Non-Pharmacological Management of Osteoporosis

Exercise, Nutrition, Fall and Fracture Prevention

Mehrsheed Sinaki
Michael Pfeifer
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Editors
Mehrsheed Sinaki
Department of Physical Medicine
and Rehabilitation
Mayo Clinic
Rochester, Minnesota
USA

Rehabilitation of Osteoporosis Program
Mayo Clinic
Rochester, Minnesota
USA

Michael Pfeifer
Institute of Clinical Osteology and Clinic
“DER FÜRSTENHOF”
German Osteology Foundation
Bad Pyrmont, Niedersachsen
Germany

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Foreword

Osteoporosis is a common disorder of the bone that predominantly affects menopausal women but also affects men and patients of all ages and races. Osteoporosis has no warning signs, and many times the first indication of the disease is a fracture with devastating consequences to the individual's health and life. Drs. Mehrsheed Sinaki and Michael Pfeifer are recognized clinical and research leaders in osteoporosis and rehabilitation. Dr. Sinaki was the first female professor at the Department of Physical Medicine & Rehabilitation, Mayo Clinic, Rochester, Minnesota, and a pioneer in the prevention of osteoporosis and rehabilitation of patients with the disorder and its associated spine deformity. Her research has helped establish clinical practice guidelines including ROPE (Rehabilitation of Osteoporosis Program-Exercise) and back-strengthening exercises to decrease risk of fracture associated with osteoporosis. Dr. Pfeifer is a Professor at the Institute of Clinical Osteology in Bad Pyrmont, Germany, with a vast range of expertise in osteoporosis. He has been essential in the establishment of multiple clinical trials testing pharmacological interventions to treat osteoporosis and in the development of orthosis to treat spine deformities and vertebral fractures associated with the disease. Together, their landmark contributions have established many of the methods currently used to prevent osteoporosis and treat patients with the disorder worldwide.

In this book, Drs. Sinaki and Pfeifer work together with an impressive group of clinicians and investigators from multiple areas of medicine to present a comprehensive understanding of osteoporosis, from the pathophysiology of the disease to the evaluation of multiple interventions to prevent the disorder and rehabilitate patients with decreased bone density and fractures. This book provides a reference when working to control symptoms, improve function, and advance the quality of life of patients with osteoporosis and the complications associated with it. I hope that you all will appreciate the deep knowledge within these pages as much as I did. Congratulations Mehrsheed and Michael for presenting the state of the art in the principles and practice of one of the most devastating diseases—osteoporosis.

Carmen M. Terzic, MD, PhD
Chair, Department of Physical Medicine and Rehabilitation
Mayo Clinic, Professor of Physical
Medicine and Rehabilitation,
Mayo Clinic College of Medicine and Science
Rochester, Minnesota, USA

Preface

Pharmacotherapy is one of the pillars of medical practice, undeniably helpful and sometimes lifesaving. The drawbacks of medication overuse are well-known, and side effects are often recognized (although unfortunately sometimes after extended exposure). Physicians' experience over long years is often rewarded by more insight, reminiscent of an admittedly strong quotation from Sir William Osler: "The young physician starts life with twenty drugs for each disease and the old physician ends life with one drug for twenty diseases."

During recent decades, the application of non-pharmacological and physical therapeutic measures has justifiably gained momentum, whether as independent measures or adjuvant to pharmacotherapy. In the mid 1990s, together with Professor Helmut W. Minne of Bad Pyrmont, Germany, we undertook an effort to start a working group in osteoporosis rehabilitation at the annual meeting of the American Society for Bone and Mineral Research (ASBMR). With the support of several colleagues from ASBMR and the Mayo Clinic Division of Endocrinology, Diabetes, Metabolism, & Nutrition and the Metabolic Bone Disease Clinic, in particular Dr. B. Lawrence Riggs, as well as the approval of the president of the society at the time, Dr. Michael Rosenblatt of Boston, we held our first meeting in San Francisco in 1998. Many more annual meetings followed. I was truly privileged with the collaborating leadership of Dr. Michael Pfeifer of Bad Pyrmont, Germany, which finally resulted in the concept of publication of this book.

We are indebted to the support of many of our colleagues in the Mayo Clinic Division of Endocrinology, Diabetes, Metabolism, & Nutrition and the Metabolic Bone Disease Clinic, including Drs. Steven Hodgson, Sundeep Khosla, and Bart Clarke, as well as European colleagues including Dr. Elizabeth Preisinger of Vienna, Austria; Dr. Mario Passeri of Parma, Italy; Dr. Piet Geusens of Maastricht, the Netherlands; Dr. Christian Kasperk of Heidelberg, Germany; Drs. Wolfgang Kemmler and Simon von Stengel of Erlangen, Germany; Dr. Yannis Dionyssiotis of Athens, Greece; Dr. Sabine Verschueren and coworkers of Leuven, Belgium; and Dr. Eiji Itoi, professor of orthopedic surgery, of Sendai, Japan. All of these authors attended our ASBMR Working Group on a regular basis and thus contributed to knowledge generation by their oral presentations on various topics, which were condensed finally into this book.

Essentially, this is a summary of all the experience we gained through our working group of over 15 years and reflects different attitudes, opinions, and non-pharmacological treatment approaches worldwide for patients suffering from vertebral fractures due to osteoporosis. Our hope is that this work may contribute to an improvement in several parameters of quality of life for patients suffering from this deleterious disease, since, due to a constantly increasing life expectancy not only in Western but also in Asian civilizations, the numbers of patients are still on the rise. This represents a major socioeconomic burden for many societies as long as treatment options are focused mainly on more or less expensive drugs. In contrast, non-pharmacological approaches are relatively inexpensive; given a fixed amount of resource, many patients may be treated.

Musculoskeletal rehabilitation is a highly promising option in the management of patients with osteoporosis. Measures to improve quality of life are relentlessly assessed and advanced. We would like to express our sincere gratitude and appreciation for the work of colleagues and old and new friends in contributing chapters to this book.

Rochester, Minnesota, USA Mehrsheed Sinaki
Bad Pyrmont, Germany Michael Pfeifer

Contents

Contributors

An Bogaerts, PhD Research Group for Musculoskeletal Rehabilitation, Department of Rehabilitation Sciences, KU Leuven, Leuven, Belgium

Bart L. Clarke, MD Consultant, Division of Endocrinology, Diabetes, Metabolism, and Nutrition, Mayo Clinic, Rochester, Minnesota, USA

Professor of Medicine, Mayo Clinic College of Medicine and Science, Rochester, Minnesota, USA

Yannis Dionyssiotis, MD, PhD Physical Medicine and Rehabilitation Department, European Interbalkan Medical Center, Pylaia, Thessaloniki, Greece

First Department of Orthopaedics, General University Hospital "ATTIKON", Chaidari, Athens, Greece

Assistant Professor of Metabolic Bone Disease and of Rheumatology, Rehabilitation Unit, University of Patras, Patras, Greece

Elizabeth A. Huntoon, MD Assistant Professor of Physical Medicine, Rehabilitation, and Orthopaedics, Vanderbilt University Medical Centre, Nashville, TN, USA

Eiji Itoi, MD, PhD Professor of Orthopaedic Surgery, Department of Orthopaedic Surgery, University of Tohoku, Sendai, Japan

Daniela H. Jurisic, MD Department of Physical Medicine and Rehabilitation, Medical College of Wisconsin, Milwaukee, Wisconsin, Italy

Active Integrative Medicine Associates, Pavia, Italy

Christian Kasperk, MD, PhD Professor of Medicine and of Endocrinology, Department of Osteology, University of Heidelberg, Heidelberg, Germany

Wolfgang Kemmler, PhD Senior Professor, Department of Medical Physics and Sports Sciences, University of Erlangen, Henkestrasse, Erlangen, Germany

Katharina Kerschan-Schindl, MD Assistant Professor, Department of Physical Medicine and Rehabilitation, Medical University Vienna, Vienna, Austria

Judith B. Kosasih, MD Professor of Physical Medicine and Rehabilitation, Medical College of Wisconsin, and Medical Director, Medical Rehabilitation, Polytrauma Support Clinic Team, Amputation Clinic Team, Zablocki Veterans' Affairs Medical Center, Milwaukee, WI, USA

Nathan K. LeBrasseur, PhD Consultant, Departments of Physical Medicine and Rehabilitation and Physiology and Biomedical Engineering, Robert and Arlene Kogod Center on Aging, Mayo Clinic, Rochester, MN, USA

Assistant Professor of Physiology and Associate Professor of Physical Medicine and Rehabilitation, Mayo Clinic College of Medicine and Science, Rochester, MN, USA

Yu Mori, MD, PhD Assistant Professor, Department of Orthopaedic Surgery, Tohoku University School of Medicine, Sendai, Miyagi, Japan

Michael Pfeifer, MD Institute of Clinical Osteology and Clinic "DER FÜRSTENHOF", Head of German Osteology Foundation, Bad Pyrmont, Niedersachsen, Germany

Elisabeth Preisinger, MD Professor of Physical Medicine and Rehabilitation, Physical Medicine and Rehabilitation, Krankenhaus Hietzing, Vienna, Austria

Meera Shah, MB, ChB Senior Associate Consultant, Division of Endocrinology, Diabetes, Metabolism, & Nutrition, Mayo Clinic, Rochester, Minnesota, USA

Assistant Professor of Medicine, Mayo Clinic College of Medicine and Science, Rochester, Minnesota, USA

Mehrsheed Sinaki, MD, MS Consultant, Department of Physical Medicine and Rehabilitation, Mayo Clinic, Rochester, Minnesota, USA

Professor of Physical Medicine and Rehabilitation, Mayo Clinic College of Medicine and Science, Rochester, Minnesota, USA

Director of Rehabilitation of Osteoporosis Program, Mayo Clinic, Rochester, Minnesota, USA

Simon von Stengel, PhD Associate Professor, Department of Medical Physics and Sports Sciences, University of Erlangen, Henkestrasse, Erlangen, Germany

Ekaterina Tankisheva, PhD Research Group for Musculoskeletal Rehabilitation, Department of Rehabilitation Sciences, KU Leuven, Leuven, Belgium

Sabine M. Verschueren, PhD Professor of Rehabilitation Medicine, Department of Rehabilitation Sciences, University of Leuven, Leuven, Belgium

Jennifer J. Westendorf, PhD Consultant, Department of Biochemistry and Molecular Biology, Mayo Clinic, Rochester, Minnesota, USA

Professor of Biochemistry and Molecular Biology and of Orthopedics, Mayo Clinic College of Medicine and Science, Rochester, Minnesota, USA

Qian Xing, MD, PhD Professor, Division of Endocrinology and Metabolic Diseases, Department of Internal Medicine, First Affiliated Hospital of Dalian Medical University, Dalian, China

Osteoporosis: Diagnosis, Risk Factors, and Prevention

1

Mehrsheed Sinaki and Michael Pfeifer

Osteoporosis is one of the most prevalent metabolic bone diseases in the world and is a major public health problem. Osteoporosis consists of a heterogeneous group of syndromes in which reduction of bone mass per unit volume results in bone fragility. The increment in bone porosity causes architectural instability of the bone and increases the likelihood of fracture. In osteoporosis, the mineral-to-matrix ratio is normal, but the bone quantity is reduced. In 2005, the direct and indirect costs of osteoporosis in the United States alone were estimated to be $17 billion. In 2025, it is projected that the costs will be $25 billion, annually [1]. Much of this expense relates to hip fractures. In 15%–20% of hip fracture cases, the outcome is fatal. In osteoporotic individuals, 50% of women and 25% of men older than 50 years could have a traumatic spine fracture during their life.

Reports from Europe in 2003 indicate that variations of a gene on chromosome 20 may cause some postmenopausal women to have osteoporosis. Research studies are in progress to identify the gene in the carriers and implement preventive measures. Meanwhile, clinicians (through nonpharmacological intervention) can add quality to the years of life of osteoporotic patients with or without fractures. Nonpharmacologic intervention could be implemented alone or along with

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M. Sinaki, MD, MS
Consultant, Department of Physical Medicine and Rehabilitation, Mayo Clinic, Rochester, Minnesota, USA

Professor of Physical Medicine and Rehabilitation, Mayo Clinic College of Medicine and Science, Rochester, Minnesota, USA

Director of Rehabilitation of Osteoporosis Program, Mayo Clinic, Rochester, Minnesota, USA
e-mail: sinaki.mehrsheed@mayo.edu

M. Pfeifer, MD
Institute of Clinical Osteology and Clinic "DER FÜRSTENHOF", Head of German Osteology Foundation, Bad Pyrmont 31812, Niedersachsen, Germany
e-mail: iko_pyrmont@t-online.de

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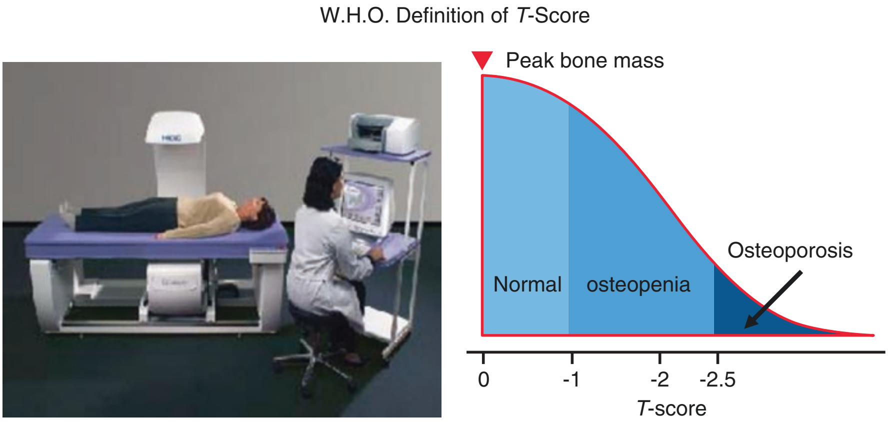

Measuring BMD

Mean based on BMD in healthy Caucasian women 20–40 years old

Fig. 1.1 *Left*—measuring BMD with DEXA machine; *right* normal peak bone mass and *T*-score defining osteopenia and osteoporosis

pharmacotherapy in cases of the need for pharmacotherapy. Clinical studies have shown that when pharmacotherapy is combined with the rehabilitative measures, the vertebral fracture rate is decreased [2].

Osteoporosis, a multifaceted disorder, requires a multidisciplinary approach to achieve the most successful management. The World Health Organization defines osteoporosis as bone mineral density (BMD) with a *T*-score 2.5 standard deviations below the peak mean bone mass of young healthy adults [1] (Figure 1.1). The *T*-score shows the amount of one's bone density compared with a young adult (at age 35 years) of the same gender with peak bone mass. The *Z* score is calculated in the same way, but the comparison is made with someone of the same age, sex, race, height, and weight. The *Z* score is adjusted for an individual's age, and the *T*-score is not. For example, a 75-year-old woman with a *Z* score of −1.0 is one standard deviation below the BMD of an average 75-year-old woman, but her *T*-score may be −3.0 because she is three standard deviations below the BMD of an average 35-year-old woman. Normal BMD is a *T*-score −1 or greater; osteopenia, a *T*-score between −1 and −2.5; osteoporosis, a *T*-score −2.5 or less; and severe osteoporosis, a *T*-score −2.5 or less with fracture. In the asymptomatic stage, osteoporosis is characterized simply by decreased bone mass without fracture. Osteoporosis usually is silent and becomes clinically symptomatic when the bone fractures.

Etiology and Pathogenesis

Bone remodeling is an ongoing process that allows removal of old bone and replacement with new bone tissue. Bone remodeling has five stages:

1. In activation: Osteoclastic activity is recruited.
2. In resorption: Osteoclasts make a cavity through eroding the bone.
3. Then in reversal: Osteoblasts are recruited.
4. During bone formation stage: Osteoblasts replace the cavity with new bone.
5. At the quiescence phase: Bone tissue remains dormant until the next cycle starts.

Peak adult bone mass is achieved between ages 30 and 35. High-turnover osteoporosis occurs due to an increased rate of bone remodeling and bone loss without equal bone formation; examples include disorders such as hyperparathyroidism and thyrotoxicosis. Of course, osteoporosis could be secondary to other health-related disorders (i.e., any increased or decreased rate of activation of the bone remodeling cycle could result in reduced bone formation). Loss and reduction of trabeculae result in increased bone porosity and fragility (Figure 1.2).

Trabecular (or cancellous) bone represents approximately 20% of skeletal bone mass and makes up 80% of the turnover media. The cortex makes up only 20% of the turnover media and is made of compact bone, which represents 80% of skeletal bone mass. Bone remodeling is initiated with the activation of osteoclasts for resorption. Then, resulting resorption sites are refilled by osteoblastic activities, a process called bone formation. There is no bone loss when the amount of bone resorbed equals the amount formed. After age 35 years, however, the remodeling process does not result in zero balance, and the normal process of remodeling results in bone loss [3].

When there is an increase in the rate of bone remodeling, such as in hyperparathyroidism or thyrotoxicosis, the rate of bone remodeling can increase, resulting in bone loss. Therefore, osteoporosis can occur after age 35 in a high turnover rate of the bone. The secondary causes of osteoporosis are associated with an increased rate of activation of the remodeling cycle. However, factors such as calcium intake, smoking, alcohol consumption, level of physical activity or physical exercise, and

Fig. 1.2 Contrast of trabeculae in healthy and osteoporotic bone. Images by David W. Dempster, PhD, ©2005

menopause are important and could contribute to the variance in peak BMD [3]. The incidence of osteoporosis-related fractures is lower in men than in women because the diameter of vertebral bodies and long bones is greater in men at maturity, and bone loss is less (about half that of women) throughout life. In addition, women have lower muscle strength than men for support of the skeletal structures [3]. Common risk factors are reflected in Box 1.1.

Box 1.1 Common risk factors for osteoporosis

- History of fracture after age 50
- Current low bone mass
- History of fracture in a primary relative
- Female
- Small stature/thin
- Advanced age
- A family history of osteoporosis
- Estrogen deficiency as a result of menopause, especially early or surgically induced
- Low testosterone levels in men
- Anorexia nervosa
- Low lifetime calcium intake
- Vitamin D deficiency
- Use of certain medications, such as oral corticosteroids and anticonvulsants
- Presence of certain chronic medical conditions
- An inactive lifestyle
- Current cigarette smoking
- Excessive use of alcohol
- Caucasian or Asian ancestry

Modified from [1]; used with permission.

Diagnosis

Osteoporosis, in general, is a preventable disorder. Maintenance of bone mass depends on several factors, including proper level of physical activity (PA), hormones, and nutrition. Early diagnosis of low bone mass and provision of measures to prevent further bone loss are essential. The diagnosis of osteoporosis requires a thorough physical examination, including height and weight measurements, location of musculoskeletal pain, family history of osteoporosis, dietary calcium intake, level of PA, and past exercise programs. Several biochemical indices are also used in the differential diagnosis of metabolic bone disease or, in some instances, for therapeutic follow-up [4].

Biochemical markers for bone formation include calcium, phosphorus, PTH (parathyroid hormone), bone-specific alkaline phosphatase, and serum osteocalcin. Resorption markers include 24-hour urinary calcium excretion (corrected by creatinine excretion), hydroxyproline, and pyridinium cross-links (in urine). The interpretation of these tests depends on intraindividual and interindividual variations. Also, indices of bone turnover show seasonal and circadian variations.

Radiographic findings of osteoporosis [5] consist of increased lucency of the vertebral bodies with loss of horizontal trabeculae, increased prominence of the cortical end plates, vertically oriented trabeculae, reduction in cortex thickness, and anterior wedging of vertebral bodies (Figure 1.3). The degree of wedging that indicates a true fracture varies from a 20% to 25% reduction in the anterior height relative to the posterior height of the same vertebra.

Other morphologic changes occur, such as biconcavity of vertebral bodies and complete compression fractures (reduction in both anterior and posterior heights by at least 25% compared with adjacent normal vertebrae) [5]. Bone scans and magnetic resonance imaging, if needed, can further define the cause of bone pain, such as stress fractures. Conventional radiographs may not reveal stress fractures nor reveal osteoporosis until at least 25%–30% of bone mineral has been lost. Consequently, evaluation of BMD through absorptiometry techniques is recommended [6].

The different methods for evaluation of bone mass have different levels of precision. Other available methods include photon absorptiometry (single or dual) (Figure 1.1), finger radiographic spectrometry, ultrasound densitometry, qualitative computed

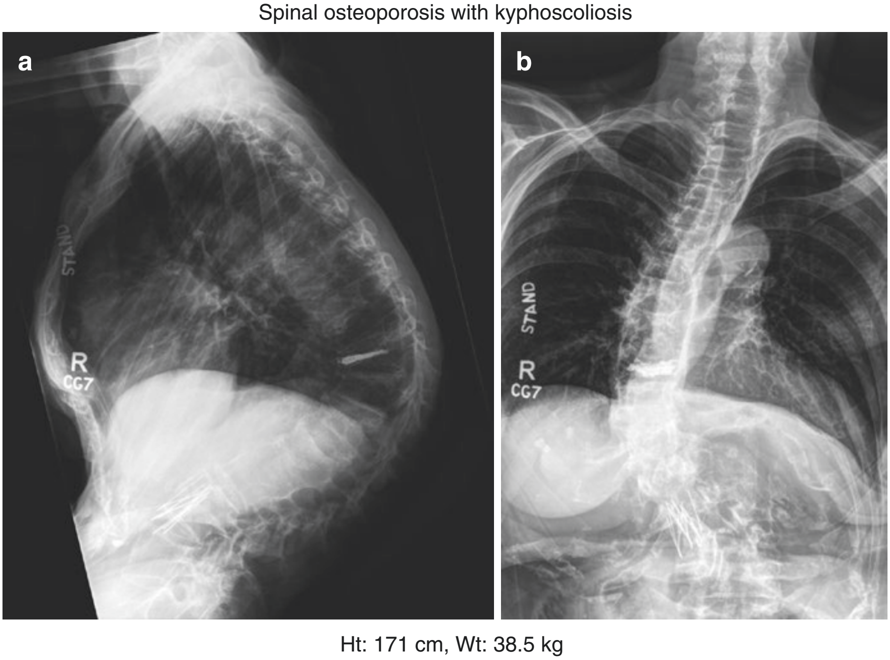

Fig. 1.3 (**a**) and (**b**) depict spinal deformities that could result from spinal osteoporosis and vertebral compression fractures

tomography, and dual-energy radiographic absorptiometry. The most commonly used technique is dual-energy radiographic absorptiometry, which has high precision and is frequently used for research and clinical evaluations to measure the BMD of the spine and hips. It is radiographically based and has a precision of approximately 1%. More

Table 1.1 Some of the diagnostic evaluations for osteoporosis

Evaluation	Details
History and physical examination	Family history of osteoporosis, type and location of pain, general dietary calcium intake, level of physical activity, height and weight
Radiographs of the chest and spine	To rule out lymphomas, rib fractures, compression fractures, etc.
Bone mineral density (spine and hip)	At menopause, every 2 years for high-risk patients, and every 5 years for low-risk patients
Complete blood cell count	To rule out anemias associated with malignancy, etc.
Chemistry group (serum calcium, phosphorus, vitamin D, parathyroid hormone, bone-specific alkaline phosphatase, osteocalcin)	To assess the level of alkaline phosphatase, which may be increased in osteomalacia, Paget's disease, bony metastasis and fracture, intestinal malabsorption, vitamin D deficiency, chronic liver disease, alcohol abuse, phenytoin (Dilantin) therapy, hypercalcemia of hyperparathyroidism, hypophosphatemia of hyperparathyroidism and osteomalacia, malabsorption, or malnutrition
Erythrocyte sedimentation rate and seroprotein electrophoresis	To determine changes indicative of multiple myeloma or other gammopathies
Total thyroxine	Increased total thyroxine concentration may be a cause of osteoporosis because of increased bone turnover
Immunoreactive parathyroid hormone	Hyperparathyroidism (accompanied by hypercalcemia)
25-Hydroxyvitamin D and 1,25-dihydroxyvitamin D3	Gastrointestinal disease, osteomalacia
Urinalysis and 24-hour urine	To check for proteinuria caused by nephrotic syndrome and for low pH resulting from renal tubular acidosis; a 24-h urine test can exclude hypercalciuria (normal calcium value in men is 25–300 mg/specimen; in women, 20–275 mg/specimen)*
Optional: bone scan, iliac crest biopsy	After tetracycline double labeling for bone histomorphometry, bone marrow biopsy may be indicated to exclude multiple myeloma and metastatic malignancy
Biochemical markers of bone turnover (Eastell)	Formation: serum osteocalcin, alkaline phosphatase (bone), procollagen type 1, C- and N-propeptides
	Resorption: serum acid phosphatase, pyridinoline, deoxypyridinoline, hydroxyproline, cross-linked telopeptides of type 1 collagen, urinary calcium, or creatinine

From [3] used with permission.
*Mayo Clinic normal values.

commonly measured is the BMD of the femoral neck, since spine bone density can be erroneously high, as in osteoarthritis of the spine [6] (Table 1.1).

Prevention

Reducing risk factors can decrease bone loss. These include positive lifestyle changes, which contribute to improvement of musculoskeletal health in general. It is suggested that the greater the bone mass at the time of menopause, the less chance for development of osteoporosis [7]. Therefore, improving muscle strength through weight-bearing exercises at a young age is beneficial [8]. Stronger back extensors and back extension-strengthening exercise could also reduce or prevent risk of vertebral fractures [9]. In addition, stronger back extensors could reduce back pain [10]. In children, stronger back extensors could decrease the risk of back pain in later years [11]. Back pain could contribute to reduced PA level and, later in adulthood, muscle and bone loss.

Proper PA plays a significant role in maintenance of musculoskeletal health. Performing strenuous flexion during a few yoga poses could result in vertebral compression and, in some cases, neck and back pain. These concerns need to be taken into consideration before prescribing an exercise program in cases of osteopenia, osteoporosis, and degenerative arthritis of the spine [12] (see Chapter 7).

Application of proper mechanical load can stimulate osteogenic activity. Axial loading of the skeleton during lifting activities at a person's job or in the care of children can be as osteogenic as mechanical-loading exercises in a gym [13].

The best preventive measures start in childhood, including proper nutrition and PA. Later in life, the level of PA plays a significant role. In women aged 30 to 40 years, BMD and muscle strength were found to be site specific. BMD of the spine was higher in women whose jobs were not sedentary [13].

One study showed a marked difference in BMD between gymnasts and volleyball players. The lower limbs are loaded differently in these two athletic activities [14]. Gymnasts had higher BMD than volleyball players, except in the pelvic bone. Swimming can improve muscle strength but not bone mass [15]. According to the theory of Frost [16, 17], a minimum threshold of mechanical loading is needed to evoke osteogenecity. This theory is referred to as that of the minimum effective strain stimulus. Lanyon [18] suggested that the greatest osteogenic effect from mechanical loading occurs when the strain is vigorous (high strain), repeated daily, short in duration, and applied to a specific bone site. There is a significant reduction of the level of PA from age 19 to 66, as shown in one study (Figure 1.4, [19]). This can contribute to age-related bone loss. Another study showed a significant correlation between the level of PA or weight-bearing involved in individual's job with BMD of the lumbar spine. Therefore, PA whether sport- or job-related could contribute to BMD ([13], Figure 1.5).

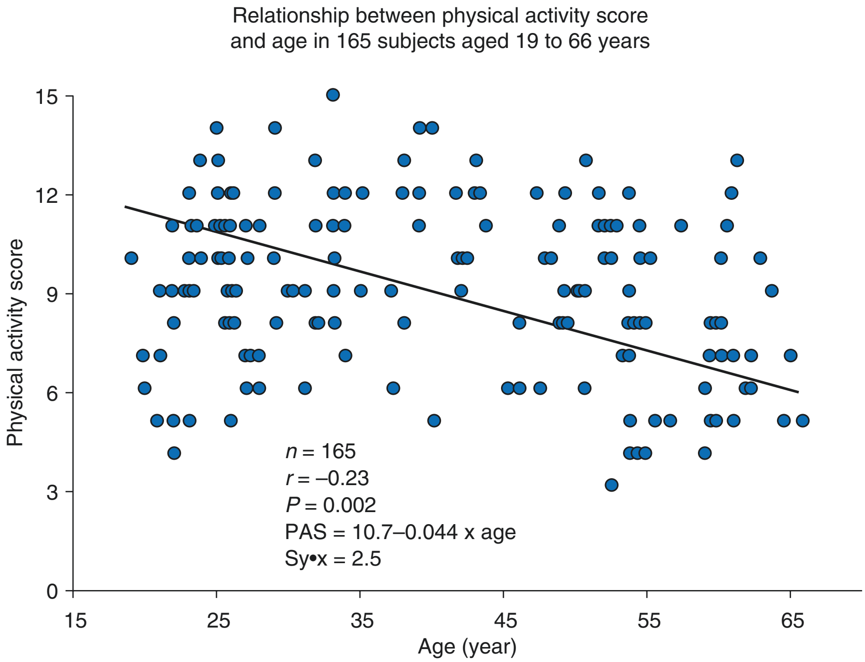

Fig. 1.4 Depicts reduction of physical activity level with increasing age in healthy population. From Sinaki M: Aging Clin Exp Res 10:249–262, 1998; used with permission.

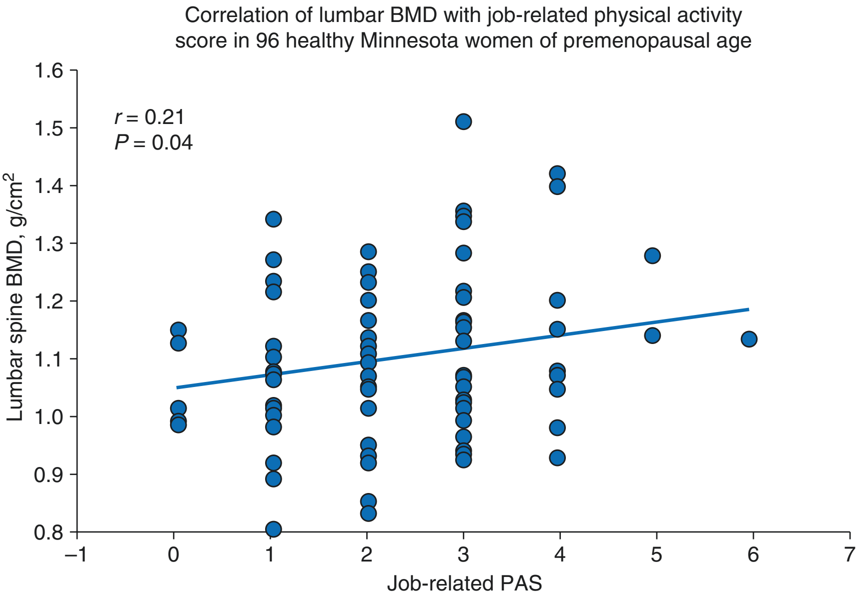

Fig. 1.5 Weight-bearing physical activity whether at job or otherwise could have positive effect on BMD of the spine. From Sinaki M, Fitzpatrick LA, Ritchie CK, Montesano A, Wahner HW. Site-Specificity of Bone Mineral Density and Muscle Strength in Women: Job-Related Physical Activity. Am J Phys Med Rehabil; 77(6):470–476, November/December, 1998; used with permission.

Maintenance of Lifelong Bone Health

Exercise is one of the factors for building and maintaining strong bones. It is well known that the risk of osteoporosis is lower for people who are active, especially for those who do weight-bearing activities at least three times a week. Exercise could also increase muscle strength and improve coordination and steadiness of gait, which helps to decrease risk of falls and situations that cause fractures.

There are different types of weight-bearing exercises with different osteogenecity effects that could be included in daily activities (e.g., walking, jogging, weight lifting, stair climbing, racquet sports, hiking, dancing). The objective of exercise needs to be defined. Compliance improves if the individual's interest is discussed prior to the recommendations. If exercise is enjoyed, it is more likely to become a habitual PA.

Healthy Bone Diet

There are a number of foods and substances that, when consumed in excess, result in excess calcium drainage from the body. These substances include caffeine and diets too high in protein from animal sources (to limit 4 oz. of meat per day would be sufficient or 0.8 g of protein per kilogram of the body weight). It is recommended by the US Department of Agriculture that all men and women over the age of 19 should get at least 0.8 g of protein per kilogram of the body weight per day (or 0.37 g per pound). This means a 130-lb woman could get 48 g of protein, such as 7 oz. of salmon.

Alcohol consumption should be limited to one drink per day (1.5 oz. of hard liquor, 12 oz. of beer, or 5 oz. of wine). Too much salt can contribute to calcium loss. To manage this concern, it is better to avoid adding extra salt to food before tasting it and reducing intake of processed foods, since they are often high in sodium.

To excrete the extra phosphates of soft drinks in urine, calcium is drawn from bones. In general, alkaline foods such as fruits, nuts, legumes, and vegetables are preferable over acidic foods such as meat, poultry, fish, dairy, eggs, grains, and alcohol. Of course, a balanced diet would take these factors into consideration.

The best source of calcium is calcium-containing foods (e.g., dairy products, leafy vegetables, nuts), but calcium supplements may also be an option. Too much calcium should be avoided, especially for patients with a history of urolithiasis. Recent studies suggest that taking high daily doses of calcium supplements (1000 mg or more) may damage the heart and have other negative health effects [20]. The type of calcium supplement and method of use is important. Calcium citrate is a highly absorbable calcium compound. It is best absorbed if taken with food. Absorption also improves if taken 500 mg at a time. Calcium ascorbate and calcium carbonate are not as easily absorbed as calcium citrate and may cause bloating. For reducing gas or constipation, increasing intake of fluids and vegetables would be of help. Vitamin D also plays a significant role in bone health. From age 18 to 70, 800 IU would be sufficient, but after 70, the amount may need to be increased to 800 IU to 1000 [21, 22].

When BMD does not improve with basic measures such as exercise, vitamin D, calcium intake, and proper nutrition, pharmacotherapy needs to be considered. There are other elemental nutrition factors that contribute to bone and muscle health and development (e.g., vitamin K and zinc), which are beyond the scope of this chapter. The authors refer the readers to the information on nutrition and maintenance of health resources.

Conclusion

Maintaining a moderate level of physical activity through a regular exercise program, combined with a balanced diet and proper calcium and vitamin D intake, is fundamental to bone and muscle health. In the case of osteoporosis and fragility, an exercise program needs to be prescribed according to the level of BMD, while being progressive and challenging. These exercises will be discussed in detail in a chapter devoted to exercise.

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Effect of Mechanical Loading on Cells: An Update

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Qian Xing and Bart L. Clarke

Introduction

It is well known that aerobic weight-bearing exercise significantly improves bone strength, increases bone mineral density, and reduces fracture risk. How biomechanical forces on the skeleton are translated into increased bone strength is less well understood, but recent studies have given insight into many aspects of the processes involved.

The osteoblasts, osteoclasts, and osteocytes that regulate the acquisition and loss of bone mineral density are each responsive to biomechanical forces on the skeleton. During skeletal growth and development, these bone cells respond to changes in biomechanical forces on the bone by contributing to modeling, in which the architecture and microarchitecture of the bone is reworked in response to alterations in biomechanical forces across the skeleton. Throughout life, osteoblasts, osteoclasts, and osteocytes respond to biomechanical forces by the process of remodeling, in which old bone with microdamage is resorbed, and newly mineralized bone is formed to fill in microstructural defects that might lead to fracture. Modeling and remodeling transform the skeleton into the structure necessary to maintain maximum bone strength for the loads it is called upon to carry.

Q. Xing, MD, PhD
Division of Endocrinology and Metabolic Diseases, Department of Internal Medicine,
First Affiliated Hospital of Dalian Medical University, Dalian, China

B.L. Clarke, MD (✉)
Division of Endocrinology, Diabetes, Metabolism, and Nutrition, Department of Internal
Medicine, Mayo Clinic College of Medicine, Mayo Clinic, Rochester, MN 55905, USA
e-mail: clarke.bart@mayo.edu

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Skeletal Anatomical Sites and Mechanical Loads

Mechanical loads applied simultaneously to the ends of long bones lead to increased forces on various sites within the bone as the length of the bone is compressed, and the bone bends to some degree in order to compensate for the increased stress. Compression and bending of the bone creates shear stress transmitted through Haversian canals and the pericellular matrix around osteocytes and osteocytic processes within the canalicular network, as fluid is displaced due to the applied load [1]. Models of this type of skeletal loading predict oscillatory fluid flow (OFF) patterns within the canalicular network, leading to shear stresses on osteocytes of 0.8 to 3.0 Pascal (Pa). High-frequency (>30 cycles per second), low-magnitude (<1 MPa) loads appear to be sufficient to generate osteocytic responses. Within the intramedullary bone marrow cavity, hydrostatic pressure compresses, and fluid flow exerts shear stress, on bone marrow-derived osteoprogenitor cells. Within blood vessel walls, mechanical strain is exerted on mesenchymal tissue-derived osteoprogenitor cells. The effect of mechanical loads on the skeleton, which increases compressive or bending forces, is to transiently deform bones, unless the forces applied exceed the ability of the bone to withstand the force, in which case fracture may occur.

The skeleton experiences relatively few high-strain (2000–3000 microstrain), low-frequency (1–3 cycles per second) events during the course of daily activity, but is exposed to nearly constant low-strain (<5 microstrain), high-frequency (10–50 cycles per second) events. These frequent low-strain, high-frequency events occur with muscle contractions necessary to maintain erect posture. As the skeleton ages and sarcopenia develops, the frequency of low-strain, high-frequency events decreases with time, possibly contributing to the bone loss that accompanies age-related deterioration of muscle function.

Sensors, Signaling Pathways, and Responses

The cells within the bone mediate bone tissue remodeling. These cells include osteocytes embedded within the bone that function as mechanosensors, osteoblasts that synthesize and secrete new bone matrix, and osteoclasts that resorb old bone affected by microdamage and their progenitors [2]. In order to fully understand the control of bone mechanobiological responses, improved understanding of the cellular and molecular bases of bone functional adaptation to stress is required.

Intracellular Signaling Pathways

Mechanical forces detected by bone cells are ultimately translated into biochemical signals that lead to downstream signaling pathway events such as phosphorylation, transcription factor translocation, or alterations in gene expression. Distal responses that occur in signaling pathways are associated with mechanotransducers that include protein kinase cascades, nuclear translocation of regulatory proteins, G-protein-regulated messengers, and second messenger systems such as intracellular Ca^{2+} and

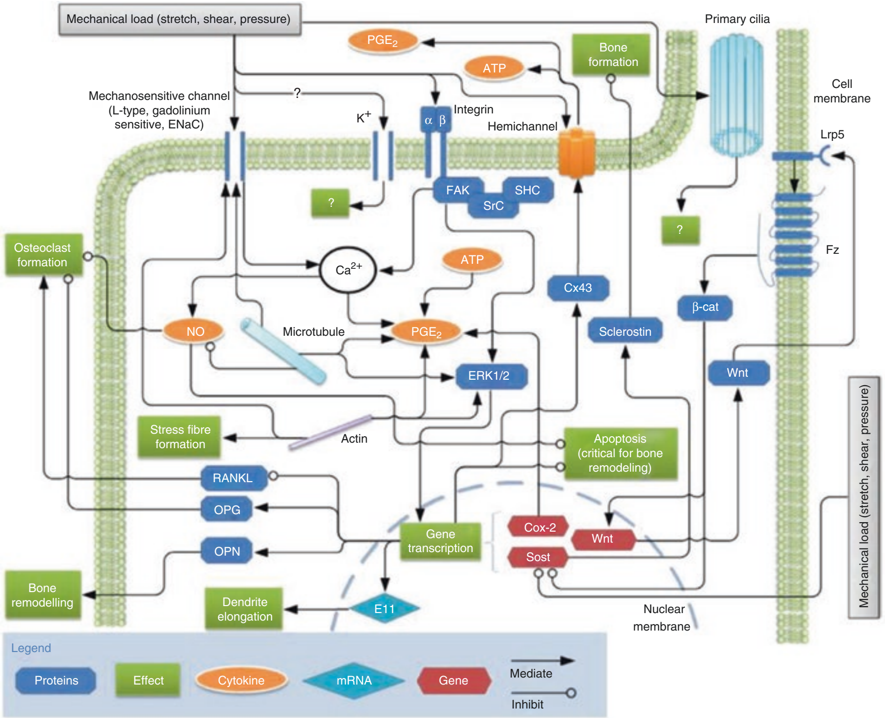

Fig. 2.1 Schematic of sensors, signaling pathways, and responses involved in osteocyte mechanobiology. Much of the current state of knowledge regarding osteocyte mechanobiology is represented in the schematic, although details are lacking in many cases. The detailed signaling mechanisms involved in osteoprogenitor mechanobiology are poorly defined. While osteoprogenitor cells appear to use many of the same sensors (e.g., integrins, ion channels, gap junctions, and primary cilia) and pathways (e.g., ERK1/2 and other MAPKs, Ca^{2+}, and Wnt) as osteocytes, their responses to distinct mechanical stimuli often differ and are not as well defined. Used with permission from Chen J-H, Liu C, You L, Simmons CA. Boning up on Wolff's Law: mechanical regulation of the cells that make and maintain bone. J Biomech. 2010;43:108–18

cAMP (Fig. 2.1). While mechanical signals are capable of activating nearly all types of signal transduction pathways within osteoblasts, osteocytes, and osteoclasts in the bone, several of the better understood pathways will be described here to give a sense of the multiple avenues by which mechanical signals regulate adaptive responses.

Protein Kinase Activation

Mechanical forces are particularly effective at activating mitogen-activated protein kinase (MAPK) cascades in nearly all types of bone cells evaluated. MAPKs are serine/threonine protein kinases necessary for bone cell differentiation, proliferation, and survival. In endothelial cells within bone, mechanical factors activate not only extracellular signal-related kinases 1 and 2 (ERK1/2) but also p38, beta-cell myeloid kinase 1 (BMK-1), and c-Jun terminal kinases (JNK). Mechanical activation of ERK1/2 has been shown to be critical for certain strain responses in bone stromal and osteoblastic cells [3]. ERK1/2 causes downregulation of receptor activator of nuclear factor kappa-B ligand (RANKL) and upregulation of endothelial nitric oxide synthase (eNOS) protein after bone cells are exposed to strain. Activation of these pathways leads to decreased bone resorption and increased bone formation.

Activation of ERK1/2 is also necessary for transforming growth factor-β (TGFβ)-induced osteogenic differentiation of mesenchymal stem cells (MSCs) into preosteoblasts and osteoblasts. ERK1/2 activation in bone cells also occurs during mechanical stimulation of voltage-sensitive calcium channels (VSCCs). Activation of ERK1/2 in osteoblastic cells by fluid shear requires Ca^{2+} influx through VSCCs and is ATP dependent. Osteocyte-like MLO-Y4 cells require association of the $\alpha_2\delta_1$ auxiliary subunit with VSCCs in order for mechanical signals to activate ERK1/2.

Protein kinase B (Akt) is a serine/threonine kinase involved in a broad range of cellular functions that is activated by a variety of growth factors, cytokines, and mechanical signals [4]. Mechanical signals that activate Akt lead to increased β-catenin activity, which causes inhibition of MSC adipogenesis, thereby causing differentiation of bone marrow MSCs toward the osteoblast lineage. Exposure to mechanical strain leading to Akt activation results in increased focal adhesion assembly in bone cells. Skeletal loading resulting in increased bone strength is influenced by refractory periods that allow regeneration of enzymes, recycling of molecules to the cell surface, and the numbers and arrangement of cytoskeletal platforms initiating the signaling cascade.

Focal adhesion kinase (FAK) is a non-receptor cytoplasmic protein tyrosine kinase (PTK) that is found in higher concentrations near focal adhesions between cells. This kinase plays an important role in signaling events involving growth factors, extracellular matrix (ECM) molecules, and stress signals [5]. FAK is found in proximity to signaling proteins including sarcoma gene (Src) family PTKs, phosphatidylinositol-3-kinases (PI3K), and paxillin. Interactions with these associated signaling proteins enable FAK to form a functional network of integrin-stimulated signaling pathways that result in activation of downstream targets, including MAPK pathways. Activation of FAK leads to autophosphorylation of FAK tyrosine 397, which leads to interactions with Src-family proteins and other molecules containing Src homology 2 (SH2) domains. Phosphorylation of FAK leads to MAPK activation by interacting with chicken sarcoma gene (c-Src), growth factor receptor-bound protein 2 (Grb2), and rat sarcoma gene (Ras), explaining why most biophysical stimuli in cell culture cause activation of MAPK pathways. Oscillatory fluid flow (OFF) has been demonstrated to cause sustained association of Src and FAK with $\alpha_v\beta_3$ integrin. Stimulation of FAK caused by this integrin association upregulates PI3K activity and modulates downstream ERK and Akt/mammalian target of rapamycin (mTOR)/p70S6K pathways, leading to increased osteoblast proliferation. FAK has also been shown to contribute to OFF-induced stimulation of osteopontin (OPN) and cyclooxygenase-2 (COX-2) expression in osteoblasts. This effect is critical for fluid shear stress-mediated increased expression of osteocalcin (OCN), core-binding factor subunit α1 (Runx2), and Osterix (Osx), demonstrating that FAK is important for osteoblast differentiation and bone formation.

β-Catenin

β-Catenin is critical for bone formation by osteoblasts, but plays other roles in bone biology. A mutation in the Wingless (Wnt) co-receptor lipid-related protein receptor-5/6 (LRP5/6) that causes constitutive activation of Wnt stimulates bone formation leading to a high bone mass phenotype known as sclerosteosis, and a dominant negative mutation of the same LRP5/6 receptor results in a low bone mass phenotype known as osteoporosis-pseudoglioma syndrome. Multiple studies have demonstrated the role of β-catenin in osteoblasts and osteocytes. β-Catenin regulates both bone formation and resorption [6, 7]. Skeletal loading has been shown to regulate levels of β-catenin in bone cells in animals and humans.

While the LRP5/6 receptor may function as a mechanoreceptor in osteoblasts, mechanical strain has been shown to control MSC differentiation via non-LRP5/6 regulation of β-catenin. Two percent mechanical strain at 10 cycles/min and continuous fluid flow at 8 dyn/cm^2 and OFF at 10 dyn/cm^2 have each been shown to stimulate β-catenin activity in osteoblasts in spite of blocked LRP5/6 receptors. Low-intensity vibration at <10με and 90 cycles per second stimulates β-catenin and suppresses fat cell differentiation, indicating that both high- and low-magnitude mechanical stimuli alter MSC fate through β-catenin. Focal adhesion-based connections with substrate mediate glycogen synthase kinase-3β (GSK3β) inhibition after loading of MSCs and osteoblasts, resulting in increased β-catenin due to reduced proteosomal degradation. Proximal signaling results in mechanical activation of mTORC2, leading to phosphorylation of Akt serine 473, leading to Akt-dependent inhibition of GSK3β (Fig. 2.2). If

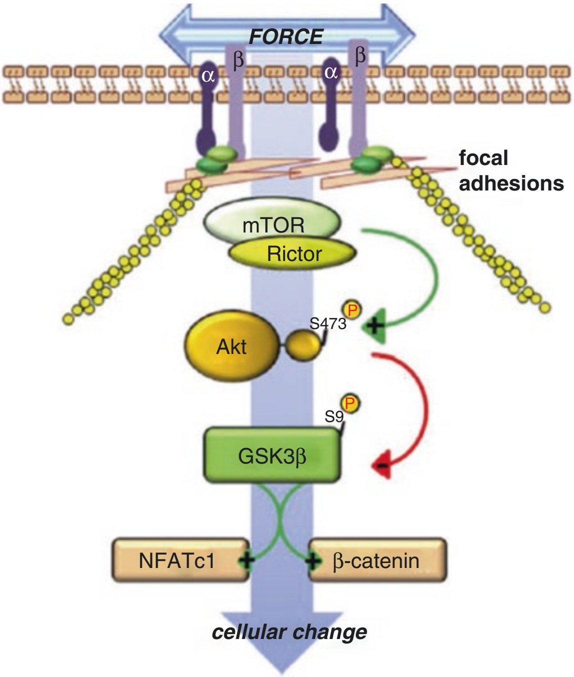

Fig. 2.2 Force-induced activation of β-catenin. Application of mechanical force to cells induces focal adhesion-dependent activation of mTORC2. mTORC2 then activates Akt, which inactivates GSK3β via phosphorylation. Inhibition of GSK3β leads to multiple downstream events, including preservation and nuclear translocation of β-catenin, as well as prolonging the nuclear residence of NFATc1. Used with permission from Thompson WR, Rubin CT, Rubin J. Mechanical regulation of signaling pathways in bone. Gene. 2012;503:179–93

mTORC2 functions as a mechanical target, there may be interactions between the cytoskeleton and metabolic responses to exercise since mTORC2 responds to insulin signaling.

GTPases and G-Protein-Coupled Receptors

Guanosine triphosphatases (GTPases) are a large family of enzymes that bind to and hydrolyze GTP. These enzymes function as switches regulating a wide variety of physiological processes. Mechanical stimuli activate heterotrimeric GTPases via G-protein-coupled receptors, resulting in increased intracellular calcium ($[Ca^{2+}]_i$), cyclic AMP (cAMP), and cyclic GMP (cGMP) (Fig. 2.3). Nitric oxide (NO) is produced by protein kinase G (PKG) after mechanical shear stress in osteoblasts [8]. PKGII was shown to be necessary for Src upregulation by phosphorylating Src homology 2 domain-containing tyrosine phosphatase-1 (SHP-1). Subsequent fluid shear stress led to recruitment of PKGII, Src, SHP-1, and SHP-2 to a β3-integrin-containing mechanosome.

Estrogen Receptors

Estrogen deficiency after menopause is a major cause of osteoporosis, and estrogen receptors (ERs) play a key role in postmenopausal bone loss. ERα mediates bone formation in response to load-bearing in vivo and regulates how osteoblasts and osteocytes respond to mechanical stimulation [9]. ER also modulates mechanically

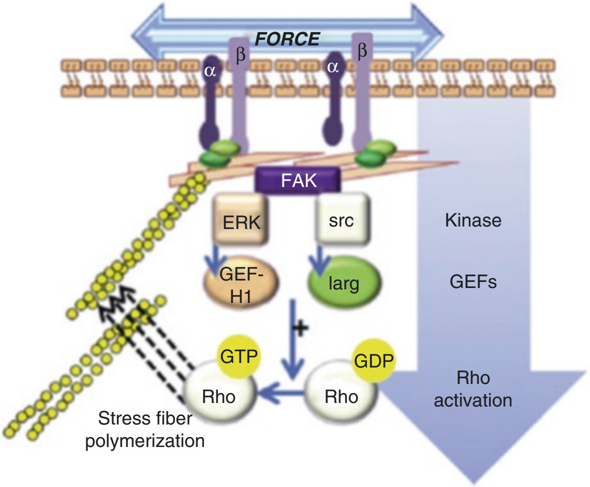

Fig. 2.3 Mechanical activation of Rho via focal adhesions. Forces transmitted through focal adhesions are known to activate signaling cascades, possibly though force-induced conformational change. Involved signaling pathways include focal adhesion kinase (FAK), ERK1/2, and Src. ERK and Src can initiate Rho signaling via activation of GEFs (here shown as GEF-H1 and Larg). GDP bound RhoA is critical for assembly of new focal adhesions and stress fiber polymerization. Used with permission from Thompson WR, Rubin CT, Rubin J. Mechanical regulation of signaling pathways in bone. Gene. 2012;503:179–93

activated signaling pathways. ERα knockout (KO) mice were shown to have reduced response to tibial loading, with severely reduced and delayed transcriptional response and a broad range of effects compared to wild-type littermates. Three hours following a brief loading regimen, wild-type mouse tibiae showed altered transcription of 642 genes, while only 26 genes were modified in ERα KO tibiae. For example, sclerostin gene (*SOST*) expression was significantly reduced after loading in wild-type mice, but unchanged in loaded tibiae of ERα KO mice.

Bone cells respond to mechanical stimuli via ERα through both genomic and nongenomic actions. ERα nongenomic actions depend on direct interaction with insulin-like growth factor-1 receptor (IGF-1R), leading to sensitization of IGF-1R and upregulation of early strain-regulated genes including COX-2. β1-Integrin expression, which is important for load-induced bone formation, is also upregulated by ERα. These interactions help explain why estrogen may help upregulate osteogenic target genes in response to mechanical stimuli.

Calcium Signaling

A rapid increase in $[Ca^{2+}]_i$ is the earliest detectable response in mechanically activated bone cells [10]. Calcium channels in the plasma membrane and intracellular organelles help regulate $[Ca^{2+}]_i$. $[Ca^{2+}]_i$ concentrations are tightly regulated to maintain a very low level of free $[Ca^{2+}]_i$, making $[Ca^{2+}]_i$ an excellent second messenger system. $[Ca^{2+}]_i$ serves as an initial signal in bone cell proliferation, mitosis, differentiation, and motility. $[Ca^{2+}]_i$ mobilization is initiated by cell membrane strain, pressure, fluid flow, and osmotic swelling. The frequency of $[Ca^{2+}]_i$ spiking is more important in bone cell response to loading than the magnitude of Ca^{2+} spikes, and a rest period between loading enhances Ca^{2+} response in osteoblastic cells.

Changes in $[Ca^{2+}]_i$ are linked to several mechanically regulated signaling cascades, including inositol-3-phosphate (IP3), adenosine triphosphate (ATP), and NO. $[Ca^{2+}]_i$ mobilization stimulates downstream signaling through protein kinase A (PKA), MAPK, and c-Fos. Prostaglandin E_2 (PGE_2) release plays an important role in mechanical bone formation, but is activated by a Ca^{2+}-independent mechanism. Other studies show that PGE_2 release is dependent on Ca^{2+} entry through the L-type VSCC, followed by release of ATP.

Influence of Mechanical Loading on Mesenchymal Stem Cell Differentiation

Mechanical strain applied to mesenchymal stem cells causes these cells to differentiate toward osteoblasts and suppresses differentiation toward adipocytes [11]. Bone formation occurs during embryonic growth and development and during postnatal bone modeling, remodeling, and repair. In order for osteoblasts to continue to fulfill their role, the skeleton or other tissues must contain a sufficiently large reservoir of osteoprogenitor cells to generate new osteoblasts from birth until death. Osteoprogenitor cells maintain their ability to differentiate from a less differentiated precursor state, or to transdifferentiate from other differentiated cell types, into osteoblast-like cells that produce a variety of proteins characterizing osteoblasts, such as Runx2, alkaline phosphatase (ALP), ON, and OCN, and synthesize bone matrix. Because osteoprogenitor cells have not yet been identified to express specific protein markers, they are difficult to identify, and the precise anatomical location of their niche remains unknown. Osteoprogenitor subpopulations have been identified in bone marrow, but also in cardiovascular tissues, including the aortic heart valve, vascular smooth muscle, and capillary beds. Mechanical signals are also thought to regulate the function and differentiation of osteoprogenitor cells in tissues other than the bone.

Substrate Deformation Effects on Osteoprogenitor Cells

Mechanical strain induces differentiation of osteogenic precursors and suppresses differentiation of osteoprogenitor cells into adipocytes. After being stretched for over 24 h, mRNA transcripts for ALP, Runx2, BMP2, BMP4, and collagen type I are significantly increased in osteogenic precursors. After cyclic stretching for 1–2 weeks, osteogenic precursor OCN and Runx2 protein levels increase, and mineralization of deposited matrix occurs. The extent of the osteogenic response depends on the size of the strain detected and mediated through FosB activation [12]. How osteoprogenitor cells respond to mechanical strain depends on their stage of differentiation. Mechanical strain at less differentiated stages leads to increased Runx2 and type I collagen mRNA expression, decreased proliferation of osteoprogenitors, and increased apoptosis, compared to exposure at more differentiated stages.

Stretching the extracellular matrix applies force to cell focal adhesions to the matrix, which results in increased FAK activity, activating downstream MAPK signaling pathways. Mechanical strain induces rapid phosphorylation of MAPK. Although mechanical strain increases MAPK activity, and inhibition of MAPK in cell culture decreases mineralization, inhibition of these pathways has little to no effect on strain-induced osteogenic differentiation in osteoprogenitor cells found in blood vessels. These findings suggest that mechanical strain also activates other signaling pathways to stimulate osteogenic differentiation.

Certain calcium channels may be activated by mechanical strain. Blockage of these calcium channels pharmacologically, or culture of osteoprogenitor cells in calcium-free media, leads to decreased strain-induced ALP upregulation. The Wnt signaling pathway may be stimulated mechanically to promote bone formation. Mechanical strain upregulates Wnt 10B and frizzled-2 receptor mRNA, which leads to increased phosphorylated β-catenin nuclear translocation in osteoprogenitor cells.

Fluid Flow Effects on Osteoprogenitor Cells

Fluid flow in the intramedullary space and Haversian canals occurs in response to mechanical strain, suggesting that fluid flow stimulates osteoprogenitor cells in these compartments also. Osteoprogenitor cells appear to be more responsive to shear stress than matrix deformation when these are both applied at the physiological ranges seen in the bone.

Although most studies have reported that fluid flow promotes osteogenic differentiation, some studies have not. In parallel plate flow chamber studies, flow-induced shear stress stimulated mRNA expression of some preosteoblast markers, but had no effect or inhibited other preosteoblast markers such as ALP, Runx2, or osteocalcin. These findings were attributed to differences in cell substrate surface chemistry and different flow patterns employed. ECM proteins and substrate materials are known to influence osteogenic differentiation, but studies have not thoroughly explored the effect of matrix proteins in combination with mechanical strain. One study demonstrated that the calcium phosphate coating on glass slides was associated with less flow-stimulated OPN and bone sialoprotein mRNA synthesis, suggesting that matrix properties affect osteoprogenitor cell mechanosensation. Osteopontin mRNA expression and ERK1/2 phosphorylation are variable, depending on whether the flow pattern is continuous, intermittent, or oscillatory and the magnitude of shear stress and flow frequency. Variable osteoprogenitor response to flow pattern may also explain some of the discrepancies seen between different studies.

The effect of flow on osteoprogenitor cells has also been evaluated in three-dimensional cell culture systems. In this case, cells are seeded into hydrogels or scaffolds and then cultured during spinning or flow perfusion. Similar to what is found in 2D systems, fluid flow stimulates preosteoblast differentiation in 3D systems. Fluid-induced preosteoblast differentiation in 3D systems also depends on substrate material. Even though 3D systems better reflect the in vivo cellular environment, the effects of shear stress and mass transport are difficult to separate. In addition, variability in pore size and interconnectivity of the scaffolds make it difficult to quantitate shear stress experienced by the cells.

Primary cilia, gap junctions, and the cytoskeleton are important in osteoprogenitor cell mechanosensing of fluid flow [13]. Primary cilia are nonmotile and project from the cell membrane into the extracellular space and move with the flow. Mechanosensing through primary cilia in osteoblast precursors is independent of calcium flux and stretch-activated channels and required for flow-induced stimulation of osteoblast differentiation, as pharmacological removal of primary cilia prevents flow-induced stimulation of OPN mRNA and PGE_2 secretion. Pharmacological inhibition of gap junctions in osteoprogenitor cells caused similar results.

Actin stress fiber formation in osteoprogenitor cells was stimulated by steady fluid flow (SFF), whereas OFF did not. Responsiveness of osteoprogenitor cells to fluid flow may depend in part on cytoskeletal tension. Osteoprogenitor cells that are more spread out on substrate surfaces are less responsive to mechanical strain than cells that are less spread out.

Fluid flow releases intracellular stored calcium and increases intracellular calcium concentration in osteoprogenitor cells, independent of activation of mechanosensitive calcium channels. This is in contrast to mature osteoblasts, in which fluid flow recruits mechanosensitive calcium channels. Fluid flow also activates ERK1/2 and p38 MAPK to stimulate osteogenesis, as inhibition of either of these kinases reduces flow-induced osteogenesis. Depletion of intracellular calcium stores pharmacologically results in decreased osteogenic response, but reduction in intracellular calcium does not affect ERK1/2 activity. These findings collectively indicate that fluid flow stimulates ERK1/2 independently of calcium signaling, but that p38 MAPK is a potential target of downstream flow-induced calcium signaling. Additionally, actin cytoskeleton disruption did not reduce intracellular calcium release in osteoprogenitor cells subjected to OFF. Instead, these cells showed increased calcium responses and increased PGE_2 release compared to untreated cells. These results demonstrate that PGE_2 release and mobilization of intracellular calcium does not depend on an intact actin cytoskeleton. One possible explanation for these results is that cytoskeleton compromise may allow greater cell deformation, which indirectly contributes to increased intracellular calcium and PGE_2 release.

