BONE TURNOVER MARKERS IN SPANISH ADULT MEN. THE CAMARGO COHORT STUDY.

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ABSTRACT

BACKGROUND. This cross-sectional study was performed to determine the reference ranges for two bone turnover markers -aminoterminal propeptide of type I collagen (P1NP) and C-terminal telopeptide of type I collagen (β-CTX)- in normal adult Spanish men as measured in serum by automated methods.

METHODS. A community-based population of 660 healthy men ≥ 50 years was evaluated. Fasting serum levels of P1NP, β-CTX, 25-hydroxivitamin D, and intact parathyroid hormone were measured on the Elecsys 2010 automated analyzer (Roche). BMD at lumbar spine, femoral neck and total hip was determined by DXA.

RESULTS. Mean age of participants was 65±9 yrs. Logarithmic transformation of both markers was performed to allow for normal distribution. Mid-95% ranges for P1NP and β-CTX were 15-78 ng/ml and 0.069-0.760 ng/ml, respectively. Median and interquartile range of serum P1NP and β-CTX were 33.5 [25.5;44.4] ng/ml and 0.27 [0.19;0.38] ng/ml, respectively. Mean values of P1NP (37.1±16.7 ng/ml) were similar to those previously described. β-CTX mean values (0.300±0.171 ng/ml) were also similar to those quoted by the manufacturers in men younger than 70 yrs, but slightly lower than those reported in subjects older than 70 yrs. Both markers were higher among osteoporotic men. After excluding from the analysis those men who were found to have BMD below -2.5 T-score, 25OHD serum level below 30 ng/ml or serum PTH above 65 pg/ml, P1NP and β-CTX ranges were 17-71 ng/ml and 0.070-0.681 ng/ml, again respectively.

CONCLUSIONS. Values obtained from this well-characterized population study provide reference ranges for serum automated P1NP and β-CTX in normal Spanish adult men.

1. Introduction

Osteoporosis is a major public health problem in the elderly that affects not only postmenopausal women but also men [1]. About 25-30% of osteoporotic fractures occur in males, and morbidity and mortality, at least after hip fracture, is greater in them than in women [2]. However, male osteoporosis has been studied less than postmenopausal osteoporosis, and was poorly recognized until the two last decades [1,3]. Bone mineral density (BMD) has proven to be as effective in men as in women in predicting the risk of fractures [3]. Nevertheless, other parameters related to bone strength and fracture risk, such as bone turnover markers (BTM) [4,5], have not been evaluated in men as much as BMD [6,7]. BTM reflect whole body rates of bone resorption and bone formation, and provide a dynamic assessment of the skeleton which may complement the static information given by BMD. Furthermore, BTM have increasingly shown to be useful in assessing the response to osteoporosis therapy, and helping to explain the mechanism of action of some hormonal and therapeutic anti- osteoporotic agents [8,9]. Reference ranges for women have been widely studied. However, there is a clear absence of this type of data regarding men.

We have recently published the reference ranges for two BMT-aminoterminal propeptide of type I collagen (P1NP) and C-terminal telopeptide of type I collagen (β-CTX)-, measured by a new fully automated serum assay in normal Spanish postmenopausal women [10]. However, to our knowledge, there is no available information about normal values in Spanish men. The Elecsys 2010 (Roche Diagnostics, GmbH, Mannheim, Germany) equipment allows the determination not only of BTM but also of 25-hydroxyvitaminD_3 (25OHD) and intact parathyroid hormone (iPTH) levels, which are of high relevance for interpretation of BTM results. Therefore, the aim of this study was: i) to evaluate these automated methods to measure the serum levels of two BTM, P1NP and β-CTX, in order to know the reference ranges for these markers in Spanish adult men, and ii) to analyze their relationship with 25OHD and iPTH serum concentrations provided by the same equipment. BMD measurements were also performed, and the relationship of their results with BTM, 25OHD and iPTH analyzed.

2. Material and methods

2.1. Study design and participants

The study population was set up with adult men included in the Camargo Cohort Study, a community-based study designed to evaluate the prevalence of metabolic bone diseases and the prevalence of risk factors for osteoporosis and fragility fractures in postmenopausal women and men older than 49 attended at a Primary Care Centre in Northern Spain. Participants were recruited while attending for medical reasons or for their regular health examination, whichever happened first. All participants were white, as are more than 95% of people in our region (Cantabria). The study was approved by the local Ethics Committee, and all subjects gave written informed consent.

