Ibn Al-Haitham Journal for Pure and Applied science https://doi.org/ 10.30526/2017.IHSCICONF.1798

Cardiovascular Risk Assessement in Osteoporotic Patients Using Osteoprotegerin as a Reliable Predictive Biochemical Marker

Noora W. Rasheed
dr.noora86@gmail.com
Al-Rafidain University College
Ooroba J. Taresh
Dept. of Physics /College of Education for Pure Science (Ibn Al-Haitham)
University of Baghdad

Abstract

Some studies indicated a relationship between increased serum levels of osteoprotegerin with arterial calcification and as a result, it leads to the risk of cardiovascular disease. In our study group we selected patients with osteoporosis, with similar age and body mass index for the assessment of the relationship between cardiovascular disease and osteoprotegerin serum level. We took into account the analysis of correlation and association between the presence of distinct patterns of atherosclerosis and associated diseases like high blood pressure, diabetes mellitus, low HDL cholesterol, increased LDL cholesterol, increased triglycerides and was the case of presence of any type of dyslipidemia, in case of pre-existent treatment.

Objective of study was the assessment of osteoprotegerin value as predictive marker for cardiovascular and metabolic risk in osteoporotic patients.

Our results showed significant correlations of parathyroid hormone, osteocalcin and biochemical markers of bone with glucose metabolism and lipid were found in our research, maintaining crosstalk between calcium and biochemical markers of bone and cardiovascular risk.

The serum level of Osteoprotegerin has been shown to have a large predictive value for the metabolic syndrome as a cardiovascular risk standard in patients with osteoporosis. The osteoprotegerin serum levels were increased in the patients with metabolic syndrome as a protective response facing the atherosclerotic lesions.

Keywords: osteoprotegerin , cardiovascular disease, metabolic syndrome

1. Introduction

Osteoporosis is a disorder characterized by decreased bone strength and increased risk of fracture, which occurs due to an imbalance in the bone remodeling process, where bone resorption exceeds bone formation [8]. Several evidences have shown in the last years a possible correlation between cardiovascular disease and osteoporosis. Studies regarding the CVD and cardiovascular mortality are associated with low bone mineral density (BMD) and bone fractures [1]. Patients affected with osteoporosis have a higher risk of CVD than subjects with normal bone mass[2]. Osteoprotegerin described as key regulators in metabolic bone disease and also have been discriminated as regulator in immunological function[3].The relationship between cardiovascular diseases and osteoprotegerin explains common risks such as age, lack of exercise, smoking and alcoholism [4]. Similarly, inflammation plays a pivotal role in both atherosclerosis and osteoporosis.[5]. Arterial calcification is a part of the atherosclerotic process leading to clinical cardiovascular disease. The presence of OPG in atherosclerotic plaques has been described, and studies have shown that it is located in areas of calcification.

Some studies indicated a relationship between increased serum levels of osteoprotegerin with arterial calcification and as a result, it leads to the risk of cardiovascular disease [6]. Vascular calcification and bone mineralization share a number of interesting anatomical and pathophysiological common features. In fact, the calcification of the arterial tissue is not just a passive process of precipitation or absorption of phosphate and calcium but it is a highly organized and regulated by mechanisms similar to those involved in bone mineralization [7].

In vitro studies show as the OPG may be important for endothelial cells survival and inhibition of calcification; it appears that the OPG protect from vascular calcification and elevated levels have been found in patients with CVD [9].

The aim of the study was to evaluate osteoprotegerin value as predictive marker for cardiovascular and metabolic risk in osteoporotic patients.

2. Materials and Methods

Analyse the subgroup of patients with measured serum Osteoprotegerin

Seventy one women (48 postmenopausal and 23 premenopausal) In our study group we selected patients with osteoporosis, with similar age and body mass index in the ELIAS hospital, Bucharest Romania, in order to evaluate the relationship between osteoprotegerin serum levels and the cardiovascular pathology. We took into account the analysis of correlation and association between the presence of distinct patterns of atherosclerosis and associated diseases like diabetes mellitus, high blood pressure, low HDL cholesterol, increased LDL cholesterol, increased triglycerides and was the case of presence of any type of dyslipidemia, in case of pre-existent treatment .

For bone metabolism, total serum calcium, total alkaline phosphates (total ALP), the parathyroid hormone (PTH), 25-Hydroxy Vitamin D (25-OH vitamin D), serum osteocalcin, serum osteoprotegerin and serum betacrosslabs. Serum osteocalcin, osteoprotegerin and 25-OH vitamin D were assessed using immunologic ELISA methods, PTH was analysed through a chemiluminometric method, while calcium and ALP were measured using spectrophotometric methods.