Hydrostatic Pressure and Compression Effects on Osteoprogenitor Cells

Osteoprogenitor cells are able to sense and respond to mechanical stress due to hydrostatic pressure or compressive loading, likely in part through membrane integrins [14]. Mechanical stress induces ALP activity and mRNA expression of Runx2, BMP2, Osx, collagen I, OCN, osteonectin, and OPN in osteoprogenitor cells. After mechanical loading for 1–2 weeks, mineralization and OCN and OPN protein expression are significantly increased compared to nonloaded cells. Osteogenic response depends on mechanical stress in a biphasic manner, suggesting that there is an optimal range of stress for induction of osteogenic differentiation. The optimal range of stress has not yet been fully characterized, as reported optimal stresses vary from 49 Pa to 11.8 kPa. Osteogenic response to hydrostatic pressure also depends on the extent of differentiation of osteoprogenitor cells, with less differentiated cells being more sensitive to hydrostatic pressure.

ERK1/2 and p38 MAPK appear to play a positive but nonsignificant role in mechanotransduction of hydrostatic pressure. Mechanical stress stimulates phosphorylation of ERK1/2 and p38 MAPK, but pharmacological inhibition of these kinases partially inhibits mechanical stress-induced osteogenic differentiation, suggesting that other signaling pathways are involved. Mechanical loading causes activation of the Wnt signaling pathway, with Wnt10B and Wnt4 mRNA expression stimulated. Stimulation of Wnt10B mRNA partially depends on ERK1/2 phosphorylation, but Wnt4 mRNA expression does not.

Substrate Stiffness Effects on Osteoprogenitor Cells

Osteoprogenitor cells sense stiffness of the ECM and change the way they respond to various stimuli, including how rapidly they proliferate [1], differentiate, and undergo apoptosis. The mechanism affecting this variable responsiveness to ECM stiffness is as yet unknown, but cellular response to matrix stiffness depends on osteoprogenitor cell differentiation. More differentiated osteoprogenitor cells appear to be more responsive to ECM stiffness. Some studies have shown that stiffer ECM promotes greater osteogenic differentiation and mineralization. One study showed that osteoprogenitor cells have a biphasic dependence on matrix stiffness, in which physiologically relevant stiffness in the range of 25–40 kPa was optimal. Another study demonstrated more significant osteogenic differentiation in this same stiffness range, compared to stiffer matrices. Differences between studies are likely due to differences in ECM surface chemistry and osteoprogenitor differentiation. Differences in differentiation potential between cell systems might also result in the biphasic response observed in primary osteoprogenitor cells, which often differentiate to myofibroblasts on stiffer ECM.

Inhibition of non-muscle myosin II decreases osteogenic differentiation on substrate of variable stiffness. MAPK activation downstream of the Ras homolog gene family member A (RhoA)-Rho-associated, coiled-coil-containing protein kinase (ROCK) signaling pathway also affects how matrix stiffness influences osteogenic differentiation. Runx2 mRNA expression by MC3T3-E1 preosteoblasts increases on stiffer substrates and correlates with increased ERK1/2 activity. Inhibition of RhoA, ROCK, and MAPK decreases Runx2 activity and inhibits osteogenesis, with resultant decreased OCN, bone sialoprotein, gene expression, ALP activity, and mineralization.

Influence of Use and Disuse on Bone Turnover

Mechanical loading significantly influences bone remodeling. Disuse or lack of loading causes an acceleration of bone turnover, with bone resorption exceeding bone formation, and subsequent rapid bone loss. This type of bone loss is observed in astronauts who spend extended periods of time in low-gravity environments or patients confined to bed rest after stroke or head injury. Bone overuse causes damage to the tissue, which in turn stimulates bone remodeling to repair microfractures. One of the important roles of bone turnover is to continuously replace and repair damaged bone tissue. Osteoclasts preferentially target regions of microdamage and remove damaged bone tissue and replaced it with new bone tissue. If damage accumulates faster than the tissue can be repaired, larger microfractures may develop and propagate to form a stress fracture.

The increased number of bone remodeling sites with skeletal disuse or overuse is preceded by programmed cell death in osteocytes [15]. The factors that initiate osteocyte apoptosis are not well understood, but these may include damage to osteocytes via microfractures in the bone matrix or lack of fluid flow during disuse. The effects of loading on bone remodeling are described by a U-shaped curve. Remodeling increases with disuse due to insufficient loading. Overuse results from overloading leading to damage. Similar to the optimal range of strain on bone cells described above, there is an optimal range of skeletal loading within which bone remodeling is reduced to a nadir. Periosteal new bone formation typically increases with increased skeletal loading.

Lack of physical use during growth limits the development of characteristic cross-sectional shape of long bones. An immobilized tibia develops a fairly round cross-sectional area, rather than the typical triangular shape. Disuse or low stress on the bone reduces bone formation on periosteal surfaces and increases bone resorption on endocortical and trabecular surfaces. These effects are associated with rapid bone loss. The effects of disuse on bone surfaces, differential response to disuse in growing and mature skeletons, and regional differences in bone loss with disuse have been evaluated in many studies. Studies in dogs have shown that casted forelimbs undergo profound bone loss resulting from disuse. In growing dogs, disuse is most apparent at the periosteal surfaces of long bones, with decreased normal appositional bone formation, resulting in smaller cross-sectional bone area and reduced second moment of inertia. In older dogs, disuse results in bone loss due to accelerated bone resorption, with loss occurring mainly on the endosteal surface of long bones. Reduction of loading of a bone in an older dog leads to a rapid expansion of the marrow cavity and a substantial worsening of cortical porosity. In both young and older dogs, bone loss is greatest in the most distal bones of the casted forelimb, indicating that skeletal sites closest to the ground lose the most bone with disuse. The osteogenic effects of mechanical loading are greatest in regions closest to the ground, likely due to direct loading of the bones. Greater pressure within the medullary cavity in the distal bones due to gravity enhances appositional bone growth. Distal regions of weight-bearing limbs have the largest anabolic response to exercise and the most severe catabolic response to disuse. These regions are the greatest distance below the heart and therefore subject to higher interstitial fluid pressure.

Human volunteers at long-term bed rest gain bone mass in their cranial bones [16]. This is due to change in the relative effect of gravity on the body when a person lies supine. Bed rest causes body fluids to shift so that dependent regions like the feet that are typically under high fluid pressure are subject to lower pressure. Sites typically under lower fluid pressure, like the head, adapt to higher pressure, which may increase bone formation or decrease bone resorption in the cranial bones. Bone loss is not equal throughout the skeleton at bed rest. Bone loss is increased in the lower extremities, particularly the calcaneus, where fluid pressure decreases substantially with bed rest.

Exercise generally stimulates an increase in bone density. Bone density measurements in professional athletes compared with non-athletes show increased bone density at the hip, or throwing arm, or kicking leg, but decreased bone density in the upper skull. Therefore, bone density in the skeleton is preserved because changes in bone density at weight-bearing sites caused by disuse or exercise are partially offset by changes in bone density at skeletal sites that do not bear weight.

Microdamage, Osteocyte Apoptosis, and Bone Resorption

Cortical and trabecular bone damage in the form of microfractures occurs throughout the skeleton each day, with the number of microfractures depending on the magnitude of the forces to which the skeleton is exposed. Immunostained iliac crest bone biopsies demonstrate microfractures that develop due to fatigue damage to the bone [2]. Microfractures may accumulate such that the bone weakens sufficiently for a fracture may occur. Microfractures typically occur along the lamellar surfaces of trabecular bone and cortical bone, and some cross osteonal units in the Haversian structure of the bone. How far microfractures propagate depends on the force applied and the mechanical properties of the affected bone.

Microfractures are believed to serve as a stimulus for osteoclast-mediated bone resorption, likely preceded by osteocyte apoptosis [17]. Osteocytes adjacent to microfractures are typically apoptotic, presumably because the adjacent microfracture disrupted the canalicular network affecting osteocyte nutrient supply. Microdamage generally correlates with strain within the bone, and bone resorption correlates with microdamage removal and repair. The osteocyte network is therefore critical for physiologic response to bone microdamage. Removal of apoptotic osteocytes during the bone resorption process, and synthesis of new bone in the area of previous microdamage, leads to the generation of new osteocytes.

Mechanotransduction in Bone

The human skeleton is both strong and tough enough to prevent fractures, but light enough to maintain mobility and functionality. Osteocytes embedded within mineralized bone sense mechanical loads applied to the skeleton. Mechanical loads are transformed into biological signals which result in bone resorption or bone formation at appropriate sites within the skeleton. Osteocytes stimulated by mechanical loads release signals coordinating the response of osteoclasts and osteoblasts, leading to adaptation of the skeleton to biomechanical forces. Wilhelm Roux first proposed that functional adaptation of the skeleton is the end result of self-organized bone cellular processes in 1881.

Osteocytes produce OCN, osteonectin, OP, and sclerostin, but have reduced expression of AP. Following mechanosensation and conversion of mechanical signals into biochemical signals, osteocytes coordinate the formation and activity of osteoblasts and osteoclasts. The intercellular communication required for this coordination involves signals including NO, PGs, BMPs, Wnts, and others.

Application of mechanical loads to the skeleton leads initially to intracellular movement of extracellular calcium through ion channels in the plasma membrane, with subsequent release of calcium from intracellular stores. The increase in intracellular calcium activates downstream signaling cascades involving phospholipase C and phospholipase A2 and is necessary for activation of calcium-/calmodulin-dependent proteins such as constitutive forms of NOS. Activation of phospholipase A2 results in arachidonic acid production and PGE_2 release. Gene transcription of c-Fos, MEPE, and IGF-1 is also modified by mechanical loading.

NO is produced by NOS, molecular oxygen, NADPH, and other cofactors during conversion of L-arginine to L-citrulline. Mechanical stimulation causes increased production of NO. NO modulates the activity of osteoblasts and osteoclasts, and inhibition of NO production by osteoblasts inhibits new bone formation. Activity of eNOS is not necessary for mechanical stimulation-induced production of NO. It is not yet clear which NOS is responsible for producing NO in mechanically stimulated osteocytes.

PGs are widely expressed in osteocytes and cells of the osteoblastic lineage and play a significant role in mechanical stimulation of new bone formation. Mechanical loading causes a rapid increase in PG production by osteocytes. Osteocyte COX produces PGs and is found in a constitutive form (COX-1) and inducible form (COX-2). Fluid shear stress on primary human bone cells does not stimulate COX-1 mRNA, but stimulates a rapid rise in COX-2 mRNA in human bone cells in vitro. Inhibition of COX-2, but not COX-1, inhibits fluid shear stress-induced PG production by primary bone cells in vitro. COX-2 has been shown to mediate the anabolic response of bone tissue to mechanical loading. PGs are released through hemichannels and purinergic receptors in response to mechanical stimuli [18].

Wnt signaling is an important modulator of mechanical stimuli-regulated bone adaptation. Wnt signaling is mediated by β-catenin pathways, kinases, or GTPases that modulate cytoskeletal organization. Activation of β-catenin signaling in response to fluid shear stress is mediated by PGE_2 in osteocytes [19]. Wnts modulate cytoskeletal organization, and β-catenin links cadherins to the actin cytoskeleton. MC3T3-E1 osteoblasts increase Wnt gene expression after mechanical stimulation by substrate deformation. Pulsating fluid flow upregulates mRNA expression of β-catenin, APC, and Wnt3a, as well as the Wnt antagonist soluble frizzled-related protein 4 (SFRP4) in MLO-Y4 osteocytes. LRP5/6, a co-receptor for Wnt signaling, functions locally in osteocytes.

Sclerostin is highly expressed in mature osteocytes and at lower levels in immature osteocytes. Sclerostin is transported to the bone surface via the canalicular network in the bone, where it inhibits new bone formation by osteoblasts. Loading of mouse ulnae in vivo results in reduced expression of sclerostin mRNA and protein by osteocytes. The magnitude of the strain stimulus is associated with sclerostin staining intensity and the number of sclerostin-positive osteocytes. Hind limb unloading resulted in a significant increase in sclerostin expression in mouse tibiae.

Mechanoreceptors

A variety of candidate mechanoreceptors have been identified that mediate the effects of mechanical strain on bone cells. Mechanosensors include any molecule, protein complex, or biological structure that can sense alterations in force on a cell. Mechanoreceptors must be able to directly contact the extracellular space or be able to detect changes in pressure or fluid shear on the cell membrane.

Proposed mechanoreceptors for bone cells include ion channels and connexins, integrins, the cytoskeleton, focal adhesions, lipid rafts, cadherins, ephrins, and primary cilia (Fig. 2.4). Ion channels in osteoblasts are stimulated by stretch or strain of the cell membrane or by parathyroid hormone. At least three classes of ion channels sensitive to mechanical signals have been identified, including gadolinium-sensitive stretch-activated cation channels, transient receptor potential channels,

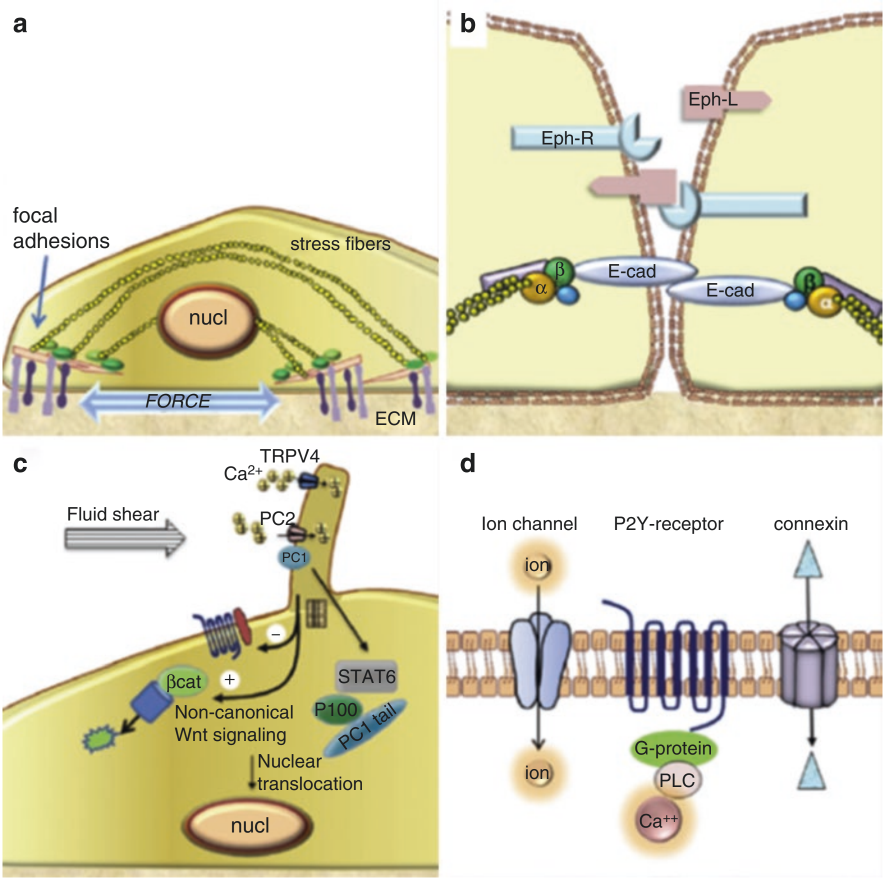

Fig. 2.4 Candidate mechanotransducer systems. (**a**) Cell cytoskeleton senses loading at the membrane through integrins that transmit force through focal adhesions and F-actin stress fibers. (**b**) Cadherins, which connect to the cytoskeleton, are examples of outside-in signaling modifiers. Ephrins exemplify an intercellular signaling system regulated by movement of components within the plasma membrane. (**c**) Primary cilia may sense flow, pressure, and strain, activating ion flux through PC1 and TRPV4, which can activate Stat signals. Cilia also modulate Wnt signaling via noncanonical antagonism that leads to β-catenin degradation. (**d**) Membrane-spanning proteins such as ion channels, purinergic receptors, and connexins can be regulated through shear and strain. Used with permission from Thompson WR, Rubin CT, Rubin J. Mechanical regulation of signaling pathways in bone. Gene. 2012;503:179–93

and multimeric L-type and T-type voltage-sensitive calcium channels in osteoblasts and osteocytes, respectively.

Membrane perturbation or shear across the cell membrane, as well as transient changes in pressure, is transmitted to the cell cytoskeleton and finally to cell adhesion proteins that attach the cell to the bone matrix. Both membrane-spanning integrins that connect the cell to the extracellular matrix, and a large number of adhesion-associated linker proteins, are potential molecular mechanotransducers.

Lipid rafts on the cell membrane are composed of various proteins that compartmentalize signals within the membrane containing several phases of liquid-ordered and liquid-disordered lipid, which may sense mechanical signals. Shear stress may cause signaling molecules in the cell membrane to translocate to caveolar lipid rafts. Degradation of caveolae internally leads to termination of both proximal and downstream signals, including those in the MAPK pathway.

Cadherins are integral membrane glycoproteins that have a large extracellular domain, single transmembrane domain, and short intracellular domain. The intracellular domain links the cadherin to the cytoskeleton by associating with multiprotein complexes that include vinculin and α- and β-catenin. Fluid shear stress reduces that amount of β-catenin bound to N-cadherin, thereby increasing the cytoplasmic availability of β-catenin. Cadherins may therefore serve to release β-catenin for nuclear translocation after mechanical stimuli are received [20].

Ephrin ligands and their cognate ephrin receptors are regulated by the cytoskeleton. Limitation of ephrin clustering within the cell membrane may modulate cellular responses to mechanical stimuli.

Osteoblasts and osteocytes possess nonmotile, microtubule-based cilia derived from centrioles. Fluid flow-induced PGE_2 signaling in osteoblasts and osteocytes, independent of intracellular Ca^{2+} changes, is dependent on cilia. Primary cilia regulate Wnt signaling by causing β-catenin degradation by noncanonical pathways, such that the loss of ciliary function leads to increased canonical Wnt signaling.

Conclusion

Mechanical loading of bone cells prevents bone loss and reduces fractures. Mechanical loads applied to the bone increase fluid flow and hydraulic pressure on bone marrow-derived osteoprogenitor cells and mechanical strain on blood vessels leading to effects on mesenchymal tissue-derived osteoprogenitor cells within the intramedullary canal and bone marrow space and shear forces within Haversian canals and the canalicular network, leading to effects on osteocytes. Mechanical loads involving stretch, shear force, or pressure stimulate bone cell mechanosensitive L-type, gadolinium-sensitive, ENaC channels, integrins, connexin-43 hemi-channels, primary cilia, and possibly potassium channels. Intracellular calcium, Wnt/β-catenin, sclerostin, Src, and ERK signaling pathways appear to mediate cellular responses to mechanical loading. Mechanical loading diverts mesenchymal stem cell differentiation from adipocytes to osteoblasts, leading to increased bone formation and reduced marrow fat. Bone use increases bone strength by stimulating bone formation, whereas disuse reduces bone strength by increasing bone turnover leading to bone resorption. Bone microdamage results in adjacent osteocyte injury and apoptosis, leading to bone resorption. Mechanotransduction in the bone by multiple mechanisms, and multiple potential mechanosensors, provides the skeleton with the flexibility and adaptability it requires to sustain loads of different weight and to avoid fracture.

Summary

Osteoporosis is a systemic skeletal disorder characterized by compromised bone strength predisposing to increased risk of fracture. Bone strength reflects integration of bone density and bone quality, and bone quality reflects architecture, turnover, damage accumulation (microfractures), and mineralization. In the USA, 44 million persons are estimated to have low bone mass, based on the 2000 census and projections from the National Health and Nutrition Examination Survey (NHANES) data, with 55% of the US population over age 50 affected. Of this number, 33.6 million are estimated to have osteopenia and ten million, osteoporosis.

The bone cells that regulate gain and loss of bone density in the skeleton are responsive to biomechanical forces. During growth and development, bone cells respond to changes in biomechanical forces by modeling the shape and architecture of the bone in response to alterations in biomechanical forces on the skeleton. During aging and senescence, these same bone cells respond to biomechanical forces by the process of remodeling, in which old bone is resorbed and new bone is laid down. The effect of both processes is reworking of the skeleton to gain or maintain maximum bone strength to support the loads carried by the skeleton.

The focus of this chapter will be the mechanisms by which mechanical loading affects bone cells. The chapter will briefly review mechanical loads borne by different skeletal anatomical sites and summarize current knowledge regarding bone cell sensors, signaling pathways, and responses to mechanical loading. The influence of mechanical loading on mesenchymal stem cell differentiation will be discussed, as will the influence of use and disuse on bone turnover. The influence of microdamage on osteocyte apoptosis and bone resorption will be summarized, and current knowledge regarding mechanotransduction in bone explored in some detail. Finally, what is known regarding potential mechanoreceptors will be briefly summarized.

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Posture Analysis in Patients with Spinal Osteoporosis

3

Eiji Itoi and Yu Mori

Introduction

Increased thoracic kyphosis, known as a dowager's hump, is commonly observed in osteoporotic patients. A dowager's hump is known to be related to respiratory dysfunction, reflux esophagitis, and postural instability. Similarly, decreased lumbar lordosis observed in patients with lumbar degenerative kyphosis is known to cause severe disability in activities of daily living such as walking disturbance because of low back pain. The measurement of thoracic kyphosis and lumbar lordosis is therefore an essential aspect to musculoskeletal assessment, helping clinicians to adequately screen for excessive kyphosis, determine baseline data, monitor progress, and guide appropriate treatment [1]. X-ray measurement has been the gold standard to assess thoracic kyphosis and lumbar lordosis [2–5]. However, X-ray measurement has several limitations. Radiation exposure is a major concern. It requires X-ray machine or X-ray generator, which needs to be located in a shielding room. The device is not handy and not always available. Because of these limitations, other non-radiographic methods have been introduced and developed. The purpose of this chapter is to review the literature to assess the reliability and validity of various methods of posture assessment commonly used.

E. Itoi, MD, PhD (✉) • Y. Mori, MD, PhD
Department of Orthopaedic Surgery, Tohoku University School of Medicine,
1-1 Seiryo-machi, Aoba-ku, Sendai, Miyagi 980-8574, Japan
e-mail: itoi-eiji@med.tohoku.ac.jp; yu-mori@med.tohoku.ac.jp

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Various Methods of Posture Assessment

X-ray Measurement

The original method described by Cobb was to measure the curvature of the spine in the coronal plane in patients with scoliosis [3]. Later, this method was applied to the spinal curve measurement in the sagittal plane [4]. The upper and lower vertebral bodies defining the curve were selected and lines were drawn, extending along the superior border of the upper end vertebra and along the inferior border of the lower end vertebra. Perpendicular lines were drawn from these two lines and the angle was measured at the intersection (Fig. 3.1). Since the fourth thoracic vertebra (T4) is the most superior thoracic vertebra that is constantly seen on lateral X-ray,

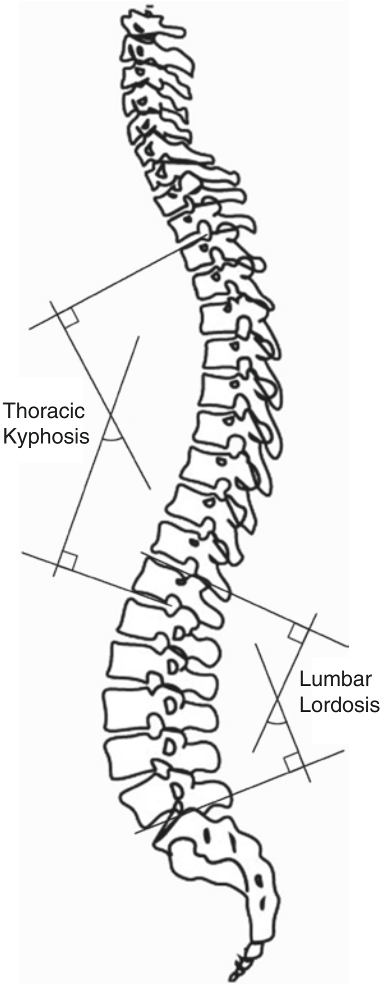

Fig. 3.1 Cobb measurement (original drawing)

T4 is usually used as the upper end vertebra and the 12th thoracic vertebra (T12) as the lower end vertebra for the measurement of thoracic kyphosis. Similarly, T12 is used as the upper end vertebra and the fifth lumbar vertebra (L5) as the lower end vertebra for the measurement of lumbar lordosis. This technique of Cobb measurement is called the constrained technique because the upper and lower end vertebrae are fixed or constrained. The constrained upper and lower vertebrae may vary according to the investigators, such as T1–T12, T2–T12, T3–T12, or T4–T12 for thoracic kyphosis, and T12–L5, T12–S1, L1–L5, L1–S1, or L2–S1 for lumbar lordosis. The other technique is called non-constrained technique, in which the end vertebra is not constrained. The most tilted vertebra, known as the transition vertebra (also called limit vertebra or interference vertebra), is determined on X-ray and used as the end vertebra for the measurement of thoracic kyphosis and lumbar lordosis. The most tilted vertebra marks the transition from the thoracic curve to the lumbar curve, and this transition does not always occur at the T12 level. This is the reason why the transition vertebra is determined in each subject such that we can measure the true angles of these two curves. This is the advantage of non-constrained technique. However, identification of the transition vertebra may sometimes be difficult and examiner dependent and could lead to low reliability for determining the transition vertebra, which can be circumvented by using the constrained technique. Both techniques are highly correlated [6], and a computer-assisted method may improve the reproducibility of non-constrained technique [6]. In the measurement methods other than X-rays, the constrained method is widely used. The Cobb measurements with high interobserver and intraobserver agreement values (kappa value) of 0.96 and 0.98, respectively [7], are considered to be the standard method and thus widely used as the gold standard to validate other methods.

A modified method of Cobb measurement is also used (Fig. 3.2) [5]. Thoracic kyphosis is defined as the angle of intersection between the inferior border (not the superior border) of T4 and that of the transition vertebra, and lumbar lordosis is defined as the angle of intersection between the inferior border (not the superior border) of the transition vertebra and the superior border of the sacrum. The reason to use only the inferior border is to let one vertebral body have one inclination angle, which is expressed by the inclination of the inferior vertebral border. According to Cobb's method, one vertebral body has two inclination angles: the superior border and the inferior border. These two inclination angles are almost the same when there is no vertebral deformity, whereas they are far separated when the vertebral body has a wedge deformity. In order to define the tilt of the transition vertebra, one inclination angle seems to be preferable.

Additional benefit of using X-ray measurement is that it visualizes not only the spinal curvature but also the shape of each vertebral body. It is especially useful to assess the patients with osteoporosis, who have a high risk of vertebral fractures. Vertebral fractures may cause a change in the spinal curvature, which may affect the back muscle and cause back muscle fatigue and pain. Also, the vertebral fractures may cause neurological disorders when compressing the spinal cord or spinal nerves.

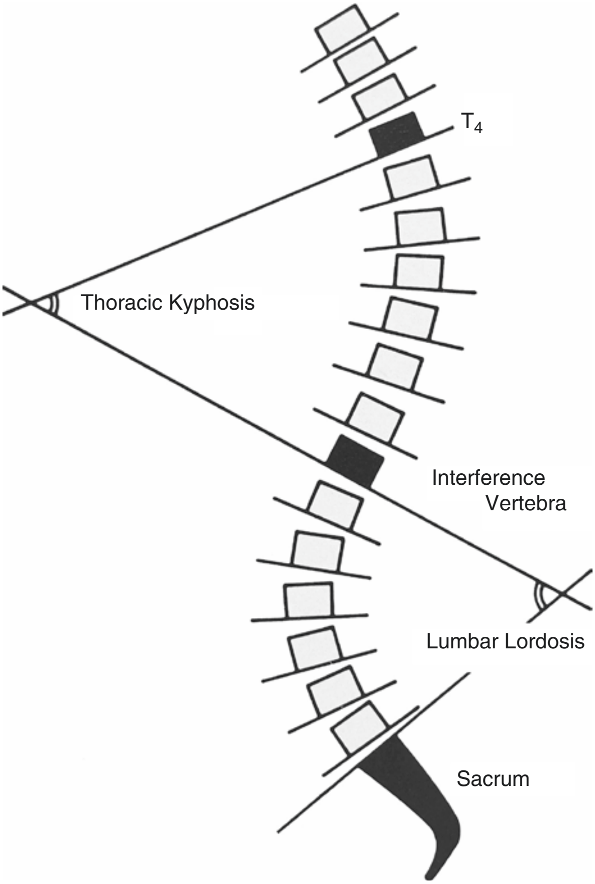

Fig. 3.2 Modified Cobb measurement [5]. One of the co-authors of this manuscript (EI) is the author of this paper in *Spine*. There is no specific method to obtain a permission to use this figure. I (EI) originally drew this figure

SpinalMouse®

SpinalMouse® (Idiag, Volketswil, Switzerland) is a device, composed of a handheld device and a computer (Fig. 3.3). The handheld device has two rollers, with which the examiner moves the device on the skin along the spinous processes. The data are transmitted to the computer and analyzed immediately. With this device, not only the contour of the spinal column or the posture but also the movement of the spinal column can be measured. The greatest advantage of this device is that it transmits real-time recording data into a computer, whereas the X-ray method requires some time to make the X-ray images available for measurements. Of course, there is no risk of X-ray radiation. There are several

Fig. 3.3 SpinalMouse®. Not only the curvature of the spine (**a**) but also the mobility of the spine (**b**, **c**) can be measured with this device. Our original photos

validation studies showing high reliability of this device with intraclass correlation coefficients (ICCs) ranging from 0.67 to 0.99, but validity is reported not to be as high as reliability with correlation coefficient ranging from 0.39 to 0.47 [8].

Because of high reliability, this device has been widely used in the clinical setting. Miyakoshi et al. demonstrated that there was a positive correlation between spinal mobility and the back muscle strength [9]. Prescription of the back strengthening exercise has been shown to improve the QOL, but no significant effect on spinal mobility [10].

Flexicurve

The flexicurve is a flexible ruler, which maintains its shape once it is bent or curved (Fig. 3.4). An examiner gently presses the flexicurve ruler onto the back of a subject, which in turn adopts the thoracic and lumbar curvatures of the subject. The examiner traces the ruler's retained shape onto a sheet of paper, measures the kyphosis height (*E*) and the length of curve (*L*), and calculates the kyphosis index by dividing "*E*" by "*L*" (Fig. 3.5) [13]. The kyphosis angle "θ" can be calculated by measuring the intersection between the perpendicular lines to the line "AB" and the line "AC" [14].

Kyphosis index showed high reliability, even in the novice testers [15]. Especially, thoracic kyphosis showed higher reliability than lumbar lordosis. Kyphosis index and kyphosis height showed high correlation coefficients (0.93, 0.89) between the testers, but kyphosis length showed lower correlation (0.56) [16]. This lower correlation comes from a difficulty of determining the upper and lower ends of the thoracic curve.

Kyphosis angle, another parameter of flexicurve method, showed high inter-rater correlation (0.831–0.942) and intra-rater correlations (0.783–0.829) [11], indicating high reliability. Also, the correlations between the flexicurve angle and the Cobb measurement in thoracic kyphosis (0.72) and lumbar lordosis (0.60) were relatively high. As both the reliability and validity are high, flexicurve kyphosis angle is considered to be a useful tool in the clinical setting.

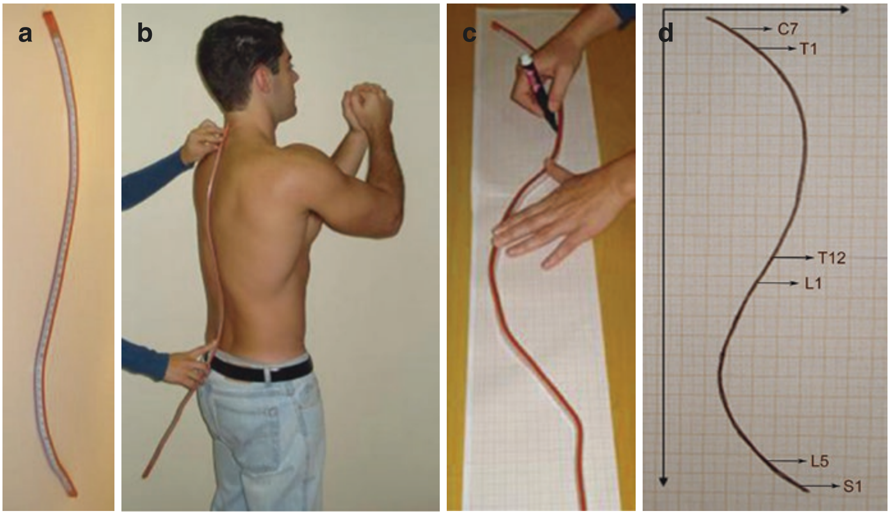

Fig. 3.4 Flexicurve ruler (from de Oliveira et al. 2012) [11]. The flexicurve ruler (**a**) is gently pressed onto the back of a subject (**b**). The ruler adopts the spinal curvature and maintains its shape (**c**), which is then traced onto a sheet of paper for various measurements (**d**). This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited

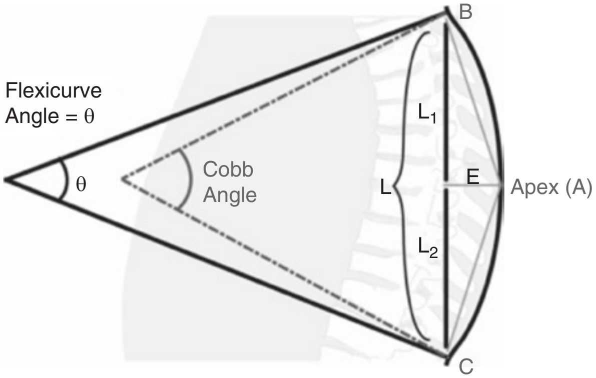

Fig. 3.5 Measurements of flexicurve (from Greendale et al. 2011) [12]. The arc BC is the thoracic flexicurve ruler, where B is the upper end vertebra (T4) and C is the lower end vertebra (T12). Then, the point A, where the distance from the line BC becomes the greatest, defines the apex "A." The height of apex "A" from the line BC is defined as kyphosis height "*E*," and the length of the line BC is defined as the kyphosis length "*L*." The kyphosis index is defined as *E*/*L*. The angle between the two perpendicular lines to the lines AB and AC is defined as kyphosis angle "*θ*". Your order details and publisher terms and conditions are available by clicking the link below: http://s100.copyright.com/CustomerAdmin/PLF.jsp?ref=d7e4d0ba-c5ca-4420-adc7-4776e9c1132f **Order Details** Licensee: Yu Mori License Date: Feb 15, 2015 License Number: 3570560006756 Publication: Osteoporosis International Title: The reliability and validity of three non-radiological measures of thoracic kyphosis and their relations to the standing radiological Cobb angle Type Of Use: Springer-owned imprint Total: 0.00 USD

Comparisons between the flexicurve and other methods have been reported. Greendale and colleagues performed a validation study among flexicurve kyphosis index, kyphosis angle, and Debrunner kyphometer and concluded that all these three methods showed high reliability and validity [12]. Barrett et al. performed a validation study between flexicurve and manual inclinometer, which demonstrated that not only the flexicurve kyphosis index and kyphosis angle but also the manual inclinometer showed high reliability [17]. All these reports support the clinical benefit of the flexicurve as well as Debrunner kyphometer and inclinometer.

Debrunner Kyphometer

The Debrunner kyphometer is a protractor with a 1-degree scale at the end of two double, parallel arms connected to blocks covering the two spinous processes each (Fig. 3.6). This protractor gives the angle of kyphosis when the blocks are placed at the upper and lower limits of the thoracic spine. The upper foot of the upper arm block is placed directly on the C7 spinous process, and the lower foot of the lower arm block is placed on the T12 spinous process, thus the upper block being at C7–T1 level and the lower block at T11–T12 level. Locating these spinous processes needs some skills. The C7 spinous process is the first prominence at the lower part of the neck by palpation. The T12 spinous process can be counted from the T8

Fig. 3.6 Debrunner kyphometer (from Kado et al.; Spine 2006) [18]. The upper block is placed on C7/T1 and the lower block on T11–T12. Your order details and publisher terms and conditions are available by clicking the link below: http://s100.copyright.com/CustomerAdmin/PLF.jsp?ref=3657549f-e548-4d3c-9763-ce372d9e5ab0 **Order Details** Licensee: Yu Mori License Date: Jun 23, 2015 License Number: 3654600617560 Publication: Spine Title: Comparing a Supine Radiologic Versus Standing Clinical Measurement of Kyphosis in Older Women: The Fracture Intervention Trial. Type Of Use: Book/Textbook Total: 0.00 USD

spinous process, which is located at the inferior angle of the scapula, or from the L4 spinous process, which intersects a line drawn between the superior borders of the iliac crests. However, it is difficult to palpate these spinous processes in obese subjects. Therefore, those with advanced training may be able to find the landmarks more easily, whereas it may be more difficult for the novice testers. This device was originally invented to measure the thoracic kyphosis, but it can also be used to measure the lumbar lordosis, or the motion of the thoracic spine and lumbar spine [19]. When measuring the lumbar lordosis, the upper block is placed at T11–T12 level and the lower block at S1–S2 level. Both the reliability and validity of Debrunner kyphometer are reported to be high [7, 18, 19]. The ICC of 0.68 indicates reasonable agreement [18], whereas the kappa values of 0.84 (interobserver agreement) and 0.92 (intraobserver agreement) [18] or the ICC of 0.91–0.94 [19] indicate high reliability. The regression coefficient of 0.76 between the Cobb measurement and kyphometer measurement indicates relatively high validity [7].

From the review of four randomized clinical trials, Purser and colleagues concluded that the Debrunner kyphometer showed high reliability not only in the healthy subjects but also in those with lower activities of daily living such as those with Parkinsonism or nursing home residents [20]. The Debrunner kyphometer is widely used in the clinical setting, such as determining the effect of yoga on kyphosis in senior men and women [14] and comparing the posture and physical activities of older community-dwelling women [21].

Arcometer

This method of curve measurement was proposed by D'Osualdo et al. [22]. The arcometer is a tool consisting of a long bar and three smaller perpendicular bars (Fig. 3.7). The first perpendicular bar is fixed at one end. The second bar, movable on a single axis, is fixed at the other end of the curve. The third bar is movable on both axes, between the other two bars. This third bar is fixed at the apex of the curve. This device provides the length of the chord and the rise of the kyphosis arc. Through a trigonometric formula, the radius of the arc and the angle of the arc are calculated.

Validation studies have demonstrated that the arcometer has high reliability and high validity in measuring the thoracic kyphosis and lumbar lordosis [1, 22]. The ICCs ranging from 0.98 to 0.99 indicate high reliability [1, 22]. The correlation coefficients between the Cobb and arcometer measurements range between

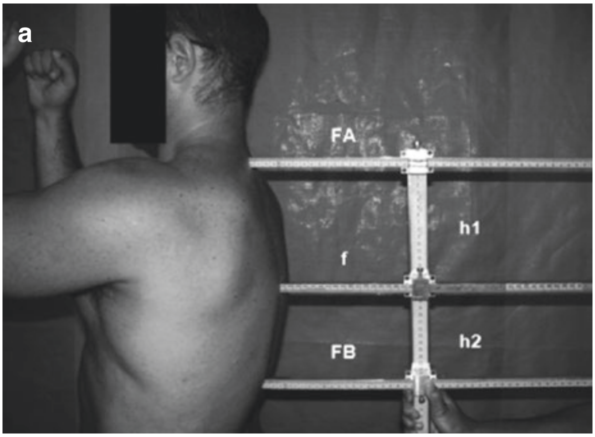
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Fig. 3.7 Arcometer. (**a**) Measurement of thoracic kyphosis. (**b**) Measurement of lumbar lordosis (From Chaise et al. 2011) [1] Creative Commons 4. http://creativecommons.org/licenses/by/4.0/deed.en

[redacted]

Fig. 3.7 (continued)

0.71 and 0.98, with the differences being smaller than 3°, which indicate high validity [1, 22].

Inclinometer

Two gravity-dependent devices called inclinometer are used to show the inclination of the specific portions of the back (Fig. 3.8). There are 2 ft on each inclinometer, and the feet of the first inclinometer are placed over the spinous processes of T1 and T2. The feet of the second inclinometer are placed over the spinous processes of T12 and L1. Thoracic kyphosis is defined as the summation of the angles recorded by these two inclinometers.

This method is reported to provide high reliability. The ICC was 0.95 for the subjects without symptoms and 0.93 for the subjects with symptoms [23]. The ICC for thoracic kyphosis was 0.91 and that for lumbar lordosis was 0.90 in patients with

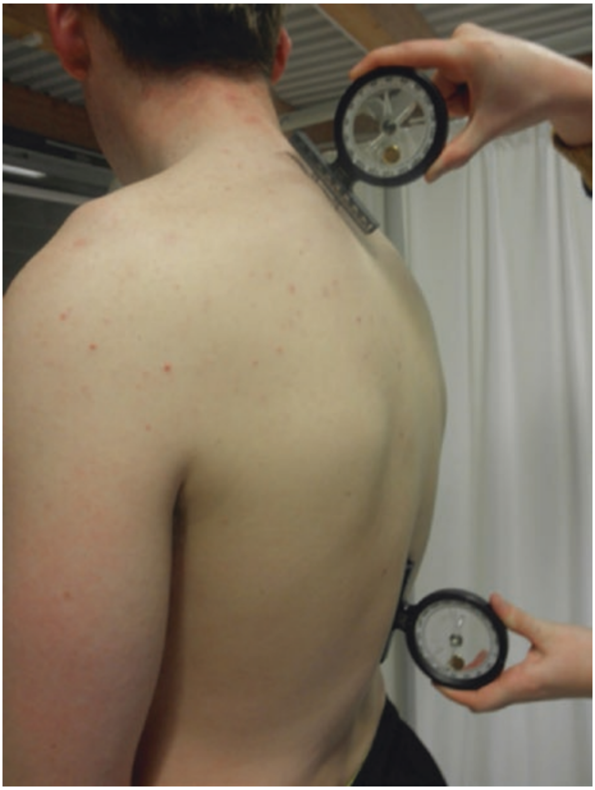

Fig. 3.8 Inclinometer. The feet of the inclinometers are placed over the spinous processes of T1/T2 and T12/L1 (from Barrett et al. 2013) [17]. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited

osteoporosis [24]. However, no validity has been reported in the literature. The validity of this method needs to be confirmed in the future study.

Systematic Review

Barrett et al. [2] performed a systematic review of 15 methods to assess thoracic kyphosis in 27 studies that satisfied the eligibility criteria. They demonstrated that the Debrunner kyphometer (ICC, 0.84–0.98), SpinalMouse® (ICC, 0.73–0.99), and flexicurve kyphosis index (ICC, 0.87–0.96) showed high reliability, whereas flexicurve kyphosis index (correlation coefficient, 0.53–0.91) and arcometer (correlation coefficient, 0.94–0.98) showed high validity [2]. They concluded that further reliability and validity studies were required to strengthen the level of evidence for the remaining methods of measurement. It is likely that these measuring methods would replace the X-ray measurement for mass screening and epidemiological studies, where devices that are handy, cost-effective, noninvasive, and validated are required.

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Parallels Between Skeletal Muscle and Bone Aging

4

Nathan K. LeBrasseur and Jennifer J. Westendorf

Sarcopenia: Age-Related Loss of Skeletal Muscle

Humans achieve peak skeletal muscle mass in midlife and then experience a progressive decline that can equal 50% by the ninth decade [1]. The loss of skeletal muscle mass, strength, and/or function with advancing age is termed *sarcopenia*. Sarcopenia underlies age-related impairments in skeletal muscle performance, physical function, and metabolism in older persons and, thus, poses a major medical and economic threat to society. In 2004, it was estimated that sarcopenia was responsible for over $18.4 billion in annual healthcare costs [2].

At a tissue level, sarcopenia is associated with a reduction in the cross-sectional area (atrophy) and the number of muscle fibers. These age-related changes are paralleled with the accumulation of fat and connective tissue within skeletal muscle. Sarcopenia is presumably multifactorial and influenced by diverse factors, including age-related changes in hormones, sex steroids, motor neurons, blood flow, chronic sterile inflammation, physical inactivity, nutrient intake, and comorbid conditions. As a result, untangling the biology of sarcopenia has proven challenging. A disruption in the balance between protein synthesis (anabolism) and protein

N.K. LeBrasseur, PhD (✉)
Department of Physical Medicine and Rehabilitation, Robert and Arlene Kogod Center on Aging, Mayo Clinic, 200 First Street SW, Rochester, MN 55905, USA

Department of Physiology and Biomedical Engineering, Robert and Arlene Kogod Center on Aging, Mayo Clinic, 200 First Street SW, Rochester, MN 55905, USA
e-mail: lebrasseur.nathan@mayo.edu

J.J. Westendorf, PhD (✉)
Department of Orthopedic Surgery, Mayo Clinic College of Medicine and Science, 200 First Street SW, Rochester, MN 55905, USA

Department of Biochemistry and Molecular Biology, Mayo Clinic College of Medicine and Science, 200 First Street SW, Rochester, MN 55905, USA
e-mail: westendorf.jennifer@mayo.edu

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degradation (catabolism) is often cited, including observations of age-associated anabolic resistance. However, the fundamental molecular mechanisms that cause the age-associated loss of skeletal muscle are not well defined [3–5].

The Age-Related Loss of Bone

Peak bone mass is achieved earlier in life (usually in the third decade) than peak muscle mass and depends on how much bone is accrued before puberty and into the third decade. While all adults lose bone mass during aging, there is a sharp drop in women at the menopause. Early bone loss is termed *osteopenia*, which is defined by bone densitometry measures 1.0–2.5 standard definitions below that of a normal 30-year-old (T score −1 to −2.5). Bone densitometry measures more than 2.5 standard deviations below normal (T scores ≤ -2.5) lead to a diagnosis of *osteoporosis* and are associated with a greater risk of fracture due to falls or normal activities, such as coughing. Two million fractures occur in the United States each year due to osteoporosis (OP) and osteopenia [6]. Up to one in four adults who lived independently before their hip fracture remains in a nursing home for at least a year after their injury [7], and 20% of hip fracture patients die within a year of their injury [8]. Medicare costs for treating osteoporotic fractures in the United States were estimated to be $22 billion in 2008 [9]. Fracture incidences and associated treatment expenses are expected to rise in the coming years as the number of people over 50 years of age with low bone mass or OP grows from 54 million today to an estimated 65 million in 2020 and 71 million in 2030 [6].

Bones are dynamic tissues that are constantly rejuvenated through bone resorption and formation. This ongoing remodeling project allows the skeleton to repair micro and macro fractures and respond to loads. Osteopenia occurs as we age because the rate of bone resorption by osteoclasts begins to exceed the rate of bone formation by osteoblasts. Progressive bone loss is multifactorial and influenced by many of the same diverse factors causing sarcopenia, including age-related changes in hormones, sex steroids, motor neurons, blood flow, physical inactivity, nutrient intake (particularly calcium and vitamin D deficiency), and comorbid conditions and medications. At the tissue level, bone loss is associated with the loss of mineralized collagenous matrix in both cancellous and cortical regions. The processes of bone formation with bone resorption are linked with osteoblasts regulating osteoclast differentiation and osteoclasts influencing the recruitment of osteoblast progenitors to sites of bone damage and repair [10].

Age-related changes in bone density coincide with the accumulation of fat within the bone marrow. Marrow adipose tissue (MAT) accumulates throughout life and is generally linked with poor bone quality [11–13]. Free fatty acids negatively impact hematopoiesis and osteoblast differentiation through lipotoxicity [14, 15]. Disuse increases marrow adiposity, while exercise and mechanical loading promote energy consumption [16–20].

Parallels in Skeletal Muscle and Bone Aging

Multiple studies have demonstrated positive associations between muscle mass and bone mineral density [21, 22] and cortical and trabecular bone geometry and microarchitecture [23]. The relatively lower muscle mass in women has been implicated in their increased prevalence of osteoporosis compared to men [24]. Common mechanical (e.g., decreased physical activity [25]), hormonal (e.g., decreased testosterone, estrogen, insulin-like growth factor-1 [IGF-1] [26–29]), and inflammatory (e.g., increased interleukin-6 and tumor necrosis factor-α [TNFα] [30–32]) stimuli have been implicated in the pathogenesis of sarcopenia and osteopenia. There also appears to be a communication network between muscle and bone. Secreted factors from muscle (called myokines) such as IGF-1 and fibroblast growth factor-2 (FGF-2) signal through receptors localized to periosteum and promote bone formation [33]. How these emerging networks are affected by aging and correlate with muscle and bone quantity and quality has not yet been explored.

Cellular Mechanisms of Skeletal Muscle and Bone Aging

Bone and Muscle Cell Differentiation

In adults, osteoblasts and myocytes originate from multipotent mesenchymal progenitors cells that reside in various places including the bone marrow, bone periosteum, vasculature (pericytes), and skeletal muscle. The progenitor cells residing in skeletal muscle are termed satellite cells and are characterized by expression of the transcription factors, Pax3 and Pax7 (reviewed in [34]) (Fig. 4.1). Satellite cells are quiescent in undamaged skeletal muscle, but are activated to proliferate and differentiate into myocytes in response to mechanical strain or damage. Myogenesis is then regulated by a series of transcription factors, including MyoD and myogenin [34]. Myocytes begin to produce skeletal muscle filament proteins and fibers and become multinucleated as they differentiate.

Osteoblasts arise from an osteo-chondroprogenitor cell that resides in bone marrow and periosteum [35]. The transcription factors, Runx2 and Osterix, are essential for osteoblast specification from the progenitor cells, but many other transcription factors coordinate osteoblast differentiation into type I collagen-producing cells that also regulate the mineralization process (reviewed in [36]) (Fig. 4.1). Terminally differentiated osteoblasts either become quiescent lining cells or osteocytes, which are embedded in the mineralized matrix, so they can respond to mechanical stimulation and structural damage [37]. Osteoblasts and osteocytes also coordinate osteoclast differentiation from hematopoietic progenitors through the production of RANKL and other molecules; inhibitors of this pathway block bone resorption and are therapeutic options for osteoporosis [38].

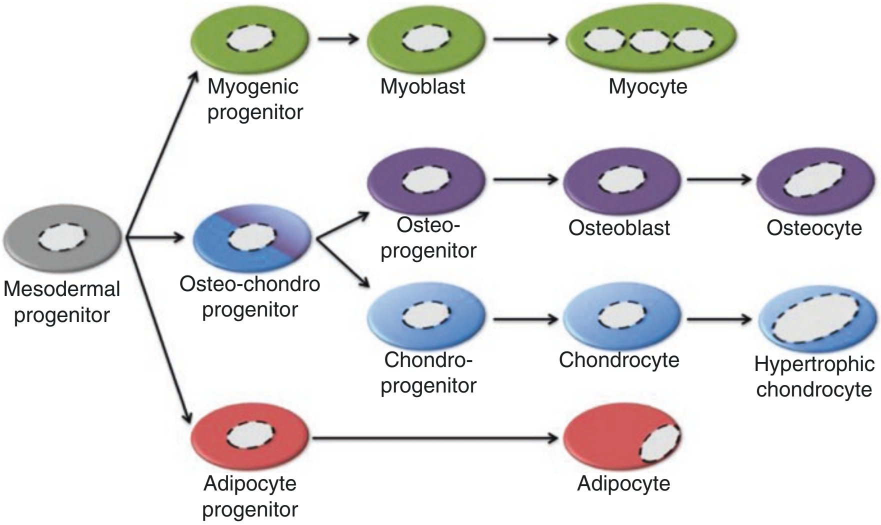

Fig. 4.1 Myocytes and osteoblasts differentiate from common mesenchymal progenitor cells

Cellular Senescence

A major problem during aging is that the functional capabilities of mesenchymal progenitor cells in bones and skeletal muscles decline. Senescence is a state of "stable" growth arrest in response to telomere erosion, DNA lesions, reactive oxygen species (ROS), and other mitogenic and metabolic stressors [39]. Activation of p16^{INK4a}/retinoblastoma protein (Rb) and/or p53/p21 tumor suppressor pathways plays a central role in senescence induction. Together these mechanisms of senescence limit excessive or aberrant growth of malignant cells. Interestingly, several senescence-inducing stressors are implicated in theories of aging (i.e., telomere erosion, DNA damage and mutation, protein aggregation, and ROS). However, instead of preventing the growth of cancers, the accumulation of senescent cells with advancing age negatively affects tissue structure and function and ultimately leads to tissue pathology. Thus, cellular senescence is an example of antagonistic pleiotropy, that is, a biological mechanism that increases odds of survival and reproduction in early life, but may have deleterious effects in later life.

Indeed, biomarkers of senescent cells (i.e., p16^{INK4a} and senescence-associated β-galactosidase (SA-β-gal)) increase in multiple tissues with chronological aging [40, 41]. Senescent cells are metabolically active and secrete a broad repertoire of cytokines and chemokines, matrix remodeling proteases, and growth factors, collectively referred to as the senescence-associated secretory phenotype (SASP) (reviewed in [42]). Though modest in number, senescent cells are presumed to underlie (a) *age-related tissue deterioration* due to their accumulation, loss of regenerative potential [43], and degradation of the extracellular matrix through the SASP; (b) *age-related hyperproliferation*, or the growth and spread of cancers, paradoxically, through components of the SASP including growth factors and matrix remodeling proteases; and (c) *inflammaging*, as cytokines and chemokines are prominent features of the SASP. Recently, it was demonstrated that targeted deletion of p16^{ink4a}-expressing cells improved multiple parameters of physical health and function, at least in a mouse model of accelerated aging [44]. Thus, cellular senescence has emerged as a potential unifying mechanism of aging and age-related diseases [45].

The contributions of cellular senescence to the aging of skeletal muscle and bone have not been thoroughly investigated. In adult skeletal muscle, satellite cells are mitotically quiescent. In response to injury and homeostatic demand, satellite cells are activated and reenter the cell cycle to generate muscle progenitor cells that repair or regenerate mature muscle fibers as well as self-renew to replenish the satellite cell population. Interestingly, the number of satellite cells does not appear to be significantly affected by aging. Instead, evidence suggests age-associated changes in the environment, or niche, which surrounds a satellite cell, compromise its ability to activate, regenerate, and replenish. While the SASP from neighboring fibroblasts, preadipocytes, endothelial cells, or other cell types may contaminate the "soil," recent data suggests that cellular senescence may also directly impact the "seed," or satellite cell. Specifically, in very old mice with sarcopenia and compromised muscle regeneration, p16^{INK4a} expression was significantly increased in satellite cells. However, when p16^{INK4a} was genetically silenced, satellite cell activation, proliferation, and self-renewal were restored [44]. The effects of eliminating senescent cells on bone strength were not assessed in this study, but there is substantial evidence that osteoblasts undergo cellular senescence during aging [46]. Modulators of SASP and cellular senescence hold great promise for increasing the health of bone and skeletal muscles.

Summary

In summary, reductions in skeletal muscle and bone occur with age and are linked to increased falls and fractures. An increased understanding of the underlying cellular mechanisms of aging, particularly cellular senescence and stem/progenitor cell renewal, is needed to stall if not reverse the effects of aging on the musculoskeletal system.

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Role of Nutrition in Musculoskeletal Health

5

Meera Shah

Nutrition plays an important role throughout life in determining bone health. Attainment of peak bone mass, typically in an individual's third decade of life, is influenced by nutrition and other factors during the bone-forming years of childhood and adolescence. In children aged 9–18, the daily recommended intake is 1300 mg of calcium and 600 international units of vitamin D, ideally obtained via a well-balanced diet [1]. In addition to diet; genetics, gender, ethnicity, physical activity, smoking status, illnesses and medications may all affect bone growth [2].

Once peak bone mass is achieved, the focus is then turned towards minimizing bone loss as naturally occurs over time. The roles of specific components of the diet in maintaining bone health are discussed below.

Calcium and Vitamin D

Bone is composed of a collagen matrix on which calcium and phosphate are deposited in the form of hydroxyapatite. Vitamin D enhances intestinal absorption of calcium and phosphate. Low concentrations of vitamin D are associated with impaired calcium absorption, higher parathyroid hormone levels and potentially excessive bone resorption.

The ideal amount of calcium and vitamin D in the diet has been debated, and the recommendations for intake are largely based on age and, in women, menopausal status. In prospective randomized trials, men and postmenopausal women taking calcium and/or vitamin D achieved improvements in bone density scores; however

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M. Shah, MB, ChB
Senior Associate Consultant, Division of Endocrinology, Diabetes, Metabolism, and Nutrition,
Mayo Clinic, Rochester, Minnesota, USA

Assistant Professor of Medicine, Department of Endocrinology, Metabolism and Nutrition,
Mayo Clinic College of Medicine, 200 First St SW, Rochester, Minnesota, USA
e-mail: Shah.Meera@mayo.edu

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Table 5.1 Calcium content of common food items

Food item, serving size	Calcium content (mg)
Milk (skim, 1%, 2% or whole), 1 cup	300
Low-fat yogurt, 6 oz. [≈180 g]	310
Cheese	
American, 1 oz. [≈30 g]	125
Cheddar, 1 oz. [≈30 g]	200
Swiss, 1 oz. [≈30 g]	270
Spinach (cooked), ½ cup	120
Broccoli (cooked), ½ cup	50
Kale (cooked), ½ cup	90
Orange juice (calcium fortified), ½ cup	250
Almonds, 1 oz. [≈30 g]	70
Salmon (canned with bones), 3 oz. [≈90 g]	180
Macaroni and cheese, 1 cup	200

this did not always translate into a reduced risk of fracture [3, 4]. Data from meta-analyses show that supplementation with vitamin D alone does not lead to improvements in bone density, thereby highlighting the importance of adequate calcium along with vitamin D supplementation [5].

Many different doses of calcium and vitamin D have been studied, and the populations at baseline have had variable dietary intake of calcium. In general, the recommendation to aim for a total of between 1000 and 1200 mg of elemental calcium and between 600 and 800 international units of vitamin D (through diet and supplements) comes from the review of data balancing efficacy with the potential risk of nephrolithiasis [1] (Table 5.1).

Calcium-containing foods are generally preferred over calcium supplementation as there is some data that supplementation increases the risk of developing kidney stones [3]. Dairy products, beans, dark leafy vegetables, nuts and tofu are good sources of calcium as are calcium-fortified foods such as orange juice (Table 5.2). These foods also tend to be good sources of vitamin D. Various calcium containing supplements are available with differing amounts of elemental calcium content. In general, supplements should not be taken in doses greater than 500 mg at a time for optimum calcium handling by the body.

Conversely, certain foods may contribute to bone loss by increasing urinary calcium excretion. Intakes of caffeine in amounts >300 mg/day (≈514 mL, or 18 oz. brewed coffee) accelerated bone loss at the spine in elderly postmenopausal women [6]. In observational studies, increased soda consumption of all types (diet, regular, caffeinated or non-caffeinated) was associated with increased risk of hip fracture in postmenopausal women. The mechanism underlying this, however, is unclear although may be related to the phosphoric acid and caffeine content of these drinks [7].

Table 5.2 Recommended dietary allowance of calcium and vitamin D (adapted from the Food and Nutrition Board of the Institute of Medicine, 2004)

Age, years	Calcium (mg/day)	Vitamin D (IU/ day)
1–3	700	600
4–8	1000	600
9–18	1300	600
19–50	1000	600
51–70 (male)	1000	600
51–70 (female)	1200	600
Greater than 70	1200	800
Pregnant and/or nursing women <19	1300	600
Pregnant and/or nursing women 19–50	1000	600

Dietary Protein

The role of protein is controversial, with studies showing both benefit and detriment to bone health, depending on the amount and sources of protein studied.

As protein intake increases, there is a greater loss of urinary calcium; however this effect is not as pronounced with dietary protein (versus intravenous amino acid infusions) and seems to be compensated by increased intestinal absorption of protein [8]. On the other hand, several studies have shown an increase in bone mineral density and reduced fracture rate with protein supplementation [9, 10]. Generally speaking, a diet containing between 1.0 and 1.5 g/kg lean body weight/ day in protein supports normal calcium homeostasis in the absence of other confounders. There is no clinically apparent difference between animal and plant sources of protein in maintaining bone health [10].

Another consideration is the effect of protein consumption on acid-base balance. The preferred sources of protein in a Western diet include meat, eggs and fish, generally considered acid-forming foods. Therefore, bone loss may be attributable, in part, to the mobilization of skeletal salts to balance the endogenous acid generated from acid-forming foods [11]. The detrimental effect of dietary acid on bone is small and can be overcome with the consumption of fruits and vegetables which have an alkalizing effect. Some suggest that the effect on bone seen with higher-protein diets could actually be more reflective of poor fruit and vegetable intake [9].

Alcohol and Bone Health

In a meta-analysis assessing the association of alcohol consumption with bone density and osteoporotic fractures, there was a lower fracture risk in persons consuming between 0.5 and 1.0 drink per day (OR 0.8, CI 0.71–0.91) when compared to abstainers. However, increasing consumption to greater than two drinks daily increased the risk by 40% (CI 1.08–1.79). This analysis was limited by the quality of the studies included, many of which did not account for potential confounders, and therefore it is difficult to ascribe a 'safe' level of alcohol consumption based on the available data [12]. One alcoholic beverage a day is equivalent to 1.5 oz. [≈40 mL] of hard liquor, 12 oz. [≈350 mL] of beer, or 5 oz. [≈140 mL] of wine.

