, and asthma is not among the most significant features which do not exist in any set is not in table 5. The relation between two significant features with osteoporosis is shown in Figure 1.

Figure 1 shows that osteoporosis is more common in older people than younger people. When age is increased, the chance of osteoporosis is also increased. The lower the menopause age, the more chance of osteoporosis. The early menopause date increased the chance of the disease. Moreover, Figure 1 represents that overweight people are at more risk of osteoporosis disease.

Table 6 represents the extracted rules between

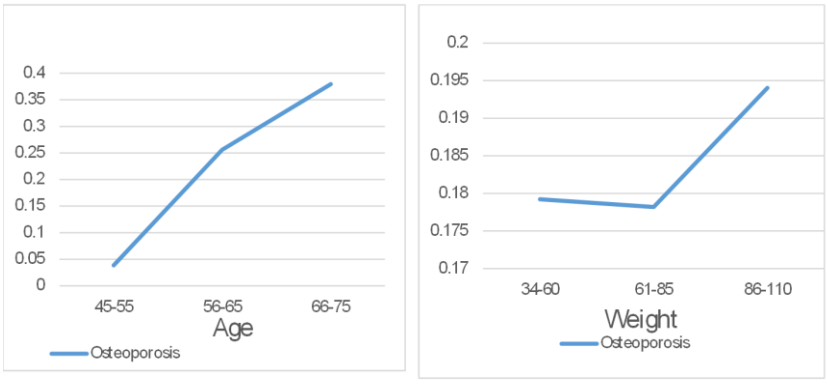
weight, age, and osteoporosis. It shows that 51 percent of people aged between 66 and 75 and the weight between 34 and 60 have osteoporosis, while only two percent of middle-weight people with age between 45 and 55 have osteoporosis.

Table 4. The set achieved by each data mining method

Method	AUC	Set
Neural Net	77%	Back Pain, Age, Low Activity, Low Calcium
Random Forest	75%	Weight Back pain, Previous Fracture, Menopause Date
Naive Bayes	74%	Age, Back Pain, Low Calcium, Weight
Linear regression	72%	Blood pressure, Age, Irregular Periods, Family History Of Osteoporosis
Support Vector Machine	69%	Low Activity, Age, Low Calcium Blood pressure
Decision Tree	66%	Age, Menopause Date, Previous Fracture LCA

Table 5. Comparison between features resulting in the performance

Features	Occurrence in Top Three highest accuracy	Occurrence in Top Three highest precision	Occurrence in Top Three highest auc	Total number of Occurrence
Age	3	3	2	8
Weight	2	3	2	7
Back Pain	0	1	3	4
Low Activity	2	1	1	4
Previous Fracture	1	1	1	3
Menopause Date	1	1	1	3
Low Calcium	1	0	2	3
LCA	1	0	0	1
Family History of Osteoporosis	1	0	0	1
Blood pressure	1	0	0	1
Thyroid Malfunction	0	1	0	1



A. Age B. Weight

Figure 1. Osteoporosis curves of three important features

Table 6. Extracted rules between weight, age, and osteoporosis

Rule	Condition	Result	Confidence
Rule 1	If age between 45 and 55 and weight between 34 and 60	Osteoporosis is True	0.19
Rule 2	If age between 56 and 65 and weight between 34 and 60	Osteoporosis is True	0.31
Rule 3	If age between 66 and 75 and weight between 34 and 60	Osteoporosis is True	0.51
Rule 4	If age between 45 and 55 and weight between 61 and 85	Osteoporosis is True	0.02
Rule 5	If age between 56 and 65 and weight between 61 and 85	Osteoporosis is True	0.13
Rule 6	If age between 66 and 75 and weight between 61 and 85	Osteoporosis is True	0.25
Rule 7	If age between 45 and 55 and weight between 86 and 110	Osteoporosis is True	0.06
Rule 8	If age between 56 and 65 and weight between 86 and 110	Osteoporosis is True	0.06
Rule 9	If age between 66 and 75 and weight between 86 and 110	Osteoporosis is True	0.2

Discussion

This study applied the data set of patients who underwent an osteoporosis diagnosis test at the Osteoporosis Diagnosis Center in Isfahan. It implemented linear regression, naive bayes, decision tree, support vector machine, random forest, and neural network on the dataset. The results of assessing these six methods using different criteria showed that support vector machine performed more accurately than other existing methods. Moreover, decision tree achieves the highest precision and neural net gets the highest AUC.

We had 12,650 four-member sets. Among these sets, each technique chose the best four-member set based on three measures consisting of accuracy, precision, and AUC. Some of the features are not in any of these sets. The results show that age is the first feature affecting osteoporosis. Results show that when the age is increased, the risk of getting osteoporosis is also increased. In general, older people are more at risk of various diseases. The paper showed that age can be considered an influential feature in the occurrence of disease in humans (30). Today, with the advent of COVID-19, older people are more prone to the disease. Studies show that the mortality rate in the elderly is high (31).