At the baseline visit, men were interviewed by investigators and all participants provided data regarding the risk factors for osteoporosis and fractures using a structured questionnaire, which included age, race, weight, height, body mass index (BMI), personal antecedents of fractures in adulthood (> 40 years), tobacco use, dairy calcium intake, alcohol consumption, physical exercise, number of falls in the previous year, presence of chronic diseases (hypertension, dyslipidemia, diabetes mellitus, urolithiasis, hyperthyroidism, hyperparathyroidism, chronic inflammatory diseases, etc); and present or past use of medications. BMI was defined as weight (kg) divided by squared height (m^2). Tobacco smoking was assessed as current smoker, former smoker or never smoker. Dairy calcium consumption was assessed by a food frequency questionnaire. Regarding alcohol consumption, participants were asked how much they had consumed during the past 30 days and how many times they had consumed three or more drinks per day during this period. Habitual physical activity was classified as high (moving, walking and working energetically and participating in vigorous exercise), moderate (walking reasonable distances, doing light housework, shopping or its equivalent, normal activities of day-to-day living but no appreciable exercise), and sedentary (little walking outside

home, or sitting in a chair most of the time). The presence of subclinical thyroid dysfunction was excluded by determination of serum free T4 and TSH levels. Full details of the Camargo cohort study have previously been reported [10,11].

Men in which the baseline assessment revealed the presence of diseases or treatments known to affect bone metabolism, such as osteoporosis, primary hyperparathyroidism, hyperthyroidism, chronic inflammatory diseases, serum creatinine > 151 μmol/L, or treatment with bisphosphonates, testosterone, strontium ranelate, teriparatide, L-thyroxin or glucocorticoids, were excluded. Therefore, those men previously diagnosed and treated for osteoporosis were left out. However, those men who were found to be osteoporotic as a result of our BMD study were included and evaluated.

2.2 Biochemical tests

Fasting blood samples were collected from each participant between 09:00 and 10:30 h. Serum was divided into 0.5-ml aliquots and stored at -40ºC. Serum total calcium (TCa), phosphate, glucose, creatinine, albumin, and total alkaline phosphatase measurements were determined by standard automated methods in a Technicon Dax autoanalyser (Technicon Instruments, CO. USA). TCa measurements were corrected for albumin concentration (cCa) following a previously published formula [12]. Serum concentrations of aminoterminal propeptide of type I collagen (P1NP), C-terminal telopeptide of type I collagen (β-CTX), 25-hydroxyvitamin D_3 (25OHD), and intact parathyroid hormone (iPTH) were determined by a fully automated electrochemiluminiscence system (Elecsys 2010, Roche Diagnostics, GmbH, Mannheim, Germany). The P1NP limit of detection was 5 ng/ml (reference range between 19 and 100 ng/ml in Spanish postmenopausal women), with intra-assay and inter-assay coefficients of variation (CV) of 3.1% and 3.5%, respectively [10, 13]. The detection limit of serum β-CTX was 0.010 ng/ml, its intra-assay and inter-assay CV being 4.2% and 4.7%, respectively, and its reference range in Spanish postmenopausal women 0.112-1.018 ng/ml [10,14]. The detection limit of

serum 25 OHD was 4 ng/ml, its intra-assay CV 5%, and its inter-assay CV 8.5%. Regarding iPTH, the detection limit was 6 pg/ml, with a manufacturers´ normal range of 15-65 pg/ml. Intra-assay and inter-assay CV were 5.4% and 5.9%, respectively [15].

2.3. DXA measurements

BMD was measured by DXA (Hologic QDR 4500, Bedford, MA, USA) at the lumbar spine (L2-L4), femoral neck, and total hip in all the 660 men who finally entered the study (see below). *In vivo* precision was 0.4-1.5% at the different measurement sites. Results were expressed as grams per square centimetre, T-score (defined as the number of standard deviations [SDs] below the mean value of young men), and Z-score (defined as the number of SDs below the mean of men of the same age). T and Z-scores were calculated using the NHANES III reference database for femur measurements [16]. Quality control was performed according to the usual standards [17].

