



Bone Remodelling Markers: Value and Limitations

Markers of bone turnover, measured in blood or urine, correlate with changes in the metabolic activity of bone. The rate of bone remodelling is important. With ageing, the quantum of bone removed/resorbed and the amount replaced/formed becomes increasingly imbalanced. Consequently, the more bone remodelling units that are active at any one time, or the greater the activity of individual units, the greater the overall rate of bone loss.

Bone turnover markers are probably predictive of the rate of bone loss and could help determine the efficacy of treatment.

Bone turnover markers:

- May predict fracture risk independently of bone mineral density, according to some studies.
- A drop in bone resorption is an early predictor of response to all anti-resorptive osteoporosis treatments initiated in general practice (bisphosphonates, denosumab or raloxifene), with these markers changing earlier than comparable markers of bone formation.
- They may be predictive of later changes in bone mineral density (BMD), and can be measured before BMD changes can be evaluated.

Which Bone Resorption Marker?

Markers measuring the rate of bone loss are degradation products of type 1 collagen cleaved during bone resorption.

Cross-linking telopeptides of collagen can be measured by immunoassays that are specific for the beginning (N terminal- called NTX) or end (C terminal- called CTX) of type 1 collagen. Whilst measuring urinary NTX and serum CTX provide comparable information there are some advantages of CTX over NTX. Consequently, serum CTX has been proposed as a reference method – see May edition of *Medical Forum*.

- The measurand in the CTX assay is clearly defined, allowing this 8 amino acid oligopeptide to become the reference method.
- Most serum CTX is from osteoclastic bone resorption (indicating high specificity).
- The assay can be performed manually or by automated methods and is only provided by one manufacturer (obviating the need for harmonisation)
- The biological and analytical variability for CTX is well documented in the literature.

Consequently, at Clinipath Pathology, we will be transitioning from the measurement of urine NTX to the measurement of serum CTX and will commence reporting serum CTX assay results soon.

Uses and Limitations

Serum CTX is a potentially useful test when investigating the cause of increased alkaline phosphatase, verifying compliance with osteoporosis treatment, improving persistence with that treatment or identifying occult secondary causes of osteoporosis such as apathetic hyperthyroidism or other metabolic bone disorders such as Paget's disease.

Samples collected fasting in the morning minimise intra-individual variation and requests ideally should include the reason for testing. Medicare currently provides a rebate for tests of bone resorption in patients with known bone disease taking treatment.



The known limitations are:

1. Not all anti-resorptive treatments suppress bone resorption to the same degree.

Provision of the type of anti-resorptive agent used and the duration of treatment is not only helpful for billing but allows us to report more specifically - whether the rate of bone resorption is typical or higher than expected for a particular anti-resorptive agent.

For example, denosumab suppresses bone resorption earlier and to a greater degree than a bisphosphonate.

2. Bone resorption is not predictive of future fracture risk in individuals

CTX can provide complementary information to bone mineral density in subpopulations but this measurement has not been currently adopted into fracture risk algorithm calculators such as FRAX or the Garvan risk calculator for individuals.

3. The measurement of serum CTX cannot be used to select treatment

This is because the baseline rate of bone remodelling is not predictive of the rate of change of bone remodelling or rate of change of bone density whilst on treatment.

4. Measurement of bone formation and bone resorption do not provide additive information

Whilst bone remodelling is a coupled process wherein bone formation and bone resorption are linked, the measurement of bone resorption or bone formation markers provide comparable information regarding the rate of bone remodelling. Measurements of both bone formation and bone resorption markers in individual patients do not help determine the degree of imbalance in bone remodelling and is therefore unnecessary.

Understanding these limitations and the potential value of measuring bone remodelling markers can be useful when making decisions regarding individual patient management in those taking treatment for osteoporosis.

Key Points

1. Bone resorption markers can assess early response to anti-resorptive treatment.
2. Information about which anti-resorptive treatment is being used and the duration of treatment is necessary if more specific advice is required.
3. Bone resorption markers results cannot be used to assess fracture risk or select treatment.

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