The second feature influencing osteoporosis is weight. The results show that osteoporosis is more common in overweight women than in other women. The study showed that the consequences of being overweight are worse for women than men (32). The study showed that osteoporosis is more common in overweight women than men (33). Women should be attentive to their weight to be less exposed to the disease. The third feature is back pain, and the fourth feature is Low Activity. Many articles have suggested a relationship between these two features and osteoporosis (34-35). Low back pain and low activity can be impressive in causing osteoporosis.

The fifth feature influencing osteoporosis is the previous fracture. This feature corresponds to the function of the human lung. Studies have shown that osteoporosis is more common in Japanese women who have lung problems (36).

The sixth significant feature was the menopause date, which affects the incidence of various diseases. The results showed an indirect relationship between menopause date and osteoporosis. In the early menopause date, the risk of osteoporosis is more than in other states. Yet, the study has shown that there is a direct relationship between menopause date and heart disease (37). The effect of this feature on the incidence of Alzheimer's disease has also been investigated (38).

Thin older people were more at risk of osteoporosis than other people. But, people with middle-weight and middle-age were at lower risk for osteoporosis. So, this study recommends the set consisting of age, weight, back pain, low activity, previous fracture, and menopause date for detecting osteoporosis patients. Moreover, support vector machine, decision tree, and neural net methods could be used for detecting this disease. Younger people should pay more attention to nutrition and sport to be less at risk of osteoporosis disease in older age.

This study used data collection about women with osteoporosis in the period 1390 to 1398 in the osteoporosis diagnosis center Isfahan. The study consists of 8258 patients' information, of which 1482 had osteoporosis. We assess the six methods consisting of decision tree, support vector machine, neural net,

random forest, naïve bayes, and linear regression. Different criteria are used such as accuracy, precision and AUC.

Support vector machine, decision tree and neural network are the best candidate techniques for predicting osteoporosis. This study recommends the set consisting of age, weight, back pain, low activity, previous fracture, and menopause date for detecting osteoporosis patients.

References

1. Camacho PM, Petak SM, Binkley N, Diab DL, Eldeiry LS, Farooki A, et al. American Association of Clinical Endocrinologists and American College of Endocrinology Clinical Practice guidelines for the diagnosis and treatment of postmenopausal osteoporosis—2016. Endocr Pract 2016;22:1-42.
2. Rachner TD, Khosla S, Hofbauer LC. Osteoporosis: now and the future. Lancet 2011;377:1276-87.
3. Sugimoto T, Sato M, Dehle FC, Brnabic AJ, Weston A, Burge R. Lifestyle-related metabolic disorders, osteoporosis, and fracture risk in Asia: A systematic review. Value Health Reg Issues 2016;9:49-56.
4. Marshall D, Johnell O, Wedel H. Meta-analysis of how well measures of bone mineral density predict occurrence of osteoporotic fractures. BMJ 1996;312:1254-9.
5. Mirzaie M, Darabi S. Population Aging in Iran and Rising Health Care Costs. Salmand 2017;12:156-69.
6. Lindsay R, Cosman F. Harrison's Principles of Internal Medicine. In: Lindsay R; Cosman F, eds. Osteoporosis. 18th ed. United States: The McGraw Hill; 2012:3131-6.
7. International Osteoporosis Foundation (IOF). Facts and Statistics, 2015. (Accessed 2015, at www.iofbonehealth.org/facts-statistics#category-14.)
8. Center JR, Nguyen TV, Schneider D, Sambrook PN, Eisman JA. Mortality after all major types of osteoporotic fracture in men and women: an observational study. Lancet 1999;353:878-82.
9. Tapak L, Shirmohammadi-Khorram N, Amini P, Alafchi B, Hamidi O, Poorolajal J. Prediction of survival and metastasis in breast cancer patients using machine learning classifiers. Clin Epidemiol Glob Health 2019;7:293-9.
10. Moeinzadeh F, Rouhani MH, Mortazavi M, Sattari M. Prediction of chronic kidney disease in Isfahan with extracting association rules using data mining techniques. Tehran University Medical Journal TUMS Publications. 2021 Sep 10;79(6):459-67.
11. Arabasadi Z, Alizadehsani R, Roshanzamir M, Moosaei H, Yarifard AA. Computer aided decision making for heart disease detection using hybrid neural network-Genetic algorithm. Comput Methods Programs Biomed 2017;141:19-26.
12. Moudani W, Shahin A, Chakik F, Rajab D. Intelligent decision support system for osteoporosis prediction. Int J Intell Inf Technol 2012;8:26-45.
13. Yoo TK, Kim SK, Kim DW, Choi JY, Lee WH, Park EC. Osteoporosis risk prediction for bone mineral density assessment of postmenopausal women using machine learning. Yonsei Med J 2013;54:1321-30.
14. Mona S, Somayeh A, Abbasi M, Ameri H. Providing a model for predicting the risk of osteoporosis using decision tree algorithms. J Mazandaran Univ Med Sci 2014;24:110-8.
15. Li H, Li X, Ramanathan M, Zhang A. Identifying informative risk features and predicting bone disease progression via deep belief networks. Methods 2014;69:257-65.
16. Guannoni N, Sassi R, Bedhiafi W, Elloumi M. A Comparison Between Classification Algorithms for Postmenopausal Osteoporosis Prediction in Tunisian Population. InInternational Conference on Information Technology in Bio-and Medical Informatics. 2016 Sep 5, Porto, Portogual: Springer, Cham, 2016:234-48
17. Pedrassani de Lira C, Toniazzo de Abreu LL, Veiga Silva AC, Mazzuchello LL, Rosa MI, Comunello E, et al. Comput Inform Nurs 2016;34:369-75.
18. Iliou T, Anagnostopoulos CN, Stephanakis IM, Anastassopoulos G. A novel data preprocessing method for boosting neural network performance: a case study in osteoporosis prediction. Inf Sci 2017;380:92-100.
19. Langarizade M, Owji L, Orooji A. Developing a decision support system for osteoporosis Prediction. J Health Adm 2019;21:87-100.
20. A Mowafy M. Osteoporosis Risk Prediction Among a Group of Postmenopausal Females: A Case-Control Study. Egypt Family Med J 2019;3:65-82.
21. Genuer R, Poggi JM, Tuleau-Malot C. Variable selection using random forests. Pattern Recognit Lett 2010;31:2225-36.
22. Friedl MA, Brodley CE. Decision tree classification of land cover from remotely sensed data. Remote Sens Environ 1997;61:399-409.
23. Montgomery DC, Peck EA, Vining GG. Introduction to linear regression analysis. New Jersey, U.S: John Wiley & Sons; 2012.
24. Rish I. An empirical study of the naive Bayes classifier. In: workshop on empirical methods in artificial intelligence. Shefield: England 2001;3:41-6.
25. Babinec T. Neural Networks and Statistical Models. Sawtooth Software Conference 1997 Nov, Sequim, WA.

