JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
© 2014 BY THE AMERICAN COLLEGE OF CARDIOLOGY FOUNDATION
PUBLISHED BY ELSEVIER INC.

VOL. 64, NO. 12, 2014
ISSN 0735-1097/$36.00
http://dx.doi.org/10.1016/j.jacc.2014.06.1183

EDITORIAL COMMENT

Cardiorespiratory Fitness and the Attenuation of Age-Related Rise in Blood Pressure

An Important Role for Effective Primordial Prevention*

Stanley S. Franklin, MD,† Gary L. Pierce, PhD‡

The blood pressure (BP) trajectory with advancing age in normotensive subjects has been well described, with increases in systolic blood pressure (SBP) and diastolic blood pressure (DBP) up to ~50 years of age and minimal changes in pulse pressure. This is followed by further increases in SBP beyond 50 years of age, while DBP plateaus and subsequently declines after 60 years of age (1,2). This pattern results in rapid elevation of pulse pressure after 60 years of age from the attendant divergent pattern in SBP and DBP.

Because cardiac output does not change substantially in normotensive adults with aging (3) and large elastic stiffness changes are minimal before 50 years of age (1,2), the hemodynamic determinants of the increases in SBP and DBP before 50 years of age have been attributed to increases in total vascular resistance and mean arterial pressure. This entire sequence is magnified in people destined to develop hypertension (1,2). Consistent with this hemodynamic pattern, hypertension in young adults is more often diastolic; however, between 50 and 60 years of age, there is a transition from isolated diastolic hypertension or combined systolic and diastolic hypertension to isolated systolic hypertension with wide pulse pressure as the predominant form of hypertension in middle-aged and older adults (4). Because mean arterial pressure changes very little during these decades (1,2), this transition in hypertensive phenotypes has been principally attributed to increased large elastic artery (i.e., the thoracic aorta and its branches) stiffness rather than continuous increases in total vascular resistance.

Interestingly, the rate of increased carotid-femoral pulse wave velocity, the gold standard measurement of aortic stiffness, increases each decade after 60 years of age (2,5) and generally precedes the onset of the rise in pulse pressure and the development of ISH (6). Not surprisingly, as shown in a Framingham Heart Study analysis, predictors of the rise in pulse pressure and ISH are more commonly derived from normal and high-normal BP (~60%) than from "burned-out" diastolic hypertension (7). Moreover, young adults with a baseline SBP <120 mm Hg have the slowest rate of increase in aortic stiffness compared with those with an SBP ≥140 mm Hg (1,5). This suggests that arterial stiffness and BP trajectory are accelerated when baseline BP is elevated, likely leading to a vicious cycle of worsening hypertension and further increases in large elastic artery stiffness in the absence of effective antihypertensive treatment (1,5). Importantly, these longitudinal studies have not considered whether certain lifestyle behaviors, such as habitual aerobic exercise/physical activity or high physical fitness, can modify the age-related BP trajectory in those without hypertension.

SEE PAGE 1245

In this issue of the *Journal*, Liu et al. (8) characterized the BP trajectory across the life span of healthy men from the Aerobics Center Longitudinal

*Editorials published in the *Journal of the American College of Cardiology* reflect the views of the authors and do not necessarily represent the views of *JACC* or the American College of Cardiology.

From the †Heart Disease Prevention Program, Division of Cardiology, University of California, Irvine, California; and the ‡Department of Health and Human Physiology, University of Iowa, Iowa City, Iowa. Both authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Study who were classified as having low, moderate, or high fitness on the basis of their baseline performance on a maximal treadmill test. The study reported that a higher fitness level significantly modified the rise in SBP trajectory across the life span. They found that SBP increased by 0.25 mm Hg per year after adjusting for body fat percentage and that the age × fitness interaction with SBP remained significant, even after additional adjustment for resting heart rate, glucose level, triglyceride level, cholesterol level, current smoking, heavy alcohol consumption, and parental hypertension. Interestingly, after the same covariate adjustments, DBP increased by 0.14 mm Hg per year. Despite a population age range of 20 to 90 years, the mean population age of 43 years in this study is consistent with the continual increase in DBP; it probably would have taken a mean age of >60 years to show a yearly decrease in DBP and a significant positive age × fitness interaction for a steeper widening of pulse pressure. Indeed, the quadratic nature of DBP and the curvilinear pattern of pulse pressure trajectory are most evident in those >60 years of age. The authors also reported that SBP increased >120 mm Hg (defined as abnormal by the authors) in men at approximately 46 years of age for those with the lowest fitness level and at approximately 54 years of age for those with a high fitness level, suggesting that a high fitness level delayed the development of "abnormal SBP" by approximately a decade compared with men with the lowest fitness level. In contrast, although DBP reached >80 mm Hg at 42 years of age in men with the lowest fitness level, DBP did not reach 80 mm Hg (defined as "abnormal DBP") in men with the highest fitness level until beyond 90 years of age. Importantly, men with hypertension at baseline or who developed hypertension during the follow-up period were excluded to ensure that BP, not hypertension, was being evaluated. Thus, the major new finding from this study is that men who were in the highest fitness category demonstrated lower SBP throughout the adult life span compared with men with moderate and low fitness levels.

