Journal of Clinical Densitometry: Assessment & Management of Musculoskeletal Health, vol. ■, no. ■, 1−14, 2014

1094-6950/■:1−14/$36.00
http://dx.doi.org/10.1016/j.jocd.2013.11.006

Review Article

Osteoporosis Update: Proceedings of the 2013 Santa Fe Bone Symposium

E. Michael Lewiecki,[*,1] *John P. Bilezikian,*[2] *Lynda Bonewald,*[3] *Juliet E. Compston,*[4] *Robert P. Heaney,*[5] *Douglas P. Kiel,*[6] *Paul D. Miller,*[7] *and John T. Schousboe*[8,9]

[1]*New Mexico Clinical Research & Osteoporosis Center, Albuquerque, NM, USA;* [2]*Columbia University College of Physicians and Surgeons, New York City, NY, USA;* [3]*University of Missouri School of Dentistry, Kansas City, MO, USA;* [4]*Cambridge Biomedical Campus, Cambridge, UK;* [5]*Creighton University, Omaha, NE, USA;* [6]*Institute for Aging Research, Hebrew SeniorLife, Beth Israel Deaconess Medical Center, and Harvard Medical School, Boston, MA, USA;* [7]*Colorado Center for Bone Research, Lakewood, CO, USA;* [8]*Park Nicollet Osteoporosis Center, Park Nicollet Clinic, Minneapolis, MN, USA; and* [9]*Division of Health Policy & Management, University of Minnesota, Minneapolis, MN, USA*

Abstract

The 2013 Santa Fe Bone Symposium included plenary sessions on new developments in the fields of osteoporosis and metabolic bone disease, oral presentations of abstracts, and faculty panel discussions of common clinical conundrums: scenarios of perplexing circumstances where treatment decisions are not clearly defined by current medical evidence and clinical practice guidelines. Controversial issues in the care of osteoporosis were reviewed and discussed by faculty and participants. This is a review of the proceedings of the Santa Fe Bone Symposium, constituting in its entirety an update of advances in the understanding of selected bone disease topics of interest and the implications for managing patients in clinical practice. Topics included the associations of diabetes and obesity with skeletal fragility, the complexities and pitfalls in assessing the benefits and potential adverse effects of nutrients for treatment of osteoporosis, uses of dual-energy X-ray absorptiometry beyond measurement of bone mineral density, challenges in the care of osteoporosis in the very elderly, new findings on the role of osteocytes in regulating bone remodeling, and current concepts on the use of bone turnover markers in managing patients with chronic kidney disease who are at high risk for fracture.

Key Words: Controversy; emerging; osteoporosis; safety; treatment.

Introduction

The Santa Fe Bone Symposium is an annual gathering of scientists, clinical researchers, and physicians of many specialties to assess the clinical implications of recent advances in knowledge of skeletal health and disease. Nonphysician participants include ancillary health care providers, dual-energy X-ray absorptiometry (DXA) technologists, and drug study coordinators, providing a broad range of perspectives on clinical trials and the management of osteoporosis. The 14th annual Santa Fe Bone Symposium was held August 9−10, 2013, in Santa Fe, New Mexico, USA. Faculty (Fig. 1) selections were based on expertise in basic science and/or clinical investigation, as well as ability to translate scientific advances to clinical care. Discussions were lively, with opportunities for all to participate throughout the symposium and in informal conversations between sessions.

It is now recognized that both type 1 and type 2 diabetes mellitus are associated with increased fracture risk. Abnormalities of bone structure in patients with type 2 diabetes might explain the increase in fracture risk that is greater than expected based on bone mineral density (BMD) measurement by DXA. Obesity, once thought to be protective for BMD and fractures, is now recognized as a risk factor for at least

Received 10/14/13; Accepted 11/01/13.
*Address correspondence to: E. Michael Lewiecki, MD, FACP, FACE, New Mexico Clinical Research & Osteoporosis Center, 300 Oak St. NE, Albuquerque, NM 87106. E-mail: mlewiecki@nmbonecare.com

Fig. 1. Faculty and moderators for the 2013 Santa Fe Bone Symposium. From left to right: Juliet E. Compston, Robert Marcus, E. Michael Lewiecki, Lynda Bonewald, John Schousboe, Robert P. Heaney, Paul D. Miller, Majorie M. Luckey, Douglas P. Kiel, John P. Bilezikian.

