

Physical Activity in Older Subjects Is Associated With Increased Coronary Vasodilation

The ADVANCE Study

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OBJECTIVES We investigated the association between physical activity and coronary vasodilation to nitroglycerin (NTG) in the ADVANCE (Atherosclerotic Disease, Vascular Function, and Genetic Epidemiology) cohort of older healthy subjects.

BACKGROUND Physical activity may exert its beneficial effects by augmenting coronary responsiveness to nitric oxide. The relationship between physical activity and coronary vasodilatory response to NTG, an exogenous nitric oxide donor, has not been studied in a community-based population with typical activity levels.

METHODS In 212 older adults (ages 60 to 72 years) without cardiovascular disease, we measured the coronary vasodilatory response to NTG using magnetic resonance angiography and physical activity using the Stanford Seven-Day Physical Activity Recall Questionnaire. The primary predictor measure was total physical activity (kcal/kg/day). The primary outcome measure was coronary vasodilatory response (percent increase of cross-sectional area post-NTG).

RESULTS Coronary vasodilation was 27.6% in more active subjects (>35 kcal/kg/day, e.g., 1 h of walking per day) compared to 18.9% in less active subjects ($p = 0.03$). Regression analysis showed a significant positive correlation between coronary vasodilation and physical activity ($p = 0.003$), with a slope (beta) of 1.2% per kcal/kg/day. This finding remained significant after adjustment for cardiac risk factors, coronary calcium, the use of vasoactive or statin medications, and analysis of physical activity by quintiles ($p < 0.05$). Coronary vasodilation was also associated with physical activity intensity ($p = 0.03$).

CONCLUSIONS In an asymptomatic, community-based cohort of older adults, increased coronary vasodilatory response was independently associated with greater physical activity, supporting the benefits of exercise on the order of 1 h of walking per day. (J Am Coll Cardiol Img 2011;4:622–9) © 2011 by the American College of Cardiology Foundation

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Manuscript received February 25, 2011; revised manuscript received April 14, 2011, accepted April 21, 2011.

It is well established that exercise reduces cardiovascular morbidity and mortality and helps prevent the development of coronary artery disease (CAD) (1-4). One possible mechanism for these beneficial effects is that physical activity favorably alters the function of the coronary vasculature. Nitric oxide (NO) is a key vasculoprotective substance, and increased responsiveness to NO may confer a cardiovascular benefit. Previous studies have demonstrated that athletes have greater coronary vasodilatory response to nitroglycerin (NTG), an NO donor, compared to physically inactive subjects (5-7). However, these studies involved invasive measures in small, select groups of men only. Thus, it is unknown if physical activity confers the same favorable coronary vasodilatory response in a broader population with more typical levels of exercise.

We and others have shown that the coronary vasodilatory response to NTG can be measured noninvasively by magnetic resonance angiography (MRA) (8-12). The ADVANCE (Atherosclerotic Disease, Vascular Function, and Genetic Epidemiology) study investigated clinical, imaging, and genetic abnormalities in an older community-based patient cohort without cardiovascular disease (13-15). Here, we report on the relationship of physical activity of this cohort to their coronary vasodilatory response to the NO donor NTG.

METHODS

Study design and population. This cross-sectional analysis was performed as part of the ADVANCE study, which investigated 1,023 healthy older adults without cardiovascular disease or other major comorbidities recruited from Kaiser Permanente of Northern California; details of this cohort have been published previously (14,15). At study baseline, all subjects underwent a comprehensive visit, including a health survey, lipid profile, blood pressure, anthropometric measurements, and coronary calcium scoring (15). A standardized and validated questionnaire, the Stanford Seven-Day Physical Activity Recall Questionnaire (PARQ) (16-19), was used to collect physical activity data. A subset of these healthy older adults ($n = 212$) underwent coronary MRA for assessment of NTG-induced coronary vasodilation (12). There were no significant differences in demographic or clinical parameters between the ADVANCE cohort and this subset (all $p > 0.2$). The study protocol was approved by the institutional review boards at Stan-

ford University and the Kaiser Foundation Research Institute. Written informed consent was obtained from all participants.

The Stanford PARQ. The Stanford PARQ is an interviewer-administered questionnaire estimating energy expenditure in kilocalories per kilogram per day (kcal/kg/day), which has been used in epidemiological, clinical, and behavioral studies since the 1980s (16,20). It has been validated in prior studies with good test-retest reliability (17,18) and used in diverse populations up to 79 years of age (19,21,22). Briefly, the PARQ is designed to estimate the amount of time that a person engages in light, moderate, hard, and very hard intensity activities during the previous 7 days. Fourteen items are used to estimate energy expenditure. The subject is guided through the recall process by a trained interviewer to determine the duration and intensity of physical activities performed. Subjects are provided with examples of various activity levels (e.g., moderate = mopping, brisk walk; hard = construction work, doubles tennis; very hard = chopping wood, running) (16). The time engaged in light activity is calculated by subtracting the time spent sleeping and performing moderate, hard, and very hard intensity activities from the total 24 h/day (16). Energy expenditure is calculated by multiplying the hours sleeping and engaging in the different physical activity categories by the average metabolic equivalent value for each intensity category (sleep = 1 MET, light = 1.5 METs, moderate = 4 METs, hard = 6 METs, and very hard = 10 METs). A standard procedure was employed for the administration, certification of staff, and scoring of the PARQ. Additionally, all staff were recertified annually in the proper administration and scoring of the PARQ.

Coronary vasodilatory response to NTG. The coronary vasodilatory response to NTG was measured by MRA, as previously described (10-12). Briefly, a 1.5-T magnetic resonance imaging (MRI) scanner equipped with a 4-channel cardiac phased-array surface coil was used (GE Healthcare, Milwaukee, Wisconsin). Real-time interactive MRI was used to prescribe in-plane and then cross-sectional views of the right coronary artery (RCA). Specifically, an imaging plane perpendicular to the long axis of the RCA was prescribed to yield the cross-sectional view. High-resolution spiral coronary MRA of the RCA in cross-section was performed with electro-

ABBREVIATIONS AND ACRONYMS

CAD = coronary artery disease

MRA = magnetic resonance angiography

MRI = magnetic resonance imaging

NO = nitric oxide

NTG = nitroglycerin

PARQ = Physical Activity Recall Questionnaire

RCA = right coronary artery

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