RESEARCH



Gastrointestinal disease is an important influencing factor of osteoporosis fracture:a retrospective study in chinese postmenopausal women



PengChao Xu¹, JiRong Ge^{2*}, Hong Jiang¹, YuJuan Lin¹, YunJin Ye², XiaoBin Huang², YanYan He² and LiPeng Xue²

Abstract

Backgroud The influencing factors of osteoporosis are complex, the incidence of osteoporosis is higher in middle-aged and elderly women, and osteoporotic fractures (OF) can seriously affect quality of life. Currently, the correlation analysis between gastrointestinal diseases and OF focuses more on diseases such as gastric cancer and inflammatory bowel disease (IBD). This study analyzed the risk factors for osteoporosis and osteoporotic fractures in 1567 postmenopausal women in Fuzhou, China. The purpose is to explore the potential influence of gastrointestinal diseases on the occurrence of OF.

Methods According to inclusion and exclusion criteria, a total of 1567 subjects were included in the analysis of OP risk factors, including 647 in the OP group and 920 in the NOP group. A total of 616 subjects were included in the analysis of correlation between OF and gastrointestinal diseases, including 132 in OF group and 484 in NF group. Statistical analysis shows that age (OR = 1.062, 95% CI = 1.045-1.080), height (OR = 0.089, 95% CI = 0.009-0.857), weight (OR = 0.981,95% CI = 0.967-0.995) and nature of work (P = 0.010) are the main risk factors for osteoporosis in postmenopausal women in southeast China, and gastrointestinal diseases (OR = 1.583, 95% CI = 1.070-2.343) and height (OR = 0.003, 95% CI = 0.000-0.104) are the main risk factors of OF.

Conclusions The main factors affecting the occurrence of OP in postmenopausal women in southeast China are individual characteristic. Gastrointestinal diseases that do not directly affect BMD increase the risk of OF in osteoporotic patients.

Keywords Osteoporosis, Osteoporotic fracture, Gastrointestinal diseases, Case control study, Chinese postmenopausal women

*Correspondence:

gejirongcn@163.com

¹Fujian University of Traditional Chinese Medicine, 1 Qiuyang Road, Minhou Upper Street, Fuzhou, Fujian, China

²Fujian Key Laboratory of Integrated Traditional Chinese and Western Medicine for the Prevention and Treatment of Osteoporosis(Fujian Academy of Chinese Medical Sciences, The Affiliated Rehabilitation Hospital of Fujian University of Traditional Chinese Medicine), Fujian Academy of Chinese Medical Sciences, 282 Wusi Road, Gulou District, Fuzhou, Fujian, China



© The Author(s) 2023. **Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by/4.0/. The Creative Commons Dublic Domain Dedication waiver (http://creativecommons.org/publicdomain/zero/1.0/) applies to the data made available in this article, unless otherwise stated in a credit line to the data.

JiRong Ge

Introduction

Osteoporosis (OP) is defined as a systemic skeletal disease characterised by low bone mass and microarchitectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture [1]. Due to the physiological characteristics of the human body, the prevalence of OP in postmenopausal women is higher than that in men of the same age [2]. As a serious consequence of OP, osteoporotic fracture is characterized by high mortality and disability rate, which significantly reduces the quality of life of patients and brings heavy economic burden [3]. Therefore, it is necessary to explore the risk factors of osteoporosis and osteoporotic fracture in postmenopausal women. In addition to the secondary osteoporosis that has been clearly and directly lead to bone loss, such as glucocorticoid treatment history, various cancers (in particular, breast cancer and cervical cancer, which mainly occur in women), thyroid diseases, inflammatory bowel disease (IBD) [4, 5]. According to the global consensus on OP and osteoporotic fracture (OF) health management, physical factors such as age, genetics, thinness can affect the onset of OP [6]. Experts agree that living situations, such as smoking, education and cognition of OP, and disease situations can also affect the occurrence of OP [7]. In addition, the concentrations of blood calcium, magnesium, and other substances are closely related to the occurrence of osteoporosis fractures [8]. Moreover, a study has found that there is a certain relationship between 25-hydroxyvitamin D levels and residential latitude [9], which indicates that region also has an important influence on the occurrence of OP.

OF are the common and most serious complications of osteoporosis. Poor bone quality, weak repair capacity, instability, and high failure rate of internal fixation are main characteristics of OF. Proximal humerus, distal radius, hip and spine are common osteoporotic fractures. The prevalence of vertebral fractures in China is about 15% in women over 50 years old [10]. It is predicted that the worldwide incidence of hip fractures will grow to 6.3 million yearly by 2050 [11]. Because the pathogenesis of OP and OF is complex and related to many factors such as individual characteristic, living situations, and disease situations, there are some differences in the incidence and influencing factors of OP and OF among people of different races and regions [12]. Although there are a large number OF risk factor analysis studies on osteoporosis and fragility fractures in the world, there are still few clinical studies on OP, OF incidence and risk factor analysis in postmenopausal women of Han nationality in southeast China. In this case-control study, individual characteristic, living situations, and disease situations were compared and analyzed in nearly 1600 postmenopausal women in Fuzhou, China. To explore the incidence and risk factors OP and OF postmenopausal women in southeast China, in order to provide evidence support for intervention and health management of OP and OF postmenopausal women in China.

