Correlation of Fat Mass with Bone Mineral Density and FRAX-based Fracture Risk among Postmenopausal Filipino Women

Davidson V. Pastrana, MD, Jerry M. Obaldo, MD

Division of Nuclear Medicine, Philippine General Hospital
E-mail address: davidson.pastrana@gmail.com, jerryobaldo@yahoo.com

ABSTRACT

Background:

Post-menopausal women experiences changes in estrogen levels affecting body metabolism, which may lead to weight gain and obesity. Moreover, one of the most prevalent diseases among this group is osteoporosis. However, the relationship between fat mass and its protective property remains unclear. This study assesses the correlation of fat mass with bone mineral density (BM) and 10-year FRAX based fracture probability among Filipino women.

Methods:

A cross-sectional review of records of post-menopausal Filipino women who underwent whole body bone mineral densitometry scans via dual-energy X-ray absorptiometry (DXA) between January 1, 2015, and December 31, 2018 in the Radioisotope Laboratory of the Philippine General Hospital was done. Pearson correlation and simple linear regression analyses were done to determine the correlation between the two outcomes – BMD and 10-year FRAX based fracture probability.

Results:

A total of 258 postmenopausal women were included in the analysis. There was a weak positive correlation of fat mass with BMD of L1-L4 vertebrae (R-score of 0.318), BMD of femoral neck (R-score of 0.3937) and hips (R - score of 0.3031). The 10-year FRAX based fracture probability for both hip and osteoporotic had very weak and weak negative correlation, respectively (R-score of - 0.06752 and - 0.29017).

Conclusion:

Despite having varying available, data on the protective effects of fat mass on fracture protection, this study showed that fat mass has a poor correlation with BMD and reduction in FRAX probability.

INTRODUCTION

Osteoporosis, described as state of low bone mineral density with deterioration of bone tissue and disruption of bone microarchitecture, which predisposes individuals to having fragility fractures [1]. In the United States alone 1.5 million were reported to have fractures from osteoporosis [2]. Even though there is no available exact number of figures for the Philippines on osteoporosis yet [3], a study conducted by Miura and Saavedra among post-menopausal women in Davao city showed a prevalence of 19.8% [4]. It is also important to note that osteoporosis is the most prevalent disease among menopausal women [5]. Through the years, dual-energy x-ray absorptiometry (DXA) has been an important and convenient tool in screening for osteoporosis, and with this technology whole body composition analysis including percent body fat became available as well. Aside from using the DXA to classify patients as to having osteoporosis, the World Health Organization (WHO) has developed the Fracture Risk Assessment Tool (FRAX®: http://www.shef.ac.uk/FRAX/), which provides a model to assess the 10-year probability of a major osteoporotic fracture (clinical spine, forearm, hip or shoulder fracture) and of a hip fracture, by using easily obtainable clinical risk factors with or without femoral neck (FN) BMD [6]. Hormonal changes happen during menopause, and an example of which is the decline of estrogen level in the body. This can affect lipid metabolism and observations point to higher prevalence of weight gain and obesity among menopausal women [7]. However, the relationship between body fat and bone mineral density (BMD) remains unclear as various studies show conflicted results on whether fat mass has protective value against osteoporosis [8-18]. This study aims to correlate the BMD and FRAX-based fracture risk values of postmenopausal Filipino women to the fat mass.

 Phil J Nucl Med 2021; 16(1):18 - 24

Osteoporosis

Osteoporosis is a disease that is described by low bone mineral density, bone tissue deterioration and disruption of its architecture, which leads to decrease in bone strength and higher risk of fracture [1]. According to WHO criteria, a person is classified as to having osteoporosis if the BMD value lies at least 2.5 standard deviations below the average value for young healthy women (T-score of <-2.5 SD) [19]. This disease has resulted in 1.5 million fracture per year in the US [2] and in Asian countries, there was notable increase in the hip fractures as well among the osteoporotic population [20].

