# C-telopeptides of type I collagen in postmenopausal women: An experience in a Tunisian Clinical Laboratory

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Télopeptide C-terminal du collagène de type I chez la femme ménopausée : une expérience d'un laboratoire clinique Tunisien

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## RÉSUMÉ

**But :** Le but de notre étude était d'évaluer l'intérêt du télopeptide C-terminal du collagène de type I (CTX) pour le diagnostic de l'ostéoporose chez les femmes post ménopausique et de définir sa valeur seuil.

**Méthodes:** Une étude transversale descriptive enrôlant des femmes ménopausées : 139 ostéoporotiques (G1) et 39 non ostéoporotiques (G2). Les 2 groupes étaient définis selon la densité minérale osseuse. Les présents marqueurs étaient mesurés: phosphatase alcaline sérique (PAL), phosphatase alcaline osseuse (PALo), télopeptide C-terminal du collagène type I (CTX). Nous avons utilisé le logiciel SPSS 10.5 pour les analyses statistiques. L'estimation de la sensibilité et de la spécificité de CTX a été présentée en courbes de ROC.

**Résultats:** Il n'y a pas de différence dans la mesure de PAL et PALo dans les 2 groupes mais CTX était statistiquement plus élevé dans G1 comparé à G2 ($p < 0.001$). Le pourcentage de femmes ostéoporotiques (G1) avec CTX > 0.500 ng/ml était plus élevé que celui des femmes non ostéoporotiques (G2). Nous avons établi une courbe ROC pour chercher la valeur seuil de CTX qui permettrait la distinction entre femmes ostéoporotiques avec haut niveau de remodelage osseux et femmes non ostéoporotiques. La valeur seuil de CTX à 0.55 pg/ml était la meilleure associant meilleure sensibilité et meilleure spécificité.

**Conclusion:** L'élévation était statistiquement significative pour CTX entre les 2 groupes; CTX apparaît ainsi être un bon marqueur du remodelage osseux dans le diagnostic de l'ostéoporose en comparaison à PAL et PALo.

La valeur seuil de CTX à 0.55 pg/ml pourrait améliorer la sensibilité et la spécificité dans la prédiction de fractures dans le futur.

**Mots-clés**
Ostéoporose ; marqueurs osseux ; diagnostic

## SUMMARY

**Aim:** The purpose of study was to evaluate the interest of C-telopeptides of type I collagen (CTX) in the diagnosis of osteoporosis in postmenopausal women and to define its cut-off value.

**Methods:** A transverse descriptive study enrolled postmenopausal women: 139 osteoporotic (G1) and 39 non osteoporotic (G2). The 2 groups were defined by bone density measurement. The following markers were measured: serum alkaline phosphatase (ALP), bone alkaline phosphatase (bone ALP), serum C-terminal telopeptide of type I collagen (CTX). Statistical analyses were performed using SPSS 10.5. The corresponding estimation of sensitivity and specificity of CTX have been presented as 'receiver Operating Curve' (ROC).

**Results:** There was no difference in the measurement of ALP and bone ALP in the 2 groups but CTX was statistically higher in G1 compared to G2 ($p < 0.001$). The percentage of osteoporotic women (G1) with CTX values > 0.500 ng/ml was higher than that of non osteoporotic women (G2). We have established a ROC curve to find the cut-off value of CTX that enables the distinction between osteoporotic women with high level of bone remodelling, and non osteoporotic women. The cut-off value of CTX 0.55 pg/ml was the best; it associated best sensitivity and specificity.

**Conclusion :** The total increase and significance for CTX was greater in the group of osteoporotic women and appeared therefore to be a good bone turnover marker in the diagnosis of osteoporosis in comparison with ALP and bone ALP.

The cut-off value of CTX 0.55 pg/ml may improve the sensitivity and specificity of prediction of future fractures.

**Key-words**
Osteoporosis; bone markers; diagnosis

**تيلوببتيد" س "نهائي لكلاجين نمط 1 عند المرأة في سن الإياس، تجربة مختبر تونسي:**

**الباحثون : ك .بوزيد ، ع .بهلوس ، آ .قلعي ، ح .فلاح ، هـ .الساحلي ، ص .السلامي ، ج .عبد المولى**

**الكلمات الأساسية : تخلخل العظام - الوسمة العظمية - تشخيص**

The level of bone mass can be estimated by measuring bone mineral density (BMD) using dual X-ray absorptiometry (DEXA)

Quantitative changes in skeletal turnover can be assessed easily and non-invasively by the measurement of serum and urinary biochemical markers; the most sensitive markers include serum osteocalcin, bone specific alkaline phosphatase, the N-terminal propeptide of type I collagen for bone formation, and the crosslinked C- (CTX) and N- (NTX) telopeptides of type I collagen for bone resorption. The purpose of our study was to evaluate the interest of C-telopeptides of type I collagen (CTX) in the diagnosis of osteoporosis in postmenopausal women and to define its cut-off value.

## MATERIAL AND METHODS

Our study enrolled 139 osteoporotic (G1) and 38 non osteoporotic (G2) post-menopausal women.

G1 was defined by bone density measurement (BMD) < -2.5 SD with or without fractures and/or -2.5 DS < BMD < -1 DS with osteoporotic fracture(s). In G2, BMD was considered > -2.5 DS. The bone mineral density (BMD) was measured by dual energy X-ray absorptiometry (DEXA) for all women.

The following biochemical markers were measured in the two groups: serum alkaline phosphatase (ALP), bone alkaline phosphatase (bone ALP), serum C-terminal telopeptide of type I collagen (CTX).

Statistical significance was defined as $p<0.05$. All statistical analyses were performed using SPSS 10.5. We used t-test of Student for comparison of means. The corresponding estimates of sensitivity and specificity of CTX have been presented as 'Receiver Operating Curve' (ROC).

