Serge Livio Ferrari
Christian Roux *Editors*

Pocket Reference to Osteoporosis

IOF International Osteoporosis Foundation

Springer

Pocket Reference to Osteoporosis

Serge Livio Ferrari • Christian Roux
Editors

Pocket Reference to Osteoporosis

Springer

Editors
Serge Livio Ferrari
Division of Bone Diseases
Geneva University Hospital
and Faculty of Medicine
Geneva
Switzerland

Christian Roux
Department of Rheumatology
Paris Descartes University
Cochin Hospital
Paris
France

ISBN 978-3-319-26755-5 ISBN 978-3-319-26757-9 (eBook)
https://doi.org/10.1007/978-3-319-26757-9

Library of Congress Control Number: 2018964428

This Springer imprint is published by the registered company Springer Nature Switzerland AG
The registered company address is: Gewerbestrasse 11, 6330 Cham, Switzerland

Preface

Every few seconds, a patient is admitted to a hospital with a fragility fracture—namely, a fracture that occurred upon a minimal trauma, such as falling from one's own height. Whether treated surgically or conservatively, the risk of another fragility fracture is increased severalfold in such patients, unless the underlying cause is recognized and appropriately managed. The bulk of fragility fractures are caused by osteoporosis, a disease that affects nearly 300 million people worldwide and is a particular burden for aging populations. In most cases, diagnosing osteoporosis and evaluating fracture risk in due time, followed by appropriate treatment, could have prevented even the first fracture. Unfortunately, disorders of bone and mineral metabolism, including osteoporosis, are seldom taught to undergraduates. The resulting relative lack of knowledge has led to under-recognizing and undertreating the disease, with commonly less than 20% of osteoporotic patients being appropriately managed. A "crisis in osteoporosis" has therefore emerged that needs to be appropriately addressed. Whether a GP or a specialist in orthopaedics, endocrinology, rheumatology, gynaecology, or other specialties, every doctor should be aware of osteoporosis and be capable of managing the disease. This book has been written by some of the most prominent authorities in this field in order to provide the basic principles about osteoporosis in a practical way, in the hope of facilitating the diagnosis and treatment of devastating disease.

Geneva, Switzerland — Serge Livio Ferrari
Paris, France — Christian Roux

Contents

Contributors

Felicia Cosman, MD Helen Hayes Hospital, West Haverstraw, NY, USA

Serge Livio Ferrari, MD Division of Bone Diseases, Geneva University Hospital and Faculty of Medicine, Geneva, Switzerland

Piet Geusens, MD Department of Internal Medicine, Maastricht University Medical Center, Maastricht, The Netherlands

John A. Kanis, MD Center for Metabolic Bone Diseases, University of Sheffield Medical School, Sheffield, UK

Eugene V. McCloskey, MD Center for Metabolic Bone Diseases, University of Sheffield Medical School, Sheffield, UK

Michael R. McClung, MD Oregon Osteoporosis Center, Portland, OR, USA

Socrates E. Papapoulos, MD Center for Bone Quality, Leiden University Medical Center, Leiden, The Netherlands

René Rizzoli, MD Division of Bone Diseases, Geneva University Hospitals and Faculty of Medicine, Geneva, Switzerland

Christian Roux, MD Department of Rheumatology, Paris Descartes University, Cochin Hospital, Paris, Paris, France

Jopp van den Bergh, MD, PhD Department of Internal Medicine, Maastricht University Medical Center, Maastricht, The Netherlands

Chapter 1
Pathophysiology of Osteoporosis

Serge Livio Ferrari

1.1 Introduction

Bone is a dynamic tissue that is continuously removed and replaced (i.e., remodeled) in order to (1) ensure adaptation of the skeleton to weight-bearing (shape is function), (2) repair microdamages (cracks) that result from mechanical stresses, and (3) allow for mobilization of calcium from the skeleton in order to maintain serum calcium homeostasis [1]. Bone remodeling is initiated by the development and activation of osteoclasts, the bone-resorbing cell, which then release growth factors capable to activate osteoblasts, the bone-forming cell. The activities of bone removal and deposition are therefore coupled within each "bone multicellular unit" or BMU. After the completion of growth, the bone size and mineral content have reached its peak and will be maintained more or less unchanged during the adult life in the absence of pathophysiological conditions thanks to moderate levels of bone remodeling that are perfectly balanced between resorption and formation within each BMU. In addition, the skeleton continuously responds to mechanical stimuli resulting from both muscle contraction and weight-bearing, by directly stimulating