Gastrointestinal diseases are highly prevalent in the Chinese population due to factors such as Chinese dietary habits:Nearly half of all new gastric cancer cases and deaths from H. pylori infection worldwide occur in China [13]. The incidence rate of chronic gastritis in China is about 20%, and the most common is chronic non-atrophic gastritis, which is nearly 50% [14]. Another study shows that [15], with the increase of age, the incidence rate of gastritis is also higher, at the same time, the incidence of osteoporosis also has the same trend, Chinese elderly women are often troubled by gastrointestinal diseases and osteoporosis. Previous studies on the correlation between gastrointestinal diseases and osteoporosis mainly focused on the diseases that have obvious effects on BMD, such as gastric cancer, post-gastrectomy, IBD [16–18]. Patients with gastric cancer who underwent gastrectomy had a significantly increased risk of OP within 10 years [19]. The incidence of OP in the elderly after gastrectomy was also significantly higher, reaching 38.2% [20]. Patients with IBD are thought to have an increased risk of bone mineral loss, resulting in osteoporosis and an increased risk of fragility fractures [21, 22]. Secondary OP and fragility fractures caused by gastrointestinal diseases have been studied extensively. Some scholars have shown through literature studies [23] that postgastrectomy, and IBD can increase the risk of bone loss and fracture. Although the correlation between these gastrointestinal diseases and OP has been recognized, it has not received much attention from the patients concerned [24], calling for the academic community to pay more attention to the health management of OP in patients with these diseases. Therefore, chronic gastrointestinal diseases that do not directly cause bone loss, such as chronic gastritis and functional gastrointestinal diseases, have less attention. Chronic gastrointestinal diseases may cause malnutrition, changes in intestinal flora, and disorders in the metabolism of trace elements, which may have a certain impact on the occurrence of OP. In addition, many scholars have noticed that proton pump inhibitor (PPI), a firstline drug for chronic gastritis, has a certain impact on the occurrence of fractures. Some scholars believe that, the possible mechanisms of PPIs leading to fracture include hyperparathyroidism caused by excessive histamine secretion and high gastrin, as well as malabsorption of minerals and vitamin B caused by hypochloremia, which may also have direct effects on bone cells [25]. In Taiwan [26] and South Korea [27, 28], there have also been clinical reports that PPI use can increase the risk of fragility fracture. Therefore, the study on the risk factors of gastrointestinal diseases and OP and OF in elderly women is also of great significance to the health management

Materials and methods

Study design and study population

The data of this retrospective study was collected from January 2012 to December 2021. Through telephone and leaflets, local women over 40 years old in Fuzhou were invited to carry their ID cards and medical records to the Osteoporosis Laboratory of Fujian Academy of Chinese Medical Sciences for BMD examination and questionnaire survey. A total of 2,729 people completed the questionnaire and BMD examination, and 1,567 were included in the study. All subjects were able to provide complete medical records and independently sign informed consent.

The inclusion criteria for this study included women aged 40-90 years old who volunteered to participate and signed informed consent from Han Chinese residents in Fuzhou. Exclusion criteria include: 1) Those who repeatedly participated in questionnaire survey and BMD examination. 2) Premenopausal or artificially menopausal women. 3) Patients with IBD, thyroid disease, rheumatoid arthritis, various kinds of cancer, serious liver, kidney or blood disease and other diseases that may cause secondary osteoporosis, and those who are receiving treatment for osteoporosis or taking other drugs that affect bone metabolism. In addition, 52 people with missing key data were excluded during data cleaning. According to the definition of osteoporosis, all subjects included in the study were divided into osteoporosis group (OP group) and non-osteoporosis group (NOP group) for osteoporosis risk factor analysis. In the OP group, 31 osteoporotic patients with non-fragility fractures were excluded according to the definition OF, and then divided into the osteoporotic fractures group (OF group) and no fracture group (NF group) for data analysis. Further details of this study are shown in flow diagram (Fig. 1).

Clinical characteristics

The data needed for the study came from questionnaires. The questionnaire mainly includes individual characteristic, living situations, and disease situations, individual characteristic includes: age, height, weight, menopausal age, BMD and T-score of lumbar vertebrae and femoral neck, occupation, nature of work and education. Living situations includes: tea consumption, coffee consumption and milk consumption, sunlight exposure, and regular exercise. Disease situations includes: hypertension, coronary heart disease (CHD), gastrointestinal diseases and knee osteoarthritis (KOA). The subjects' medical history were recorded by inquired about the subjects' medical history and checked their medical records, including OF, hypertension, CHD, gastrointestinal disease and KOA. The above contents were collected by trained doctors and carefully filled in a unified questionnaire. Height and weight of each subject were measured with calibrated instruments accurate to 0.1 cm and 0.1 kg, respectively. After measuring the height and weight, calculate the body mass index (BMI) according to the formula: BMI=weight (kg) / height² (m²).

BMD examination

All subjects undergo unified BMD examination at our research institution. Dual-energy X-ray absorptiometry (DXA) (Discovery W, Hologic Inc., USA) was used to measure BMD of the first to fourth lumbar vertebrae and left femoral neck. The T-score was alculated according to the reference range of the instrument manufacturer. The examination is conducted by two professional doctors who are uniformly trained to reduce deviations. The coefficient of variation (CV) for repeated measurements was approximately 1.0%.

Definitions

The diagnosis of osteoporosis was based on the T-score in the lumbar vertebrae or femoral neck. A T-score ≤ -2.5 indicates osteoporosis, osteopenia is diagnosed as -2.5 < T-score< -1.0, and a T score ≥ -1.0 indicates normal [29]. All subjects were divided into NOP group (NOP) and osteoporosis group (OP) according to T-score. Osteoporotic fractures are defined in reference to the European OP Guidelines [30]: fragility fractures of the spine, hip, distal forearm and proximal humerus following osteoporosis were recorded as osteoporotic fractures. The OP group was divided into NF group and OF group according to the occurrence of osteoporotic fracture. According to the International Statistical Classification of Diseases and Related Health Problems (ICD) (tenth revision, ICD-10). Gastrointestinal diseases included in this study: Esophagitis (ICD-10 code K20), gastritis and duodenitis (ICD-10 code K29), gastroesophageal reflux (ICD-10 code K21), gastric ulcer (ICD-10 code K25), duodenal ulcer (ICD-10 code K26), gastrojejunal ulcer (ICD-10 code K28) and peptic ulcer with unspecified site (ICD-10 code K27). The above definitions of gastrointestinal diseases refer to the Chinese medical textbook: Internal Medicine-Gastroenterology & Hepatology [31]. Other chronic diseases include: hypertension (ICD-10 code I10), CHD (ICD-10 code I25), KOA (ICD-10 code M17). Hypertension was defined as systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg or intake of antihypertensive drugs. The diagnosis of coronary heart disease was based on the guidelines of



Fig. 1 Flow diagram of this study

the European Society of Cardiology and Chinese Society of Cardiology of Chinese Medical Association: the subjects had discomfort related to myocardial ischaemia, including location, character, duration and relationship to exertion and other exacerbating or relieving factors. All subjects had a resting 12-lead ECG recorded allowing for detection of ST-segment changes [32, 33]. The diagnosis of KOA is mainly determined by history, physical examination, and imaging studies [34], that includes knee pain, friction when moving, morning stiffness, and osteophyte at the edge of knee joint shown by X-ray. Participants were asked during the questionnaire survey and their medical records were checked to determine if they had any of the above diseases and records were kept. BMI category were generally classified into underweight (<18.5 kg/m²), normal weight (18.5~23.9 kg/m²), overweight (24~27.9 kg/m²), and obese (\geq 28 kg/m²) in accordance with the criteria of the Working Group on Obesity in China [35]. In terms of daily drinking, 200ml is defined as the limit and divided into three groups: no drinking, occasional drinking (0-200ml), regular drinking (>200ml/day). According to China's national conditions, the occupations of participants are divided into five categories: farmers, workers, cadres, intellectuals and others; The education level is divided into below junior high school group, below bachelor degree group and bachelor degree or above.

