Bone Strength: The Whole Is Greater Than the Sum of Its Parts

K. Shawn Davison,* Kerry Siminoski,† J.D. Adachi,‡ David A. Hanley,§ David Goltzman,‖ Anthony B. Hodsman,¶ Robert Josse,** Stephanie Kaiser,†† Wojciech P. Olszynski,‡‡ Alexandra Papaioannou,§§ Louis-George Ste-Marie,‖‖ David L. Kendler,¶¶ Alan Tenenhouse,*** and Jacques P. Brown†††

Objective: To summarize the current knowledge regarding the various determinants of bone strength.

Methods: Relevant English-language articles acquired from Medline from 1966 up to January 2005 were reviewed. Searches included the keywords bone AND 1 of the following: strength, remodeling, microcrack, structur*, mineralization, collagen, organic, crystallinity, osteocyte, porosity, diameter, anisotropy, stress risers, or connectivity. Abstracts from applicable conference proceedings were also reviewed for pertinent information.

Results: Bone strength is determined from both its material and its structural properties. Material properties such as its degree of mineralization, crystallinity, collagen characteristics, and osteocyte viability have substantial impacts on bone strength. Structural properties such as the diameter and thickness of the cortices, the porosity of the cortical shell, the connectivity and anisotropy of the trabecular network, the thickness of trabeculae, and the presence of trabecular stress risers and microcracks impact bone strength in diverse manners. Remodeling activity either directly or indirectly impacts all of these processes.

Conclusions: Bone strength is dependent on numerous, interrelated factors. Remodeling activity has a direct impact on almost all of the components of bone strength and requires further investigation as to its impact on these factors in isolation and in unison.

 Semin Arthritis Rheum 36:22-31

Keywords: *bone, strength, mineralization, architecture, porosity, remodeling, anisotropy, osteocyte, collagen, crystallinity, connectivity, microcracks, stress riser*

*Clinical Research Scientist, Department of Medicine, Laval University, Sainte Foy, Quebec, Canada.

†Associate Professor of Radiology and Diagnostic Imaging and Internal Medicine, Department of Radiology and Diagnostic Imaging and Division of Endocrinology and Metabolism, Department of Internal Medicine, University of Alberta, Edmonton, Alberta, Canada.

‡Professor, Department of Medicine, Director, Hamilton Arthritis Centre, St. Joseph's Healthcare–McMaster University, Hamilton, Ontario, Canada.

§Department of Medicine, University of Calgary, Calgary, Alberta, Canada.

‖Department of Medicine, McGill University, Montreal, Quebec, Canada.

¶Professor, Department of Medicine University of Western Ontario, Director, London Regional Osteoporosis Program, St. Joseph's Health Centre, London, Ontario, Canada.

**Associate Physician-in-Chief, St. Michael's Hospital, Professor of Medicine, University of Toronto, Toronto, Ontario, Canada.

††Associate Professor of Medicine, Division of Endocrinology and Metabolism, Dalhousie University, Halifax, Nova Scotia, Canada.

‡‡Clinical Professor of Medicine, University of Saskatchewan, Director, Saskatoon Osteoporosis Centre, Saskatoon, Saskatchewan, Canada.

§ §Associate Professor Department of Medicine, McMaster University, and Hamilton Health Sciences, Hamilton, Ontario, Canada.

‖‖Associate Professor of Medicine, Faculty of Medicine, Université, de Montréal, Endocrinologist, Centre de Recherche du CHUM, Hôpital Saint-Luc, Montreal, Quebec, Canada.

¶¶Assistant Professor, Department of Medicine (Endocrinology), University of British Columbia, Vancouver, British Columbia, Canada.

***Professor Emeritus, Department of Medicine, McGill University, Montreal, Quebec, Canada.

†††A Clinical Professor of Medicine, Laval University, CHUL Research Centre, Sainte-Foy, Quebec, Canada.