2.4. Statistical analyses

Results were expressed as mean ± SD or median [interquartile range] for quantitative variables, and percentages of the population for qualitative variables. Kolmogorov-Smirnov test was used to test for normality of the data set distribution. As expected in adult men, serum β-CTX and P1NP were not distributed normally with a frequency distribution skewed toward the lowest values (Figure 1A and 1B). Thus, these variables underwent logarithmic transformation before statistical analyses. Chi-squared or Fisher's exact test were performed in order to identify differences in categorical variables between subgroups. Mann-Whitney U-Test was used to compare BTM between the groups of men distributed by serum levels of iPTH, vitamin D, or osteoporosis status. One-way ANOVA was undertaken to assess correlation between BTM and age strata. Bonferroni's test for multiple comparisons was performed when significant differences were found. Significance levels less than 5% were

considered significant. All analyses were performed using SPSS for Windows (SPSS Inc, Chicago, IL, USA).

3. Results

3.1. Subjects

A total of 703 men, aged 50-92, were initially recruited. Forty-three of them were excluded because their baseline study revealed the presence of diseases or treatments known to affect bone metabolism, or even treatments addressed to bone metabolic diseases, including osteoporosis. The remaining 660 men entered into the study, and their baseline characteristics are listed in table 1.

3.2. Serum P1NP and β-CTX levels

Median and interquartile range of serum P1NP and β-CTX in adult men were 33.5 [25.5;44.4] ng/ml and 0.27 [0.19;0.38] ng/ml, respectively (Table 2). Moreover, mean value of P1NP was 37.1 ng/ml (± 16.7) and mean value of β-CTX: 0.300 ng/ml (± 0.171). Neither of them was distributed normally, but skewed toward the lowest values (Fig.1A, and 1B). After log- transformation, data took on a normal, Gaussian distribution, and the geometric mean ± 2SD was used to determine the 95% range. The limits of this range were 15-78 ng/ml for P1NP, and 0.069-0.760 ng/ml for β-CTX. These values were similar to those obtained by our group in Spanish premenopausal women (mean P1NP: 41.1±18.5 ng/ml, and β-CTX: 0.271±0.139 ng/ml), but significantly lower than those observed in postmenopausal women of similar age (63±9) from our region (mean P1NP: 47.7 ± 19.9 ng/ml, and β-CTX: 0.387 ± 0.197 ng/ml; ($p<0.001$) [10]. Thus, serum P1NP and β-CTX levels in adult men were, respectively, 22% and 23% lower than those obtained in postmenopausal women.

P1NP and β-CTX ranges were also calculated after excluding from the analysis those men who were found to have a BMD below -2.5 T-score, a 25OHD serum level lower than 30 ng/ml or a PTH serum above 65 pg/ml. The corresponding values were 17-71 ng/ml and 0.070-0.681 ng/ml, quite close to those of the whole population, although in both cases the upper value was somewhat lower (about 10%).

3.3. Changes in serum P1NP and β-CTX with age

Considering all men as a whole, no significant correlation between age and either P1NP or β–CTX concentrations was found. Both markers remained stable until the age of 80 years, although a significant rise ($p=0.03$) in β–CTX levels was observed in participants older than this. (Fig.1C and 1D). In fact, the average levels in men older than 80 years were 22% higher than those observed in men aged 50-60 years (Table 3).

3.4. Comparison of BTM between subgroups

P1NP and β–CTX values were also compared among subgroups based on serum 25OHD (above or below 30 ng/ml, levels generally considered to be the threshold for optimal vitamin D status), serum PTH (below or above 65 pg/ml), and presence or absence of osteoporosis (defined as BMD >-2.5 T in lumbar spine, femoral neck or total hip). As expected, the two markers were higher in men with osteoporosis than in those without ($p<0.01$), the difference being 16% for P1NP and 26% for β–CTX. Men with PTH levels above 65 ng/ml also had higher levels of both P1NP and β–CTX ($p<0.05$), and a positive relationship was observed between iPTH and BTM values (P1NP: $r=0.135$; $p<0.001$; β–CTX: $r=0.252$; $p<0.001$). However, no significant differences were seen in either marker among subgroups of men based on serum 25OHD levels (Table 3). Finally, we did not find any relationship between smoking habits, alcohol consumption, physical activity, and the other characteristics of the population studied (Table 1) and bone turnover markers (data not shown).