Statistical analysis

EpiDate 2 (the EpiData Association, Odense M, Denmark) was used to enter and proofread data repeatedly, and SPSS 26 (IBM, Inc., New York, USA) software was used for data analysis. The results are expressed as the average standard deviation or quantity (percentage). Independent sample t test or Mann-Whitney U test were used according to whether continuous variables conform to normal distribution. Pearson chi-square test and Fisher exact probability method were used to measure the difference in frequency. Logistic regression analysis was carried out with OP and OF as dependent variables to investigate the factors affecting OP and OF. First, the independent variables were screened by P>0.2. Univariate regression analysis was used to exclude variables without statistical significance and eliminate mediary variables. Multicollinearity was assessed using stepwise regression. For continuous variables, the linear condition was assessed. The -2 log-likelihood ratio was used to test the overall significance of the model. The Hosmer-Lemeshow test evaluated the model's goodness-of-fit. Except screening the independent variables, all statistical hypothesis tests were two-sided and performed at the 0.05 significance level.

Table 1 Demographic data with participants.(mean + SD)

Results

A total of 1,567 subjects were enrolled after excluding 1,162 subjects who did not meet the criteria.Further details are shown in flow diagram (Fig. 1). Statistically, subjects in the OP group had a higher mean age than those in the NOP group, while height, weight, and menopause age were significantly smaller than those without osteoporosis (P<0.001). In addition, BMD in OP group was significantly lower than that in NOP group (P<0.001) (Table 1).

The OF group and NF group were grouped based on 647 subjects in the OP group. After excluding 31 subjects with non-osteoporotic fractures, 616 subjects were included in this study. The data in Table 2 show the baseline of OF group and NF group. The age of NF group was lower (P<0.001) and higher height (P<0.002), the femoral neck had higher BMD (P<0.001).

Among the 132 subjects, 37 (28.03%) suffered spinal fracture, 13 patients with humerus fracture (9.85%). there were 40 patients with ulna and radius fracture (30.30%), 8 patients with hip fracture (6.06%), 25 patients with other lower limb fractures (including tibia, calcaneus and so on) (18.94%), and 9 patients with multiple site fractures (6.82%).

Comparison of influencing factors between OP group and NOP group

Individual characteristic, living situations, and disease situations of the two groups were preliminarily compared, and the preliminary screening of risk factors was conducted according to the results, as shown in Table 3. Set p < 0.2 is the factor that may affect OP. The risk factors included in the analysis were age, height, weight, nature of job, education, tea consumption, coffee consumption, milk consumption and CHD. The above factors were analyzed by univariate and multivariate regression analysis, and the adjusted results showed that the increase of age was a risk factor for OP, the increase of height and weight

	Total	Osteoporosis	Non-osteoporosis	P value	Number of
	(n = 1567)	(n=647)	(n = 920)		missing sample data
Age	62.86±6.80	64.54±6.83	61.69±6.53	0.000	0
(years)					
Height	1.558 ± 0.05	1.548 ± 0.06	1.565 ± 0.05	0.000	0
(m)					
Weight	56.39 ± 8.45	56.36 ± 8.21	58.12 ± 8.55	0.000	0
(kg)					
BMI	23.62 ± 3.09	23.50 ± 3.06	23.71±3.11	0.205	0
(kg/m ²)					
Menopause age (years)	50.35 ± 3.60	49.92 ± 3.69	50.65 ± 3.51	0.000	0
Lumbar vertebra BMD (g/cm2)	0.781 ± 0.15	0.660 ± 0.08	0.867±0.13	0.000	4
Femoral neck BMD (g/cm2)	0.696 ± 0.13	0.631±0.12	0.743±0.11	0.000	11

statistical method: Mann-Whitney U-test

Table 2 Demographic data with osteoporotic fracture group and no fracture group.(mean ± SD)

	Total (n=616)	Osteoporotic fracture (n=132)	Osteoporosis without fracture (n=484)	P value	Number of missing sample data
Age (years)	64.72±6.81	68.17±7.19	63.79±6.40	0.000 ^a	0
Height (m)	1.548±0.06	1.534±0.06	1.551 ± 0.05	0.002 ^b	0
Weight (kg)	56.41±8.15	55.16±8.12	56.75±8.13	0.079 ^a	0
BMI (kg/m ²)	23.53±3.03	23.41 ± 3.05	23.56±3.03	0.615 ^a	0
Menopause age (years)	49.86 ± 3.71	49.47 ± 3.92	49.96±3.66	0.216 ^a	0
Lumbar vertebra BMD (g/cm2)	0.660 ± 0.08	0.652 ± 0.09	0.662±0.08	0.689 ^a	2
Femoral neck BMD (g/cm2)	0.631 ± 0.12	0.584±0.11	0.644±0.12	0.000 ^a	4

a: Mann-Whitney U-test, b: independent t-test

could reduce the occurrence of OP, and the nature of work may also affect the occurrence of OP (Table 4).

Comparison of influencing factors between OF group and NF group

In the analysis of these two groups, we first analyzed the association of osteoporotic fractures with chronic disease. Through analysis, we found that gastrointestinal diseases may have an impact on the OF occurrence (Table 5). We adjusted the regression coefficient between gastrointestinal diseases and OF by further comparing factors such as individual characteristic, living situations. Through screening, the main influencing factors included in the analysis are age, height, weight, occupation, tea consumption, milk consumption and regular exercise (Table 6). Before the regression analysis, age, a mediary variable that could increase the incidence of gastrointestinal diseases, OF and OP, was excluded, and the OR value of gastrointestinal diseases to OF was adjusted through the remaining influencing factors, and the regression equation only included height and gastrointestinal diseases. After adjusting, the OR value OF gastrointestinal diseases for OF was 1.583, p=0.022, indicating that gastrointestinal diseases can significantly improve the risk of OF. That gives us a new hint of health management and education for osteoporosis patients in the future (Table 7).

