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Muscle Forces or Gravity—What Predominates Mechanical Loading on Bone?

INTRODUCTION

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Abstract

This paper describes the background, rationale, significance and objective of the recent American College of Sports Medicine (ACSM) symposium entitled “Muscle Forces or Gravity—What Predominates Mechanical Loading on Bone?” (55th Annual Meeting, Indianapolis, May 28, 2008) and introduces a series of papers representing the positions taken by three of the speakers at that symposium. Our goal is to reinvigorate discussion on a topic that will inform many, provoke some and, most importantly, stimulate ideas that will encourage progress in the field of exercise prescription for bone.

Keywords: Bone strain; exercise and bone; bone mineral density, bone strength

The task of prescribing exercise to improve bone strength and reduce risk of fracture has proven challenging. Despite the availability of considerable data to suggest that bone responds to a variety of mechanical loads, many factors limit our ability to translate the evidence into effective practice for all. Obvious confounders include age and sex specific responses, along with nutrition, hormone status, medications and disease states. More notably, in recent years an ersatz theoretical dichotomy regarding the predominant source of mechanical loads on bone (muscles or gravity) has clouded understanding of the issue. While issues of genetic and environmental confounds are difficult to address, critique of empirically-based theory is a more straightforward exercise. Thus, in the following series of papers, the contribution of muscle forces and gravity-derived forces to the mechanical environment of bone is examined and the practical implications explored.

Since 1987 when Harold Frost first proposed the “mechanostat theory” and began to assert that “Bone strength and ‘mass’ normally adapt to the largest voluntary loads on bones. The loads come from muscles, not body weight” (5, p. 1539), the notion has increasingly pervaded the literature. This contemporary focus on the muscle-bone relationship, however, does not reflect the full gamut of evidence and opinion from almost a century of research in the field. In fact, early observations of bone loss associated with bed rest (3) and space flight (14, 15), fostered the assumption that forces arising from the effect of gravity on body mass predominate the mechanical loads that govern the maintenance of skeletal integrity. A myriad of experimental animal models in the years that followed reinforced the notion that extrinsic loads have a potent ability to provoke an adaptive response from bone. On what basis then, did the pendulum begin to swing towards a muscle focused theory?

The most likely origin of the trend was the recognition that, owing to a disparity in moment arm length, the magnitude of muscle forces on bones during simple movements necessarily exceed those from ground (or substrate) reactions in order to resist or effect movement at a joint. Indeed, if our original question is interpreted to mean “What is the source of the largest physiological loads on bone?” the answer is quite simple. Muscle.

Positive correlations between muscle and bone mass are frequently reported (8, 13, 32). As common genetic determinants for lean tissues undoubtedly contribute to this association (illustrated by relationships between muscle and bone in different parts of the body (27, 28)) the association is perhaps not unexpected and causality cannot be implied. One would expect the effect of growth and aging on the bone-muscle relationship to be enlightening, but study findings have not been entirely consistent. That is, peak bone growth velocity has been reported both to *coincide with* and *to follow* muscle growth velocity (23, 25). Similarly, both observations that age-related bone loss occurs *earlier* and *later* than loss of muscle strength have been reported (2, 17, 18). A large scale, prospective, longitudinal trial tracking bone and muscle mass over the lifespan, using three dimensional computed tomography or magnetic resonance measures, will be necessary to resolve the issue.

Recently, computer modeling has suggested that muscle forces influence the development or maintenance of normal skeletal morphology (1, 6, 12, 19). Paradoxically, models have also shown that *removing* muscle loads will *increase* internal bone stresses during movement (4, 21); a prediction that is supported by the observation that principal strains on the canine tibiae can increase 30% with leg muscle fatigue (35). That muscles both impart and neutralize forces on long bones during gait has yet to be fully rationalized.

There is compelling experimental evidence of the important influence of muscle loads on bone. Physical “unloading” following muscle paralysis has been clearly associated with a dramatic reduction in muscle and bone mass in affected limbs (33). For non-weight bearing sites, the effects of muscle disuse and reuse on bone mass are quite evidently reflective and causal (22, 26). The issue of load source predominance is blurred, however, by the observation that in the weight bearing skeleton, bone loss post-paralysis preferentially occurs at locations normally exposed to primarily compressive forces during gait on the paretic side, and amount of loss is dependent on the amount of body weight born on the paretic leg (9). In fact, it is difficult to distinguish between the influence of reduced muscle versus ground reaction force loading on a paralyzed limb that is unable to bear weight.