3.5. BMD in adult men according to BTM values

The relationship between BTM and BMD was also analyzed categorizing men in quartiles according to bone marker levels, and comparing their BMD values. Adult men with P1NP and β-CTX levels in the lowest quartile had a lumbar spine BMD 4% and 7% greater than in the highest (P1NP: 1.044±0.141 g/cm^2 vs. 1.003±0.155 g/cm^2; p=0.09; β-CTX: 1.060±0.153 g/cm^2 vs. 0.984±0.161 g/cm^2; p<0.05). A similar pattern was seen at the femoral neck (P1NP: 0.833±0.124 g/cm^2 vs. 0.807±0.141 g/cm^2; p= 0.3; βCTX: 0.849±0.112 g/cm^2 vs. 0.786±0.130 g/cm^2; p<0.001) and the total hip (P1NP: 1.007±0.131 g/cm^2 vs. 0.961±0.132 g/cm^2; p<0.01; β-CTX: 1.021±0.124 g/cm^2 vs. 0.937±0.127 g/cm^2; p<0.001). Therefore, lumbar spine and femoral neck BMD differences between the highest and lowest quartiles were significant when based on β-CTX but not on P1NP concentrations.

4. Discussion

We describe the reference ranges for two of the main bone markers (P1NP and β-CTX) measured by a new automated serum assay, in 660 Spanish adult men in which mineral metabolic disorders, bone metabolic diseases (other than previously unknown osteoporosis) and treatments known to affect bone metabolism had been ruled out. Median value of P1NP was 33.5 [25.5;44.4] ng/ml, and β-CTX 0.27 [0.19;0.38] ng/ml. Mean serum P1NP and β-CTX were 37.1 ng/ml (± 16.7) and 0.300 ng/ml (± 0.171). The ± 2SD range limits (after log-transformation) were 15-78 ng/ml for P1NP and 0.069-0.760 ng/ml for β-CTX.

Manufactures of the automated serum P1NP assay have not yet developed –or at least published- their own reference values in men, so we cannot compare our own results with them. When compared with other researcher's findings, we have found similar mean and reference values to those described by Garnero et al [13] in 64 men aged 40-65 years (mean ± SD: 38.1±18.4 ng/ml; reference limits 13.9 and 85.5 ng/ml), in a study performed with the same methodology. Our results are also similar to those published more recently by Bauer et al [7] in 947 men older than 65 years who were

randomly selected from the Osteoporosis in Men study (MrOS), a large cohort of community-dwelling older men (74±6 years) from the USA (mean ± SD: 39.0±24.9 ng/ml). Therefore, P1NP values assessed by Elecsys automated method appear to be similar in Caucasian men in different countries.

In contrast, serum β-CTX determined by the automated assay technique shows some differences between publications. Our results are very similar to those quoted by manufacturers in normal adult men younger than 70 years (0.304±0.200 ng/ml for men between 50-70 years), but lower than those reported in men older than 70 (0.394±0.230). In our sample, men younger and older than 70 show mean values of 0.296 ng/ml (±0.168) and 0.312 ng/ml (±0.177), respectively. Our values are also slightly lower than those reported by Bauer et al [7] in the subgroup of participants of the MrOS (0.41±0.21 ng/ml) previously referred to, aged 74±6 years. In contrast, Chen et al [18] reported a mean value of 0.24 ng/ml (range 0.16-0.39) in frail elderly (older than 80) men from Sydney, Australia. At this age, β-CTX levels in our sample are 0.365 ng/ml (±0.162).

We have previously published our reference range for both BTM, P1NP and β-CTX, in women, and compared our results with those of studies performed in other latitudes [10]. We found a superimposable pattern: P1NP results are similar for all Caucasian women studied, but β-CTX shows clear differences.

We have no straightforward explanation for this different behaviour of the two BTM. Speculation could be made that bone resorption markers may be more influenced by the particular characteristics of participants included in each study, such as age, weight, smoking habits, physical activity, etc.