Menopause

Menopause signifies the end of the reproductive potential of a woman [21] and is defined as amenorrhea for 12 months after the last menstrual period, as a result of depletion of pool of follicles and estrogen production [7]. Numerous symptoms appear during menopause, such as hot flashes, sleep and mood changes, metabolic problems – increase in body weight, insulin resistance and glucose and lipid metabolism, which increases the risk of type 2 diabetes, osteoporosis, cardiovascular and oncological diseases [7].

Estrogen promotes fat oxidation in the skeletal muscles and inhibits hepatic and muscle lipogenesis [9]. The amount of this hormone declines in menopause, hence it is expected that it will result in increase in visceral fat mass and abdominal obesity [7]. Zhao et al in 2008, noted there is unclear benefit of fat mass on the BMD [8]. Several studies showed a positive correlation of BMD values with fat mass [9-13] while other studies contrasted that excessive fat mass may not be beneficial [14-18].

FRAX

The guidelines have veered away from solely using BMD values for managing osteoporosis. Clinical risk factors are now also being used to determine risk of developing fractures and which patients would need treatment. And with this, FRAX, a tool developed by WHO, has been useful in identifying individuals who may need to start treatment even in the absence of BMD values [22]. A 10-year FRAX-based hip fracture probability of at least 3%, or a major osteoporosis-related fracture probability of at least 20% are considered clinically significant and are recommended for pharmacologic treatment [23].

A study conducted by Zhang et al in 2012 among central south Chinese postmenopausal women showed negative relationship between the FRAX values and fat mass, however, lean mass had a better impact on the risk of fractures. [24] In another study done in Canada neither lean mass nor fat mass affected the prediction of major osteoporosis and hip fractures based on FRAX scores analysis. [25]

This study aims to determine the correlation of fat mass with BMD values and with the FRAX-based 10-year fracture among post-menopausal Filipino women patients in the Philippine General Hospital.

MATERIALS AND METHODS

Study Design and Sample Population

This is a cross-sectional review of records of post-menopausal Filipino women who underwent whole body bone mineral densitometry scans via dual-energy X-ray absorptiometry (DXA) between January 1, 2015, and December 31, 2018 in the Radioisotope Laboratory of the Philippine General Hospital. Only a total of 258 post-menopausal female patients' records were identified available during the given time period and were included in the analysis.

Patients who had vertebral fixations and hip surgery with metal implants were excluded in the study for this will affect the accuracy of the BMD values measured by the DXA machine. Patients under the age of 40 were also excluded due to unavailability of computed FRAX probability. Moreover, those with identified conditions that may cause secondary bone loss and may affect bone density will not be included in the study. These conditions are as follows: hypogonadism, primary hyperparathyroidism, thyrotoxicosis, hypercortisolism, vitamin D deficiency, malignancy, chronic renal diseases, prolonged steroid use and liver diseases.

Age, height, weight, computed BMI, bone mineral density values of L1-L4 vertebrae, bilateral femoral necks and total hips, FRAX score with bone mineral density value, total fat mass (in kilograms and percentage) values generated by the DXA machine from the whole body composition scan.

Ethical Approval

The University of the Philippines Research Ethics Board gave ethical approval for the conduct of this study.

Statistical Analysis

The encoded data in Microsoft Excel for Mac version (Edmonton, Washington, USA) was imported to the STATA 15 (StataCorp, Lakeway Drive, College Station, Texas, USA). The means and standard deviations were used to summarize all normally distributed data while the medians and interquartile ranges were used to summarize all non-normally distributed data. Pearson correlation and simple linear regression analyses were done to determine the correlation between the two outcomes – BMD and FRAX – with the following potential confounders: age in completed years, height in centimeters, weight in kilograms, and BMI in kg/m2. The beta coefficients for the primary effect variable and potential confounders were reported along with its standard error, 95% confidence interval, R-score, and p-values. A p-value of less than 0.05 is considered statistically significant.

RESULTS

Table 1 shows the demographic characteristics of the post-menopausal women. The means ± standard deviations of all participants in terms of age, weight, height and body mass index (BMI) are 64.310 ± 9.001, 57.756 ± 10.555, 152.800 ± 5.876 and 24.678 ± 4.044, respectively.

