Past, Present and Future of Muscle–Bone Interactions

Bjoern Buehring

Published online: 29 April 2014
© Springer Science+Business Media New York 2014

As a consequence of primary shape variations and continuous loading, or even due to loading alone, bone changes its inner architecture according to mathematical rules and, as a secondary effect and governed by the same mathematical rules, also changes its shape.

Julius Wolff (1836–1902), in *The Law of Bone Transformation (Das Gesetz der Transformation der Knochen)*, Berlin, A. Hirschwald, 1892.

The interest in muscle–bone interactions has grown in recent years and expanded from the original mechanical theories such as Wolff’s Law and Frost’s Utah Paradigm to theories of mechanosensation, cellular interactions through cytokines and hormones to shared genetic traits to name a few. As such, it is very timely for this journal to publish a special issue on this topic.

I feel honored to have been invited by the editorial board of Clinical Reviews in Bone and Mineral Metabolism to serve as a guest editor for this issue and deeply grateful to the authors who accepted my invitation to contribute.

In the included five articles the reader will find well-written summaries of historical aspects of Wolff’s law and the mechanostat theory. Furthermore authors appraise the current knowledge in important areas pertaining to muscle–

bone interactions such as muscle and bone imaging techniques, genetics, and biochemical pathways as well as strength and weakness of exercise interventions and development of osteoporosis and sarcopenia criteria. Lastly these articles offer thought provoking suggestions where this growing field might and should be heading.

After reading and reviewing these articles I have noticed two overarching themes:

- a. There is a reason why we call it the “musculoskeletal system”. On the one hand muscle and bone function as separate organ systems (e.g. glucose versus calcium metabolism/creating loads versus being loaded). There are outcomes that are more closely linked muscle (independence, mobility) or bone (fracture) and both organ systems have syndromes/diseases connected to them (sarcopenia, osteoporosis). However on the other hand more and more data highlight the multiple interactions, close links, common pathophysiological links between muscle and bone on genetic, cellular and biochemical and biomechanical levels. This also becomes evident in shared epidemiologic data, shared risk factors and shared treatment interventions.
- b. Things are more complicated than I (we) thought. Muscle and bone are not only connected on a biomechanically they clearly communicate on a biochemical level as well. Furthermore, muscle and bone are not only hormonal target organs, there is increasing evidence that they act as secretory organs which produce cytokines and hormones. Next, although there are common genetic traits, pathophysiological and risk factors there likely are primary muscle disorders, primary bone disorders and mixed disorders. This might explain why certain interventions such as exercise or nutrition work well in some patients but

B. Buehring (✉)
Osteoporosis Clinical Research Program, Division of Geriatrics
and Gerontology, Department of Medicine, University of
Wisconsin, 2870 University Ave, Suite 100, Madison, WI 53705,
USA
e-mail: bbuehring@medicine.wisc.edu

B. Buehring
GRECC, William S. Middleton Memorial Veterans Hospital,
Madison, WI, USA

not in others. Exercise remains an area which theoretically should be very beneficial for both muscle and bone, however real world efficacy remains below expected outcomes. This might not be only be due to problems with adherence and the choice of exercise intervention but there also appear differences between genders and the age at which the intervention is applied.

These two themes appear in all of the articles included in this issue:

1. Dr. Blank highlights in his manuscript titled “Bone and Muscle Pleiotropy: The Genetics of Associated Traits” the genetics behind muscle and bone mass and structure and how genes could influence both tissues directly or by influencing one tissue which then influence the other tissue. He gives a brief overview over the mechanostat and then gives clinical and animal examples of gene mutations that lead to different phenotypes in bone and muscle. He closes his review with a section on how to use genetic tools to improve our knowledge in muscle and bone interaction.
2. Dr. Rittweger’s and Dr. Ferretti’s manuscript “Imaging Mechanical Muscle–Bone Relationships—How to See the Invisible” focuses on concepts how to classify bone/muscle disorders and calculate muscle–bone strength indices. It combines a more detailed summary of the mechanostat theory and applies it in new ways to quantify muscle–bone interactions through imaging. The authors review the various methods how to image muscle and bone and proposes an approach how to bridge the gap between theoretical explanation of muscle–bone interactions and actual, measureable muscle–bone ratios.
3. The manuscript “Physiology of Mechanotransduction: How Do Muscle and Bone “Talk” to One Another?” by Drs. Isaacson and Brutto describes the communication between muscle and bone on a cellular/cytokine/hormonal level. It not only describes how mechanical signals created by muscle contraction and gravity act on bone, but puts bone and muscle into a broader context of the entire body. It reviews the effects that bone and muscle have on other organs and how other organs have effects on bone and muscle. It suggests that the mechanostat plays an important role in muscle and bone physiology but that non-mechanical stimuli have a major impact as well. It provides evidence that muscle and bone have endocrine and paracrine functions and that we are only beginning to understand. The authors argue persuasively that the role of the musculoskeletal system in obesity and diabetes is topic needing further study.
4. Dr. Demontiero and colleagues’ manuscript continues the transition from the more basic and transitional science focus at the beginning of this special issues to the clinical side. Their work entitled “Clinical Outcomes of Impaired Muscle and Bone Interactions” focuses on the clinical aspects of sarco-osteoporosis as an example of “impaired muscle bone interactions”. It gives an overview how sarcopenia and osteoporosis are connected to each other and why they should be evaluated together. The paper proposes ways of diagnosing sarcopenia and sarco-osteoporosis and outlines possibilities how muscle and bone diseases could be assessed clinically. It closes with a discussion of possible treatment options.
5. One of the most promising non-pharmacological interventions to treat muscle and bone diseases, namely exercise, is discussed in detail in the final manuscript “The Influence of Muscular Action on Bone Strength via Exercise” by Dr. Ireland and colleagues. This review focuses on the impact exercise has on bone. It highlights the important mechanical stimuli muscle force provides for bone modeling and remodeling and gives several examples that provide evidence for this theory. The authors then nicely review the impact of exercise on bone in children and adolescents and compare these effects to those in older adults. Further more it compares the effect of exercise on bone between genders. The manuscript discussed barriers to exercise and several important areas in which more research is needed including optimization of exercise modalities and intensity as well as personalizing exercise program to individuals.

In closing, I hope that you, the reader, find this special issue both worthwhile reading as an overview of important topics of muscle–bone interactions as well as useful as a resource for review and stimulation of new research ideas and new ways of approaching muscle and bone disorders clinically. The ultimate goal in my opinion should be that the increased knowledge and improved clinically care in the field of muscle and bone result in reduced fall and fracture risk as well as increased mobility, independence and thus better quality of life—outcomes that our aging population deeply cares about.