On the other hand, it is of interest that serum levels of P1NP and β-CTX in our adult males were similar compared to those previously described in Spanish premenopausal women (P1NP: 41.1±18.5 ng/ml; β-CTX: 0.271±0.139 ng/ml), as well as those described in young women from other countries [10,14,19].

We found no change in either of the two BTM with age, apart from a late increase in β-CTX only just after the age of 80. Szulc et al (6, 20) have reviewed the changes of BTM with age in men. According to them, BTM in men show

their lowest levels between 50 and 60 years. Thereafter, age-related increase, stability or decrease of bone resorption markers, have been described. Concerning serum bone formation markers, they remain roughly stable between 40 and 60 years, independently of the marker studied. Over 60 years, they remain stable or increase slightly in cohorts including very old men (6, 21). The reasons for these discrepancies are not clear, but they may probably be related to differences in the characteristics of the participants –for instance, the inclusion of men with different degrees of renal function-, along with the fact that some of the samples studied are small in number, so that a few discordant participants may have a great influence in the final results. In this regard, the number of patients assessed in our study may be considered reassuring.

The participants of our study were also divided into groups according to their serum 25OHD and iPTH levels. No significant differences were seen in either P1NP or β-CTX between men with serum 25OHD above or below 30 ng/ml. Consistent with our results, Chen et al [18] did not find any relation between bone markers and serum 25-OH vitamin D in elderly men. Regarding PTH stratification, men with PTH values above 65 pg/ml showed a higher level of P1NP (7%) and β-CTX (15%). This probably reflects the increase of bone remodelling mediated by high levels of PTH. Finally, as we have previously commented on, and has been widely described for other BTM [7,22-24], both P1NP and β-CTX were higher in osteoporotic men than in men with BMD greater than -2.5 T. The difference was smaller for P1NP (about 16%) than for β-CTX (26%). Moreover, we found an inverse relationship between quartiles of bone markers and bone mineral density, with a difference between extreme quartiles of 3 to 8 %.

Our study has some limitations. Specifically, men were recruited from a Primary Care Centre. In our health care system however, people of a certain age are asked to visit their family doctors regularly, at least once a year; therefore, after this period of time, all men older than 50 are expected to have attended the clinic. Hence our cohort may be considered representative of the general population. On the other hand, before being included in our cohort, men were carefully studied from the mineral and bone metabolism point of view, and excluded if any diseases or treatments known to affect this were present.

Among the strengths we want to emphasize, it is worth mentioning that the subjects of our analysis met the criteria for BMT reference individuals recommended by the Clinical and Laboratory Standards Institute (NCCLS) [25]. The sample was large enough (more than 600 men), the participants were well-characterized, and all men provided data regarding their risk factors for osteoporosis and fractures. Finally, all samples were obtained at the same time of the day and in a fasting state. Thus factors to minimize biological variability were controlled.

In conclusion, in our study we report the mean, median, and reference ranges for two BMT (P1NP and β-CTX) from a well characterized population of Spanish adult men, using a new automated technique. For serum P1NP these values were similar to those previously described. Serum β-CTX levels were also similar to those previously reported by the equipment manufacturers in males aged 50-70 years, but slightly lower than those reported for men older than 70 years. Both markers were higher in men with greater PTH levels and in men found to have osteoporosis in the course of our study. We believe that our reference ranges can serve as useful standards for bone turnover in adult males in our country.

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No conflict of interest was declared

List of abbrevations

P1NP: aminoterminal propeptide of type I collagen

β-CTX: C-terminal telopeptide of type I collagen

25OHD: 25-hydroxivitamin D

iPTH: intact parathyroid hormone

BMD: bone mineral density

LS: lumbar spine

FN: femoral neck

TH: total hip

DXA: dual X-ray absorptiometry

NHANES III: Third National Health and Nutrition Examination Survey

BMT: bone turnover markers

SD: standard deviation

BMI: body mass index

TCa: serum total calcium

cCa : albumin-corrected serum total calcium

CV: coefficients of variation

NCCLS: Clinical and Laboratory Standards Institute

Figure 1. Frequency distribution of serum P1NP (A) and β-CTX (B) in adult men. Age-related changes in serum P1NP (C) and β-CTX (D) in men

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Table(s)