In terms of BMD of all participants, the hips exhibited the highest mean (0.838 ± 0.181), followed by the L1-L4 vertebrae (0.791 ± 0.179), then lastly by the femoral necks (0.730 ± 0.142). FRAX (osteoporotic) showed a higher mean (3.129 ± 1.744) when compared to the FRAX (hip) (1.058 ± 1.275). Furthermore, the means ± standard deviations of the total fat mass in % and kg are 40.603 ± 6.941 and 23.602 ± 6.829, respectively.

The correlation of BMD (L1-L4) with weight is moderately positive, while its correlation with fat mass (kg) and BMI is weakly positive. Furthermore, the correlation of BMD (L1-L4) with height and fat mass (%) is considered very weakly positive.

Among the different variables in analysis of BMD of the femoral neck with the different variables, only age showed a negative β-coefficient (- 0.0066) and R-score (- 0.4196), thereby exhibiting a low negative correlation. The correlation of BMD (femoral neck) with weight is moderately positive, while its correlation with fat mass (kg) and BMI is weakly positive. Furthermore, the correlation of BMD (femoral neck) with height and fat mass (%) is considered very weakly positive. The correlation of BMD (femoral neck) with fat mass (%) is not statistically significant ($p = 0.063737$), while the rest of the correlations are considered statistically significant ($p < 0.05$).

The correlation of BMD (total hips) with weight, fat mass (kg) and BMI is weakly positive. Furthermore, the correlation of BMD (total hips)) with height and fat mass (%) is considered very weakly positive. The correlation of BMD (hips) with fat mass (%) is likewise not statistically significant ($p = 0.082811$), while the rest of the correlations are considered statistically significant ($p < 0.05$).

For FRAX (hips) inverse pattern when compared with the BMD tables. The correlation of FRAX hip (%) with weight and BMI is considered weakly negative, while its correlation with fat mass (%), fat mass (kg) and height is very weakly negative. The correlation of FRAX hip with fat mass (kg) is likewise not statistically significant ($p = 0.2836$), while the rest of the correlations are considered statistically significant ($p < 0.05$).

The correlation of FRAX with the fat mass and other clinical variables showed a similar pattern with Table 2. As before, only age showed a positive β-coefficient (0.08992) and R-score (0.4642), thereby exhibiting a low positive correlation. The correlation of FRAX osteoporotic (%) with weight and BMI is considered weakly negative, while its correlation with fat mass (%), fat mass (kg) and height is very weakly negative. All the correlations made in this table are considered statistically significant, since all p-values are less than 0.05.

TABLE 1. Demographics and clinical characteristics in terms of BMD, FRAX and total fat mass of post-menopausal wom-

Characteristic	Means (SD)	Standard Error	95% CI
Age (completed years)	64.310 ± 9.001	0.560	63.212 to 65.408
Weight (kg)	57.756 ± 10.555	0.657	56.468 to 59.044
Height (cm)	152.800 ± 5.876	0.366	**56.468 to 59.045**
Body Mass Index (kg/m^2)	24.678 ± 4.044	0.252	24.185 to 25.172
BMD (L1-L4)	0.791 ± 0.179	0.011	0.769 to 0.812
BMD (Femoral Necks)	0.730 ± 0.142	0.009	0.713 to 0.902
BMD (Total Hips)	0.838 ± 0.1813	0.011	0.816 to 0.860
FRAX hip	1.058 ± 1.275	0.079	0.903 to 1.213
FRAX osteoporotic	3.129 ± 1.744	0.108	2.917 to 3.341
Total Fat Mass (%)	40.603 ± 6.941	0.432	39.756 to 41.450
Total Fat Mass (kg)	23.602 ± 6.829	0.425	22.769 to 24.435

TABLE 2. Correlation of BMD (L1-L4, femoral neck, and total hip) and FRAX with Fat Mass and other clinical variables

