Psychosocial Impacts on Bone Turnover in Adult Men: Preliminary Findings From the MIDUS Study

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MIDUS Midlife in the United States

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ABSTRACT

Recent work demonstrates that bone remodeling is, at least in part, regulated centrally in the hypothalamus. As osteoporosis ultimately results from disordered bone remodeling, it is plausible that psychosocial factors, both negative (e.g., depression) but also positive (e.g., purpose in life), could impact skeletal health. This work investigates correlations between psychosocial variables and serum bone turnover markers in adult male participants in MIDUS (Midlife in the US), a nationally representative cohort study of aging. In this preliminary analysis, serum turnover markers (BSAP, P1NP and NTx) in 247 men were correlated with positive and negative psychosocial variables. Additionally, a bone balance index (BBI), developed by deriving turnover marker T-scores and defining bone balance as formation T-score minus resorption T-score, was used to investigate associations between bone balance and psychosocial variables. A negative BBI favors resorption.

In men age ≥ 66 years (n = 75) measures of positive psychosocial status are negatively correlated with serum NTx while aspects of psychological ill-being are positively linked with NTx. In this group, the BBI is consistent, with negative psychological factors favoring resorption while positive variables favor formation. In contrast, among younger men (age 35-49, n = 61) the relationship between psychosocial factors and BBI is opposite to that in older men in that positive psychosocial factors are associated with increased bone resorption and a negative BBI.

In conclusion, psychosocial factors may play an important role in osteoporosis pathogenesis in men. Differential associations between bone turnover and psychosocial status may exist at various ages.

INTRODUCTION

Osteoporosis ultimately results from unbalanced bone remodeling where resorption exceeds formation. As bone remodeling is, at least to some extent, regulated centrally, it is plausible that psychosocial factors impact bone balance. Though negative impacts have received the most study (e.g., depression being associated with low BMD), it is possible that positive psychosocial factors could favorably impact bone formation, thereby being associated with lower fracture risk. These possibilities have received limited study. As such, the purpose of this preliminary work is to investigate potential impacts of psychosocial factors on markers of bone turnover.

MIDUS II (Midlife in the United States) is a population-based nationally representative survey of midlife adults. To this multi-disciplinary psychosocial survey, a biomarker component was added which expanded data collection to include measurement of multiple biologic parameters including bone mineral density by DXA and serum markers of bone turnover. This preliminary report investigates relationships between markers of bone turnover and psychosocial factors (both positive and negative) in men.

METHODS

Subjects

- Adults participating in Midlife in the US (MIDUS-II)
  - Men participating in the Biomarker Project were evaluated

Psychosocial Assessment

- Comprehensive multi-disciplinary assessment performed; selected components presented here
  - Reported data obtained via self-administered questionnaires
- Assessment of positive psychosocial factors; multiple dimensions of psychological well-being and positive affect were evaluated including:
  - Purpose in Life Scale – Seven questions related to purpose and direction in life
  - Self-acceptance – Seven questions regarding confidence, evaluation of achievements and comparison to others
- Assessment of negative psychosocial factors; multiple dimensions of depressive symptomatology, anxiety, loss of interest and negative affect were evaluated including:
  - General Distress-Depressive Symptoms – 12 questions related to mood and general outlook
  - Loss of Interest – Eight questions related to self-worth, motivation and engagement
  - CES-D Depression Scale – 20 questions related to issues such as self-worth, anxiety, mood and interactions with others

Bone Turnover Markers

- Serum obtained by standard venipuncture in the fasting state (no food or drink since midnight) between 0600-0700
- Markers of bone turnover measured using commercially available kits as follows:
  - Bone Specific Alkaline Phosphatase (BSAP); Metra BAP EIA immunoassay, Quidel (San Diego, CA)
- N-Telopeptide of Type 1 Collagen (NTx)
  - Osteomark ELISA/EIA immunoassay, Wompole Laboratories (Princeton, NJ)

Bone Balance Index (BBI)

- Developed to potentially evaluate imbalances between bone formation and resorption
- T-scores for BSAP and NTx created using data from the first 500 participants in the MIDUS II Biomarker Project
  - Men younger than 50 years used as a gender-specific normative group for calculation of mean and SD
- BBI defined as formation (BSAP) T-score minus resorption (NTx) T-score
  - Positive values favor formation while negative values favor resorption

Statistical Methods

- Subjects were arbitrarily grouped into 3 age categories; 35-49, 50-65 and ≥ 66 years
- Scatterplots of bone turnover markers and BBI with psychosocial parameters were examined and data windsorized to normalize outliers
- Relationships between bone turnover markers and psychosocial variables were evaluated using Pearson's correlation with SPSS (Chicago, IL)
- Linear regression analyses were performed for purposes of data presentation

RESULTS

Subjects

- Adults participating in Midlife in the US (MIDUS II)
  - Preliminary male data from the Biomarker project; total n = 247; age 59.3 ± 12.1 (mean ± SD); 90% were Caucasianxxx
  - Age 39-49; n = 61; 44.3 ± 3.8 (mean age ± SD)
  - Age 50-65; n = 111; 57.5 ± 4.3 (mean age ± SD)
  - Age ≥ 66; n = 75; 74.3 ± 5.6 (mean age ± SD)

