Sclerostin and bone in diabetes mellitus type 2

In the current number, García-Martín et al.1 from the working group of Dr. Muñoz of Granada report that blood levels of sclerostin – the protein coded for by the gene SOST, which inhibits the osteoblast Wnt pathway - depend on the sex, the age and the renal function of patients with diabetes mellitus type 2 (DM2). They also demonstrate, contrary to expectations, a negative relationship with the markers for bone remodelling, and a positive relationship with bone mineral density (BMD). Finally, they show that blood levels of sclerostin are lower in patients with DM2 and osteoporosis irrespective of the presence or absence of fractures.

DM2 is a disease of high prevalence – up to 12-15% of the adult population in our country2 - and with an enormous impact on morbi-mortality and quality of life. Its relationship with micro-vascular complications – retinopathy, nephropathy and diabetic neuropathy – and macro-vascular complications – coronary artery, peripheral arterial and cerebrovascular disease - is well known. Most recently, new complications have been recognised to be clearly related to diabetes, among which osteoporosis or diabetes-related metabolic bone disease is a notable example.

Metabolic bone disease in subjects with DM2 is characterised by the presence of an increased average bone mineral density (BMD) in spite of which the number of fractures – especially appendicular – is clearly higher than expected. Obviously, this situation has been interpreted as a change in bone quality, that is, in the characteristic materials and structures of the bone tissue, related more or less directly with the chronic hyperglycemia from which those with DM suffer3. Hence, the work of García-Martín et al.1 may indicate that the increase in sclerostin in subjects with DM2 results in a reduction in remodelling which, although reducing bone loss and increasing BMD, results in bone which is less biomechanically effective. On the other hand, over the last decade the skeleton has been shown to have new and unexpected functions in relation to the rest of the organism. We have assisted in this process in the discovery and characterisation of fibroblast growth factor 23 (FGF23), basically produced by the osteocytes, not only as a phosphaturic factor, but also a hormone originating in the bone-inhibiting calcitropic hormones – PTH and D3 hormone. Among these new functions is emerging the role of bone tissue in the control of energy metabolism which happens through the secretion of osteocalcin (BGP), which we should also consider to be a hormone produced by osteoblasts, which regulates the secretion of insulin, sensitiveness to insulin and the use of energy. The signalling pathway for insulin in the osteoblasts (OB) drives glucose homeostasis in the body, the negative regulation of the carboxylation of BGP and its bioavailability, showing a typical negative hormonal feedback.

The work collected in this number suggests a role of sclerostin in the appearance of bone disease in DM2. Other contributions from the same group have demonstrated the presence of higher concentrations of sclerostin in subjects with DM2 in comparison with controls which, in addition to being related to BMD and markers for bone remodelling, are correlated with the period of time over which the diabetes has developed and with glycemic control (measured as HbA1c)6. So, this research demonstrates that sclerostin is increased in subjects with DM2, correlated with the duration and control of the disease, which makes this molecule, at the very least, a potential mediator in the genesis of diabetes-related bone disease. Its exact role among other hormone
mediators released by the bone (which we should start calling osteokines, if not bone hormones) is yet to be elucidated and, what is even more attractive, could bring us close to discovering the nexus between metabolic bone disease and the high cardiovascular risk in DM2.

**Bibliography**