Discussion

With the continuous progress of aging population in China, the occurrence of OP and OF in our country has become an important national health problem. This retrospective study showed that the prevalence of osteoporosis and osteoporotic fracture in postmenopausal women in Fuzhou was 41.29% and 20.40% respectively. Accroding to the incidence in Fuzhou, the occurrence of OP and OF does have an important impact on the life of local elderly women. In comparison of baseline data between the groups, it was interesting to note that femoral neck BMD in the OF group was significantly lower than that in the NF group, while lumbar vertebrae BMD was not significantly different (Table 2). From the clinical perspective, a large number of elderly women find themselves suffering from osteoporosis, the initial symptoms were mostly waist pain. In terms of bone structure, the lumbar vertebrae had a higher proportion of cancellous bone, but the data here showed a more pronounced change in femoral neck BMD. The cause of this problem may be related to waist strain and osteophyma. Besides, hip fracture can greatly affect the athletic ability and mental state of the elderly [36, 37]. In previous concepts, it was often described as the dying fracture of the elderly. Combined with the results of this study, femoral neck BMD is a greater accuracy in the prevention of OF, and regular femoral neck BMD examination is more necessary in osteoporotic patients.

In the first part, the analysis results of OP show that the risk factors of OP in postmenopausal women in southeast China mainly include age, height, weight and nature of work. In OP health management and education for elderly women, we should remind older women, shorter height and lighter weight to pay more attention to the prevention and treatment of OP. In terms of the influence of living situations on OP, the impact of occupation and educational level on osteoporosis may be related to the economic status of the subjects. In addition, there may be some relationship between the amount of tea consumed, sunlight exposure, cardiovascular disease and BMD, but the statistical difference in this study is not significant. In the studies of other scholars, the effect of tea consumption on bone mineral density is still inconclusive [38-40], but sunlight exposure [41] and cardiovascular disease [42–44] may both have an impact on the prevalence of osteoporosis. In general, personal physical quality still has a greater impact on the occurrence of OP. Therefore, in the prevention and treatment education of OP, We should focus on this part of the population.

 Table 3
 Comparison of individual characteristic, living situations and disease situations influencing factors between the osteoporosis group and non-osteoporosis group

Variable	Osteoporo-sis (n,%)	Non-osteo-porosis(n,%)	X ² test	P value	Number of missing sample data
Individual characteristic					
BMI					
Underweight	25,45.5%	30,54.5%	2.758	0.430	0
Normal	366,42.6%	494,57.4%			
Overweight	202,38.5%	323,61.5%			
Obese	54,42.5%	73,57.5%			
Occupation					
Farmer	40,50.6%	39,49.4%	3.215	0.522	3
Worker	188,40.0%	282,60.0%			
Cadre	99,41.2%	141,58.8%			
Intellectual	136,41.6%	191,58.4%			
Others	183,40.8%	265,59.2%			
Nature of work					
Manual labour	212,42.2%	290,57.8%	5.329	0.070	0
Mental labour	318,39.0%	498,61.0%			
Both above	117,47.0%	132,53.0%			
Education					
Below junior high school	297,44.3%	374,55.7%	5.960	0.051	0
Below bachelor degree	310,39.9%	467,60.1%			
Bachelor degree or above	40,33.6%	79,66.4%			
Living Situations					
Tea consumption					
No or drinking occasional	560,41.0%	805,59.0%	4.679	0.096	3
0–200ml/day	43,51.8%	40,48.2%			
>200ml/day	43,37.1%	73,62.9%			
Coffee consumption					
No or drinking occasional	630,41.3%	894,58.7%	3.784	0.151	1
0–200ml/day	5,25.0%	15,75.0%			
>200ml/day	12,54.5%	10,45.5%			
Milk consumption					
No or drinking occasional	366,39.2%	567,60.8%	4.269	0.118	1
0–200ml/day	61,46.6%	70,53.4%			
>200ml/day	219,43.6%	283,56.4%			
Sunlight exposure					
<1 h/day	424,41.2%	604,58.8%	0.559	0.756	5
1–3 h/day	209,41.8%	291,58.2%			
>3 h/day	12,35.3%	22,64.7%			
Regular exercise					
No	241,41.2%	344,58.8%	0.003	0.954	13
Yes	406,41.3%	576,58.7%			
Disease Situations					
Hypertension					
No	450,40.6%	659,59.4%	0.792	0.673	2
No examination	25,43.9%	32,56.1%			
Yes	171,42.9%	228,57.1%			
CHD					
No	570,40.5%	837,59.5%	3.911	0.141	0
No examination	29,51.8%	27,48.2%			
Yes	48,46.2%	56,53.8%			
Gastrointestinal diseases					
No	385,40.9%	557,59.1%	0.171	0.679	0
Yes	262,41.9%	363,58.1%	_		

Table 3 (continued)

Variable	Osteoporo-sis	Non-osteo-porosis(n,%)	X ² test	P value	Number of
	(n,%)				missing sample data
КОА					
No	327,41.4%	462,58.6%	0.024	0.988	3
No examination	194,41.0%	279,59.0%			
Yes	125,41.4%	177,58.6%			
Fracture					
No	483,37.8%	795,62.2%	34.291	0.000	1
Yes	163,56.6%	125,43.4%			

statistical method: Pearson Chi-Square

Table 4 Multivariate Logistic regression analysis for the effect of independent variables on osteoporosis

