

Collagen Cross Links, N-Telopeptide (NTx), Urine

Test Codes:	2 nd Morning Void	10922
	24 Hour Urine	90080

Clinical Use

- Monitor therapeutic response in patients with metabolic bone disorders
- Predict future bone mineral density (BMD)
- Predict therapeutic response prior to initiation of antiresorptive therapy
- Detect bone metastasis in patients with various malignancies

Clinical Background

Osteopenia and osteoporosis are characterized by low bone mineral density (BMD) leading to bone fractures that may result in full recovery or chronic pain, disability, and even death. Healthy levels of BMD are maintained by a balance between bone resorption and bone formation. N-telopeptide (NTx), the amino-terminal cross-linked peptide of type I collagen, is released during bone resorption and has been correlated with BMD T-scores.¹ Multiple studies have shown that NTx not only correlates inversely with BMD response to therapy, but also is an early marker or predictor of BMD response. Thus, therapeutic response can be determined within 3 to 6 months of therapy rather than 1 to 2 years.²⁻⁴ Studies have also demonstrated that elevated pretreatment NTx values predict positive response to therapies such as hormone replacement therapy in postmenopausal women.^{4,5} In patients with malignancies, elevated levels of NTx may indicate bone metastases.⁶⁻⁸

The above clinical utility was established based on urinary measurements.⁹⁻¹²

Individuals Suitable For Testing

- Individuals who are about to begin antiresorptive therapy
- Individuals who are currently receiving antiresorptive therapy
- Individuals with suspected bone metastasis

Specimen Requirements

2nd Morning Void: 2 mL urine in a sterile screw cap container (1 mL minimum). Do not use preservatives. Acidified specimen is not acceptable. Discard the first morning void specimen. Collect the second morning void, mix well.

24 Hour Urine: 2 mL refrigerated urine from a 24-hour urine collection. Do not use preservatives. Acidified specimens are not acceptable. Keep refrigerated during collection.

CPT Codes*

- 82523, 82570

Method

- Enhanced Chemiluminescence
- Utilizes an immobilized monoclonal anti-NTx antibody
- Results are reported in nanomoles of bone collagen equivalents per mmol creatinine
- Synonyms: type I collagen cross-linked N-telopeptide, NTx

Interpretive Information

Increased N-telopeptide results in urine indicate an increased rate of bone resorption. Such increases may be observed in osteopenia, osteoporosis, celiac disease, Paget's disease, primary hyperparathyroidism, rheumatoid arthritis, and growth hormone deficiency (non-adult onset). Early postmenopausal women (<3 years postmenopausal) with second morning void NTx levels ≥ 67 nmol/mmol creatinine experience the greatest benefit from hormone replacement therapy (HRT). A $\geq 30\%$ decline in second morning void N-telopeptide concentration following 6 months of HRT is indicative of a positive therapeutic response in postmenopausal women. 88% of women with such a decline were shown to have maintained or increased their BMD at 1 year.⁴ Similar declines in NTx and similar correlation with BMD was observed post alendronate therapy.²

An N-telopeptide result within the premenopausal reference range does not rule out osteoporosis or the need for therapy.

References

1. Schneider DL and Barrett-Connor EL: Urinary N-telopeptide levels discriminate normal, osteopenic, and osteoporotic bone mineral density. *Arch Intern Med* 157:1241-1245, 1997.
2. Greenspan SL, Parker RA, Ferguson L, et al: Early changes in biochemical markers of bone turnover predict the long-term response to alendronate therapy in representative elderly women: a randomized clinical trial. *J Bone Miner Res* 13:1431-1438, 1998.
3. Amama EA, Taga M, and Minaguchi H: The effect of gonadotropin-releasing hormone agonist on type I collagen C-telopeptide and N-telopeptide: the predictive value of biochemical markers on bone turnover. *J Clin Endocrinol Metab* 83:333-338, 1998.
4. Chesnut CH III, Bell NH, Clark GS, et al: Hormone replacement therapy in postmenopausal women: urinary N-telopeptide of type I collagen monitors therapeutic effect and predicts response of bone mineral density. *Am J Med* 102:29-37, 1997.
5. Rosen CJ, Chesnut CH III, and Mallinak NJS: The predictive value of biochemical markers of bone turnover for bone mineral density in early postmenopausal women treated with hormone replacement or calcium supplementation. *J Clin Endocrinol Metab* 82:1904-1910, 1997.
6. Miura H, Yamamoto I, Takada M, et al: Diagnostic validity of bone metabolic markers for bone metastasis. *Endocr J* 44:751-757, 1997.
7. Westerhuis LW and Delaere KP: Diagnostic value of some biochemical bone markers for the detection of bone metastases in prostate cancer. *Eur J Clin Chem Clin Biochem* 35:89-94, 1997.
8. Demers LM, Costa L, Chinchilli NM, et al: Biochemical markers of bone turnover in patients with metastatic bone disease. *Clin Chem* 41:1489-1494, 1995.
9. Gertz BJ, Clemens JD, Holland SD, et al: Application of a new serum assay for type I collagen cross-linked N-telopeptides: assessment of diurnal changes in bone turnover with and without alendronate treatment. *Calcif Tissue Int* 63:102-106, 1998.
10. Scariano JK, Glew RH, Bou-Serhal CE, et al: Serum levels of cross-linked N-telopeptides and aminoterminal propeptides of type I collagen indicate low bone mineral density in elderly women. *Bone* 23:471-477, 1998
11. Prestwood KM, Thompson DL, Kenny AM, et al: Low dose estrogen and calcium have an additive effect on bone resorption in older women. *J Clin Endocrinol Metab* 84:179-183, 1999.
12. Clemens JD, Herrick MV, Singer FR, and Eyre DR: Evidence that serum NTx (collagen-type I N-telopeptides) can act as an immunochemical marker of bone resorption. *Clin Chem* 43:2058-2063, 1997.

*The CPT codes provided are based on AMA guidelines and are for informational purposes only. CPT coding is the sole responsibility of the billing party. Please direct any questions regarding coding to the payor being billed.