



## The effects of antihypertensive medications on physical function

Paul D. Loprinzi<sup>a,\*</sup>, Jeremy P. Loenneke<sup>b</sup>

<sup>a</sup> Physical Activity Epidemiology Laboratory, Department of Health, Exercise Science, and Recreation Management, The University of Mississippi, MS, United States

<sup>b</sup> Keiser Ermin Applied Physiology Laboratory, Department of Health, Exercise Science, and Recreation Management, The University of Mississippi, MS, United States

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### ABSTRACT

**Objective.** Limited research has examined the effects of antihypertensive medication use and physical function. These studies provided mixed findings while employing a convenience sample and limiting their examination to few indices of physical function and few classes of antihypertensive medications. The purpose of this study was to examine whether several antihypertensive medication classes were associated with several measures of physical function in a national sample of U.S. middle-to-older age adults.

**Methods.** Data from the 1999–2002 and 2011–2012 NHANES were used. Antihypertensive medication use was assessed from an interviewer, and included angiotensin converting enzyme (ACE) inhibitors, peripherally-acting antiadrenergic agents and centrally-acting antiadrenergic agents. Physical function-related parameters included objectively-measured lower extremity isokinetic knee extensor strength (IKES), objectively-measured grip strength, laboratory-assessed walking performance (8 and 20 ft walk tests) and self-reported physical activity engagement.

**Results.** Those on ACE inhibitors had a 37% reduced odds (OR = 0.63, 95% CI: 0.48–0.83,  $P = .002$ ) of engaging in moderate-to-vigorous physical activity, had reduced knee extensor strength ( $\beta = -15.4$ , 95% CI:  $-27.2$  to  $-3.4$ ,  $P = .01$ ) and took longer to complete the 20 ft ( $\beta = .42$ , 95% CI: 0.02–0.81,  $P = .04$ ) and 8 ft walking tests ( $\beta = .22$ , 95% CI: 0.05–0.39,  $P = .01$ ). Those on peripherally-acting antiadrenergic agents had reduced grip strength ( $\beta = -4.8$ , 95% CI:  $-9.1$  to  $-0.5$ ,  $P = .02$ ).

**Conclusions.** Antihypertensive medication use, particularly ACE inhibitors, is associated with various measures of reduced physical function. Clinicians are encouraged to monitor the long-term mobility function of their patients on antihypertensive medications.

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### 1. Introduction

It is reported that 1 out of 3 American adults (77.9 million) have high blood pressure (Go et al., 2013). A number of medications are prescribed to reduce cardiovascular complications associated with hypertension. Of these, the angiotensin converting enzyme (ACE) inhibitors may have the potential to concurrently improve both cardiovascular health and muscle function. ACE inhibitors prevent the conversion of Angiotensin I to Angiotensin II in the renin-angiotensin system. Angiotensin II, in animal models, can promote muscle loss by an inhibitory effect on the insulin like growth factor-1 (IGF-1) system and by stimulating catabolism via the atrogenes (Yoshida et al., 2010). In humans, those with the II genotype of the ACE gene have low serum ACE levels and display better endurance performance as well as greater

endurance following training (Woods et al., 2000). ACE inhibitors have also been found to be associated with increased muscle size and strength in those with hypertension (Onder et al., 2002; Di Bari et al., 2004), which is an important finding as muscular strength is associated with various health outcomes (Loprinzi et al., 2015) and reduced lower extremity muscular strength is linked with impaired mobility (Batista et al., 2012), which in turn is associated with quality of life and premature mortality (Rizzoli et al., 2013; Masel et al., 2010).