Table 1. Baseline characteristics of the population studied

	N=660	Range
Age (years)	65±9	50-92
Weight (kg)	82±11	45-121
Height (cm)	168 ± 6	150-189
BMI (kg/m^2)	28.9± 3.4	19-41
Waist's perimeter (cm)	102 ± 9	74-134
Arm spam (cm)	173 ± 9	125-197
History of falls (last year) (%)	15	-
Any fracture > 40 years (%)	15	-
Physical activity		
Sedentarism (%)	1	-
Moderate (%)	31	-
High (%)	68	-
Current smoking (%)	18	-
Current alcohol consumption (%)	47	-
Dairy calcium consumption (mg/day)	500 [300;700]	0-2000
Calcium supplements (%)	1	-
Vitamin D supplements (%)	1	-
Dyslipemia (%)	32	-
Diabetes mellitus (%)	18	-
Urolithiasis (%)	14	-

Data are presented as mean ±SD, median [interquartile range], or number (percentage)

Table 2. Biochemical parameters and bone mineral density (BMD) in adult men

	N= 660	**Range**
Glucose (mmol/l)	5.22 [4.77;5.88]	3.38-15.87
Creatinine (μmol/l)	96 [86;106]	53-150
Calcium (mmol/l)	2.40 [2.33;2.45]	2.12-2.62
Phosphate (mmol/l)	0.99 ± 0.15	0.55-1.61
Albumin (g/l)	45 [44;47]	30-53
cCa (mmol/l)	2.25 [2.20;2.33]	2.10-2.55
Alkaline phosphatase (U/l)	62 [53;74]	16-283
25OHD (ng/ml)	24 ± 8	4-61
iPTH (pg/ml)	52 [40;63]	14-107
P1NP (ng/ml)	33.5 [25.5;44.4]	10.1-132.2
β-CTX (ng/ml)	0.27 [0.19;0.38]	0.02-1.31
BMD, LS (g/cm^2)	1.021 ± 0.154	0.580-1.733
BMD, LS (T-score)	-0.83 ± 1.40	-4.897-5.55
BMD, LS (Z-score)	0.02 ± 1.46	-4.20-6.68
BMD, FN (g/cm^2)	0.817 ± 0.123	0.430-1.342
BMD, FN (T-score)	-0.82 ± 0.91	-3.71-3.02
BMD, FN (Z-score)	0.28± 0.23	-2.33-3.92
BMD, TH (g/cm^2)	0.981 ± 0.127	0.544-1.393
BMD, TH (T-score)	-0.33 ± 0.86	-3.24-2.33
BMD, TH (Z-score)	0.27 ± 0.89	-2.74-3.40

Data are presented as mean ± SD or median [interquartile range].

cCa : albumin-corrected serum total calcium; P1NP: aminoterminal propeptide of type I collagen ; β-CTX: C-terminal telopeptide of type I collagen; 25OHD: 25-hydroxyvitamin D; iPTH intact parathyroid hormone. BMD, LS: bone mineral density at the lumbar spine; BMD, FN: bone mineral density at the femoral neck, BMD, TH: bone mineral density at the total hip.

Table 3. Subgroup analysis of serum P1NP and β-CTX among adult men according to age, serum levels of 25OHD and PTH, and the presence or absence of osteoporosis