Vitamin K

Vitamin K is a cofactor for the metabolism of osteocalcin, an important component of the bone extracellular matrix [13]. Vitamin K has also been shown to positively affect calcium homeostasis and may work synergistically with vitamin D [14]. Epidemiologically, vitamin K has been shown to be beneficial to bone health with higher vitamin K intake associated with higher bone mineral density and lower risk of fracture [15]. However, data from randomized controlled trials assessing the efficacy of vitamin K supplementation on improving bone density and /or reducing fracture risk has been inconsistent [16]. The safety profile of vitamin K, however, is excellent, and few adverse events were reported with supplementation in patients not on oral anticoagulants [17]. Good sources of dietary vitamin K are green leafy vegetables and dairy products.

Phosphorus, Magnesium, and Strontium

Adequate phosphorus is important for bone health. Phosphorus is found in common foodstuffs (e.g. dairy, vegetables, cereals) and is used as food additive (e.g. ham, processed cheese); hence phosphorus deficiency is relatively rare. Excess phosphorus intake, however, may be deleterious to bone [18].

Strontium ranelate supplementation was approved for the treatment of osteoporosis in Europe. However due to the higher than expected numbers of myocardial infarction and venous thromboembolism, the European Medicines Agency recommended restriction in the use of strontium in 2014 to patients who cannot be treated with other medicines approved for osteoporosis. The highest concentrations of strontium in the diet are found in fish, seafood, nuts and vegetables.

Magnesium is another mineral that influences bone structure and turnover. However, there is no data to support magnesium supplementation to enhance overall bone health. Dietary sources of magnesium include green leafy vegetables, legumes and whole-grain products, nuts, seeds, and fish.

Conclusion

Maintaining well-balanced nutrition throughout all stages of life is a key aspect of good overall bone health.

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Exercise for Prevention of Bone Loss: The Role of Sports Medicine

6

Wolfgang Kemmler and Simon von Stengel

Introduction

Physical activity and especially physical exercise are considered as cornerstones of musculoskeletal health [1, 2]. Indeed, dedicated exercise protocols can affect *all* fracture parameters, i.e. fall risk [3], fall impact [4, 5], and bone strength [6, 7], and should thus be considered as optimum candidates for non-pharmacological fracture prevention. Some evidence for the general anti-fracture efficacy of exercise was provided by dedicated exercise trials [8, 9] and a corresponding meta-analysis [10], but the optimum strategy (if there is any) on how to prevent fractures in elderly subjects is still under discussion. Although some researchers postulate to focus more on falls than on osteoporosis to prevent fractures [11], the most promising and feasible exercise strategy is to select types of exercise that address both factors, falls, and osteoporosis. This approach, however, ought to consider the requirements and determining factors of each individual. That is, the need for fall prevention is higher for elderly subjects with several fall risk factors, while for early postmenopausal women with distinct bone loss, this topic is of lesser relevance [12]. But even with careful adaptation of the exercise program to subjects' changing bone, health, and fitness status, effectivity may still decrease over the time. This could specifically be the case where the limitations of higher age collide with the specification of the exercise program. In the Erlangen Fitness and Osteoporosis Prevention Study (EFOPS), the overall aim was to evaluate the effect of a multipurpose exercise program on clinical low-trauma fractures in postmenopausal women starting to exercise in their early postmenopausal years. In detail, we intended to answer the following research questions:

W. Kemmler, PhD (✉) • S. von Stengel, PhD
Institute of Medical Physics, Friedrich-Alexander University of Erlangen-Nuremberg,
Henkestrasse 91, Erlangen 91052, Germany
e-mail: wolfgang.kemmler@imp.uni-erlangen.de; simon.von.stengel@imp.uni-erlangen.de

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1. Can exercise reduce the risk of osteoporotic fractures in postmenopausal women?
2. Is there an optimal exercise program to increase or maintain bone mineral density?
3. Are there temporary limitations on the effectivity of exercise on bone?
4. Can exercise program that focuses on fracture reduction relevantly affect other risk factors with advancing age?
5. Are high-intensity anti-fracture exercise programs attractive and feasible?

Methods

The EFOPS is a nonrandomized semi-blinded controlled exercise over 16 years so far. The study complied with the Helsinki Declaration of "Ethical Principles for Medical Research Involving Human Subjects" and was approved by the ethics committee of the University of Erlangen (Ethikantrag 905, 4209, 4914 B) and the Federal Bureau of Radiation Protection (S9108–202/97/1). After detailed information all study participants gave written informed consent. EFOPS was registered under www.clinicaltrials.gov (NCT01177761). In this publication we will present the results and experiences after 16 years of exercise meanwhile organized in the setting of a noncommercial health club ("Sportverein"). Special emphasis is placed on the design of the exercise program and its adaptation to the increasing age and correspondingly changing requirements and determining factors of our cohorts.

Participants

Figure 6.1 shows the participant flow of the study. We queried population registers to contact all women from Erlangen and surroundings in the age between 48 and 60 in the form of individual letters describing the study objectives.

Inclusion criteria were a time window of 1–8-year postmenopause and osteopenia at the total hip or lumbar spine as measured by dual X-ray absorptiometry (DXA) using the WHO *T*-score definition (-2.5 SD $<$ *T*-Score ≤ -1.0 SD). Exclusion criteria were diseases and use of medication affecting bone metabolism, known osteoporotic fractures, current or recent athletic activity (defined as participation in sport competitions within two decades before study start), inflammatory diseases, history of cardiovascular disease, and very low physical capacity as defined by ergometry (<75 W).

The participants were free to join the exercise or the control group. On hundred thirty-seven early postmenopausal (1–8 years) women were finally included in the study and 86 women joined the exercise and 51 the control group. Participants of the control group were requested to continue their habitual lifestyle, while participants of the exercise group underwent the training regime described below.

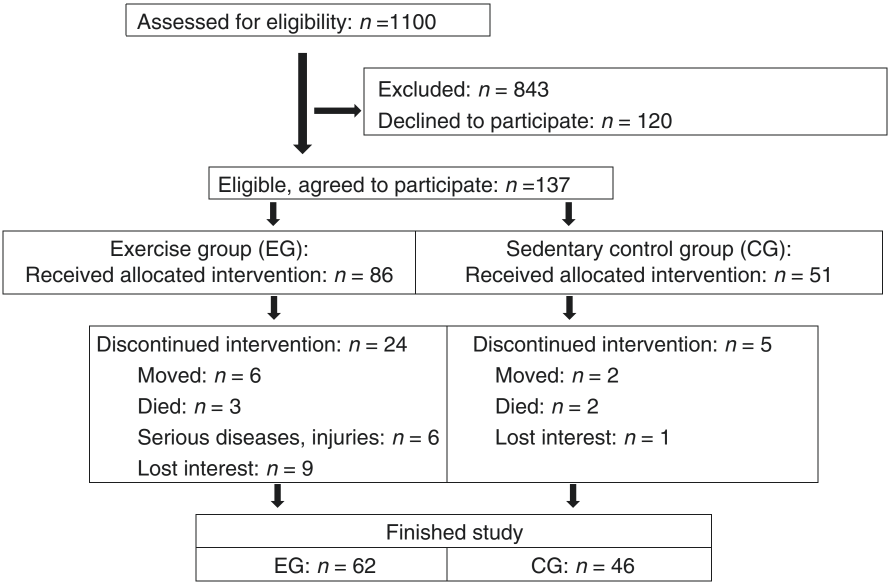

Fig. 6.1 Brief chart of participants flow through the EFOPS exercise trial

Intervention and Changes of the Exercise Program During the Study Course

Certified trainers monthly or (after year 4) bimonthly briefed by the principal investigator supervised all the joint exercise sessions over the 16-year period. Each subject of the EG kept an individual training log that was checked every 12 weeks in order to determine participants' attendance and compliance with the exercise protocol. Apart from study years 4 and 5 (see below), the EFOPS protocol scheduled two joint group classes of 60–65 min on nonconsecutive days and two home training sessions of 20–25 min consistently for 49–50 weeks per year. Exercise intensity was regularly adapted (see below) to subjects' physical performance.

Group Classes

The joint exercise session started with a 20–25-min warm-up/endurance sequence. This sequence focused on running/gaming variations, dancing, and low- and (after 4–5 months of conditioning) high-impact aerobic dance exercises with short intervals (2–3 min) at heart rates (HR) of 80–85% HRmax intermitted by 1–2 min of moderate heart rates (70–80% HRmax). During the high-impact aerobic dance, peak ground reaction forces (peak GRF) of ≈2–3 × body weight were realized. The number of these moderate- to high-impact loads during this session was progressively increased during the first 3–4 study years (up to 150) and decreased (90–110) during the last 3 study years.

While general coordination exercises were consistently applied by traditional dances and aerobic dance during the initial session, the focus slightly shifted from bone to fall-relevant exercises including exercises for dynamic balance. This approach was supported by a dedicated short (3–5 min) sequence that specifically focused on static and dynamic balance exercises introduced after 10 years of exercising.

In order to specifically address bone by high ground reaction forces, a short high-impact sequence (3–5 min) was introduced after a conditioning phase of 6 months. After a 3-month lasting adaption phase of rope skipping, 4 different sets of 15 simple multidirectional jumps/session (e.g., closed leg jumps, lateral one leg jump, jumping jacks) were carried out. Subjects were encouraged to focus on intensive takeoff and soft landing with flexed ankles and knees without heel strikes. Complexity and impact of the prescribed jumping exercises progressively increased up to a peak GRF of ≈4–4.5 × body weight during the first 4 years, while less challenging jumping exercises (peak GRF ≈ 3–3.5 × body weight) with higher demands on balance and coordination (e.g., lateral jumps with predefined rhythm) were introduced during the last 3 study years.

The main part of the exercise program, however, was the resistance sequence that covered 35–40 min of the group session. This training consisted of two different types of resistance training: in one of the two group sessions, exercises were carried out on machines (Techno Gym, Gambettola, Italy), and in the other one isometric exercises, elastic bands, and free weights were used. The following dynamic exercises were performed in the session using resistance machines: horizontal leg press, leg curls, bench press, rowing, leg adduction and abduction, abdominal flexion, back extension, lat pulley, hyperextension, leg extension, shoulder raises, and hip flexion. During the second resistance training session, isometric (12–15 exercises, 2–4 sets, 6–10 s) and elastic band exercises (3 exercises with 2–4 sets and 15–20 reps.) were carried out. In addition, three resistance exercises using free weights (squat/deadlift, one hand dumbbell rowing, and dumbbell chest press) were performed according to the periodized protocol described below.

After 9 months of conditioning, we consistently applied a structured exercise schedule with 12 weeks of linearly or nonlinearly periodized high-intensity resistance training [13] on machines (9–10 exercises, 1–4 sets, 4–12 repetitions with 70–90% one-repetition maximum (1-RM)) and 4–6 weeks of lower intensity (50–55% 1-RM) but higher volume (13 exercises, 2–3 sets, 20–25 repetitions) or correspondingly with free weights. After a dedicated study section during years 4 and 5 [14, 15] that focused on movement velocity (i.e., strain rate [16]) during resistance exercise, applying three-group and one-home training session, movement velocity was also consistently manipulated. Periods of fast (explosive movement during the concentric phase) and slow (up to 4 s during concentric and eccentric phase) velocity were applied, while higher loads (≥1 RM) were always with movement velocities of 2–4 s per movement phase. Exercise intensity prescribed in the participants' individual training logs was either based on regular 1-RM tests (first 5 years; [13]) or the repetition number combined with the rate of perceived exertion (Borg CR-10 scale, [17]) [13]. Of high importance, although the applied exercise program would be denominated as an “HIT” resistance exercise program nowadays, apart from one 12-week period [13], we did not intend subject’s complete exhaustion by the maximum number of repetitions.

Home Sessions

Except for years 4 and 5 (one-home training session/week only), the 20–25-min home training was consistently prescribed twice per week. The session was structured in a short warm-up sequence including rope skipping (3–5 min) and an isometric and dynamic exercise element. During the latter sequence, isometric exercises primarily focused on trunk stability (e.g., crunches, forearm planks), while dynamic exercises using elastic bands or gravity focused on upper back and upper and lower limbs. Stretching (eight muscle groups, 20 s continuous stretching) was conducted at the end of the resistance exercises. All exercises were carefully practiced in the group sessions beforehand. Home training protocols were changed every 3 (up to year 4) to 6 months.

Calcium and Vitamin D Supplementation

Based on dietary protocols (see below), all study participants received calcium (Ca) and vitamin D (Vit-D) in order to ensure an intake of at least 1000 mg/day Ca (first 10 years, 1500 mg/day) and 500 IU/d Vit-D. Due to funding limitations, after 5 years of free supplementation, participants were directed to resources for low-priced Ca and Vit-D supplements.

Measurements

Except for the assessment of clinical overall fractures, the measurements detailed below were performed at baseline and, during the course of the intervention, repeated after years 1, 2, 3, 4, 5, 8, 12, and 16. All assessments were determined in a blinded fashion, i.e., researchers and research assistants were unaware of the status (EG or CG) of the participant.

Anthropometry

Height, weight, and waist circumference was measured using calibrated devices. Body composition was determined by multi-frequent bio-impedance technique (Tanita BF 305, Tokyo, Japan).

Bone Mineral Density

BMD at the lumbar spine (LS) and the femoral neck (FN) was measured by dual energy X-ray absorptiometry (DXA) using standard protocols of the manufacturer (QDR 4500a; Hologic, Bedford, USA). LS scans (L2–L4) and FN scans were independently analyzed by two experienced researchers. Long-term (16-year) coefficient of variation for BMD at the LS was 0.5% as determined by weekly "spine phantom" measurements.

CHD Risk

The 10-year risk index of myocardial infarction or coronary death was calculated using the algorithm suggested by the NCEP ATP III Panel [18] that includes categories of age, total cholesterol, HDL cholesterol, systolic blood pressure, treatment for hypertension, and smoking status.

Questionnaires

Baseline questionnaires determined demographic parameters, pre-study physical activity and exercise levels, and health risk factors with special regard to bone and quality of life parameters. Follow-up questionnaires conducted after 1, 2, 3, 4, 5, 8, 12, and 16 years were specifically designed to detect changes in confounding parameters that may affect the study endpoints (e.g., medication, diseases, lifestyle, physical activity, exercise, dietary pattern, and Ca−/Vit-D supplementation).

Clinical Overall Fractures

All fractures during the last 16 years were retrospectively determined by questionnaires combined with structured interviews after 4, 8, 12, and 16 years. In order to verify the fracture, subjects were asked to provide a medical report. Low-trauma fracture was defined as a fracture occurring spontaneously without high load or falls from a standing height or lower [19]. Among the low-trauma fractures, we further checked for major osteoporotic fractures (i.e., vertebral, humerus, forearm, proximal femur/hip) according to the WHO Fracture Risk Assessment Tool (FRAX®, [20]). Fractures caused by vehicle/bicycle accidents or bicycle falls, falls from a higher level, or other more serious trauma were excluded from the analysis.

Dietary Intake

The consumed food was weighted precisely and reported by the participants. The analysis of the protocols was performed by research assistants using Prodi-4.5/03

Expert software (Nutri-Science, Hausach, Germany). However, due to participants' unwillingness to regularly perform this laborious procedure and the minor annual differences for calcium and vitamin D uptake, we decided to stop assessing dietary intake by this method and started to use a standardized calcium and vitamin D questionnaire [21], initially biyearly and later in 4 yearly intervals. A validation of this questionnaire with results of the 5-day dietary assessment resulted in corresponding differences of 10% for calcium and 15% for vitamin D uptake.

Statistical Analysis

Estimated sample size calculation was based on the number of clinical low-trauma fractures. In order to detect a rate ratio of 0.5 for overall fracture rate ratio [22, 23], about 50 patients/group/12 years were required (5% error probability, 80% statistical power). Fisher's exact test was used to determine differences between EG and CG for the number of subjects with fractures (risk ratio). The total number of fractures (rate ratio) was compared using negative binominal regression. A completer analysis including all subjects with 16-year follow-up data was calculated. However, for research question (3), only subjects with complete BMD values for baseline, years 4, 8, 12, and 16, were considered. According to their distribution, intragroup BMD changes were analyzed by paired *t*-tests or Wilcoxon rank tests. Differences between the groups were consistently determined using Welch *t*-tests. Effect sizes (ES) were calculated using Cohen's *d* [24]. All tests were two sided with a *p*-value of less than 0.05 considered as statistically significant.

Results

Can Exercise Reduce the Risk of Osteoporotic Fractures in Postmenopausal Women?

Only a handful of exercise studies determined fracture risk or rate as a primary or secondary study endpoint (review in [10]). Two of these trials [8, 9] reported significant positive findings. Sinaki et al. [8] detected a significant positive effect for vertebral compression fractures after 2 years of supervised back-strengthening exercises followed by a non-monitored period of 8 years of self-selected physical activity in women aged 58–75 years. Addressing both fall risk and bone strength, Korpelainen et al. [9] reported significant differences between EG and CG concerning "overall fractures" (EG, 6, vs. CG, 16; rate ratio, 0.34; $p = 0.019$) after 30 months of exercise with 160 women, 70–73 years old. Finally, after 12 months of home exercise with subjects 75 years and older, Robertson et al. [25] observed significant effects for "serious injuries resulting from a fall" in favor of the EG (EG, 2, vs. CG, 9 fractures; rate ratio, 0.25; $p = 0.03$). However, the same exercise protocol did not result in significant between-group differences ($p = 0.26$) in somewhat older subjects [26]. However, the limitation of the latter two studies was that their statistical power to address clinical fractures was insufficient; so there is some likelihood that their positive results were promoted by random.

In the present study, however, the high amount of "participant years" (1650) allows us to address clinical fractures, clinical low-trauma fractures, and major osteoporotic fractures according to FRAX® [20]. In summary, risk and rate ratio for all the fracture parameters given above were significantly positive in favor of the exercise group. Most impressive, the number of clinical major osteoporotic fractures decreased by 63% in the EG (rate ratio, 0.37; 95% CI, 0.14–0.88; $p = 0.027$). Comparable data was observed for total clinical low-trauma fractures; 24 fractures occurred in the CG vs. 13 fractures in the EG (rate ratio, 0.42; 95% CI, 0.20–0.86; $p = 0.018$).

We are aware that a comparison with pharmacological studies as a benchmark is not fully feasible given the latter's featured high(er) evidence levels and more dedicated inclusion criteria, but it provides an insight into the dimensions of exercise-induced fracture reduction achieved. Zoledronate, probably the most potent bisphosphonate actually [27], decreases the total clinical fracture rate by 33% [28] which is comparable with the anti-fracture efficacy reported for denosumab (32%) [29] and teriparatide (35%) [30]. However, it would be completely inappropriate to conclude exercise that may be a true alternative to pharmaceutical therapy, since the large proportion of frail elderly, as the classical addressees, are unable or simply unwilling to start and maintain lifelong, frequent, and intense exercise programs [31, 32] comparable to the EFOPS protocol.

Is There an Optimal Exercise Program to Increase or Maintain Bone Mineral Density

In the EFOPS we aimed to transfer approved exercise strategies generated by animal studies [12] and athletic exercise performance to our exercise program. Our exercise strategy was rather pragmatic: since most people are unwilling to spend a lot of time for prevention activities [33], the available time should be used most effectively. In order to optimize training effects under the constraints of a limited exercising volume, we applied modern training strategies [34] developed for athletic performance [35, 36]. One central feature of our exercise protocol was a regular change and adaptation of the training regimen, which required a periodization to structure the macro- as well as the mesocycles [34]. Although this strategy was specifically applied during the resistance sequence, we also periodized the other training sequences by varying the length of the high-impact sequences or the number of jumps per session. However, it is to be emphasized, that despite high exercise intensity, subjects did not exercise until complete exhaustion. Also, during the resistance sequence individual training plans did not call for the maximum possible repetitions for a given workload. We attribute the low injury rate of our study to this "non-exhaustive" strategy as well as to the conditioning period at the start of the study and to the intermediate regeneration phases.

While the effect of exercise types and most strain parameters have been evaluated in the meantime, the optimum design and composition of an exercise program to increase bone strength is still under debate [37, 38]. In this context, one basic question simply is how frequent the exercise sessions should be applied (per week). This decision has a twofold impact on the results of exercise programs: primarily because of its direct impact on the given endpoint of an exercise program and secondarily by affecting feasibility of the program and thus the participant's compliance [39]. Based on the 12-year results of EFOPS, we structured retrospectively two exercise groups according to the overall exercise frequency. Changes of a BMD at lumbar spine and femoral neck (DXA) were compared between the low-frequency exercise group (LFG, 1.5 to <2 sessions/week) and the high-frequency exercise group (HFG, ≥2 to 3.5 sessions/week). The results showed changes of BMD at lumbar spine (HFG, 1.1 ± 4.7%, vs. LFG, −4.1 ± 3.0%; $p = 0.001$) and femoral neck (−4.4 ± 3.9% vs. −6.7 ± 3.5%, $p = 0.045$). Of importance, BMD changes of the LFG did not differ from the data of the non-training control group (LS, −4.4 ± 5.2%; FN, −6.9 ± 5.0%). Although this result might not be generalizable across all exercise types and cohorts, it indicates that an overall exercise frequency of at least two sessions per week may be crucial, even if exercise is applied with high intensity/impact [32].

Another research question that refers to the strain parameter "strain rate" was evaluated during the 4 and 5 study years [14, 15]. In this randomized controlled trial, we evaluated the effect of the movement velocity during the resistance sequence (strength (ST), 4 s (concentric)/4 s (eccentric), vs. power (PT), explosive/4 s). After 2 years of exercise, significant between-group differences were determined for LS-BMD (PT, −0.3%, vs. ST, −2.4%; $p = 0.01$). Also the incidence of pain indicators at the lumbar spine was more favorable in the PT group.

Although final evidence had been generated by another study of our group (TRACE study, [40]), we also addressed the relevance of block periodization in the EFOPS. Shortly, block periodization bases on two main determinants. From a scientific point of view, there is some experimental evidence that regular "unloading periods" (4 weeks within a 12-week exercise program) may be even more effective to increase bone strength than continuously applied loading [41] because of bone desensitization to frequent and high mechanical stimuli. From a pragmatic point of view, these "bone unloading periods" can be used to address other relevant training aims/risk factors of the elderly (i.e., falls, cardiometabolic risk factors) more specifically. Even though we do not directly compare the effects of a block periodized vs. a non-block periodized study group (but block periodized (EG) vs. sedentary control (CG)), the study results for LS-BMD as determined by QCT (total BMD: EG, −0.3 ± 2.1%, vs. CG, −2.1 ± 2.2%; $p = 0.015$; trabecular BMD: −0.7 ± 3.4% vs. −4.7 ± 4.9%; $p = 0.001$) and DXA (−0.1 ± 2.2% vs. −2.0 ± 2.0%, $p = 0.002$) were promising.

In summary, our appraisal on how to increase or maintain bone mineral density most favorably included the following items:

1. General application of multipurpose exercise program with special regard to bone.
2. Application of exercise type with relevant joint and (if applicable) high ground reaction forces.
3. High-intensity (HIT) strategy, however, without work to failure.
4. Implementation of 6 months of conditioning before HIT.
5. Progression of the exercise program with special regard to intensity.
6. Consequent and consistent variation/manipulation of the exercise program with respect to exercise type and parameters (e.g., intensity, movement velocity).
7. Regular rest periods and (if applicable) the implementation of block periodization.
8. Regular tests to monitor changes of short- and long-term aims of the exercise program, use of corresponding feedback to define next trainings, aims, and steps

Are There Temporary Limitations of Effectivity of Exercise on Bone?

Another aspect of our research was whether exercise consistently prevents loss of bone mineral density or whether there are periods of reduced effectiveness. To answer this question, we structured EFOPS in four periods of 4 years. As given, we only included participants with complete BMD data for baseline 4-, 8-, 12-, and 16-year follow-up. Figure 6.2 gives the result of the corresponding comparison for LS and FN.

In summary, after a slight increase of BMD at LS and FN in the EG during the first 2 years [42], we observed a largely linear decrease of BMD during the study course. Finally, we observed an overall decrease of −2.2 ± 3.1% ($p = 0.02$) after 16 years of continuous, supervised exercise with an average training frequency of 2.2 ± 0.4 sessions/week. However, BMD changes were quite homogeneous in the EG with reductions ranging between 0.49 and 0.61%. BMD reductions in the CG

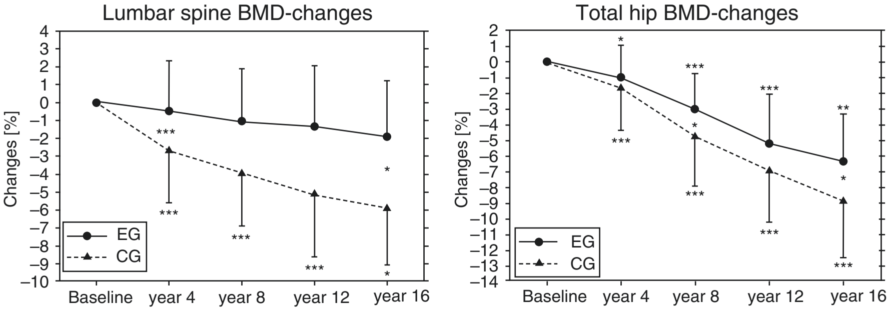

Fig. 6.2 BMD changes at LS and FN during the study course. Asterisks (*$p < 0.05$; $p < 0.001$) indicate either (top of the SD) significant different from the period before or (between the curves) significant group difference (EG vs. CG) for the corresponding period

(6.6 ± 3.1, $p < 0.001$) were most pronounced during the first period with a gradual leveling-off afterward. About half of the total LS-BMD reduction took place during the first 4 years (i.e., during early menopause).

During the first 4 years, reductions of FN-BMD (EG, 0.862 ± 0.077 to 0.810 ± 0.074, vs. CG, 0.853 ± 0.088 to 0.775 ± 0.090 g/cm^2; $p < 0.001$) were less distinct than at the LS, but increased significantly ($p \leq 0.022$) during phase 2 (5–8 years). While the CG demonstrated a constant BMD decrease between 2.4 and 3.1% during periods 2–4, a reduction of BMD loss ($p = 0.051$) during the last 4 years (i.e., phase 4 compared with phase 3) was observed for the EG.

In summary, the BMD gap between EG and CG increased progressively throughout the study course, although we failed to determine significant differences for all isolated 4-year periods (LS-BMD, first and final period only; FN-BMD, second and final period). We are unable to refer these periods of (slightly) reduced effectivity to changes of our exercise program. Even the most pronounced reduction of bone-specific contents realized after year 12 was not related to a decreased effectivity during the final period. In conclusion, our sophisticated exercise program adapted to subjects' priorities demonstrated a highly significant and clinically relevant long-term effect on BMD at lumbar spine and femoral neck. However, compared with the comfortable option of pharmaceutical intervention, more time and effort have to be invested in order to favorably affect BMD through exercise. With respect to the generalizability of our results, this suggests that "exercise" will be still reserved for motivated postmenopausal females.

Which Impact on Cardiometabolic Risk Factors Features an Exercise Program That Focuses on Fracture Reduction in Postmenopausal Women?

Multi-morbidity of the elderly is an increasing problem in the Western world [43]. Besides musculoskeletal problems, metabolic and cardiac diseases largely contribute to the high morbidity of our elderly population [44, 45]. Uniquely "exercise" represents a complex agent that in general affects most, if not all, of the relevant risk factors and diseases of the elderly [1, 46, 47]. However, it is not trivial to design a multipurpose exercise training that favorably affects the most relevant early menopausal risk factors (i.e., bone loss and cardiometabolic diseases) that may fundamentally differ with respect to their sport-scientific addressing. Examining our exercise protocol, the endurance/jumping sequence can be considered as a high-intensity interval training (HIIT) [48], a method with high relevance for cardiometabolic prevention and rehabilitation [49–51]. Further, the high relevance of resistance training for cardiometabolic is also accepted [52]. Both components were regularly and frequently applied in the EFOPS trial; thus a positive effect on relevant cardiometabolic markers should be achieved.

During the first study years, we focused on isolated cardiometabolic risks (e.g., blood lipids, blood pressure, waist circumference) which were consistently positively affected [42, 53]. However, in parallel to the osteoporotic fracture issue, the large number of participant years enabled us to select more meaningful cardiometabolic endpoints. Thus, finally (years 12 and 16, respectively), we addressed the metabolic syndrome according to the International Diabetes Federation (IDF) [54] and the "hard coronary heart disease" risk (i.e., risk of myocardial infarction and coronary death during the next 10 years [18]). The latter parameter significantly deteriorated in both study arms ($p < 0.001$); however, the changes were significantly less unfavorable in the EG, compared with the CG (5.00 ± 2.94% vs. 6.90 ± 3.98%; $p = 0.017$). Ignoring the subjects' increasing age, which is however considered as a core risk factor by the hard CHD risk score, changes were no more significantly negative in the EG, contrarily to the CG. In parallel, metabolic syndrome Z-score [55] that did not include the variables sex and age and may be thus more sensible for "true" changes of cardiometabolic risk did not relevantly change in the EG but significantly deteriorate in the CG (EG, −0.42 ± 1.03%, $p = 0.003$, vs. CG, 1.61 ± 1.88%, $p = 0.001$).

In summary, the EFOPS strategy of a consistently applied high-intensity training program complies with our philosophy of multipurpose exercise programs, able to favorably address the most important risk factors of the menopause and of increasing age.

Are High-Intensity Exercise Programs for Osteoporosis Safe, Attractive, and Feasible?

Finally, we aimed to clarify an important issue with respect to high-intensity exercise training programs. Reviewing the literature, there is some evidence that high-impact [56]/high-intensity training [57] may lead to joint and/or low back pain.

In summary, we cannot verify this estimation; in fact, we determined positive effects on pain frequency and intensity for the lumbar spine and main joints that, however, reached significance only for the LS region [58]. This result is not trivial since LS and joint pain incidence in (early) postmenopausal females is very high. In a study by Raspe et al. [59], 35–40% of German women between the age of 50 and 59 years reported back pain and 45–50% reported joint pain. In our cohort pain incidence was even higher, 60% suffer from back pain (cervical, thoracic, and lumbar spine) and 68% from joint pain (knee, hip, and shoulder). Thus, exercise programs that generate pain reduction are of high relevance for this cohort. Our result that high-intensity exercise training, even with intermitted "power" training (i.e., high movement velocity) phases, did not lead to complication but even improve dedicated pain parameters has been recently confirmed by an exercise trial with subjects with hip arthritis [60]. Thus, our results do not support the statement "what is good for the bones is bad for the joints" [56], at least if certain rules are adhered to. These include: (1) careful incrementing of exercise intensity and impact, (2) avoiding complete exhaustion from maximizing the number of repetitions under a given load, (3) including intermittent "recreational exercise periods," (4) proper variation of intensity and volume within the heavy-load periods, and (5) replacing exercises with very high ground reaction forces by less challenging high-impact movements in the course of advancing age. However, the latter was not applied for intense joint reaction forces reported to be less critical for elderly subjects [61, 62].

The attractiveness of the exercise program is easy to determine since subjects “vote with their feet”; thus, high attendance and low dropout rates indicate a high attractiveness of the program. The overall dropout rate of the EFOPS exercise group (Fig. 6.1) was 28%; however, taken into account that only nine subjects quit the study due to study-related reasons (loss of interest!), compared with other much shorter exercise trials [6, 63], the commitment was very impressive. The attendance rate per se averaged only 57%, but, taking into account that four sessions per week were prescribed by the EFOPS protocol, the average number of sessions effectively conducted per week was 2.15 ± 0.40. In total about two third of the EG participants exercised more than two sessions/week/year. Of importance, the number of group session attended (≈1.6) per week did not change during the 16-year period.

Besides effectiveness and attractiveness, feasibility is a further determinant of successful exercise programs. In general, we consider that the application of high-intensity training is feasible at least if educated trainers lead the sessions. However, even if this might be a specific problem of the complex German rehabilitation exercise practice, the requirement of resistance machines is problematic. Of lesser relevance, the use of resistance machines may increase the organizational and financial expenditure for the exercise groups. More important, the application of resistance machines within the framework of institutional rehabilitation by exercise according to SGB IX (Social Security Code) § 44 is not allowed. Since the vast majority of corresponding groups were largely co-financed by public health funds, the corresponding use of resistance machine is rare. This determinant, however, prevents the broad application of the EFOPS protocol that based on dedicated resistance exercise training on machines, at least in osteoporosis rehabilitation groups in Germany.

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Exercise for Patients with Established Osteoporosis

7

Mehrsheed Sinaki

> *Bone, to be maintained, needs to be mechanically strained—within its biomechanical competence.*
>
> *M. Sinaki [1]*

> *To succeed we need to treat the patient—* ***NOT*** *the disease,* ***NOT*** *the BMD,* ***NOT*** *the musculoskeletal status.*
>
> *M. Sinaki*

Physical activity (PA) is any contraction of striated muscles that consumes energy. PA is beneficial to an individual's overall health and has been reflected in literature for hundreds, if not thousands, of years. Exercise as medicine was promoted by Galen (130–200 C.E.), one of the most prominent ancient physicians. A philosopher and Persian physician, Avicenna (C 980), has also written extensively on *philosophy* and *medicine*, advocating exercise as medicine in his *Book of Healing*.

More than a century ago, in 1892, a German scientist named Julius Wolff described the effect of mechanical loading on bone structure and orientation of trabeculae. In his book, *The Law of Bone Remodeling*, Wolff discussed the theory of the remodeling of the internal architecture of the bone and the development of the law of bone remodeling [2]. Since then, investigators have shown that mechanical

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M. Sinaki, MD, MS
Consultant, Department of Physical Medicine and Rehabilitation, Mayo Clinic, Rochester, Minnesota, USA

Professor of Physical Medicine and Rehabilitation, Mayo Clinic College of Medicine and Science, Rochester, Minnesota, USA

Director of Rehabilitation of Osteoporosis Program, Mayo Clinic, Rochester, Minnesota, USA
e-mail: sinaki.mehrsheed@mayo.edu

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loading regulates bone mass and architecture. Until recently, little had been known about the signals that are involved in mechanical loading in the process of bone formation (see Chapter 2). In this chapter, we are interested in the combination of exercises that address mechanical loading and muscle strengthening without resulting in vertebral compression fracture (VCF). Needless to say, the appendicular muscles also need to be strengthened to improve locomotion, self-care, compliance with activities of daily living, and prevention of falls. In addition to general well-being, safe strength training, and safe stretching, cardiovascular (CV) fitness, axial stability, and coordination need to be considered.

In recent years, medical researchers have been studying the effects of different PAs and exercises on musculoskeletal health. In recent decades, the significance of exercise has been established as an important determinant of muscle strength, bone mineral density (BMD), and CV health. The considerable role of exercise in weight management and reducing the risk of hypertension, type 2 diabetes, and breast and colon cancer has also been emphasized. Additional benefits of exercise (besides musculoskeletal) include mood enhancement and reducing the effects of dementia. It has also been recognized that various types of exercise produce various results. In cases of osteopenia/osteoporosis and fragility, PAs such as swimming, though not osteogenic enough, are important for improving muscle strength and reducing musculoskeletal pain (Figure 7.1) [3]. However, overly strenuous flexion exercises of the spine and weightlifting could result in vertebral compression fracture (Figure 7.2) [4]. With the potential for fracture in mind, for PA to be safe for people with osteopenia/osteoporosis and to have the proper

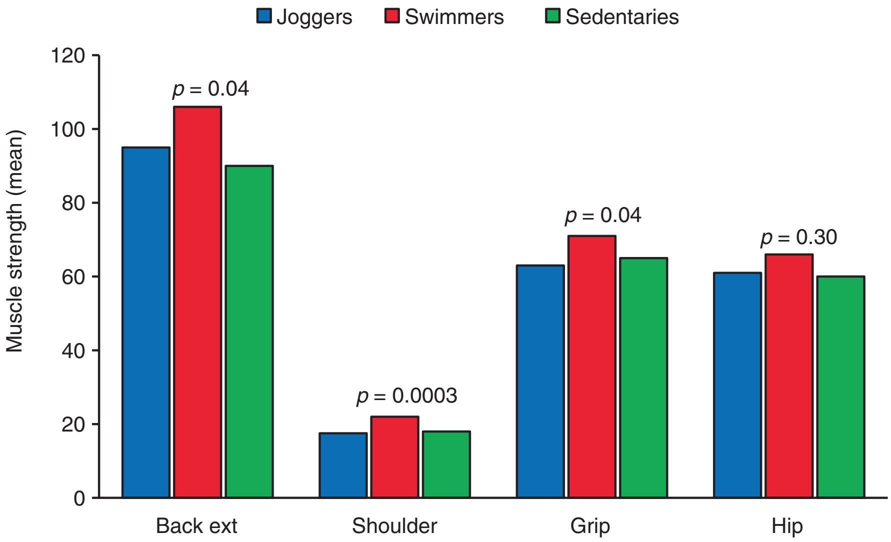

Fig. 7.1 Comparing muscle strength in three groups of female college students (swimmers, joggers, and sedentary). From Emslander HC, Sinaki M, Muhs JM, Chao EY, Wahner HW, Bryant SC, Riggs BL, Eastell R. Mayo Clin Proc. 1998; used with permission.

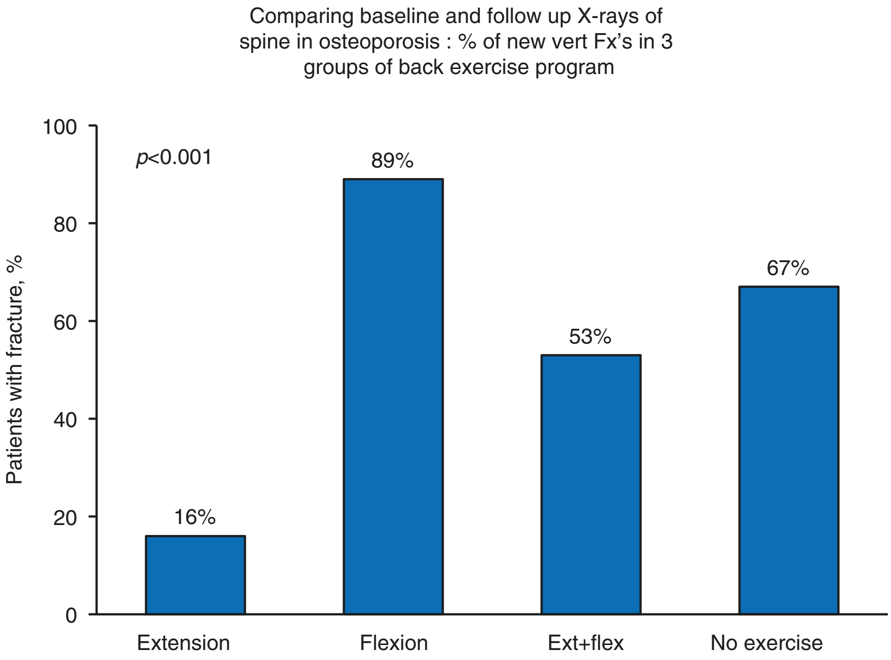

Fig. 7.2 Comparing baseline and follow-up X-rays of the spine in four groups of osteoporotic women after participation in therapeutic back exercises. Percentage of new vertebral fractures in spinal extension; spinal flexion combined with extension; spinal flexion only; and no exercise). *y*-Axis reflects percentage of patients with new vertebral fracture. Figure shows higher percentage of fracture in subjects who performed spinal flexion exercises as therapeutic back exercise program. Data from Sinaki M, Mikkelsen BA: Arch Phys Med Rehabil: 1984.

effect for building muscle and bone, exercise needs to be prescribed, and the feasibility of recreational PA needs to be discussed with patients. This chapter will address the benefits and shortcomings of recreational exercises, as well as recommendations for therapeutic exercise programs for osteopenia/osteoporosis-related musculoskeletal challenges.

Role of Muscles

Skeletal structures are kinematically acted upon by muscles. Therefore, the role of muscles in skeletal health is remarkable. The health and development of musculoskeletal structures begin in childhood. Axial and appendicular muscle strength in boys and girls is about the same until age 10 years, when a discrepancy begins to develop [5]. One study showed that back pain can develop in children who have low back strength [6]. Reduction of muscle strength is affected

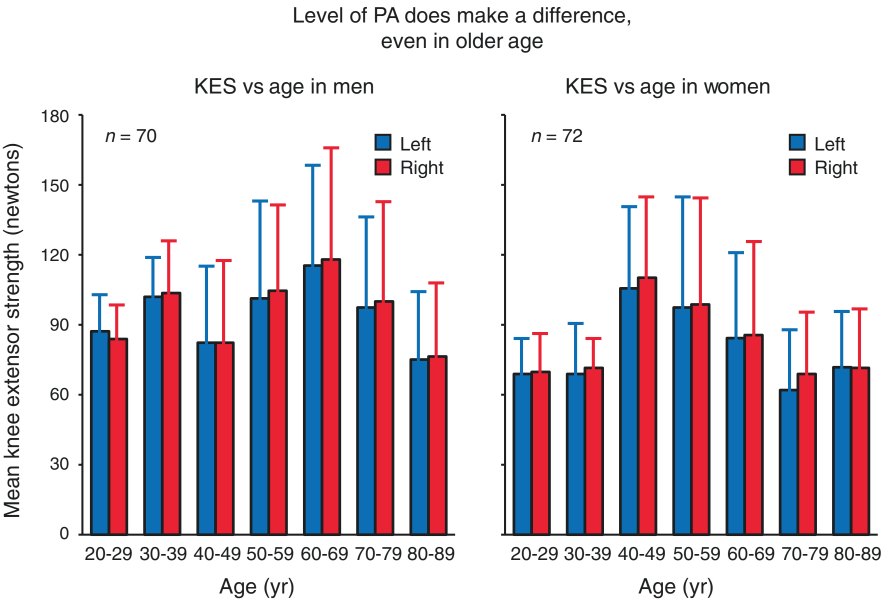

Fig. 7.3 Level of physical activity affects lower extremity strength in men and women after age 50. Data from [8]. Sinaki M, Nwaogwugwu NC, Phillips BE, Mokri MP. Effect of gender, age, and anthropometry on axial and appendicular muscle strength. American Journal of Physical Medicine & Rehabilitation. 2001 May; 80(5):330–8.

by the aging process in men and women. Sarcopenia affects type II fibers ("fast twitch") more than type I fibers. This expands the type I motor neuron units at the expense of type II fibers [7]. The consequences of these changes are less muscle strength and agility and the reduction in endurance for daily activities that comes with age (Figure 7.3) [8].

In the matter of age-related challenges, women are more affected than men since they initially have lower muscle strength than men [8]. In that study, back and upper and lower extremity muscle strengths were measured in healthy men and women aged 20 to 89 years. Comparison of the two sexes showed that women's muscle strength was lower than men's at all ages. Indeed, the back extensor strength of women at different decades ranged from 54% to 76% that of men.

Along with disequilibrium, muscle and bone loss becomes challenging. Axial muscle strength decreases by about 50% from age 30 to 80 in women, and by age 80, women lose about 50% of axial bone mass [9]. The combination makes women more predisposed to osteoporosis and fragility than men. Furthermore, in both sexes, the amount of body sway increases with reduction of proprioception and increased propensity for falls. This results in reduced participation in PA with aging (Figure 7.4) [10]. Kyphosis can increase the risk (and fear) of falls in osteoporotic individuals [11, 12]. It can also decrease vital capacity of the lungs and contribute to back pain due to mechanical strain [13].

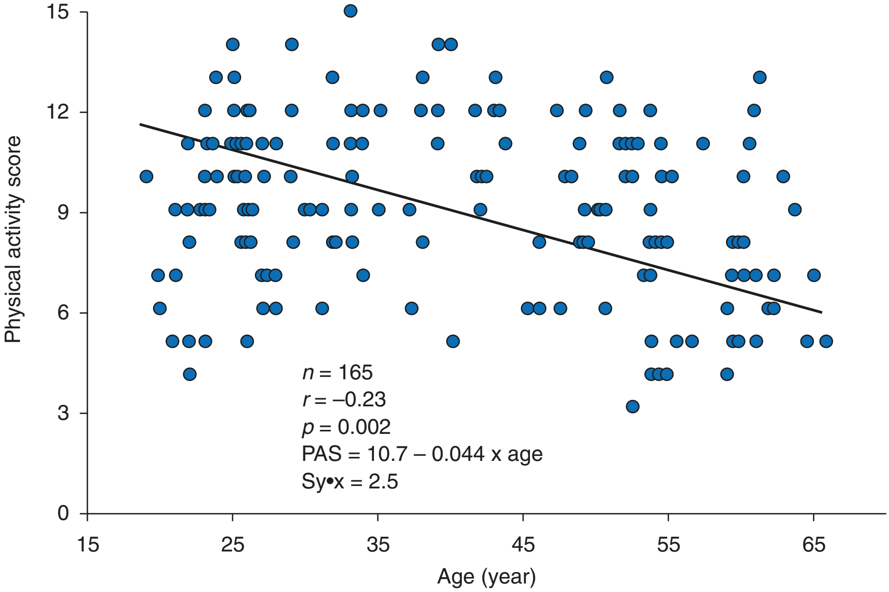

Fig. 7.4 Relationship between physical activity score and age in 165 subjects aged 19 to 66 years [10]. With aging, level of PA decreased significantly. From Sinaki M: Aging Clin Exp Res 10:249–262, 1998; used with permission.

Management of Osteoporosis

Comprehensive successful management of osteoporosis requires a combination of the Rehabilitation of Osteoporosis Program-Exercise (ROPE) and pharmacotherapy as needed. Antiresorptive agents (to reduce bone loss) and anabolic agents (to build bone) have each been more effective for increasing bone mass and decreasing bone fracture when combined with ROPE. The choice of pharmacotherapy depends on the status of the patient's overall health, status of bone cells, BMD, and fragility.

Role of Exercise in the Treatment of Osteoporosis

The objective of using exercise in the treatment of osteoporosis is to improve muscle strength for axial and appendicular stability and to induce proper mechanical strain for maintenance of bone health. Therefore, a strengthening exercise program specifically for back extensors and upper and lower limbs is recommended (Figure 7.5). A back extension exercise program specific to one's musculoskeletal

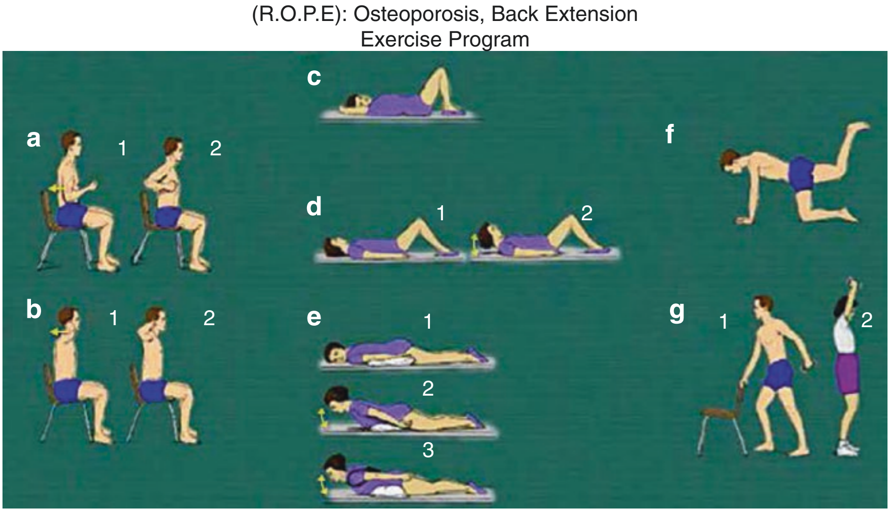

Fig. 7.5 Some back extension exercise choices for Rehabilitation of Osteoporosis Program-Exercise (ROPE). From Sinaki M. Spinal osteoporosis. In: Sinaki M (ed). Basic clinical rehabiliation medicine. Burlington (ON CA): BC Decker. 1987:201–17. Used with permission.

competence and pain status can be performed in a sitting position and later advanced to the prone position (Figure 7.5). When fragility is resolved, back extension is performed against resistance applied to the upper back. To decrease pain and immobility present in acute vertebral fracture, the use of spinal orthoses becomes inevitable. Therapeutic exercise should address osteoporosis-related deformities of axial posture, which can increase risk of falls and fractures.

Strengthening of the major appendicular muscles decreases fragility and improves participation in PA. The effect of strengthening exercises is augmented by proper intake of cholecalciferol and calcium. Thus, the role of a therapeutic exercise program is to increase muscle strength safely, decrease immobility-related complications, and prevent falls and fractures. As with pharmacotherapy, therapeutic exercises need to be prescribed.

Exercise intensity in patients with established osteoporosis is closely based on bone density and muscle strength. Neuromuscular, cardiovascular, and general health also play a substantial role in initiating the program; these health considerations are reviewed to avoid further exercise-induced injury.

There are common definitions of bone density [14]. In general, BMD evaluation and *T*-scores of the spine and hips define the severity of osteoporosis. A *T*-score of −1 to −2.5 indicates osteopenia, and a *T*-score less than −2.5 indicates osteoporosis. If a vertebral fracture is present, osteoporosis is then considered severe. To apply safe mechanical forces to the bone, we need to consider that without mechanical strain, differentiation of osteogenic precursors to osteoprogenitor cells will be suppressed, and the osteoprogenitor cells could change into adipocytes. The adaptability observed between *adipocyte* and *osteoblast* differentiation is necessary for bone formation under mechanical strain [15].

We have observed several patients with weak/deconditioned back muscle strength who suffered vertebral fracture despite a BMD score above −2.5. On the other hand, several patients with strong back muscle strength and BMD below −2.5 did not demonstrate vertebral fracture. Thus, the role of muscle strength in the prevention of vertebral fracture could be of great significance [16].

Tables 7.1, 7.2, and 7.3 were developed to facilitate the consideration of different exercise programs without overstraining when BMD is low and in the presence of fragility. These tables provide some guidelines for planning an exercise program with consideration of BMD, muscle strength, cardiovascular fitness, and neuromuscular health status.

A positive correlation exists between strength of back extensors and BMD of the spine (Figure 7.6) [17]. In a back exercise study, participants' activities of daily

Table 7.1 Suggested rehabilitation guidelines based on bone mineral density (T scores): reduction to −1 SD (normal)[a]

No treatment
Patient education, preventive measures
Lifting techniques
Proper diet (calcium and vitamin D)
Jogging (short distances)
Weight training
Aerobics
Abdominal and back-strengthening exercises
Conditioning of erector spinae muscles

Modified from [1]; used with permission.

[a] T-score: standard deviation below peak normal young adult bone mass

Table 7.2 Suggested rehabilitation guidelines based on bone mineral density reduction of −1 SD to −2.5 SD (osteopenia)[a, b]

Consultation for treatment
Patient education, preventive interventions
Pain management
Back-strengthening exercises
Limit load lifting (≤10–20 lbs)
Aerobic exercises: walking 40 min/day
Strengthening exercises: weight training three times a week
Postural exercises: weighted kypho-orthosis combined with pelvic tilt and back extension
Frenkel exercises, prevention of falls
Tai chi, if desired
Antiresorptive agents, if required

Modified from [1]; used with permission.

[a] *T*-score: standard deviation below peak normal young adult bone mass

[b] Osteopenia or osteoporosis as defined by the World Health Organization [14].

Table 7.3 Suggested rehabilitation guidelines based on bone mineral density reduction of −2.5 SD or more (osteoporosis)[a, b]

Pharmacologic intervention
Pain management
Range of motion, strengthening, coordination
Midday rest, heat or cold, stroking massage, if needed
Back extensor strengthening
Walking 40 min/day, as tolerated; Frenkel exercises
Aquatic exercises once or twice a week
Fall prevention program
Postural exercises: weighted kypho-orthosis program with pelvic tilt and back extension
Prevention of vertebral compression fractures (orthoses, as needed)
Prevention of spinal strain (lifting ≤5–10 lbs)
Evaluation of balance, gait aid
Safety and facilitation of self-care through modification of bathrooms (grab bars) and kitchen (counter adjustment); occupational therapy consultation
Start strengthening program with 1–2 lbs and increase, as tolerated, to 5 lbs in each hand
Spinal proprioceptive extension exercise dynamic program, if needed
Hip protective measures
Prescribe a patient-specific therapeutic exercise program
Start appropriate pharmacologic intervention

Modified from [1]; used with permission.

[a] *T*-score: standard deviation below peak normal young adult bone mass

[b] Osteopenia or osteoporosis as defined by the World Health Organization [14].

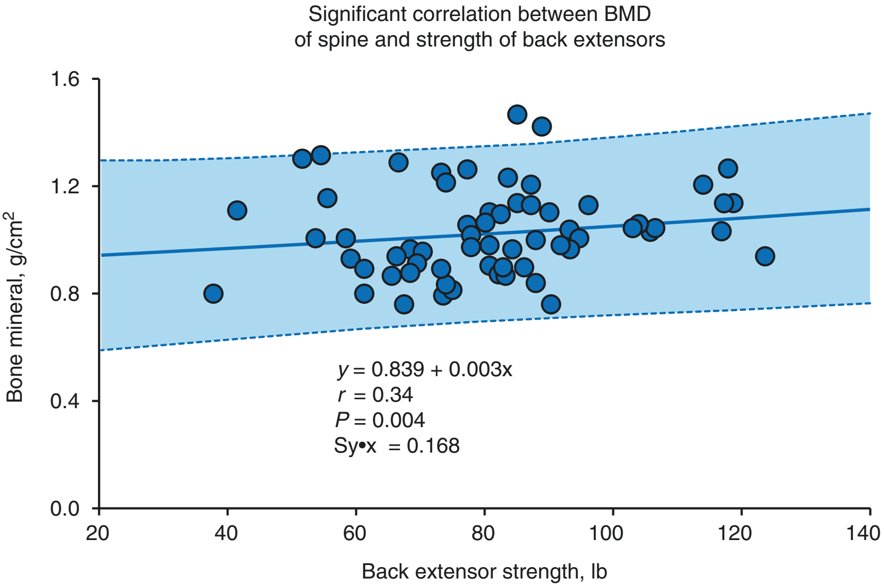

Fig. 7.6 Positive correlation of bone mineral density of the spine with back extensor strength. Data from Sinaki M, McPhee MC, Hodgson SF, Merritt JM, Offord KP. Mayo Clin Proc. 1986

living, posture, and body shape improved with exercise [18]. A study from the author and coinvestigators shows that several factors, including age, grip strength, and kyphosis, affect the level of PA and quality of life in patients with postmenopausal osteoporosis [19]. Statistical analysis has shown that back extensor strength, which is mainly provided by lumbar extensors, and lumbar spinal mobility are the most important factors for improving quality of life [19].

Loading of the spine through lifting weight in the upper extremities needs to be done with proper technique, as shown in Figure 7.5 [20]. Back extension exercises from a prone position with weight applied to the upper back improves back strength considerably, and the effect has been shown to last for years [16]. In addition, if performed properly, the exercise itself does not cause back pain [21]. Back extensor strengthening exercise can decrease the risk of vertebral fracture after vertebroplasty (Figure 7.7) [22]. Improvement of axial muscle support improves posture and helps reduce the risk of vertebral fracture as well as falls. The major supportive muscles are extensors (more than flexors); the ratio of strength is about 2/1.5:1 [23]. Spinal extension exercises should be used along with exercises to reduce lumbar lordosis [24, 25]. One study showed that progressive resistive back-strengthening exercises can improve back strength considerably. A recent randomized controlled trial showed the most effective, safe back-strengthening exercise to be the method of Sinaki et al [26]. However, according to several other studies, the most effective back-strengthening exercise continues to be progressive resistive back extension

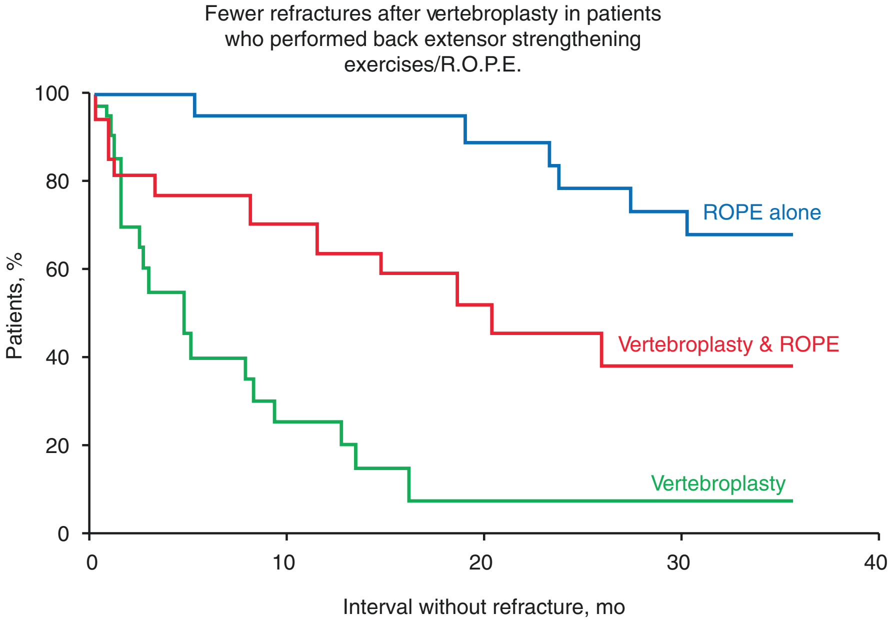

Fig. 7.7 Comparing the follow up in vertebroplasty group vs. vertebroplasty and ROPE vs. ROPE alone. Data from Huntoon EA, Schmidt CK, Sinaki M: Significantly fewer refractures after vertebroplasty in patients who engage in back-extensor-strengthening exercises, *Mayo Clin Proc* 83:54–57, 2008.

exercises [27–29]. Weakness of the abdominal muscles is fairly common, and in cases of osteopenia or osteoporosis, this can be addressed with modified isometric strengthening such as partial lift of the trunk rather than strenuous flexion of the spine (Figure 7.5). Strenuous spinal flexion during daily activities and spinal flexion exercises need to be avoided in patients with osteoporosis (Figure 7.2) [4]. In that study, which compared the effect of flexion and extension exercises on the spine, it was demonstrated that even without pharmacotherapy, patients with osteoporosis who performed back extension exercises had a considerably lower rate of fracture than those who performed spinal flexion exercises or no exercise. This issue again became a concern when several patients who were in good health, but had osteopenia, suffered vertebral compression fracture when they participated in yoga spinal flexion position exercises (Figure 7.8) [30].

Fig. 7.8 Common yoga positions. The various positions can cause extreme spinal flexion (**b**, **d**, **e**), extreme cervicothoracic strain (**b**, **e**), kinetic thoracic and shoulder strain (**a**, **g**, **h**), and kinetic low back strain (**h**). Panels **(c)** and **(f)** are safe if done properly. Sinaki M. Yoga spinal flexion positions and vertebral compression fracture in osteopenia or osteoporosis of spine: case series. Pain Pract 2013;13(1):68–75. (**i**) Yoga spinal flexion positions and vertebral compression fracture. Panel i from Sinaki, M.: Yoga spinal flexion positions and vertebral compression fracture in osteopenia or osteoporosis of spine: case series. Journal of Pain Practice 2013;13(1):68–75. Acute back pain after yoga flexion position exercises. Spinal radiographs showed a vertebral compression fracture (VCF) at L2, post vertebroplasty cement in place without aberrant cement in canal or evidence of impingement). Please see reference [30] for clarification.

Fig. 7.8 (continued)

i Yoga spinal flexion positions and vertebral compression fracture in osteopenia or osteoporosis of spine: case series

- Ant wedging
- Fx
- Neck pain
- Back pain

New Hypothesis: The Most Effective Exercise to Reduce the Risk for Vertebral Fracture

While we intend to improve back extensor strength in osteoporosis through mechanical loading, we also need to prevent further vertebral compression fracture in the course of performing the prescribed exercise. After a 10-year follow-up study, the author developed the following hypothesis: “Back progressive resistive exercises performed in a prone position (nonloading) rather than in a vertical loading position can decrease risk of vertebral compression fractures through improvement of horizontal trabeculae” (Figure 7.9a) [16, 31]. An effective progressive resistive exercise (PRE) program can decrease the risk of vertebral fractures in healthy osteopenic individuals, particularly women. We have sought and measured the efficacy of PRE on paravertebral muscles from prone position, designed for increasing back strength without inducing back pain or vertical loading compression fracture. Women who performed PRE increased their back extensor strength more than controls who performed other exercises excluding PRE (Figure 7.9b, c) [26, 32]. This exercise regimen is recommended to improve posture and decrease the risk of further vertebral fractures. Of course, the exercise is prescribed and needs to be modified according to BMD and status of an individual’s musculoskeletal health. The bone-safe resistive exercise is a part of ROPE. Compliance with this program has been effective in reducing kyphosis and preventing vertebral fractures. When pharmacotherapy becomes necessary in the comprehensive management of osteoporosis, the treatment is more effective for reduction of vertebral fractures if combined with ROPE (Figure 7.10) [33].

