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**Positive correlations between free vitamin D and bone variables in a group of young Lebanese men**

**Article type: Letter to the Editor**

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Dear Editor,

Vitamin D deficiency is a major public health problem in many countries (1-7). The prevalence of vitamin D deficiency is also very common in Lebanese adults (1-7). Although vitamin D is very important for bone health, several studies have failed to find a positive relationship between 25-hydroxyvitamin D [25(OH)D] and bone mineral density (8-10). However, we have previously shown that serum vitamin D is a positive determinant of composite indices of femoral neck strength in young adults (11, 12). Bone strength is not only influenced by bone mineral density (BMD) but also by bone geometry (13). Several DXA-based variables other than BMD can predict fracture risk in elderly subjects such as bone mineral apparent density (BMAD), cross-sectional area (CSA) of the femoral neck, compressive strength index (CSI), bending strength index (BSI), impact strength index (ISI) and trabecular bone score (TBS) (14, 15). In order to maintain healthy bones, adequate serum vitamin D levels should be maintained (16). Approximately 90% of 25(OH)D is bound to binding protein (16, 17). In general, the free fraction of a hormone is the biological active component (16, 17). Accordingly, one would expect the bone strength variables to correlate more strongly to free fraction of vitamin D than to total vitamin D (18, 19). In line with this hypothesis, Powe et al. (20) have shown that free vitamin D is positively correlated to BMD in a group of young adults. Johnsen et al. (21) have obtained similar results in a population of postmenopausal women. These previous studies did not focus on evaluating other bone health parameters such as bone geometry and architecture. In a recent study, we have demonstrated free vitamin D serum level is a stronger positive determinant of bone parameters and hip bone strength indices in young female adults than total serum Vitamin D (22). The aim of the current study was to explore the relationships between serum free vitamin D and several bone parameters (bone mass, BMD, hip bone geometry

indices, composite indices of femoral neck strength and TBS) in a group of young Lebanese men.

Forty young men whose ages ranged from 18 to 35 years participated in the present study. The 40 participants were recruited from 2 private universities located in North Lebanon. All participants were nonsmokers and had no history of major orthopedic problems or other disorders known to affect bone metabolism or physical tests of the study. Other inclusion criteria included no diagnosis of comorbidities and no history of fracture. An informed written consent was obtained from the participants. The current study was approved by the University of Balamand Ethics Committee. Weight and height were measured, and body mass index (BMI) was calculated. BMC (in gram) and BMD (in gram per square centimeter) were determined for each individual by DXA (GE Healthcare, Madison, WI, USA) at whole body (WB), lumbar spine (L1–L4), total hip (TH), and femoral neck (FN). Femoral neck (FN) cross-sectional area (CSA), FN cross-sectional moment of inertia (CSMI), and L1–L4 TBS were also evaluated by DXA (22). In our laboratory, the coefficients of variation were <1% for BMC and BMD (22). Composite indices of FN strength were calculated as previously described (14, 15). FN compressive strength index (CSI), FN bending strength index (BSI), and FN impact strength index (ISI) were calculated (14, 15). Compressive strength  $((FN\ BMD * FN\ width) / weight)$  and bending strength  $((FN\ BMD * [FN\ width]^2) / (hip\ axis\ length * weight))$  express the forces that the FN has to withstand in weight-bearing, whereas impact strength  $((FN\ BMD * FN\ width * hip\ axis\ length) / (height * weight))$  expresses the energy that the FN has to absorb in an impact from standing height (14, 15). Free vitamin D, vitamin D binding protein and total vitamin D were measured as previously described (22).

Free vitamin D was positively correlated to WB BMC ( $r = 0.39$ ;  $p = 0.02$ ), WB BMD ( $r = 0.35$ ;  $p = 0.04$ ), TBS ( $r = 0.43$ ;  $p = 0.01$ ), TH BMD ( $r = 0.47$ ;  $p = 0.003$ ), FN BMD ( $r = 0.45$ ;  $p = 0.006$ ), ISI ( $r = 0.41$ ;  $p = 0.01$ ), CSA ( $r = 0.45$ ;  $p = 0.006$ ) and CSMI ( $r = 0.41$ ;  $p = 0.01$ ). Vitamin D binding protein was positively correlated to TBS ( $r = 0.44$ ;  $p = 0.008$ ) and CSI ( $r = 0.51$ ;  $p = 0.001$ ). Total vitamin D was not correlated to bone variables. The present study conducted on a group of young Lebanese men mainly shows that serum free vitamin D is a positive determinant of several bone variables (BMC, BMD, TBS and bone geometry indices). Although the strengths of the associations between free vitamin D and bone variables were moderate, this is the first study to show positive associations between serum free vitamin D and several DXA variables in young men. This correlation is of great importance making free vitamin D a variable to test routinely in youth. Accordingly, our study suggests that treatment for free vitamin D deficiency may improve bone health in youth, and therefore bone fragility fractures at a later age would be reduced. Enough evidence is now present to support the realization of a larger-scale powered study evaluating the association between free vitamin D and bone parameters in young and elderly populations. Such correlations, if present, should make free vitamin D dosing a routine in young and elderly subjects, especially if diagnosing a deficiency and treating it could improve bone quality and therefore reduce fragility fracture incidence at a later age.

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