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Author
Budoff, Matthew J

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EXERCISE CAPACITY AND BIOLOGICAL AGE

Matthew Budoff, MD

Endowed Chair of Preventive Cardiology

Los Angeles Biomedical Research Center

Professor of Medicine

David Geffen School of Medicine at UCLA

Address for correspondence:

Matthew Budoff, MD

Los Angeles Biomedical Research Institute at Harbor-UCLA

1124 W Carson St, Torrance, CA 90502

Phone: 310-222-24107

Fax: 310-787-0448

E-mail: mbudoff@labiomed.org

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The concept of vascular or biologic age in risk prediction should be credited to Scott Grundy, who originally wrote up this concept in 2001[1] and incorporated this into practice guidelines via the National Cholesterol Education Program (NCEP) 2004 update.[2] The original concept, was that coronary artery calcium (CAC) scores, by demonstrating the vascular age of the patient, should replace chronologic age as a better surrogate of risk and atherosclerosis. Conceptually, this made a lot of sense, as age is used as an atherosclerosis surrogate for cardiovascular risk in the risk stratification tools. That CAC is better than age is intuitive, as CAC is a better measure of coronary plaque burden, and thus a direct risk marker for CVD events. Grundy concluded that "the degree of plaque burden could be used to replace age as a risk factor in Framingham scoring for risk prediction". This concept has been born out with multiple studies using CAC demonstrating superiority of CAC to predict CV risk.[3],[4],[5] Incorporating CAC into the Multi-Ethnic Study of Atherosclerosis (MESA) clearly improves risk stratification and discrimination over scores based on chronologic age.[6],[7] Grundy's simple conclusion **"**Use of coronary calcium scores will thus make it possible to improve selection of persons for intensive intervention with risk-reducing medical therapies. Their use will improve the efficacy of intervention and enhance cost-effectiveness of medical preventive therapies"[1], resonates strongly today within the cardiovascular preventive community and is incorporated into the 2013 American College of Cardiology/American Heart Association (ACC/AHA) guidelines for treatment of cholesterol[8].

Various studies have proposed distinct ways to define and measure vascular age, with the concept that this better reflects an individual's exposure to cardiovascular risk factors.[9] Studies have looked into the effects of vascular age as a tool to improve cardiovascular risk prediction but most have been limited by size or scope. Large studies will be required before its clinical use can be justified. The paper by Blaha goes a long way to validate the 'biological age', using a

large cohort and long follow up to demonstrate the importance of age-defined exercise capacity.[10] Blaha et al derived fitness-associated biologic age as a tool to improve risk prediction in those symptomatic persons undergoing stress testing. They studied a retrospective cohort including 57,085 patients who underwent clinically-referred treadmill stress testing from 1991-2009. Fitness-associated biologic age was derived as the chronologic age with equivalent mortality or MI risk. Approximately 10% of the population died and 3% suffered a myocardial infarction over the follow up period. Univariate models demonstrated improved predictive accuracy compared to chronologic age for both mortality (C-statistic: 0.81 vs. 0.77, P<.001) and MI (C-statistic: 0.72 vs. 0.68, P<.001).

While the study is very well done, the study applicability suffers from use of symptomatic population. While that is the only appropriate population to perform exercise treadmill patients on, use of symptomatic cohorts have intrinsic limitations. Some of the patients had underlying coronary artery disease, and may have halted exercise not due to true exercise capacity issues, but partially related to development of chest pain, ongoing shortness of breath, or a myriad of causes associated with patients with suspected CAD. The prior studies of biologic age, demonstrating significant improvement substituting vascular age of CAC instead of chronologic age, were largely or solely done in asymptomatic populations. Use of exercise treadmill testing in asymptomatic persons is largely considered inappropriate, with the exception of exercise prescription purposes.[11] So, for the symptomatic population, this is a clever, readily available test to help patients understand their cardiovascular risk and relative age, and hopefully promote better behaviors to improve exercise capacity and thus morbidity and mortality.

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