26. Auria L, Moro RA. Support Vector Machines (SVM) as a Technique for Solvency Analysis. Berlin, Germany: DIW Berlin Discussion, 2009:811.
27. Mastrogiannis N, Boutsinas B, Giannikos I. A method for improving the accuracy of data mining classification algorithms. Comput Oper Res 2009;36:2829-39.
28. Alvarez SA. An exact analytical relation among recall, precision, and classification accuracy in information retrieval. Boston College, Boston, Technical Report 2002:1-22.
29. Huang J, Ling CX. Using AUC and accuracy in evaluating learning algorithms. IEEE Trans Knowl Data Eng 2005;17:299-310.
30. Loeber R, Keenan K. Interaction between conduct disorder and its comorbid conditions: Effects of age and gender. Clin Psychol Rev 1994;14:497-523.
31. Shahid Z, Kalayanamitra R, McClafferty B, Kepko D, Ramgobin D, Patel R, et al. COVID- 19 and older adults: what we know. J Am Geriatr Soc 2020;68:926-9.
32. Miller MM, Allison A, Trost Z, De Ruddere L, Wheelis T, Goubert L, et al. Differential effect of patient weight on pain-related judgements about male and female chronic low back pain patients. J Pain 2018;19:57-66.
33. Zhao LJ, Liu YJ, Liu PY, Hamilton J, Recker RR, Deng HW. Relationship of obesity with osteoporosis. J Clin Endocrinol Metab 2007;92:1640-6.
34. Vuori IM. Dose–response of physical activity and low back pain, osteoarthritis, and osteoporosis. Med Sci Sports Exerc 2001;33:S551-86.
35. Chilibeck PD, Vatanparast H, Cornish SM, Abeysekara S, Charlesworth S. Evidence-based risk assessment and recommendations for physical activity: arthritis, osteoporosis, and low back pain. Appl Physiol Nutr Metab 2011;36:S49-79.
36. Watanabe R, Tanaka T, Aita K, Hagiya M, Homma T, Yokosuka K, et al. Osteoporosis is highly prevalent in Japanese males with chronic obstructive pulmonary disease and is associated with deteriorated pulmonary function. J Bone Miner Metab 2015;33:392-400.
37. Stampfer MJ, Colditz GA, Willett WC. Menopause and heart disease. Ann N Y Acad Sci 1990;592:193-203.
38. Tang MX, Jacobs D, Stern Y, Marder K, Schofield P, Gurland B, et al. Effect of oestrogen during menopause on risk and age at onset of Alzheimer's disease. Lancet. 1996;348:429-32.