some types of fractures, suggesting that excessive body weight, as well as excessive thinness, may have adverse skeletal effects. There has been a great deal of misunderstanding and controversy on the balance of benefits and risks with nutritional therapy for osteoporosis. The limitations of randomized controlled clinical trials of nutritional supplements and concepts for improved trial designs are presented. DXA has been identified as the ''gold standard'' for BMD measurement, and is also a technology that can diagnose vertebral fractures, measure lean and fat body mass, analyze hip structure, and generate data for trabecular bone score (TBS), providing information on fracture risk that is independent of BMD. The care of osteoporosis in the very elderly presents special challenges, particularly with regard to frailty, overuse of prescription medications, and limitations of data in this population. The management of patients with chronic kidney disease (CKD) who are at high risk for fracture has been hampered by difficulties in defining the underlying bone disease without a bone biopsy. Potential uses of bone turnover markers in patients with CKD who are unable or unwilling to have a bone biopsy are reviewed. Osteocytes are now recognized as having a key role in regulating bone remodeling with potential implications for identifying new targets for treatment. These and other topical issues are presented here, providing a comprehensive update of the best available medical evidence and expert opinion on potential applications in the care of patients in clinical practice.

Previous reviews of Santa Fe Bone Symposium presentations have been published in this journal and elsewhere *(1–8)*. Enduring medical educational materials with continuing medical education and continuing education credits have been developed as monographs in print and electronic formats *(9–11)*, online slides with audio recordings *(12–14)*, and most recently as recorded audiovisual webcasts.

Diabetes and Bone

John P. Bilezikian, MD

The list of known risk factors for osteoporosis does not typically include type 2 diabetes mellitus. In fact, type 2 diabetes mellitus, often associated with obesity, has long been thought to be protective for bone. If there was a relationship between type 2 diabetes mellitus and osteoporosis, the global epidemic of diabetes *(15)* would argue for an increasingly ''at-risk'' population for osteoporosis over the next 2 decades. The evidence at this time strongly indicates, in contrast to previous impressions, that type 2 diabetes mellitus is, in fact, a risk factor for the fragility fracture.

The relative risk for sustaining virtually any kind of fragility fracture in type 2 diabetes mellitus is higher than in matched control subjects, ranging from 1.28 to 1.44 for fractures of the hip, foot, upper arm, ankle, and spine *(16)*. The increase in relative risk is evident even though BMD in type 2 diabetes mellitus is, on average, 5% higher than age-matched controls. In subjects taking insulin, BMD is even higher *(16,17)*. Despite the relatively higher BMD in individuals with type 2 diabetes mellitus, the risk of fracture increases with declining BMD *(8)*, as it does in those without diabetes. It would seem that the curve representing the well-delineated relationship between BMD and fracture has been displaced to the ''right'' in patients with diabetes. Fractures are related to BMD but they occur at higher BMD values *(16,18)*. TBS is a textural analysis of the lumbar spine DXA image that provides a higher predictive value in diabetes for fracture risk than BMD alone at any skeletal site *(19)*. This recent observation implies that patients with type 2 diabetes have microarchitectural skeletal abnormalities that reduce bone strength independently of bone mass.

With type 2 diabetes mellitus becoming established as a risk factor for fragility fracture, a number of potential mechanisms need to be considered. Fall risk is increased in patients with type 2 diabetes mellitus due to associated conditions that include peripheral neuropathy, impaired renal function, poor vision, uncertain balance, and hypoglycemia in some patients receiving aggressive therapy to reduce blood glucose levels. Although these risk factors for falls are undoubtedly present in many patients with type 2 diabetes mellitus, when falls are accounted for, it appears that they do not entirely account for the increase in fracture risk *(8,16,20,21)*. Some drugs used to treat diabetes, particularly the thiazolidinediones, may alter the balance between early lineage cells committed to either the adipocyte or osteoblast pathway in favor of the adipocyte line. The ''A Diabetes Outcome Progression Trial'' findings, in fact, showed that patients taking rosiglitizone had a higher risk of facture in the lower and upper limbs than did those taking either metformin or glyburide *(22)*. However, the thiazolidinediones have been used for only a relatively brief period in the history of diabetes therapeutics and one would be hard pressed to invoke this mechanism for the vast majority of subjects with type 2 diabetes mellitus who demonstrate increased fracture risk.