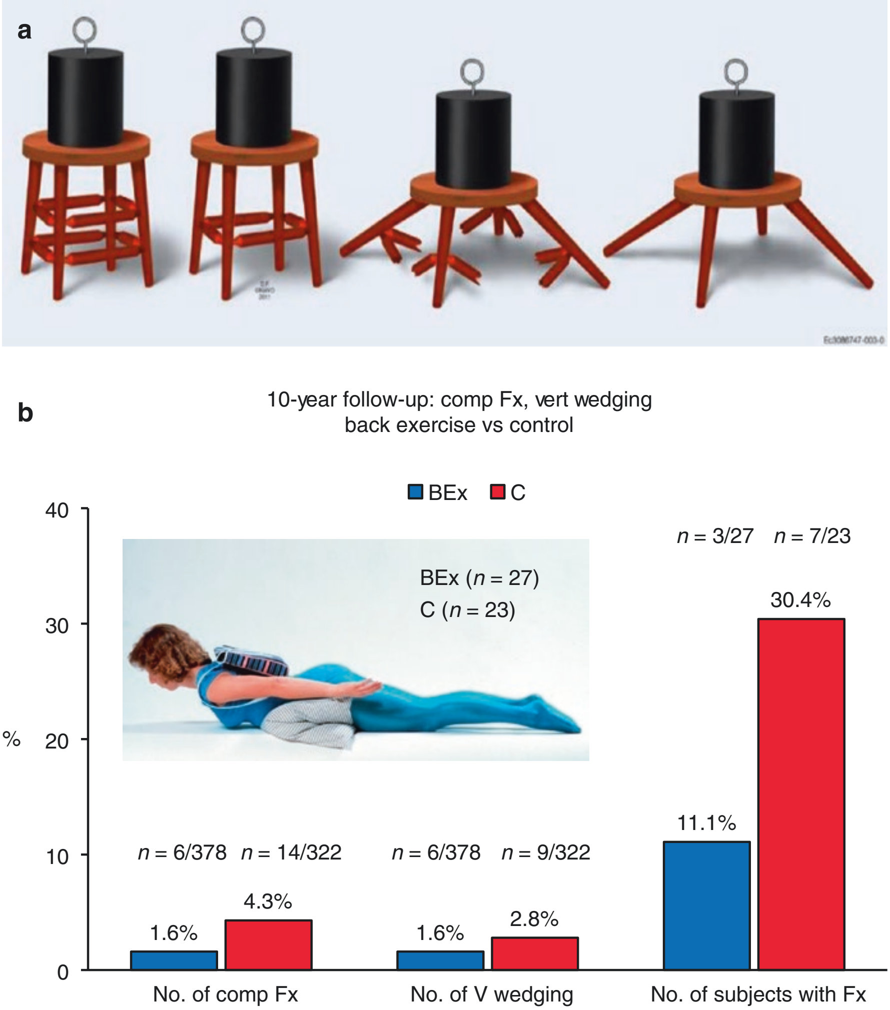

Fig. 7.9 (**a**) Schematic demonstration of contribution of horizontal trabeculae to bone strength and decreasing risk of vertebral fracture under vertical compression on the spine. (**b**) At 10-year follow-up, the number of vertebral compression fracture (comp fx) was 14 in 322 vertebral bodies examined (4.3%) in controls (C) and 6 fractures in 378 vertebral bodies examined (1.6%) in the back exercise (BEx) group ($p = 0.0290$). The number of controls with vertebral fractures was three times greater than BEx group. Model demonstrating the BEx with a backpack containing weights as used in this study [24]. From Sinaki M, Itoi E, Wahner H, Wollan P, Gelzcer R, Mullan B, Collins D, Hodgson S. Stronger back muscles reduce the incidence of vertebral fracture: A prospective 10-year follow-up of postmenopausal women. Bone 30(6):836–841, June 2002. (**c**) Rate of change in BES (pounds per year) in women 50 and over who performed progressive resistive back exercise vs. controls who performed other exercises [17]. From Sinaki M, Wahner HW, Offord KP, Hodgson SF: Efficacy of Nonloading Exercises in Prevention of Vertebral Bone Loss in Postmenopausal Women: A Controlled Trial. MC Proc. 64(7):762–769, July, 1989

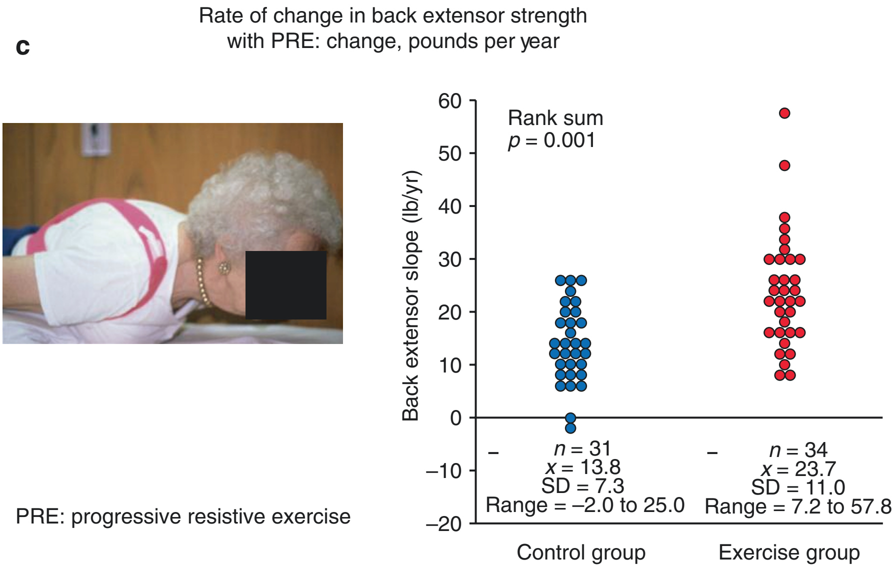

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Fig. 7.9 (continued)

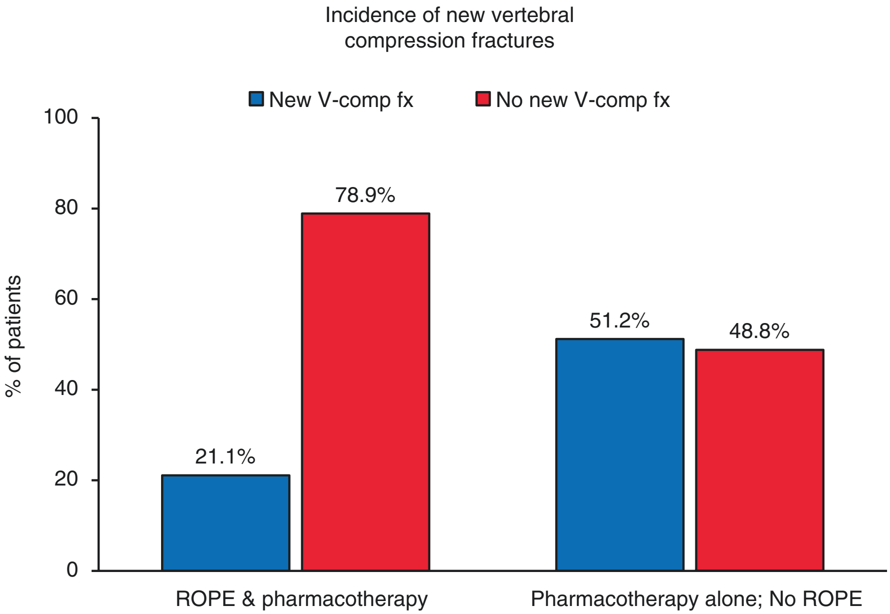


Fig. 7.10 Comparing women with osteoporosis who performed ROPE and pharmacotherapy versus those who used only pharmacotherapy. From Figueroa DAK, Sinaki M. Significant reduction of vertebral fractures: Comparison of rehabilitation of osteoporosis program-exercise (ROPE) versus No-ROPE, with or without pharmacotherapy. J Bone Miner Res. 2007 Sep; 22(Suppl 1):S462. Used with permission.

Risk of Falls in Osteoporosis and Exercise Program for Prevention

Sarcopenia and osteoporotic fractures create musculoskeletal challenges that cannot be managed with pharmacotherapy alone. Improvement of balance along with bone-enhancing exercise programs and pharmacotherapy (when indicated) can improve the level of an individual's PA and mobility. Postural deformities have been shown to impair quality of life of osteoporotic individuals. Kyphotic posture has been demonstrated to contribute to propensity to falls in osteoporotic individuals. Proprioceptive balance training combined with strengthening exercises for back extensors and the lower extremities can reduce falls and prevent fractures.

Falls are not uncommon. More than one-third of persons aged 65 years or older fall each year. One out of ten falls results in hip fracture, subdural hematoma, head injury, or other injuries. In general, there is no fracture without falls, except in special cases of spontaneous iatrogenic or secondary pathologic fractures. Avoidance of falls is still the best prevention. We need to ask all of our older patients, particularly those aged 70 and older, about gait difficulties, falls, and balance disorder. The patient should be observed during the "get up and go" test (i.e., getting out of a chair and walking). Since falls are usually multifactorial, evaluation for fall prevention needs to include quick, clinical evaluation of patient's cognition through a mini-mental test as well as assessment of muscle strength and neuromuscular and cardiovascular health. Risk of falls consists of extrinsic and intrinsic factors (Tables 7.4, 7.5, and 7.6).

Table 7.4 Extrinsic factors

Inappropriate footwear
Insufficient ambulatory aids
Environmental (i.e., poor illumination, unevensurface, loose carpeting, slippery floor, etc.)
Pets

From [39]

Table 7.5 Intrinsic factors

Visual impairment
Vestibular changes
Impaired proprioception
Cognitive decline/CNS degeneration
Postural changes, imbalance, gait unsteadiness
↓ coordination, ↓ agility
↓ muscle strength (48% risk)
↓ joint flexibility
Orthopnea → postural hypotension → cardiovascular deconditioning
Iatrogenically reduced alertness: ↓ antidepressants, use alternatives if possible, ↓ use of allergy and sleep medications

Age-related musculoskeletal and neuromuscular changes play a significant role in the development of malposture. Therefore, other interventions are needed to address musculoskeletal challenges of bone loss. From [39]

Table 7.6 Reducing the incidence for falls

Identify high-risk activities
Reduce antidepressants; use alternatives, if possible
Decrease dose of diuretics
Avoid hyponatremia
Avoid over-the-counter sleep and allergy medications
Manage postural hypotension
Manage gait and balance disorders
Improve muscle strength; increase level of physical activity
Improve coordination
Use gait aids, if necessary
Improve back strength; prevent hyperkyphosis
Use hip protectors, when necessary
Emphasize proper intake of vitamin D and calcium
Increase bone mass

From [34]

Spinal Proprioceptive Extension Exercise Dynamic (SPEED)

Hyperkyphosis can increase risk of falls [11]. Another exercise program developed by the author that has been helpful is SPEED (Spinal Proprioceptive Extension Exercise Dynamic) program [35]. The efficacy of the SPEED program has been evaluated through gait laboratory tests and computerized dynamic posturography. In this study, the evaluations were carried out at baseline and follow-up. Through implementation of the SPEED program in cases of osteoporosis, balance disorder, and kyphosis, we can decrease kyphosis and back pain and increase the level of PA. Reduction of body sway and reduction of use of hip strategy and fear of falls would increase velocity of gait [11]. The SPEED program consists of mechanical intervention to stimulate proprioception of the vertebral facet joints for improvement of static/dynamic vertebral alignment to reduce kyphosis and risk of falls. A weighted pouch is applied below the T10 vertebra to induce an individual's perception of upright posture for proper recruitment of back extensors to decrease kyphosis (Figure 7.11a). A study of patients' gait in the Gait Evaluation Laboratory (Figure 7.11b) showed improvement of velocity. The fear of falls decreased as well (Figure 7.11c). Their balance was evaluated through the use of a computerized dynamic posturography machine and showed significant improvement (Figure 7.11d, e). This weighted kypho-orthosis (WKO) increases a patient's perception of induction of physiologic/normal vertebral facet joints and orientation to one another, which plays an important role in dynamic and static healthy upright posture. The weighted support contributes to the mechanical reduction of kyphosis and provision of proper spine alignment for better recruitment of paraspinal muscle contraction. This daily home-based program consists of application of a WKO while performing ten repetitions of back extension exercises in a sitting (unsupported) position. Each back contraction needs to last 5 seconds, followed by 5 seconds of relaxation. This procedure reduces kyphosis without increasing lumbar lordosis. Individuals also need to perform specific proprioceptive exercises for the lower extremities for 10 minutes

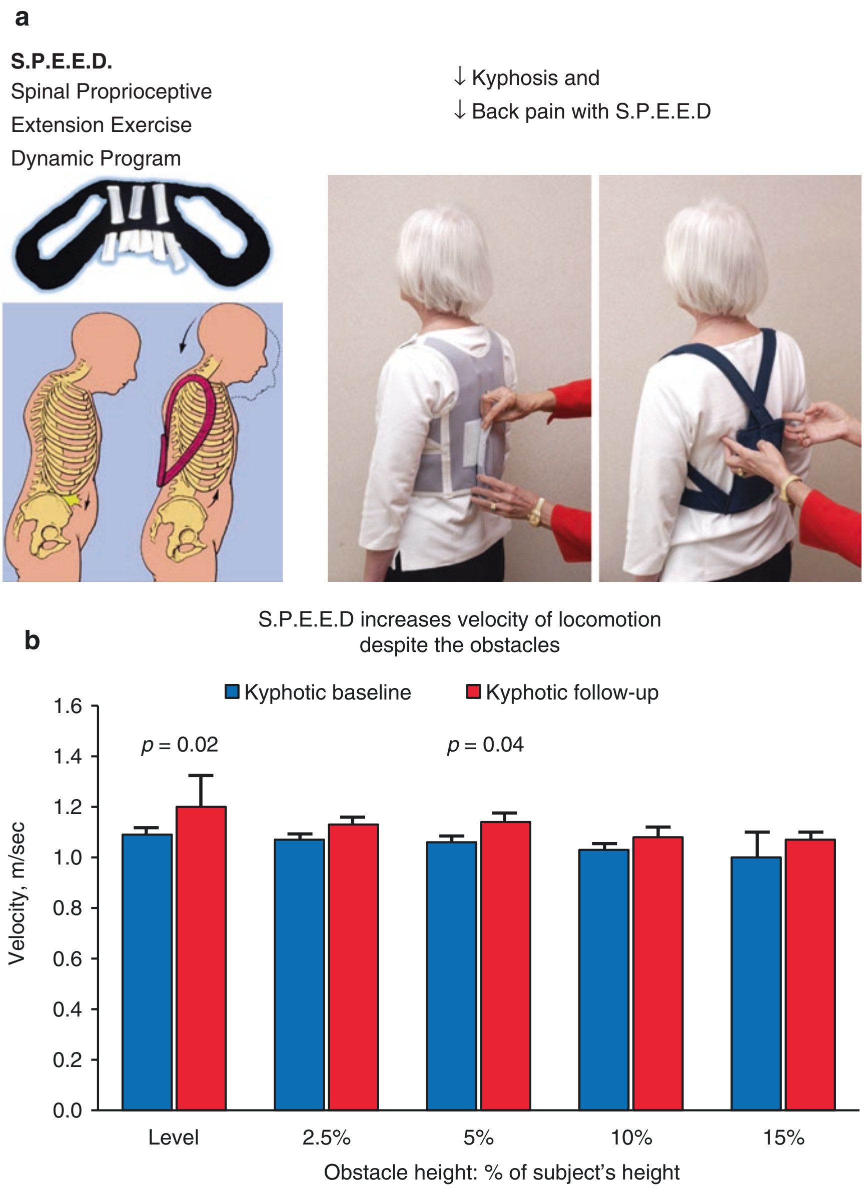
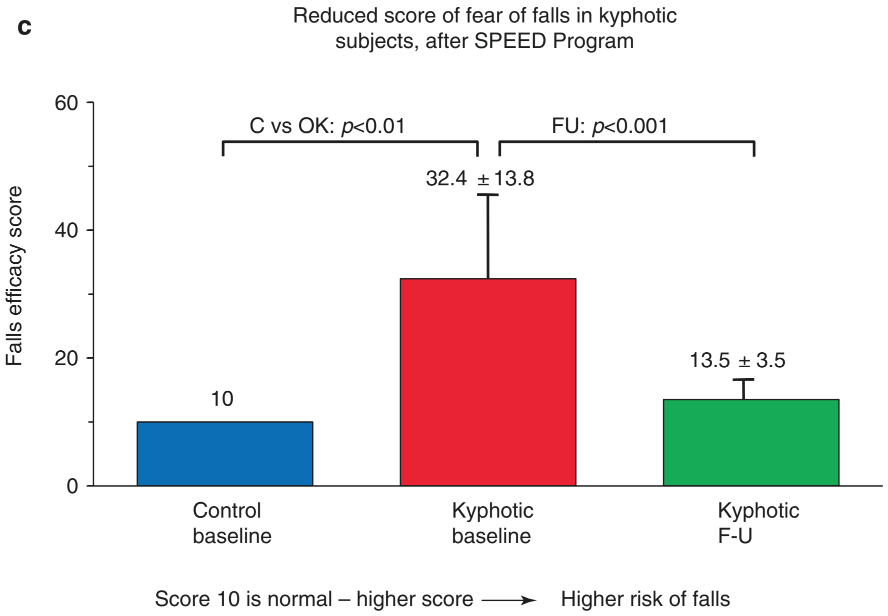
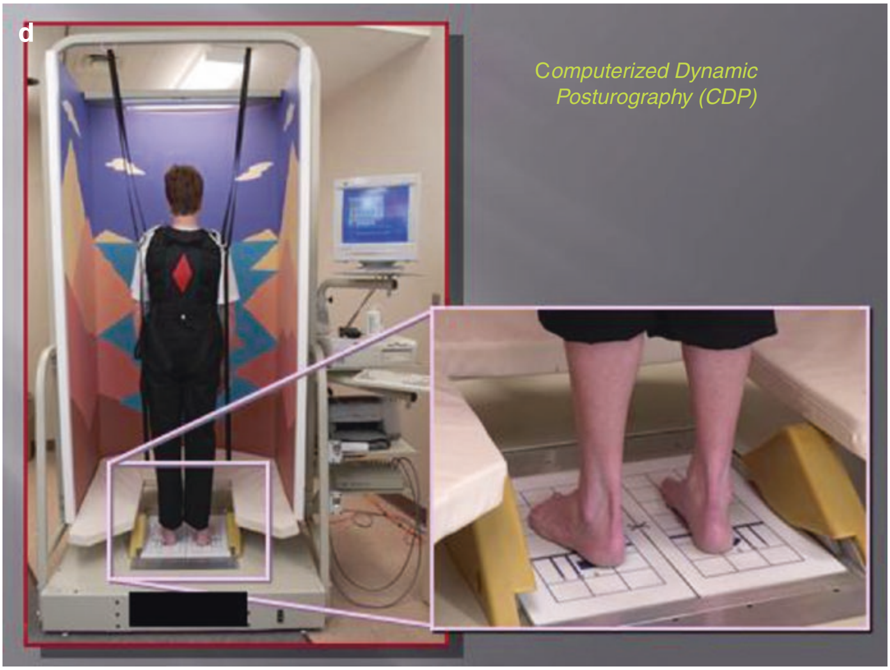


Fig. 7.11 (**a**) Weighted kypho-orthosis applied in SPEED program. (**b**) Velocity improved with SPEED despite increase in obstacle heights. Panel b from Sinaki M, Brey RH, Hughes CA, Larson DR, Kaufman KR. Balance disorder and increased risk of falls in osteoporosis and kyphosis: significance of kyphotic posture and muscle strength. Osteoporos Int. 2005;16(8):1004–10. (**c**) Change in fear of falls. Panel c from Sinaki M, Brey R, Hughes C, Larson D, Kaufman K. Significant reduction in risk of falls and back pain in osteoporotic kyphotic women through a spinal proprioceptive extension exercise dynamic (SPEED) program. Mayo Clinic Proc. 2005 July;80(7):849–855. (**d**) CDP machine. (**e**) Equilibrium score (CDP) change with SPEED Panel e from Sinaki M, Brey R, Hughes C, Larson D, Kaufman K. Significant reduction in risk of falls and back pain in osteoporotic kyphotic women through a spinal proprioceptive extension exercise dynamic (SPEED) program. Mayo Clinic Proc. 2005 July;80(7):849–855.





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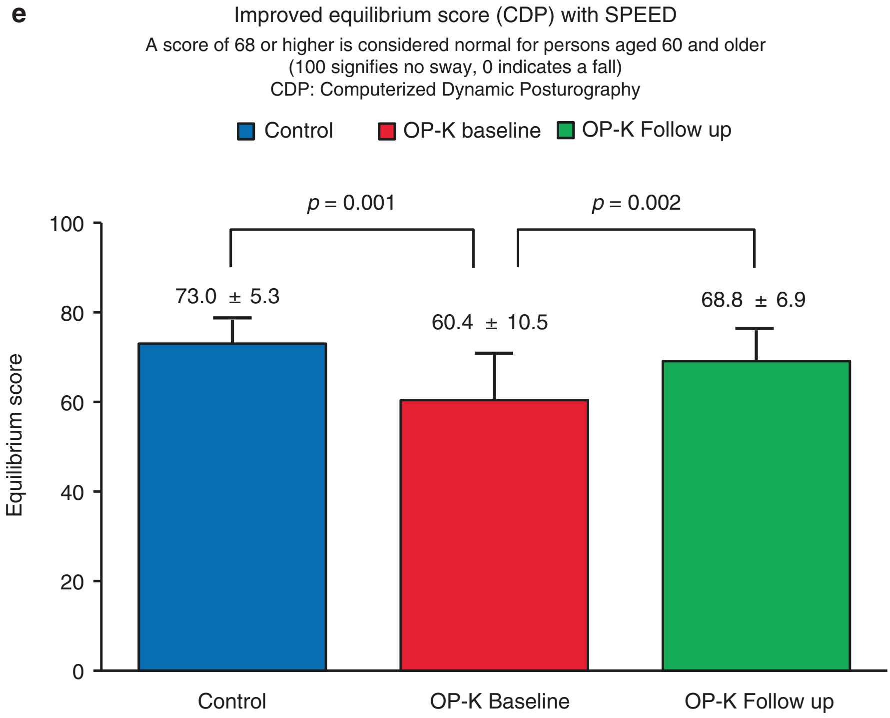

Fig. 7.11 (continued)

twice daily to improve balance. This combination has shown to decrease risk of falls. The WKO consists of a fitted harness with 1 kg of weight or more as tolerated and required according to the patient's stature and physique (body build) to decrease kyphosis. The pouch is suspended between T10 and L4 vertebrae of the spine. Individuals are instructed to wear the WKO daily for 20–30 minutes in the morning and 20–30 minutes in the afternoon while performing the postural exercises. The frequency but not the duration of application of WKO could be increased. To improve patient compliance, their height and/or degree of kyphosis could be measured at baseline and on a monthly basis for provision of feedback to the patient. This would verify the efficacy of the program and allow advancement of the back exercise program, if needed. The degree of thoracic kyphosis is measured through the Cobb method of measuring the angle formed between the lines extended from top edge of T4 and bottom edge of T12 or interference vertebrae [35]. Comparison of the Cobb angle from baseline with follow-up in the kyphotic group showed decreased thoracic kyphosis.

Recreational Exercises with Osteoporosis in Mind

Not all recreational exercises are safe for the osteoporotic spine. Strenuous flexion in some yoga positions can increase torque pressure applied to the vertebral bodies and result in anterior wedging or worse, compression fracture (Figure 7.8a, b) [30]. While physical therapeutic exercise programs are preferred to be osteogenic, they need also to be designed on the basis of an individual's exercise interest, skeletal biomechanical competence, and cardiovascular health status. Therefore, if there are any health-related concerns, to avoid injury, the exercise program for osteopenic/osteoporotic individuals needs to be prescribed.

Participation in bone-safe PA is ideal for musculoskeletal health. To contribute to bone health, PA needs to be weightbearing. PAs should not engage the osteoporotic spine in strenuous flexion. Recreational activities such as golfing or hot yoga could expose the spine to compressive forces with some flexion maneuvers. Also, high-impact recreational activities such as downhill skiing should raise concern. In the past, we have reported individual cases of women with osteoporosis who did not follow medical advice to avoid strenuous flexion of the spine or wear a back brace during such activities for protection. These patients sustained spinal fractures and returned for evaluation of severe back pain [36]. Another popular recreational exercise is yoga. With increasing popularity of yoga, we have seen more cases of patients who sought medical advice after experiencing severe back pain during yoga. These patients who were in good health and had osteopenia suffered vertebral compression fractures when they participated in spinal flexion position exercises during yoga [30]. To maintain the intended flexion position of the spine during some yoga maneuvers, forceful flexion of the spine creates a closed-chain maneuver under mechanical stress induced through forceful muscle contraction. Achieving paraspinal muscle relaxation and maximum stretchability of the longitudinal ligaments could be harmless in a healthy spine but not in a spine challenged by osteoporosis.

Osteoporotic women generally have weaker back extensors than healthy women of comparable age (Figure 7.12) [37]. Choice of PAs needs to be individualized. Swimming can improve skeletal muscular support, but is not osteogenic (Figure 7.1) [3]. Short periods of stationary biking are not sufficiently osteogenic either, but can

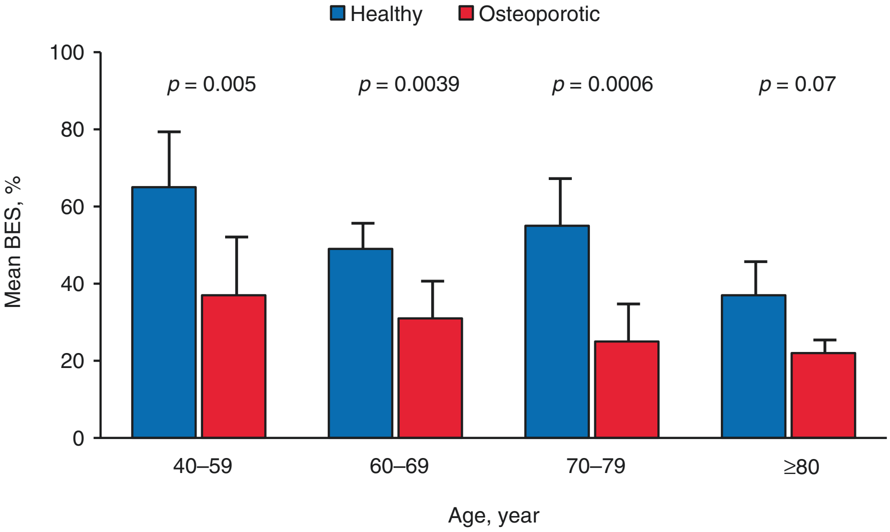

Fig. 7.12 Mean back extensor strength in healthy women and women with osteoporosis. Data from Sinaki M, Khosla S, Limburg PJ, Rogers JW. Muscle strength in osteoporotic versus normal women. Osteoporos Int. 1993;3:8–12.

fulfill the need for cardiovascular fitness without straining the osteoporotic frame [38]. Walking for 40 minutes at least three times a week is effective for maintaining lower limb bone density.

Summary

Musculoskeletal changes that are related to osteoporosis/osteopenia can be prevented or mitigated through implementation of proper osteoporosis rehabilitation programs. The PA and exercise interventions recommended here are evidence based and are the result of controlled trials and studies. In addition, the author has included a few caveats. The latter are intended to emphasize avoidance of overstraining the spine beyond its biomechanical competence when interested in osteogenicity of exercise and PA.

The author would like to inspire readers to contemplate the reliability of studies, so that they could depend on the results more comfortably, whether the focus is on well-controlled research studies with lower numbers of patients and frequent follow-up to monitor compliance or the studies with large numbers (hundreds) of patients with infrequent follow-up that may jeopardize proof of compliance.

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8

Management of Fractures in Osteoporosis: Role of Rehabilitative Measures

Mehrsheed Sinaki

Osteoporosis is a multifaceted metabolic bone disease and is a major public health problem in the United States. The direct and indirect cost of osteoporosis in the United States alone is estimated to be more than $14 billion annually [1]. Much of this expense relates to hip fractures. In 15% to 20% of hip fracture cases, the outcome is fatal, despite recent advances in surgical and nonsurgical interventions. Therefore, prevention of hip fracture remains of utmost importance. Osteoporosis may go unnoticed until a fracture occurs or a vertebral compression fracture is incidentally detected on a chest radiograph. Falls are the major cause of fractures in osteoporotic individuals; however, spontaneous fractures also can occur in certain cases of osteoporosis and fragility.

In the typical aging process, there is an imbalance between resorption and formation, since osteoblastic activity is not equal to osteoclastic activity. The result of the remodeling process is bone loss during each cycle of remodeling. Risk of fracture increases severalfold with each 7 years of incremental aging. Following menopause, there is exponential bone loss from the axial skeleton in women for 3 to 4 years. This loss decreases between 1% and 2% per year and then gradually decreases to 1% per year. With each standard deviation of bone mineral density (BMD) loss, risk for vertebral fracture increases greater than 1.5- to 2-fold, and the risk for hip fracture increases 2.6-fold. Several factors, such as age, loss of bone and muscle strength, reduction of proprioception, and, finally, falls, can contribute to osteoporosis-related fractures.

It has been estimated that after menopause, a woman's lifetime risk of sustaining an osteoporotic fracture is 50%, while the risk for men is 30%. The highest incidence of fracture is in white females. The female to male ratio is about 7:1 for vertebral fractures, 2:1 for hip fractures, and 5:1 for Colles fractures. The most

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M. Sinaki, MD, MS
Consultant, Department of Physical Medicine and Rehabilitation, Mayo Clinic, Rochester, Minnesota, USA

Professor of Physical Medicine and Rehabilitation, Mayo Clinic College of Medicine and Science, Rochester, Minnesota, USA

Director of Rehabilitation of Osteoporosis Program, Mayo Clinic, Rochester, Minnesota, USA
e-mail: sinaki.mehrsheed@mayo.edu

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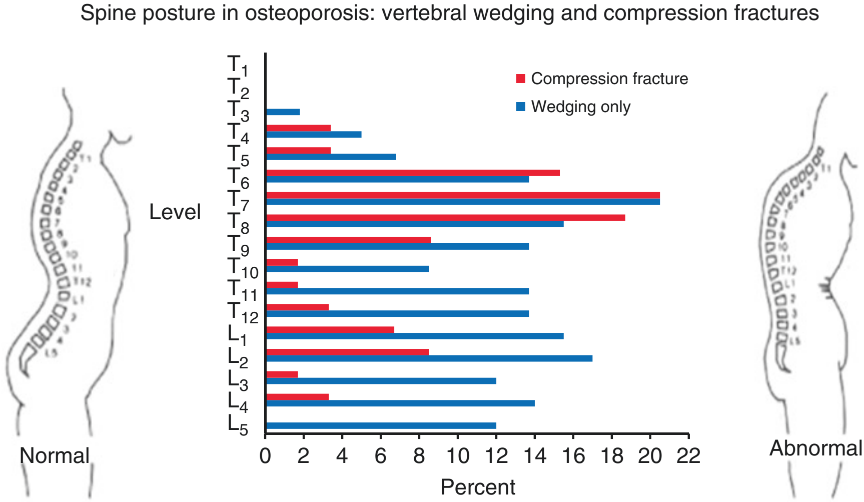

Fig. 8.1 The most common areas for vertebral fractures in osteoporosis are the mid-thoracic and thoracolumbar spine. Osteoporosis-related incidence of wedging and compression fractures at various levels of the spine on radiographic evaluation. (From Sinaki M, Mikkelsen BA. Postmenopausal spinal osteoporosis: flexion vs extension exercises. Arch Phys Med Rehabil, 1984; 65(10):593–6; used with permission.)

common areas for vertebral fractures in osteoporosis are the mid-thoracic and upper lumbar or thoracolumbar spine (Figure 8.1) [2].

Isometric muscle strength decreases by 50% from age 30 to 80; this includes reduction of type II muscle fibers. Axial bone mass also decreases by 50% in women and by 30% in men by age 80 (Figure 8.2). The combination of weaker and slower muscles with lower bone mass creates fragility and postural deformities, resulting in increased risk of falls and fractures. Furthermore, in addition to the bone and muscle loss, aging attenuates vestibulospinal reflexes and affects proprioception. Kyphosis contributes to relative imbalance between the body's center of gravity and the base of support, thus increasing unsteadiness of gait. Consequently, body sway and fear of falls increase, resulting in decreased participation in physical activities. As with pharmacotherapy, therapeutic exercise is an essential parameter in the management of osteoporosis, especially after a fracture.

Falls and fractures are multifactorial; therefore, multifaceted approaches are required to prevent and manage them. Reducing sedative pharmacotherapy decreases iatrogenically affected alertness and falls in the geriatric population. Axial strength and stability are of primary importance. Muscle and bone loss, along with age-related disequilibrium, falls, and fractures, require innovative approaches for management. Imbalance and postural sway are two important risk factors for falls. Strengthening lower extremity muscles can decrease the risk of falls.

A spinal extensor strengthening program should be performed with progressively resistive exercises, as tolerated. The combination of reducing kyphosis, increasing back strength, and reorienting the facet joints for proper upright posture would be of help. Spinal proprioceptive extension exercise dynamic (SPEED) program (Figure 8.3) (see Chapter 7) has demonstrated improvement of back extensor

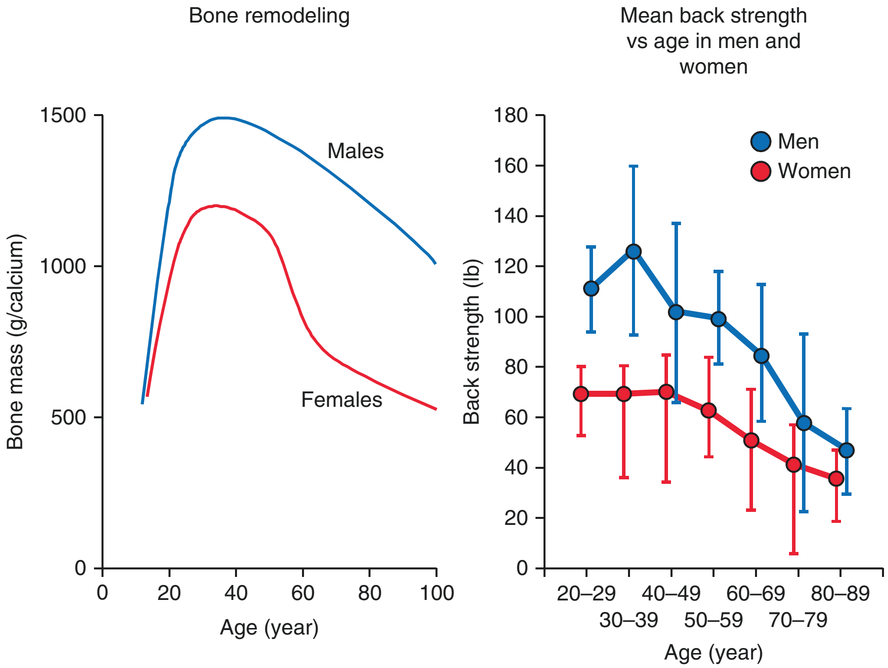

Fig. 8.2 Axial bone and muscle loss with aging in men and women. From Riggs BL, Melton LJ 3rd. Involutional osteoporosis. N Engl J Med. 1986;314(26):1676–86. (*left*). From Sinaki M, Nwaogwugwu N, Phillips, B, Mokri M. Effect of gender, age, and anthropometry on axial and appendicular muscle strength. Am J Phys Med Rehabil. 2001;80:330–8. (*right*)

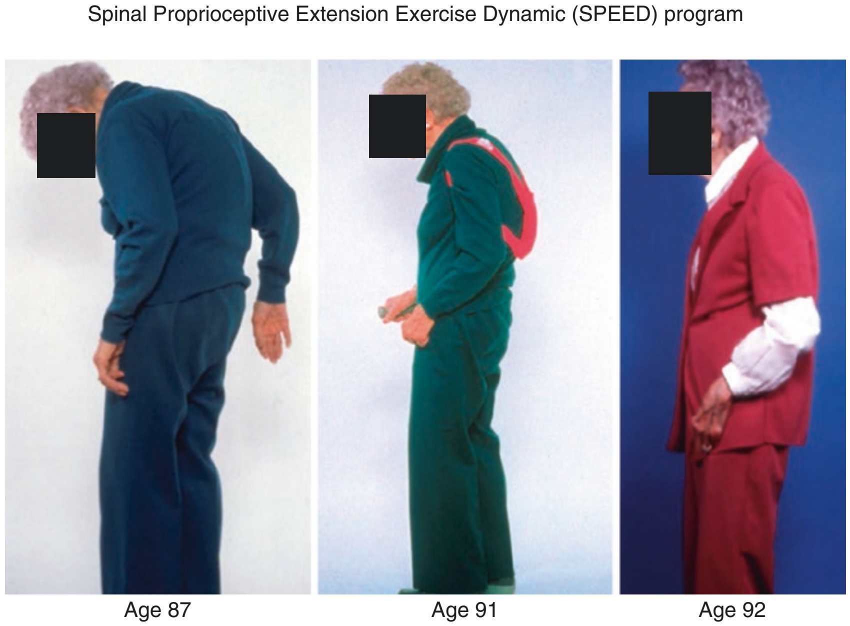
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Fig. 8.3 An 87-year-old woman with kyphotic posture at baseline (left), 4 years later with kypho-orthosis (center), and 5 years later at age 92 (right) after compliance with SPEED program strength, reduction of back pain, and improvement of locomotion and balance. Fracture risks related to osteoporosis or osteopenia can be prevented or mitigated through implementation of a properly devised muscle strengthening exercise program. Mechanical loading is vital for osteoblastic activity. This has been reflected in our previous publication, "*Bone, to be maintained, needs to be mechanically strained—within its biomechanical competence*" (Figures 8.4, 8.5, and 8.6) [3].

T Score –1 to –2.5 SD
Suggested rehab guidelines

- Walking ex, ↓ fall risk
- Aerobic ex's weight training
- Therapeutic: back extension exercise
- Frenkel exercises (if needed)
- Weighted kypho-Orthosis
- Lifting precautions
- ↓ pain

Fig. 8.4 To maintain or improve bone mass, a safe, progressive, mechanical loading exercise program is recommended. From Sinaki M. Osteoporosis. In: Cifu D (editor). Braddom's Physical Medicine and Rehabilitation, 5th ed. New York: Elsevier. 2015:747–68; used with permission

T Score ≥–2.5 SD
Suggested rehab guidelines

- Fall prevention–pain management
- Aquatic exercises
- Range of motion, flexibility
- Coordination and Frenkel exercises
- Walking exercises
- Weighted Kypho-Orthosis and hip pads (if needed)
- Therapeutic exercises
- Weight training (start with 1–2 lbs)
- Load lifting limitations (5–10 lbs)

Practical exercise for rehabilitation of osteoporosis

Fig. 8.5 To maintain or improve bone mass, a safe, progressive, mechanical loading exercise program is recommended. From Sinaki M. Osteoporosis. In: Cifu D (editor). Braddom's Textbook of Physical Medicine and Rehabilitation, 5th ed. New York: Elsevier. 2015:747–68; used with permission

Fig. 8.6 To maintain or improve bone mass, a safe, progressive, mechanical loading exercise program is recommended. From Sinaki M, Wahner HW, Offord KP, Hodgson SF. Efficacy of nonloading exercises in prevention of vertebral bone loss in postmenopausal women: a controlled trial. Mayo Clin Proc. 1989;64:762–9; used with permission

Table 8.1 Factors contributing to risk of falls

Extrinsic
Environmental: obstacles, slippery floors, uneven surfaces, poor illumination, stairs not well defined, pets, icy sidewalks, wearing stable, nonslip shoes
Extraskeletal: inappropriate footwear, obstructive clothing
Intrinsic
Intraskeletal: lower extremity weakness (neurogenic or myopathic), balance disorder (vestibular disequilibrium, peripheral neuropathy, hyperkyphosis), visual impairment, bifocal use, vestibular changes, cognitive decline, decreased coordination (cerebellar degeneration), postural changes, imbalance, gait unsteadiness, gait apraxia, reduced muscle strength, reduced flexibility, orthopnea, postural hypotension, cardiovascular deconditioning, iatrogenically reduced alertness
Avoiding excessive alcohol consumption
Being physically active to maintain strength and balance

From Sinaki M. Prevention of hip fracture: physical activity. In Ringe JD, Meunier JP (editors). Osteoporotic fractures in the elderly: clinical management and prevention. Stuttgart: Georg Thieme Verlag; 1996:99–115; used with permission.

Therefore, after any fracture, whether vertebral or appendicular, a safe mechanical loading stimulus needs to be initiated as soon as possible. Bone cells are responsive to biomechanical forces; therefore, weight-bearing is important for the healing process while avoiding misalignment.

Clinicians can add quality to the life of patients with osteoporosis through a multidisciplinary approach. Prevention and management requires a team effort inclusive of the primary physician, endocrinologist, orthopedic surgeon, physiatrist, orthotist, occupational and physical therapist, and, of course, the patient and/or the patient's caregiver. Management includes treatment of the present fracture and prevention of future fractures. It has been reported that once a vertebral fracture occurs, subsequent vertebral fractures are more likely to occur [4].

Prevention of falls is the primary objective of a rehabilitation course. When a diagnosis of osteoporosis is made, provision of patient education materials that reflect fall prevention issues can benefit the patient and their family and/or caregiver. Table 8.1 notes contributors to the risk of falls.

Fractures in Osteoporosis

Appendicular fractures typically require immediate attention and could not go unnoticed (with the exception of some minor stress fractures). The fact that a fracture results from osteoporosis should not affect the method of orthopedic management.

Management of an osteoporotic spine fracture requires immobilization of the involved vertebral bodies and analgesia. Fortunately, vertebral fractures heal by becoming more condensed and do not require any specific treatment process, as is usually the case for appendicular fractures. In any fracture, the duration of immobilization should be limited but sufficient to ensure the fracture-healing process. It is important to avoid prolonged immobilization, which can contribute to further bone loss. Therefore, bracing the spine or use of proper gait aids during the initial stage becomes significant. There are several types of gait aids and spinal supports or braces for different indications (see Chapter 10 [Spinal Orthotic]) (Table 8.2).

Rib Fractures

Rib fractures are not uncommon in older adults with osteoporosis and are very painful. About 25% of rib fractures result from major trauma such as a car accident. Fragility also increases the risk of rib fracture with lesser trauma. Every attempt should be made to prevent displacement of the fractured bone ends, as they can puncture the lungs or cause swelling and other injuries to the adjacent organs. Nontraumatic events such as the repeated strain of a coughing spell or swinging a

Table 8.2 Reducing the incidence of falls

Identify high-risk activities
Reduce antidepressants; use alternatives, if possible
Decrease dose of diuretics
Avoid hyponatremia
Avoid over-the-counter sleep and allergy medications
Manage postural hypotension
Manage gait and balance disorders
Improve muscle strength; increase level of physical activity
Improve coordination
Use gait aids, if necessary
Improve back strength; prevent hyperkyphosis
Use hip protectors, when necessary
Emphasize proper intake of vitamin D and calcium
Increase bone mass

From Sinaki M. Falls, fractures, and hip pads. Curr Osteoporos Rep. 2004 Dec; 2(4):131–7; used with permission.

golf club may also cause rib fracture. In osteoporosis, the fracture can also occur with falls or an affectionate hug. Rib cage pain occurs with palpation of the area and/or taking a deep breath. Emergency care is indicated if there is shortness of breath, especially if it is worsening [7].

Treatment

To decrease the risk of lung infection, pain needs to be managed for the ability to breathe deeply and to cough. Application of proper trunk support or a rib cage binder can reduce chest wall pain and facilitate breathing and reduce the risk of developing pneumonia. Pneumonia is the most prevalent and serious complication of rib fractures in older adults. If simple pain management is sufficient, one can use acetaminophen (Tylenol), ibuprofen (Advil, Motrin, etc.), or naproxen (Aleve) for pain relief. Opioids are better avoided, as they can result in constipation. Application of analgesic patches may be more helpful. For severe posttraumatic fractures, an injection or continuous infusion of pain-blocking drugs should be considered. Complications can be serious. One study of older adults showed that about 19% of those who sustained a fracture of three to four ribs died from complications [7].

Most non-displaced rib fractures heal within 6 weeks. Although pain will gradually subside over this time, the patient could experience exacerbation of pain with exertional activities until complete healing and alignment of the ligamentous structures is achieved.

Considering the severity of complications of rib fractures, preventing avoidable risks is an ultimate goal. This could include reducing the risk of falls by removing tripping hazards from the home and avoidance of excessive alcohol consumption. Maintenance of musculoskeletal health through consumption of adequate calcium and vitamin D, as well as regular weight-bearing physical activity such as walking to improve posture, balance, and strength, can be beneficial.

Hip Fracture

The most life-threatening fracture in osteoporosis is the hip fracture. Aging and reduction of BMD are considerable predictors of risk of hip fracture. With reduction of one standard deviation of BMD, the risk of osteoporotic fracture of the spine increases from 1.5- to 2-fold, and the risk of hip fracture increases 2.6-fold. Also with every 5 to 7 years of increment in age, the risk of fracture doubles [8].

Hip Fracture Definition and Description

The term, *hip fracture*, applies to fractures of the femoral head to the proximal portion of the femoral shaft.

Etiology and Types

The most common etiology is a fall from a standing position (~90%); in other words, there is no fracture without a fall. The classification of the type of hip fracture is based on the anatomic location. Intracapsular fractures involve the femoral neck and head; extracapsular fractures are intertrochanteric and/or subtrochanteric [9].

Epidemiology

Incidence of hip fracture in the world is about 1.6 million/year and in the United States about 300,000/year. White women with osteoporosis living in premorbid facilities (i.e., nursing homes) have a higher risk for falls, especially with the presence of dementia. Risk of hip fracture increases with age. The mean age of hip fracture for women is 77 years of age, and for men it is 72 years of age. Mortality in the first year postfracture ranges from 15% to 36%.

Pathogenesis

Intracapsular fractures have a higher rate of nonunion/malunion and avascular necrosis of the femoral head. Subtrochanteric fractures have a greater need for intramedullary (IM) nails or rods. When hip fracture is suspected after a fall, anteroposterior and lateral hip x-rays are required. Infrequently, computed tomography or magnetic resonance imaging may also be obtained. In addition, some laboratory tests such as complete blood count, electrolyte levels, and ratio of blood urea nitrogen to creatinine (BUN/Cr) could be helpful. An increased ratio may be due to a decrease in the flow of blood to the kidneys, such as congestive heart failure or dehydration. Coagulation studies are performed for prevention of deep venous thrombosis (DVT). The prothrombin time (PT) with international normalized ratio test measures the length of time it takes for a clot to form in a sample of blood. Partial thromboplastin time (PTT) test is ordered for unexplained bleeding or clotting [10].

Management

After hip fracture, surgical repair depends primarily on the type of fracture.

The options for repair include percutaneous pinning, using IM nails, open reduction/internal fixation (ORIF), partial hemiarthroplasty, or total arthroplasty. Postacute phase rehabilitation includes safe, independent ambulation and performance of activities of daily living (ADLs). The rehabilitation program needs to address weight-bearing precautions, mobility-related issues such as transfers/ambulation, use of proper gait aids, osteoporosis education inclusive of ADLs, and use of adaptive equipment to prevent falls. Medical management would include pain management (simple analgesics), DVT prophylaxis, wound healing, and decubitus preventive measures [10, 11].

Following a hip fracture or issues related to prolonged immobility, there is always a risk of thromboembolic complications, which can be a cause of postfracture mortality. The author encourages practitioners who treat patients for hip fracture to review the prophylactic thromboembolic measures for reducing this risk. National and international guidelines for prevention of complications are available.

The management course includes consideration for the level of weight-bearing, avoidance of contracture, and deconditioning of the supportive muscles of the involved hip and lower extremity.

The recommendations should be modified at the discretion of the orthopedic surgeon according to the patient's status of health, the type of procedure, and the status of healing of the bone or soft tissues. Following hip fracture surgery, most patients bear weight on the affected extremity as tolerated. In general, range of motion (ROM) needs to be applied to the joint with stable fixation. If a cast has been applied, the joints proximal and distal to the casted area need to be mobilized through ROM exercises. When possible, isometric muscle contraction needs to be initiated to avoid muscle loss or development of contractures. Exercise and gait training through physical therapy sessions is necessary. Proper positioning in bed plays a considerable role, and the expertise of occupational therapists is of great help to patients. This includes facilitation of self-care and ADLs through provision of home instructions and the use of home aid devices such as raised toilet seats and chairs and installation of grab bars to prevent falls.

Immobility-related issues regarding prevention of DVT through proper anticoagulation and safe progressive mobilization need to be addressed by the physician.

Post-hip Fracture Rehabilitation Course

During the postoperative healing phase (1–7 days) after ORIF, it is better to avoid passive range of motion. Following endoprosthesis, it is better to avoid internal rotation and adduction past the midline. Active assistive ROM and later active ROM to the hip, knee, and ankle are applied. Isometric contraction of the gluteals and quadriceps and isotonic-strengthening exercises to the ankle muscle groups are applied.

Weight-bearing, as tolerated, on the stable impacted fracture or endoprosthesis is recommended. Muscle strength can increase by 5% to 12% per week with submaximal or maximal strengthening exercises [12, 13].

If the patient is kept on bed rest and performs isometric contractions, the loss of strength is approximately 0.3% per week. In cases of complete bed rest with no strengthening exercises, the loss is about 1.5% per day. Isometric contractions are recommended when possible to mitigate the immobility-related muscle loss.

Every effort is worth it to prevent risk of falls. Data from our unpublished study indicates that stronger hip extensors are correlated with fewer falls in

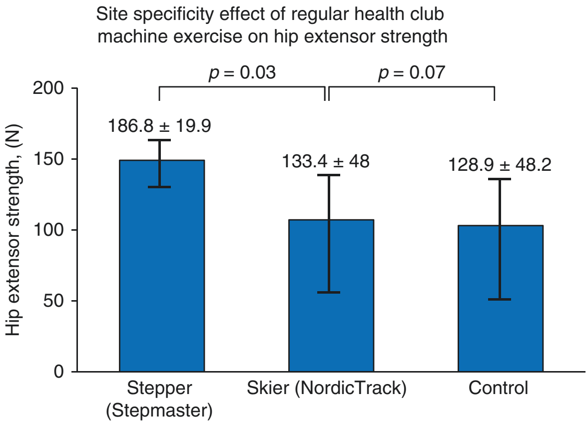

Fig. 8.7 Individuals who used the Step Master showed more significant increase in their hip extensor strength [14]

postmenopausal women. Another study [14] shows that some exercise machines can improve hip extensor strength more than others (Figure 8.7). These exercise machines could be used for site-specific strengthening exercises if needed.

Sacral Insufficiency Fracture

Fractures of the sacral alae and pubic rami are not uncommon.

Pelvic fractures such as those to the pubic rami are particularly common in patients with a combination of fragility and osteoporosis. These fractures can occur with minimal strain or trauma. Healing typically occurs without invasive procedures. Ambulatory activities need to be reduced, and a wheeled walker is recommended to decrease pain. Weight-bearing is limited and is dictated by the level of pain in the pelvic area. Application of heat and analgesic massage with use of topical pain relievers is recommended for reduction of pain and facilitation of the healing process. Efforts are made not to use sedatives or analgesics that can contribute to risk of falls, especially in elderly patients.

Tibial Shaft Fracture Treatment

The main objective for treatment of tibial shaft fractures is restoration of normal alignment. Following IM rod and external fixation, a cast is applied. A rehabilitation course of 2 to 3 months consists of ROM exercises to both the knee and ankle. Progressive resistive exercises of the quadriceps, ankle plantar, and dorsiflexors are initiated. While still in the cast, isometric strengthening is applied.

With external fixation while in a cast, gait instructions are provided to perform touch weight-bearing only. In cases of IM rod fixation, weight-bearing, as tolerated, is frequently allowed.

Management of Stress Fracture or Ankle Fracture

In cases of stress or ankle fractures, range of motion to the ankle is avoided, and a cast or brace is applied. After 1 to 7 days, ROM is applied to knee and metatarsophalangeal joints.

Muscle strengthening does not include strengthening of ankle or foot groups. It is, however, recommended to perform isometric strengthening of the quadriceps as tolerated. At this stage, avoidance of weight-bearing during ambulatory activities is recommended, and proper gait aids need to be used. After the healing process is complete, isometric strengthening of the ankle stabilizers could be helpful.

Forearm Fractures

Most forearm fractures caused by osteoporosis are the result of a fall on an outstretched hand. Orthopedic management could include ORIF followed by casting and later application of a splint to aid in protection of the healing area along with a progressive musculoskeletal rehabilitation program. The program needs to avoid overstraining while preventing the development of contractures. Complete bone healing takes 2 to 3 months. The postoperative musculoskeletal rehabilitation course takes 3 to 6 months. If dislocation has occurred along with the fracture, the rehabilitation course will take longer to allow complete healing of the ligamentous structures. Strengthening exercises play an important role in the recovery phase. Muscle contraction also contributes to the healing of the fractured area and postfracture mobilization.

Soft Tissue Injuries

Skeletal fractures may be concomitant with soft tissue injuries. However, soft tissue injuries may also occur alone and mainly include sprains and strains. The injured area needs to be protected to decrease the pain level. Voluntary relaxation and contraction exercises need to be induced. In cases of muscle strain, strenuous muscle contractions need to be decreased to prevent further soft tissue injuries.

If there are related tendinous injuries, they typically occur at the weakest stage of healing (during the first 14 days) and could be disrupted with a simple muscle pull.

It would take 6 to 8 weeks to begin to see healing of the muscle function. Muscle contraction can then move the tendon without overstrain. After 6 months of healing, maximum strength is achieved, and return-to-normal tensile strength and function can be gradually attained.

Vertebral Wedging and Compression Fracture

The distribution of the weight on vertebral bodies depends on their anatomical location in spine. In the thoracic spine, the pedicle facet complex of the anatomical unit of spine bears 20% of the intervertebral load. The remaining 80% is absorbed by the intervertebral disk [15]. Increasing age decreases the resilience of the intervertebral disks. Therefore, the increased compressive forces on the spine are transferred directly to the osteoporotic vertebral bodies during flexion of the spine and result in further compression fracture of vertebral bodies [2]. Vertebral compression can result in two types of back pain: acute or progressive and chronic. Chronic back pain and kyphotic posture can develop insidiously as a result of vertebral microfractures under repetitive strain. In kyphosis, the ligamentous structures of the spine contain pain fibers, and their persistent stretch is perceived as pain. The resulting kyphotic posture increases the risk for falls (Figure 8.8) [16]. Vertebral compression in the form of wedging deformity is stable. In cases of compression fracture, there is concern related to stability of the alignment and the presence of concomitant neurologic deficit (Figure 8.9) (Tables 8.3 and 8.4).

During the acute phase, in some cases, there is initially concern related to the development of ileus, and this needs to be taken into consideration. At this stage, there is sometimes also the need for an overnight nasogastric suction to prevent uncomfortable distension. If a patient is unable to void, the use of intermittent catheterization or, in some cases, a Foley catheter is recommended.

Next, proper bracing to immobilize the fractured area, as well as proper positioning to decrease pain whether in or out of bed, is recommended. Proper realignment

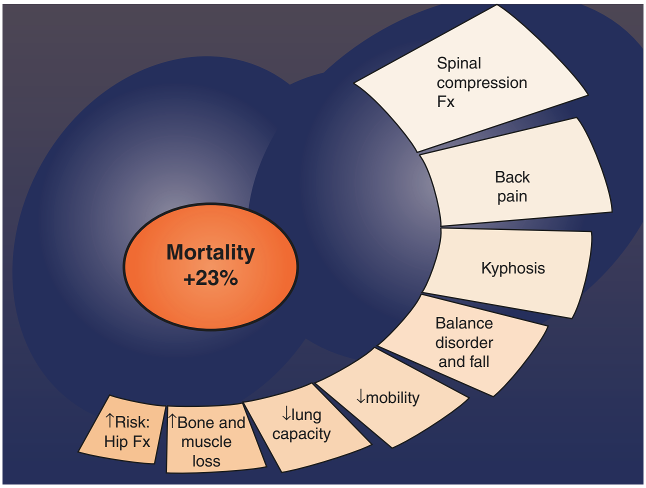

Fig. 8.8 Vertebral fracture increases kyphosis which increases risk of falls which could contribute to hip fracture and increased mortality. Fx indicates fracture; ↑, increased; ↓, decreased

Fig. 8.9 Vertebral fractures (red arrows) and severe kyphosis depicted in spine x-ray of the woman in Figure 8.3

Table 8.3 Management of acute pain in patients with osteoporosis

Bed rest (2 days): substantial bone loss is not likely to occur with 2 days of bed rest
Analgesics: avoid constipating medicines, such as codeine derivatives
Avoidance of constipation
Physical therapy: initially cold packs, then mild heat and stroking massage
Avoidance of exertional exercises
Knowledge of lifting and standing principles to avoid excessive spinal strain
Back supports if needed to decrease pain and expedite ambulation
Gait aids if needed

From Sinaki M. Osteoporosis. In: Cifu D (editor). Braddom's Textbook of Physical Medicine and Rehabilitation, 5th ed. New York: Elsevier. 2015:747–68; used with permission.

Table 8.4 Management of chronic pain in patients with osteoporosis

Improve faulty posture; may need weighted kypho-orthosis
Manage pain (ultrasound, massage, or transcutaneous electrical nerve stimulation)
If cause of pain is beyond correction, apply back support to decrease painful stretch of ligaments
Advise patient to avoid physical activities that exert extreme vertical compression forces on vertebrae
Prescribe a patient-specific therapeutic exercise program
Start appropriate pharmacologic intervention

From Sinaki M. Osteoporosis. In: Cifu D (editor). Braddom's Textbook of Physical Medicine and Rehabilitation, 5th ed. New York: Elsevier. 2015:747–68; used with permission.

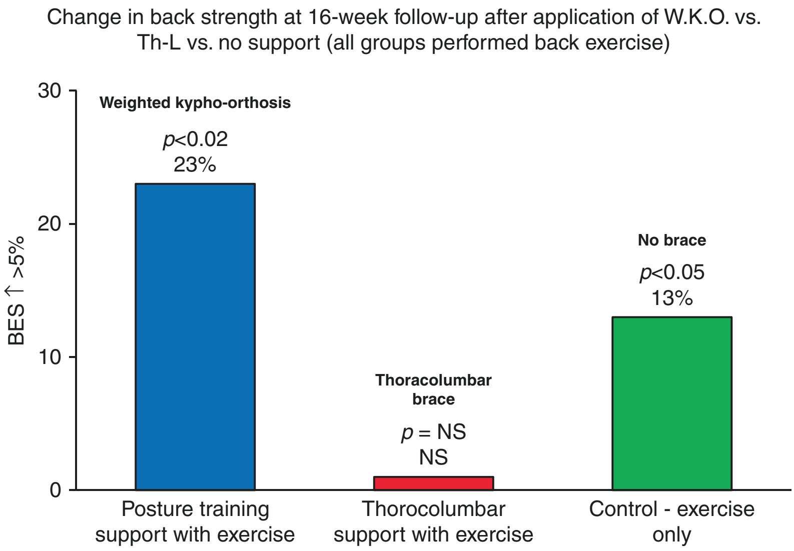

Fig. 8.10 Three groups performed back extension exercises; two groups who did not use a thoracolumbar brace improved their back extension strength significantly. From Kaplan RS, Sinaki M, Hameister M: Effect of Back Supports On Back Strength in Patients With Osteoporosis: Controlled trial; A Pilot Study. Mayo Clin Proc. 1996;71:235–241; used with permission

of the spine and prevention of deformity is critical. With application of bracing, the prevention of pressure sores needs to be considered.

After approximately 6 weeks of wearing the brace, active extension of the spine is allowed through isometric contraction of paraspinal muscles. Isometric pain-free strengthening could also be attempted. Every effort is made to avoid induction of pain, which could result in paraspinal muscle co-contraction and further exacerbation of pain and related immobility. When pain is managed, weaning from and discontinuation of the brace needs to be addressed. Isometric back extension exercises while wearing the back support is recommended. This would decrease muscle loss related to overuse. In one controlled randomized study, those patients who wore thoracolumbar support for back pain had less back strength than those who used posture training support and recruited their back muscles for support of the spine (Figure 8.10) [17].

Neurologic deficits need to be prevented. Initiation and patient compliance with a home-based program is necessary for reduction of risk of further falls and fractures [18].