	Univariate Logistic regression				Multivariate Logistic regression			
	В	Crude OR	95%CI	Р	В	Adj. OR	95%CI	Р
Age	-4.364	1.066	1.049-1.082	<0.001	0.060	1.062	1.045-1.080	<0.001
Height	-5.818	0.003	0.000-0.020	<0.001	-2.422	0.089	0.009-0.857	0.037
Weight	-0.025	0.975	0.963–0.987	<0.001	-0.019	0.981	0.967-0.995	0.007
Nature of work				0.070				0.010
Manual labour								
Mental labour	-0.135	0.873	0.697-1.095	0.241	-0.198	0.821	0.648-1.039	0.104
Both above	0.193	1.212	0.893-1.646	0.216	0.252	1.287	0.939-1.765	0.117
Education				0.052				
Below Junior high school								
Below bachelor degree	-0.179	0.836	0.678-1.031	0.093				
Bachelor degree or above	-0.450	0.638	0.423-0.960	0.031				
Теа				0.099				
No or drinking occasional								
0–200ml/day	0.435	1.545	0.991-2.409	0.055				
>200ml/day	-0.166	0.847	0.572-1.253	0.405				
Coffee				0.161				
No or drinking occasional								
0–200ml/day	-0.749	0.473	0.171-1.308	0.149				
>200ml/day	0.532	1.703	0.731-3.966	0.217				
Milk				0.119				
No or drinking occasional								
0–200ml/day	0.300	1.350	0.935-1.950	0.110				
>200ml/day	0.181	1.199	0.962-1.494	0.106				
CHD				0.144				
No								
No examination	0.456	1.577	0.924-2.693	0.095				
Yes	0.230	1.259	0.844-1.878	0.260				

According to the analysis results of OF in the second part. We suggest that we should pay more attention to the impact of gastrointestinal diseases on OF. With the progress of an aging society, an increasing number of middle-aged and elderly people are also suffering from gastrointestinal diseases and osteoporosis. The stomach and intestines are the main organs for ingesting nutrients and maintaining human life activities. The normal function is closely related to the health status of the human body. With the growth of age, the function of the digestive system gradually weakens, and the prevalence rate of gastrointestinal diseases is also increasing [45]. This often leads to weight loss, weakness, and other issues in the elderly. In addition, with the deterioration of physical functions, muscles begin to lose, and the motor function of the elderly is gradually declining [46]. The frequent occurrence of gastrointestinal diseases and the decline in the health status of the elderly lead to a decrease in their musculoskeletal mass. These problems directly affect the BMD and bone quality of the elderly, and even lead to fragility fractures.

Because of Chinese dietary habits and not used to separate meals, the prevalence of Helicobacter pylori infection and gastrointestinal diseases are very high in China

Table 5	Comparison of	f disease situations influencing	a factors between the osteo	porotic fracture grou	p and no fracture group
---------	---------------	----------------------------------	-----------------------------	-----------------------	-------------------------

Variable	Osteoporotic fracture (n,%)	Osteoporosis without fracture(n,%)	X ² test	P value	Number of missing sample data
Hypertension					
No	83,19.6%	341,80.4%	2.876	0.237	1
No examination	5,20.0%	20,80.0%			
Yes	43,25.9%	123,74.1%			
CHD					
No	115,21.2%	427,78.8%	0.819	0.664	0
No examination	5,17.9%	23,82.1%			
Yes	12,26.1%	34,73.9%			
Gastrointestinal o	liseases				
No	68,18.4%	301,81.6%	4.920	0.027	0
Yes	64,25.9%	183,74.1%			
KOA					
No	69,22.5%	237,77.5%	1.361	0.506	1
No examination	35,18.4%	155,81.6			
Yes	27,22.7%	92,77.3%			
statistical mathed.	Chi Causto				

statistical method: Pearson Chi-Square

[13]. Nutritional issues or calcium phosphorus metabolism abnormalities caused by gastrointestinal diseases often lead to secondary osteoporosis and the occurrence of OF [47]. Numerous studies have confirmed the importance of these factors in the occurrence of OF. For example, the effects of gastrectomy on the nutritional status of the elderly [20], the effects of anti-breast cancer drugs on bone metabolism [5], and the effects of IBD on bone mineral loss [23] were mentioned above. However, doctors have not paid enough attention to gastrointestinal diseases that do not directly cause bone loss. The patients included in this study were excluded from various gastrointestinal diseases that directly caused bone loss, including various cancers, post-gastrectomy, and IBD. Through statistical analysis, however, our study suggests that even diseases that have little direct impact on BMD may significantly increase the risk of fracture in osteoporotic patients. At present, there are not many studies on the relevant mechanism of this condition, but in the process of sorting out relevant literatures, we still found some relevant studies [24]: A review summarizes possible pathways by which PPI affects bone metabolism, PPI may affect BMD through histamine secretion and hyperparathyroidism. But in addition to its effect on BMD, could gastrointestinal diseases contribute to the predisposition of osteoporotic patients by affecting bone mass or nerve or muscle function? Whether the physical and mental state of the elderly with gastrointestinal diseases more lead to the occurrence of OF, and what is its biological mechanism? This question deserves further study.

The results of this study suggest that when OP occurs, we should take drug intervention as early as possible, and change the diet structure and lifestyle to have limited effect on the occurrence of OP. To avoid the occurrence of OF as much as possible, we should focus on patients with chronic gastrointestinal disease and check BMD of the femoral neck regularly. Provide more targeted health education and attention to patients with gastrointestinal diseases. Of course, this study also has some shortcomings: 1) Since no accurate incidence of osteoporotic fractures has been reported in the literature in China, this study uses the data of spinal fragile fractures in the estimation of sample size. As a result, there may be some error between the calculated sample size and the actual required sample size. Furthermore, in order to increase the sample size, this study has a long time span. 2) As a single-center retrospective study, it is difficult to exclude some confounding factors, especially the influence of different regions on OP and OF, and it is also difficult to obtain a direct causality between gastrointestinal diseases and OF. 3) In the data collection of large samples, although we try our best to obtain objective data, there may be some selection bias and recall bias. In future studies, we may consider using multi-center, large sample, short-term or prospective cohort studies to further explore the relationship between gastrointestinal diseases and OF, or further explore the possible mechanism of chronic gastrointestinal diseases affecting the occurrence OF, with a view to improving the quality of life and health management of OP and OF patients.