Clinical Variable	BMD (L1-L4)		BMD Femoral Neck		BMD Total Hip		FRAX (hip)		FRAX (major)	
	R-score	p-value	R-score	p-value	R-score	p-value	R-score	p-value	R-score	p-value
Fat mass (kg)	0.3108	p < 0.00001	0.3937	p < 0.00001	0.3031	p < 0.00001	-0.06752	0.2836	-0.29017	p < 0.00001
Fat mass (%)	0.0497	p < 0.00001	0.1156	0.063737	0.1082	0.082811	-0.1937	0.001844	-0.1268	0.043166
Height	0.2545	0.000035	0.2700	0.000011	0.2362	0.000128	-0.2111	0.000647	-0.2262	0.000252
Weight	0.5227	p < 0.00001	0.5224	p < 0.00001	0.4625	p < 0.00001	-0.4678	p < 0.00001	-0.4076	p < 0.00001
BMI	0.4756	p < 0.00001	0.4753	p < 0.00001	0.4231	p < 0.00001	-0.4325	p < 0.00001	-0.3578	p < 0.00001
Age	-0.2226	0.000326	-0.4196	p < 0.00001	-0.3695	p < 0.00001	0.4108	p < 0.00001	0.4642	p < 0.00001

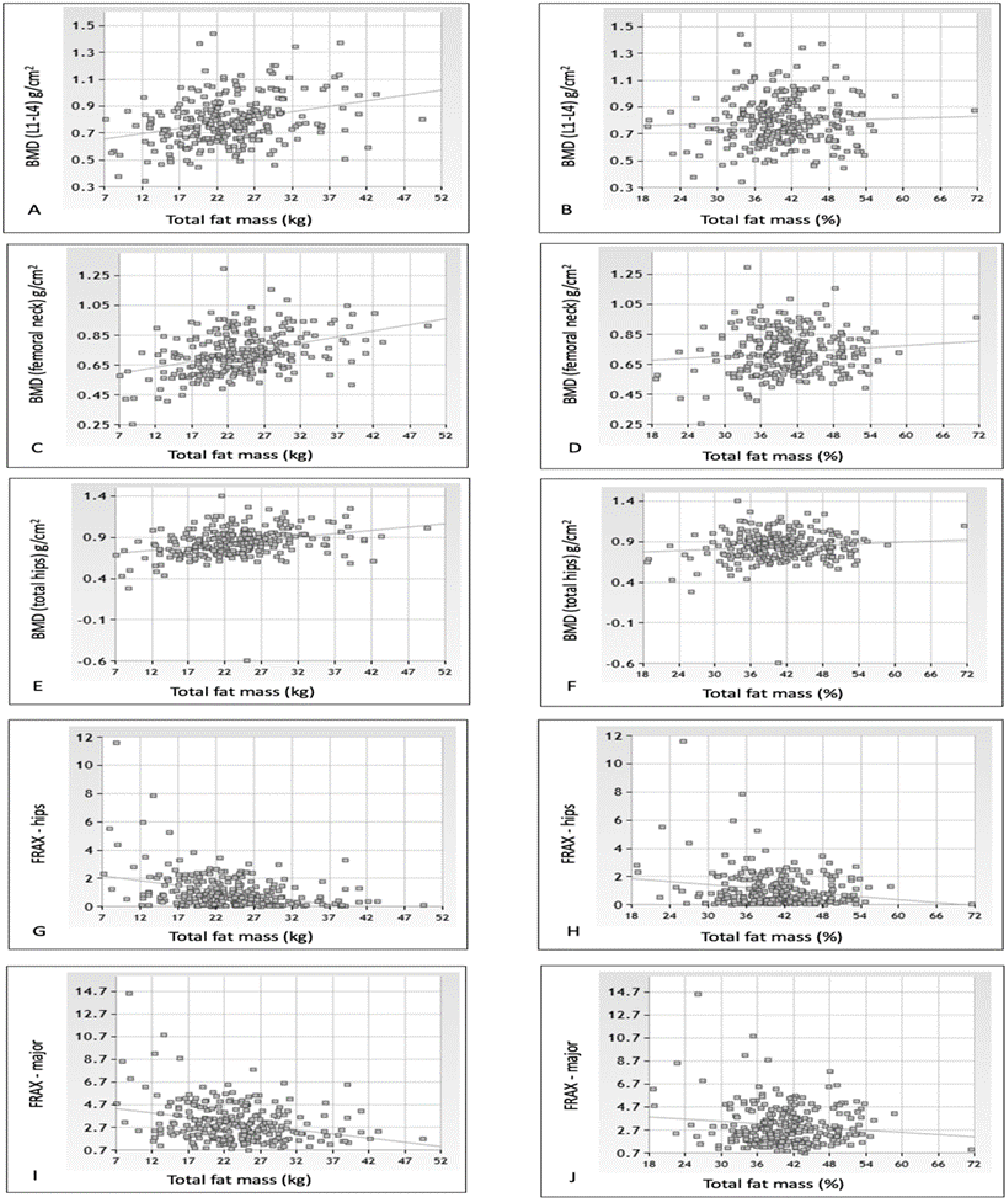

Figure 1. Scatter plots of fat mass (total in kg and percentage) vs BMD (L1-L4, femoral neck and total hips) and 10-year probability of fracture with bone mineral density (hips and major). (A) R-score = 0.3108 , P < 0.00001 ;(B) R-score = 0.0497, P < 0.00001; (C) R-score = 0.3937, P < 0.00001; (D) R-score = 0.1156, P= 0.063737; (E) R-score = 0.3031, P < 0.00001; (F) R-score = 0.1082, P = 0.082811; (G) R-score = -0.06752, P = 0.2836; (H) R-score = -0.1937, P = 0.001844; (I) R -score = -0.29017, P < 0.00001; (J) R-score = -0.1268, P = 0.043166

DISCUSSION

To the best of our knowledge, this is the first study identifying the possible correlation of fat mass to bone mineral density and 10-year FRAX based-fracture risk among post-menopausal Filipino women. Our findings showed that most post-menopausal women in this study has a mean of 40.6029 ± 6.9414 percentage fat mass. Though there is no specific recommendation on what the ideal percentage body fat mass is, a percentage of more than 30% for women equates to obesity [26].

Increase in body weight in the form of central obesity and changes in metabolism happen during menopause. This is attributed to the rapid decrease in estrogen in the body. Though not only it is hormonal, different environmental, genetic and lifestyle factors should be considered in weight gain and fat accumulation during this period [7]. According to Zhao in 2008, overweight individuals were said to have higher BMD values than individuals who weigh less. It