Ethics statement. Our research involved human participants and has been approved by Elias Hospital Ethics Committe. All clinical investigation has been conducted acccording to the principle expressed in the Declaration of Helsink Statistical analysis. Data analysis are presented as mean and standard deviation. Clinical characteristics were compared using the *t* Student test. Significant was defined at the 0.05 level of confidence. All calculations were performed using the Statistical Package for Social science software (SPSS).

3. Results and Discussion

Serum total calcium did correlate to the time spent in postmenopausal period in these patients. Comparing to the all group analysis, there is no meaningful difference between these findings: years since menopause are highly correlated to age.

Serum total calcium was found to be directly correlated with urinary calcium excretion, in accordance to the previously described correlation with PTH and osteocalcin. Calcemia was also significantly corelated with serum osteocalcin in all group analysis; instead in the OPG group a correlation to the crosslaps has the same meaning, that serum total calcium is correlated to an increased bone turnover.

Serum 25 OH vitamin *D levels* were found to be negatively correlated with age (table 2) in the OPG subgroup. Increased age is a well known risk factor for low 25 (OH) vitamin D levels which was confirmed in our data.Several factors found in the elderly people may be the cause of this aspect: low sun exposure due to invalidity, skin alteration with age, decreased activation of vitamin D in the kidney[4]. The inverse relationship between PTH and 25 (OH) vitamin D was not significant anymore compared to the extended group; the explanation might be the lower case number or the lower prevalence of vitamin D defficiency in this subgroup which alleviates it.

Serum Osteocalcin levels were found to be directly correlated to HDL-cholesterol in the OPG subgroup (table 1), a relationship explained by the utility of osteocalcin in the evaluation of the cardiovascular risk, an intensively explored aspect in the latest years[10]. Compared to the extended group, osteocalcin was no more correlated to blood calcium, PTH levels and serum crosslaps The Osteoprotegerin serum levels were found to be directly and significantly correlated to HDL –cholesterol, total ALP and serum PTH (Table 1). These correlations sustain the protective role of the OPG for cardiovascular diseases and, in the same time, the link to the bone metabolism.

Table (1): A Comparison between study subgroups according to the Mets presence criteria among OPG available subjects: clinical, lipid and glucose parameters

Biochemical parameter	Control group (no Mets)	Study group (Mets present)
Age* (years)	61 [19]	70 [17.5]
BMI** (kg/m^2)	24.5 [4.7]	26.3 [3.7]
Years since menopauze*	40 [45]	41 [48]
Blood glucose* (mg/dL)	87 [12]	107 [17]
Total cholesterol** (mg/dL)	200 (53.8)	231.8 (42.89)
HDL Cholesterol* (mg/dL)	56 [18]	58 [17]
LDL Cholesterol** (mg/dL)	119 (43.3)	138 (43.1)
Triglicerides** (mg/dL)	94.4 (35.1)	146.1 (52.5)

Table (2):A Pearson correlation coefficients between calcium and bone, clinical, lipid andglucose parameters in osteoprotegerin subgroup

	Age (yrs)	BMI (kg/m^2)	Years since menopause (yrs)	Blood glucose (mg/dL)	Total cholesterol (mg/dL)	HDL Cholesterol (mg/dL)	LDL Cholesterol (mg/dL)	Triglicerides (mg/dL)
Serum total Calcium (mg/dL)	0.151	-0.176	-0.546*	-0.200	-0.169	0.395	-0.283	-0.233
Calcium urine excretion (mg/24 hrs)	-0.098	0.268	0.373	0.080	-0.544	-0.425	-0.181	0.008
Total ALP (UI/L)	0.310	0.090	0.103	0.211	0.134	-0.103	0.090	0.143
PTH (pg/mL)	0.065	0.128	0.090	0.491**	0.127	0.225	0.030	0.268*
25OH Vit D (ng/mL)	-0.358**	-0.100	0.261	-0.152	-0.170	-0.101	-0.128	-0.267
Osteocalcin (ng/mL)	-0.194	-0.116	0.206	-0.011	0.035	0.344*	-0.035	-0.136
Crosslaps (ng/mL)	-0.598	0.458	0.212	-0.101	0.040	0.830**	-0.586	-0.008
Osteoprotegerin (pmol/L)	0.101	0.078	-0.079	0.245	0.246	0.333*	0.264	0.023
*. Correlation is significant at the 0.05 level (2-tailed).								
**. Correlation is significant at the 0.01 level (2-tailed).								