Indications for Bracing in Postvertebral Fracture

Acute pain requires immobilization of the area to decrease pain and fracture-related edema. Reduction of pain decreases paraspinal muscle co-contraction. Bracing and prevention of movement of vertebral bodies in the fractured area

Fig. 8.11 *Left to right*: Spinomed, thoracolumbar brace, and lumbar brace

decreases muscle guarding. Therefore, proper bracing is highly appreciated by the patients at this stage and, above all, contributes to their independence in self-care.

There are several types of braces that can be prescribed according to the area of fracture [19]. Some braces extend to the thoracic spine for immobilization and pain management, while others are used to decrease movement in the lumbar spine (Figure 8.11). However, there is one principle that all braces need to be utilized for in postfracture stage and that is to prevent kyphotic posturing. Following spinal fracture, one usually finds more comfort in contracting the spinal flexors in order to avoid the contraction of spinal extensors, which could cause more pain in the area of fracture. After subsidence of the acute phase, the isometric contraction of the back extensors is gradually introduced into management while the patient is still wearing the brace. By 6 weeks of postfracture, the patient is encouraged to start weaning off the brace for a period of 1 hour at a time and then gradually increasing that time to half of the day. At this stage, a weighted kypho-orthosis for postural training would be helpful (Figure 8.12). During this period, patients are instructed to continue with isometric contraction of their back extensors. Strengthening of the back extensors will substitute for the support that was provided through application of a spinal brace. Progressive, resistive spinal exercises can improve back strength, decrease hyperkyphosis, and reduce risk of vertebral fracture [20, 21].

Fig. 8.12 Weighted kypho-orthosis in the form of vest with pouch or shoulder straps with pouch applied below T10 (inferior angle of scapulae), as helpful to the patient. From Sinaki M: Critical Appraisal of Physical Rehabilitation Measures After Osteoporotic Vertebral Fracture. Osteoporos Int. 2003; 14:773–779; used with permission

Summary

Every effort should be made by the managing medical team to prevent immobility-related complications, decrease pain, and later decrease or discontinue the application of a brace as pain subsides. Mechanical loading and weight-bearing are needed for prevention of bone loss. Regular strength training has been demonstrated to slow the loss of muscle function. Poor compliance with an exercise regimen often interferes with improvement. Periodic follow-up may improve a patient's adherence to the recommended measures for prevention of falls and fractures.

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9

The Role of Orthotics in Osteoporosis

Michael Pfeifer

Introduction

Vertebral fractures due to osteoporosis are the most common fractures in the elderly and are characterized by compression fractures of the anterior spinal column at the mid-thoracic spine and thoracolumbar junction. In the majority of patients, they cause acute pain and disability. In the longer term, changes in vertebral body shape can progress and result in spinal deformity such as loss of height and thoracic hyperkyphosis. Hyperkyphotic posture itself imposes stress on the anterior spinal column that increases the risk of new fractures and also disturbs normal balance, thereby increasing the risk of falls and other fractures. Hyperkyphosis and vertebral fractures due to osteoporosis are both associated with increased mortality and a range of adverse symptoms including chronic pain and fatigue, reduced back extensor strength, respiratory compromise, and depression, which all reduce physical function and quality of life [1, 2].

Optimal management for these conditions is uncertain. Pharmaceutical treatment is essential but cannot address deficits in back extensor strength, balance, and posture to improve function or reduce the risk of falls. Surgical interventions such as kypho- or vertebroplasty are commonly used in acute and painful vertebral fractures. Current reviews, however, deliver inconsistent messages about the benefits of surgery when there is no neurologic compromise and highlight insufficient evidence. Conservative management in a rehabilitation setting is often not standardized. Usually, it includes analgesia, short and temporary bed rest of up to 2 days, physiotherapy, and the use of spinal orthoses such as a brace or a corset [1, 2].

M. Pfeifer, MD
Institute of Clinical Osteology and Clinic "DER FÜRSTENHOF", Head of German Osteology Foundation, Bad Pyrmont 31812, Niedersachsen, Germany
e-mail: iko_pyrmont@t-online.de

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Spinal Orthoses

Spinal orthoses are used immediately after vertebral fracture, in the subacute phase, and during the longer-term rehabilitation process of vertebral fractures due to osteoporosis. The main goals of orthotic treatment may be any combination of improving posture, reducing pain and fatigue, and promoting function or social participation. In any case, limiting of motion should be avoided. Orthoses can be recommended for 2–3 months after a vertebral fracture to stabilize the injured vertebra and promote fracture healing while allowing the individual to mobilize. Thus, a certain training effect especially on the back extensor muscles is guaranteed. The primary function is to alter posture; namely, to reduce excess flexion and promote more neutral lumbar and thoracic alignment. This aims to diminish the load on the affected anterior column and vertebral body in order to relieve pain and fatigue and to promote healing in an optimal alignment, thereby reducing subsequent deformity. Reducing excess kyphosis may also improve balance and facilitate trunk muscle activity to improve strength and function and reduce the risk of falls and further fractures [3, 4].

Many types of spinal orthoses are available; they may be custom-made or prefabricated, and they can be described according to the area of the spine they affect, by their properties or by their product names (Table 9.1). Rigid, semirigid, and flexible orthoses are all prescribed after acute fracture, while semirigid and flexible orthoses are used in longer-term rehabilitation [2]. Most rigid orthoses, however, apply some degree of 3-point pressure to restrict motion and correct posture [5]. These devices and their mode of action are associated with low compliance due to immobilization of the trunk muscles resulting in further loss of muscle mass and much more important some restrictions in breathing. These restrictions in breathing are already a well-known phenomenon and complication of vertebral compression fractures which limit thoracic motion [1, 5]. Flexible orthoses provide increased sensory feedback about posture and serve as a psychological reminder to the person about their condition. This reminder stimulates patients to bring themselves in an upright position by contracting their trunk muscles, which—in part—belongs to the principle of biofeedback and thereby results in a strengthening of the trunk muscles [3, 4]. The major problem with all of these orthoses, however, is the fact that they have never been tested in well-designed randomized controlled trials (RCTs). Therefore, Table 9.1 provides an overview of orthoses, which have been tested in randomized and nonrandomized clinical trials [3–14].

Selection of Clinical Trials

Randomized controlled trials (RCTs) and pilot RCTs, controlled clinical trials without true randomization, and experimental studies with prospective control groups were included. Unlike in pharmaceutical RCTs, a so-called true randomization may be very difficult to perform, since “placebo orthoses” cannot be used. These clinical trials were identified by a literature search of the following electronic databases up until July 2016: PubMed, MEDLINE, EMBASE, AMED, CINAHL, and the Cochrane Library. Broad terms related to the population and interventions of interest were searched. The population of interest was studies of spinal orthoses for adults with a diagnosis of vertebral osteoporosis or osteopenia with or without vertebral fractures due to osteoporosis. Studies that compared spinal orthoses with inactive control groups were included as were studies in which orthoses were used in addition to an intervention received by all participants (e.g., exercise). Primary outcomes of interest included measures of body structure and impairment related to fracture consolidation, pain, spinal muscle strength and endurance, spinal curvature, and height, as well as measures of physical activity, function, and parameters of quality of life. Secondary outcomes were related to adverse events and treatment compliance. Observational studies, studies of people with traumatic vertebral fractures, camptocormia, or hyperkyphosis of different etiology were excluded. Finally, 12 studies were included (Table 9.1).

Findings

In the treatment of acute vertebral fractures due to osteoporosis, rigid orthoses are burdensome to the individual and present risks. They are associated with skin breakdown, respiratory compromise, hernia, pain and discomfort, and low compliance [5]. If used for longer periods, there is a potential risk of further demineralization and atrophy of off-loaded trunk muscles with a subsequent increased risk of future fractures. Complications with casting are well recognized and were reported, but the high rate of complications reported with a 3-point orthosis was concerning [5]. On the other hand, there is evidence that a flexible backpack orthosis such as Spinomed might be well tolerated and improve pain function even after an acute fracture [3, 4, 8]. Given the lack of evidence of benefits and poor tolerability of rigid orthoses, any fracture studies should collect data about adverse effects and adherence. Especially, direct comparison studies between rigid and flexible orthoses in the treatment of acute vertebral fractures due to osteoporosis should be performed in the near future.

With respect to rehabilitation, there is qualified support for the use of a flexible backpack orthoses such as Spinomed in women with previous fractures and hyperkyphosis. Two trials were specifically designed to investigate possible effects and efficacy in the treatment of women suffering from postmenopausal osteoporosis. Both trials were adequately powered, and outcomes were prespecified and analyzed appropriately, but uncertainty over the presence of observer bias means caution is needed [3, 4]. However, the extent of improvements in trunk strength, balance, and pain described could be considered as clinically relevant and were associated with increases in function and quality of life. Evidence from nonrandomized studies echoed these findings. Improvements attributable to the orthosis occurred mainly during the first 6 months but were maintained at 12 months with continued use, which could suggest the orthosis might provide longer-term benefits.

Table 9.1 Characteristics of included studies and their main findings

Authors, publication, Year, country, setting	Study design/Randomization	Population characteristics	Intervention	Outcomes	Main conclusions
1. Orthoses for rehabilitation of acute vertebral fractures due to osteoporosis					
Li et al., 2014, Hongkong, inpatients [5]	RCT pilot study	Women (n=51) aged > 55 years with acute vertebral fractures 1. Group 1 (n=27): 82 ± 8.3 years; Number of VFs: 15 single, 7 two, 5 three or more 2. Group 2 (n=21): 81 ± 6.6 years; Number of VFs: 10 single, 9 two, 5 three or more	3 weeks all: Week 1 rigid Orthosis 1. Backpack (Spinomed) up to 3 h daily, then LS brace rest of day for 2 weeks 2. LS brace throughout day for 2 weeks	Baseline and 3 weeks Primary outcome not specified Thoracic kyphosis, back pain (VAS), FIM, Elderly Mobility Scale, modified Ambulation Category Compliance	Pain, mobility, and activities of daily living improved significantly within each group. No significant differences between groups significant difference
Meccariello et al., 2013, Italy, inpatients [6]	Nonrandomized Controlled clinical Trial	Men (n=18) and women (n=25) with acute vertebral fractures 1. Group 1 (n=23): 10 men, 13 women; mean age 81.5 years 2. Group 2 (n=20): 8 men, 12 women; mean age 82.8 years	12 weeks 1. Three-point orthosis for 10 weeks while upright, weaned 2 weeks, trunk exercises 2. Backpack (Spinomed) for 10 weeks while upright, weaned 2 weeks, trunk exercises	Baseline, 1, 3, 6 months Primary outcome not specified Vertebral fracture height Thoracic kyphosis Delmas index (stiffness) Back pain (VAS), Oswestry Low Back Pain Disability Questionnaire	No difference in vertebral deformity or kyphosis between groups at any time Group 2 significantly less pain and disability at 3 and 6 months complications: 14/23 (60.8%) 3-point 3/20 (15%) Spinomed

Talic et al., 2012, Bosnia and Herzegovina Inpatient Clinic [7]	Nonrandomized Controlled clinical Trail	Men (*n*=21) and women (*n*=38) aged 52–80 years with acute vertebral fractures due to osteoporosis 1. Group 1 (*n*=25): 10 men, 15 women; 65.4 ± 7.7 years 2. Group 2 (*n*=34): 15 men, 23 women; 66.8 ± 7.8 years	Up to 16 weeks 1. Cast 2. Three-point orthosis	Baseline, every 2 weeks, up to 16 weeks, Primary outcome not specified Length of immobilization pain, complications; outcomes for pain not presented	Complications with casting 16% (4/25). Significantly longer duration of immobilization in orthosis group
2. Orthoses for rehabilitation of subacute vertebral fractures due to osteoporosis					
Dionyssiotis et al., 2014, Greece, Outpatients [8]	Nonrandomized Controlled clinical trial Inclusion criteria as for Pfeifer	Women (*n*=50) aged > 50 years with subacute VF due to OPO, Kyphosis angle > 55° 1. Group 1a (*n*=10): 72.3 ± 8.3 years Group 1b (*n*=10): 72.6±8.5 years 2. Group 2 (*n*=20) 3. Group 3 (*n*=10): 61.0 ± 10.5 years	6 months 1. Backpack (Spinomed) for 2 h daily (Group 1a) Spine-X orthosis (Group 1b) 2. Garment orthosis (Spinomed active) 2 h daily 3. No orthosis	Baseline, 1, 6 months Primary outcome not specified. Back pain (VAS), back extensor and abdominal flexor strength. Compliance via diary and questionnaire	Group 1a significantly improved pain (9%), abdominal flexor (12%) and extensor (13%) strength compared with group 3 Overall compliance 66%: Spinomed 90%, Spine-X 30%

(continued)

Table 9.1 (continued)

Authors, publication, Year, country, setting	Study design/Randomization	Population characteristics	Intervention	Outcomes	Main conclusions
Pfeifer et al., 2004, Germany, Community-dwelling Patients [3]	RCT 12-months trial with planned crossover at 6 months	Women (n=62) aged > 60 years with subacute vertebral fractures. Kyphosis angle > 60° 1. Group 1 (n=31): 72.8±7.1 years 2. Group 2 (n=31): 72.3 ± 6.7 years Number of VF: 2.0 ± 2.8 years	12 months 1. Backpack (Spinomed) for 2 h daily 2. No orthotic care	Baseline, 3, 6, 12 months Primary outcome: Change in back extensor strength. Secondary outcomes: Changes in abdominal flexor strength, thoracic kyphosis, postural sway, vital capacity, forced expiratory volume in 1 s Questionnaires regarding pain, daily activity, well-being	Significant improvements in orthosis via control group in back extensor strength (73%), abdominal strength (58%), pain (38%), kyphosis angle (11%), body sway (25%), well-being (15%), and daily living (27%). High compliance No complications
Pfeifer et al., 2011, Germany, Community-dwelling Patients [4]	RCT 12 months trial with planned crossover at 6 months	Women (n=108) > 60 years with VF within the last 6 months Kyphosis angle > 60°. 1. Group 1 (n=36): 72.8 ± 7.3 years Number of VF: 2.1 ± 2.7 2. Group 2 (n=36): 72.3 ± 6.7 years Number of VF: 1.6 ± 2.8 3. Group 3 (n=36): 69.7 ± 8.9 years Number of VF: 1.1 ± 1.2 years	12 months 1. Backpack (Spinomed) for 2 h daily 2. Garment orthosis (Spinomed active) for 2 h daily 3. No orthotic care	As for Pfeifer 2004 (see above)	Significant improvements in both orthosis groups versus control in back extensor strength and abdominal strength, pain, balance, kyphosis angle, well-being, and daily living. No significant differences between orthoses Compliance high in both orthosis groups 1 and 2

3. Orthoses in longer-term rehabilitation					
Gündogdu et al., 2013, Turkey, Outpatients [9]	RCT pilot study	Women (n=29) with vertebral osteoporosis, with and without past vertebral fractures Kyphosis angle > 50° 1. Group 1 (n=14): 71.5 ± 1.5 years Number of VF: 1.0 ± 0.7 2. Group 2 (n=15): 68.3 ± 8.9 years Number of VF: 1.1 ± 0.8	12 weeks 1. Kypho-Orthosis: Omuz Retraksyon ortezi for 8 h daily plus home exercise 2. Home exercise	Baseline, 1, 3 months Primary outcome not specified. Height, thoracic kyphosis TUG, single leg stand, Berg Balance Scale, Kinesthetic ability QUALEFFO	Significant greater height at 3 months in orthosis group Improvements in other outcomes within both groups at 3 months. Only seven participants (50%) wore orthosis as prescribed
Hübscher et al., 2010, Germany, community-dwelling Patients [10]	RCT	Women (n=72) with vertebral osteoporosis, with and without past vertebral fractures 1. Group 1 (n=38): 74.2 ± 8.1 years Number of VF: 1.5 ± 2.0 2. Group 2 (n=34): 74.1 ±7.7 years Number of VF: 0.9 ± 1.2	6 months 1. Garment orthosis (Osteomed) daily 2. No orthosis	Baseline, 3, 6 months. Primary outcome: Postural sway: center of pressure fluctuation via force plate. Others: back extensor and quadriceps strength, QUALEFFO, back pain (VAS), physical activity, falls	Postural sway unchanged Back strength and pain improved significantly in orthosis group only. Physical activity, quadriceps strength, falls, and quality of life unchanged Dropouts due to orthosis discomfort

(continued)

Table 9.1 (continued)

Authors, publication, Year, country, setting	Study design/Randomization	Population characteristics	Intervention	Outcomes	Main conclusions
Kaplan et al., 1996, USA, Outpatients [11]	RCT pilot study	Women (n=45) aged > 40 years with vertebral osteoporosis or osteopenia with and without past vertebral fractures 1. Group 1 (n=15): Øage 68.1 years 2. Group 2 (n=15): Øage 64.2 years 3. Group 3 (n=15): Øage 70.1 years	16 weeks All postural exercises 1. Thoracolumbar corset while awake 2. Weighted kypho-orthosis for 4 h twice daily 3. Exercise alone	Baseline, 8, 16 weeks Primary outcome not specified. Back extensor strength, grip strength, physical activity scale, compliance	Back extensor strength improved significantly within both groups 2 (23%) and 3 (13%), not in group 1. High compliance in the WKO group 2 versus poor compliance in corset group 1
Raeissadat et al., 2014, Iran, Outpatients [12]	Nonrandomized controlled clinical trial	Women (n=31) with vertebral osteoporosis with and without past vertebral fractures, no VF within last 6 months, Kyphosis angle 35–55° 1. Group 1 (n=11): Øage 65.6 years 2. Group 2 (n=20): Øage 62.4 years	4 weeks All advice to walk 30 min daily 1. Weighted kypho-orthosis for 30 min twice daily plus back extensor exercises 2. Back extensor exercises	Baseline, 4 weeks, Primary outcome not specified, functional reach test, TUG, unilateral stance test	Orthosis plus exercise group showed significantly better balance performance on TUG and functional reach test compared with exercise alone.

Schmidt et al., 2012, Germany, community-dwelling patients [13]	RCT	Women (n=69) with vertebral osteoporosis and back pain, with and without previous VF. No acute vertebral fractures 1. Group 1 (n=35): 74.0 ± 8.3 years Number of VF: 1.4 ± 2.0 2. Group 2 (n=34): 74.1±7.7 years Number of VF: 0.9±1.2	6 months 1.Garment orthosis (Osteomed) Daily 2. No orthotic care	Baseline, 3, 6 months, Primary outcome not specified. Gait analysis: force plate in walkway, speed, step length, width. Pain-related limitation in activities (VAS) Compliance	In orthosis group, significant reduction double-support phase of gait cycle and limitation in activity reduced for most restricted 30%. No other changes. Withdrawals due to orthosis discomfort, good compliance retained
Sinaki and Lynn, 2002, USA Outpatients [14]	RCT pilot study	Women (n=7) aged 70–83 years with vertebral osteoporosis, with and without VF, Kyphosis angle 50–65° 1. Group 1 (n=2) 2. Group 2 (n=5)	4 weeks 1. Back extensor exercises 2. Weighted kypho-orthosis daily for 2 h plus back extensor exercises.	Baseline, 4 weeks, Primary outcome not specified. Thoracic kyphosis angle, pain (VAS), physical activity Back, knee, and grip Strength, balance, Computerized dynamic Posturography	Improvements in balance in 3 participants in group 2 with abnormal balance at baseline. Changes in pain, physical activity, and strength across groups

Abbreviations: *VF* vertebral fracture, *QUALEFFO* Quality of Life Questionnaire of the European Foundation for Osteoporosis, *TUG* Timed Up and Go test, *VAS* Visual Analog Scale

Modified according to [15]

These spinal backpack orthoses apply pressure mainly over the shoulders to generate an extension moment about the spine, increase feedback about body position, and improve posture. A more normal spinal alignment could facilitate the activity of trunk muscles during daily activities and explain the increases in back extensor and abdominal flexor muscle strength without the inclusion of specific exercises. Supporting this, an experimental follow-up study found a semirigid backpack orthoses had no effect on strength in women with poor walking ability and with fixed spinal curves [2]. For the orthosis to be effective, an individual may need some ability to change kyphosis angle and be active during wear. Stronger abdominal muscles would help reduce the load on the anterior spinal column and, together with stronger back extensor muscles, could contribute to the improvements in thoracic kyphosis and height seen without the orthosis.

In summary, there appears to be some promise in the use of a flexible backpack orthosis for women with vertebral fractures due to osteoporosis with or without severe hyperkyphosis. These orthoses appear to be well tolerated, being used for relative short periods of the day (2–4 h). Future studies may investigate whether gains in postural stability translate into improvements in clinical balance and the frequency of falls and fractures.

Whether the garment Osteomed orthosis is able to provide benefits is uncertain. Hübscher et al. [10] found back extensor strength increased wearing the orthosis, and earlier work suggests that the sensorimotor stimulation provided by the orthosis helps recruit back extensor muscles and adopt a more erect posture. However, whether the orthosis can increase back strength sufficiently to be clinically relevant is not known. Changes in strength were relatively small, and physical activity levels and quality of life were unaffected. Similarly, whether the small improvement in gait stability reported by Schmidt et al. [13] could increase functional mobility or reduce falls is unknown, since the study may have been underpowered to detect changes. Small improvements in pain were described, in line with previous studies by the same research group. The orthosis has no direct biomechanical effects but provides proprioceptive feedback about posture.

This is in total contrast to the garment Spinomed active orthosis in which a backpad reminds patients to bring themselves in an upright position and thus stimulates especially back extensor strength. A system of belts with Velcros is replaced by textile elements in the garment in order to guarantee similar efficacy with respect to the flexible backpack orthoses Spinomed. As a result, in the corresponding RCT, no significant differences in outcome parameters were observed between Spinomed and Spinomed active. Additionally, high compliance and few complications are reported with flexible backpack orthoses across studies. Compliance was also an issue in studies of garment orthoses. Withdrawals might occur if treatments are perceived as painful, ineffective, or burdensome. Considering this, Dionyssiotis et al. [8] reported lower compliance with garment orthoses, noting that some women had difficulty managing the orthosis when toileting. These facts highlight the importance of fitting and an adequate education of patients. The garment Spinomed active orthosis may be tailored individually according to different body sizes and shapes. This is extremely helpful with respect to compliance.

Furthermore, there is good evidence that using a weighted kypho-orthosis (WKO) combined with an exercise program can improve balance for women with vertebral osteoporosis and increased kyphosis [12, 14]. A WKO has no rigid elements and thus cannot passively correct posture. However, the weight below the scapula creates an extension moment and feedback about alignment. These factors could facilitate back extensor muscles and encourage movements of the center of gravity within the base of support to aid stability. Additionally, in contrast to other spinal orthoses, the WKO has no pelvic strap, thus allowing the individual to recruit hip strategies as part of balance control. Studies in populations with hyperkyphosis also report that a WKO may positively affect balance and reduce the risk of falls. A WKO may improve balance and is a lightweight, comfortable, and relatively inexpensive device that appears to have only few side effects.

Conclusions

This literature search concerning the potential role of orthoses for rehabilitation and treatment of vertebral fractures due to osteoporosis provided no support for traditional rigid thoracolumbar corsets, which were poorly tolerated. In addition, there is some evidence that these rigid corsets may even worsen the condition especially in the long term. Wearing these corsets may result in further loss of muscle mass and strength followed by loss of bone and bone strength. Both together may worsen functional abilities of patients.

On the other hand, flexible backpack orthoses may improve functional capabilities of patients suffering from acute or subacute vertebral fractures due to osteoporosis. These orthoses generate an extension moment about the spine, increase feedback about body position, and improve posture. This results in an improvement in trunk strength, balance, and pain, which is associated with increases in functional capabilities and parameters of quality of life. Especially, individually tailored garment orthoses such as Spinomed active may guarantee high compliance and adherence in the long-term phase of rehabilitation.

Finally, there is good quality evidence that weighted kypho-orthoses (WKO) together with an exercise program may improve balance for women with vertebral osteoporosis and hyperkyphosis. A weight below the scapula creates an extension moment and feedback about alignment. Both factors facilitate back extensor muscles and encourage movement of the center of gravity within the base of support to aid stability. Missing pelvic straps allow patients to recruit hip strategies for improvement of balance control. This may positively affect balance and reduce fall risk.

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Vibration Training as Means to Counteract Age-Related Muscle and Bone Loss

10

Sabine Verschueren, An Bogaerts, and Ekaterina Tankisheva

In the human environment, people are exposed to many kind of vibrations (e.g., in trains, in cars, using motor saws). For a long time, it was thought that vibrations were detrimental for health. However, in recent years several studies have shown that a vibratory stimulus used in a particular way may even enhance health-related parameters. In the early 1970s, Russian scientists elucidated that mechanical vibration of the human muscle was efficient in improving neuromuscular performance [1]. They used vibration training in combination with resistance training to increase muscle strength of the Russian Olympic team.

Vibration training became a hype and was commercialised in Europe in the late 1990s, leading to a wide variety of available vibration systems and applications in fitness, rehabilitation and sports. Soon after that, the first scientific studies appeared to assess the beneficial effects of vibration training on the musculoskeletal system that were put forward by the different vibration platform companies.

What Is Vibration and How Does it Stimulate the Musculoskeletal System?

Vibration is a mechanical oscillatory motion characterised by its biomechanical parameters.

The biomechanical parameters, which define the intensity of the vibrations, are amplitude and frequency, where velocity and acceleration can be derived from. The amplitude of the vibrations is the peak-to-peak displacement of the motion and is expressed in millimetres; the frequency describes the repetition rate of the cycles of the oscillations and is expressed in Hertz (cycles.sec^{-1}) [2].

S. Verschueren, PhD (✉) • A. Bogaerts, PhD • E. Tankisheva, PhD
Research Group for Musculoskeletal Rehabilitation, Department of Rehabilitation Sciences, KU Leuven, Leuven, Belgium
e-mail: sabine.verschueren@kuleuven.be

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Depending on how vibrations are applied on the human body, vibration training can be divided into two categories.

In ‘direct—or local—vibration training’, the muscle belly or tendon is vibrated by a direct contact with the vibrating source, which is held in the hand or fixed to an exterior support [3–6].

In ‘indirect vibration training’, vibrations are transmitted to the body by a vibrating source that does not make a direct contact with the muscles, for example performing a biceps curl with a vibrating lever [7, 8] and whole-body vibration (WBV) training.

Vibration applied directly to the muscle belly or tendon during vibration exercise provokes a phase-oriented discharge from both primary and secondary endings of the muscle spindles [9], which depends on the prestretch of the muscles and increases with muscle length. This muscle spindle discharge elicits in turn the alpha-motoneurons, resulting in a reflexive muscle contraction known as the tonic vibration reflex—TVR [9]. It is well known that the TVR has both monosynaptic (Ia, primary afferents) and polysynaptic (II, secondary afferents) components and thus fosters contractions of the homonymous muscle [10]. The TVR is continuously activated and the muscles contract and relax until the vibration stops [11]. Stretched muscles are more sensitive to vibration stimulation [12] and, therefore, respond to vibration with a stronger contraction [13]. The magnitude of the TVR also depends on the applied vibration frequency [14]. Other mechanisms have also been proposed to explain the effect of vibration stimulation on muscle response as for example an inhibition of the agonist-antagonist co-activation by means of Ia-inhibitory neurons and stimulation of central motor structures [14]. Additional explanations for the higher electromyography (EMG) response during vibration compared to no vibration are an increase in motor-unit synchronisation and/or an increase in the sensitivity of the stretch reflex during vibration [14].

Whole-body vibration (WBV) training is the most common and well-studied training approach. WBV is typically used to stimulate muscle strength and power of lower limbs. During WBV training (Fig. 10.1), static and dynamic exercises, mainly for the lower body, are performed on a platform that generates vibrations with a frequency between 20 and 60 Hz and peak-to-peak amplitudes from 1 to 10 mm. Depending on the posture on the platform (e.g., squat, one-legged squat, etc.), specific muscle groups are trained.

During whole-body vibration, the mechanism of muscle stimulation seems more complicated than the underlying mechanism of the tonic vibration reflex seen by direct vibration on the muscle tendon or belly. The vibration stimulus from the platform is attenuated by the body structures, and the vibration signals that reach the target muscles are considerably reduced.

The muscle response is stronger for the muscles that are closer to the vibration source due to the stronger stimulus [15]. In general, the indirect whole-body vibration stimulation may stimulate more muscle groups at the same time, whereas the effects of directly applied vibration are more localised [7].

Fig. 10.1 Squat on a WBV platform

Until now, two different types of commercially available vibration training platforms are recognised. The first type (e.g., Power Plate®) produces vertical synchronous vibrations (VV—vertical vibrations), and the signal is transferred simultaneously (to both legs at the same time). The second type (e.g., Galileo®) produces side-alternating vibrations (RV—rotational vibrations) and delivers the signal asynchronous (first to one leg and then to the other one) which results in an asymmetric perturbation of the legs. It is still a matter of debate which type of platform induces higher muscle activation and results in better training effects. It is suggested that higher peak accelerations can better be tolerated when side-alternating vibrations are applied as a result of the rotational movements around the pelvis and lumbar spine, which diminish the transmission of the signal to the trunk [16, 17]. However, it should be taken into account that RV devices often employ lower frequencies compared with VV devices and those lower frequencies are considered as unsafe due to the possible body resonance [18]. Body resonance may occur when the applied vibration frequency reaches the natural resonance frequency of the human body (natural frequency is determined by the stiffness and mass of the human body) and could be harmful to the body [19].

Immediate Effects of WBV on Muscle Activity

Several studies have tried to evaluate the WBV training stimulus from an efficacy perspective and therefore have demonstrated immediate effects on leg muscle activity during vibration stimulation [13, 20–23]. Muscle activation during vibration may be measured by recording the EMG signals of different target muscles. Most of the vibration studies used surface electromyography to measure muscle activity during whole-body vibration. EMG signals can be used to verify if different vibration parameters (amplitude, frequency) result in different muscular responses.

In our laboratory we showed that vertical WBV exposure can induce an increase in muscular activity of numerous muscles, including rectus femoris, vastus medialis, vastus lateralis and gastrocnemius when a frequency of 35 Hz and amplitude of 2.5 mm was applied [23]. Greater muscle activation was found when a one-leg squat (knee angle of 125°) was performed compared with a high squat (125°) and a low squat (90°) (Fig. 10.2).

In a study of Abercromby and colleagues, the effects of two different commercially available platforms with the same vibration parameters (30 Hz, 4 mm) were tested, and the main outcomes showed that vertical vibrations led to significantly greater muscle responses of vastus lateralis and gastrocnemius than rotational vibrations, whereas muscle activation of tibialis anterior was higher when rotational vibrations were applied [20]. Cardinale and Lim studied the neuromuscular responses to three different vibration frequencies −30, 40 and 50 Hz—in a group of professional female volleyball players while performing a half-squat position on the vibration platform (knee angle 100°) [13]. The findings of that study reported an increase in muscle activity of vastus lateralis compared with no vibration. The highest muscle response of vastus lateralis was found when a frequency of 30 Hz was applied in comparison to 40 and 50 Hz.

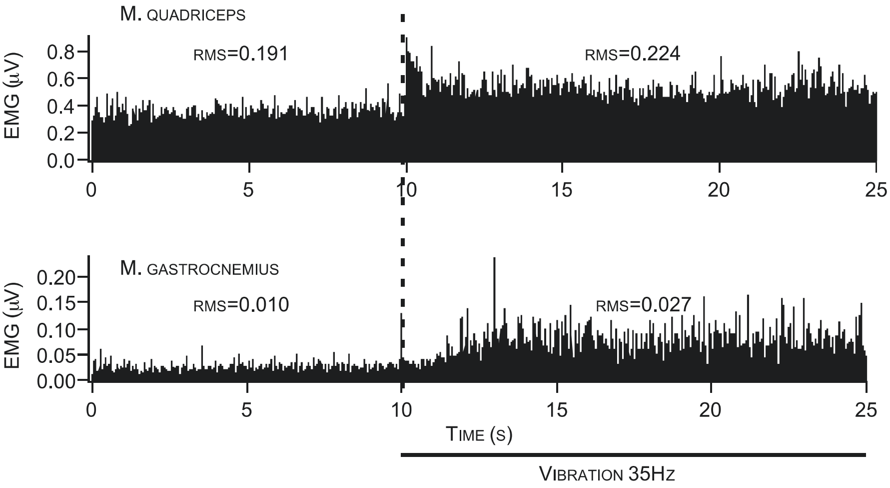

Fig. 10.2 EMG activity of the quadriceps and gastrocnemius muscle in a representative subject while performing a squat with and without vibration (starting after 10 sec); unpublished data

In contrast to the previous studies, Pollock et al. [22] demonstrated that higher amplitude vibration and higher frequencies are associated with greater EMG responses compared to no vibration. WBV training (RV platform) was performed at frequencies between 5 and 30 Hz at high (5.5 mm) and low (2.5 mm) amplitudes, and EMG signals of several lower-limb muscles were recorded. Likewise, Hazell et al. reported a significantly greater muscle response of vastus lateralis, biceps femoris and tibialis anterior when frequency of 45 Hz was applied compared with 25 Hz and 35 Hz [21]. WBV included 25, 35 and 45 Hz frequencies with 4-mm amplitude, and a series of dynamic squats (unloaded with no WBV, unloaded with WBV, loaded with no WBV and loaded with WBV) were performed.

In general, the presented vibration studies applied different vibration frequencies and amplitudes and different EMG filtering. Therefore, it remains unknown which vibration parameters elicit the most beneficial muscle activation; some studies reported that a frequency of 30 Hz is recommended to induce a higher muscle response, while others reported a significant frequency effect, in which the 45 Hz frequency elicited significantly greater muscle activity than lower frequencies.

Effects of Whole-Body Vibration Training on Muscle Strength/Mass, Cardiovascular Fitness, Bone Density and Postural Control in the Older Population

In the following literature overview, we will summarise the effects of WBV training on muscle and bone parameters that have been reported by now, with a main focus on the elderly population. Some research groups assessed the effects of vibration training on different patient populations (Parkinson, stroke, MS, etc.); however, these studies will not be covered in this chapter.

Muscle Strength/Mass

The increased muscle activity during vibration training caused by the TVR, leading to a mechanical overload, may result in improvements in neuromuscular parameters after long-term WBV training. For obtaining increases in strength by WBV, it is evident that the load of a WBV training programme, determined by training volume and training intensity, must be high enough to create an overload on the muscle, resulting in a supercompensation situation, which can end in an increased force-generating capacity. In general, the training load of a WBV programme is low at the beginning but increases gradually according to the ‘overload’ principle [24]. Training volume can be increased by increasing the duration of one vibration session, the number of series per exercise or the number of different exercises. Training intensity can be increased by shortening the rest periods between the exercises, increasing the amplitude and/or frequency of vibration and increasing the load on the muscles (e.g., by changing the execution form from two-legged to one-legged exercises).

Several studies evaluated the effects of long-term WBV training, on muscle strength in the elderly population (Table 10.1). We will go into some of those studies in more detail.

Table 10.1 Whole-body vibration training in elderly—studies focussing on strength

Study	Age (years)	Population	Frequency (Hz)	Amplitude (mm) or acceleration (*g*)	Platform	Duration	Outcomes
Bautmans, 2005 [45]	77.5	Nursing home residents	30–50	2–5 mm	VV	6 weeks (3x/wk)	No changes in isokinetic leg extension
Bogaerts, 2007 [25]	67.3	Community-dwelling men	35–40	2.5–5 mm	VV	1 year (3x/wk)	An increase in jump performance, isometric knee-extension strength, thigh muscle mass
Machado, 2010 [26]	79	PMW	20–40	2–4 mm	VV	10 weeks (3–5x/wk)	No changes in isotonic muscle strength An increase in isometric muscle strength and in thigh muscle cross-sectional area
Roelants, 2004 [24]	58–74	PMW	35–40	2.5–5 mm	VV	6 months (3x/wk)	An increase in CMJ, isometric and isokinetic muscle strength
Russo, 2003 [29]	60.7	PMW	12–28	NR	RV	6 months (2x/wk)	An increase in muscle power No changes in bone characteristics

Study	Age (years)	Population	Frequency (Hz)	Amplitude (mm) or acceleration (*g*)	Platform	Duration	Outcomes
Trans, 2009 [27]	60.4	Female patients, diagnosed with knee osteoarthritis	30–35	NR	VV	8 weeks (2x/wk)	An increase in isometric knee-extension strength
Verschueren, 2011 [37]	70	PMW, + vitamin D	30–40	1.6–2.2 *g*	VV	6 months (3x/wk)	No muscle hypertrophy of the lower limb
Von Stengel, 2012 [28]	68.5	PMW	25–35	1.7–2 mm	NR	18 months (2x/wk)	An increase in isometric extension strength but no additive effects compared to the same exercises without vibration

Note: *CMJ* countermovement jump, *NR* not reported, *PMW* postmenopausal women, *RV* rotational vibrations, *VV* vertical vibrations (Tankisheva, unpublished summary table thesis)

In community-dwelling postmenopausal women (58–74 years), we performed a 6 months WBV training study [24]. Eighty-nine postmenopausal women were randomly assigned to a WBV group (n = 30), a resistance training group (RES, n = 30) or a control group (n = 29). The WBV group and the RES group trained three times a week for 24 weeks. The WBV group performed unloaded static and dynamic knee-extensor exercises on a vibration platform (35–40 Hz, 1.7–2.5 mm, total duration 3–30 min). The RES group performed dynamic leg press and leg extension exercises increasing from low (20 repetitions maximum (RM)) to high (8RM) resistance. The control group did not participate in any training. *Isometric and dynamic knee-extensor strength* increased significantly in the WBV group by 15.0% and 16.1%, respectively, and in the RES group by 18.4% and 13.9%, respectively, after 24 weeks of training, with the training effects not significantly different between these groups. Countermovement jump height enhanced significantly in the WBV group by 19.4% and in the RES group by 12.9% after 24 weeks of training. Most of the gain in knee-extension strength and speed of movement and in countermovement jump performance had been realised already after 12 weeks of training. The results of WBV were thus comparable with those achieved by conventional resistance training. As can be seen in Table 10.1, several later studies, in different age categories, also found significant increases in isometric knee-extension strength [25–28]. The additional effect of vibration training compared with the same exercises performed without vibration did however not reach significance in the study of von Stengel [28].

Russo et al. [29] found an improved *muscle power and velocity of movement* in older women after 6 months WBV (10–28 Hz, 3x 1–2 min, 2x/week).

Most studies suggest that especially untrained or older individuals with low fitness levels could benefit from WBV. This assumption is supported by a review article of Rehn et al. [30]. Nine of the 14 analysed WBV studies reported an increase in leg strength or power, whereby eight of these studies included untrained or elderly subjects.

In a meta-analysis of 13 RCTs, it was concluded that **whole-body vibration is beneficial for enhancing leg muscle strength among older adults** [31]. More specifically they found a significant treatment effect on knee-extension dynamic strength (standardised mean difference = 0.63), leg extension isometric strength (standardised mean difference = 0.57) and functional measures of leg muscle strength such as jumping height (standardised mean difference = 0.51) and performance in sit-to-stand (standardised mean difference = 0.72) among older adults compared with no intervention.

As such, WBV training in older community-dwelling women appears to be a safe, suitable and efficient strength training method with a low starting threshold for those who are not attracted to or not able to perform conventional resistance training. The major part of the subjects who followed a WBV training programme was very enthusiastic and motivated to continue after the end of the study, indicating that WBV has a potential for application in the geriatric and therapeutic sector [24].

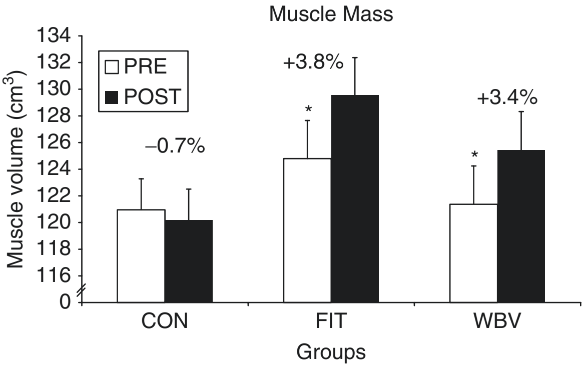

Fig. 10.3 Muscle mass in the control group (CON), the fitness training group (FIT) and whole-body vibration group (WBV) at baseline (PRE) and 1 year later (POST). *Significant pre-post difference within group ($p < 0.05$); adapted from Bogaerts et al. 2007 [25]

Several studies have assessed the effect of WBV on **lean body mass** (LBM), as measured with DXA, and did not find any effect of WBV training. For example, in our study in 2004 [32], after 6 months of vibration training, increases in maximum strength were reported, but no changes occurred in the total body LBM. In a study of von Stengel [28], increases in LBM were found both for a training group with vibration as a group that performed similar exercises without vibration. However, the effect of resistance training on LBM was not enhanced by the addition of a vibration stimulus.

In contrast, in studies in which local muscle mass was determined with CT scan, increases in muscle mass at the thighs were reported [25, 26], which indicates that the effects of WBV training on muscle mass might be rather site specific. In our 1-year training study, we assessed the effects of WBV training on the muscle mass of the upper leg measured by CT. We compared the results of the WBV group (n = 31, 67.3 ± 6 0.7 years) with those of a fitness (FIT) group (n = 30, 67.4 ± 0.8 years) and a control (CON) group (n = 36, 68.6 ± 0.9 years). Muscle mass increased significantly in the WBV group (3.4%) and in the FIT group (3.8%) with the training effects not significantly different between the groups. No significant changes were found in the CON group (see Fig. 10.3).

Cardiovascular Fitness

Almost no studies assessed the effects of vibration on cardiovascular fitness. In one of our studies [33], 220 community-dwelling adults (mean age 67.1 years) were randomly assigned to a WBV group, fitness group or control group. The WBV group exercised on a vibration platform, and the fitness group performed cardiovascular, resistance, balance and stretching exercises. The control group did not participate in any training. To investigate whether WBV might be a cardiovascular stimulus in that population, we assessed HR during training. Heart rate increased significantly up to 62% of heart rate reserve (HRR) in a traditional vibration session and up to 80% of HRR in a more dynamic training session, in which 15 s of traditional

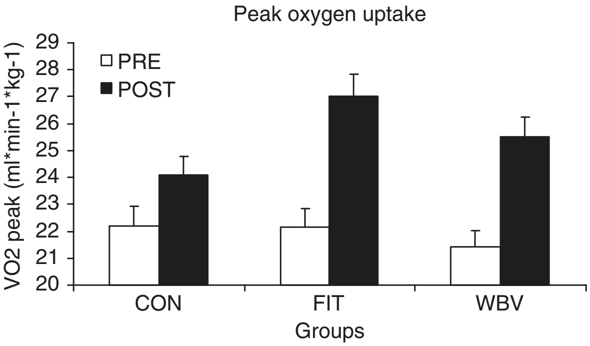

Fig. 10.4 VO2 peak in the control group (CON), the fitness training group (FIT) and whole-body vibration group (WBV) at baseline (PRE) and 1 year later (POST). *Significant pre-post difference within group ($p < 0.05$); adapted from Bogaerts et al. 2009 [33]

standing exercises on the platform was alternated with 15 s stepping on and off the vibrating platform. After 1 year of training, peak oxygen uptake (VO2peak) and time-to-peak exercise (TPE) as measured during progressive bicycle ergometry increased significantly both in the WBV and fitness groups. Both training groups improved similarly in VO2peak (see Fig. 10.4). The fitness group improved significantly more in TPE than the WBV group.

Bone Density

Rubin showed in animals that exposure to high-frequency (30 Hz) and low-amplitude (0.2 g) vibrations may lead to an improved quality and quantity of the bone [34]. Based on these results, WBV training with its high-frequency (25–60 Hz) and high-amplitude (1–10 mm) stimulation was put forward as a potential tool in the prevention and/or treatment of osteoporosis.

We performed a study of 6 months WBV training (35–40 Hz, 2.02–5.09 g, 3–30 min, 3x/week) in postmenopausal women (age, 58–74 years) that were randomly assigned to a whole-body vibration training group (WBV, n = 25), a resistance training group (RES, n = 22) or a control group (CON, n = 23) [32]. The WBV group and the RES group trained three times weekly for 24 weeks. As mentioned before, the WBV group performed static and dynamic knee-extensor exercises on a vibration platform. The RES group trained knee extensors by dynamic leg press and leg extension exercises, increasing from low (20 RM) to high (8 RM) resistance. The CON group did not participate in any training. We found a net gain of 1.5% in hip bone density (measured on DXA), compared to a control group that did not follow an exercise intervention. No changes in hip BMD were observed in women participating in resistance training or age-matched controls (−0.60% and −0.62%, respectively; not significant). Serum markers of bone turnover did not change in any of the groups.

Similarly, Gusi reported an increased bone density in older women following 8 months of low-frequency WBV training (12.5 Hz, 3 mm, 3–30 min, 3x/week) [35]. Because of the lack in change in bone density of the lumbar spine, a local effect of vibration training was suggested. In a 1-year prospective randomised placebo-controlled trial of Rubin and co-workers, daily exposure to high-frequency (30 Hz), low-magnitude (2 mm) mechanical signals in postmenopausal women inhibited the decline in bone mineral density of the hip and spine that normally follows menopause [36].

In a later study on an older population (113 institutionalised elderly females aged >70 years), we did not find any additional effect of WBV on hip BMD compared with vitamin D supplementation [37]. Because of the old age of the study population, the intensity and volume of the WBV programme was increased very carefully and relatively slowly to avoid major overload of the musculoskeletal system. The intensity and volume of the programme was clearly lower than in previous studies and may probably thus not have allowed the optimisation of the bone response. Also, the amplitude of the vibrations remained lower (<2.2 g). Several other studies could also not show improvements in bone density in elderly, which could possibly be explained by the insufficient loading of the skeletal system (e.g., by a too low vibration amplitude or too low training frequency) [29, 38].

In a recent study on the effects of WBV on the *bone quality* in osteopenic women as assessed by HR-pQCT of the tibia, WBV did not lead to measureable improved bone quality in osteopenic postmenopausal women after 12 months of training compared to controls [39]. Slatkovska et al. [40] performed a 1-year trial using low-magnitude vibration (0.3 g) at 90 or 30 Hz (thus a different vibration training protocol with higher frequency and lower amplitude and vertical vibration) with postmenopausal women and did also not find changes in bone structure measured by HR-pQCT.

In the systematic review of Merriman [41] and the later meta-analysis of Slatkovska [42], the conclusion on the effects of WBV on the bone is that the evidence provided suggests that **WBV may improve or maintain bone density at the hip but not at the lumbar spine**. Both vertical and rotational vibration might be effective, but a dose-response relationship appears to exist, with studies with longer exposures and higher compliance to training demonstrating the most consistent evidence. However, a more recent meta-analysis of Lau in 2011 [31] concluded that data so far suggest that **whole-body vibration has no overall treatment effect on bone mineral density in older women**. The discrepancy may lie in inclusion and combination of different papers into the analysis and slightly different methods for doing the meta-analysis. It needs to be mentioned that the differences in training protocols applied in the different studies as well as different outcome measures make comparison of results of different studies very difficult. Where a meta-analysis can be performed separately on different outcomes, it still combines studies in which different training protocols are tested (frequencies, amplitudes, duration of vibration in one session, etc.).

Postural Control and Risk of Falls

As mentioned above, a relevant number of WBV studies have examined the effects of vibration training on various aspects of lower-limb muscle strength among different populations [25, 26, 32]. Neuromuscular performance is highly related to body balance and mobility function [43], and this, together with the evidence that vibration can improve proprioceptive function [44], could explain why vibration exercises might also benefit balance and risks of falls. Therefore, in the next paragraph, we will focus on studies that have assessed effects of WBV on postural control and risk of falls.

In older individuals including postmenopausal women or community-dwelling adults, WBV training appears to improve specific aspects of postural control [25, 32, 45]. Postural control was assessed via different balance tests for dynamic balance (timed up-to-go test, sensory organisation test, tandem walk test chair rising) [25, 45–48], static balance (balance master system, balance index, posturography on force plates) [46, 49, 50] and functional balance (Tinetti test) [45, 48].

In frail institutionalised elderly (mean age 77.5 year), Bautmans et al. [45] showed significant improvements in balance and mobility measures after 6 weeks WBV (35–40 Hz, 2–5 mm, 3x30–45 sec, 3x/week), but failed to show improvements in knee-extensor muscle strength. Runge et al. [51] found an improvement of 18% in chair-rising time in a geriatric population after 2 months of WBV (27 Hz, 7–14 mm, 3x2 min, 3x/week), and Bruyere et al. [45] reported enhancements in gait, balance and time to get up and go performance after 6 weeks WBV (10 or 26 Hz, 3 mm, 4x1 min, 3x/week) combined with physical therapy.

However, findings have again been inconsistent, with no effect of WBV on dynamic and static postural control in several other studies [15, 47, 50, 52]. The meta-analysis of Rogan et al. [53] on the effects of WBV on postural control in the elderly showed thus not unexpectedly only weak to moderate evidence as a result of either vertical or rotational vibration training on static, dynamic and functional balance. Thus firm and clear conclusions concerning the most beneficial protocol for improvement of postural control cannot be made at this stage.

Effects of Local Vibration Training on Muscle Strength/Mass and Bone Density

Whole-body vibration may not be an adequate training method for a large segment of the adult's populations including frail elderly, adults that are in a wheelchair or bedridden individuals and patients with knee osteoarthritis who are unable to stand on a whole-body vibration platform. These older adults have a high risk for osteoporosis and sarcopenia and, thus, are at high risk for falls and fractures. Therefore, a different form of vibration training—local vibration training—can be applied in an attempt to broaden the impact of vibration intervention to frail elderly.

So far, most studies reported the beneficial effects of WBV on muscle performance, whereas only very few research groups studied the possible beneficial effects of locally applied vibrations on muscle performance [54, 55]. Pietrangelo et al. studied the effects of locally applied vibrations on the thigh muscles in male and female elderly diagnosed with sarcopenia [54]. Vibration application at frequency of 300 Hz lasted 12 weeks/1–3x/wk for 15 min. The researchers showed an improvement in isometric muscle strength, which was higher in the female than in the male participants. Brunetti et al. have shown that vibration of three applications (of 10 min) every day over three consecutive days on the quadriceps enhances the single-limb stability in young male patients with anterior cruciate ligament (ACL) reconstruction (100 Hz, < 20 μm) [55]. Balance control was assessed using the centre of pressure from a force plate, and the centre of pressure averaged speed (mm/s) was estimated. Whether this improved balance due to local vibration would also hold in an older population remains to be determined.

In a recent pilot study performed in our lab, we investigated the effect of 6 months local vibration training on bone mineral density, muscle strength, muscle mass and physical performance in postmenopausal women (66–88 y) [56]. The study was organised as a randomised controlled trial for postmenopausal women who lived in daily care service flats and rest homes.

Thirty-five postmenopausal women were randomly assigned to either a vibration (n = 17) or a control group (n = 18). The vibration group received a 6-month local vibration treatment with custom-made shakers (30 and 45 Hz, 1.71–3.58 g). The vibration was applied on the mid-thigh and around the hip in supine lying position once per day, 5 days/week. Overall, the results showed a net benefit of 13.84% in isometric muscle strength at 60° knee angle in favour of the vibration group compared to the control group. However, no significant changes in bone mineral density (measured with DXA), muscle mass (measured on CT scan) or physical performance (measured by modified physical performance test) were found in both groups.

Six months of local vibration training improved thus some aspects of muscle strength, but had no effect on bone mineral density, muscle mass and physical performance in postmenopausal women. The specific vibration protocol used in the present study can be considered as safe and suitable for a local vibration training programme; however, future larger studies are needed to further assess the potential of local vibration training.

Conclusion and Practical Applications

Based on the above, WBV training can be put forward as an efficient training method for enhancing muscle strength, muscle mass and some aspects of postural control and cardiorespiratory fitness in community-dwelling older men and women. Most of the improvements found were comparable (not superior) with the gains found after an equal number of fitness/resistance training sessions. With respect to the effects of WBV on bone density, several meta-analyses come to opposite conclusions, so further study is warranted.

These positive results, the low training load during WBV, the low dropout rate and the easy way to master, create a potential for WBV training as an efficient alternative for fitness training in community-dwelling older individuals. However, this does not imply that every community-dwelling older person has to set up a vibration platform at home. Because of the strict in- and exclusion criteria for participation in a WBV programme, approval of the general practitioner is essential. Additionally, WBV training must always be performed under the supervision of a professional instructor. Furthermore, as a variety of vibration platforms are available with a wide range in cost prices, people must be informed about the differences in the quality of the vibration stimulus between these platforms.

The positive effects found in community-dwelling individuals are not yet confirmed in more frail, institutionalised elderly women. We could for example only show a surplus value of vibration training upon calcium and vitamin D supplementation in the enhancement of functionality parameters [37]. Up to now, we cannot recommend WBV training as an efficient training method in the enhancement of musculoskeletal parameters in institutionalised older women. Also in this specific population, group sessions are not appropriate. Due to safety concerns, these frail subjects require individual coaching. However, the very high compliance rate, the low dropout rate and the enthusiasm of the subjects underscore the feasibility of WBV training also in this geriatric population.

To conclude we can say that sufficient evidence is available on the benefits of WBV on the musculoskeletal system in general, but that additional studies are needed to determine safe and most effective parameters for WBV in older adults [41].

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Application of Electrical Modalities on Muscle Stimulation

11

Wolfgang Kemmler and Simon von Stengel

Introduction

Physical activity and especially physical exercise are considered as cornerstones of musculoskeletal health [1, 2]. Recent studies [3, 4], however, indicate that a training frequency of at least 2 h/week/year must be generated and maintained in order to achieve relevant positive results for maintaining or increasing muscle or bone mass in older adults. This need for high training frequency, however, collides with the (low) sports participation rates of older adults [5]. Although the sports participation level has slightly increased [6] for the elderly population, surveys demonstrated that less than a quarter of women 70 years and older, which may be the most prominent risk group for sarcopenia and osteoporosis, regularly "exercise" [5]. Moreover, in a lifelong "sport-abstinent" cohort of subjects, the willingness and insight to start regular and intense exercise programs are rather limited. However, from a socioeconomic point of view, it is important that "exercise programs" dedicated to this target group be developed. "Alternative" training technologies, such as whole-body vibration (WBV) or even more promisingly whole-body electromyostimulation (WB-EMS), which are able to amplify light exercise stimuli to an effective degree [7], may be a time-effective, customizable, and joint-friendly option, especially for older, less sport-affine, and/or vulnerable subjects.

Despite its promising potential, in contrast to whole-body vibration technology with its considerable amount of recent studies, there is hardly any international research into whole-body electromyostimulation (WB-EMS). Therefore, this

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W. Kemmler, PhD (✉) • S. von Stengel, PhD
Department of Medical Physics and Sports Sciences, University of Erlangen,
Henkestrasse 91, Erlangen 91052, Germany
e-mail: wolfgang.kemmler@imp.uni-erlangen.de

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chapter addresses the potential of WB-EMS for impacting “musculoskeletal risk factors” of the elderly based on selected randomized controlled trials of our research group.

Overall Methodology

All the studies listed here [8–11] are randomized controlled trials (RCTs) in a single-blinded, parallel-group design. The studies were all reviewed and approved by the Ethics Committee of the Friedrich-Alexander University Erlangen-Nuremberg and—in the case of radiation-relevant outcomes—by the Federal Bureau of Radiation Protection. After detailed information all participants gave their written informed consent. The TEST investigations are reported and registered at www.clinicaltrials.gov as RCTs.

WB-EMS Intervention

In contrast to the classical local application, whole-body electromyostimulation (WB-EMS) exercises considerably larger areas. The vest and cuff electrodes of the WB-EMS technology (Miha bodytec, Gersthofen, Germany) used in our studies allow simultaneous but dedicated control and innervation of 8–10 muscle groups with a total electrode area of up to 2800 cm^2 (Fig. 11.1).

From the multitude of possible compositions of the current parameters (impulse type, frequency, duration, width, and rise), we applied a similar protocol in all studies that was based on bipolar pulse mode. Based on the available literature, the stimulation frequency was selected at 85 Hz [12, 13], the impulse width at 350 μs [12], and the impulse rise as direct (rectangular application) [14]. Impulse duration

Fig. 11.1 WB-EMS equipment (Miha bodytec, Gersthofen, Germany)

ranged between 4 and 6 s with a 4-s break between the impulses. However, in two trials (TEST I and II), an adjuvant continuous 7 Hz-WB-EMS program was applied. Total exercise duration of a session (with breaks) was 18–25 min, taking into account the setup time for WB-EMS a typical session lasted not more than 30 min. Of importance, the equipment used allows a dedicated intensity of the current per muscle group addressed (Fig. 11.2).

Unfortunately, we are unable to prescribe the exact stimulation intensity (in mA) due to regional and individual disparities of current sensitivity. Thus, to achieve an adequate intensity of the EMS application, participants were requested to exercise at a rate of perceived exertion (RPE) between "somewhat hard" and "hard" (see below) (Table 11.1).

Exercises were carried out in a dynamic mode without additional weights

The number of repetitions per exercise varied between 6 and 8 repetitions per set, with 1–2 sets/exercise being performed. As mentioned above, based on our intensity requirements, the EMS application should be perceived as "strenuous (hard) to very strenuous (very hard)" (RPE 5–7 on the 10-step (cr10) Borg Scale [15]).

Fig. 11.2 WB-EMS operator device (Miha bodytec, Gersthofen, Germany)

Table 11.1 Exercises performed during WB-EMS (examples)

Exercise	Primary loaded region
1. Squat, arm flexion, and extension	Leg extensors, flexors, buttocks, arm flexors, extension
2. Squat and crunch	Leg extensors, flexors, buttocks, abdomen
3. Squat, latissimus pulleys (down) und shoulder press (up)	Leg extensors, flexors, buttocks, arm flexor, arm extensor, shoulder, chest, upper back
4. Squat, butterfly (down) und reverse fly (up)	Leg extensors, flexors, buttocks, chest, upper back
5. Lunges, chest press, and vertical rowing	Leg extensors, flexors, buttocks chest, upper back

Measurements and Test Procedures

The status of each participant (WB-EMS or control group) was not apparent for the investigators; corresponding questioning was not allowed. Measurements at study start and for follow-up were always performed and evaluated by the same researcher at the same time of day (±2 h).

Statistical Procedures

In all studies, a formal sample size analysis appropriate for the primary study endpoint was calculated. The intention-to-treat (ITT) principle, the completer analysis, and the per-protocol method were used to analyze the data of the trials. Baseline values are reported as means and standard deviations. Within-group changes between baseline and follow-up were reported as relative changes (text) or absolute changes (tables). Depending on the data distribution, analysis of variance with repeated measures, *t*-tests, and corresponding parameter-free methods were used. The distribution of data was always tested graphically and statistically. A significance level of $p < 0.05$ is considered significant. Effect sizes were calculated using Cohen's *d* [16]. SPSS versions 16.0–21.0 (SPSS Inc., Chicago, IL, USA) were used for all statistical procedures except for the ITT analysis and the multiple imputation performed in TEST V.

Study 1

Training Und Electromyostimulation Trial I (TEST I) [8]

Motivation and Study Aim

The aim of this pilot study was to detect the effect of WB-EMS training on body composition, physiological and functional parameters, as well as on feasibility and participant acceptance in older women with considerable exercise training experience. Our hypothesis was that an adjuvant WB-EMS training significantly increases the effects of conventional multifunctional exercise training [17] on (a) muscle mass, (b) fat mass, and (c) muscle strength.

Methodology

The TEST I (Training and Electromyostimulation) study is a randomized, controlled, single-blinded intervention study over 14 weeks. The study was conducted from February to August 2008 at the Institute of Medical Physics.

Study Endpoints

- Lean body mass (LBM)
- Body fat mass
- Maximum isometric trunk (back) and leg extensor strength

Table 11.2 Baseline characteristics of the TEST I study groups

Variable	WB-EMS ($n = 15$)	CG ($n = 15$)
Age [years]	65.6 ± 5.6	63.3 ± 5.4
BMI [kg/m^2]	26.1 ± 4.4	24.7 ± 2.6
Lean body mass (LBM) [kg][a]	40.7 ± 4.1	41.1 ± 3.4
Energy intake [kJ/day][b]	7689 ± 1722	7824 ± 1640
Vitamin-D intake [μg/day][b]	6.4 ± 2.1	7.1 ± 2.4
Exercise volume [min/week]	179 ± 58	147 ± 43

[a] Via skinfold thickness [18]

[b] Via four nutritional analyses

Participants

Thirty women 60 years and older (64.5 ± 5.5 years) from the Erlangen-Nuremberg region with more than 3 years' training experience in conventional resistance exercise training were randomly assigned to a WB-EMS exercise group ($n = 15$) or a non-EMS-exercising control group ($n = 15$). Both groups maintained their conventional exercise training, however.