The mechanisms by which fitness can influence the trajectory of BP over the life span likely differ in normotensive subjects <50 years of age, 50 to 60 years of age, and >60 years of age; indeed, this may be related to the hemodynamic factors that mediate changes in BP components across the life span. For example, assuming similar genetic influences across age groups, lower SBP in young adults with higher fitness levels from habitual aerobic exercise/physical activity may result almost exclusively from a tonically lower total vascular resistance. In middle-aged adults (50 to 60 years of age) who remain physically active, lower SBP would likely be sustained by a combination of lower vascular resistance and less aortic stiffness in comparison to their age-matched, low-fitness peers. Beyond 60 years of age, higher fitness levels from aerobic exercise minimize the rise in SBP and pulse pressure, perhaps almost exclusively by attenuating the age-related increase in elastic artery stiffness (9) or as reflected by lower aortic stiffness (carotid-femoral pulse wave velocity) (5) and carotid stiffness (carotid beta-stiffness index) (10) as demonstrated in highly fit older adults compared with their sedentary age-matched peers. Furthermore, a previous paper by the authors of the present study (11) reported higher incidence rates of hypertension (per 10,000 human-years adjusted for age) of 89.8, 78.4, and 64.6 for low, middle, and high cardiorespiratory fitness, respectively (trend $p < 0.0001$), suggesting that maintaining a higher fitness level may reduce the incidence of hypertension across the adult life span.

A limitation of the present study was the exclusion of women. There is some evidence that men have a steeper rate of increase in aortic stiffening beyond 50 years of age compared with women (5); therefore, fitness may have a different modifying effect on SBP and DBP trajectory with aging in women than in men. This should be addressed in future studies. Second, fitness is a highly heritable trait that is also influenced by the volume of recent habitual aerobic exercise or physical activity. Therefore, the proportional contribution of genetics versus habitual aerobic exercise/physical activity on higher fitness levels that mediated the lower SBP observed in this cohort across the life span cannot be determined from this study. Third, there is a "healthy cohort effect" in the selection of men who underwent repeated cardiopulmonary testing and who maintained a certain level of cardiorespiratory fitness over a long period. These men may also have consumed a healthier diet, including chronically lower sodium intake. Lastly, the mechanisms by which cardiorespiratory fitness attenuates arterial stiffening and overall cardiovascular health are complex and poorly understood.

The current study shows that higher fitness levels were associated with lower SBP throughout the life span that cannot be explained by differences in body fatness or other risk factors for cardiovascular disease. Indeed, habitual aerobic exercise/physical activity may even counteract the burden of cardiometabolic abnormalities that accelerate artery

JACC VOL. 64, NO. 12, 2014
SEPTEMBER 23, 2014:1254–6

stiffening—characterized as "early vascular aging"—and therefore slow the onset and severity of ISH. Future studies should investigate fundamental mechanisms of cardiorespiratory fitness that result in "primordial" prevention of systolic hypertension with advancing age.

REPRINT REQUESTS AND CORRESPONDENCE: Dr. Stanley S. Franklin, Heart Disease Prevention Program, C240 Medical Sciences (Offices C340A-B), University of California, Irvine, California 92697-4079. E-mail: ssfranklinmd@earthlink.net.

REFERENCES

1. Franklin SS, Gustin W IV, Wong ND, et al. Hemodynamic patterns of age-related changes in blood pressure. The Framingham Heart Study. Circulation 1997;96:308–15.

2. Mitchell GF, Wang N, Palmisano JN, et al. Hemodynamic correlates of blood pressure across the adult age spectrum: noninvasive evaluation in the Framingham Heart study. Circulation 2010; 122:1379–86.

3. Rodeheffer RJ, Gerstenblith G, Becker LC, et al. Exercise cardiac output is maintained with advancing age in healthy human subjects: cardiac dilatation and increased stroke volume compensate for a diminished heart rate. Circulation 1984; 69:203–13.

4. Franklin SS, Larson MG, Khan SA, et al. Does the relation of blood pressure to coronary heart disease risk change with aging? The Framingham Heart Study. Circulation 2001;103:1245–9.

5. AlGhatrif M, Strait JB, Morrell CH, et al. Longitudinal trajectories of arterial stiffness and the role of blood pressure: the Baltimore Longitudinal Study of Aging. Hypertension 2013;62:934–41.

6. Kaess BM, Rong J, Larson MG, et al. Aortic stiffness, blood pressure progression, and incident hypertension. JAMA 2012;308:875–81.

7. Franklin SS, Pio JR, Wong ND, et al. Predictors of new-onset diastolic and systolic hypertension: the Framingham Heart Study. Circulation 2005; 111:1121–7.

8. Liu J, Sui X, Lavie CJ, et al. Effects of cardiorespiratory fitness on blood pressure trajectory with aging in a cohort of healthy men. J Am Coll Cardiol 2014;64:1245–53.

9. Tanaka H, Dinenno FA, Monahan KD, et al. Aging, habitual exercise, and dynamic arterial compliance. Circulation 2000;102:1270–5.

10. Pierce GL, Casey DP, Fiedorowicz JG, et al. Aortic pulse wave velocity and reflecting distance estimation from peripheral waveforms in humans: detection of age- and exercise training-related differences. Am J Physiol Heart Circ Physiol 2013;305:H135–42.

11. Chase NL, Sui X, Lee DC, et al. The association of cardiorespiratory fitness and physical activity with incidence of hypertension in men. Am J Hypertens 2009;22:417–24.

KEY WORDS blood pressure, exercise, hypertension, longitudinal studies, physical fitness, vascular stiffness