was explained that greater fat mass imposes greater mechanical stress so that the bone adapts by increasing its mass to accommodate the heavier load. In addition, adipose tissues were said to expresses estrogen, resistin, leptin, adiponection, and interleukin-6, which may be involved with bone metabolism, contributing to the relationship between fat and bone [8]. With this premise, fat could be a protective from bone fracture and osteoporosis. This was supported by various studies that leave a general consensus that heavier individuals are said to be more protected against fractures and osteoporosis [27-29].

However, in this study, there was a weak positive correlation between BMD (L1-L4, femoral neck and hip) and fat mass. The reduction in the 10-year FRAX based fracture risk (hip and osteoporotic) showed very weak negative correlation. Theoretically, given that the increased fat mass may possibly be protective to osteoporosis and probable fracture, this was not observed in the study. In contrast to the possibility that fat mass could be protective, a study done by Hsu and colleagues in 2006, noted a higher percentage fat mass showed negative effect on bone mass in contrast with the positive effect of weight-bearing.

Looking into other parameters in the correlation analyses, only weight had moderately positive correlation with the BMD of L1-L4 vertebrae and femoral neck. An all other parameters showed weak correlation with BMD and 10-year FRAX based fracture risk (hip and osteoporotic).

With this study showing that weight has moderately positive correlation to BMD, and having fat mass weakly correlated to BMD and FRAX risk reduction, perhaps this could be taken into account the importance of other components of weight. Ilesanmi-Oyelere and colleagues in 2018 found that among postmenopausal women lean mass has been the strongest predictor for femoral neck, spine and whole body BMD [30]. This may suggest that with the weak correlation of fat mass among postmenopausal Filipino women with BMD and FRAX based risk reduction, and importance of weight to promote increase in BMD, lean mass should be of more focus on protective against fractures. Increasing body fat for fracture protection may not be advised for increased body fat may also be attributed to other diseases.