## RESULTS

Descriptive statistics for all variables relating to serum bone turnover (CTX, ALP and bone ALP) of the two groups including mean, standard deviation (SD), minimum and maximum of all parameters are shown in table 1.

**Tableau 1 :** comparison of results of bone markers in the 2 groups.

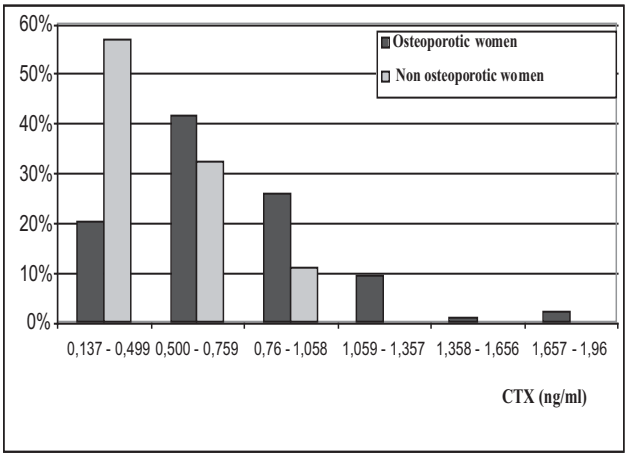
| Biochemical markers | | Osteoporotic (G1, n=139) | non osteoporotic (G2, n=38) |
|---|---|---|---|
| **CTX** | M (ng/ml) | 0,710* | 0,479 |
| | SD | 0,316 | 0,201 |
| | Min (ng/ml) | 0,161 | 0,137 |
| | Max (ng/ml) | 1,960 | 1,000 |
| **ALP** | M | 90 | 83 |
| | SD | 29 | 23 |
| | Min | 47 | 45 |
| | Max | 224 | 148 |
| **Bone ALP** | M ($\mu$g/l) | 19.7 | 19.1 |
| | SD | 8.9 | 9.2 |
| | Min ($\mu$g/l) | 7.05 | 8.6 |
| | Max ($\mu$g/l) | 80 | 52.4 |

*: p< 0,001, M: mean value, SD: standard deviation, Min: minimum, Max: maximum.

CTX were higher in osteoporotic women (G1) compared to G2; the difference was statistically significant between the 2 study groups ($p <0.001$) (table 1).

The percentage of osteoporotic women (G1) with CTX values > 0.500 ng/ml was higher than that of non osteoporotic women (G2) (Fig.1).

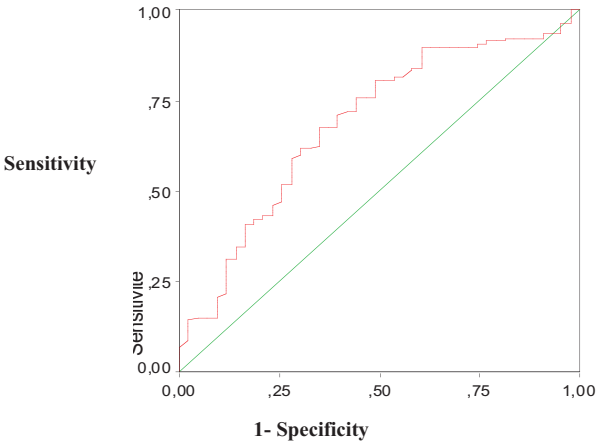
**Figure 1 :** Results of CTX in the 2 groups




If we consider the cut off of 1.008 ng/ml for non osteoporotic menopausal women determined by the provider of CTX kit, the specificity and the positive predictive value (PPV) of CTX in the diagnosis of osteoporosis will be 100%, confidence intervals at 95% are respectively [85-100] and [78- 100]. In menopausal women, without any bone diseases, a high value of CTX is indicative of presence of osteoporosis. Sensitivity and negative predictive value (NPV) are respectively 13% [8- 28] and 18% [13-20]. Thus, in osteoporosis, it's possible to find low values of CTX.

We have established a ROC curve to find the cut-off value of CTX that enables the distinction between osteoporotic women with high level of bone remodelling, and non osteoporotic women. The cut-off value of CTX 0.55 pg/ml was the best; it associated the best sensitivity and specificity (Fig.2).

**Figure 2 :** ROC curve for determination of cut-off value of CTX



## DISCUSSION

Biochemical bone-turnover markers are released during bone formation or resorption. Their concentration in serum or urine reflect bone remodeling activity. They don't replace dual energy absorptiometry (DEXA) for the diagnosis of osteoporosis [1] but can potentially be used as surrogate markers of the rate of bone formation or bone resorption [2].

We have compared three bone markers in osteoporotic and non osteoporotic women and we have found that CTX was statistically the best to compare osteoporosis in the two groups. In an other study, Garnero showed that the use of CTX in association with BMD measurement is helpful in risk assessment, especially in those women who are not identified as at risk by BMD measurement alone [3]. The cut-off value of CTX 0.55 pg/ml may improve the sensitivity and specificity of prediction of future fractures.

Now, multiple approaches are able to classify the level of bone turnover in the training set with 80% sensitivity and 100% specificity. The finding of serum protein fragments which elevation leads to the increase of osteoclast activity and presumably an increase risk of fracture can provide a novel approach to evaluate high bone turnover states [4].

## CONCLUSION

Bone marker measurements are non invasive, inexpensive compared to measurement of BMD and can be repeated often. The total increase and significance for CTX was greater in the group of osteoporotic than in non osteoporotic women and appeared therefore to be a good bone turnover marker in the diagnosis of osteoporosis in comparison with ALP and bone ALP.

The cut-off value of CTX 0.55 pg/ml may improve the sensitivity and specificity of prediction of future fractures.

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