Conclusions

In general, the main factors affecting the occurrence of OP in postmenopausal women in southeast China are individual characteristic. Living situations and disease situations may have some influence on the occurrence of OP, but their effects are limited. Our study shows that there is a close relationship between gastrointestinal diseases and the occurrence OF, and even gastrointestinal diseases that do not directly affect bone density can

Variable	Osteoporotic fracture (n,%)	Osteoporosis without fracture(n,%)	X ² test	P value	Number of missing sample data
BMI					
Underweight	7,31.8%	15,68.2%	2.987	0.393 ^b	0
Normal	78,22.3%	272,77.7%			
Overweight	35,18.2%	157,81.8%			
Obese	12,23.1%	40,76.9%			
Occupation					
Farmer	13,33.3%	26,66.7%	6.449	0.168 ^a	1
Worker	39,21.5%	142,78.5%			
Cadre	18,19.1%	76,80.9%			
Intellectual	32,25.2%	95,74.8%			
Others	30,17.2%	144,82.8%			
Nature of work					
Manual labour	41,20.3%	161,79.7%	2.378	0.304 ^a	0
Mental labour	71,23.8%	227,76.2%			
Both above	20,17.2%	96,82.8%			
Education					
Below Junior high school	58,20.5%	225,79.5%	0.456	0.796 ^a	0
Below bachelor degree	67,22.6%	230,77.4%			
Bachelor degree or above	7,19.4%	29,80.6%			
Tea consumption					
No or drinking occasional	122,22.8%	412,77.2%	4.679	0.085 ^a	1
0–200ml/day	6,15.0%	34,85.0%			
>200ml/day	4,9.8%	37,90.2%			
Coffee consumption					
No or drinking occasional	130,21.7%	469,78.3%	0.846	0.786 ^b	0
0–200ml/day	0,0.0%	5,100.0%			
>200ml/day	2,16.7%	10,83.3%			
Milk consumption					
No or drinking occasional	66,18.9%	284,81.1%	4.269	0.118 ^a	1
0–200ml/day	18,29.5%	43,70.5%			
>200ml/day	48,23.5%	156,76.5%			
Sunlight exposure					
<1 h/day	88,22.0%	312,78.0%	0.622	0.758 ^b	2
1-3 h/day	42,20.6%	162,79.4%			
>3 h/day	1,10.0%	9,90.0%			
Regular exercise					
No	56,24.6%	172,75.4%	2.110	0.146 ^a	0
Yes	76,19.6%	312,80.4%			

Table 6 Screening of risk factors for osteoporotic fractures Variable Osteoporotic fracture Osteoporotic fracture

a: Pearson Chi-Square, b: Fisher Exact Test

increase the incidence of OF. Therefore, health education of OP and OF should be emphasized in patients with gastrointestinal diseases to reduce the occurrence of adverse events.

Table 7 Multivariate Logistic regression analysis for the effect of independent variables on osteoporotic fractures

	Univariat	e Logistic regre	ssion		Multivariate Logistic regression B Adj. OR 95%CI 0.460 1.583 1.070-2.343 -5.838 0.003 0.000-0.104			
	В	Crude OR	95%CI	Р	В	Adj. OR	95%CI	Р
Gastrointestinal diseases	0.437	1.548	1.051-2.281	0.027	0.460	1.583	1.070-2.343	0.022
Height	-5.648	0.004	0.000-0.121	0.002	-5.838	0.003	0.000-0.104	0.001
Weight	-0.025	0.976	0.952-1.000	0.047				
Occupation				0.177				
Farmer								
Worker	-0.599	0.549	0.258-1.168	0.119				
Cadre	-0.747	0.474	0.204-1.098	0.082				
Intellectual	-0.395	0.674	0.310-1.465	0.319				
Others	-0.875	0.417	0.192-0.903	0.026				
Теа				0.098				
No or drinking occasional								
0–200ml/day	-0.518	0.596	0.244-1.453	0.255				
>200ml/day	-1.008	0.365	0.128-1.045	0.060				
Milk				0.121				
No or drinking occasional								
0–200ml/day	0.588	1.801	0.977-3.322	0.059				
>200ml/day	0.281	1.324	0.870-2.015	0.190				
Regular exercise	-0.290	0.748	0.505-1.107	0.147				

Acknowledgements

We thank all the participants for their willingness to accept the questionnaire survey.

Authors' contributions

All authors contributed to the study conception and design. PCX drafted the manuscript and participated in the questionnaire, medical records collecting. JRG provided to the study conception and critical revision of the manuscript. HJ and YJL were responsible for entered data and participated in the questionnaire, medical records collecting. YJY and XBH assisted with bone mineral density measurement. YYH and LPX were responsible for the questionnaire and medical records. The final version was reviewed and approved by all the authors.

Funding

Funding for the study came from the National Natural Science Foundation of China (81674007,82274563). The funding body has no specific restrictions in the design of the study and collection, analysis, and interpretation of data and in writing the manuscript.

Data Availability

The datasets generated and/or analysed during the current study are not publicly available due to personal protection laws. Subsets or aggregation of these data will not include information that could compromise research participants' privacy and are available from the corresponding author on reasonable request.

Declarations

Competing interests

The authors have no relevant financial or non-financial interests to disclose.

Ethics approval and consent to participate

All methods were carried out in accordance with the Declaration of Helsinki. This retrospective study performed using the data from the questionnaire survey. All participants signed informed consent to obtain necessary personal information when receiving free BMD examination. This study was approved by the Ethics Committee of Clinical Research on Traditional Chinese Medicine of Fujian Academy of Chinese Medical Sciences (approval number: 2016KY020-02).

Consent for publication

Not applicable.

Received: 31 March 2023 / Accepted: 28 July 2023 Published online: 18 August 2023

