Title: The effectiveness of serum cross-linked N-telopeptide (NTx) and aminoterminal procollagen extension propeptide (PINP) measurements for identifying osteoporosis in elderly women

Author(s): David Berndt, Burton Dunlap, William Jarrard, Jung Park, Ashley Schlafstein, Akhilesh Venkatesan

Clinical Question: Can screening for serum cross-linked N-telopeptide (NTx) and aminoterminal procollagen extension propeptide (PINP) identify decreased bone mineral density in elderly women effectively when compared with whole-body femoral neck and lumbar spine dual emission X-ray absorptiometry?

1 and 2) PICO Parts:
  P – elderly women
  I – serum cross-linked N-telopeptide(NTx) and aminoterminal procollagen extension propeptide(PINP)
  C – Whole-body femoral neck and lumbar spine dual emission X-ray absorptiometry
  O – lowered bone mineral density

a. Database(s) searched: Ovid Medline
b. Keyword Search Terms used: N-telopeptide, diagnosis
c. MeSH Search Terms used: Osteoporosis

3.) Methods description
- Setting: New Mexico Aging Process Study at the University of New Mexico Health Sciences Center from 1993-1999
- Population: Elderly women at risk for osteopenia
- Sample size:
  - 196 ambulatory, community-dwelling female volunteers aged 60-90 years between 1993 and 1999; 93% Caucasian, 7% Hispanic ancestry
  - Exclusion criteria: recent myocardial infarctions; diagnosis of coronary disease; uncontrolled hypertension; malignancy; chronic obstructive pulmonary disease; immobile; receiving chemotherapeutic, cardiac, respiratory, thyroid, glucocorticoid, or antipsychotic medications
  - There was no mention of the number of patients that were excluded from the study or why
- Study design: Prospective cohort study - Compared sensitivity and specificity of two different diagnostic techniques on identifying a set level of decreased bone mineral density. Performed the two tests on both patients with the decreased bone mineral density and healthy controls (not having decreased bone density).

4.) Methods interpretation (Validity):
  a. Was there an independent “blind” comparison with a reference standard?
     i. The study included the gold standard of bone mineral density (BMD) measured by dual X-ray absorptiometry (DXA)
     ii. The study was non-blinded
  b. Did the sample include an appropriate spectrum of patients to whom the diagnostic/screening test will be applied in clinical practice?
     i. The purpose of this study was to determine the effectiveness of measuring serum levels of cross-linked N-telopeptides of bone collagen (NTx) and aminoterminal procollagen extension propeptide (PINP) to identify postmenopausal women with low BMD. This study did not include a diverse
demographic that was representative of the health of postmenopausal women. In addition to the exclusion criteria above, the subjects consisted of 93% caucasian and 7% hispanic women and as a whole the subjects were attributed to having exemplary health behaviors including diet, lifestyle, and exercise habits.

ii. The study also states that the prevalence of the osteopenia is low amongst the study participants and postulates that they would be better served with a pool of applicants better representative of the general population.

c. Did the results of the diagnostic/screening test evaluated influence the decision to perform the reference standard?
   i. All participants of the study were evaluated with both the screening test and the reference standard

d. Were the methods for performing the diagnostic/screening test described in sufficient detail to permit replication?
   i. There was adequate detail of preparation of the patient
      1. Study applicants were described as having a healthy diet, exercise regimen, and lifestyle, but no details were provided.
      2. Pre-existing diseases and medications that precluded participation in the study were listed
      3. The authors described how they positioned the bodies of the subjects prior to scanning
   ii. There was sufficient detail regarding administration of the test
      1. The authors provided sufficient detail in the methods section for the reproduction of the study.
      2. Both the non-reference and reference groups were measured via DXA and had serum levels checked for NTx and PINP.

iii. There was sufficient detail regarding analysis or interpretation of the results
   1. The authors provided the names of the software programs used in statistical analysis of the data. They detailed which program yielded each method of analysis.

5.) Results

Of the 12 women classified as having a low bone mineral density (BMD) based on the measurements of total body, femoral neck, and spine values; all were classified as having a serum NTx higher than the cutoff 15.0 nmol as hypothesized. Per the NTx test, the negative predictive value is high, yet the positive predictive value is fairly low in this study perhaps due to the patient sample having only slightly decreased BMD. Only 10 out of the 12 women with decreased BMD, per femoral neck and spine values, were correctly identified as having low BMD using the PINP tests. Again, the positive predictive value was low but the negative predictive value approached 1.0.

Both the NTx and PINP tests for decreased BMD were only slightly effective. The NTx marker test had a stronger predictive value than the PINP test overall, but they both revealed minimal positive predictive power. These two tests would be of productive use in ruling someone out of having a decreased BMD, yet the tests would not be as effective in diagnosing a patient with low BMD.

6.) Translational applications

Until the study is validated on a larger scale it will be of little use to our patients. However, it has the potential to diagnose osteoporosis without exposing patients to radiation as a result of DXA.