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Editorial

An update on sclerostin and kidney

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Introduction

Bone diseases commonly detected in chronic renal failure patients and increases a patient's risk for cardiovascular calcification, fracture and mortality. Excessive vascular calcification between hemodialysis individuals plays a predictive and contributive role in consequent cardiovascular incidents and all-cause mortality (1,2). The relationship of bone turnover and cardiovascular disease, is defined by various traditional, injurious determinants of vascular calcification among chronic renal failure patients, such as, increasing age, diabetes mellitus, length of the time patients on hemodialysis, excessive vitamin D therapy, chronic inflammation, net positive calcium and phosphate balance, and finally and dyslipidemia (1-3). Renal osteodystrophy, disturbed calcium and phosphate homeostasis, in association with elevated fibroblast growth factor 23, vitamin D deficiency and elevated plasma parathyroid hormone have been established as crucial cardiovascular risk factors and represent chronic kidney disease - mineral and bone disorder syndrome (1-4).

Current evidences, established that, chronic kidney disease-mineral bone disorder is an active extra-endochondral ossification process. In fact, dysregulation of osteogenic signaling, accelerates the conversion of vascular smooth muscle cells to osteo/chrondrocytic-like cells, resulted to the development of dystrophic mineralization and eventually vascular calcification (2-6). Recent investigations, showed the role of Wnt signaling pathway, to the pathogenesis of bone metabolism and vascular calcification. The (canonical) Wnt–β-catenin route appeared as the main component of Wnt signaling with thoughtful influences on the skeleton. Principally, canonical signaling is started by the binding of Wnt ligands to the dual receptor complex comprising frizzled (FZD) protein and either low-density lipoprotein receptor-related protein 5 or 6 (LRP5/6) (2-6).

Recent data, showed that, Wnt directly influences both the osteoclast and the osteoblast bone cell lineages and likewise indirectly influences these cells across cross-talk in the bone environment, making an overall increase in osteoblastogenesis concurrently with a diminish in osteoclastogenesis, hence ensuing in an enhanced bone formation and lessened bone resorption. Therefore, Wnt signaling activation has an anabolic and anticatabolic bone property (1-5).

Recently much attention, has been directed toward sclerostin, which is produced by the osteocyte and has anti-anabolic properties on bone formation. Sclerostin is a glycoprotein (22 kDa) product of the SOST gene in osteocytes. Sclerostin is a Wnt signaling pathway antagonist which leads to a negative regulation of bone formation by inhibiting differentiation and proliferation of osteoblasts (5-7). Hence, it is possible that, sclerostin which is expressed in osteocytes and some chondrocytes is able to inhibit bone formation by osteoblasts. Additionally, sclerostin prevents osteoblast proliferation and differentiation enhancing their apoptosis through canonical Wnt signaling blocking. However, sclerostin as a soluble blocker of canonical Wnt signaling, is crucial for bone physiology (1-4). Interestingly, various experimental and clinical investigations, propose that the Wnt pathway could also play a role in atherosclerosis and vascular calcification (4-6).

More recent data, showed, sclerostin is detectable in atherosclerotic plaques and found to be expressed in calcifying vasculature that suggests a participation in transdifferentiating from vascular smooth muscle towards osteocyte-like cells. Thus the net results of actions of sclerostin consisting of a decrease in bone formation by blocking osteoblast proliferation and differentiation and importantly, promoting osteoblast apoptosis. Furthermore, high serum value of sclerostin have been accompanied with incident fractures consisting hip fractures in postmenopausal women (5-9). Thus, inhibition of sclerostin is believed to be a promising new attitude for the treatment of osteoporosis. Blocking of sclerostin with anti-sclerostin antibodies enhances bone mass in rodents, primates, and also in humans. Accordingly, anti-sclerostin antibodies are presently in clinical elaboration for the therapy of osteoporosis. However, the important questions is the role of sclerostin in chronic kidney disease - mineral and bone disorder syndrome (3-7). The current finding imply that, serum sclerostin levels rise in patients with chronic kidney disease and those on hemodialysis. Whether this is due to reduced clearance or surplus production has not yet been fully evaluated. It is possible that, sclerostin increasing may related to parathormone resistance in chronic renal failure with other factors like vitamin D deficiency. Circulating sclerostin levels were elevated when the glomerular filtration rate (GFR)

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Implication for health policy/practice/research/medical education

Sclerostin is a Wnt signaling pathway antagonist which leads to a negative regulation of bone formation by inhibiting proliferation and differentiation of osteoblasts. It can be assumed that, sclerostin which is expressed in osteocytes and some chondrocytes is able to inhibit bone formation by osteoblasts. Additionally, sclerostin prevents osteoblast proliferation and differentiation enhancing their apoptosis through canonical Wnt signaling blocking. Since chronic kidney disease-metabolic bone disorder induces cardiovascular disease and mortality in chronic kidney disease patients, the association of serum sclerostin levels and the future outcome may become a crucial entity.

Keywords: Sclerostin, Kidney, Chronic kidney disease, Fibroblast growth factor 23

dropped, due to poorly understood mechanisms involving either increased production or kidney accumulation. This accumulation may reach 3–4 times higher in individuals with end-stage kidney failure compared with healthy individuals (2-7). Moreover in patients on regular hemodialysis, sclerostin has been detected to be increased and related to the bone quality impairment. More recent investigation, demonstrated that, increased plasma levels of sclerostin, were found to be associated with reduced bone turnover and osteoblast proportion in hemodialysis patients. Sclerostin also has been proved to be upregulated during vascular smooth muscle cell calcification in vitro (6-10). Likewise, it was indicated that high serum sclerostin was accompanied with the degree of aortic valve calcification and that in aortic valve tissue. Importantly, sclerostin zealously co-localized with areas of calcification in hemodialysis individuals (8-10).

Conclusion

Since chronic kidney disease-metabolic bone disorder induces cardiovascular disease and mortality in hemodialysis individuals and chronic renal failure patients, the association of serum sclerostin levels and the future outcome may become a crucial entity.

Author's contribution

HN was the single author of the paper.

Conflict of interests

The author declared no competing interests.

Ethical considerations

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