References

- Consensus. development conference: diagnosis, prophylaxis, and treatment of osteoporosis. Am J Med. 1993;94(6):646 – 50.doi: https://doi. org/10.1016/0002-9343(93)90218-e.
- Barker KL. Toye F,Lowe CJ.A qualitative systematic review of patients' experience of osteoporosis using meta-ethnography[J]. Archives of Osteoporosis 2016,11(1):33–46doi: https://doi.org/10.1007/s11657-016-0286-z.
- Compston J, Cooper A. C Cooper, UK clinical guideline for the prevention and treatment of osteoporosis[J]. Archives of Osteoporosis 2017, 12(1):43. doi: https://doi.org/10.1007/s11657-017-0324-5.
- Stein E, Shane E. Secondary osteoporosis. Endocrinol Metab Clin North Am. 2003;32(1):115–34. https://doi.org/10.1016/s0889-8529(02)00062-2. vii.
- Scaturro D, de Sire A, Terrana P, et al. Early Denosumab for the prevention of osteoporotic fractures in breast cancer women undergoing aromatase inhibitors: a case-control retrospective study. J Back Musculoskelet Rehabil. 2022;35(1):207–12. https://doi.org/10.3233/BMR-210012.
- Management of Osteoporosis in Postmenopausal Women. The 2021 position Statement of the North American Menopause Society" Editorial Panel. Management of osteoporosis in postmenopausal women: the 2021 position statement of the North American Menopause Society. Menopause. 2021;28(9):973–97. https://doi.org/10.1097/GME.000000000001831.
- Baccaro LF, Conde DM, Costa-Paiva L, Pinto-Neto AM. The epidemiology and management of postmenopausal osteoporosis: a viewpoint from Brazil. Clin Interv Aging. 2015;10:583–91.
- Scaturro D, Vitagliani F, Terrana P, et al. Does the association of therapeutic exercise and supplementation with sucrosomial magnesium improve posture and balance and prevent the risk of new falls? Aging Clin Exp Res. 2022;34(3):545–53. https://doi.org/10.1007/s40520-021-01977-x.
- Arantes HP, Kulak CA, Fernandes CE, Zerbini C, Bandeira F, Barbosa IC, Brenol JC, Russo LA, Borba VC, Chiang AY, Bilezikian JP, Lazaretti-Castro M. Correlation between 25-hydroxyvitamin D levels and latitude in brazilian postmenopausal women: from the Arzoxifene Generations Trial. Osteoporos Int. 2013;24(10):2707–12. https://doi.org/10.2147/CIA.S54614.
- Zhang H, Hu Y, Chen X, et al. Expert consensus on the bone repair strategy for osteoporotic fractures in China. Front Endocrinol (Lausanne). 2022;13:989648. https://doi.org/10.3389/fendo.2022.989648.

- Friedman SM, Mendelson DA. Epidemiology of fragility fractures. Clin Geriatr Med. 2014;30(2):175–81. https://doi.org/10.1016/j.cger.2014.01.001.
- Kanis JA, Harvey NC, Johansson H, Odén A, Leslie WD, McCloskey EV. FRAX Update. J Clin Densitom. 2017 Jul-Sep;20(3):360–7. https://doi.org/10.1016/j. jocd.2017.06.022.
- Hu Y, Zhu Y, Lu NH. The management of Helicobacter pylori infection and prevention and control of gastric cancer in China. Front Cell Infect Microbiol. 2022;12:1049279. https://doi.org/10.3389/fcimb.2022.1049279.
- Fang JY, Du YQ, Liu WZ, Ren JL, Li YQ, Chen XY, Lv NH, Chen YX, Lv B. Chinese society of Gastroenterology, Chinese Medical Association. Chinese consensus on chronic gastritis (2017, Shanghai). J Dig Dis. 2018;19(4):182–203. https:// doi.org/10.1111/1751-2980.12593.
- Marques-Silva L, Areia M, Elvas L, Dinis-Ribeiro M. Prevalence of gastric precancerous conditions: a systematic review and meta-analysis. Eur J Gastroenterol Hepatol. 2014;26(4):378–87. https://doi.org/10.1097/ MEG.0000000000000065.
- Krela-Kaźmierczak I, Szymczak A, Łykowska-Szuber L, Eder P, Linke K. Osteoporosis in gastrointestinal Diseases. Adv Clin Exp Med. 2016 Jan-Feb;25(1):185–90. https://doi.org/10.17219/acem/33746.
- Rychter AM, Ratajczak AE, Szymczak-Tomczak A, Michalak M, Eder P, Dobrowolska A, Krela-Kaźmierczak I. Associations of Lifestyle factors with Osteopenia and osteoporosis in polish patients with inflammatory bowel disease. Nutrients. 2021;13(6):1863. https://doi.org/10.3390/nu13061863.
- Seo GH, Kang HY, Choe EK. Osteoporosis and fracture after gastrectomy for stomach cancer: a nationwide claims study. Med (Baltim). 2018;97(17):e0532. https://doi.org/10.1097/MD.00000000010532.
- Park KB, Jeon CH, Lee HH, Chin H, Song KY. Prediction of risk of osteoporosis after gastrectomy for gastric cancer. BJS Open. 2021;5(6):zrab123. https://doi. org/10.1093/bjsopen/zrab123.
- Kawabata R, Takahashi T, Saito Y, Nakatsuka R, Imamura H, Motoori M, Makari Y, Takeno A, Kishi K, Adachi S, Miyagaki H, Kurokawa Y, Yamasaki M, Eguchi H, Doki Y. Analysis of the risk factors for osteoporosis and its prevalence after gastrectomy for gastric cancer in older patients: a prospective study. Surg Today. 2022 Sep 6.doi: https://doi.org/10.1007/s00595-022-02581-w.
- Targownik LE, Bernstein CN, Leslie WD. Inflammatory bowel disease and the risk of osteoporosis and fracture. Maturitas. 2013;76(4):315–9. https://doi. org/10.1016/j.maturitas.2013.09.009.
- Targownik LE, Bernstein CN, Leslie WD. Risk factors and management of osteoporosis in inflammatory bowel disease. Curr Opin Gastroenterol. 2014;30(2):168–74. https://doi.org/10.1097/MOG.00000000000037.
- Oh HJ, Ryu KH, Park BJ, Yoon BH. Osteoporosis and osteoporotic fractures in gastrointestinal disease. J Bone Metab. 2018;25(4):213–7. https://doi. org/10.11005/jbm.2018.25.4.213.
- Schüle S, Rossel JB, Frey D, Biedermann L, Scharl M, Zeitz J, Freitas-Queiroz N, Kuntzen T, Greuter T, Vavricka SR, Rogler G, Misselwitz B. Swiss IBD cohort study. Widely differing screening and treatment practice for osteoporosis in patients with inflammatory bowel diseases in the swiss IBD cohort study. Med (Baltim). 2017;96(22):e6788. https://doi.org/10.1097/ MD.00000000006788.
- Thong BKS, Ima-Nirwana S, Chin KY. Proton Pump inhibitors and fracture risk: a review of current evidence and mechanisms involved. Int J Environ Res Public Health. 2019;16(9):1571. https://doi.org/10.3390/ijerph16091571.
- Lin SM, Yang SH, Liang CC, Huang HK. Proton pump inhibitor use and the risk of osteoporosis and fracture in stroke patients: a population-based cohort study. Osteoporos Int. 2018;29(1):153–62. https://doi.org/10.1007/ s00198-017-4262-2.
- Kim JJ, Jang EJ, Park J, Sohn HS. Association between proton pump inhibitor use and risk of fracture: a population-based case-control study. PLoS ONE. 2020;15(7):e0235163. https://doi.org/10.1371/journal.pone.0235163.
- Park DH, Seo SI, Lee KJ, Kim J, Kim Y, Seo WW, Lee HS, Shin WG, Yoo JJ. Longterm proton pump inhibitor use and risk of osteoporosis and hip fractures: a nationwide population-based and multicenter cohort study using a common data model. J Gastroenterol Hepatol. 2022;37(8):1534–43. https://doi. org/10.1111/jgh.15879.
- Kanis JA, Melton LJ 3rd, Christiansen C, Johnston CC, Khaltaev N. The diagnosis of osteoporosis. J Bone Miner Res. 1994;9(8):1137–41. https://doi. org/10.1002/jbmr.5650090802.
- 30. Kanis JA, Cooper C, Rizzoli R, Reginster JY, Scientific Advisory Board of the European Society for Clinical and Economic Aspects of Osteoporosis (ESCEO) and the Committees of Scientific Advisors and National Societies of the International Osteoporosis Foundation (IOF). European guidance for the diagnosis