Address reprint requests to: Dr. K. Shawn Davison, R.R. #5, Site 505, Box 26, Saskatoon, SK S7K 3J8. E-mail: ebmedicine@gmail.com

 0049-0172/06/$-see front matter
doi:10.1016/j.semarthrit.2006.04.002

The World Health Organization definition of osteoporosis put forth in 1993 was "a systemic skeletal disease characterized by low bone density and microarchitectural deterioration of bone tissue, leading to enhanced bone fragility and a consequent increase in fracture risk" (1). This definition highlighted bone mineral density (BMD) as an important component of fracture risk, but it also recognized that there are other factors that contribute to fracture susceptibility. In the more recent 2000 NIH Statement on Osteoporosis, Diagnosis, and Therapy, osteoporosis was defined as "a skeletal disorder characterized by compromised bone strength predisposing to an increased risk of fracture" (2). This newer definition intimates the paradigm shift that has been evolving for the past decade, that measures of bone strength are essential for fracture prediction and that, while BMD is a surrogate of bone strength, it explains only a portion of it.

A bone of sufficient strength does not fracture under normal loading conditions, which includes mild to moderate trauma such as a fall from standing height or less. In simple terms, fracture occurs when local stresses exceed material strength. Fracture can occur either when strength remains constant and the stress to the bone is increased (traumatic fracture) or when the stress on the bone is constant and the strength of the bone is decreased (atraumatic fracture). Occasionally, there are situations where there is both weakened bone and high stresses, such when an osteoporotic individual suffers a fracture from a motor-vehicle accident. Both the material strength and the local stresses placed on bone are dictated by a myriad of interrelated factors.

Bone strength is altered in one of two ways: by changing the tissue-level material properties of the bone or by changing the structural properties of the bone, and thus the local stresses, through adjustment of the rates of bone resorption and formation (bone remodeling).

This review seeks to document the material and structural components of bone strength in an attempt to better understand the mechanisms of fragility fracture.

MATERIALS AND METHODS

Relevant English-language articles acquired from Medline from 1966 up to January 2005 were reviewed. Searches included the keywords "bone" AND 1 of the following: "strength," "remodeling," "microcrack," "structur*," "mineralization," "collagen," "organic," "crystallinity," "osteocyte," "porosity," "diameter," "anisotropy," "stress risers," or "connectivity." All abstracts gathered were reviewed for relevance and those deemed applicable were collected in their full form and reviewed for inclusion in the review. The references cited in collected articles were also scanned for relevant articles that may not have been captured in the Medline search. Relevant conference proceedings were scanned to allow for the capture of recent data that may not have yet been published in its full form. Due to the relative infancy of many of the topics presented in this review, meta-analyses were not completed as they would not lead to any reliable conclusions.

RESULTS

Material Properties of Bone

The material properties of bone encompass the properties of the constituents of bone itself and are independent of the bone's size or shape (3). Since bone is essentially a composite of organic and inorganic materials, the investigation of the mechanical properties of either the organic or the mineral phase separately does not give an accurate representation of the properties of the composite as a whole. However, isolation investigations can provide valuable insight as to the roles of the different components of bone tissue with regard to bone strength.

Mineralization

The mineral phase of bone is responsible for both mechanical and homeostatic functions. Despite common perceptions, bone matrix is not uniformly mineralized, but rather displays a range of mineralization at any given skeletal site. The mean degree of mineralization of bone (MDMB) at a particular remodeling site is largely dependent on its stage of secondary mineralization (4). In an active remodeling sequence, the osteoclasts resorb bone from the remodeling space after which osteoblasts quickly fill the space with a collagenous osteoid. Primary mineralization generally begins 5 to 10 days after osteoid deposition and is typified by a rapid, linear rate of mineralization that proceeds until the remodeling cavity has been filled to 50 to 60% of the mineralization maximum. Following primary mineralization, the rate of mineralization slows and a phase of secondary mineralization begins; secondary mineralization progressively continues for a number of years, if not decades. Mineralization is rarely, if ever, complete and typically stabilizes around 90 to 95% of the maximum level (5).

The MDMB and the distribution of mineralization is similar in trabecular and cortical bone, between genders, and over age (6). With normal aging the distribution of mineralization is relatively homogeneous and of higher degree due to reduced bone turnover, but the true volumetric density of the bone tissue is similar because of reduction of bone tissue per volume leading to a similar MDMB (g/cm^3). Roschger and coworkers (7), using quantitative backscattered electron imaging, reported that there were no differences in trabecular BMD distribution between ethnicities, skeletal site, age (>25 years of age), or gender and that the intraindividual variance between sites was exceedingly small. However, significant interindividual differences were observed in patients with bone disease, such as osteomalacia, when compared with controls. Based on these findings, it was suggested that diagnostic transiliac biopsies would be generally representative of the entire skeleton with regard to mineralization and could be employed to ascertain the average mineralization of