While our findings were contradicting with different studies with different population, having a data set reference for Filipino women could still be of value and may help contribute in creating future recommendations.

LIMITATIONS OF THE STUDY

One limitation of the study is the relatively small number of subjects included in the analysis. It could be recommended for future analysis that more subjects be included by possibly including data from other institutions.

CONCLUSION

Among postmenopausal Filipino women, fat mass has a weak and positively correlation with bone mineral density and weak negative correlation with FRAX related fracture risk. Weight showed moderately positive correlation on lumbar and femoral neck BMD. In relation to this, lean mass may be a better factor to check for its protective capability.

REFERENCES

1. NIH Consensus Development Panel on Osteoporosis Prevention, Diagnosis, and Therapy. Osteoporosis prevention, diagnosis, and therapy. JAMA 2001; 285: 785-95.
2. Black, D. M., & Rosen, C. J. (2016). *Postmenopausal Osteoporosis. New England Journal of Medicine, 374(3), 254–262.*doi:10.1056/nejmcp1513724.
3. Tito, Torralba (2004). Clinical management of osteoporosis in the Philippines. Clinical calcium 14(9):134-7.
4. Miura, S., Saavedra, O.L. & Yamamoto, S. Arch Osteoporos (2008) 3: 17. https://doi.org/10.1007/s11657-008-0018-0.

4. Miura, S., Saavedra, O.L. & Yamamoto, S. Arch Osteoporos (2008) 3: 17. https://doi.org/10.1007/s11657-008-0018-0.

5. JI, Meng-Xia and Yu, Qi (2015). Primary osteoporosis in postmenopausal women. Chronic Dis Transl Med. 2015 Mar; 1(1): 9–13. doi: 10.1016/j.cdtm.2015.02.006.

6. Sherman, Sherry Defining the menopausal transition The American Journal of Medicine (2005) Vol 118 (12B), 3S–7S doi:10.1016/j.amjmed.2005.11.002.

7. Jarosław Kozakowski, Małgorzata Gietka-Czernel, Dorota Leszczyńska, and Agnieszka Majos (2017) Obesity in menopause – our negligence or an unfortunate inevitability? Prz Menopauzalny. 2017 Jun; 16(2): 61–65. 2017 Jun 30. doi: 10.5114/pm.2017.68594.

8. Zhao LJ, Jiang H, Papasian CJ, Maulik D, Drees B, Hamilton J, Deng HW. (2008) Correlation of obesity and osteoporosis: effect of fat mass on the determination of osteoporosis. J Bone Miner Res. 2008;23:17–29.

9. Reid IR, Ames R, Evans MC, Sharpe S, Gamble G, France JT, Lim TM, Cundy TF (1992) Determinants of total body and regional bone mineral density in normal postmenopausal women—a key role for fat mass. J Clin Endocrinol Metab 75:45–51.

10. Reid IR, Plank LD, Evans MC (1992) Fat mass is an important determinant of whole body bone density in premenopausal women but not in men. J Clin Endocrinol Metab 75:779 –782.

11. Khosla S, Atkinson EJ, Riggs BL, Melton LJ III (1996) Relationship between body composition and bone mass in women. J Bone Miner Res 11:857–863.

12. Douchi T, Oki T, Nakamura S, Ijuin H, Yamamoto S, Nagata Y (1997) The effect of body composition on bone density in preand postmenopausal women. Maturitas 27:55–60.

13. Douchi T, Yamamoto S, Oki T, Maruta K, Kuwahata R, Nagata Y (2000) Relationship between body fat distribution and bone mineral density in premenopausal Japanese women. Obstet Gynecol 95:722–725.

14. De Laet C, Kanis JA, Oden A, Johanson H, Johnell O, Delmas P, Eisman JA, Kroger H, Fujiwara S, Garnero P, McCloskey EV, Mellstrom D, Melton LJ III, Meunier PJ, Pols HA, Reeve J, Silman A, Tenenhouse A (2005) Body mass index as a predictor of fracture risk: A meta-analysis. Osteoporos Int 16:1330–1338.