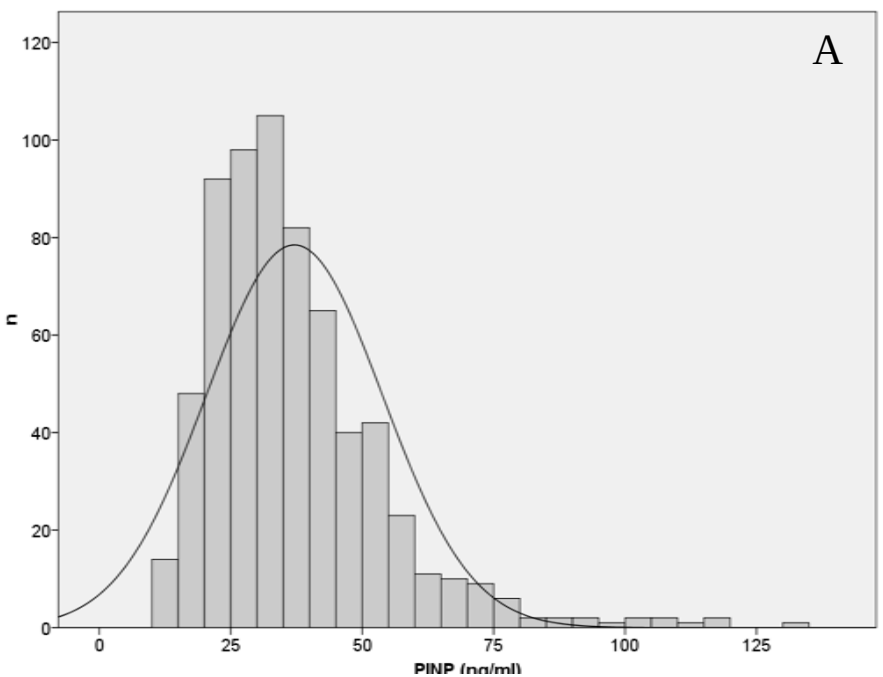
		N	Serum P1NP (ng/ml)	Serum β-CTX (ng/ml)
Age (years)		660		
	50-59	203	34.1 [25.9;43.9]	0.261 [0.181;0.382]*
	60-69	267	33.1 [25.4;45.0]	0.263 [0.194;0.363]*
	70-79	149	32.1 [24.6;43.5]	0.269 [0.185;0.386]*
	>80	41	37.8 [29.3;48.9]	0.335 [0.238;0.475]
25OHD		660		
	<=30 ng/ml	531	32.8 [25.3;43.5]	0.265 [0.197;0.373]
	>30 ng/ml	129	36.8 [26.3;47.2]	0.291 [0.196;0.393]
iPTH		660		
	<=65 pg/ml	514	32.1 [24.9;44.5]	0.261 [0.183;0.377]
	>65 pg/ml	146	34.5 [28.0;44.1]*	0.309 [0.235;0.418]**
Osteoporosis		660		
	Yes	88	38.9 [28.8;51.5]**	0.354 [0.235;0.471]***
	No	572	32.7 [25.0;43.1]	0.260 [0.182;0.366]

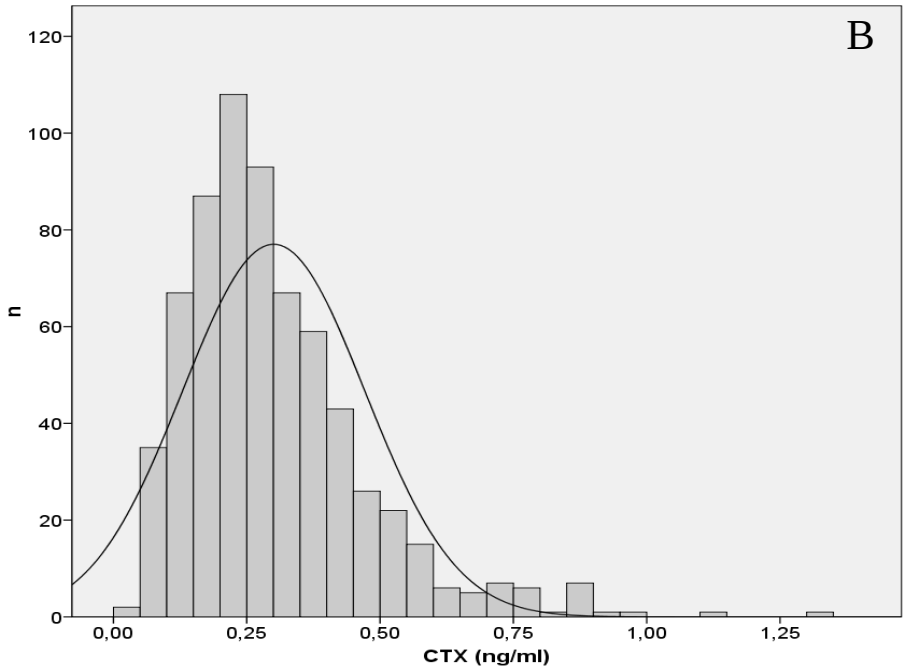
Data are presented as median [interquartile range]