Not all studies, however, have demonstrated a favorable effect of ACE inhibitors on physical function. This discrepancy across studies may be explained by an inverted J-shape relationship between physical function and the activity of the renin-angiotensin system or may be related to the performance task measured. To illustrate, previous studies noting a favorable effect of ACE inhibitors on physical performance have largely measured exercise capacity by using a walk test (Hutcheon et al., 2002; Ahimastos et al., 2006; Sumukadas et al., 2007); however, not all studies support this finding. Sumukadas et al. failed to find an enhancement of exercise capacity (walk test) or grip strength with ACE inhibitors compared to those receiving a placebo (Sumukadas et al., 2014). Lastly, one study reported a negative association between ACE inhibitor use

\* Corresponding author at: Physical Activity Epidemiology Laboratory, Department of Health, Exercise Science, and Recreation Management, The University of Mississippi, 229 Turner Center, MS 38677, United States.

E-mail address: [pdloprin@olemiss.edu](mailto:pdloprin@olemiss.edu) (P.D. Loprinzi).

and measures of physical performance (e.g. chair stand, grip strength) (Gray et al., 2012).

These mixed findings warrant the need for additional work on this topic. Specifically, there is a need to examine the effects of ACE inhibitors, as well as other anti-hypertensive medications, on multiple concurrent indices of physical function (e.g., muscular strength, free-living physical activity, laboratory-based ambulatory performance). To our knowledge, no such systematic study exists. Therefore, the purpose of this study was to comprehensively examine the effect of antihypertensive medication (ACE inhibitors, centrally- and peripherally-acting antiadrenergic agents) use on various indices of physical function, including objectively-measured lower extremity muscular strength, free-living physical activity, laboratory-based walking velocity performance, and grip strength.

## 2. Methods

### 2.1. Design and participants

Data were extracted from several cycles of the National Health and Nutrition Examination Survey (NHANES). All outcome measures were not consistently evaluated across the same NHANES cycles. Cycles 1999–2002 included assessments of physical activity and lower extremity muscular strength; cycle 2001–2002 included assessments of walking performance; and cycle 2011–2012 included an assessment of grip strength. See the Fig. 1 for the analyzed sample sizes for each analytic model. For all analyses, the sample included those 50 yrs of age and older as few participants under this age were on antihypertensive

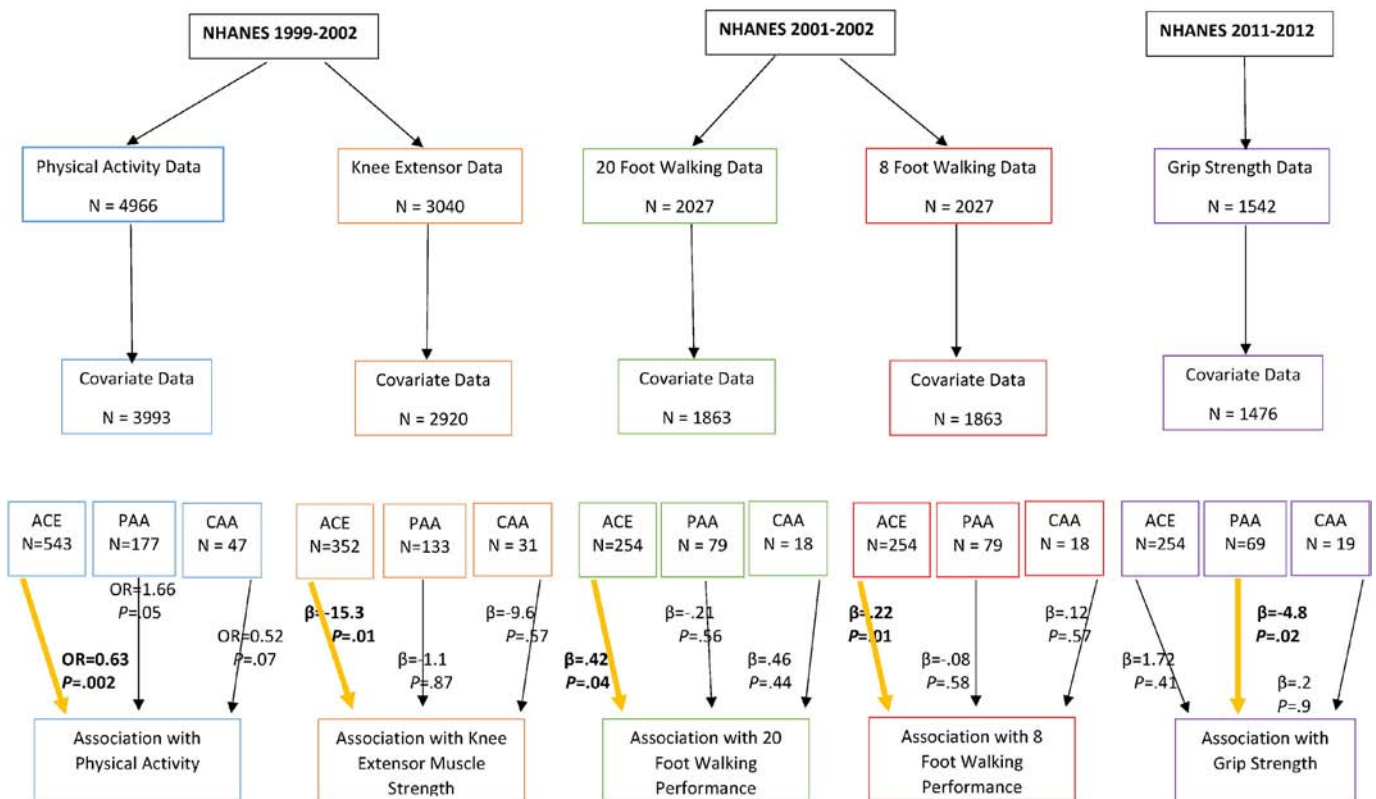
medication and only those 50+ yrs were eligible for the lower extremity muscular strength test, walking tests, and grip strength test. Procedures were approved by the National Center for Health Statistics review board. Consent was obtained from all participants.

