**Procollagen type 1 amino terminal propeptide (P1NP) – an overview**

**ABSTRACT**

Around 200 million people worldwide have osteoporosis, and osteoporotic fractures account for 8.9 million of all fractures. The key to effective treatment and the identification of osteoporotic patients at high risk of fracture is early diagnosis of osteoporosis. The quantitative study of Bone Mass Density (BMD) by Dual Energy X-Ray Absorptiometry (DXA) provides the foundation for the diagnosis of osteoporosis and the evaluation of fracture risk. Bone strength is only partially revealed by the gold standard approach of BMD evaluation of bone mass by DXA. The clinical use of bone biomarkers in conjunction with bone mineral density assessment has given detailed information for the diagnosis of osteoporosis. The tissue of the bone is dynamic and constantly changes over the course of a person's life. During the processes of bone remodelling, bone biomarkers such as formation, resorption, and regulator are released. The rate of bone production and resorption may now be accurately and sensitively assessed using a variety of biomarkers. Procollagen type 1 amino-terminal propeptide (P1NP), one of the bone markers, has been shown to be a more sensitive bone biomarker for determining the rate of bone production in osteoporosis. A clinical application for P1NP testing is currently being developed.

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**INTRODUCTION**

Over the past decade, researchers have done studies on biomarkers of bone turnover. Bone formation biomarkers, bone resorption biomarkers and regulators of bone turnover are produced during the bone remodelling process. Biomarkers of enzymes, proteins, and by products throughout the bone remodelling process have been used to study bone metabolism. The rate of bone production and resorption may now be accurately and sensitively assessed using a variety of biomarkers (Fig 1.)



Fig 1. Biochemical biomarkers of bone turnover. *Blue* boxes/arrows represent bone formation markers: bone-specific alkaline phosphatase (BALP); osteocalcin (OC); propeptides of type I procollagen (P1NP and P1CP). Orange boxes/arrows represent bone resorption markers: pyridinoline (PYD); deoxypyridoline (DPD); carboxy-terminal crosslinked telopeptide of type 1 collagen (CTX-1); amino-terminal crosslinked telopeptide of type 1 collagen (NTX-1); hydroxyproline (HYP); hydroxylysine (HYL); bone sialoprotein (BSP); osteopontin (OP); tartrate-resistant acid phosphatase 5b (TRAP 5b); cathepsin K (CTSK). *Green* boxes represent regulators of bone turnover: receptor activator of NF-κB ligand (RANKL), osteoprotegerin (OPG), dickkopf-1 (DDK-1) and sclerostin. 1

The bone biomarkers are useful in assessing osteoporosis when the Bone Mass Density (BMD) of Dual Energy X-Ray Absorptiometry (DXA) measurement is insufficient to make the diagnosis.

The huge potential to improve the early assessment of those at high risk for osteoporosis is therefore demonstrated by the combination of BMD testing by DXA and biomarker detections. P1NP is one biomarker that has highest potential as a sensitive and stable bone marker for the early detection of osteoporosis among these biomarkers. It is also a bone formation biomarker that has been recommended by both the International Osteoporotic Foundation (IOF) and International Federation of Clinical Chemistry (IFCC). Major advantages of using P1NP as a bone biomarker include its low individual variability and high essay precision.

P1NP, a biomarker for bone growth, physiologically represents bone anabolic activity. Its levels decrease with aging, however there is an increase in postmenopausal age and osteoporosis due to increased bone production and resorption, which leads to higher levels of P1NP. The degree of P1NP expression represents the development of new bone.

Type 1 collagen, the most widespread protein in bone, produces P1NP as a byproduct. 35% of the bone matrix is organic and 65% is inorganic, with collagen type 1 making up the majority of the organic portion. Measuring collagen synthesis byproducts is an intriguing method for studying bone development. P1NP is cleaved from type 1 procollagen by proteases outside the osteoblast after the osteoblast produces new type 1 collagen. While some P1NP enter the bloodstream, others deposit straight into the bone matrix. Collagen type 1 and P1NP both decreased as osteoblast production decreased. The need for P1NP expression level measurement rises along with the popularity of bone metabolism research.

The organic bone matrix (>90%) contains type 1 collagen, which is produced in bone from procollagen type 1. Fibroblasts and osteoblasts produce type 1 procollagen. The N- and C-terminal extensions of procollagen type 1 are removed by certain proteases as it is converted to collagen. The P1CP and P1NP procollagen type 1 are then conjugated to the bone matrix. A specific indicator of type 1 collagen deposition is the bone formation biomarker P1NP. The intracellular space is where P1NP is released during the synthesis of type 1 collagen and eventually ends up in the bloodstream. P1NP is often produced in a trimeric configuration (derived from the trimeric collagen structure), which is quickly broken down to a monomeric form by thermal degradation defects. Using radioimmunoassay or the enzyme-linked immunosorbent assay (ELIZA), P1NP antibodies are utilized to identify the trimeric structure of the protein. To evaluate the rate of bone production in osteoporosis, P1NP has proven to be a more sensitive bone biomarker.

A clinical application for P1NP testing is currently being developed. The primary protein in bone is type 1 collagen, which is produced inside osteoblast. P1NP is created when proteases interact with type 1 procollagen, and as a result, serum P1NP concentration reflects the amount of freshly produced bone. Therefore, illnesses like osteomalacia and multiple myeloma that have a high rate of bone turnover may cause an increase in serum levels of P1NP. P1NP levels in the serum may dramatically rise as a result of teriparatide therapy. P1NP had therefore been proposed as a reference serum marker of bone development.

**CONCLUSION**

P1NP, a marker of bone development, has been linked in numerous studies to multiple myeloma, bone metastasis from tumors, and other bone metabolic disorders. Moreover, its detection is unaffected by interference from food, circadian rhythm, hormones, and other elements. Bone biomarkers have the potential to be extremely effective indicators for assessing osteoporosis therapy and potentially assisting in the early-stage clinical diagnosis of osteoporosis. As a result, P1NP is a fresh and reliable bone diagnostic marker for the early identification of osteoporosis.

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