Exclusion criteria were epilepsy, cardiac pacemaker, serious circulatory disorders, abdomen/groin hernia, tuberculosis, cancer, serious neurological disturbances, inflammatory diseases, bleeding tendencies, medication or diseases affecting muscle metabolism, inflammatory diseases, tuberculosis, tumor, severe neurological disorders, and large-scale skin injuries in the area of the electrodes. Table 11.2 shows the initial characteristics of the groups.

Intervention

While the control group (CG) maintained their intense physical training (two sessions of 60 min; two home-training sessions of 20 min) described in detail elsewhere [17, 19], the treatment group (WB-EMS) additionally performed a 14-week EMS program with EMS application every 4–5 days (three training sessions in 2 weeks) with the strain parameters given above.

Measurements

Anthropometry

Body height, weight, and circumference values of the subjects were measured using calibrated devices. The muscle mass was indirectly measured via resting metabolic rate (RMR) as assessed by spirometry [20, 21]. The RMR was measured after 12 h of fasting and with 24-h abstinence of heavy physical activity between 7:00 and 9:00 during the last 15 min of a 30-min rest lying in a supine position. The measurement was carried out using mobile spirometry (Viasis, Conshohocken, USA).

For the determination of body fat and fat-free mass, the skinfold thickness at different body areas was measured using a calibrated caliper (Lange, Cambridge, USA). Tests were performed twice, and the mean value of both tests was included in the analysis. Based on these data, body composition parameters were calculated using the 7-point skinfold method suggested by Durnin-Womersley [18].

The maximum isometric strength of the trunk and leg extensors was evaluated by a "Schnell m3-tester" (Schnell, Peutenhausen, Germany) as per the test protocol of Tusker [22].

A detailed questionnaire was used to assess well-being, pain frequency, and intensity at different skeletal sites, prestudy exercise levels, normal daily activity levels, diseases, and medication. The follow-up questionnaires also contained sections to monitor disease incidence, changes in disease severity and intake of medication, lifestyle changes, or sport activities outside the TEST training program.

Statistical Procedures

The formal sample size analysis of the TEST I study was based on the parameter "resting metabolic rate" (RMR). An intention-to-treat (ITT) analysis was performed, in which all the participants were included with baseline data.

Results

All the participants were able to complete the training according to the protocol. The attendance rate for the conventional training protocol was comparable between the groups and ranged at 81%. The corresponding rate for the WB-EMS training attendance was 98%. The mean overall intensity of the EMS application over the intervention period was rated by the participants as "hard" to "very hard" (6.0 ± 0.5 on the cr10 Borg Scale [15]).

During the intervention period, no adverse events or changes occurred that may affect our results.

Table 11.3 listed the results of the ITT analysis for the study endpoints.

In summary, our hypotheses (a–c) cannot be fully confirmed. Based on (a) muscle mass, the two assessment methods showed slightly different results. Only the caliper tests [18] resulted in a marginally significant difference between WB-EMS and the control group which maintained its conventional exercise training (CG). Although our results showed a strong tendency for more favorable changes of body fat mass in the WB-EMS group, our hypothesis (b) cannot be verified, while for (c) muscle strength, our hypothesis can be fully confirmed.

Summary and Conclusion of the TEST I Study

The aim of the present study was the general evaluation of the effectiveness, feasibility, and acceptability of WB-EMS in elderly women with considerable experience in (resistance) training and correspondingly pronounced perceived exertion appraisal. The study design prescribed an adjuvant WB-EMS application in parallel to an intense, conventional multipurpose exercise training protocol focusing on muscle strength. Particularly noteworthy appears that the adjuvant WB-EMS training generated (significant) positive effects on muscle and body fat even in this powerful cohort of elderly females with high baseline fitness levels. Moreover, muscle strength was also significantly improved by the WB-EMS application, whereas no

Table 11.3 Baseline values, intragroup changes, and intergroup differences for resting metabolic rate (RMR) and lean body mass and strength

	WB-EMS (n = 15) ((MV ± SD)	CG (n = 15) (MV ± SD)	Difference MV (95% CI)	p	ES
Resting metabolic rate RMR (kcal/h)					
Baseline	61.6 ± 10.6	60.0 ± 9.7	–	–	–
Difference (p)	−0.1 ± 4.8 (.991)	−3.2 ± 5.2 (0.038)	−3.2 (−7.0–0.6)	0.095	0.62
Lean body mass [kg][a]					
Baseline	41.78 ± 4.58	43.60 ± 4.80	–	–	–
Difference (p)	0.17 ± 0.75 (.388)	−0.40 ± 0.78 (.060)	0.56 (0.11–1.11)	0.046	0.75
Body fat mass [%][a]					
Baseline	34.78 ± 5.40	33.62 ± 7.47	–	–	–
Difference (p)	−1.12 ± 1.8 (0.031)	−0.01 ± 1.50 (0.974)	1.10 (−0.13–2.33)	0.077	0.67
Isometric maximum strength trunk extensors [N]					
Baseline	116.3 ± 33.8	119.5 ± 40.0	–	–	–
Difference (p)	11.5 ± 12.8 (0.015)	−7.6 ± 12.2 (0.054)	−19.2 (−32.4–6.0)	0.006	1.53
Isometric maximum strength leg extensors [N]					
Baseline	827 ± 209	889 ± 191	–	–	–
Difference (p)	80 ± 77 (0.001)	−40 ± 90 (0.106)	−121 (−184–57)	0.001	1.43

[a] Results of the ITT analysis via skinfold thickness [18]

corresponding significant effects were determined for the CG. Finally, the exceptionally high attendance rate of the WB-EMS group indicates excellent acceptance of this alternative training technology. The main limitations of this study, however, were the suboptimal evaluation methods of body composition that resulted from applying the gold-standard procedure "dual-energy X-ray absorptiometry" (DXA) in TEST II and III.

Study 2

Training Und Electromyostimulation Trial II (TEST II) [9]

Motivation and Study Aim

The primary goal of TEST II study was to determine the effect of WB-EMS on body composition in males with the metabolic syndrome 65 years and older. Our hypothesis was that WB-EMS training was significantly more favorable for positively affecting (a) (appendicular) muscle mass, (b) body fat mass, and (c) muscle strength/aerobic capacity compared with whole-body vibration training (control group).

Methodology

The TEST II study is a randomized, controlled, single-blinded intervention study over 14 weeks. The study was conducted from March to October 2009 at the Institute of Medical Physics (IMP) of the FAU.

Study Endpoints

- Appendicular skeletal muscle mass (ASMM)
- Abdominal (AF) and total (TF) body fat mass
- Maximum isometric strength of the trunk and leg extensors and maximum aerobic capacity (VO_2peak)

Participants

After applying the inclusion criteria, (a) male, age 65–75 years; (b) metabolic syndrome according to International Diabetes Federation [23]; and (c) largely untrained with respect to strength and endurance training (< 1 h/week) and exclusion criteria for WB-EMS (above) and WBV application (e.g., endoprostheses, retina diseases), 28 men were enrolled in the study (Fig. 11.1). Stratified for age, participants were randomly assigned to the groups “WB-EMS” (*n* = 14) and “WB-vibration (WBV)” (*n* = 14). Table 11.4 gives the initial characteristics of both groups.

Intervention

While the WB-EMS group performed the 15-min WB-EMS protocol (see above) every fourth to fifth day for 14 weeks, a 15-min WB-vibration training with a corresponding training frequency was implemented for the control group. The focus of the WBV exercise program which included low-amplitude movements was on improving flexibility and—to a lesser degree—strengthening. The WBV was performed on Vibrafit devices (Solms, Germany) which applied vertical vibration at a frequency of 30 Hz (amplitude, 1.7 mm). Using video animation mainly, stretching exercises were performed. Some slight squat movements were also be performed on the plates with a perceived exertion of moderate (4–5 on the Borg cr10 scale [15]). After an initial introduction of two to three sessions, vibration training was no longer fully supervised but regularly controlled by research assistants instead.

Table 11.4 Baseline characteristics of the TEST II study group

Variable	WB-EMS (*n* = 14) (MV ± SD)	WB-vibration (*n* = 14) (MV ± SD)
Age [years]	69.1 ± 2.7	69.7 ± 3.0
BMI [kg/m^2]	28.1 ± 4.4	27.6 ± 2.7
Lean body mass (LBM) [kg][a]	64.4 ± 6.1	61.7 ± 6.5
Energy intake [MJ/day][b]	11.02 ± 2.41	11.23 ± 2.30
Vitamin-D intake [μg/day][b]	4.8 ± 4.1	5.4 ± 4.4
Exercise volume [min/week][c]	32 ± 27	29 ± 31

[a] Via DXA assessment

[b] Via 4-day dietary analysis

[c] Resistance- and endurance-type exercise only

Measurements

Anthropometry

Body height, weight, and circumference values of the participants were measured using calibrated devices. Total and regional body fat and lean body mass were determined using a whole-body DXA scan (Hologic QDR 4500a, Discovery-upgrade, Bedford, MI, USA). The segmentation of the appendicular skeletal muscle mass (ASMM) was conducted according to Heymsfield et al. [24]. The abdominal "region of interest" (ROI) was set at between the upper end of the iliac crest and the lower edge of the lumbar spine.

Procedures for the measurement of isometric strength and the design of the questionnaire are comparable to the TEST I procedure and thus have been omitted here. In addition, maximum isometric power of the leg extensors ("leg press") and plyometric jumps was assessed using a force plate (MTD-Systems, Neuburg v. Wald, Germany). The maximum oxygen uptake (VO_2peak) (Oxycon mobile, Conshohocken, USA) of the subjects was determined during a cross-trainer step test, in which the resistance was increased by 20 Watt every 3 min at a constant frequency of 120–130 rpm up to a voluntary maximum.

Statistical Procedures

The formal sample size analysis of the study was based on the study endpoint "appendicular skeletal muscle mass" (ASMM). In contrast to the original publication [9], the data for this article were calculated using a "completer analysis," where all cases with follow-up data were included.

Results

Only one participant (WB-EMS) could not be included in the final analysis, because cardiac risk factors that precluded participation were detected after the randomization procedure. Attendance rates in the WB-EMS group were 78 ± 8% and 72 ± 10% in the WBV group. The mean overall intensity of the EMS application over the intervention period was rated "hard" to "very hard" (6.1 ± 0.4 on the cr10 Borg Scale [15]), while the WBV group perceived their exercise program as being significantly less intense (4.7 ± 0.6).

Table 11.5 shows the results for the appendicular skeletal muscle mass (ASMM) and also for total (TF) and abdominal fat mass (AF). ASMM (and LBM) and TF differ significantly between the groups, with more favorable changes in the WB-EMS group. Differences for the AF did not reach significance, however. Unfortunately, a relevant reduction of body fat and muscle mass induced by energy restriction (−500 or −750 kcal/day for 4 or 6 weeks) in two participants of the WBV group may slightly confound our results.

Maximum isometric strength of the trunk and leg extensors and power of the leg extensors (leg press) significantly increased by 12% (leg extensor power) to 21% (leg extensor strength) ($p = 0.001$) in the WB-EMS group, while for the WBV group, only slightly positive changes (3% to 7%, $p > 0.081$) were observed. For all strength/power parameters, significant intergroup differences were determined.

Table 11.5 Baseline values, intragroup changes, and intergroup differences for body composition

	WB-EMS (MV ± SD)	WBV (MV ± SD)	Difference MV (95% CI)	*p*	ES
Appendicular skeletal muscle mass (ASMM)[kg]					
Baseline	29.73 ± 2.48	26.66 ± 3.06	–	–	–
Difference (*p*)	0.270 ± 0.433 (0.037)	−0.287 ± 0.642 (0.119)	0.557 (0.131–0.982)	0.012	1.02
Abdominal body fat (AF)[g]					
Baseline	3820 ± 1368	3765 ± 1792	–	–	–
Difference (*p*)	−237 ± 197 (0.001)	−91 ± 224 (0.153)	146 (−18 to 310)	0.079	0.69
Total body fat (TF)[%]					
Baseline	25.95 ± 3.49	27.37 ± 5.65	–	–	–
Difference (*p*)	−1.25 ± 0.93 (0.001)	−0.42 ± 1.12 (0.118)	0.83 (0.05–1.64)	0.037	0.81

Results of the completer analysis

VO_2peak increased by 4.3 ± 3.0% ($p = 0.001$) in the WB-EMS group, which was significantly more favorable ($p = 0.003$) compared with changes of the WBV group (−0.4 ± 3.1%, $p = 0.633$).

Thus, hypotheses (a) and (c) can be fully confirmed, while hypothesis (b) can be verified only for total, but not for abdominal, body fat.

Summary and Conclusion TEST II Study

The central aim of the TEST II study was to compare the effectiveness of the two alternative training technologies "WB-EMS" and "WB-vibration" with respect to muscular parameters and body fat in untrained, unfit, and mainly overweight/obese men 65 years and older. With one exception (abdominal fat mass), this comparison was clearly decided in favor of the WB-EMS group. Of importance, however, attendance rates for both technologies range in the normal high area of data given for conventional exercise programs [25], which is rather remarkable when considering the less sport affine status of this cohort. Thus, besides the clinical effectiveness of WB-EMS, an essential benefit of this innovative technology may be its attractiveness for subjects who are unable or unwilling to exercise conventionally.

Study 3

Training Und Electromyostimulation Trial III (TEST III) [10, 11, 26]

Motivation and Study Aim

The previous TEST studies showed relatively high effects on muscle mass and strength; thus, there is at least some evidence that suggested favorable effects of WB-EMS application on bone mass. In the TEST III study, we focused on lean, sport-abstinent women with osteopenia 70 years and older as one of the most vulnerable cohorts for osteoporosis and sarcopenia. Our hypotheses were that WB-EMS exercise training significantly affects bone mineral density at (a) the lumbar spine and (b) the femoral neck compared with a control group without bone-relevant exercise regimen.

Methodology

The TEST III trial is a randomized, controlled, single-blinded intervention study over 54 weeks. The study was conducted at the Institute of Medical Physics (IMP) of the FAU between November 2010 and August 2012.

Study Endpoints

- Bone mineral density at the lumbar spine (LS) und femoral neck (FN)
- Total and appendicular lean body mass

Participants

After application of the inclusion criteria, (a) female, ≥ 70 years of age, living independently, (b) BMI < 24 kg/m², and (c) osteopenia (BMD < 1 SD *T*-Score), and the exclusion criteria, (a) exercise <60 min/week, (b) medication/diseases with relevant effect on bone metabolism, (c) febrile diseases and acute bacterial and viral infections, and (d) contraindications for WB-EMS application (see above), a total of 76 women were included in the study. Participants were randomly assigned to a WB-EMS ($n = 38$) and a "control group" ($n = 38$). Table 11.6 shows the baseline characteristics of both groups.

Intervention

While the WB-EMS group performed a 20-min WB-EMS training protocol every fourth to fifth day over 54 weeks, the control group (CG) conducted two 10-week training courses (one session with 60 min/week) with an intermittent 10-week break. The focus of the low-intensity exercise program of the CG was to perform the identical physical exercises/movements that were prescribed by the WB-EMS protocol (see above) in order to determine the isolated effect of WB-EMS. In addition, exercises to increase flexibility, coordination, and relaxation were applied in the CG.

Table 11.6 Baseline characteristics of the TEST III study groups

Variable	WB-EMS ($n = 38$) (MV ± SD)	CG ($n = 38$) (MV ± SD)
Age [years]	74.7 ± 3.7	74.7 ± 4.4
BMI [kg/m²]	22.1 ± 1.5	22.1 ± 1.2
Lean body mass (LBM) [kg][a]	35.2 ± 4.3	35.4 ± 3.5
Energy intake [kJ/day][b]	6490 ± 1771	6605 ± 1632
Vitamin-D intake [µg/day][b]	4.7 ± 5.1	5.7 ± 6.9
Calcium intake [mg/day][b]	986 ± 276	966 ± 266
Exercise volume [min/week]	34 ± 22	31 ± 19

[a] DXA assessment
[b] 4-day dietary analysis

Measurements

Body height, weight, and circumference values of the subjects were measured using calibrated devices. The bone mineral density (BMD) of the lumbar spine, the proximal femur (tHip ROI), and for the total body was determined by DXA technology (Hologic QDR 4500a, Discovery-upgrade, Bedford, MI, USA). Body fat and lean body mass were determined by DXA total body scan. Appendicular skeletal muscle mass (ASMM) was analyzed and calculated according to Heymsfield et al. [24]. The abdominal "ROI" has been set at between the upper edge of the iliac crest and the lower edge of the lumbar spine. Maximum isometric strength of the leg extensors ("leg press") was measured by a force plate (MTD-Systems, Neuburg v. Wald, Germany).

Statistical Procedures

The formal sample size analysis was based on the study endpoint "bone mineral density at the lumbar spine." We conducted a completer analysis, which included all participants with 12-month data as well as a "per-protocol analysis," excluding subjects with a relevant change of covariates (see below) that may affect our study endpoints.

Results

Six subjects of the WB-EMS and ten subjects of the control group were not available for the final examination and could not therefore be included in the completer analysis. With respect to the per-protocol analysis, three persons were excluded due to (a) a diet-related weight loss of 13% and 17% (WB-EMS) or (b) to osteoanabolic therapy (CG). The participation rate in the WB-EMS group was 79 ± 18% and 74 ± 33% in the CG. The mean overall intensity of the EMS application over the intervention period was rated as "hard" to "very hard" (5.9 ± 0.5 on the cr10 Borg Scale [15]), while the CG rated their exercise program as "moderate" to "somewhat hard" (3.7 ± 0.3).

Table 11.7 shows the results of the completer analysis for bone mineral density, LBM, ASMM, and leg strength. In summary, significant WB-EMS effects were determined for muscular parameters (LBM, ASMM, strength), while bone mineral density was less favorably affected. In detail, (non)significant effects were determined only for the lumbar spine ROI borderline, while no relevant group differences were determined for the total hip ROI with respect to BMD changes.

The per-protocol analysis generally confirmed the results of the completer analysis, however, as expected intergroup differences were more pronounced (BMD lumbar spine ROI: $p = 0.016$; BMD tHip-ROI: $p = 0.416$).

Thus, hypothesis (a) that WB-EMS generates significantly higher positive changes of bone mineral density at the lumbar spine compared with an active control group can be confirmed, while hypothesis (b) with the same assumption for the proximal femur must be rejected.

Table 11.7 Baseline values, intragroup changes, and intergroup differences for bone mineral density, body composition, and leg strength

	WB-EMS (MV ± SD)	Control group (MV ± SD)	Absolute difference MV (95% CI)	*p*	ES
Bone mineral density at the lumbar spine [mg/cm2]					
Baseline	884 ± 175	835 ± 103	–	–	–
Difference (p)	5 ± 21 (0.140)	−5 ± 20 (0.167)	10 (0.4 to 20.7)	0.050	0.49
Bone mineral density at the hip (tHip-ROI) [mg/cm2]					
Baseline	762 ± 175	754 ± 94	–	–	–
Difference (p)	−6 ± 14 (0.032)	−8 ± 15 (0.016)	1.9 (−5.8–7.7)	0.756	0.10
Lean body mass (LBM) [kg]					
Baseline	35.15 ± 4.32	35.42 ± 3.52	–	–	–
Difference (p)	0.273 ± 0.589 (0.014)	−0.296 ± 0.977 (0.121)	568 (157–979)	0.008	0.71
Appendicular skeletal muscle mass (ASMM) [kg]					
Baseline	15.80 ± 2.12	15.85 ± 1.72	–	–	–
Difference (p)	0.062 ± 0.346 (0.322)	−0.233 ± 0.475 (0.015)	294 (82 to 508)	0.009	0.71
Isometric leg strength (leg-press) [N]					
Baseline	604 ± 185	523 ± 171	–	–	–
Difference (p)	60 ± 73 (0.001)	1 ± 70 (0.969)	59 (21 to 97)	0.003	0.82

Results of the completer analysis

Summary and Conclusion TEST III Study

The main outcome of the TEST III study was the only small-to-moderate effect of WB-EMS training on bone density. Due to the (apparently) close interaction between the muscle and bone [27, 28] and highly significant effects of EMS on muscle mass and strength at locally corresponding areas of the skeleton [26], we had expected much stronger effects. One may argue that the low impact of (WB-) EMS on bone mineral density may be caused by a suboptimum setting of strain parameters. Although the most favorable composition of EMS for triggering bone adaptation has yet to be established, a recent study which directly compared different frequencies of EMS[1] in an animal disuse model [13] determined the most favorable effect on bone parameters (e.g., volume fraction, connectivity, trabecular number/thickness) to be 20 and 50 Hz.[2]

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[1] 1 Hz vs. 20 Hz vs. 50 Hz vs. 100 Hz vs. disuse control (“hindlimb suspension”) vs. aged matched control.

[2] The effect of 100 Hz was also significant but slightly lower…

Study 4

Training Und Electromyostimulation Trial V (TEST V)

The aim of the present study was to evaluate the effect of active vs. passive WB-EMS application on muscle strength and body composition in elderly women with low muscle mass and decreased functional capacity. Our hypothesis was that an active WB-EMS program in a supine position is significantly more effective for increasing (a) isokinetic muscle strength of the leg extensors and flexors, (b) muscle mass, and (c) fat mass compared with a control group with passive WB-EMS application only.

Methodology

The presented study is a subproject of the FORMOSA study, a controlled, randomized, and single-blinded 12-week study with two treatment arms. The study was conducted at the Institute of Medical Physics (IMP) of the FAU between July 2014 and October 2014. The TEST V study has not been published yet; thus, some features and particularities of this study will be given more detail compared with the already mentioned parts (TEST I–III) of the TEST family.

Study Endpoints

- Isokinetic leg muscle strength (primary study endpoint)
- Total and appendicular lean body mass (experimental endpoint)
- Total fat mass (experimental endpoint)

Participants

A total of 28 of eligible persons were included after the application of the inclusion criteria: (a) female, older than 70 years of age, (b) untrained status ($\leq$ 1 h exercise training/week), (c) low muscle mass (−1 SD *T*-score Teschler score (13)), and (d) $\geq$1 fall in the past 6 months or $\geq$1 osteoporotic fracture. Subjects were excluded in the event of (a) pathological cardiac changes or inflammations, (b) relevant medication/diseases affecting muscle metabolism, (c) the absence of $\geq$1 week during the intervention period, (d) alcohol and drug abuse, and (e) the presence of a contraindication to WB-EMS.

After detailed study information, 25 subjects were willing to participate in the study and conducted a WB-EMS conditioning training session. One person perceived the training as unpleasant and quit the study, so that finally 24 women were randomly assigned to two study arms: (1) active WB-EMS group (n = 12) and (2) passive WB-EMS group (n = 12). Table 11.8 shows the baseline characteristics of both groups.

Intervention

The WB-EMS training was carried out lying supine on comfortable armchairs with adjustable foot- and backrest (Fig. 11.3). “Time under load” was consecutively augmented by linearly increasing the duration of the WB-EMS session from 10 min to 16 min. The active WB-EMS training group executed 8–10 different slight

Table 11.8 Baseline characteristics of the TEST III study groups

Variable	Active WB-EMS group (MV ± SD)	Passive WB-EMS group (MV ± SD)
Age [years]	77.1 ± 4.8	75.8 ± 5.4.8
BMI [kg/m^2]	180.7 ± 7.2	180.9 ± 5.7
Body fat [%][a]	37.1 ± 6.9	35.9 ± 6.0
Sarcopenia score [kg/m^2][b]	6.17 ± 0.14	6.09 ± 0.07
Grip strength [kg]	22.3 ± 2.1	21.3 ± 2.6
Exercise volume [min/week]	25 ± 31	20 ± 37

[a] BIA technique

[b] According to Baumgartner et al. [29] (ASMM/body height)

Fig. 11.3 WB-EMS armchairs to exercise in a supine position

movements with 1–2 sets and 6–8 reps. The amplitude of the movements and the corresponding intensity was prescribed rather low in order to focus on the isolated effect of WB-EMS. Movements included leg extension and flexion with fixed thigh (only) against gravity, arm extension, and flexion exercises without any additional weight applied with the elbow on the armrest or movements performed in an upright (sitting) position using a gymnastic stick ("military press," "lat-pulls"). The back and abdominal muscles were addressed by slight pressure against the moveable seat back or low-amplitude raising of the body from a semi-recumbent position. In contrast, no movements were performed in the passive WB-EMS group; however, subjects of both groups were asked to isometrically contract their muscles immediately before and during the 4-s impulse.

Measurements

Body height, weight, and circumference values of the participants were assessed with calibrated devices. Body fat and lean body mass (LBM) were determined using modern multifrequency Bio-Impedance Analysis (BIA) technique (Inbody 770, Seoul, Korea). The analysis and calculation of the appendicular muscle mass (ASMM) were conducted according to Heymsfield et al. [24].

The (leg) strength diagnostics were performed in an isokinetic mode using the leg press module of ConTrex (PHYSIOMED, Schnaittach, Germany). Maximum isokinetic strength (0.6 m/s) of the leg extensors and flexors (knee angle 30° to 90°) was determined by a five-repetition maximum test. The highest value of the five repetitions was included in the analysis.

Statistical Procedures

The formal sample size analysis is based on the study endpoint "maximum isokinetic strength of the leg extensors." An intention-to-treat (ITT) analysis was performed with the statistical software program R (R Development Core Team Vienna, Austria) in combination with a multiple imputation by the program Amelia II [30].

Results

Two subjects, one each per group, quit the study after 4 and 7 weeks due to personal reasons not related to the WB-EMS application. The training frequency was similar in both groups (11.3 ± 1.7 sessions or 94 ± 11%). The individual exercise intensity of the active EMS group was reported to be 5.5 ± 0.4 on the cr10 Borg Scale [15]; the corresponding RPE of the passive EMS group was rated slightly lower (5.1 ± 0.6).

Table 11.9 gives the results for isokinetic maximum strength of the leg extensors and flexors as assessed by the isokinetic leg press device.

In summary, we determined highly significant improvement ($p < 0.001$) of leg extensor strength within the groups (active 24 ± 10% vs. passive 13 ± 9%), albeit with highly significant differences ($p = 0.001$) between the groups in favor of the active application method. Similarly, a significant improvement was determined for leg flexors (active 19 ± 12% vs. passive 11 ± 11%); group differences were not significant however (p =0.088) (Table 11.9).

Baseline LBM, ASMM, and body fat mass did not differ relevantly between the groups. LBM increased in the active WB-EMS group by 3.8 ± 7.0% ($p = 0.172$) and remained largely unchanged in the passive EMS group (−0.2 ± 6,6%, $p = 0.837$).

Table 11.9 Baseline values, intragroup changes, and intergroup differences for isokinetic leg strength

	Active WB-EMS (MV ± SD)	Passive WB-EMS (MV ± SD)	Difference MV (95%-KI)	*p*	Effect size
Maximum isokinetic strength of the leg extensors [N]					
Baseline	1184 ± 191	1149 ± 277	–	0.721	–
Difference	284 ± 88 ($p = 0.001$)	150 ± 73 ($p = 0.001$)	134 (64–202)	0.001	1.67
Maximum isokinetic strength of the leg flexors [N]					
Baseline	484 ± 155	477 ± 163	–	0.915	–
Difference	93.5 ± 52.1 ($p = 0.001$)	52.3 ± 52.0 ($p = 0.005$)	41.2 (−2.8–85.3)	0.065	0.79

Results of the ITT analysis

The difference between the groups was not significant ($p = 0.197$). ASMM showed a similar trend with an increase in the active ($2.3 \pm 7.3\%$, $p = 0.431$) and a reduction ($-2.5 \pm 9.2\%$, $p = 0.216$) among the passive EMS group, again without significant difference between the groups however ($p = 0.201$). Body fat did not change significantly in the active EMS group ($-0.3 \pm 1.3\%$, $p = 0.923$), while in the passive EMS group, a significant rise ($1.1 \pm 1.3\%$, $p = 0.011$) was observed. The difference between the groups was borderline (not) significant ($p = 0.061$). Of importance, the weight gain of the active EMS group is fully explained by the increase of LBM, while the weight gain of the passive EMS group correlates with an increase in body fat mass. In summary, hypothesis (a) can be at least partially confirmed, while hypotheses (b) and (c) have to be rejected although (strong) tendencies for more favorable results for active WB-EMS application were detected.

Summary and Conclusion TEST V Study

Although not consistently significant, the TEST V study at least demonstrated the general superiority of an "active" WB-EMS application compared with passive EMS application on muscle strength and—to a lesser degree—on body composition. However, with respect to strength development, both groups showed highly significant and clinically meaningful changes of maximal isokinetic strength of the leg flexors and extensors. With respect to the varying group differences, we put this difference down to the fact that during isokinetic testing the leg-flexion movement is hard to coordinate, an aspect that may explain the relatively high variance of the results for leg flexion (Table 11.9). A comparison of the TEST V study results with studies which also determined maximum strength changes of the leg extensors after WB-EMS application in the elderly [8, 9, 26] indicated significantly higher values for the present study. We attribute this difference to the higher specificity and sensitivity of the isokinetic leg press compared with a conventional isometric strength measurement and the remarkably weak baseline strength of the test subjects.

Although a tendency for higher effects of active WB-EMS on body composition parameters was detected, significance levels (5%) were not reached. In this context one may argue that the relatively short intervention period of 12 weeks may have prevented more striking results; however, significant hypertrophic effects were reported after 3–5 weeks even with respect to muscular parameters [31]. A more problematic aspect may be that the BIA technique did not reach the sensitivity of the originally intended DXA assessment, although modern, multifrequency BIA technique was reported to be a reliable and valid method to assess body composition [32]. However, one should not overlook that body composition was regarded as an experimental endpoint of the TEST V study only. Thus, the formal sample size calculation did not address changes of muscle mass, which may lead to a simple "underpowering" of the study for detecting significance between group differences for this parameter.

General Discussion and Conclusions of the TEST Series

The aim of the TEST study series was (or still is) to evaluate the effectiveness, applicability, and attractiveness of the efficient, flexible, and highly customizable WB-EMS technology on musculoskeletal risk factors in the elderly. Addressing the effectiveness of this novel technology on musculoskeletal parameters resulted in a slightly heterogeneous scenario: While various measurement methods generally confirm the significant and highly relevant effect of WB-EMS training on muscular parameters in elderly subjects with different status and conditions, the corresponding effect on bone mineral density is rather disappointing. The latter finding may have several reasons. Most relevant, although state of the art, our WB-EMS protocol may be at least suboptimal at least for addressing the "bone." However, due to a lack of bone-specific comparative literature, the extent to which higher training frequency [4], higher amperage [33], and/or slightly lower frequencies [13 12,466] would have led to more favorable effects on bone density cannot be decided. The present human EMS studies with application of local EMS or functional electrostimulation (FEMS) under "disuse conditions" related to severe spinal cord injuries (e.g., [34–38]) did not allow a dedicated comparison with our study with elderly subjects for two main reasons: (1) It can be assumed that bone strain threshold will be extremely low in the corresponding immobilized skeletal area; thus, even very low strain may overwhelm this threshold and induce positive effects. (2) At least with respect to functional FEMS, it remains unclear whether the observed positive BMD changes at the lower extremities were due to WB-EMS or more to a corresponding mechanical loading during leg extension (FEMS "leg press") or FEMS cycling. Thus, a direct comparison with studies which included cohorts without corresponding limitations, correspondingly higher strain threshold, and largely isolated muscle stress without substantial axial loading of the bone is not appropriate.

Revisiting muscular parameters, a comparison with results derived by conventional (resistance) exercise training programs further substantiates the relevance of our results. In summary, the effects of both types of exercise on muscle mass of older subjects resulted in comparable positive changes of LBM [39]. Of interest, these results remained consistent after a dedicated comparison with high-intensity (> 70% 1RM) exercise protocols (e.g., [25, 40–42] with their pronounced positive effect on muscle mass.

With respect to "muscle strength," a corresponding appraisal of the affectivity of WB-EMS is more difficult due to the variety of possible endpoints in this area. Although we do not systematically review the literature for older adults, data of meta-analysis or reviews [43–45] suggest a slight superiority of conventional resistance training for maximum strength and an even more pronounced effect for muscular power. Regarding bone parameters, however, the superiority of dedicated conventional "state-of-the-art" exercise programs [46] for increasing bone mineral density [25, 47, 48] is indisputable.

In addition to the effectiveness of the method, acceptance by the participants is a key criterion for successful interventions. Considering the “attendance rate” as a relevant criterion, WB-EMS exhibited participation rates in the upper range of conventional exercise programs [25, 48]. The “dropout rates” among our RCTs were also well below the corresponding rate of interventions of comparable duration [25, 49]. Considering the aspect that most of our trials addressed subjects with low sport affinity will further increase the significance of these data. Limitations of present WB-EMS that may restrict practicability and feasibility of a WB-EMS training programs in health-related settings such as relatively high costs due to WB-EMS equipment and low trainer/trainee ratio (TEST-Trials: 1:2 and 1:3[3]) may be compensated by low spatial requirements (4 m^2 per WB-EMS device) and high flow rates of participants due to low application time (≈20 min). Finally, with respect to safety and tolerability of WB-EMS application, rigorous response to contraindications, careful progression of the intensity of the WB-EMS procedure, and adequate preparation of the participant for the WB-EMS session will prevent orthopedic, cardiac, or metabolic problems during WB-EMS. In this context the TEST V trial demonstrated the effectiveness, applicability, feasibility, and safety of WB-EMS for impacting muscle strength and (to a lesser extent) muscle mass in a setting that focuses specifically on (very) frail subjects.

As some may argue that our enthusiasm for WB-EMS may be bordering on the exaggerated, we would like to clarify our position with respect to WB-EMS application in the elderly. We strongly feel that WB-EMS should not be regarded as an “alternative” to but as an “enhancement” for intensive exercise programs for elderly subjects who are either unable or unwilling to exercise conventionally. This appraisal based on the limitation of WB-EMS, namely, its narrower, focuses on muscular parameters rather than the much more comprehensive effects of multipurpose exercise programs which may impact most if not all [1] health risk and protective factors of the elderly, a highly relevant aspect for our multi-morbid elderly population [50]. Thus, WB-EMS application in a healthcare setting should focus on subjects with a lack of disposition to conventional sports activities.[4] For these subjects WB-EMS may be an appropriate option for improving their body composition and muscular strength for independent and healthy aging. Taking further into account that WB-EMS technology will become more feasible, sophisticated, and cost-effective over the coming years, the application of WB-EMS should be seriously considered for healthcare settings as a mean of exercise training dedicated to improving body composition and strength parameters in the elderly.

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[3] That is, one instructor supervised two to three participants.

[4] …which is however the majority of the older population [6].

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Osteoplastic Procedures for the Treatment of Vertebral Fractures

12

Christian Kasperk

Introduction

Osteoplastic Procedures

Osteoplastic techniques such as balloon kyphoplasty and vertebroplasty use a quickly solidifying resin (polymer from polymethylmethacrylate (PMMA)) or calcium phosphate cements to stabilize a painful osteoporotic compression fracture, to relief the patient instantly from the vertebral fracture-associated pain and to prevent any further loss of vertebral height [1]. The extent of the pain relief depends on the identification of additional causes for local back pain like degenerative changes of the vertebral morphology which cannot be treated by any osteoplastic procedure [2]. Calcium phosphate cements ("biocements") should only be used in osteoporotic compression fractures which do not convey shear stress but rather sole compressive forces to the implant (i.e., type A.1 vertebral compression fractures). An advantage of calcium phosphate cements is the resorbability of this material in case a cement leakage out of the vertebral body occurred, whereby the intravertebral calcium phosphate implants remain stable and intact for years [2]. In malignoma-associated osteolytic lesions and pathologic fractures, only PMMA should be used. An important aspect of osteoplastic procedures is the immediate stability for the treated fractured vertebra. Usually osteoplastic procedures in osteoporosis patients are performed at thoracic vertebrae 5–12 and lumbar vertebrae 1–5. Cervical vertebral fractures are uncommon in osteoporosis but rather occur after trauma or due to pathological lesions of the spine and are not a standard situation for any osteoplastic technique. During osteoplastic procedures the patient is positioned horizontally (face down with pillows under the shoulder and iliac crest) in a hyperlordotic

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C. Kasperk, MD, PhD
Division of Osteology, Department of Medicine I and Clinical Chemistry,
University Hospital Heidelberg, INF 410, 69120 Heidelberg, Germany
e-mail: Christian.kasperk@med.uni-heidelberg.de

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position. Patients with, for example, an instable thorax, painful rib fractures, cervical vertebral or dens fractures and instability or with an abdominal aortic aneurysm should therefore not be treated by osteoplastic techniques.

The pain relief by osteoplastic procedures most likely results from destruction of the intravertebral pain fibres. Therefore, new and also old vertebral fractures even when more than 1 year old can successfully be treated by these procedures [3] as long as there is an anamnestic causal association to the vertebral fracture-associated local pain. An MRI oedema in the bone marrow may be favourable for a preoperative judgement whether lost vertebral height can be restored; however, it is not a prerequisite for an osteoplastic procedure as long as there is a clear anamnestic and anatomical association of the vertebral fracture with the location of the pain at the spine [4].

Remarkably, osteoplastic procedures are associated with a decreased mortality, whereby kyphoplasty appears to be more favourable in this regard than vertebroplasty [5, 6].

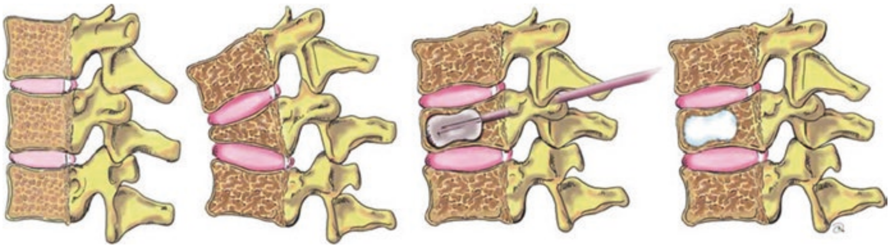
Balloon Kyphoplasty

In 1998 balloon kyphoplasty has been introduced for the stabilization of vertebral fractures [7]. Today it is an established osteoplastic procedure for routine therapy of vertebral fractures or lesions on the basis of a primary or secondary osteoporosis.

Usually balloon kyphoplasty is performed in general anaesthesia after intubation of the patient. The balloon catheter is inserted into the fractured vertebral body via a trans- or extrapedicular approach. The balloon catheter is then inflated using a contrast fluid under fluoroscopic control until the balloon extends to the endplates of the vertebral body. The balloon is deflated and removed from the vertebra so that within the fractured vertebral body, which is somewhat reheightened by the balloon expansion procedure, an empty void remains. As muscle relaxation during general anaesthesia and the positioning of the patient prevent any compressive forces on the spine that might cause a collapse of the space created by the balloon, the cavum remains even after removal of the balloon. Hyperlordosis as a consequence of the positioning of the patient and general anaesthesia in complete muscle relaxation support the reheightening process of partially collapsed or fractured vertebrae.

As the amount of contrast fluid is known that was used to inflate the balloon, the volume of the balloon-created space is known, and the same volume of PMMA plastic or other “cement” material is inserted into the void, whereby only polymethylmethacrylate (PMMA) is used in malignoma-associated osteolytic lesions (Fig. 12.1). As PMMA and calcium phosphate cements solidify rapidly within the treated vertebral body, embolic events from PMMA or calcium phosphate cement are rare events.

Kyphoplasty



Vertebroplasty

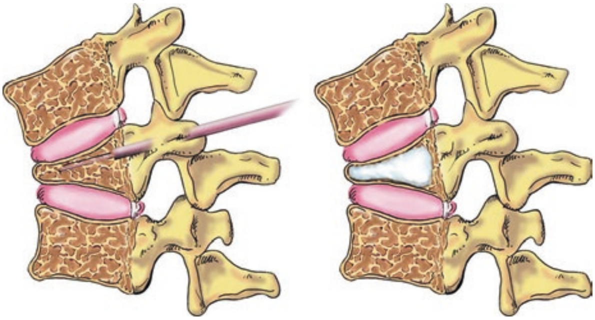


Fig. 12.1 Kyphoplasty: Kyphoplasty attempts to reheighten osteoporotic vertebral compression fractures by a balloon catheter, thus creating a void of defined volume, and stabilizes the vertebral body—after removal of the balloon catheter—by injection of an instantly hardening resin like polymethylmethacrylate or calcium phosphate cement, whereby the volume of the applied implant is equal to the volume of the first created void. Vertebroplasty: During vertebroplasty the instantly hardening resin (polymethylmethacrylate) is directly injected into the fractured vertebral body

Vertebroplasty

Vertebroplasty was established in 1984 for the internal stabilization of vertebral fractures and vertebral lesions [8, 9]. This technique is often applied by interventional radiologists in analgosedation under fluoroscopic or computer tomographic guidance.

Via a trans- or extrapedicular approach, a canula is placed within the fractured vertebra, and the PMMA plastic material is directly injected into the treated vertebra under fluoroscopic control.

In contrast to balloon kyphoplasty, vertebroplasty does not rely on the generation of a cavum of defined void within the treated vertebral body. Due to low viscosity of the PMMA plastic material and the overall technical procedure, a significant reheightening of the treated vertebra is not expected. The distribution of the PMMA plastic material within the treated vertebral body cannot be controlled; therefore PMMA leakages are more frequent after vertebroplasty. A typical location for PMMA leakages after vertebroplasty is the venous plexus surrounding the vertebrae which – for most cases – does not have any clinical consequences.

Comparison of Kyphoplasty and Vertebroplasty

The major technical difference between these two osteoplastic techniques is the usage of a balloon catheter for balloon kyphoplasty as described above in more detail. The balloon creates a void of defined volume within the fractured vertebra that is subsequently filled with plastic (or "cement") material of high viscosity to internally stabilize the fractured vertebral body. Leakages of the used plastic or cement material are therefore significantly less likely after balloon kyphoplasty. Another advantage for balloon kyphoplasty is the compression of spongious bone material during the intravertebral expansion of the balloon which creates a condensed spongiosa layer surrounding the void which may close possible cortical perforations of the vertebral body and allows bone repair to occur on the surface of the implanted plastic or cement material. In case of malignant disease and pathological osteolytic lesions, the malignant tissue is compressed and relocated to subcortical areas supporting local control, e.g., by radiation or chemotherapy.

The extent and the direction of dissemination of the PMMA material are less controllable in vertebroplasty leading to leakages mainly in venous plexus surrounding the vertebrae or into the muscle tissue. The direction of the dissemination is determined by areas within the vertebral body providing the lowest resistance which may predispose to leakages. Vertebroplasty may be more beneficial for the patient at an early time point when the vertebral body containing a pathological lesion shows signs of collapse (e.g., MRI bone oedema) but has not lost much of its initial height, yet.

Indications and Contraindications

Osteoplastic techniques such as the balloon kyphoplasty or vertebroplasty should be considered if a patient suffers from severe to moderate pain due to a vertebral fracture or due to an osteolytic lesion which cannot be sufficiently controlled by pain medication [10]. In addition, it should be considered if these minimally invasive procedures could potentially prevent future neurological complications due to instable vertebral bodies compromising the function of the spinal cord or spinal nerves. This situation occurs most often in secondary osteoporosis by malignant diseases such as multiple myeloma which destroy the biomechanical stability of the vertebral bodies. Osteoplastic procedures are not successful to treat spine pain which is caused by degenerative spine diseases [11–13].

In order to perform osteoplastic procedures, the cortical bone of the analysed vertebral body should be intact – particularly the ventral and dorsal wall of the respective vertebral body – to prevent leakages of plastic or cement material into the spinal canal. Pedicular structures also have to be intact to apply the osteoplastic insertion instruments safely under fluoroscopic control. There should be no major degenerative changes of the spine that would compromise the fluoroscopic visibility of crucial vertebral structures and orientation by the surgeon during surgery.

Osteoplastic procedures are contraindicated in case of local or systemic infections. In particular spondylodiscitis has to be excluded preoperatively as cause of a vertebral destruction. For most traumatic vertebral fractures without primary or secondary osteoporosis, osteoplastic procedures are not recommended because bone fragments will be dislocated such that neurological complications may occur or the morphological stability of the entire vertebral body may be jeopardized.

Randomized Controlled Studies of Osteoplastic Procedures for Vertebral Osteoporotic Fractures

No randomized, sham-controlled and blinded studies have so far been published on vertebral fractures and pain for malignancy-induced vertebral compression fractures. There is one unblinded randomized, controlled study in patients with multiple myeloma demonstrating a beneficial effect of kyphoplasty for at least 12 months as compared to nonstandardized conservative management of painful vertebral fractures due to multiple myeloma ([14], abstract).

There are three randomized, controlled studies on osteoplastic procedures published for osteoporotic painful vertebral compression fractures.

The randomized FREE study ([15]) investigated the balloon kyphoplasty in 300 patients with a mean age of 73 years. Ninety-five percent of the patients were diagnosed with primary and 5% with secondary osteoporosis. Patients had one to three vertebral fractures with a mean time interval between diagnosis of vertebral fracture and the kyphoplasty procedure of 5 weeks. All treated vertebrae had a minimum height reduction of 15% and a bone marrow oedema in MRI. About 138 patients after balloon kyphoplasty had postoperatively and also after 12 months a significant reduction in back pain and up to 6 months after kyphoplasty an improved mobility compared to the conservatively treated group. This study did not evaluate vertebral augmentation or a possible improvement of the kyphosis angle of the spine.

A double-blind randomized, sham-controlled study was published by R. Buchbinder et al. [16] investigating vertebroplasty in 78 patients with a mean age of 76 years with painful osteoporotic vertebral fractures. Patients had one to two vertebral fractures not older than 12 months, and MRI confirmed bone marrow oedema or fracture line. Thirty-five patients received vertebroplasty, and 36 patients underwent a sham procedure (local skin and periosteal anaesthesia, synthetic material prepared to induce the PMMA smell in the operating room). In this study no statistical difference of pain reduction between vertebroplasty and sham treatment group was noted postoperatively for 3 and 6 months after vertebroplasty.

Kalmes et al. [17] investigated vertebroplasty in a randomized blinded, sham-controlled study in 131 patients at a mean age of 73 years with osteoporotic vertebral fractures. The patients were diagnosed with one to three vertebral fractures. The verum group ($n = 68$) received mainly monopedicular vertebroplasty; for some vertebrae that did not contain “satisfactory amounts” of synthetic material, a bipedicular vertebroplasty was performed. A sham procedure was performed for control patients, and a crossover of the patients was allowed after 1 month or at a later time point if pain reduction was not sufficient. Whereas the pain reduction was not significantly different between the two groups, more patients (*n* = 27) in the sham-operated control group crossed over to verum. Only eight patients of the verum group crossed over to the alternative treatment.

In a competitive randomized study comparing balloon kyphoplasty to vertebroplasty [18], 50 patients per group at a mean age of 73 years were treated with vertebroplasty or balloon kyphoplasty. In the postoperative period as well as after 3 months, there was no significant difference in pain reduction between the two techniques. Vertebrae treated with balloon kyphoplasty were found to have a better vertebral augmentation and an improvement of the degree of the kyphosis.

In a nonrandomized, controlled study (*n* = 40), balloon kyphoplasty was compared to a standardized control treatment (*n* = 20) for painful osteoporotic vertebral fractures. Balloon kyphoplasty was superior to conservative treatment regarding pain reduction over a period of at least 12 months and with regard to mobility in the first 6 months after kyphoplasty [3, 19]. All vertebrae in the control group exhibited a progression of vertebral compression fracturing, whereas after balloon kyphoplasty, a small but significant vertebral augmentation was recorded. Eighty-nine percent of the patients treated by balloon kyphoplasty after an interdisciplinary selection of patients exhibited a marked reduction of pain [20]. Kyphoplasty reduces vertebral pain after osteoporotic vertebral fractures and improves mobility for at least 3 years after the procedure. The long-term risk of new vertebral fractures after kyphoplasty of chronically painful vertebral fractures is reduced versus controls [11, 12].

Studies Using Kyphoplasty and Vertebroplasty in Patients with Multiple Myeloma

Published reports on the outcome after minimally invasive osteoplastic procedures (kyphoplasty and vertebroplasty) in patients with back pain due to multiple myeloma are based on prospective and retrospective, uncontrolled and unblinded cohort studies. In Tables 12.1, 12.2, and 12.3 an overview on published trials utilizing kyphoplasty and vertebroplasty in patients with multiple myeloma is presented, including series with ≥10 patients with multiple myeloma.

In some of the published studies, the indication for an intervention is evaluated by an interdisciplinary team, and preoperative spine X-rays, MRI and CT scans are needed for this interdisciplinary assessment [21]. Inclusion criteria for both kyphoplasty and vertebroplasty are localized painful vertebral fractures refractory to conservative treatment including opiate analgesia and/or physical therapy. In many cases a desired more effective reheightening of a recently fractured vertebra leads to the selection of kyphoplasty instead of vertebroplasty as the most appropriate procedure. Typical exclusion criteria for both interventions (kyphoplasty and vertebroplasty) included unstable fractures (i.e., with a destruction of the posterior wall of the vertebral body) or with retropulsed tumour tissue or bone fragments, epidural compression of neural elements, stenosis of the spinal canal, radicular pain, failure to localize

Table 12.1 Kyphoplasty in patients with multiple myeloma

Author	Number of patients (mean age) anaesthesia	Number of levels treated	Follow-up	Outcome clinical *1	Outcome radio-morphological	Complications
Prospective reports						
Pflugmacher et al. (2006a, b + 2007)	23 (63.5) GA	59	24 months	*64% pain reduction* VAS decreased from 8.6 to 2.4 (postoperatively) and to 3.1 (24 months) *57% improved disability* ODI improved from 78.1 to 37.3 (postoperatively) and to 33.6 (24 months)	Postoperative height improvement in 61% of vertebral bodies with height restoration of 3.5 mm (from 25 to 28.5 mm) After 2 years slight height decrease by 1.0 mm Postoperative correction of kyphosis in 76.5% of patients by 8° After 2 years slight loss of correction in 53.1% of patients by 3° Adjacent fractures in two patients	Cement leakage 10%
	20 (62.4) GA	48	12 months	*62% pain reduction* VAS decreased from 8.2 to 2.2 (3 days) and to 3.1 (12 months) *56% improved disability* ODI improved from 71.5 to 27.5 (3 days) and to 31.2 (12 months)	Postoperative height improvement in 64.5% of vertebral bodies with height restoration of 4.3 mm (47.3% of lost height) After 1 year slight height decrease in 43.7% (21/48) of treated vertebral bodies by 1.1 mm Postoperative correction of kyphosis in 78.4% of patients by 6.3° After 1 year slight loss of correction in 42% of patients by 1.8° One adjacent fracture after 2 weeks	Clinically asymptomatic cement leakage in 10.4%
Lane et al. (2004)	19 (60.4) GA	46	3 months	*33% improved disability* ODI reduced from 48.9 to 32.6 Improvement in 84.2% (16/19 patients) No improvement with preoperative ODI < 28	53.4% restoration of midvertebral height loss (in 42 of 46 levels) 37.8% restoration of anterior vertebral height loss (in 35 of 46 levels)	Cement leakage in 26.3% No clinical sequelae

(continued)

Table. 12.1 (continued)

Author	Number of patients (mean age) anaesthesia	Number of levels treated	Follow-up	Outcome clinical *1	Outcome radio-morphological	Complications
Dudeney et al. (2002)	18 (63.5) No information on anaesthesia	55	7.4 months (mean)	From SF36-questionnaire: Pain improved from 23.2 to 55.4 Physical function improved from 21.3 to 50.6	34% restoration of lost height	No major complications 4% asymptomatic cement leakage
Retrospective reports						
Astolfi et al. (2009)	30 (63) GA [$n = 13$] + LA [$n = 17$]	45	4 years (median)	*56% pain reduction* VAS reduced from 8.7 to 2.8 (1 month), 2.1 (3 years), 3.8 (5 years) Complete pain relief in 59% Pain recurred in 10% between 3 and 12 months *58% improved disability* ODI improved from 87 to 45 (1 month), 21 (3 years), 37 (5 years) SF36 improved from 23 to 76.5 (1 month), 77.2 (3 years), 67.8 (5 years)	55% restoration of lost height, maintained to 5 years 6.8° correction of segmental kyphotic angle, decrease of 1.7° after 5 years Follow-up fractures in 14 Pat (31.1%) after 18 months (mean)	Transiently increased back pain and pyrexia immediately postoperatively in two patients Two (4.4%) asymptomatic cement leakages No major complications

Astolfi S, Scaramuzzo L, Logroscino CA. A minimally invasive surgical treatment possibility of osteolytic vertebral collapse in multiple myeloma. Eur Spine J. 2009;18(Suppl 1):115–21

Dudeney S, Lieberman IH, Reinhardt MK, Hussein M. Kyphoplasty in the treatment of osteolytic vertebral compression fractures as a result of multiple myeloma. J Clin Oncol. 2002;20:2382–7

Lane JM, Hong R, Koob J, Kiechle T, Niesvizky R, Pearse R, Siegel D, Poynton AR. Kyphoplasty enhances function and structural alignment in multiple myeloma. Clin Orthop Relat Res. 2004;426:49–53

Pflugmacher R, Kandziora F, Schroeder RJ, Melcher I, Haas NP, Klostermann CK. Percutaneous balloon kyphoplasty in the treatment of pathological vertebral body fracture and deformity in multiple myeloma: a 1-year follow-up. Acta Radiol. 2006a;47:369–76

Pflugmacher R, Schleicher P, Schröder RJ, Melcher I, Klostermann CK. Maintained pain reduction in five patients with multiple myeloma 12 months after treatment of the involved cervical vertebrae with vertebroplasty. Acta Radiol. 2006b;47:823–9

Pflugmacher R, Schulz A, Schroeder RJ, Schaser KD, Klostermann CK, Melcher I. A prospective two-year follow-up of thoracic and lumbar osteolytic vertebral fractures caused by multiple myeloma treated with balloon kyphoplasty. Z Orthop Ihre Grenzgeb. 2007;145:39–47

Table 12.2 Vertebroplasty in patients with multiple myeloma

Author	Number of patients (mean age)	Number of levels treated	Follow-up	Outcome clinical *1	Outcome radio-morphological	Complications
Prospective reports						
Ramos et al. (2006)	12 (66) LA	19	3.2 years (median) [2–56 months]	*67% pain reduction* VAS reduced from 7.5 to 3.7 (1 day) and to 2.5 (3 years) 92% showed ≥75% pain reduction within 3 months *52% improved functional status* ECOG [0–4] reduced from 3.1 to 2.5 (1 day) and to 1.5 (3 years)	No further collapse of treated or neighbouring vertebrae at the last follow-up	Leakage in 94% (16/19) of patients No clinical or neurological symptoms
Diamond et al. (2004)	7 (69) LA	14	6 weeks	*75% pain reduction* VAS [0–25] reduced from 19 to 4 After 1 day six of seven patients (86%) had ≥50% decreased pain score *50–60% improved functional status* BI improved from 11.9 to 18.7 Of seven patients three cease pain medication, three reduce analgesic >50% after 1 day	No information provided	No complications No paravertebral or foraminal leakages
Retrospective reports						
McDonald et al. (2008)	67 (66.2) LA + conscious sedation	114	12 months	Pain “at rest” improved from 3.9 by 2.7 (25%) (1 week) [69%] Pain “at activity” improved from 8.5 by 5.3 (48%) (1 week) [62%] RDQ improved from 19.5 by 11 (48%) (1 week) [56%] 70% of patients reported improvement in mobility after 1 week Clinical outcomes maintained for 1 year of follow-up Narcotics discontinued 16%, decreased 49%, increased 5%	No information provided	12 patients (17%) showed subsequent vertebral compression fractures, 6 within 12 months, 7 adjacent, 5 symptomatic treated with second VP 19% asymptomatic cement leakage

(continued)

Table 12.2 (continued)

Author	Number of patients (mean age)	Number of levels treated	Follow-up	Outcome clinical *1	Outcome radio-morphological	Complications
Thang et al. (2008)	27 (65) LA: if 1 level treated GA: if >1 level treated	117	1 month (41 months)	1 month: *72% pain reduction* VAS reduced from 7.5 to 2.1 70–100% pain reduction in 70% 0–49% pain reduction in 16.7% *55% improved functional status* ECOG [1–5] reduced from 1.9 to 0.86 Opiate consumption interrupted in 59.3%, partially reduced in 22.2% 70.4% decrease in opiate dose	No evidence for progression at treated site after median follow-up of 41 months	No major complications One cement leakage L5 nerve root correlated with appearance of a transient sensory defect, which resolved within 3 weeks Eight clinically not relevant cement leakages (24%)
	50 (62.7) Cancer patients 14 MM LA + conscious sedation	129	3 months (median)	Outcomes of myeloma subgroup not reported separately Pain reduction in 82% of patients Improved mobility in 52% of patients	No information provided	No major complications Increased pain in seven patients (with preoperative mild to moderate epidural involvement) immediately after VP in three patients, treated with epidural steroid injection of steroid infusion, after several weeks in four patients, treated by neuroforaminal epidural nerve root block)

Diamond TH, Hartwell T, Clarke W, Manoharan A. Percutaneous vertebroplasty for acute vertebral body fracture and deformity in multiple myeloma: a short report. Br J Haematol. 2004;124:485–7

McDonald RJ, Trout AT, Gray LA, Dispenzieri A, Thielen KR, Kallmes DF. Vertebroplasty in multiple myeloma: outcomes in a large patient series. AJNR Am J Neuroradiol. 2008;29:642–8

Ramos L, de Las Heras JA, Sánchez S, González-Porras JR, González R, Mateos MV, San Miguel JF. Medium-term results of percutaneous vertebroplasty in multiple myeloma. Eur J Haematol. 2006;77:7–13

Thang NNT, Abdo G, Martin JB, Seium-Neberay Y, Yilmaz H, Verbist MC, Rufenacht D, Sappino AP, Dietrich PY. Percutaneous cementoplasty in multiple myeloma: a valuable adjunct for pain control and ambulation maintenance. Support Care Cancer. 2008;16:891–6

Table 12.3 Reports including both kyphoplasty and vertebroplasty in patients with multiple myeloma

Author	Number of patients (mean age) anaesthesia	Number of levels treated	Follow-up	Outcome clinical[a]	Outcome radio-morphological	Complications
Retrospective reports						
Köse et al. (2006)[b]	34 KP: 18 (63.7) VP: 16 (62.2) LA + midazolam if needed	KP: 22 VP: 28	12 months	*KP: 73% pain reduction* KP: VAS [0–50] improved from 36 to 12.1 (6 weeks), 8.6 (6 months), 9.7 (12 months) *VP: 64% pain reduction* VP: VAS improved from 37.8 to 15.3 (6 weeks), 12,2 (6 M), 13.5 (12 months) → Significant better improvement after KP after 6 + 12 months compared to VP Decreased need of analgesics	Mean height restoration 54% No collapse of adjacent vertebrae	One superficial wound infection, resolved No neurological or pulmonary complications No cement leakage

(continued)

Table 12.3 (continued)

Author	Number of patients (mean age) anaesthesia	Number of levels treated	Follow-up	Outcome clinical[a]	Outcome radio-morphological	Complications
Fourney et al. (2003)[c]	56 (64) Cancer patients KP: 15 VP: 34 KP + VP: 7 (at separate levels) 21 MM: KP: 11 VP: 6 KP + VP: 4 KP: GA VP: GA or LA	97 KP: 32 VP: 65	4.5 months (median) [1 day—19.7 months]	Outcomes of myeloma subgroup not reported separately *Entire study group* VAS reduced from 7 to 2 Immediate pain improvement or complete relief after 84% of procedures (VP: 86%; KP: 80%) Maintained improvement through 1 year No significant functional improvement Decreased analgesic usage at 1 month	42% restoration of lost height and 4.1° improved kyphosis after kyphoplasty	9.2% (6/65) asymptomatic cement leakage after vertebroplasty No leakage after kyphoplasty No procedure-related clinical complications (2x subsequent spinal surgery not related to procedures)

VAS Visual analogue scale (pain) [0–10]; differing ranges are indicated in brackets, *ODI* Oswestry Disability Index [0–100], *ECOG* Eastern Cooperative Oncology Group scale [1–5] – functional status, *BI* Barthel Index, disability score [0 (worst disability)–20 (no disability)], *RDQ* Roland-Morris Disability Questionnaire [1–23], *SF36* Short Form 26 Health Survey [%], *MM* multiple myeloma, *LA* local anaesthesia, *GA* general anaesthesia, *KP* kyphoplasty, *VP* vertebroplasty

[a] % pain reduction and improved disability/functional status represents the percentage of change of the last reported follow-up compared to the preoperative value

[b] (Köse 2006): Indications for Kyphoplasty: >50% loss of vertebral height. Vertebroplasty: <50% loss of vertebral height

[c] (Fourney 2003): Indications for Kyphoplasty: (1) kyphosis >20°, (2) disruption of posterior vertebral cortex, (3) significant vertebral collapse. Vertebroplasty: (1) severe vertebral collapse, when insertion of balloon device not possible, (2) GA or longer procedure time not tolerated

Fourney DR, Schomer DF, Nader R, Chlan-Fourney J, Suki D, Ahrar K, Rhines LD, Gokaslan ZL. Percutaneous vertebroplasty and kyphoplasty for painful vertebral body fractures in cancer patients. J Neurosurg. 2003;98(1 Suppl):21–30

Köse KC, Cebesoy O, Akan B, Altinel L, Dinçer D, Yazar T. Functional results of vertebral augmentation techniques in pathological vertebral fractures of myelomatous patients. J Natl Med Assoc. 2006;98:1654–8 symptomatic levels at the spine, intolerance to being positioned prone, significant medical contraindications (e.g., coagulopathy) or local or systemic infection. While kyphoplasty is typically performed in general anaesthesia, vertebroplasty was usually conducted in local anaesthesia in most patients. The treated levels by both kyphoplasty and vertebroplasty are mainly located in the thoracic and lumbar spine. There are few reports on vertebroplasty in cervical vertebral bodies (e.g., Pflugmacher et al. Acta Radiol. 2006;47:823–9); however, cervical vertebral bodies are not treated routinely by osteoplastic procedures. The reported cement leakage rates are somewhat higher after vertebroplasty treatment (0–94%) compared to kyphoplasty (0–26%). In two retrospective studies, the included patients with multiple myeloma were treated either by kyphoplasty or by vertebroplasty (or both at different levels) [Fourney 2003 and Köse 2006; Table 12.3]. Köse et al. report a significantly better pain improvement after kyphoplasty compared to the vertebroplasty group after 6 and 12 months. However, due to the retrospective design and small group size as well as a possible selection bias by different indications for kyphoplasty and vertebroplasty, no direct comparison of efficacy and safety of both procedures is possible on the basis of these trials.

