

EMERGING APPROACH OF BONE REMODELLING INDICES

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ABSTRACT

The field of osteoporosis, especially of primary type, tidily connected with estrogen deprivation and aging, is complex and dynamic. Bone turnover markers (BTM) have been and still are a hot spot on this panorama, because no straight cut lines are found yet. We aim to briefly introduce the current status of BTM, as a short commentary. BTM have a high inter- and intra- individual variation, they are rather expensive for daily practice, they are not necessary to diagnose osteoporosis. Low or normal levels do not necessary mean that a person will not suffer fragility fracture while a higher level is associated with an increased fracture risk. Moreover, BTM seem better players for clinical studies to point out the efficacy of anti-osteoporotic drugs rather than helping each patient's decision. BTM prematurely detect remodelling variations before DXA. No algorithm or calculation model of fracture prediction has incorporated yet BTM, most probably due to heterogeneity of reports. Traditional BTM are alkaline phosphates, osteocalcin, and collagen- derived fragments. New BTM, that proved useful, are represented by P1NP. Atypical BTM like osteoprotegerin, sclerostin, and serotonin are still far from daily practitioners' assessment. Regardless classical or modern, the way that BTM represent a reflection of skeleton health is still an emerging subject.

Keywords: bone turnover marker, serotonin, osteoporosis

INTRODUCTION

The field of osteoporosis, especially of primary type tidily connected with estrogen deprivation and aging, is complex and dynamic. Bone turnover markers (BTM) have been and still are a hot spot on this panorama because no straight cut lines are found yet. (1,2,3)

OBJECTIVE

We aim to briefly introduce the current status of BTM, a domain where questions are still unanswered.

MATERIAL AND METHOD

This is a short commentary regarding a modern theme in menopausal osteoporosis field using PubMed.

GENERAL CONTEXT

Some facts about BTM are widely recognised like: a high inter- and intra- individual variation is found, they are rather expensive for daily practice, they are not strictly necessary to obtain the diagnosis of osteoporosis while a lower or normal levels do not necessary mean that a person will not suffer an osteoporotic fracture but a higher level is associated with an increased fragility fracture risk. (4-6) Moreover, BTM seem better players for clinical studies to point out the usefulness of anti-osteoporotic drugs rather than helping each patient's decision. (7) Meta-analysis on menopausal females showed mild negative correlation between BTM and BMD (Bone Mineral Density) at DXA (Dual-Energy X-Ray Absorptiometry); the most useful results are for alkaline phosphatase, osteocalcin, CTX (blood C-terminal cross-linking telopeptides of type I collagen), NTX (urinary N-terminal cross-

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linking telopeptides of type I collagen) while subjects with menopausal osteoporosis may be found with higher levels of alkaline phosphatase as well as those with prevalent fractures (like osteocalcin and CTx). (8) BTM prematurely detect remodelling variations before DXA - BMD does thus the role on fracture prediction. (9) However, no algorithm or calculation model has incorporated yet BTM, most probably due to heterogeneity of reports.

DISCUSSION

When it comes to BTM, the concept of “traditional” and “new” (or atypical) BTM is constantly changing because of promising indices that finally did not reach the everyday clinical approach like osteoprotegerin, sclerostin, serotonin while others that became very useful like P1NP. (9-12) As classical BTM are recognised alkaline phosphates, osteocalcin and collagen segments derivatives. (8,9) P1NP was proposed as standard of bone formation three years ago in order to be included in all clinical trials and many of recent anti-osteoporotic drugs studies embraced it. (10,11) Osteopontin is connected to bone resorption and menopausal subjects with osteoporosis have been found with higher levels than women with osteopenia at DXA while females with prevalent vertebral fragility fractures

have an elevation when compare with those without fractures. (12) Overall, a negative correlation with BMD was established although nowadays the marker is not routinely used. (12,13) Sclerostin inhibit the Wnt/ β catenin pathway of bone remodelling with a secondary increase of bone loss especially in menopause. (14,15) It is blocked by different bone regulators as TGF- β 1 (which is a mediator of bone turnover and decrease with age). (14) Sclerostin elevates during menopausal stages and it is linked to favour the balance of bone resorption instead of bone formation. (15) Circulating serotonin as measured after blood with drawn has been found in some studies to be correlated with bone loss and low bone mineral density in menopausal women and people taking selective serotonin reuptake inhibitors. (16,17) However, its skeleton influence is a cocktail derived from distant effects ordered by brain serotonin, paracrine actions and direct influence of gut 5-hydroxytryptamine, that is why its assays might not be very relevant for its complex actions on bone. (16,17)

CONCLUSION

Regardless traditional or atypical, the way that BTM represent a reflection of skeleton health is still an emerging subject.

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