Among calcium and bone biochemical markers, 25 (OH) vitamin D and Osteoprotegerin serum levels were significantly different across the study groups (table3).

Table(3):A Comparison between study subgroups according to the Mets presence criteria among OPG available subjects: bone markers parameters.

Biochemical parameter	Control group (without Mets)	Study group (Mets present)
Serum total Ca** (mg/dL)	9.3 (0.5)	10 (0.8)
24 hrs urine calcium* (mg/24 hrs)	158 [151]	118 [168]
Total ALP* (UI/L)	87 [90]	134 [109]
iPTH* (pg/mL)	77.2 [13.3]	80.6 [16.9]
25 HO Vit D* (ng/mL)	30 [39]	17.4 [11.1]
Osteocalcin* (ng/mL)	10.4 [12.4]	10.1 [10.1]
Crosslaps* (ng/mL)	0.448 [0.137]	0.132 [0.389]
Osteoprotegerin baseline** (pmol/L)	5.15 (0.54)	5.6 (0.68)

Osteoprotegerin levels were higher in the Mets group it has been suggested that increased level of OPG in patients with cardiovascular risk is due to the protective effect of Osteoprotegerin, but mechanisms are still under debate.

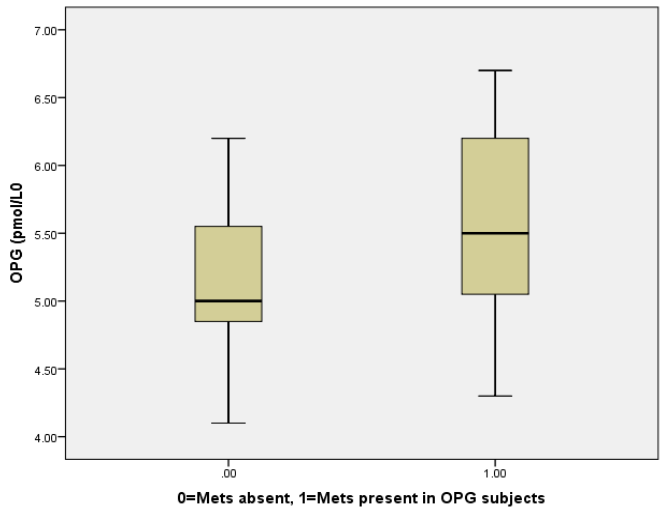

Figure (1): Correlation of OPG (pmol/L) with the occurence of metabolic syndrome.

For more information about the Conference please visit the websites:
http://www.ihsciconf.org/conf/
www.ihsciconf.org

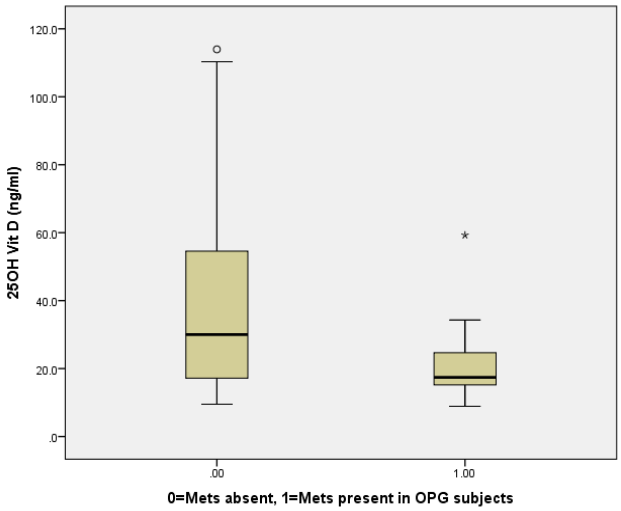

Figure (2): Correlation of 25 (OH) vitamin D (ng/mL) with the occurence of metabolic syndrome.

Relationships between OPG and 25 (OH) vitamin D with the presence of metabolic syndrome as an indicator for cardiovascular risk was further analysed in order to exclude aother cofounding factors. Due to correlations between OPG and total ALP, PTH and HDL cholesterol, suggesting that OPG difference between Mets segregated
groups may be mediated by one of these parameters, a discriminant analysis was performed (table 4) . Results showed a significant predictive value for OPG and 25 (OH)
vit D for Mets. PTH was not significantly predictive. Cholesterol parameters were not included in this analyse because the significant difference found between Mets subgroups were due to selection criteria (Mets definition).