There is no randomized, blinded, sham-controlled clinical study to confirm the use of osteoplastic procedures in myeloma cases or other malignant entities causing osteolytic vertebral lesions. However, evidence from one randomized trial in myeloma patients [14] and evidence provided from randomized trials in patients with primary osteoporosis are the current basis for the identification of myeloma patients most likely to benefit from osteoplastic procedures.

In a retrospective evaluation of myeloma patients treated with chemotherapy and stem cell transplantation, the additional benefit on pain and vertebral stability was evaluated when the patients received in addition to conventional pain medication kyphoplasty or radiation. This study showed that additional kyphoplasty was more effective than additional radiotherapy or systemic therapy alone in terms of pain relief, reconstruction of pain-associated disability and reduction of fracture incidence of the entire lumbar and thoracic spine [22].

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Bone and Fall-Related Fracture Risk

13

Elisabeth Preisinger and Katharina Kerschan-Schindl

Introduction

Accidental falls in the elderly are a major public health concern because they may result in fracture, loss of autonomy, and institutionalization. Additionally, falls are the second leading cause of accidental or unintentional injury deaths worldwide [1]. The fact that the mean age of the population is increasing almost everywhere in the world emphasizes the importance of prevention and management of falls.

Our sensory-motor control mechanisms are challenged several times a day because of some kind of perturbations. Usually we do not even recognize that. However, with increasing age the postural control system experiences a functional decline and the risk of stumbling and falling increases. An unintentional movement to the floor or lower level, not as a result of a major intrinsic event (such as stroke) or overwhelming hazard, may be defined as a fall [2]. A fall can be divided into three different phases: the initiation, the fall itself, and the impact on the ground.

Epidemiology of Falls and Fall-Induced Injuries

Above the age of 65 years, about 30% of the self-dependent elderly and half of those living in residential care facilities or nursing homes fall at least once a year; the percentage increases further with increasing age, and about half of the fallers are

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E. Preisinger, MD (✉)
Department of Physical Medicine and Rehabilitation, Hietzing Hospital and Neurology Center Rosenhuegel, Wolkersbergenstraße 1, 1130 Vienna, Austria
e-mail: elisabeth.preisinger@wienkav.at

K. Kerschan-Schindl, MD
Department of Physical Medicine and Rehabilitation, Medical University Vienna, Waehringer Guertel 18-20, 1090 Vienna, Austria
e-mail: katharina.kerschan-schindl@meduniwien.ac.at

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recurrent fallers [3]. The injurious outdoor fall rate is supposed to be similar in both genders; however, the rate of injurious indoor falls has been shown to be about twice as high in females compared to males [4]. Of course, the majority of falls do not lead to an injury, but in 20% some medical attention is necessary and 5% result in a serious injury, for instance, a fracture [3].

Bone- and Fall-Related Fracture Risk

Except for most of the vertebral fractures, the nature of the fall and the bone structure are essential parts concerning the risk of a fragility fracture. A fracture occurs if the applied load during the impact of the fall is higher than the structural capacity of the bone. A 10% decrease of bone mineral density (BMD) increases fracture risk 2- to 2.5-fold [5], but most of the fragility fractures occur in subjects without osteoporosis. It is surprising that only 3% of elderly subjects attending an emergency department because of a fragility fracture have no other fracture risk factor than osteoporosis according to the WHO [1], 7% only have a bone-related risk factor, and the majority, one quarter, has one or more fall-related risk factors [6]. Fracture history, mother with fracture history, low body weight (<60 kg), immobility, and regular use of glucocorticoids are summarized as bone-related risk factors. Fall-related risk factors are described below.

The direction of the fall is another important point concerning the probability of a serious injury. Falling sideways increases the risk of a hip fracture fivefold and a fall directly on the trochanter even 30-fold [5]. Of course, the energy-striking bone also depends on the characteristics of the landing surface (e.g., forest soil vs pavement or street) and the thickness of the surrounding soft tissue absorbing some of the energy.

Etiology of Falling

Endogenous and Exogenous Risk Factors of Falling

The number of known risk factors is quite large, and most falls in the elderly are results of an interplay of predisposing and precipitating factors. Elderly subjects, female subjects, and white subjects are more prone to suffering from a fall-related fracture than their younger, male, or black counterparts.

Any acute or chronic disease like a neurologic disorder, rheumatic disease, or a cardiovascular problem raises the risk of falling. With advancing age, the likelihood of diseases or impairments in muscle or joint function, vestibular system, vision, etc. increases. All these factors negatively influence postural stability. Because of diseases and impairments, elderly subjects often have to take several medications. Unfortunately, “taking drugs” negatively influences the risk of falling to a high extent (OR 4.24) [7]. Especially, central nervous system-acting

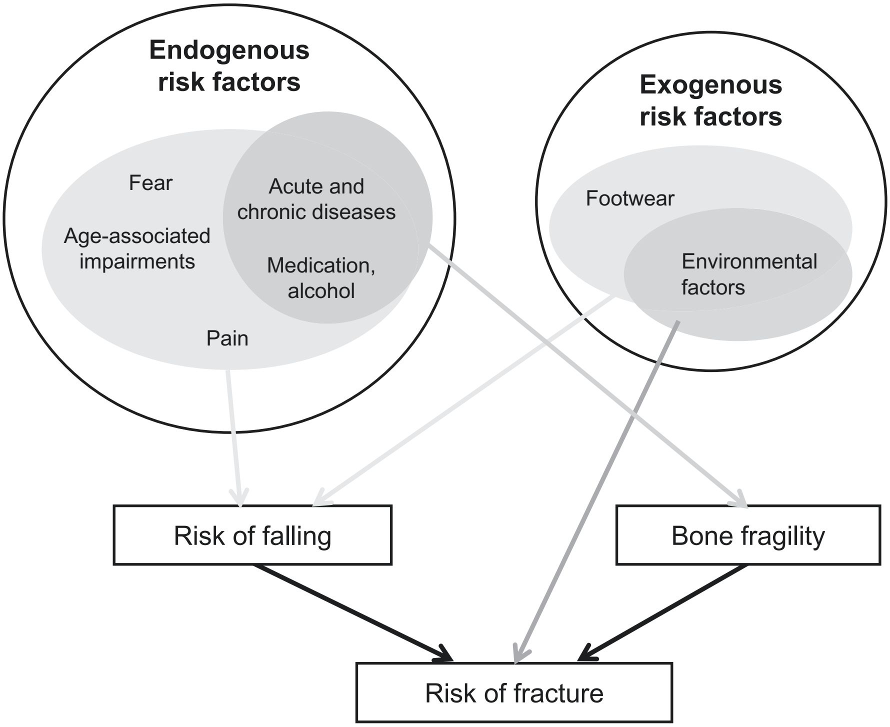
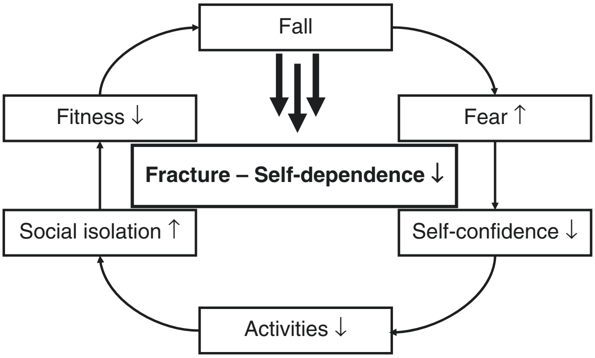


Fig. 13.1 Risk factors for a fracture

agents are fall-risk increasing. Polypharmacy is a serious problem: The overall odds ratio of a hip fracture among patients using 10 or more agents is 8.42 compared to those taking no or just one compound per day [8]. Nevertheless, pain relieved—with or without medication—is indispensable not only to elevate psychological well-being and quality of life but also to reduce the risk of falling; a meta-analysis demonstrated that pain is associated with an increased odds ratio of falling (OR 1.56) [9]. Acute and chronic diseases, age-associated impairments, the intake of substances with a negative influence on postural stability, and psychological distress lead to a reduction in vigilance and can be summarized as endogenous risk factors. Environmental factors such as poor lightening, door sills, stairs, wet floors, or outdoor weather conditions further exacerbate the risk of falling. Of course, the footwear also is an important point in the phase of fall initiation (Fig. 13.1).

The risk of falling increases with the number of prevalent risk factors and with a history of previous falls. An important point is that half of the subjects who have fallen have fear to fall again, and one quarter reduces daily activities because of this fear [2, 10] which has a negative impact on social life and physical fitness which again increases the risk of falling and fall-related fractures (Fig. 13.2).

Fig. 13.2 Consequences of a fall



Physiology of Balance and Postural Strategies

To maintain balance during everyday activities, it is necessary to keep the body's center of gravity over its base of support during upright standing, movement, and walking. Balance is regulated and controlled via interplay of the sensory and motor systems. The central nervous system (CNS) steadily receives information from visual, acoustic, vestibular, and proprioceptive perceptions. This afferent component of the sensory-motor system leads the CNS to induce continuous reactive efferent mechanisms, changes of the motor system. Thus, postural control underlies a continuous feedback mechanism.

Since the regulation is very complex, it is susceptible to flaws. With increasing age we experience a decline in all components of this mechanism. Loss of vision and hearing and a decline in several peripheral receptors reduce the input to the CNS. The age-associated loss of muscle mass and function has an impact on the efficacy of the efferent part of this sensory-motor system. The CNS also underlies age-associated loss of function, and the vigilance of the superior management system is often reduced because of interfering factors like pain or fear. Additionally, an increase of the thoracic kyphosis, shortening or weakness of some muscles, and reductions in hip and knee extension lead to a displacement of the center of gravity; it is shifted forward. All these age-related changes lead to deficits in balance with increased swaying and to more complex postural reactions compared to subjects at younger age.

In young subjects, small disturbances of balance lead to an activation of the muscular activity in the ankle region (i.e., ankle strategy); older people tend to activate muscles in the hip region (i.e., hip strategy) [2, 10]. If it is not possible to regain balance with these postural strategies, one has to take a step. Elderly have to do so at a lower amount of perturbation, and older subjects have to take multiple smaller steps to restore balance, whereas younger subjects respond by a compensatory single step [10]. Apart from anterior-posterior perturbations, disturbances of the equilibrium in the lateral direction have been investigated [11]: Young subjects responded with large roll movements of the trunk in the opposite direction of the tilt platform and abduction of the ipsilateral arm to keep the center of gravity over their base of support. In the elderly, trunk roll was in the same direction as support-surface motion with abduction of the arm in the direction “downhill,” making elderly subjects more prone to losing control of their balance.

A large proportion of falls in the elderly occur while walking, a balance-displacement activity. Older adults may be less capable of weight shifting, and, thus, the gait tends to be stiffer with slower velocity, increased double support time, and smaller steps. Another important point leading to an increased risk of falling induced by an unevenness of the ground is that the minimum foot clearance (distance between lowest point of the foot of the swing leg and the ground) is lower and shows a higher variability during walking in elderly compared to younger men [12, 13].

Screening and Fall Risk Assessment

A key component in preventing falls is the identification of important factors which may increase the risk of falls. An assessment of fall risk should be integrated into the history and physical examination of all geriatric patients, including those not specifically being seen for a problem with falling [14]: All older patients (65 years and more of age) should be asked at least once a year about falls, frequency and circumstances of falling. Older individuals should be asked about difficulties with walking or balance. Older persons presenting with a single fall should be evaluated for gait and balance. A multifactorial fall risk assessment should be performed for community-dwelling older persons who cannot perform a standardized gait and balance test or who report recurrent (two or more) falls in the past year or who report difficulties with gait or balance or who seek medical attention or present to the emergency department because of a fall.

Multifactorial Fall Risk Assessment

The multifactorial fall risk assessment should be performed by a clinician (or clinicians) with appropriate skills and training. It should include a comprehensive history, a physical examination, a functional assessment, and an environmental assessment (Fig. 13.3).

Several studies report that the most important consideration in the history is a previous fall, which places the patient at increased risk of future falls. For patients presenting with a fall, important components of the history include the activity of the faller at the time of the incident; prodromal symptoms, like lightheadedness, imbalance, and dizziness; and where and when the fall occurred. Loss of consciousness is associated with injurious falls and may be caused by orthostatic hypotension, cardiac disease, or neurologic disease. Identification of underlying chronic diseases that increase fall risk is important. Examples of these age-related chronic conditions include Parkinson disease, chronic musculoskeletal pain, knee osteoarthritis, dementia, stroke, and diabetes.

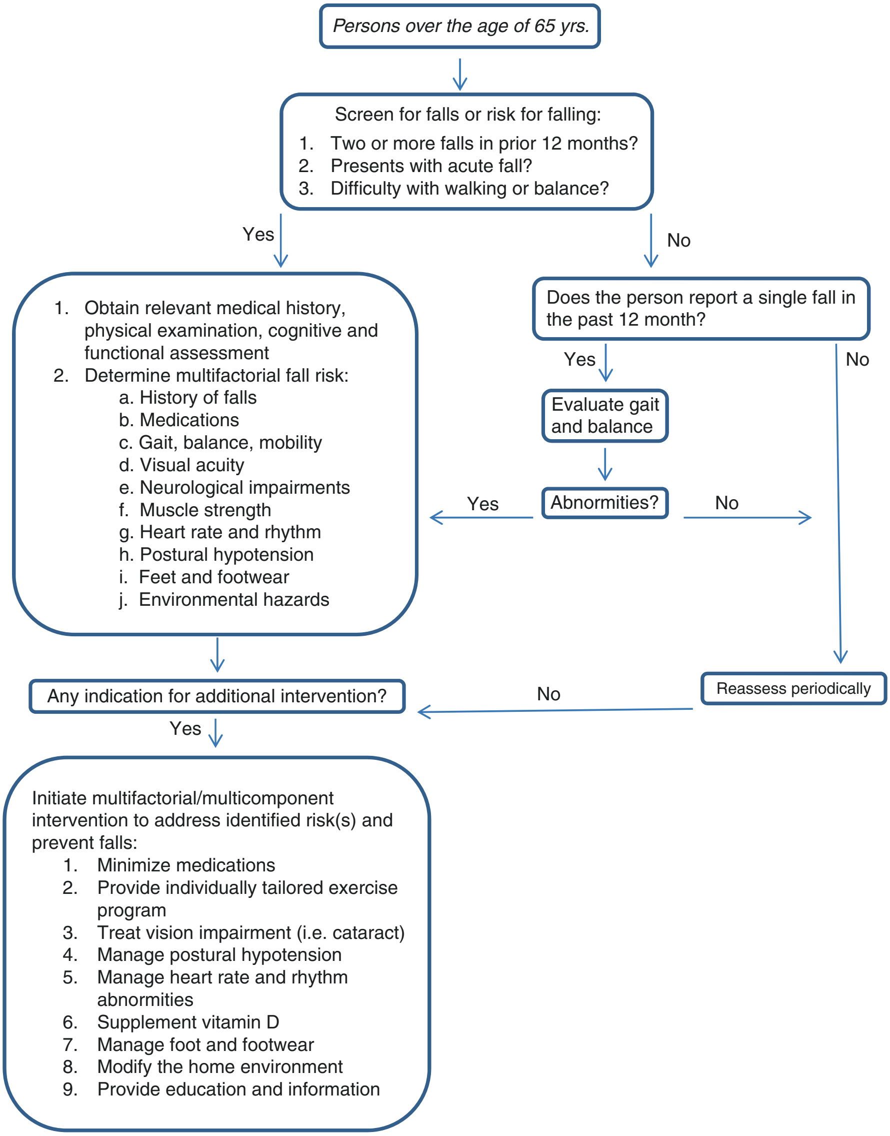


Fig. 13.3 Prevention falls algorithm. Adapted from: The Prevention of falls in Older Persons: Clinical Practice Guideline from the American Geratrics Society. www.americangeriatrcs.org

Information on previous falls should be collected to identify patterns that may help target risk factor modification strategies. A complete medication history should be taken, with specific focus on psychotropic medications, sedative hypnotics, antidepressants, and antihypertensive medications. Timing of medication administration and alcohol use to past falls should be determined. Environmental factors that may have contributed to the fall should also be identified; information on lighting, floor covering, door thresholds, railings, and furniture may add important clues.

The physical examination should include neurologic and joint functions, muscle strength, cardiovascular status, vision, the feet, and footwear. The most important aspect of the physical examination in the patient who has fallen is an assessment of integrated musculoskeletal function. This can be obtained by performing one or more tests of postural stability.

Tests of Postural Stability

The "Get Up and Go" test is one of the best known tests. A 2013 meta-analysis of 53 studies (n = 12,800) showed a mean difference of 3.59 s between institutionalized fallers and non-fallers [15]. However cutoff points distinguishing fallers from non-fallers showed considerable variation between the studies. The test is best used as part of a global assessment of an individual's fall risk. In practical terms, the observation of deficiencies in various individual components may isolate areas for targeted intervention. The test is performed by observing the subject rising from a standard arm chair, walking a fixed distance of 10 ft. (3 m) across the room, turning around, walking back to the chair, and sitting back down. Observation of the different components of this test may help to identify deficits in leg strength, balance, vestibular dysfunction, and gait. The timed part of the test records the mean time (in seconds) from initial getting up to reseating. Patients are compared to the mean time of adults in their age group [16] (Table 13.1).

The "Performance Oriented Mobility Assessment tool (POMA or Tinetti Assessment Tool)" is a scored instrument that assesses balance and gait, using an ordinal scale from zero to two ("0" for the most impaired performance, "1" if slight impairment, and "2" if independent) [17]. The items range from being able to maintain balance when someone slightly pulls on an individual to walking normally with assessment of step continuity and path deviation. No reliable cut point has been established for the POMA score in the prediction of falls.

The "Functional Reach" test is another practical approach to testing integrated neuromuscular base of support that has predictive validity for falls [18]. Functional reach is the maximal distance one can reach forward beyond arm's length while maintaining a fixed base of support in the standing position. The individual makes a fist and extends the arm forward as far as possible without taking a step or losing balance. The total reach is measured along the yardstick and recorded. In its original description, the functional reach correlated with other physical performance measures, including walking speed, tandem walking, and standing on one foot.

Table 13.1 Reference values for the Timed Up and Go Test

Age (years)	Mean time (s)
60–69	8.1 (7.1–9.0)
70–79	9.2 (8.2–10.2)
80–99	11.3 (10.0–12.7)

Bohannon RW. Reference Values for the Timed Up and Go Test: A descriptive metaanalysis. J Geriatr Phys Ther 2006; 29(2):64–8 [16]

The “Short Physical Performance Battery (SPPB)” characterizes lower extremity function [19]. It includes measures of standing balance (timing of tandem, semi-tandem, and side-by-side stands; four-meter walking speed and ability; and time to rise from a chair five times). The SPPB captures a wide range of functional abilities, and summary scores <9 have independently predicted disability in ADL and mobility at one to 6 years of follow-up and are also predictive of falls.

Other tests are the “Berg Balance test.” It is performed easily in the rehabilitation setting or outpatient clinic [20]. The scale predicted risk of multiple falls in older patients in one study. A more comprehensive performance-oriented assessment of balance includes measures of sitting and standing balance, ability to withstand a nudge on the sternum, and ability to reach up, bend down, and extend the back and neck. Each of these performance measures attempts to identify components of postural stability that complement the standard physical examination. Difficulty in performing divided attention tasks such as “walking while talking” may also identify individuals at high risk for falling. A preliminary study in 60 older people found that those who had difficulty walking while reciting the alphabet or walking while reciting every other letter of the alphabet were at significantly increased risk for falls (odds ratio [OR] 7.02 and 13.7, respectively) [21].

General Physical Examination

Other aspects like orthostatic hypotension should be excluded. The blood pressure and heart rate should be taken supine and after one and 3 min of standing. Some information may be derived from sitting vital signs if the patient is unable to stand. An assessment of visual acuity should be performed. Hearing may be assessed using the whisper test or a handheld audiometer. Eighth cranial nerve deficits may be associated with vestibular dysfunction. Examination of the extremities may uncover deformities of the feet that contribute to the risk of falling, such as bunions, callouses, arthritic deformities, and sensory neuropathies. A targeted neurologic examination including evaluation of lower extremity strength, gait, and postural stability may identify persons with an increased risk of falls. Individuals who report a history of falls in the past year tend to have a greater number of abnormalities on a neurologic examination [22]. Leg weakness may increase the risk of falling by more than fourfold.

Diagnostic Testing

Diagnostic testing may be indicated based upon the history and physical examination, including evaluation of postural stability, gait, and mobility. There is no standard diagnostic evaluation of an individual with a history of or at high risk for falls. Only balance problems can be tested by posturography. Laboratory tests such as a hemoglobin concentration and serum urea nitrogen, creatinine, and glucose concentrations can help to rule out causes of falling such as anemia, dehydration, and neuropathy related to diabetes. Serum 25-hydroxyvitamin D levels can identify individuals with vitamin D deficiency who will benefit from vitamin D supplementation. There is no proven value of routinely performing ambulatory cardiac monitoring in individuals who have fallen. Similarly, the decision to perform echocardiography, brain imaging, or radiographic studies of the spine should not be considered routine, but should be driven by findings during the history and physical examination.

Preventing Falls

In general, evidence suggests that interventions individually tailored to target risk factors and impairments are more effective than those applied as a standard package [23].

In reviewing the studies of fall prevention, many trials use the number of fallers in active versus placebo groups, whereas other studies use the rate of falls in the active versus placebo groups. Since individuals who sustain multiple falls have a different risk profile than individuals who sustain a single fall, it seems more relevant to clinical practice to favor those studies that examined fall rates as the outcome [24]. A 2012 systematic review evaluated 159 randomized trials of interventions to reduce the incidence of falling and involved 79,193 older persons living in the community [25]. Authors concluded that group- and home-based exercise programs and home safety interventions reduce rate of falls and risk of falling in community-dwelling elderlies. Exercise both reduces risk of falls and prevents injuries related to falls. In care facilities, mostly vitamin D supplementation is effective in reducing the rate of falls [26]. Exercise in subacute hospital settings appears effective, but its effectiveness in care facilities remains uncertain due to conflicting results, possibly associated with differences in interventions and levels of dependency. There is evidence that multifactorial interventions reduce falls in hospitals, but the evidence for risk of falling was inconclusive. Evidence for multifactorial interventions in care facilities suggests possible benefits.

Exercise Programs

Multiple meta-analyses of randomized trials conducted in various populations, nursing home patients, as well as community-dwelling older adults find that various exercise regimens tend to reduce the risk of falls and that exercise programs that include balance components are most effective [25]. Exercise both reduces risk of falls and prevents injuries related to falls. Exercise interventions can be grouped into different categories: (a) strength training or resistance training exercise, (b) endurance training, (c) flexibility training or range of motion exercises or stretching exercises, and (d) motor control exercises or complex exercises such as gait training, balance training, Tai Chi, dancing, and general physical activity.

Exercise classes incorporating multiple categories of exercise both reduced the rate of falls (rate ratio, RaR, 0.71, 95% CI 0.63–0.82) and risk of falling (risk ratio, RR, 0.85, 0.76–0.96). Home-based exercises that included more than one type of exercise also decreased the fall rate and fall risk [25]. In one trial involving subjects 70 years and older with a history of a significant fall in the past year, a program that integrated balance and resistance training into everyday home activities resulted in a 31% decrease in the rate of falls (RaR 0.69, 95% CI 0.48–0.99) compared to sham control and was more effective than a structured exercise program done three times a week. Tai Chi, which contains elements of motor control exercise, flexibility, and balance training, was found effective in the systematic review and other studies, although may be less effective in frail older adults at high risk for falls. In one meta-analysis, greater relative effects of exercise in decreasing fall rates were seen for exercise programs that incorporated balance challenges and used a higher dose of exercise. A large trial conducted in New Zealand compared Tai Chi to low-level exercise that did not incorporate any exercise specifically targeted to balance and found that both the Tai Chi and the low-level exercise reduced the risk for falls by 58% [27].

Programs that include multitasking exercises during balance/gait interventions have shown some benefit. One trial compared a walking intervention termed “trail walking exercise” with regular walking, both in combination with a standard exercise program [28]. The trail walking procedure is a complex task walking exercise in which an individual walks sequentially from one numbered flag to another, thereby incorporating the dual task of walking and being challenged with an “executive” function. After a six-month period, incidence of falling showed an 80% reduction in the trail walking group. A trial among community-dwelling older adults of a dual task exercise done to rhythm from piano music improved balance and functional test results and decreased risk of falling and number of falls by about 50%; the benefit persisted 6 months after the intervention [29].

Medication Modification

One placebo-controlled trial found that gradual withdrawal of psychotropic medications reduced the rate of falls (RaR 0.34, 95% CI 0.16–0.73), but not the risk of falling [25]. Risk of falling was decreased (RR 0.61; 95% CI 0.41–0.91) in one trial that evaluated medication review combined with multiple other physician-focused interventions (academic detailing, provider feedback on prescriptions, and financial reward). However, there is no evidence that medication assessment and withdrawal in the absence of other management interventions will reduce the risk of falling.

Vitamin D

Although the evidence is not definitive, because of low risk of harm, we suggest that older patients be given cholecalciferol (vitamin D3) supplements for fall prevention, which can be given daily, weekly, or monthly with the dose adjusted to achieve the dosing equivalence of at least 1000 units daily, in agreement with 2014 guidelines from the American Geriatrics Society for fall prevention [30]. Men and women over age 65 years with low serum 25-hydroxyvitamin D concentrations (<10 ng/mL [25 nmol/L]) are at greater risk for loss of muscle mass, strength, and hip fractures [31]. Vitamin D supplementation may improve bone mineral density and muscle function. However, the effect of vitamin D on risk of falls remains unclear. A 2012 meta-analysis of trials of interventions to prevent falls showed that vitamin D supplementation in community-dwelling adults did not reduce risk of falling (risk ratio 0.96, 95% CI 0.89–1.03, 13 trials) or the rate of falls (rate ratio 1.00, 7 trials), but may have had some effect in people with lower pretreatment vitamin D levels [25]. It is important to ask about dietary supplements (some of which contain vitamin D) that patients may be taking, as well as assessing other contributors to vitamin D status such as dietary intake, the presence of obesity, and sun exposure before prescribing extra vitamin D, since the amount of supplemental vitamin D should take these factors into account.

Multiple and Multifactorial Interventions

In a meta-analysis of six studies, home safety assessment and interventions decreased the rate (RaR 0.81, 95% CI 0.68–0.97) and risk (RR 0.88, CI 0.80–0.96) and were most effective for individuals at higher fall risk and when delivered by an occupational therapist [25]. In a subsequent cluster randomized trial, a standardized set of home safety interventions, installation of stair handrails, grab rails in bathrooms, improved lighting, slip-resistant deck surfacing, nonslip bathmats, etc., resulted in a 26% decline (RR 0.74, 95% CI 0.58–0.94) in injuries caused by falls over a 3-year period, compared with study of households that were wait-listed for the intervention. Vision assessment and correction did not reduce risk or rate of falls in four trials. One randomized trial found that substituting single lens for multifocal glasses during outdoor and walking activities decreased the rate of falls in active older adults. Nonslip devices worn on shoes in winter weather conditions decreased the rate of falls in the outdoors (RaR 0.42, 95% CI 0.22–0.78). Educating older people about fall prevention as a sole intervention did not reduce the rate or risk of falls in a systematic review [25]. A systematic review of "cognitive motor interference" (CMI) interventions (practicing a simultaneous cognitive and motor task) to prevent falls concluded that CMI training reduced falls and improved gait, balance, and reaction time [32].

Several Interventions Targeting Patients with Specific Morbidities

For fallers with carotid sinus hypersensitivity, insertion of a cardiac pacemaker decreased the rate of falls (RaR 0.42, 95% CI 0.23–0.75) [25]. For patients with cataracts, expedited surgery for the first eye reduced the rate of falls (RaR 0.66, 0.45–0.95), but cataract surgery for the second eye was not associated with a decrease in the rate of falls [25]. Data from a Medicare database comparing hip fracture rates in patients with cataract who did or did not undergo cataract surgery found a 16% decrease in the adjusted odds ratio for hip fracture within 1 year in patients who had surgery and a 23% decrease for patients with severe cataract. Compared with usual care, oral nutritional supplementation for 3 months for malnourished older patients (BMI <20 kg/m^2 or significant recent unintentional weight loss) who had been recently hospitalized decreased the number of falls and number of fallers. The intervention included vitamin D, a protein supplement, and nutritional counseling. Postural hypotension is a fall risk, and treatment has shown benefit [14]. Treatment may include medication reduction, fluid optimization, elastic stockings, or medications such as fludrocortisone or midodrine. For community-dwelling older patients with disabling foot pain, a multifaceted podiatry intervention (podiatry care, orthotics, footwear subsidy, foot and ankle exercises, and falls education) led to a 36% reduction in the incidence of falls compared to patients who received usual care.

Preventing Complications of Falls

The above measures can reduce a large number of falls, but do not prevent them entirely. Additional aids should be considered for preventing fall complications.

Hip Protectors

Hip protectors have been studied as a method of preventing hip fractures. A meta-analysis of randomized trials that included both community-dwelling and nursing home patients found no evidence that they were effective in reducing hip fractures in studies in which randomization was by individual patient within an institution or among patients living at home [33]. Hip protectors may fail to prevent injury because they are often not worn, or injury occurs in circumstances that would have precluded use of hip protectors.

Assistive Devices

Providers are often motivated to recommend assistive devices (walkers or canes) to their aging patients with gait and balance impairments related to decline in neuromuscular function with aging and/or chronic disease. Some individual patients are obviously benefited by such devices, in terms of mobility. However, evidence that assistive devices reduce the risk of falls is lacking. There are no randomized placebo-controlled trials of assistive devices to prevent falls. Observational studies have noted an association between the use of assistive devices and increased risk for falls. This most likely represents an inherent bias because individuals with the most impaired gait and balance are most likely to be prescribed these devices. It should be possible that using a walker or cane can interfere with compensatory stepping, which may result in an increased risk for falling.

Time on Floor

A study of 1100 individuals over age 72 found that 47% of the 313 who experienced non-injurious falls were unable to get up for at least 1 h after falling [34]. Prolonged time on the floor was associated with serious injury, hospital admission, and move to long term care. Call alarm systems have been promoted to prevent "long lies" after falls. These systems may include alarm buttons worn on the person or in the room. Their effectiveness is uncertain. Sometimes very old fallers who could not get up and had some type of call alarm system did not use it.

Anticoagulation

A decision analysis has concluded that a predisposition to falls, with potential head trauma, is rarely a contraindication to the use of anticoagulants in older adult patients with atrial fibrillation (AF) [35]. Even when taking anticoagulants, the risk of subdural hematoma is so low that persons with an average risk of stroke from AF must fall approximately 300 times in a year for the risks of anticoagulation to outweigh its benefits.

Conclusion

With advancing age the risk of falling and fall-related injuries increases. Most fragility fractures are caused by falling from a standing or sitting position. The sensory-motor system is complex, and many age- and disease-associated changes have a negative impact on balance. Thus, a fall risk screening or assessment has to be performed in older patients with osteoporosis. Multifactorial/multicomponent interventions have to address identified risk factors in order to effectively prevent falls.

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Rehabilitation After Hip Fracture

14

Yannis Dionyssiotis

Hip Fracture: An Important Clinical Entity

Hip fractures represent one of the most important causes of morbidity and mortality among the elderly. After a hip fracture, approximately half of the previously independent elderly victims will become partly dependent and ultimately a third totally dependent. A previously normal subject becomes disabled and the quality of his life is diminished. Hip fractures lead to an overall 12–20% reduction in expected survival with 5–20% excess mortality within the first year after the fracture and are also a major problem for the economics of modern medical care [1, 2].

Extraskeletal clinical factors related to falls increase hip fracture risk. Unsteady gait or slow gait speed because of lower limb dysfunction or neuromuscular impairment, decreased physical activity, use of medications like long-acting barbiturates or benzodiazepines, visual problems and type of fall (direct hip impact and falls to the side) can contribute to the likelihood of experiencing a hip fracture [2]. The ability to respond rapidly and effectively is reduced in older people compared with younger adults. A decrease of reaction time during aging is expected. Studies of reaction time in stepping in older people typically have observed a delay in step initiation and execution timing. Coordination time has also been linked to lower extremity fracture risk [3].

Bone loss is an important factor associated with hip fracture. A previous osteoporotic fracture is an important predictor for future fractures, including those of the hip. Diminished mobility and independence experienced after hip fracture produces a rapid and major deterioration in health-related quality of life (Fig. 14.1).

Y. Dionyssiotis, MD, PhD
Physical Medicine and Rehabilitation Department, European Interbalkan Medical Center,
10 Asclepiou Street, Pylaia, Thessaloniki 57001, Greece

First Department of Orthopaedics, General University Hospital "ATTIKON",
Chaidari, Athens, Greece

Assistant Professor of Metabolic Bone Disease and of Rheumatology, Rehabilitation Unit,
University of Patras, Patras, Greece
e-mail: yannis_dionyssiotis@hotmail.com

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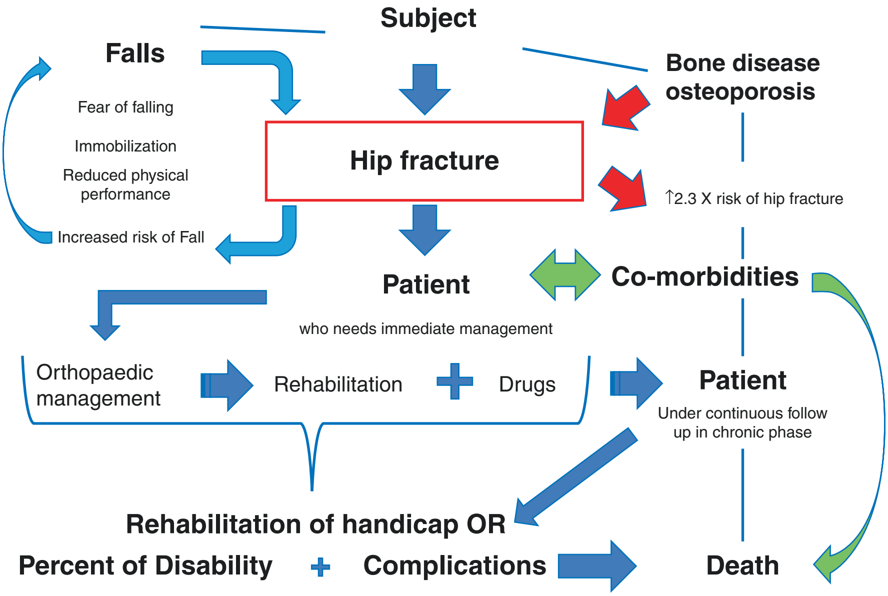

Fig. 14.1 Hip fracture is an important clinical entity. Schematic presentation © Dionyssiotis 2015 (for detailed explanation see text)

Rehabilitation After Hip Fracture

A Comprehensive Approach in the Fall Clinics

Depending on the country, this term includes also rehabilitation, ortho-geriatric and orthopaedic departments for the management of the older adults presenting with hip fracture. According to the country, different healthcare professionals retain the responsibility for the management of the patients throughout the care pathway after hip fracture. In most countries, in-hospital stay is usually short (on average a week), and post-acute rehabilitation is performed in different settings, such as other in-hospital wards, i.e., geriatric or rehabilitation department; out-of-hospital facilities, i.e., rehabilitation clinics; physical therapy units; or home-based services. Some countries support most sophisticated models, i.e., rehabilitation wards specifically designed for the rehabilitation of geriatric patient (Geriatric Rehabilitation Unit) or even orthopaedic geriatric patients (Geriatric Orthopaedic Rehabilitation Unit) [4].

Rehabilitation is a goal-oriented and time-limited process that focuses on making a functionally impaired person to reach the optimum mental, physical and social functional level. The aim of the rehabilitation team is to restore the functional level of people who sustained a fracture as a consequence of falling and to avoid falls and fall-related fractures by educating groups under high risk (Fig. 14.2).

Rehabilitation after surgical stabilization of a hip fracture is crucial in optimization of post-injury mobility, restores prefracture function and avoids long-term institutionalization. Patient's medical history concerning other co-morbidities and data about frequency, characteristics and number of previous falls during the last year are important [3].

The degree of healing varies widely depending on the age, concomitant diseases of the patient and other factors such as thyroid hormone levels, nutritional status, etc. Common conditions that disturb the healing fracture include diabetes, circulatory disorders, anaemia, hypothyroidism, nutritional deficiency-malnutrition (lack of vitamin C or D, insufficient protein intake) and long-term use of alcohol and tobacco. Drugs which may also disturb the healing fracture including non steroidal anti-inflammatory drugs (NSAIDs), glucocorticoids and antibiotics (ciprofloxacin) [5]. Rehabilitation physicians are facing life-threatening medical complications such as cardiopulmonary problems, deep vein thrombosis and ischaemic attack in hip-fractured subjects, but also variable complications such as hip pain, uneven limb length, heterotopic ossification, decubitus ulcers and neurological complications which possible occur after hip fracture and should be treated. A thorough clinical examination of gait and balance disorders is also necessary to inspect current impairments or disabilities and organize the rehabilitation process [3] (Table 14.1).

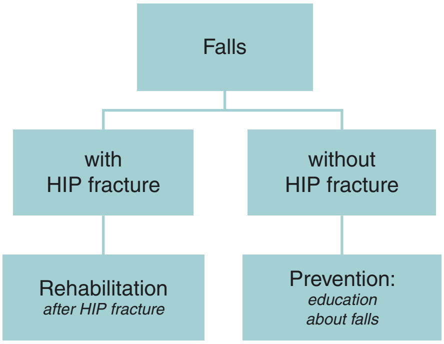

Fig. 14.2 The dual role of rehabilitation (Modified with permission from: Dionyssiotis Y et al., J Musculoskelet Neuronal Interact. 2008)

Table 14.1 A combination of medical and rehabilitation interventions is necessary after hip fracture

Rehabilitation interventions	Medical interventions
Physical modalities (mainly for complications, i.e., hip pain, heterotopic ossification, decubitus ulcers etc.)	Not exclusively rehabilitation interventions but can be done in the rehabilitation department (or ortho-geriatric or orthopaedic) in a hospital setting
Therapeutic exercise and comprehensive rehabilitation programme	

Physical Therapy: Exercise Programme

Immediately after the operation, breathing exercises to reduce the risk of atelectasis and other pulmonary complications while the patient is still in bed should be started. Breathing exercises can be either energetic or passive when a physical therapist helps the patient. The individuals are also given spirometers and are instructed to take deep breaths, keeping the inhaled air inside for a couple of seconds and then exhale. The following primary exercises are important for increasing circulation to legs and to prevent blood clots, to strengthen muscles and to improve hip movement and should be started gradually from the first day after surgery with an intensity that does not exceed the limits of pain tolerance (for analytical descriptions, please see Table 14.2). They should be performed in a supine body position with the lower limbs partially abducted. The patient is encouraged to bend his operated limb. "Pump-like" energetic exercises (ankle pumps), ankle rotations and straight leg raises for the lower extremities are basic in the programme. However, upper extremities and trunk strengthening must also be part of the rehabilitation programme, to assure that patient has adequate strength in the arms for moving around in bed, for standing up from a chair and for walking when using a walker or crutches. Exercises to keep trunk muscles strong may help avoid back problems, which may arise from the initial uneven weight bearing. Abdominal and dorsal muscles should also be exercised isometrically and then energetically, in order to minimize the risk of low back pain during weight-bearing exercises.

However there are some limitations on range of motion (ROM) after surgery depending on the surgical procedure (hip fractures stabilized with internal fixation do not require ROM precautions). The patient is instructed to avoid (a) hip flexion greater than 70–90° for 6 weeks, (b) inner and/or outer hip rotation and adduction exceeding the neutral position for at least a 6-week period (in posterior approach), (c) forward bending and lying on the operated hip's side for the first 2 weeks and (d) putting the lower extremities in a crosswise position. By the third day after surgery, the patient should start training from a sitting position. While standing down during transfer from bed to chair, the hip must be abducted. Weight bearing should start later on at 6th to 10th day, when the patient is capable of standing on his feet by himself. Partial weight bearing should be preserved for 6–12 weeks. Most of the patients are more likely to start using a walker frame and then progressively move to using crutches. In the partial weight-bearing stage of rehabilitation, the operated hip is allowed to bear only a load of 30 kg. Gradually, the patients will be allowed to start walking on crutches for 4–6 weeks. Complete weight bearing depends on the surgical procedure. Usually the patient is scheduled after total hip arthroplasty after a period of 6 months and after open reduction and internal fixation after 3 months [3].

Regular weight-bearing exercise can preserve bone mass and conserve or improve bone mineral density (BMD) in older adults and could also reduce hip fracture risk by decreasing the risk of fall in the elderly population [2]. After their strength is regained, they should follow balance-specific, individually tailored and targeted training for dynamic balance, strength, bone, endurance, flexibility, gait and functional skills; training to improve 'righting' or 'correcting' skills to avoid a fall; backward chaining; and functional floor exercises [3].

Table 14.2 Early postoperative exercises

Early postoperative exercises				
Exercise	Description	Frequency	Comments	Duration
Ankle pumps	Slowly push the foot up and down	Several times as often as every 5 or 10 min	Keeps calf muscle flexible while ‘pumping’ the muscles to help circulation	Begin immediately after surgery and continue until fully recovered
Ankle rotations	Move ankle inwards towards the other foot and then outwards away from the other foot	Repeat five times in each direction 3–4 times per day	Helps circulation	Begin immediately after surgery
Bed-supported knee bends	Slide heel towards the buttocks, bending the knee and keeping the heel on the bed	Repeat five times, 3–4 times per day	Do not let the knee roll inwards	Begin immediately after surgery
Quad set	Try to straighten the knee	Hold for 5–10 sec Repeat the exercises 10 times, 3 times/day	Tighten the thigh muscle	Begin immediately after surgery
Straight leg raises	Tighten the thigh muscle with your knee fully straightened on the bed. As thigh muscle tightens, lift the leg several inches off the bed	Hold for 5–10 sec Slowly lower leg Repeat the exercises 10 times, 3 times/day	Repeat until thigh feels fatigued	Begin immediately after surgery
Buttock contractions	Tighten buttock muscles	Hold to a count of 5	Repeat until thigh feels fatigued	Begin immediately after surgery
Abduction exercise	Slide the leg as far as the patient can and then back	Repeat the exercise 10 times	Do not exceed the neutral position for at least 2 weeks	Begin immediately after surgery

Prevention of Falls

Falls can also result in deterioration of physical functioning and quality of life due to injury or due to fear of falling. We need to assess possible intrinsic, extrinsic risk factors for falls and the exposure to risk of the individual. As important as identifying risk factors is appreciating the interaction and probable synergism between multiple risk factors because the percentage of persons falling increased from 27% for those with no or one risk factor to 78% for those with four or more risk factors. Prevention may be even more effective when multiple risk factors of falls are taken into account. Most multifactorial fall prevention programmes have been successful in reducing the incidence of falls and risk factors of falling, especially when prevention has been individually tailored and targeted to populations at high risk of falling [6]. Interventions to prevent falls may be planned to reduce a single internal or external risk factor of falling or be broadly focused to reduce multiple risk factors simultaneously [7].

Tai Chi is a promising type of balance exercise [8, 9]. However it requires further evaluation before it can be recommended as the preferred method for balance training. Although Tai Chi is probably the exercise programme, we would least recommend to people who have previously suffered fractures because they show a level of frailty that means they could not fully participate in Tai Chi unless it was adapted so much it was no longer dynamic balance training (Skelton D, personal communication). However, as ageing is related with reduced physical functioning (frailty), exercise prescription for falls prevention, except balance and strength training, may include exercises to increase the functional capabilities in all elderly. Suggested solutions are low-intensity balance exercises (tandem walking and standing on one's foot) combined with coordination exercises. Individuals who are frail and severely kyphotic or suffer from pain or poor balance may benefit from water exercise (hydrotherapy). People are also advised to undergo strengthening exercises of the quadriceps, hip abductors/extensors, back extensors and the arm muscles [10].

Occupational Therapy

When older patients at increased risk of falls are discharged from the hospital, a facilitated environmental home assessment should be considered. House modifications as well as the use of accessories minimizing the risk of falling are key elements of occupational therapy (OT). Hip fracture patients should have OT training for skills adaptation and a home visit to get individualized support to improve the ability to perform activities of daily living ADL and to speed up both mental and social recoveries. More advanced skills (e.g., driving, vocation, avocations) may take a longer period of recovery or may need to be modified to permit performance. Driving skills are best delayed until at least 8 weeks postfracture. Patients are urged to keep on training even after they are discharged and their period of rehabilitation is over [3].

Hip Protectors

Anatomically designed external hip protectors disperse the energy of a fall into adjacent soft tissue. The effectiveness of the provision of hip protectors in reducing the incidence of hip fracture in older people is still not clearly established, although they may reduce the rate of hip fractures if made available to frail older people in nursing care. It remains unknown from studies identified to date if these findings apply to all types of hip protectors. Some cluster-randomized trials have been associated with high risk of bias. Poor acceptance and adherence by older people to hip protectors have been key factors contributing to the continuing uncertainty [11].

Recommendations: Guidelines

Two evidence-based clinical practice guidelines suggesting possible treatments and rehabilitation pathways for hip fracture patients agree that it would be best if they underwent multidisciplinary rehabilitation [12–14].

However two Cochrane reviews recently published challenged these guidelines [15, 16]. The first review included 13 studies involving a total of 2498 elderly patients, mainly women, who had undergone surgery for hip fracture. In 11 studies, patients underwent rehabilitation either totally or primarily in nursing or hospital environment. Although there was a trend for better outcome after multidisciplinary rehabilitation, the results were not statistically significant and therefore cannot be considered as definitive. In a study that compared multidisciplinary rehabilitation at home with the usual inpatient care, the participants had a shorter hospital stay, but longer periods of rehabilitation. Overall, the results of this analysis show that multidisciplinary rehabilitation can help older people recover after a hip fracture. However, the results are not conclusive and more research is needed [15]. In the second Cochrane review, main results included the independence in activities of daily living or focus on social and psychological issues of older people recovering from hip fracture. The transition from early phase to rehabilitation and community needs further investigation because studies are small and of different quality [16].

However, multidisciplinary rehabilitation programmes are targeted particularly at frail older people with multi-morbidity and physical function impairment. A more general systematic review of inpatient rehabilitation for older patients found that multidisciplinary inpatient rehabilitation provided to general (eight trials) or orthopaedic populations (nine hip fracture trials) reduces mortality, improves physical function and reduces risk of nursing home placement; these favourable findings were found in both hip fracture and general geriatric patients [17, 18].

On the other side, Feehan et al. stated that improved functional results in the early phase exist with inpatient and interdisciplinary rehabilitation programmes after hip fracture. Better functional results and better gait followed a program including early mobilization, load, aerobics, balance, and strength training after a hip fracture [19].

The review on nutritional supplementation after hip fracture again points out the weakness of the available evidence for this group of patients. The review found out that it is unlikely that nutritional supplements are beneficial for those older hospital patients who are well nourished; however, there is evidence of benefit for those who are underweight [17].

Monitoring Hip-Fractured Subjects and Prognosis

Patients who have fallen should have their medications reviewed. Particular attention to medication reduction should be given to older persons taking four or more medications and to those taking psychotropic medications because are linked to the occurrence of falls. Reducing the total number of medications to four or fewer, if feasible, has also been demonstrated to reduce the risk of falling [20, 21].

Follow-up sessions should be organized at the end of the first, third and sixth month post-surgery and continue at least 1 year as a remainder in the patient's life. Patients will return to their premorbid level of basic functions within 4–6 weeks of the fracture. The Functional Independence Measure (FIM) scale assesses many parameters concerning hip fractures. Through FIM, factors like mobility and self-care ability were found to be correlated with the intra-hospitalization time span. Moreover, bladder issues and locomotion are correlated with expenditure, while problems with urinary bladder, clothing and mental status are associated with the patient's functionality [22, 23].

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Postural Changes in Osteoporosis: Musculoskeletal Consequences

15

Mehrsheed Sinaki

Axial posture is not static but rather a dynamic process affected by orientation of different anatomical units in relationship to one another at any given time. Posture can be influenced by multiple factors, including aging, sex, bone loss, muscle strength, and occupation. These factors can affect the intensity of recruitment of muscles, whether for static upright position or locomotion. The most disfiguring effect of axial loss of bone and muscle strength is the anterior wedging or fractures of the mid-thoracic or thoracolumbar vertebral bodies. This can result in thoracic hyperkyphosis and shift of cervical spine to the front of the line of gravity. The line of gravity normally passes through an aligned cervical spine. The human upright posture has a phylogenetic history. The chief factor in providing upright posture is the development of extensors during the cycle of evolution. This includes the extensors of the back, hips, and knees. The most effortless posture in humans is when anatomical structures that participate in upright posture are aligned with the line of gravity or close to it. In normal posture, this line of gravity passes from C1 to C6, then to T9 to lumbosacral perpendicular to the horizontal line connecting the hip joints (or slightly behind hip joints), and then in front of knee joints and ankle joints. Needless to say, any posture is not static and can change backward and forward in relation to the line of gravity (Figure 15.1).

In kyphosis and forward thrust of the head, weight of the head will add to the deforming forces of the spine and further development of kyphosis (Figure 15.2). Therefore, exacerbating forces of gravity on misaligned spine can increase thoracic kyphosis and cause further contraction of the posterior neck muscles and extensors to maintain upright posture [1, 2].

M. Sinaki, MD, MS
Consultant, Department of Physical Medicine and Rehabilitation, Mayo Clinic,
Rochester, Minnesota, USA

Professor of Physical Medicine and Rehabilitation, Mayo Clinic College of Medicine and Science,
Rochester, Minnesota, USA

Director of Rehabilitation of Osteoporosis Program, Mayo Clinic, Rochester, Minnesota, USA
e-mail: sinaki.mehrsheed@mayo.edu

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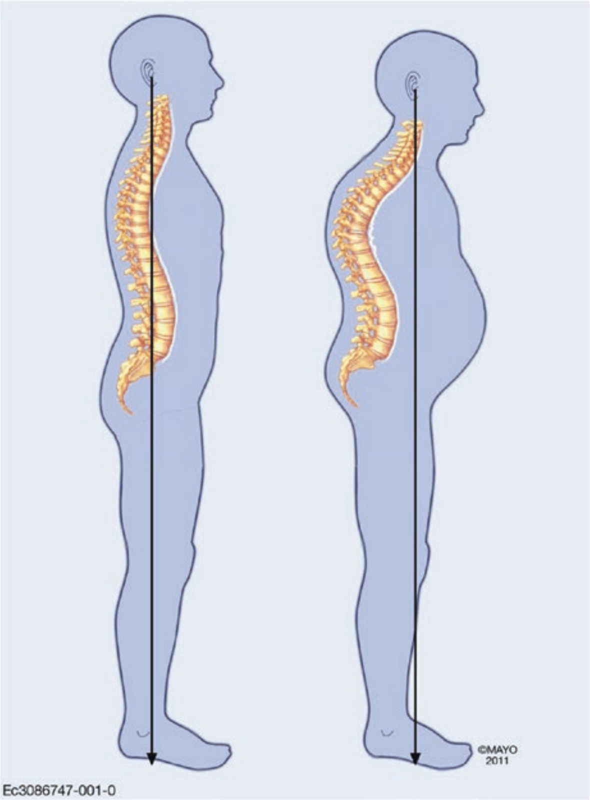

Fig. 15.1 Orientation of the body to the line of gravity in normal vs. kyphotic posture

In our outpatient clinic, some of the osteopenic and osteoporotic patients exhibit acquired kyphosis and experience cervicalgia and headaches. Some patients also complain of low back pain, flank pain, or both and demonstrate fear of falls due to unsteadiness of their gait [3]. These patients usually have undergone work-up for etiology of their headaches, and if all other causes are ruled out, we evaluate them in our tertiary facilities to address their symptoms. Age-related sarcopenia and osteoporotic fractures create musculoskeletal challenges that cannot be managed with pharmacotherapy alone. Some headaches are related to overuse of posterior cervical muscles in the setting of malposture of the spine [4]. To address the forward positioning of the head and neck, we have noted positive results from mechanical intervention aimed at reduction of thoracic kyphosis.

Cervicalgia and Related Headaches

Headaches can be complex, and their etiology needs detailed work-up. In this chapter, I discuss the headaches related to overuse of posterior cervical muscles in the setting of malposture related to axial bone loss and thoracic kyphosis. Forward posture of the head and neck can result in contraction of posterior neck muscles. In normal posture, a periodic inertia of alignment of vertebral bodies with the line of

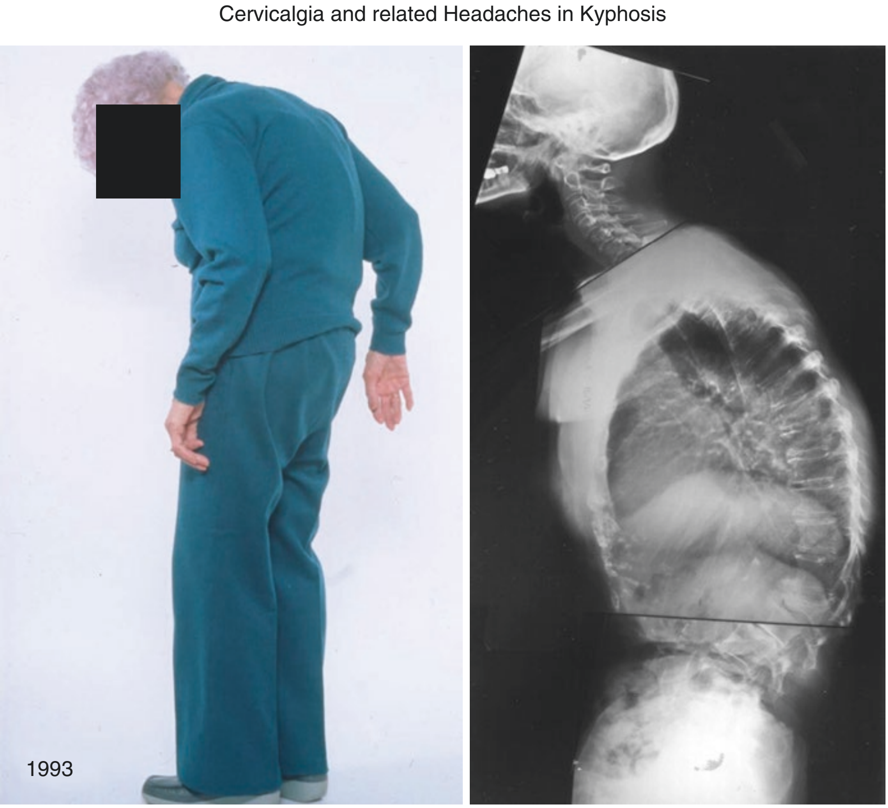

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Fig. 15.2 Forward thrust of the head and weight of the head will contribute to the deforming forces of the spine in development of kyphosis

gravity results in the relaxation of posterior neck muscles. In kyphosis, the persistent contraction of posterior cervical muscles results in pain at their attachments in the suboccipital area. In some cases, suboccipital nerve entrapment could occur, which results in occipital neuralgia and headaches. Patients may complain of headaches in the frontal area with a lack of relaxation of frontalis muscles [5].

Treatment

Injections of pain-relieving or anti-inflammatory substances to the suboccipital area have been successful in reducing pain; however, the effect is not long lasting. Therefore, the etiology needs to be determined, and in the case of hyperkyphosis, correction of the kyphotic posture is necessary. It is difficult to decrease kyphosis as it is not easy for the patient to resume proper posture without preparing the spinal extensors to maintain the alignment. Also, after getting used to the kyphosis, the body's spatial orientation recognizes the malposture as its normal posture; therefore, any attempt at correction of misalignment requires thoughtful planning.

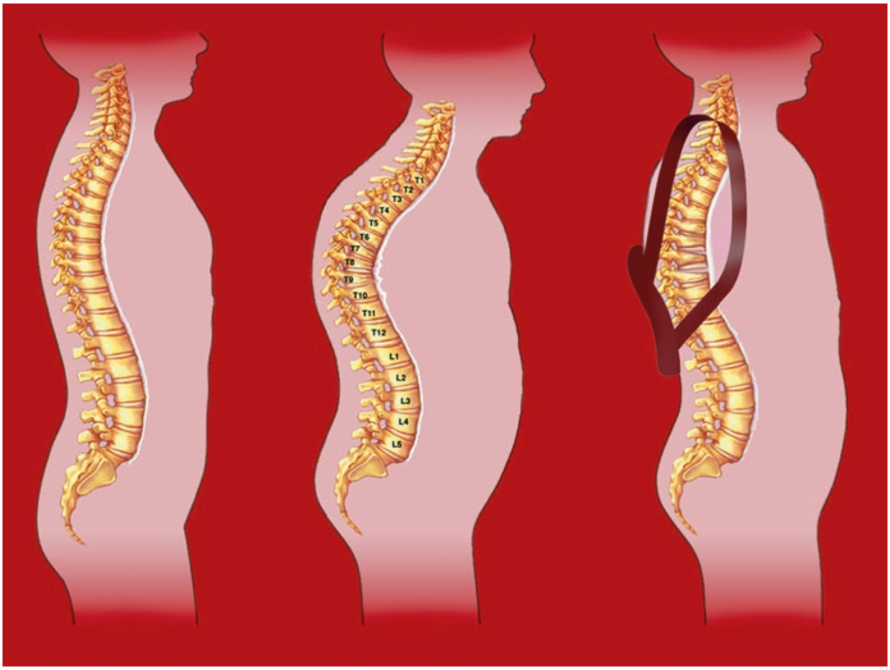
Intervention with Mechanical Loading, Postural Training and Back Extension Exercise

Fig. 15.3 Mechanical intervention is accomplished through a properly positioned mechanical load using a WKO support below the scapulae or at the tenth thoracic vertebra (Th–10), to reduce forward thrust forces and facilitate contraction of spinal extensors

Proper intervention should be biomechanical and include realignment of the spinal facet joints to the correct posture through application of a weighted kypho-orthosis (WKO) support used for short periods of time (20 min), the same time used as in the trial of the spinal proprioceptive extension exercise dynamic (SPEED) program (Chapter 7) (Figure 15.3). In the SPEED program, after the trial, if the patient feels some pain relief, the attempt is considered successful, and it is worthwhile to pursue the instructions for daily or twice a day implementation at home. The weight in the pouch is based on the patient's stature and need for mechanical correction; it also plays an important role and needs to be sufficient for reduction of kyphosis but not too heavy to cause shoulder pain or any other pain. The WKO device needs to be fitted below the scapulae at the T10 vertebral body. Recruiting the paraspinal back extensors could be facilitated through this dynamic intervention for reduction of kyphosis. Relaxation of the posterior neck muscles and contraction of thoracic paraspinal extensors would gradually ameliorate the patient's myofascial pain in the occipitocervical area as the persistent contraction of these muscles is reduced or relieved. The exercise program should address contraction of the back extensors performed in a sitting position while wearing the WKO support.

In one clinical trial (data not published), after preliminary evaluations, patients were provided with instructions to improve their occipito-cervico-thoracolumbar kinetic chain alignment (posture) through specific muscle-strengthening exercises.

Mechanical intervention included the use of WKO when necessary and posture training through re-education of axial muscles with the use of WKO. Reduction of muscle overuse in the posterior cervical spine can decrease suboccipital attachment pain and pressure over the neurovascular structures [4, 6].