and management of osteoporosis in postmenopausal women. Osteoporos Int. 2019;30(1):3–44. https://doi.org/10.1007/s00198-018-4704-5.

- Tang CW, Zhang ST. Internal Medicine-Gastroenterology & Hepatology. Beijing: People's Medical Publishing House.(in Chinese; 2015.
- Messerli FH, Mancia G, Conti CR, Pepine CJ. Guidelines on the management of stable angina pectoris: executive summary: the task force on the management of stable angina pectoris of the european society of cardiology. Eur Heart J. 2006;27(23):2902–3. https://doi.org/10.1093/eurheartj/ehl308. author reply 2903.
- Chinese Society of Cardiology, Chinese Medical Association. Editorial Board, Chinese Journal of Cardiology. [Guideline for diagnosis and treatment of patients with chronic stable angina (no abstract)]. Zhonghua xin xue guan bing za zhi. 2007;35(3):195–206. (In Chinese).
- Michael JW, Schlüter-Brust KU, Eysel P. The epidemiology, etiology, diagnosis, and treatment of osteoarthritis of the knee. Dtsch Arztebl Int. 2010;107(9):152–62. https://doi.org/10.3238/arztebl.2010.0152.
- 35. Chinese Nutrition Society Obesity Prevention and Control Section; Chinese Nutrition Society Clinical Nutrition Section. Zhonghua Liu Xing Bing Xue Za Zhi. 2022;43(5):609–26. https://doi.org/10.3760/cma.j .cn112338-20220402-00253. (In Chinese)doi:, Chinese Preventive Medicine Association Behavioral Health Section; Chinese Preventive Medicine Association Sports and Health Section. [Expert Consensus on Obesity Prevention and Treatment in China].
- Alexiou KI, Roushias A, Varitimidis SE, Malizos KN. Quality of life and psychological consequences in elderly patients after a hip fracture: a review. Clin Interv Aging. 2018;13:143–50. https://doi.org/10.2147/CIA.S150067.
- Dyer SM, Crotty M, Fairhall N, Magaziner J, Beaupre LA, Cameron ID, Sherrington C. Fragility Fracture Network (FFN) Rehabilitation Research Special Interest Group. A critical review of the long-term disability outcomes following hip fracture. BMC Geriatr. 2016;16(1):158. https://doi.org/10.1186/ s12877-016-0332-0.
- Chen S, Chen T, Chen Y, Huang D, Pan Y, Chen S. Causal Association between Tea Consumption and Bone Health: a mendelian randomization study. Front Nutr. 2022;9:872451. https://doi.org/10.3389/fnut.2022.872451.
- Huang YP, Chen LS, Feng SH, Liang YS, Pan SL. Tea consumption and the risks of osteoporosis and hip fracture: a population-based longitudinal follow-up study. Osteoporos Int. 2023;34(1):101–9. https://doi.org/10.1007/ s00198-022-06569-7.
- Sun K, Wang L, Ma Q, Cui Q, Lv Q, Zhang W, Li X. Association between tea consumption and osteoporosis: a meta-analysis. Med (Baltim). 2017;96(49):e9034. https://doi.org/10.1097/MD.00000000009034.
- Lee HJ, Kim CO, Lee DC. Association between daily sunlight exposure and fractures in older korean adults with osteoporosis: a Nationwide Population-Based cross-sectional study. Yonsei Med J. 2021;62(7):593–9. https://doi. org/10.3349/ymj.2021.62.7.593.
- Rodríguez-Carrio J, Martínez-Zapico A, Cabezas-Rodríguez I, Benavente L, Pérez-Álvarez Ál, López P, Cannata-Andía JB, Naves-Díaz M, Suárez A. Clinical and subclinical cardiovascular disease in female SLE patients: interplay between body mass index and bone mineral density. Nutr Metab Cardiovasc Dis. 2019;29(2):135–43. https://doi.org/10.1016/j.numecd.2018.09.007.
- Chai H, Ge J, Li L, Li J, Ye Y. Hypertension is associated with osteoporosis: a case-control study in chinese postmenopausal women. BMC Musculoskelet Disord. 2021;22(1):253. https://doi.org/10.1186/s12891-021-04124-9.
- Rodríguez-Gómez I, Gray SR, Ho FK, Petermann-Rocha F, Welsh P, Cleland J, Iliodromiti S, Ara I, Pell J, Sattar N, Ferguson LD, Celis-Morales C. Osteoporosis and Its Association With Cardiovascular Disease, Respiratory Disease, and Cancer: Findings From the UK Biobank Prospective Cohort Study. Mayo Clin Proc. 2022;97(1):110–121.doi: 10.1016/j.mayocp.2021.07.019.
- Grassi M, Petraccia L, Mennuni G, et al. Changes, functional disorders, and diseases in the gastrointestinal tract of elderly. Nutr Hosp. 2011 Jul-Aug;26(4):659 – 68. doi: 10.1590/S0212-16112011000400001.
- Cruz-Jentoft AJ, Sayer AA. Sarcopenia. Lancet. 2019;393(10191):2636–2646. doi: 10.1016/S0140-6736(19)31138-9.
- 47. Merlotti D, Mingiano C, Valenti R, et al. Bone Fragility in Gastrointestinal Disorders. Int J Mol Sci. 2022;23(5):2713. doi: 10.3390/ijms23052713.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.