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Good vibrations and strong bones?

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THE HUMAN PHYSIOLOGY of bone perfusion has been neglected. The issue may be explained in part by technical difficulties in assessing bone blood flow in vivo. Currently available techniques may be rather expensive, and the access of interested scientists to these techniques may be limited. Another possible explanation for the neglect is the fact that the integration between cardiovascular and bone research fails because each research area is narrowly focused on its own organ or tissue system. This state of affairs is unfortunate given the potentially important interactions between the cardiovascular system and bone. Indeed, bone and vascular disease frequently coexist in the same patients. Osteoporosis risk is increased in patients with atherosclerosis and vice versa. The correlation is probably explained in part by a common underlying mechanism rather than a spurious association. Bone perfusion may be such a common mechanism.

Perfusion appears to be matched to the metabolic demands of the bone. For example, increased bone turnover and inflammation are associated with an increased blood flow. Blood flow decreases as bone turnover normalizes or the inflammation has resolved. Failure of the vasculature to respond to metabolic needs of the bone might predispose to bone disease. Alterations in vascular function and in intraosseous angiogenesis may be contributory. Several studies suggest a correlation between bone perfusion and bone density. Studies used different methodologies and are, therefore, difficult to compare. In one study (8), magnetic resonance imaging was used to obtain an indirect measure of bone marrow perfusion at the level of the lumbar spine. Bone marrow perfusion was correlated with bone mineral density in postmenopausal but not in premenopausal women. In another study (2), decreased bone marrow perfusion was associated with progression of collapse of fractured vertebra in patients with osteoporosis.

Perhaps “bone vascular disease” contributes to osteoporosis. One might further speculate that interventions that improve bone vascular function may have a beneficial effect on bone structure. The anatomic structure of blood small blood vessels within the bone is similar to the structure of blood vessels in other tissues. These vessels may be susceptible to the same genetic and environmental risk factors.

If bone vascular disease and, thus, alterations in perfusion were a cause of excessive bone loss, atherosclerosis risk factors should also increase the risk for osteoporosis. Indeed, smoking, diabetes mellitus, elevated low-density lipoprotein cholesterol, reduced high-density lipoprotein cholesterol, and hyperhomocystinemia are associated with increased cardiovascular risk and reduced bone mineral density (4). Both the risk for cardiovascular disease and the risk for osteoporosis increase sharply after menopause. A study in rabbits suggests that experimental “postmenopause” through oophorectomy leads to changes in

bone vascular function. In this study (1), oophorectomy increased the responsiveness of isolated vascular rings from small bone arteries to norepinephrine and to endothelin. However, whether vascular damage to the bone vasculature explains the association between osteoporosis and cardiovascular risk factors in humans is unknown.

Interestingly, treatment of some cardiovascular risk factors appears to have a beneficial effect on osteoporosis. For example, smoking cessation leads to an improvement in markers of bone turnover within a 6-wk period (5). Lipid-lowering therapy increases bone mineral density (3). Thiazide diuretics appear to lower the bone fracture rate (7). Moreover, beta blockers appear to do the same (6). Finally, estrogen replacement therapy improves bone density and endothelial function in humans.

If bone perfusion has an important effect on bone density, could an increase in bone perfusion also increase bone density? How can bone blood flow be increased? In this issue of the *American Journal of Physiology-Regulatory, Integrative and Comparative Physiology*, Stewart et al. (9) reviewed the literature on bone perfusion and bone mass. The few available publications seem to suggest that increased venous pressure and increased perfusion tend to increase bone mass. They reasoned that an increase in leg and, perhaps, bone perfusion may contribute to the recently described increase in bone mass with whole body vibration (10). To address this issue, they assessed changes in leg hemodynamics and fluid shifts using strain-gauge and impedance plethysmography before and during whole body vibration. The vibration was elicited by placing the subjects on a vibrating platform. Whole body vibration increased blood flow to the lower body while subjects were in the supine position. Furthermore, the intervention reversed the decrease in leg blood flow in the upright position. Finally, leg vibration shifted the microvascular filtration relation to higher pressures, both in the supine and in the upright position. The shift is probably explained by improved lymphatic drainage. Thus whole body vibration substantially altered leg hemodynamics.

The study by Stewart et al. (9) necessarily has some limitations. The authors did not measure bone perfusion directly. It is difficult to know whether the change in leg blood flow is associated with a change in bone perfusion. I would suggest comparing “cheap” leg blood flow measurements with “costly” more direct measurements of bone blood flow in future studies. It would be tremendously helpful to have inexpensive methods that could be used to obtain hemodynamic measurements that are relevant for bone hemodynamics. Furthermore, the authors did not provide data linking changes in hemodynamics and bone turnover. Perhaps more questions were raised than answered. Nevertheless, the study is of importance because it may generate interest in studying the interaction between bone and the cardiovascular system. Promising clinical and epidemiological data linking vascular disease and osteoporosis ought to be supported by solid physiological work. Equally important, the study suggests that even in the era of molecular medicine, a simple and “old-fashioned” physiological method

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is still useful to raise new scientific hypotheses. A final question for those who will not be interested in bones: Do good vibrations add to angiogenesis elsewhere?

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