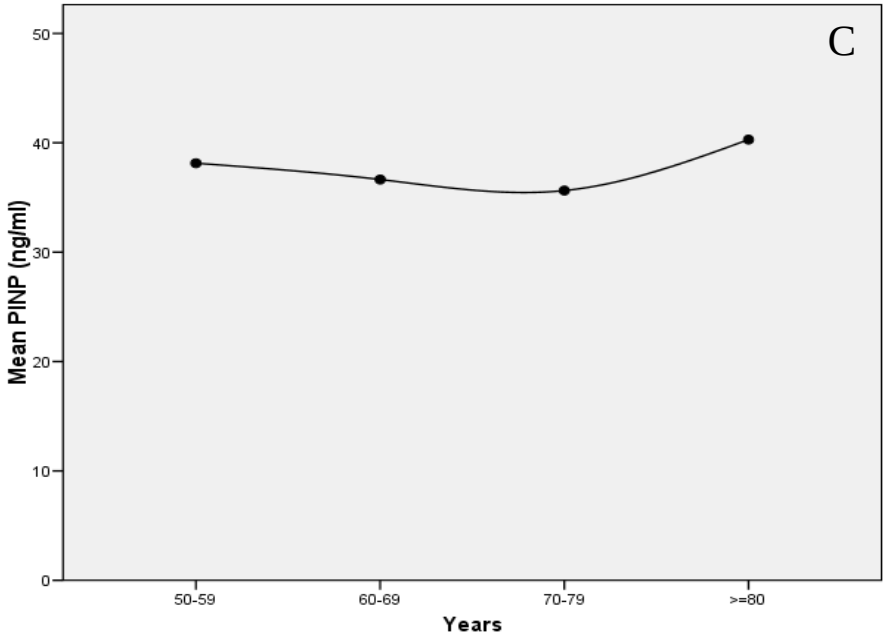
*p<0.05; **p<0.01; ***p<0.001. In age subgroups, comparisons were made with the oldest group (>80 years).

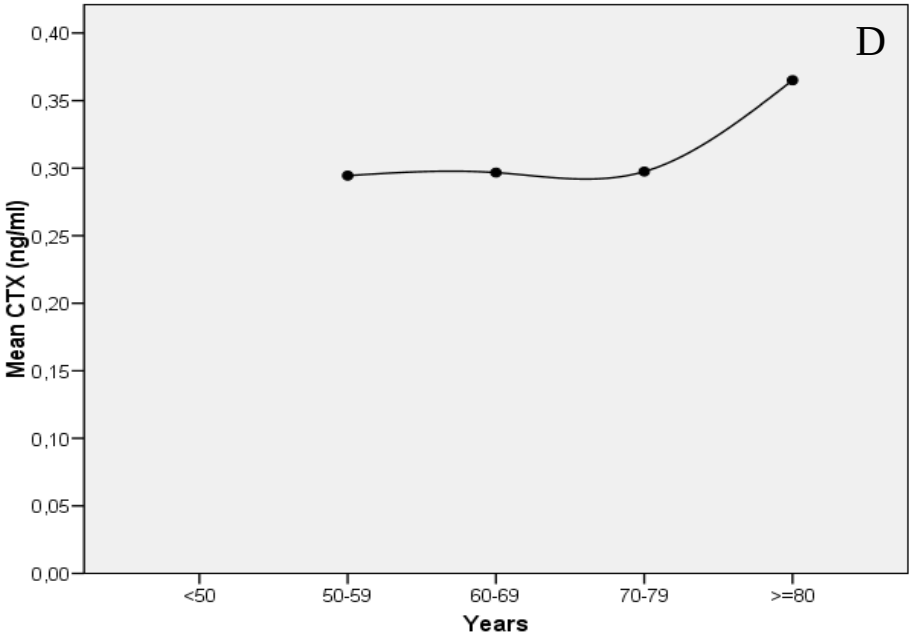
P1NP: aminoterminal propeptide of type I collagen; β-CTX: C-terminal telopeptide of type I collagen; 25OHD: 25-hydroxyvitamin D; iPTH: intact parathyroid hormone.

Figure(s)


A
n
PINP (ng/ml)


B
n
CTX (ng/ml)


C
Mean PINP (ng/ml)
Years
50-59
60-69
70-79
>=80


D
Mean CTX (ng/ml)
Years
<50
50-59
60-69
70-79
>=80