

# UNDERCARBOXYLATED OSTEOCALCIN AND SECONDARY HYPERPARATHYROIDISM IN POSTMENOPAUSAL PATIENTS ON HEMODIALYSIS

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## OBJECTIVES

Osteocalcin (also known as non-collagenous bone matrix gla protein)(OC), is a vitamin K-dependent Ca<sup>2+</sup>-binding protein, produced by osteoblasts. OC biosynthesis is tightly regulated by 1,25-dihydroxy-vitamin D<sub>3</sub>. OC carries three gamma-glutamic acid residues (Gla) at positions 17, 21, and 24, which are target for vitamin K-dependent carboxylation and OC activation. Carboxylated OC is known to mediate strong binding to bone hydroxyapatite crystals[1]. During bone resorption the OC that is incorporated into the bone matrix is released into the circulation, and, hence, is considered as a marker of bone turnover, rather than a specific marker of bone formation[2,3]. The marked elevation of OC in patients with renal failure has been regarded as a combination of impaired clearance and increased skeletal production[4,5]. In subclinical vitamin K deficiency part of the OC in serum remains undercarboxylated (ucOC) and thus inactive in respect to bone metabolism[6]. The objective of the present study was to assess the ucOC levels in postmenopausal hemodialysis (HD) patients with and without secondary hyperparathyroidism.

## METHODS

We recruited 52 menopausal women: 26 on HD and 26 controls similar to the HD patients along criteria such as food intake, physical activity, medication use and other risk factors for osteoporosis. The mean age was 65±1.30 years and 59±0.95 years respectively. Serum levels of ucOC [ng/ml] were measured by EIA kit of TAKARA Bio.Inc. (Japan) before the HD session. Intact parathormone (iPTH) levels [ng/L] were measured on Immulite 2000 using chemiluminiscent (CLIA) kit. Statistical analysis was performed by Student's t-test and Pearson's correlation.

## RESULTS

Table 1. Serum ucOC levels [ng/ml] in HD patients

Control group [1]	HD patients without secondary hyperparathyroidism (SHPT) [2]	HD patients with SHPT not treated by cinacalcet and calcitriol [3]	HD patients with SHPT treated with cinacalcet and calcitriol [4]
3.01±0.36 n=26	12.318±8.106 n=6	14.630±7.824 n=10	23.723±6.911 n=7
		3:2 p-NS	4:3 p<0.02

Serum ucOC in HD patients (16.45±1.62 ng/mL, n=26) was significantly increased in comparison with the levels in control group members (3.01±0.36 ng/mL, n=26), p<0.0001. Serum ucOC levels [ng/ml] in HD patients are presented in table 1. Correlations between ucOC and different parameters in HD patients are presented in table 2.

Table 2. Correlations between ucOC and different parameters

Parameter	Pearson r	p
Parathormone	0.52	0.008
HD duration	0.77	0.0001
Age	- 0.49	0.01

## CONCLUSIONS

1. Serum levels of ucOC in HD patients were significantly increased in comparison with the healthy controls and a strong positive correlation was found between ucOC and iPTH as well as between ucOC and HD duration.
2. In the initial stages of secondary hyperparathyroidism (iPTH <300 ng/l), serum ucOC levels were the same as in the patients without secondary hyperparathyroidism.
3. The treatment of secondary hyperparathyroidism with cinacalcet and calcitriol leads to significant increase of ucOC, most probably due to increased bone turnover.

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