S. L. Ferrari (✉)
Division of Bone Diseases, Geneva University Hospital and Faculty of Medicine, Geneva, Switzerland
e-mail: serge.ferrari@unige.ch

S. L. Ferrari, C. Roux (eds.), *Pocket Reference to Osteoporosis*,
https://doi.org/10.1007/978-3-319-26757-9_1

bone formation (i.e., without prior resorption), a process known as bone modeling. This process in particular is responsible for the increased bone diameter and bone mass observed in physically active individuals, furthermore in athletes. It is controlled by osteocytes, which are terminally differentiated osteoblasts that have lost their capacity to form new bone but are entrenched in the bone and form a dense network of "sensing" cells capable to respond to mechanical stimuli, as well as to microdamages, and control both modeling and local remodeling processes [2].

1.2 The Pathophysiological Bases of Osteoporosis

Osteoporosis is a systemic skeletal disorder characterized by a decrease of bone mineral mass together with alterations of bone microstructure, particularly a reduction in the number and/or thinning of trabeculae with a loss of trabecular bridges, cortical thinning, and increased cortical porosity [3, 4]. These alterations are mainly the result of increased bone turnover triggered by the dramatic decline of estrogen levels in postmenopausal women. In men, aging and the decline in both testosterone and estrogen levels also play a role. At the cellular level, these endocrine disturbances lead to the activation of new BMUs that spread throughout cancellous and cortical bone surfaces. Moreover, within these foci of bone remodeling, a mismatch appears between the activity of osteoclasts and osteoblasts, resulting in a negative bone mineral balance (Fig. 1.1). Eventually, the senescence of osteocytes [5], together with the decline in physical functions with aging, may lead to a decrease of modeling-based bone formation.

In recent years, the key molecular mechanisms involved in the bone remodeling and modeling processes and the coupling between osteoblasts and osteoclasts have been elucidated. Among them, the Wnt/LRP5/beta-catenin

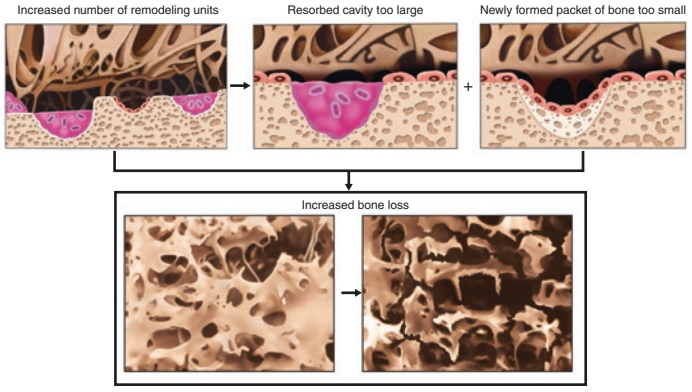

FIGURE 1.1 Increased bone remodeling causes bone loss

canonical signaling pathway [6] and the RANKL/RANK/OPG system [7] have emerged as playing essential roles in, respectively, bone-forming and bone resorption processes. In addition, the role of the immune system and the central nervous system on the regulation of bone turnover starts to be better appreciated. In turn, these remarkable progresses in the understanding of the pathophysiology of osteoporosis have delineated new targets for therapeutic developments.

1.3 The Role of Osteoclasts

The osteoclast (OC) is a bone tissue-specific multinucleated cell that differentiates from hematopoietic stem cells similar to those giving rise to monocyte/macrophage. Mature osteoclasts adhering to the bone surface both produce and secrete HCl, which acidifies and dissolves the bone mineral, and proteolytic enzymes, mainly metalloproteases and cathepsin K, which digest the bone matrix, releasing in the circulation-specific collagen fragments, such as CTx, which in turn are used as clinical markers of bone turnover.