Table(4):Astandardized Canonical Discriminant Function

Coefficients and significance in predicting Mets occurance

	Coefficient	Sig.
PTH, pg/mL	0.144	0.193
OPG (pmol/L)	0.673	0.022
25(OH) Vit D (ng/mL)	-0.765	0.009

Excluding the non-osteoporotic patients, we exclude the influence of the bone mineral density status onto this evaluation. Even the link is not very specific, we had a confirmation through our data of the possible predicted value of osteoprotegerin as an independent risk for cardiovascular diseases

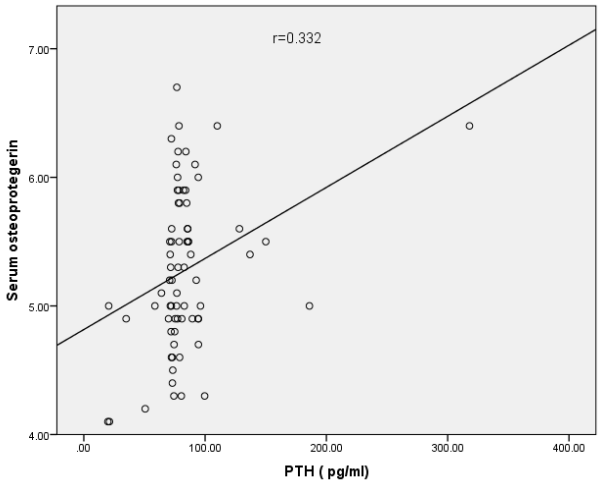

Figure (3): The Pearson Correlation's coefficient between serum osteoprotegerin and PTH (pg/mL)

4. Conclusions

Significant correlations of parathyroid hormone, osteocalcin and biochemical markers of bone with glucose metabolism and lipid were found in our research, Maintaining crosstalk between calcium and biochemical markers of bone and cardiovascular risk.

The serum level of Osteoprotegerin has been shown to have a large predictive value for the metabolic syndrome as a cardiovascular risk standard in patients with osteoporosis. The osteoprotegerin serum levels were increased in the patients with metabolic syndrome as a protective response facing the atherosclerotic lesions.

25 Hydroxy Vitamin D serum levels have great predictive values of cardiovascular and metabolic risk in our research maintaining the broad role of vitamin D outside bone metabolism.

References

[1] V. Baldini; M. Mastropasqua; CM. Francucci; E D'Erasmo., Cardiovascular disease and osteoporosis. 2005;28:69-72.

[2] R. Baron; Anatomy and ultrastructure of bone. IN: Favus MJ, ed. Primer on the Metabolic Bone Diseases and Disorders of Mineral Metabolism. 2nd ed. New York: Lippincott, Raven 1993:3-9

[3] D. L.Bartel, D.; D. T., and M., K. T. The musculoskeletal system. In Orthopaedic biomechanics: mechanics and design in musculoskeletal systems. Pearson.2006;22.

[4] P.Assantachai, --- W.Angkamat, --- P. Pongpim, --- C.Weattayasuthum, --- et al. Risk factors of osteoporosis in institutionalized older Thai people. 2006:17:1096-1102.

[5] I .Samy; McFarlane, et al. Osteoporosis and cardiovascular disease.2004, 23;1–10.

[6] G. J.Atkins; K. J, Welldon and P. Halbout, , et. al.. Strontium ranelate treatment of human primary osteoblasts promotes an osteocyte-like phenotype while eliciting an osteoprotegerin response. 2009;20: 653–664.

[7] JB. Arlet; M .Courbebaisse; G .Chatellier and D. Eladari, et al. Relationship between vitamin D deficiency and bone fragility in sickle cell disease: A cohort study of 56 adults.2013;52:206-211.
[8] Adler RA. Osteoporosis in men. In: Adler RA, editor. Osteoporosis — pathophysiology and clinical management. 2nd edition.2010; 545–57.
[9] JF.Aloia; SA.Talwar; S .Pollack; M .Feuerman; Yeh JK. Optimal vitamin D status and serum parathyroid hormone concentrations in African American women.2006;84(3): 602.
[10] American Society for Bone Mineral Research President's Committee on Nomenclature. Proposed standard nomenclature for new tumor necrosis factor family members involved in the regulation of bone resorption. 2000