### 2.2. Antihypertensive medication

During a household interview, participants were asked if they were taking any prescription medication, and if so, how long (# of days) they were taking the medication. Participants self-reporting medication use were asked to show the interviewer the medication container(s), in which the interviewer then entered the product's complete name from the container into a computer. If no container was available, the interviewer asked the participant to verbally report the name of the medication. Due to the availability of data, antihypertensive medication use was defined as taking ACE inhibitors (e.g., captopril, enalapril, fosinopril, quinapril, ramipril, benazepril, lisinopril, moexipril,trandolapril, perindopril), peripherally acting antiadrenergic agents (e.g., guanethidine, prazosin, reserpine, terazosin, guanadrel, doxazosin, tamsulosin, alfuzosin, silodosin) and/or centrally acting antiadrenergic agents (e.g., clonidine, guanabenz, methyl dopa, guanfacine).

### 2.3. Peak lower extremity muscle strength

In the 1999–2002 NHANES cycles (Fig. 1), a Kin Com MP dynamometer (Chattanooga Group, Inc.) was used to assess isokinetic knee extensor strength (IKES) at peak force in newtons (at a speed of 60 degrees/s). A total of 6 measurements of muscle strength of the right quadriceps



**Fig. 1.** Participant (all participants ≥50 yrs) flow chart and results examining the association between antihypertensive medication and physical activity, knee extensor strength, walking performance and grip strength. In a logistic regression, those on ACE inhibitors had a 37% reduced odds (OR = .63, P = .002) of engaging in physical activity in the last 30 days. In a linear regression, those on ACE inhibitors had reduced knee extensor strength ( $\beta = -15.4$ , P = .01). In a linear regression, those on ACE inhibitors took longer to complete the 20 ft ( $\beta = .48$ , P = .04) and 8 ft walking tests ( $\beta = .22$ , P = .01). In a linear regression, those on peripherally-acting antiadrenergic agents had reduced grip strength ( $\beta = -4.8$ , P = .02). For all analyses across all cycles, covariates included: age, gender, race-ethnicity, BMI, diabetes, mean arterial pressure, coronary artery disease, smoking and duration of medication use. ACE = Angiotensin-converting-enzyme inhibitor; PAA = Peripherally-acting antiadrenergic agents; CAA = Centrally-acting antiadrenergic agents.

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