Positive Psychosocial Factors

- Purpose in Life
  - Correlated with serum NTx; negatively in men age ≥ 66 years ($p < 0.05$; Figure 1a) but positively in men age 35-49 years ($p < 0.001$; Figure 1b)
  - Correlated with BBI; relationship favors formation in men age ≥ 66 years ($p < 0.05$; Figure 1c) but resorption in men age 35-49 (p , 0.01; Figure 1d)
  - No correlation with NTx or BBI in men age 50-65 (data not shown)
- Self-acceptance
  - Correlated with serum NTx; negatively in men age ≥ 66 years ($p < 0.05$; Figure 2 a) but positively in men age 35-49 years ($p < 0.01$; Figure 2b)
  - Correlated with BBI; relationship favors formation in men age ≥ 66 years ($p < 0.05$; Figure 2c) but resorption in men age 35-49 ($p < 0.01$; Figure 2d)
  - No correlation with NTx or BBI in men age 50-65 (data not shown)

Negative Psychosocial Factors

- Depressive Symptoms
  - Correlated with serum NTx; positively in men age ≥ 66 years ($p < 0.01$; Figure 3a) but no correlation in men age 35-49 (data not shown)
  - Correlated with BBI; relationship favors resorption in men age ≥ 66 years ($p < 0.05$; Figure 3b) but no correlation in men age 35-49 (data not shown)
  - No correlation with NTx or BBI in men age 50-65 (data not shown)
- Loss of Interest/CES-D Depression Scale
  - Correlated with serum NTx; positively in men age ≥ 66 years ($p < 0.01$; data not shown) but no correlation in men age 35-49 (data not shown)
  - Correlated with BBI; relationship favors resorption in men age ≥ 66 years ($p < 0.05$; data not shown) but favors resorption in men age 35-49 ($p < 0.10/0.05$; data not shown)
  - No correlation with NTx or BBI in men age 50-65 (data not shown)

FIGURES

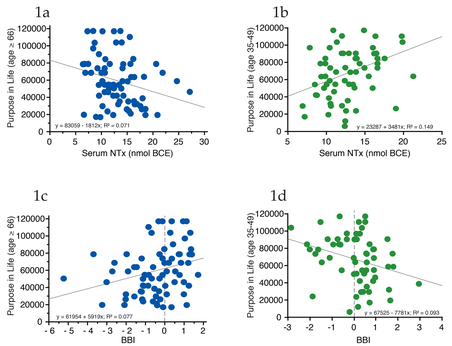

Figure 1a-d: ***Relationship of Bone Turnover with Positive Psychosocial Factors; Purpose in Life.*** Serum NTx is negatively related to purpose in life in men over age 65 (1a). However, in men age 35-49 a reverse relationship is observed (1b). Consistent with this, a bone balance index (BBI) identifies a relationship of positive purpose in life with bone formation in men ≥ 66 (1c). Similar to the NTx relationship, a bone balance index favors resorption in men age 35-49 (1d).

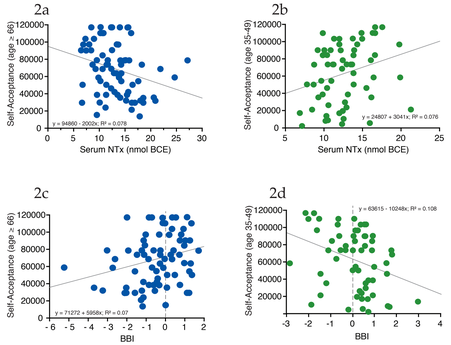

Figure 2a-d: ***Relationship of Bone Turnover with Positive Psychosocial Factors; Self-acceptance.*** Serum NTx is negatively related to self-acceptance in men over age 65 (2a). However, in men age 35-49 a reverse relationship is observed (2b). Consistent with this, a bone balance index (BBI) identifies a relationship of positive self-acceptance with bone formation in men ≥ 66 (2c). Similar to the NTx relationship, a bone balance index favors resorption in men age 35-49 (2d).

FIGURES

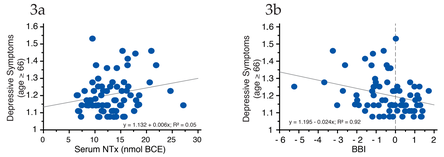

Figure 3a-b: ***Relationship of Bone Turnover with Negative Psychosocial Factors; General Distress-Depressive Symptoms.*** Serum NTx is positively related to depressive symptoms in men over age 65 (3a). Consistent with this, a bone balance index (BBI) identifies a relationship of depressive symptoms with bone resorption in men ≥ 66 (3b).

SUMMARY

- Serum measures of bone turnover are related psychosocial parameters.
- This relationship differs by age.
- In men over age 65:
  - Measures of positive psychosocial status are associated with lower serum NTx and a bone balance index favoring formation.
  - Measures of negative psychosocial status are correlated with higher NTx concentrations and a bone balance index favoring resorption.
- In men age 35-49:
  - Measures of positive psychosocial status are associated with higher serum NTx and a bone balance index favoring resorption.

CONCLUSIONS

- The relationship of psychosocial factors with bone turnover appears to differ by age in men.
- In older men, positive psychosocial factors appear to favorably impact bone balance while negative psychosocial status may adversely impact bone balance.
- Psychosocial factors may be important, but previously underappreciated, risk factors for bone loss and therefore fracture risk.

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