15. Goulding A, Jones IE, Taylor RW, Williams SM, Manning PJ (2001) Bone mineral density and body composition in boys with distal forearm fractures: A dual-energy x-ray absorptiometry study. J Pediatr 139:509–515.

16. Mobley SL, Ha E, Landoll JD, Badenop-Sevens NE, Clairmont A, Goel P, Matkovic V (2005) Children with bone fragility fractures have reduced bone mineral areal density at the forarm and hip and higher percent body fat. J Bone Miner Res 20:S34.

17. Hsu YH, Venners SA, Terwedow HA, Feng Y, Niu T, Li Z, Laird N, Brain JD, Cummings SR, Bouxsein ML, Rosen CJ, Xu X (2006) Relation of body composition, fat mass, and serum lipids to osteoporotic fractures and bone mineral density in Chinese men and women. Am J Clin Nutr 83:146 –154.

18. Blum M, Harris SS, Must A, Naumova EN, Phillips SM, Rand WM, Dawson-Hughes B (2003) Leptin, body composition and bone mineral density in premenopausal women. Calcif Tissue Int 73:27–32.

19. Assessment of fracture risk and its application to screening for postmenopausal osteoporosis. Report of a WHO Study Group. Geneva, World Health Organization, 1994 (WHO Technical Report Series, No. 843).

20. Mithal, A., & Kaur, P. (2012). *Osteoporosis in Asia: A Call to Action. Current Osteoporosis Reports, 10(4), 245 – 247.* doi:10.1007/s11914-012-0114-3 .

21. Sherman, Sherry Defining the menopausal transition The American Journal of Medicine (2005) Vol 118 (12B), 3S –7S doi:10.1016/j.amjmed.2005.11.002.

22. Kanis, J.A., Johnell, O., Oden, A. et al. (2008) FRAXTM and the assessment of fracture probability in men and women from the UK. Osteoporosis International, 19, 385–397.

23. Cosman, F., de Beur S.J. et al, (2014). Clinician's Guide to Prevention and Treatment of Osteoporosis. Osteoporos Int (2014) 25:2359–2381 DOI 10.1007/s00198-014-2794-2.

24. Zhang, Z., Shen, X., Zhang, H., Li, S., Zhou, H., Wu, X., Liao, E. (2012). The relationship between body composition and fracture risk using the FRAX model in central south Chinese postmenopausal women. Clinical Endocrinology, 77(4), 524 –530. doi:10.1111/j.1365-2265.2012.04399.x

25. Leslie, W., Orwoll, E., Nielson, C., Morin, S., Majumdar, S., Johansson, H., Odén, A., McCloskey, E. and Kanis, J. (2014). Estimated Lean Mass and Fat Mass Differentially Affect Femoral Bone Density and Strength Index but Are Not FRAX Independent Risk Factors for Fracture. *Journal of Bone and Mineral Research*, 29(11), pp.2511-2519.

26. Shah NR, Braverman ER. (2012) Measuring adiposity in patients: The utility of body mass index (BMI), percent body fat, and leptin. PLoS ONE. 2012;7(4):e33308.

27. Bainbridge KE, Sowers M, Lin X, Harlow SD. (2004) Risk factors for low bone mineral density and the 6-year rate of bone loss among premenopausal and perimenopausal women. Osteoporos Int. 2004;15(6):439–446.

28. Ho SC, Chan SG, Yip YB, Chan CS, Woo JL, Sham A (2008). Change in bone mineral density and its determinants in pre - and perimenopausal Chinese women: The Hong Kong Perimenopausal Women Osteoporosis Study. Osteoporos Int. 2008;19(12):1785–1796.

29. Hui SL, Perkins AJ, Zhou L, et al. (2002) Bone loss at the femoral neck in premenopausal white women: Effects of weight change and sex-hormone levels. J Clin Endocrinol Metab. 2002;87(4):1539–1543.

30. Ilesanmi-Oyelere BL, Coad J, Roy N, Kruger MC. (2018). Lean Body Mass in the Prediction of Bone Mineral Density in Postmenopausal Women. Biores Open Access. 2018 Oct 10;7(1):150-158. doi: 10.1089/biores.2018.0025. PMID: 30327744; PMCID: PMC6188582.