All patients who were enrolled in the SPEED program had fewer headaches and reduced use of analgesics. There was a notable improvement in their posture and decreased pain from 8 to 1.3 on pain scale of 0 to 10. On follow-up radiographs, no new vertebral compression fractures were seen.

We concluded that application of WKO provides static reduction of kyphosis, facilitation of neck extensor counterstrain, trapezius relaxation, and cervicogenic pain relief (Figure 15.3). Of course, proper application of the WKO with the appropriate amount of weight in the pouch is necessary to ensure proper fitting of the WKO to avoid shoulder discomfort.

Headaches are complicated, and their etiology requires elaborate work up. We have presented headaches related to myofascial pain due to overuse of posterior cervical muscles in the setting of kyphotic posture of the osteoporotic spine. Any rehabilitative or mechanical intervention (or both) that can decrease the use of pharmacotherapy and analgesics in elderly patients is highly recommended and would decrease the risk of falls related to sedation effect in this age group.

Iliocostal Impingement Syndrome or Flank and Back Pain in Kyphosis

Iliocostal impingement syndrome is not uncommon and is associated with thoracic hyperkyphosis and kyphoscoliosis related to spine deformities in osteopenia or osteoporosis (Figure 15.4). This impingement can be a very painful and disabling condition that affects quality of life for many kyphotic individuals. Spinal deformities can develop with axial bone and muscle loss and under repetitive strain beyond biomechanical competence of the spine. Sarcopenia of aging and anterior wedging of the mid-thoracic vertebral

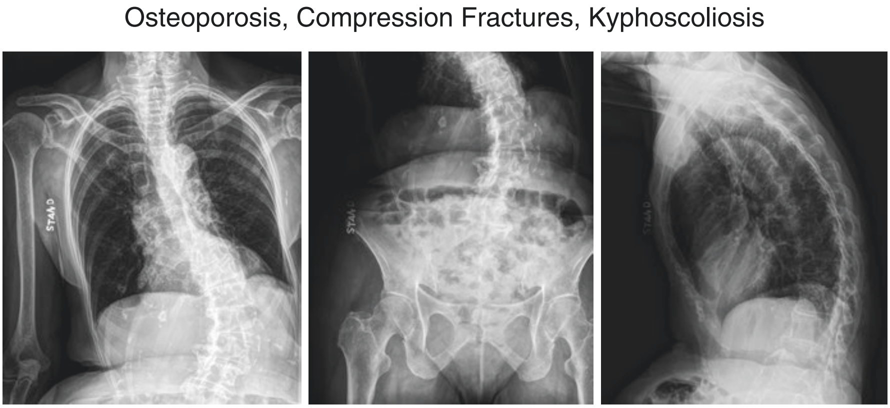

Fig. 15.4 Spinal radiographs of a patient with flank and back pain and unsteady gait. Hyperkyphosis and kyphoscoliosis contribute to iliocostal impingement.

bodies or compression fractures result in kyphotic posture which enhances flank impingement resulting in a dull, nagging pain. This is most often seen in osteoporotic individuals of small stature as the space between the lower rib cage and pelvis is diminished resulting in ligamentous impingement at the iliocostal angle or flank pain [7, 8].

Treatment

Rehabilitation of osteoporosis has been of some help, but initiation of back exercises for strengthening paraspinal muscles is very difficult when the patient cannot use these muscles due to severity of kyphosis and pain (Figure 15.5) [9].

Strengthening back extensors can reduce kyphosis. One study showed a negative correlation between thoracic angle of kyphosis and back extensor strength (Figure 15.5).

To date, treatment of iliocostal impingement syndrome has included injections, use of belts, and surgical resection of the lower ribs. Injections have been used to decrease pain in the insertions of the tendons on iliac crest or pain-generating ligamentous structures. The most invasive procedure has been resection of ribs 11 or 12 [10, 11]. These procedures can all be of help in most cases as a temporary remedy if kyphosis is not addressed and the source of pressure and impingement is not removed. Therefore, recurrence of pain is not unusual [7].

In a clinical study of a group of osteoporotic women with complaints of aggravating pain in the flank area, a WKO support and back-strengthening program focusing on posture improvement were used [12]. The pain level gradually improved in those who were compliant with the program. In the report, we discussed our diagnostic and

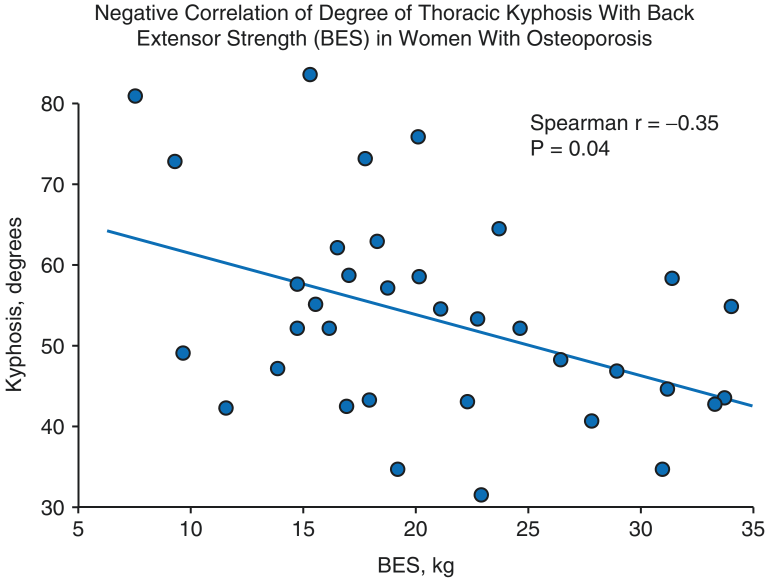

Fig. 15.5 Stronger back extensors can decrease thoracic kyphosis. From Sinaki M, Wollan P, Scott R, Gelczer R. Can strong back extensors prevent vertebral fractures in women with osteoporosis? Mayo Clin Proc. 1996;71(10):951–956; used with permission.

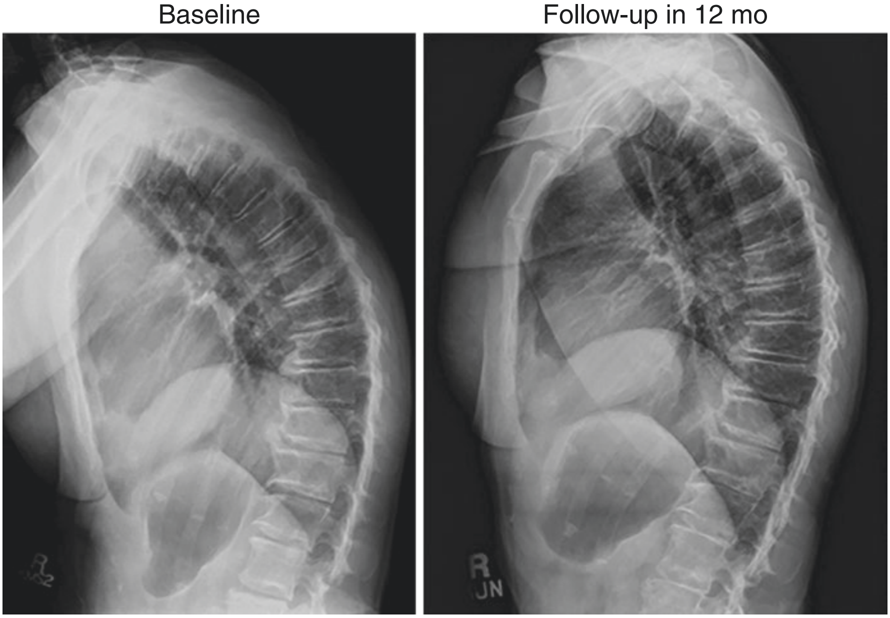

Fig. 15.6 Radiographs depict reduction of thoracic hyperkyphosis from baseline (*left*) to 12-month follow-up (*right*). Radiographic evidence of kyphosis before treatment (*left*) and 12 months after initiating treatment (*right*) with weighted kypho-orthosis and exercise program

treatment approach to iliocostal impingement syndrome which has proven successful in our patient population (see also Chapters 7 and 8). We have reported successful management of iliocostal impingement syndrome in a case series of 38 women [11]. We are having success with more cases; therefore, this technique of the SPEED program could be implemented for reduction of kyphosis as described in Chapters 7 and 8.

Radiographs obtained at baseline, before treatment (Figure 15.6, left), and 12 months after initiating treatment (Figure 15.6, right) show evidence of reduced kyphosis with the use of WKO support and an exercise program.

After initial detailed instruction, patients find the SPEED program to be convenient and easy to perform. This program has been shown to be successful for recruiting the use of back extensors for reduction of kyphotic posture. Patients who report immediate pain relief after the initial trial are suitable for further WKO use. Those who comply with the program report improved physical function and gradual long-term relief of their aggravating flank pain.

Kyphotic Posture Can Increase Risk of Falls

Equilibrium is multifactorial. Figure 15.7 shows the factors that contribute to gait steadiness. Aging affects vestibulospinal reflexes which, when intact, protect against falls. Participation in regular physical activity has been shown to develop or maintain the efficiency of the reflexes involved in postural control [13].

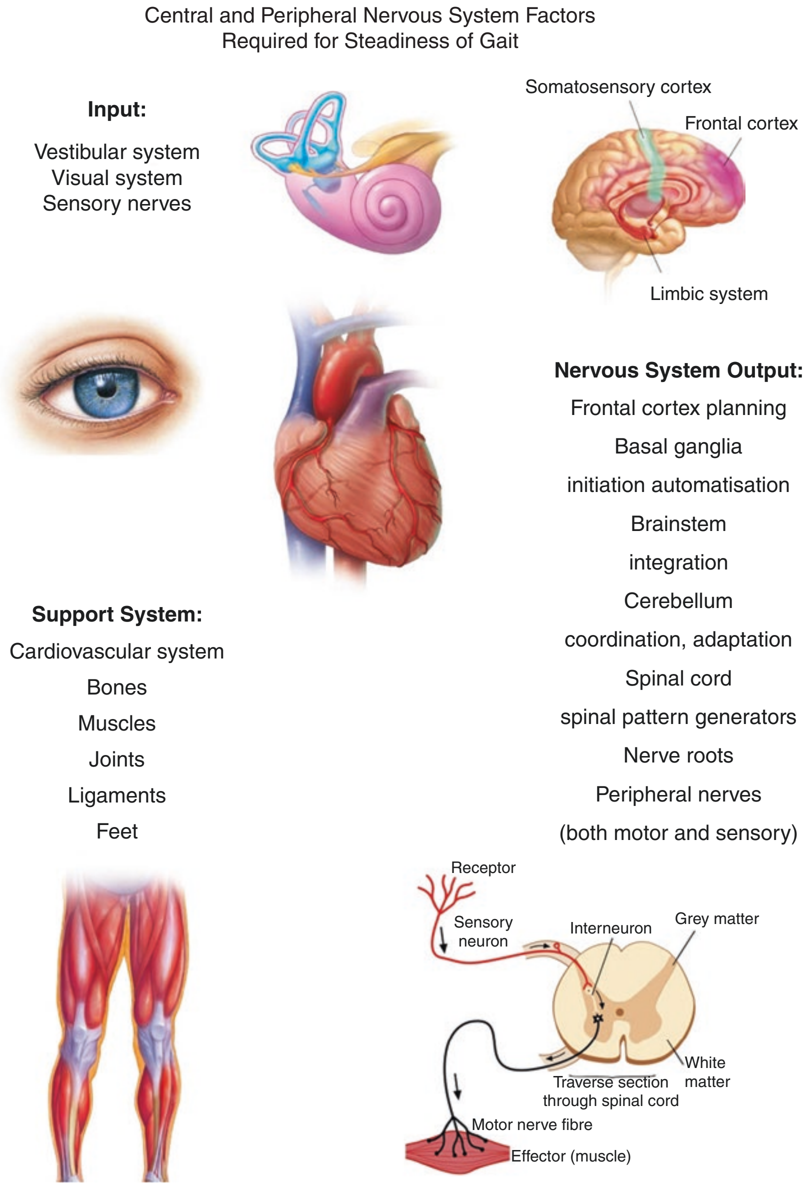

Fig. 15.7 This illustration indicates physiologic factors whose function contributes to normal locomotion

The proprioception generated within joints, ligaments, and muscles contributes to awareness of the orientation of functional units of the spine or axial posture. This is fundamental to posture, balance, and steadiness of locomotion. Reorientation of zygapophysial or facet joints requires change in proprioception of these joints which needs to be utilized for improvement of posture and balance. The osteoporotic kyphotic patients in one study sensed a greater propensity for falling than did the controls, according to their subjective falls efficacy scores [14].

Fear of falls has been substantiated through computerized dynamic posturography, which objectively measures balance [3].

In another study of proprioceptive dynamic posturography, balance improved with enhancement of postural proprioception and with reduced hip strategy. In normal balance, ankle strategies are recruited rather than hip strategies [15].

Strengthening of the lower extremity muscles can reduce the risk of falls [16]. Kyphotic posture in persons with osteoporosis contributes to the risk of falls [14]. Patients with osteoporosis and kyphosis have more postural sway and greater use of hip strategies than ankle strategies to maintain balance than persons without kyphosis, which contributes to an increased risk of falls (Figure 15.8) [17]. This author believes that strengthening hip extensors and quadriceps can reduce the risk of falls and facilitate getting in and out of the sitting position.

A study showed that reducing kyphosis through proprioceptive training can reduce back pain and risk of falls and contribute to improvement of level of physical activity (Figures 15.9 and 15.10) [18].

In summary, kyphosis results in relative imbalance between the body's center of gravity and base of support, increasing unsteadiness of gait. Furthermore, aging attenuates vestibulospinal reflexes and also affects proprioception; these changes result in body sway and fear of falls, which would decrease participation in physical

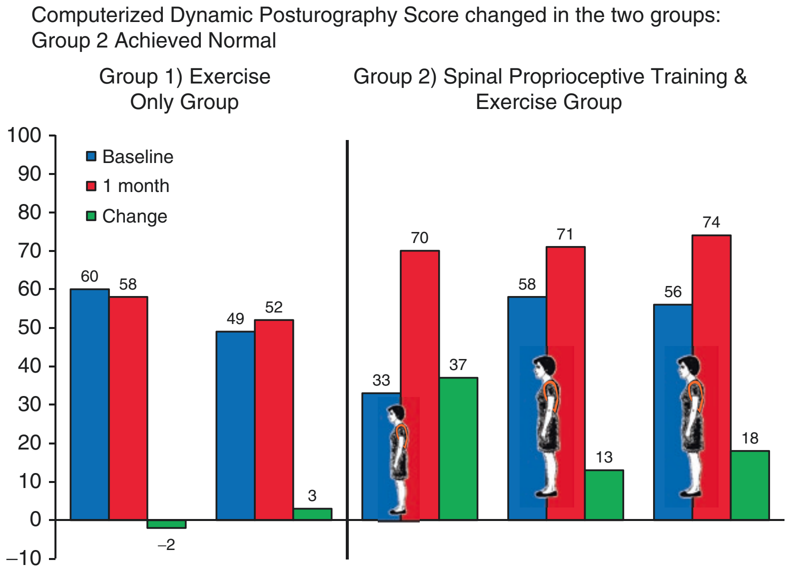

Fig. 15.8 Both groups performed back extension exercises. Group 2, in addition, used weighted kypho-orthosis. Computerized dynamic posturography scores became normal only in group 2. From Sinaki M, Lynn S. "Reducing the risk of falls through proprioceptive dynamic posture training in osteoporotic women with kyphotic posturing: a randomized pilot study. Am J Phys Med Rehabil. 2002;81(4):241–246.

Fig. 15.9 The application of weighted kypho-orthosis (WKO) support can provide greater steadiness in some patients. Panel (**a**), on the *left*, depicts a patient with kyphosis and balance disorder, in the setting of parkinsonism and osteopenia. Panel (**b**) shows patient's upright posture after application of a WKO. Panels (c) and (d) show proper application of 2 types of WKO: vest and shoulder-strap models.

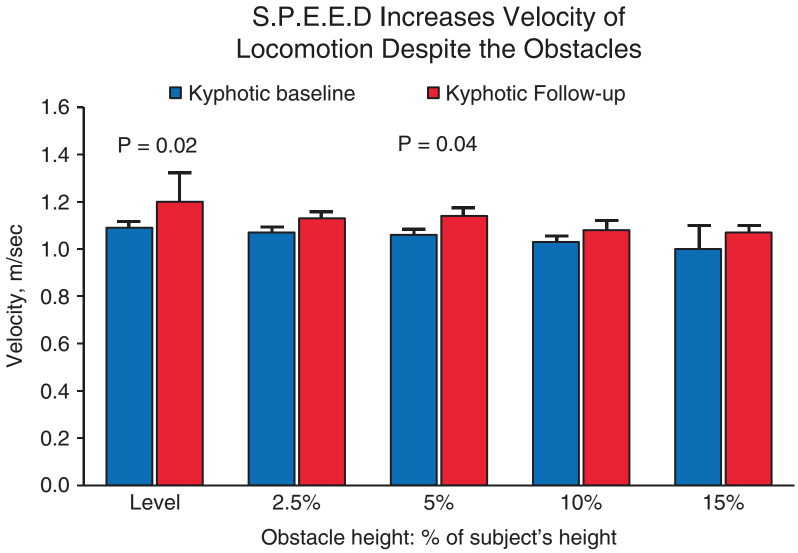

Fig. 15.10 After trial of the spinal proprioceptive extension exercise dynamic (SPEED) program, kyphotic subjects showed improved velocity of locomotion at different obstacle heights in the gait lab weighted kypho-orthosis trial for steadiness of gait.

activities and could contribute to an individual's deconditioning. Therefore, measures that can improve posture and decrease disequilibrium can contribute to a reduction in risk of falls. Needless to mention, rehabilitative and/or mechanical interventions that can decrease the use of pharmacotherapy and analgesics in elderly patients are highly recommended. It is well known that analgesics in elderly patients would increase risk of falls related to sedation effect.

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Pain Management and Acupuncture After Vertebral Fractures

16

Elizabeth A. Huntoon

Osteopo rosis can affect the vertebra at all levels; however, vertebral compression fractures (VCFxs) usually occur in the mid-thoracic or thoracolumbar transition zone of the spine. This condition affects women more than men and increases in incidence as the population ages [1]. Non-painful VCFxs are oftentimes found incidentally on routine imaging studies while investigating other medical conditions [2] and may remain asymptomatic until the patient develops kyphosis and/or back pain. Patients that present with painful VCFxs are faced with treatment challenges such as undesirable medication side effects, toxicities, or lack of efficacy. As the population ages, the incidence of general back pain increases [3] so do the referrals to pain clinics where patients may be recommended to try oral medications as well as injections, which often contain steroids. Several articles have attempted to describe the relationship of joint- or spine-related steroid injections to the development or advancement of osteoporosis. Glucocorticoid-induced osteoporosis is an important topic in pain medicine since many patients who present to pain clinics are medically fragile and often have conditions that require chronic steroid use prior to or concurrent with their visit to the pain clinic. These patients present a special challenge to the pain physician, since glucocorticoid-induced osteoporosis is considered the most common iatrogenic form of the disease [4–6]. Despite this risk, spinal injections have been used safely and effectively in select patients with VCFxs with refractory pain.

E.A. Huntoon, MS, MD
Department of Physical Medicine and Rehabilitation, and Orthopaedic Surgery, Vanderbilt Medical Group, Vanderbilt Bone and Joint, 206 Bedford Way, Franklin, TN 37064, USA
e-mail: elizabeth.a.huntoon@vanderbilt.edu

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Spine Injections

Patients with refractory back pain may have pain related to the fractured bone or may have additional pain generators located within the back/spine area. These pain generators may be identified as the disc, facet joint, sacroiliac joint, myofascial trigger points, sacral bone pain, or hip pain; once identified these areas can be addressed specifically with image-guided interventional spine procedures such as epidural injections, nerve blocks, facet joint injections, medial branch blocks, facet rhizotomy, sacroiliac joint injections, hip injections, and myofascial trigger point injections. Patients who have undergone procedures such as vertebral augmentation oftentimes have complete or significant relief of their back pain; however, persistent pain after vertebral augmentation is found in a small percentage of patients [7]. Persistent pain after vertebral augmentation may be attributed to failure of the procedure and recurrent fracture or may be related rather to an old or a new pain generator, such as an irritated sacroiliac or lumbar facet joint. Kamalian et al. found that 29 out of 124 patients (23%) had persistent pain after vertebral augmentation. The source of pain was most often attributed to the sacroiliac and/or lumbar facet joints, and most of the patients with persistent pain in this study responded to injections [8].

Facet joints (also referred to as zygapophysial joints) are paired synovial joints formed by articulation of the inferior articular process of one vertebra with the superior articular process of a more caudal vertebra. They allow the spine to move in flexion, extension, and rotation. The facet joint is innervated by the medial branch of the dorsal ramus of spinal nerves [9, 10]. One approach to determining if the facet joint is a pain generator is to perform a medial branch block or an intra-articular facet joint injection. Bogduk et al. looked at a biomechanical model of the spine and found that the posterior elements (the facet joints, lamina, spinous processes, and the associated ligaments) of the vertebral column sublux cephalad or caudad in response to deformity of a vertebral body. They concluded that the pain of a vertebral compression fracture may thus arise in part from the posterior elements as a result of the increased stress across this area [11]. Mitra et al. looked specifically at the thoracic facet joints and postulated that these facet joints may be abnormally stressed due to the increasing thoracic flexion moment in anterior compression fractures, which may serve as a secondary pain generator; they found that patients with thoracic compression fractures received significant long-lasting relief after receiving fluoroscopically guided intra-articular facet joint injections [12]. Facet radiofrequency ablation (RFA) is a more advanced procedure that destroys the medial branch of the dorsal ramus, thus rendering the joint insensate and providing long-term pain relief that is sometimes permanent, when the facet joint is found to be the main pain generator. Improvement in symptoms after either a facet joint injection or medial branch nerve block is a necessary precursor to proceeding with RFA. The reported adverse events associated with facet joint injections are vasovagal reactions, injection site soreness, sleeplessness, elevated blood glucose levels, elevated blood pressure [13], epidural spread of the injectate, epidural abscess [14], discitis, and other infections [15–17].

Epidural steroid injections (ESIs) have been used for many years in the treatment of back pain as well as radicular pain [18]. Despite their widespread use, there still remains some controversy as to the efficacy of these injections in the management of back pain. Cohen et al. performed a comprehensive review of the literature and found that ESIs did appear to prove pain relief and improvement of function for 6 weeks. ESIs can be administered via the intralaminar or the transforaminal approach with the transforaminal approach appearing to be more effective and non-particulate steroids associated with less risk than particulate steroids [19]. Other researchers also found evidence that epidural steroid injection was moderately effective for short-term (but not long-term) symptom relief [20, 21]. Carette et al. published early on in 1997 that epidural injections of methylprednisolone, as compared with saline injections, provided mild-to-moderate improvement in leg pain and sensory deficits and reduced the need for analgesics, but did not change the level of function or prevent surgery [18]. Complications and adverse events after ESIs can be mild (blood glucose and blood pressure elevations, headache, dural punctures) or catastrophic such as the fungal contamination of steroid preparations in 2012 in the United States that resulted in 650 cases of fungal infection with 39 reported deaths as a result [19]. Stroke, penetration of the spinal cord, infections, spinal cord infarct, paralysis, and death have also been reported [22–26].

Vertebral Augmentation

Many interventional pain physicians are trained to perform vertebral augmentation (VA) procedures such as vertebroplasty and kyphoplasty for VCFx patients with refractory back pain. Vertebroplasty consists of percutaneous injection of the fractured vertebral body with polymethylmethacrylate (PMMA) or bone cement.

Kyphoplasty is similar to vertebroplasty but involves an inflatable balloon that is percutaneously placed to first create a cavity in the vertebrae, which is then filled with the bone cement. Theoretically, the cavity allows the cement to be injected under less pressure and minimizes extravasation. Vertebral augmentation is indicated for patients who are neurologically intact, who have pain that is confirmed to be emanating from a known vertebral compression fracture, who are failing other conservative measures, and who cannot tolerate analgesics including opioids [27]. Multiple studies have shown significant improvements in pain reduction and function as a result of VA [28–30].

A meta-analysis performed by Anderson et al. found significantly greater pain relief, faster onset of pain relief, improved functional recovery, and improvement in quality of life measures with VA compared with control subjects [31]; the procedure was also found to be cost-effective when performed in patients hospitalized for VCFx pain [32]. A multicenter study in Europe consisting of 300 patients found that patients treated with balloon kyphoplasty had less pain and reduced analgesic use as well as faster return of physical function [33].

The complications of percutaneous VA include infection, bleeding, and allergic reactions from the PMMA or contrast medium, as well as cement extravasation, embolism, neurologic complications, and new fractures. The factors that contribute to cement extravasation include the level of injection, the severity of fracture, and the amount of cement injected. Meta-analyses have demonstrated better adverse event profiles with kyphoplasty, with cement leakage rates from 7% to 9% in kyphoplasty compared with 19.7–41% in vertebroplasty [34, 35]. Although some leakage of cement is common, severe outcomes occur in only a small percentage of patients. CT studies show that cement extravasation occurs in most patients (i.e., 18–88%) but is of minimal significance [36, 37]. Kyphoplasty is associated with a lower rate of cement extravasation because of the higher viscosity of the PMMA that is used, the lower injection pressure employed, and the inflatable balloon that seals pathways for cement leakage [37]. Pulmonary embolism may result from leakage of cement into the paravertebral veins and bone marrow or embolism of fat particles. The VERTOS II trial reported cement leakage had occurred in 97 of the 134 individuals in the study; 54 patients volunteered to undergo CT of the chest. Asymptomatic pulmonary cement emboli were found in 14 of these patients. The authors found that the only risk factor for embolism was cement leakage to the azygos vein [29]. Neurologic complications occur in <1% of patients, but when complications are present, the patient may require surgery. Neurologic complications include radiculopathy, spinal claudication, paraplegia, and death and can present acutely or may occur in a delayed manner [38]. The increased risk of subsequent VCFxs after VA was found to be related to cement leakage [39, 40] and increased stiffness of the augmented vertebral body, which results in a biomechanical change of the segments with increased pressure over adjacent levels [41, 42]. Baroud et al. showed that the augmented vertebral body became at least 35 times stronger and 12 times stiffer than control levels, causing increased pressure over adjacent levels by 13–18% [43]. Another study found that subsequent fractures were related to low bone mineral density and low body mass [44].

Acupuncture

Acupuncture is becoming increasingly popular as a noninvasive, non-pharmacologic approach to manage many different types of pain including neuropathic pain, visceral pain, and musculoskeletal pain. It is a type of intervention that involves penetration of the skin with needles on or over certain points of the body, collectively known as acupoints. These points are considered to be located along channels or meridians that traverse all parts of the body. The original acupuncture points have been described in ancient Asian texts and atlases for the past 2500+ years. Thousands of points are known throughout the surface of the body; however, usually only several hundred are used on a regular basis. There is a considerable overlap between these traditional acupoints and locations defined in modern physical medicine such as trigger points. Meridians are thought to course through the myofascial layer of the body and send branches to one another and the organs they influence. Dr. Dorscher investigated the overlap of the principal meridians and anatomically derived myofascial trigger point locations and found a strong correlation between the two systems [45]. Acupuncture points are often palpable as either mild depressions in the fascial plane or small, and sometimes tender, subcutaneous nodules. Finger-pressure massage of selected points is called acupressure. Electroacupuncture

(EA) is a form of acupuncture that incorporates a pulsating electrical current to acupuncture needles as a means of stimulating the acupoints.

Acupuncture needles are placed at various depths depending on the type of acupuncture being used. Stimulation of the needle is accomplished by a variety of different means: manual manipulation, electricity, laser, ultrasound, and heat. Heating can be accomplished by infrared lamps placed over the patient or by burning of dried, powdered herb—*Artemisia vulgaris* (moxa), referred to as moxibustion. The goal of acupuncture is to access and stimulate the vital energy within the body known as Qi (pronounced “chee”). Qi is felt to permeate all things and is thought to reside within the meridians. When it is disrupted, it is described as stagnant. The smooth movement of Qi is essential for health, and any disruption of the smooth flow is considered to be responsible for the development of disease or pain; thus, the goal of acupuncture is to improve Qi flow by first identifying and then unblocking the source of stagnation.

Different types of acupuncture can be used depending on the patients’ physical and energetic needs, as well as the location of the problem. Auricular acupuncture, scalp acupuncture, and Korean hand acupuncture are all different forms of acupuncture that use the ancient Chinese philosophy that the human body is regarded as a microcosmic reflection of the macrocosm of the universe which is further refined in the body with body parts thought to contain entire representations of the whole body within their specific location. For example, the entire body is represented within the auricle as well as on the volar surface of the hand.

Acupuncture has gained popularity in the past decade as a treatment for back pain from all etiologies. In 1998, the National Institutes of Health (NIH) published a consensus paper on the use of acupuncture for a variety of different health conditions. At that time acupuncture was found to be a useful adjunct for the treatment of back pain [46]. Since then the results of multiple studies have supported the use of acupuncture for the treatment of both acute and chronic back pain. In 2014, Vickers and Linde published a “Clinical Evidence Synopsis” in JAMA describing the effective use of acupuncture for chronic pain. They included 29 trials published between the years 1996 and 2008, which involved 5624 men and 12,535 women. After analysis of the data, the authors concluded that acupuncture was associated with improved pain outcomes compared with sham acupuncture and no-acupuncture controls in back pain patients [47]. In a study that looked at elderly patients who had non-fracture-related back pain for more than 12 weeks, Meng et al. found that patients who received acupuncture had a significant decrease in their Roland Disability Questionnaire score as well as fewer medication-related side effects when compared to the control group [48].

There are many proposed physiological and neurobiological mechanisms for the etiology of acupuncture effects within the body. For the treatment of musculoskeletal conditions, including back pain, neurobiological theories involve the activation/deactivation of different parts of brain as well as the release of bioactive compounds or neurotransmitters such as frequency-dependent release of opioid peptides in the CNS during electroacupuncture (EA) stimulation [49]. The established research on the neuro-physiological correlates of acupuncture has pointed toward endogenous opioids as the principal biological mediators of the therapeutic actions of this ancient technique; however, many other bioactive compounds have also been implicated and may be activated or released in response to different types of acupuncture stimulation. Electroacupuncture blocks pain through peripheral, spinal, and supraspinal mechanisms. Endogenous opioids are released from many cells in the body and are thought to desensitize peripheral nociceptors, decrease proinflammatory cytokines in peripheral sites, and decrease cytokines and substance P in the spinal cord [50]. Opioids also activate the descending inhibitory system, the main neurotransmitters of which are serotonin and norepinephrine [51]. Electroacupuncture (EA) stimulates different neurochemicals at different frequencies; low-frequency (2–20 Hz) stimulation causes the release of endorphins resulting in analgesia mediated by the mu receptor system that is blocked by naloxone. High-frequency stimulation (>100 Hz) causes the activation of the dynorphin system mediated by the κ-opioid receptors [52, 49]. Electroacupuncture also increases endogenous cannabinoid CB2 receptors (CB2R) to upregulate opioids in inflamed skin tissue and also increases the levels of endogenous anandamide in inflamed tissue [53]. Anandamide is a molecule which acts as a neurotransmitter and which has a structure very similar to that of tetrahydrocannabinol, the active constituent of cannabis.

Functional magnetic resonance imaging (fMRI) has shown interesting correlation between the activation and deactivation of specific areas of the cerebrum and cerebellum with acupuncture. These fMRI signals are thought to reflect changes in metabolic activity via observation of changes in blood flow to specific areas of the brain, which indicate the anatomic areas of the brain activated or deactivated during acupuncture [54–57].

Most neuroimaging studies have demonstrated that acupuncture can significantly modulate brain activation patterns in healthy subjects; however, Shi et al. looked at patients with experimental low back pain and compared fMRI during baseline (no pain) to fMRI scans during acupuncture and during sham (tactile stimulation of BL 40 point). The authors concluded that the results showed broad deactivation in most areas of the limbic system and activation in the somatosensory system in the acupuncture group, compared to the no-pain and sham groups [58].

Acupuncture treatments are associated with very low risk of adverse events; however, any time needles are introduced through the skin, there is a potential risk of infection or organ, nerve, or blood vessel injury. Infection, pneumothorax, nerve damage, cardiac tamponade, osteomyelitis, empyema, and psoas abscess have been reported [59–62] as well as less serious adverse events, such as dizziness, bruising or bleeding, pain at insertion sites, and contact dermatitis [63]. Pneumothorax is considered the most common of the serious adverse events reported. Delayed presentation of symptoms may contribute to under-recognition of this problem [64]. A prospective study in Germany that included 97,733 patients receiving 760,000 treatments reported only two cases of pneumothorax and one vasovagal reaction. Additional adverse events that were considered to be potentially associated with the acupuncture treatments were an acute hypertensive crisis and an exacerbation of depression [65]. One study that looked specifically at patient's perceptions of adverse events related to acupuncture rather than physician reported events found that 682 out of 6348 patients reported at least one adverse event over the 3-month survey period. The most common patient's reported events were severe tiredness and exhaustion, pain at the site of needling, and headache [66].

Overall the incidence of serious adverse events related to acupuncture is relatively small when performed by trained practitioners.

Trigger Point Injections

Myofascial trigger points (MTPs) are defined as localized, hyper-irritable spots in a taut band of the muscle, identified by a "twitch" response when the trigger point is located by palpation. These MTPs can be treated with stretching of the muscle, coolant spray, injections, or neuromuscular re-education. Some treatments include the use of transcutaneous electrical nerve stimulation (TENS) or myofascial release therapies such as deep tissue massage. In 2004 a group of researchers combined trigger point needling with acupuncture in a group of elderly back pain patients, including patients with osteoporosis and VCFxs. They compared needling at trigger points identified by palpation versus acupuncture points and found that deep trigger point acupuncture therapy was more effective than superficial trigger point acupuncture therapy or traditional acupuncture alone [67].

Exercise and Bracing

Exercise and physical therapy are a significant component of the rehabilitation world and often utilized as adjuncts to treatment programs within multidisciplinary pain clinics. Several studies have shown that exercise reduces the risk of vertebral and nonvertebral fractures [68, 69]. Sinaki et al. specifically linked back extensor strengthening exercises to a lowered risk of VCFx in healthy postmenopausal women [69], and Huntoon et al. found a reduced refracture rate in women with osteoporotic VCFxs as well as women who had undergone vertebroplasty and who had participated in a specific back extensor strengthening program [70]. Bracing of osteoporosis-related vertebral fractures reduces pain by decreasing postural flexion, stabilizing the spine, restricting axial rotation, and reducing back fatigue [71]. There is controversy surrounding which type of bracing affords the best, reliable pain reduction; however the type of brace used is predicated in part on the location of the fracture, the patients' body habitus, and patients' comfort with the orthosis. Braces are thought to improve bone healing in part by immobilization as well as by allowing reduced pain during mobilization [72].

Summary

Pain management physicians are often tasked to care for the fragile elderly who may have back pain related to osteoporotic vertebral compression fractures that are refractory to conventional medical management. Spine injections are available as pharmacologic interventions that may be better tolerated than oral analgesics in the medically frail, who do not tolerate oral analgesics. Vertebral augmentation and acupuncture are two safe, non-pharmacologic interventions that are often offered as tools to help these patients manage their pain. Bracing and exercise are also routinely offered to back pain patients in the pain clinic.

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Tai Chi and Feldenkrais: Therapeutic Movement-Based Mind-Body Practices

17

Judith B. Kosasih and Daniela H. Jurisic

Introduction

It is well established that lifestyle intervention such as physical activity plays an integral role in bone health and that exercise has the potential to be a safe and effective way to avert bone loss in postmenopausal women and promote bone health [1]. In osteoporosis management, there is a growing need to find an exercise option that is safe, low cost and effective and has multiple benefits such as health preservation, disease treatment, and promotion and maintenance of wellness. First and foremost, it is vital that an exercise is chosen that best fits the individual to function as a sustainable lifestyle skill with long-term benefits. Second, a physician's guidance in any exercise prescription is invaluable to address safety, efficacy, and compliance to ensure effective activation toward lifestyle changes and exercise adherence.

This chapter will specifically highlight Tai Chi and—to a lesser extent—Feldenkrais as two forms of therapeutic "movement for health" strategies in exercise. Further understanding of these two movement practices would guide physicians in effective clinical utilization and lifestyle prescription. At the end of the chapter, exercise prescription guidelines are outlined which may facilitate clinical decision

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J.B. Kosasih, MD (✉)
Department of Physical Medicine and Rehabilitation, Medical College of Wisconsin,
Milwaukee, WI 53226, USA

Clement J. Zablocki Veterans Affairs Medical Center,
5000 W. National Ave., Milwaukee, WI 53295, USA
e-mail: judith.kosasih@va.gov

D.H. Jurisic, MD
Department of Physical Medicine and Rehabilitation, Medical College of Wisconsin,
Milwaukee, WI 53226, USA

Active Integrative Medicine Associates, Pavia, Italy

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making based on research-based evidence, providers' clinical expertise, and patient's choice, values, and preferences.

Tai Chi and Feldenkrais have been chosen for several reasons. First, they have been considerably studied in connection with osteoporosis. Notwithstanding methodological limitations, these exercises show growing evidence of safety first, and then efficacy. Second, Tai Chi and Feldenkrais are based on identifiable principles that have health promotion as their goal, thus facilitating their safety and use in a medical context. Third, these movement therapies focus more on the quality than the quantity of movements. This point is important as it may spur further research on the possible relationship with the quality beyond the quantity of bone formation and retention in osteoporosis.

Tai Chi

Background

The National Center for Complementary and Integrative Health (NCCIH), previously known as National Center for Complementary and Alternative Medicine (NCCAM), reports that Tai Chi can improve health well-being and has benefits to a wide variety of health condition, including osteoporosis [2]. The 2007 National Health Statistic Reports found that approximately 2.3 million American adults reported having practiced Tai Chi in the 12 months preceding the survey [3]. The subsequent 2015 survey report demonstrated a linear increase in the use of Tai Chi throughout the years of 2002–2012 as popular complementary health approaches among American adults in the 12 months preceding the survey [4].

History and Basic Concepts of Tai Chi

Tai Chi, also known as T'ai Chi Chuan, T'ai Chi Quan, T'ai Chi, or Taijiquan, originated in China as a synthesis of ancient Chinese martial arts and meditative techniques. Tai Chi has the unique integration of ancient Chinese culture, martial arts, breathing and meditative techniques, and traditional Chinese medicine (TCM) philosophy. Tai Chi practice involves movement of the body with the purpose of cultivating and enhancing health through improving the harmony of the various forms of energy present both in the person and their external environment. As a mind-body method, Tai Chi promotes a range of beneficial physiological effects through purposeful regulation of breathing focus, relaxed patterns of movement (body focus), and focused awareness [5]. These body's self-regulatory and self-healing mechanisms were described in eastern TCM as inner medicine to balance the body energy (Qi) and restore homeostasis. In western medicine these terms imply up-regulating immune function, improving circulatory efficiency of blood and lymph, and stimulating the balanced release of endogenous neurohormones and neurotransmitter production [5, 6].

There are various types of Tai Chi named after their proponents (Chen, Yang, Wu/Hao, Wu, and Sun) and many simplified adaptations from these lineages [7, 8]. Traditional complex Tai Chi forms can be challenging to learn. The Tai Chi Fundamentals® (TCF®) is a modified Tai Chi program with basic movements to train proper body mechanics for practicing Tai Chi and train functional movements used in activities of daily living. This program provides a systematic progression from simple movement patterns to graduated levels of increasing difficulty within one's capabilities (Figs. 17.1, 17.2, and 17.3) [9, 10]. There are more complex forms using dozens of movements practiced by advanced or master Tai Chi practitioners with more precision and skills (Figs. 17.4 and 17.5). Although many styles of Tai Chi exist, most share fundamental principles of using controlled muscle relaxation in a series of slow, gentle, flowing movements integrated with mindfulness and breathing awareness as a mind-body practice. Tai Chi incorporates unilateral and bilateral weight shifts in slow continuous forms of integrated body central core movements while emphasizing the quality of transition between one movement and another. It requires the person to learn and perform movements through perception of movements rather than through visual observation training, thereby, enhancing memory and cognitive functions [11]. Tai Chi is practiced to enhance relaxation skills, mental focus, physical posture, and alignment, with positive effects on muscle strength, flexibility, endurance, coordination, and balance, which collectively improve overall physical functioning and psychological well-being [5, 7, 8]. Practiced by millions of Chinese for centuries, Tai Chi has gained increasing popularity worldwide in the recent years. Due to the promising health benefits, low cost, and apparent safety, Tai Chi has been widely adapted and practiced in both Eastern and Western countries as a low-impact, weight-bearing, and mind-body physical activity suitable for people of all ages, genders, and physical abilities. Tai Chi may be performed alone or in a group (Fig. 17.2). It conveniently does not require any equipment. The aim is not just to promote the individual's growth of skills but also to facilitate the development of lifelong practice where optimal benefit can be achieved. Regularly practiced in a group setting, Tai Chi may enhance quality of life through socialization skills and community enjoyment. The medical community has recognized that Tai Chi is effective when integrated into the existing rehabilitation treatment plans at hospitals [10] partnering with community-based programs [12], and incorporated into home exercise programs [13].

Tai Chi Movement Patterns and Poses

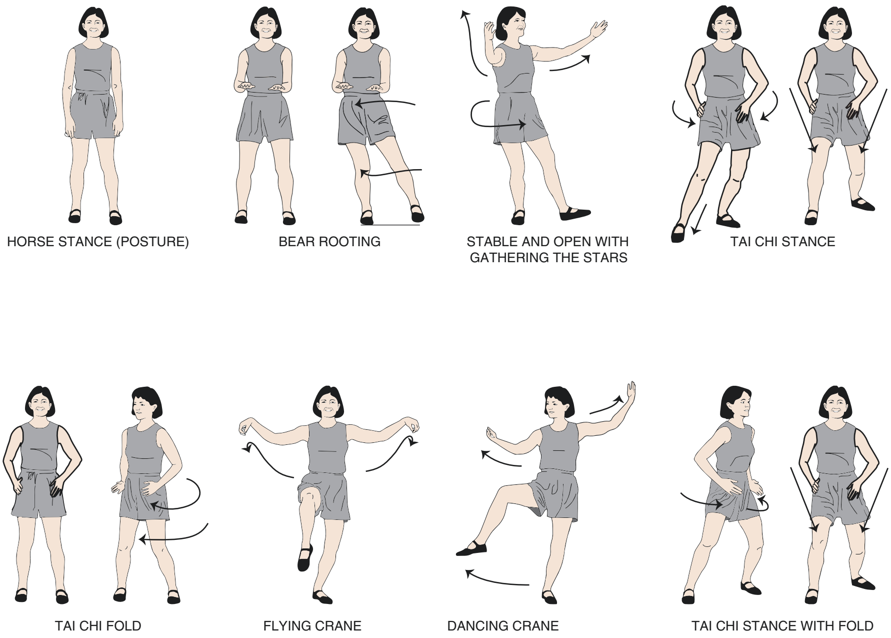

Fig. 17.1 TCF®'s Program: 12 basic moves train body mechanics for practicing Tai Chi and for functional movements used in activities of daily living

Fig. 17.2 Participants practice together in a TCF® class, first learning easier movements, then progressing to more difficult ones, depending on the stability and coordination

Fig. 17.3 Tricia Yu demonstrates TCF® basic move: dancing crane

Fig. 17.4 Tricia Yu demonstrates traditional Tai Chi form move: bend bow and shoot tiger

Fig. 17.5 Tricia Yu demonstrates traditional Tai Chi form move: sweep lotus with leg

Training and Certification

Currently, there is no official Tai Chi licensure granted by national or state professional boards. There are no official standards for Tai Chi training instructors. Various Tai Chi organizations offer training and certification with different criteria and levels of certification [2]. Usually, students are taught by a Tai Chi master and then teach others after certification or with a master's approval. A Tai Chi "train the trainer" method has been described to train health-care providers the Tai Chi skills and certify the educated trainee to teach Tai Chi classes for patient care and education [10].

Literature Reviews on Tai Chi Benefits

Throughout the world, there has been an increasing number of research studies and published reviews that investigate the effectiveness of Tai Chi for a number of clinical indications [14]. The evidence map of Tai Chi by the Department of Veterans Affairs [14] (September 2014) is a comprehensive review of 107 studies in multiple clinical areas and medical populations. This report stated that the three largest research areas addressed Tai Chi on general health benefits, psychological well-being, and interventions in older adults. A review of 77 randomized control trials (RCT) did not provide treatment effect estimates across studies but emphasized that the studies consistently demonstrated significant clinical benefits of Tai Chi and Qigong in multiple areas including bone health, cardiopulmonary fitness, balance and factors associated with fall prevention, quality of life, and self-efficacy (defined as "the confidence a person feels in performing one or several behaviors and the perceived ability to overcome the barriers associated with the performance of those behaviors) [5].

Accordingly, there has been increasing interest in studying Tai Chi effects on bone health and improvement in bone mineral density, especially as prevention, treatment management, or health maintenance options in osteoporosis. Cross-sectional studies [15] revealed that early menopausal women who regularly practiced Tai Chi for more than 3 years and over 3 hour per week showed improved neuromuscular function (greater quadriceps muscle strength and longer single-limb balance) as well as higher bone mineral density at the weight-bearing skeletal sites, primarily at the spine, greater trochanter, and proximal femur, as measured by dual-energy x-ray absorptiometry (DEXA). Follow-up studies showed that regular practice of Tai Chi slowed the rate of postmenopausal bone loss. These studies reflect that increased benefits are realized with longer years of Tai Chi practice. Similarly, Song et al. [16] reported that Tai Chi benefits on lower limb muscle strength, bone mineral density, and balance function in elderly women increased significantly with longer months of Tai Chi practice, ongoing for 8 months and even beyond 12 months. They suggested that as a fitness promotion, Tai Chi is suitable as long-term exercise, whereas its short-term effect is less obvious. While two RCTs [17] suggested that Tai Chi may be an effective, safe, and practical intervention to maintain bone mineral density in postmenopausal women, no treatment effect estimates were reported. A larger review of five RCTs [18] found inconclusive findings across studies and outcomes with the recommendation for future research with larger subject numbers and longer follow-up. Wayne et al. [12] suggested that the improved balance benefits of Tai Chi observed in the older population may apply to relatively younger and healthier osteopenic women as a preventative approach. Their report also suggested that in combination with the modest effects of BMD, "Tai Chi is a potentially valuable intervention for prevention of falls and fall-related fractures in postmenopausal osteopenic women and goes beyond most fracture intervention that target only the skeleton." Most importantly, there is consensus that the apparent safety of Tai Chi compared to pharmacological approaches shows suitability for sustainable long-term management in osteoporosis [18].

Other musculoskeletal benefits of Tai Chi practice have been studied in people with osteoarthritis [19], which often coexist with osteoporosis, and rheumatoid arthritis [20]. Twelve weeks of Tai Chi reduced pain and improved physical function, self-efficacy, depression, and health status in people with knee osteoarthritis [19]. A Cochrane review of Tai Chi concluded that it does not exacerbate symptoms of rheumatoid arthritis and produces statistically significant and clinically relevant improvements in ankle plantar flexion range of motion [20]. Based on self-reported scores of patients with fibromyalgia [21], 12 weeks of Tai Chi practice improved sleep quality, musculoskeletal pain, depression, activities of daily living, and quality of life.

Across these reviews, the most promising Tai Chi benefits were reported for both fall prevention outside of institutions (significantly reduced risk of falling) and positive effect on cognitive performance. A 2012 Cochrane review on fall prevention in older people living in the community found that Tai Chi significantly reduced the risk of falling and that overall exercise intervention significantly reduced the risk of sustaining a fall-related fracture [22]. In contrast, another Cochrane review in 2012 [23] included two Tai Chi studies that both reported no significant difference in the risk of falling in elderly in care facilities and hospitals. These reports imply that Tai Chi appears to be more effective in people who are less frail and are not a high risk of falling. Numerous variables influence efficacy outcomes, including different styles of Tai Chi, dosage of intervention, instructor factor (instructor's training and skill level), setting or population characteristics (community vs. hospitals or nursing homes), intervention duration (short term vs. long term), intervention intensity, comparator (exercise vs. non exercise), poor and inconsistent reporting of adverse events, and patient's participation (compliance and preference) [14].

In addition to physical and psychological benefits, there is evidence for positive effects of Tai Chi on improved cognitive functions. A review of 11 RCTs found enhanced cognitive performance in older adults: a large effect size in executive functions of cognitively healthy adults compared to no intervention, a moderate effect size compared to exercise controls, and smaller but statistically significant effects of global cognitive function in cognitively impaired adults compared to non-intervention controls [11]. As with physical benefits, long-term utilization of Tai Chi offers a safe, nonpharmacological approach to improve cognitive function in older adults. However, further research with longer follow-up intervals is needed before definitive conclusion can be drawn.

Effective balance is one of the most commonly reported benefits following the practice of Tai Chi, including improvement of balance control ability and flexibility of older adults. This is likely due to enhanced postural stability, somatosensory awareness, and neuromuscular control [24]. A review of 27 RCTs concluded that in people over age 55, Tai Chi improved static and dynamic balance and the functional factors which affect balance, but it did not provide specific treatment effect estimates [25]. The optimum amount of Tai Chi practice (dosage) to achieve significant improvement in balance remains unclear. Recent studies confirmed that exercise such as Tai Chi performed to reduce falls should be done at least twice a week and that the style of Tai Chi is less important than the cumulative length of time it is being practiced [26]. This implies the cumulative benefits of Tai Chi during long-term practice. The intensity and duration of Tai Chi sessions need to be tailored to the health status of the participants; frail elderly people may need lower intensity sessions over a longer time span [24]. Improved postural stability achieved with Tai Chi appears based on increased responsiveness in the proprioception, especially in the ankle and knee joints [25]. Responsive proprioception is possibly the most important factor relating to balance ability [27], implying that Tai Chi training in elderly could improve balance ability through better proprioception. The exact mechanism for improving balance capacity remains unclear. Further studies on movement analysis, neuromuscular, and neuroplasticity aspects of Tai Chi are needed to understand unique features of multidimensional Tai Chi characteristics. Patients with mild to moderate Parkinson's disease [13] participating in Tai Chi exhibit less balance impairments as well as improved functional capacity and reduced falls than individuals engaged in resistance training or stretching. Follow-up analysis of these Parkinson's patients found that Tai Chi improved patients' perceptions of health related benefits, which in turn correlated with better exercise adherence [28].

A large systematic review of Tai Chi clinical studies by Yang et al. [8] reported 507 studies published between 1958 and 2013 in 21 countries. The majority (62.5%) of studies were conducted in China, followed by the United States (20.5%). The clinical studies of Tai Chi covered the top ten diseases and conditions: hypertension, diabetes, osteoarthritis, osteoporosis or osteopenia, breast cancer, heart failure, chronic obstructive pulmonary disease, coronary heart disease, schizophrenia, and depression, as well as the practice of Tai Chi in healthy participants for the purpose of health maintenance. Most diseases studied were in the circulatory system, musculoskeletal system, and connective tissue, which relate to the impact of the physiological and biomechanical processes of Tai Chi training. This includes effects on lower extremity strength and flexibility, proprioception, neuromuscular, and cognitive-motor coordination. In this review, Yang style Tai Chi was the most common, and Tai Chi was frequently practiced in two to three 1-hour sessions per week for 12 weeks. Tai Chi was used alone in more than half of the studies or applied in combination with other therapies, including medications, health education, and other physical therapies in other studies. The majority of the included studies in this review demonstrated significant health benefits of Tai Chi in prevention, treatment, and rehabilitation. The review concluded that "the quantity and evidence base of clinical studies on Tai Chi is substantial," with the majority of studies (94.1%) reporting positive effects of Tai Chi and no serious adverse events related to Tai Chi. However consistent with the evidence map of Tai Chi report [14], there was a wide variation in Tai Chi intervention studied (style, intensity, duration, learning, and practicing methods). There was similar consensus on the recommendation that "design, conduct, and reporting of Tai Chi intervention should be standardized" to ensure reproducibility. It was recommended that future studies should have large enough samples and sufficiently long follow-up periods to support meaningful conclusions.

In terms of safety reporting, most of the studies did not address adverse events nor did they report any adverse effects associated with Tai Chi interventions. A systematic review of adverse event reports in randomized trials [29] concluded that Tai Chi is unlikely to result in serious adverse events, but it may be associated with minor musculoskeletal pain and soreness, especially in the early days of the intervention. Overall, the consensus indicates that Tai Chi is perceived to be safer than invasive treatments or pharmacological approaches.

Discussion

Research examining the physiological and psychological benefits of Tai Chi is growing rapidly. There is a growing evidence supporting the effectiveness and therapeutic benefits of Tai Chi on promoting overall physical and psychological well-being, symptom management, and as an adjunct therapy for a variety of conditions. Some of the inconclusive and equivocal findings to conclude whether Tai Chi is effective for specific diseases and health conditions are due to factors such as small treatment effect, methodological flaws of studies, or insufficient follow-ups. There also is an inherent challenge on how to best study the clinical application of Tai Chi and the optimum outcome measures. Research on Tai Chi is methodologically difficult when Tai Chi is considered a mere exercise therapy and is evaluated by the same criteria as conventional exercise. Tai Chi movement practice and its mind-body transformative experience often have effects beyond “body” effects and may need different assessment tools and outcome measures. There are potential subtle changes and improvements with adherence to regular Tai Chi participation, which may not be readily measured with conventional assessment tools. This may involve qualitative lifestyle changes, proactive self-management, and coping skill improvements that are not easily quantifiable but evident to the practitioners. This may be the reason why the effects of Tai Chi on “health” or “health perception” end up being addressed more frequently with more consistent results. Despite the inconclusiveness of some of the review findings, the consensus is that Tai Chi is worthy of further investigation. Further studies of possible neuroplasticity induced by perception-based learning are needed to understand more about the impact of Tai Chi. Current studies have shown that as a fitness measure, Tai Chi seems to be more suitable for long-term exercise, as its short-term effect is less obvious [16]. This reinforces the need for early intervention of behavioral activation and lifestyle changes for optimum benefits. Current research tends to focus on older adults and postmenopausal women and demonstrates that Tai Chi benefits are greater with increased years of practice. Consequently, research on the optimum timing of intervention is lacking. Future research on Tai Chi may also need to focus on the younger population—“start as young as you can”—to maximize long-term health benefits, including bone health in younger healthier osteopenic women as a potential preventative intervention. In addition, since Tai Chi focus more on the quality of movements, further research is needed on the possible relationship with the quality—not just the quantity—of bone formation and retention in osteoporosis.

Conclusions

Extensive research studies have been done on the unique application of Tai Chi for multiple clinical conditions. Evidence to date suggests that Tai Chi is a promising safe nonpharmacological and lifestyle intervention in the studied areas, including osteoporosis. Our overview aims to raise awareness that there are inherent challenges and limitations to Tai Chi research due to the nature of Tai Chi as a complex, multicomponent mind-body intervention. Despite the lack of vigorous evidence in the literature, Tai Chi continues to be widely practiced as a form of exercise for health and fitness, especially due to its multidimensional benefits in physical, psychological well-being, and cognitive functions. When prescribed, embraced, and practiced properly, Tai Chi can be an effective option for helping people with osteoporosis and can be an ideal lifelong skill for long-term health benefits and wellness.

Feldenkrais Method: Another Movement-Based Mind-Body Practice

The Feldenkrais method, often referred to simply as "Feldenkrais" is the result of Moshè Feldenkrais' decades-long (1904–1984) process of study and application of his original thesis concerning human movement and quality of life [30]. Feldenkrais claimed that the basis of the approach was founded in the human potential for learning how to learn [31]. There are two basic principles: first, the body, emotions, and mind are inextricably interconnected, such that changing one of these would change the others. The second is that each person is able to choose the most functional, effortless, and pain-free series of movement for each motor task. This is accomplished by shifting the movements from "automatic" to "aware" through guided practice of a series of movement and sensation-based explorations, whereby a perception is first discerned and then "catalogued" by the patient as either *favorable* or *unfavorable*. A favorable movement is identified through its ease and effortlessness, and an unfavorable movement is identified through sensations such as strain, pain, or discomfort.

It is useful to note that Moshè Feldenkrais was an international expert in both Judo and Jujitsu, both martial arts which spring from a common philosophy regarding mind-body relationship, similar to that of Tai Chi. His extensive writing on these martial arts underlines a basic shared principle that somatic perception is the basis for learning optimal effortless movement, regardless of the individual's level of health or illness. Feldenkrais was a physicist and an engineer by training. Although his own personal knee injury provided momentum for his research and for the consolidation of his method, it was not developed as a physical therapy to apply to specific medical diagnoses. Feldenkrais is used to improve movement patterns rather than to treat specific injuries or illnesses. This means that in studying the applicability of the Feldenkrais method to a specific diagnosis group, such as osteoporosis, similar methodological problems arise as those regarding Tai Chi.

There are two Feldenkrais teaching methods: Awareness Through Movement and Functional Integration. Both aim to increase the students' awareness of themselves and to expand the students' pain-free movement repertoire. In Awareness Through Movement, the student is directed verbally, in absence of visual reinforcement, through a series of simple movements (such as rotation of the head or flexion of the knee) first done through the entirety of all the student's pain-free range. The movement is then deconstructed into partial movements to increase somatic perception and awareness then reconstructed. Usually the student feels an immediate sensation of increased comfort within that specific movement. All aspects of the teaching are important, including the speed and inflection of the teacher's voice, the quietness of the surrounding teaching environment, and the smoothness of the passage from one exercise to another. Awareness Through Movement is usually offered as a group practice of about 10–12 students. In Europe the sessions are approximately 60–75 min, whereas in the United States, the sessions are about 30–60 min. The second method, Functional Integration, is a hands-on, one-on-one technique used for awakening somatic sensation and resetting movement through increased perception. The perceptual feedback is augmented through the teacher's precision of touch during the movement. In accordance with the basic principles of Feldenkrais, the student's movement is not forcibly corrected or impeded in any way. Functional Integration lessons last about 60 min.

Research on the efficacy of Feldenkrais, specifically for osteoporosis patients, is more limited than that regarding Tai Chi, with similar methodological obstacles. Despite the limited literature to support the use of Feldenkrais, there are two current studies to be noted. Ullmann et al. studied the effect of the Feldenkrais method on gait biomechanics, fear of falling, mobility, and balance in 47 community-dwelling patients aged 65 and older. They found that participants of the Feldenkrais group demonstrated significant improvement in all domains except for gait biomechanics when compared to wait list controls [32]. Hillier and Worley reported a systematic review of literature published about the Feldenkrais method [31]. The 20 RCTs included were appraised using the Cochrane risk of bias approach and trial findings analyzed individually and collectively where possible. The findings were reported as positive though generic. They were interpreted as reinforcing Feldenkrais' proposal that his method is based on a learning paradigm rather than disease-based mechanisms.

In addition to the traditional Feldenkrais method, there is a separate method called "Bones for Life" [33], intended to improve bone quality. It was developed by Ruthy Alon, one of Feldenkrais' first students. The method incorporates the principle of somatic perception of comfort to learn improved quality of movement, as measured by diminished fear of falling and decreased sense of effort during walking. The exercises, however, are more active and make use of assistive "wraps" around both the upper and lower girdles to enhance proprioceptive sensation. This method is being taught throughout Europe and the United States. Currently, there are no RCTs available; however, the results of small clinical trials are promising. The Bones for Life method has been well accepted in Europe, both for ease of execution and aesthetic appeal. Patients who have had difficulty in tolerating the slow rhythm intrinsic in learning Feldenkrais as well as Tai Chi often find Bones for Life less difficult.

Reflection

In considering a possible prescription of Tai Chi or Feldenkrais as a lifestyle-changing movement practice for the individual patient, the criteria to consider are the following:

1. Is the patient willing to consider a form of physical activity whose efficacy depends on consistency of practice and has willingness and ability to learn through somatic perception rather than cognitive-visual memorization?

2. Is the patient comfortable learning a physical practice which is based on a philosophy that they may not share?
3. Is the physician knowledgeable enough or does he/she want to become knowledgeable enough to engage in real dialogue about benefits, risks, and confidence level toward the practice and the instructor and help problem solve complications that might occur?
4. Is the instructor willing to interact on any level (minimally a simple phone call to, ideally, a formalized integrative interaction) with the physician to enhance consistency of treatment plans, patient's performance, and outcomes?
5. Is the exercise prescription specific enough and a good fit for the patient? Patients who have never been active and are contemplating becoming active might be more successfully motivated by more detailed and personalized description of benefits. The best form of movement is the one the patient is most likely to do and keep doing. This would promote compliance and integration into lifestyle practices and thereby assist the patient to transition from the role of "patients" to the role of "proactive healthy people."

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