Buying into healthy blood vessels: exercise and aging

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Submitted 2 June 2014; accepted in final form 30 June 2014

IMAGINE FOR A MOMENT YOU ARE the chief executive of a major pharmaceutical company. You know that: 1) cardiovascular disease is a major killer, and 2) worldwide increases in longevity and adoption of “Western” diets in the developing world will likely increase the number of individuals needing treatment for cardiovascular disease. You also know that the pathophysiological effects of cardiovascular disease are caused in part when large blood vessels lose their elasticity and get stiffer and when small blood vessels in the microcirculation lose their ability to vasodilate. If your vice president of business development came to you with a story about a startup that had developed a therapy that made the large arteries less stiff and improved the ability of the microcirculation to vasodilate in people at risk for cardiovascular disease, my guess is that your interest in acquiring the company that developed this therapy would be high. It might even be higher if your vice president told you that the major side effects of this therapy included lower blood pressure, better blood lipids, and less diabetes (8).

While the scenario was different, the 2013 Adolph Lecture presented by Douglas R. Seals, told a version of that story and a review based on his lecture is in this month’s Journal of Applied Physiology (10). The Seals narrative focuses primarily on work done in his laboratory over about 20 years showing that regular aerobic exercise can prevent both large-artery vascular stiffening and preserve microvascular function in older adults (11). An especially important part of the story is that both the vascular stiffening and microvascular dysfunction associated with aging can be either fully or partially reversed with what might be termed “adult fitness” style exercise programs (4, 5, 11).

In most cases, the human studies are complemented by what might be described as reverse translational experiments in animal models that provide mechanistic insights into the how’s and why’s of both the effects of aging and the effects of exercise on vascular function. Along these lines, the mechanisms responsible for large vessel remodeling, including the cross linking of collagen, are summarized. Likewise, the role of exercise training in preserving endothelial and thus microvascular function via several mechanisms, including improved nitric oxide bioavailability, are highlighted (11). In many cases, common mechanisms explain how both large and small blood vessels go bad with aging and how exercise blunts and potentially restores this loss of function.

As I listened to the lecture in 2013 and had my memory refreshed by the Seals review, four highlights hit me.

First, the use of master athletes as a model of what might be described as aging in the absence of physical inactivity. For many organ systems, comparison studies between younger and older athletes can shed light on minimal rates of aging. For example, the age-related decline in peak heart rate is only minimally affected by lifelong training (12). By contrast, vascular function is largely preserved (5, 10, 11). These studies help solve the problem that aging is frequently studied in the context of one or more coexisting diseases that are associated with aging, but by no means an obligatory part of it.

Second, the guidelines work. The exercise interventions used in the Seals laboratory are typically similar to the general recommendations from various public health advocacy groups and governmental entities for exercise training in middle-aged and older adults (4). In other words, 30–60 min of moderately vigorous physical activity most days of the week is an effective way to preserve and improve vascular health in middle-aged and older adults.

Third, aging is different for men and women. The generally positive effects of exercise on arterial blood vessels both large and small are not as clear cut in postmenopausal women as they are in middle-aged and older men (10). Perhaps this is a result of the loss of endogenous estrogen production and complex interactions between the autonomic nervous system and vascular endothelium in aging women. Clearly, there are major gaps in knowledge when it comes to aging, exercise, and the cardiovascular system in women (1, 7).

Fourth, exercise is about twice as protective in preventing cardiovascular disease as it “should be” based on how it affects traditional risk factors like blood pressure and lipids (8, 11). Healthier blood vessels are likely one major explanation for the extra protection against cardiovascular disease afforded by exercise. Less stiff and more compliant large blood vessels are likely part of the reason that baroreflex function and heart rate variability are relatively preserved in active older people. Preservation of heart rate variability and the associated improved vagal tone has powerful anti-arrhythmic effects. Additionally, while exercise training will not normalize every risk factor in every participant, it still offers impressive protection in those with elevated risk factors (9).

If I now return to my initial scenario of the drug company executive, it is easy to think about how, in the right hands, a pill-based therapy as powerful as endurance exercise might be marketed across the world in a highly profitable way. However, it is in fact unlikely that a polypill with all of the positive primary effects and secondary (side) effects of exercise will ever emerge (2, 6). So, the unstated question from the 2013 Adolph lecture is how best to promote and even market exercise and physical activity across the world when the economic incentives for doing so are far more diffuse than developing a drug, but the costs in terms of death, disability, and medical care costs of doing nothing are staggering (3, 13).

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).
AUTHOR CONTRIBUTIONS

Author contributions: M.J.J. drafted manuscript; M.J.J. edited and revised manuscript; M.J.J. approved final version of manuscript.

REFERENCES