A number of well-controlled animal models have provided the opportunity to examine the effect of extrinsic mechanical loads (to mimic non-muscular load-induced strain) on the adaptive responses of bone. Those models have repeatedly demonstrated direct cause and effect of extrinsic loading (24, 30). The effect of ground/substrate reaction forces on skeletal adaptation has also been examined, both observationally and via intervention animal and human trials. In the human domain, athletes engaging in chronic weight-bearing training exhibit greater bone mass than those engaging in non-weight bearing activities, despite similar forceful muscle activity (29). Exercise interventions report that weight bearing training improves lower extremity BMD while resistance training activities does not (10, 11); and that, despite enhancing muscle strength, high-resistance upper extremity strength training does not always increase upper extremity bone mass or strength (7). On the other hand, some have reported a positive relationship between the response of bone and the response of muscle to exercise training (16, 34).

Ultimately, the most meaningful interpretation of the original question, “What predominates mechanical loading on bone?” is likely to be “What source of bone strain predominates the adaptive stimulus?” This question is clearly more problematic than the determination of the source of the largest loads on bone. In fact, it has become apparent that larger is not necessarily better. It is well-recognized that the rate at which bone is exposed to strain can influence the adaptive response to an even greater extent than the absolute magnitude of the strain (20, 31). The relative rates at which ground reaction forces and muscle contraction forces are typically applied have also been well described. The next logical step is the integration of those observations in order to determine the form of loading that imparts the most favorable strain characteristics at each skeletal site, and the extent to which the optimal loading profile can be captured and applied. No small feat!

The objective of the recent American College of Sports Medicine (ACSM) symposium “Muscle Forces or Gravity—What Predominates Mechanical Loading on Bone?” the primary proceedings of which are presented in the following papers, was to revisit how we attribute the sources of mechanical loads on bone, and to examine the bearing of the evidence on effective exercise prescription. Symposium speakers were approached on the basis of their impressive track records in the relevant fields. Associate Professor Stefan Judex (State University of New York Stony Brook, Department of Biomedical Engineering), and Assistant Professor Alexander Robling (Indiana University, School of Medicine) were well-credentialed to present “*The Case for the Predominance of Gravitational Loads*” and “*The Case for the Predominance of Muscle Loads*,” respectively. Professor Charles Turner (Indiana University, Department of Biomedical Engineering) presented “*The Rejoinder to Both Cases*” and Professor Wendy Kohrt (University of Colorado, Division of Geriatric Medicine) spoke to “*Translating Theory into Practical Application*.” Professor Turner was

unavailable to submit a summary of his rejoinder paper; however, Professor Kohrt has synthesized the ideas presented in the debate into a paper of practical relevance.

It is important to note that speakers Judex and Robling were asked to present opposing sides of the issue. As such, their individual papers do not represent a comprehensive review of the literature and will appear one-sided if read in isolation. Judex and Robling find common ground with respect to the inherent link between gravitational and muscle loading on the skeleton, and the fact that the relative contribution of each to the bone loading milieu has yet to be fully determined. They also concur that the evidence for a link between muscle forces and *non-weight bearing* bone mass is strong. The authors' perspectives diverge with respect to the postulate that muscle force is both sufficient and necessary to stimulate bone or prevent loss at all sites; and on the degree of cause and effect of muscle and bone growth velocity. Further experimentation with transgenic mouse models with a muscular phenotype may be the most appropriate strategy to examine remaining questions at the tissue level. It will also be important to re-examine the skeletal consequences of novel exercise programs specifically designed to target muscle-derived versus gravity-derived bone loading. The acquisition of real bone strain data from clinically relevant bone sites during those targeted activities would add immeasurably to what could be concluded about the relative contribution of each source of loading. To date the challenges associated with the conduct of such trials, including sample size sufficiency (to accommodate broad subject heterogeneities), and an understandable reluctance of subjects to volunteer for the highly invasive procedures associated with direct measurement of strain from bone, have proved difficult to overcome.

In reality, the available evidence suggests that to espouse either source of bone strain as the predominance adaptive stimulus is not only overly simplistic, but neglects their intrinsic

interdependence. That is, while it is accepted that substantial local and joint reaction forces are applied to bone by muscle contraction, it is also intuitive that the primary purpose of those contractions is to resist the force of gravity and substrate reactions. The goal of effective exercise prescription for bone will be difficult to achieve without acknowledgement of this inextricable relationship. If the ultimate goal of biological research is the translation of findings into effective healthy practice, theoretical clarity is a good place to start. The following series of papers present broad evidence for the sources of mechanical loading of bone in order to provide a theoretical basis from which we can move forward with practical exercise prescription.

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