

SERUM BRAIN NATRIURETIC PEPTIDE (BNP) CORRELATES WITH OPG LEVELS AND INFLUENCES BONE MASS AND BODY SEGMENT LENGTHS IN ELDERLY SUBJECTS

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Natriuretic peptide family consists of 3 structurally related endogenous ligands, atrial, brain, and C-type natriuretic peptides (ANP, BNP, and CNP), and is thought to be involved in a variety of homeostatic processes, including longitudinal bone growth. BNP is a 32-aminoacid peptide that is markedly elevated in patients with congestive heart failure and acute coronary syndrome (ACS). Even though cardiac myocytes constitute the major source of BNP, this peptide is synthesized and released by bone marrow stromal cells at physiologically relevant levels *in vitro*. Moreover, BNP receptors have been described in osteoblasts and BNP knockout mice exhibit cardiac fibrosis and bone malformations. The aim of this study was to characterise the relationship between plasma BNP, bone mineral density (BMD), and bone turnover markers in 150 subjects. BNP levels significantly increased with age ($r=0.25$; $p<0.01$) both in males and females and were higher in postmenopausal than premenopausal women. Of interest, BNP highly correlated with OPG levels ($r=0.85$, $p<0.0001$) and total body BMD ($r=0.30$, $p<0.001$). Negative correlations between BNP and urinary calcium or phosphate excretion were also observed in both sexes. When subjects were grouped according to BNP quartiles, we observed significantly higher OPG levels and lower RANKL/OPG ratio in subjects within the high BNP quartile. No major differences were observed concerning bone alkaline phosphatase and serum CTX. Moreover, in postmenopausal women with BNP in the highest quartile, the average total body BMD was from 4% to 14% higher than in women in the other BNP quartiles ($p<0.005$). A similar but not significant trend was observed in men. Sitting height measured by a stadiometer was significantly related to BNP levels ($r=0.24$; $p<0.05$). Finally, to further explore the relationship between OPG and BNP we evaluated their levels in 50 patients affected with ACS. A similar positive correlation between OPG and BNP was observed ($r=0.38$; $p<0.01$) and both markers significantly correlated with left ventricular systolic function and the severity of disease. These data confirm experimental observations demonstrating a skeletal effect of BNP and further support the reported link between bone and cardiovascular disorders.