#### ARTICLE IN PRESS

JAMDA xxx (2016) 1-4



# **JAMDA**

journal homepage: www.jamda.com



## Original Study

# Gait Performance in Hypertensive Patients on Angiotensin-Converting Enzyme Inhibitors

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#### ABSTRACT

Keywords: Ace inhibitors physical performance *Objective*: To examine the relationship between angiotensin-converting enzyme inhibitor (ACEI) use and gait performance in older adults.

Design: Cross-sectional survey.

Setting: Community.

Participants: A total of 281 community-dwelling older adults with hypertension enrolled in an aging study.

Measurements: Quantitative variables used to define gait performance included velocity (cm/s), stride length (cm), swing time (s), stride length variability (SD), and swing time variability (SD).

*Results*: There were 72 hypertensive participants on ACEIs and 209 were on other antihypertensive medications. Linear regression analysis adjusted for age, sex, and potential confounders revealed that hypertensive participants on an ACEI walked 7.29 cm/s slower (P = .016) and stride length was 6.86 cm shorter (P = .006) compared with those not on ACEIs. There were no significant differences on the other gait variables examined.

*Conclusion:* ACEI use was associated with worse gait performance in elderly hypertensives. Biological mechanisms need to be explored, and clinicians should consider monitoring gait speed in hypertensive patients on ACEIs.

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Poor gait performance is associated with multiple adverse outcomes including falls, hospitalization, and mortality in older adults. Biological derangements in inflammation, oxidative stress, and vascular pathways are implicated in the occurrence of gait and mobility disorders, as well as in slowing of gait in aging. Hedications, such as angiotensin-converting enzyme inhibitors (ACEIs), that are commonly used to treat hypertension and act on these biological pathways could, therefore, influence gait performance in older patients. Although it is plausible that ACEIs may improve gait function,

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previous studies in older adults with hypertension have shown mixed results. Some studies have reported an improvement in gait performance in older adults on ACEIs,<sup>6,7</sup> whereas others show no improvement or a decline in gait performance in older adults on ACEIs.<sup>8,9</sup> These studies have been based in a single sex,<sup>6,8</sup> or included patients taking ACEIs with high cardiovascular risk profiles<sup>9</sup> or functional limitations.<sup>8,9</sup> Furthermore, although there are many facets and domains that characterize gait performance and that show differential relationships with outcomes such as cognitive decline, falls, or frailty,<sup>10–12</sup> most previous studies in hypertensive populations have reported associations of ACEI use with gait speed only. Establishing the relationship between ACEIs and gait performance has implications in developing clinical guidelines for the long-term management of older hypertensive patients in clinical settings.

### **Materials and Methods**

**Participants** 

We performed a cross-sectional study in community-dwelling residents 65 years and older with hypertension enrolled in the

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This study was supported by grants from the National Institute on Aging (R01AG036921–01A1: R. Holtzer, PI, and R01AG044007–01A1: J. Verghese, PI) and an intramural grant from Resnick Gerontology Center, Albert Einstein College of Medicine. CJG is supported by supplement R01AG044007–02S1 from the National Institute on Aging. The funding sources have no role in the study design; in the collection, analysis and interpretation of data; in the writing of the report; and in the decision to submit the article for publication.

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"Central Control of Mobility in Aging" (CCMA) study, a longitudinal study at Albert Einstein College of Medicine in the Bronx, New York. The main aim of the CCMA study was to determine cognitive processes and underlying brain substrates of mobility in aging. Study design has been previously reported.<sup>13</sup> In brief, potential participants were initially screened by telephone, including cognitive tests (AD8 Dementia Screening interview)<sup>14</sup> and the Memory Impairment Screen (MIS)<sup>15</sup> to exclude participants with dementia, then invited for further in-person testing in our research center. Participants were included if they were 65 and older, English speaking, ambulatory, resided in the community, and planned to be in the area for the next 3 years. Exclusion criterion for the parent study included presence of dementia (self-reported, detected on the CCMA telephone cognitive screen, <sup>13</sup> or diagnosed by study clinicians at in-house visits), mobility limitations requiring assistive devices, history of severe neurological or psychiatric disorders, significant loss of vision or hearing, recent or planned surgical procedures that could affect mobility, or serious chronic or acute illnesses. Additional inclusion criteria for the current analysis were the presence of hypertension as determined by self-report of physician diagnosis of hypertension, medication indication for hypertension, and review of medical records for reports of diagnosis of hypertension. An in-house blood pressure was performed and recorded by the study physician. Written informed consent was obtained from all participants, and the study protocol was approved by the local institutional review board.

#### Clinical Evaluations and Medications

Participants received detailed clinical, cognitive, and mobility assessments at their baseline in-house visit and at yearly follow-up visits. They were also interviewed about medical conditions, cognitive status, and had neurological examinations performed by the study clinician. Presence or absence of physician-diagnosed chronic illnesses (depression, chronic obstructive lung disease, osteoarthritis) and vascular diseases (diabetes, heart failure, myocardial infarction, or stroke) were recorded. ACEI and other medication use was ascertained by the study clinician at the in-person visit. Medication history was further confirmed by review of medication bottles, interviewing family members when available, and any available medical records. The Morisky Medication Adherence scale, 16 a reliable and validated medication adherence scale, was administered to 97 CCMA participants, and 81.4% had high or medium adherence to medications. Between the in-house study visits, participants' mobility, medical, and fall status were tracked by bimonthly telephone calls.

#### Quantitative Gait Assessments

Gait parameters were quantitatively assessed using the GAITRite system (CIR Systems, Havertown, PA). Participants walked on a 20foot instrumented walkway without any attached monitors, which also included 4 feet of nonrecording surface at either end to account for initial acceleration and terminal deceleration. Participants were instructed to walk at their normal pace for 1 trial. None of the participants included in this analysis used an assistive device during their walking trial. This system has been used in our previous studies and has excellent reliability. 12 Velocity (cm/s), stride length (cm), swing time (seconds), stride length variability (SD), and swing time variability (SD) were examined. These 5 parameters were chosen as they show differential relationships with outcomes such as cognitive decline, falls, or frailty. 12,17,18 Moreover, these variables load the highest on 3 previously described gait domains, <sup>17</sup> pace (velocity, stride length), rhythm (swing time), and variability (stride length variability and swing time variability).

#### Statistical Analysis

Baseline characteristics in hypertensive participants on and not on ACEIs were compared using descriptive statistics. Linear regression analysis was used to determine the relationship between ACEI use and gait performance at cross-section, adjusting for age (years), sex, and educational level (years) and other potential confounders. The covariates to be included in the models were chosen if they were significant at a *P* value of .05 or less in the univariate analyses (see Table 1). Model assumptions were examined analytically and graphically, and were adequately met. All analyses were performed on SPSS version 21 (IBM SPSS Statistics, IBM Corporation, Chicago, IL).

#### Results

Of the 513 CCMA participants evaluated between June 2011 and December 2014, 281 had hypertension as per our study criteria. All participants in this study with hypertension were on antihypertensive medications for this indication when evaluated by study clinicians. Table 1 lists the baseline characteristics of the 72 patients with hypertension on an ACEI and 209 who were not on an ACEI. The mean age was  $76.0 \pm 6.5$  years in the ACEI group and  $77.0 \pm 6.9$  years in the No ACEI group. Table 1 shows that participants who were not on an ACEI were more likely to be prescribed an angiotensin receptor blocker (ARB). Those on an ACEI were more likely to be on a thiazide diuretic (P = .039) compared with patients with hypertension not on an ACEI. Blood pressure control was comparable between patients on ACEI and non-ACEI medications (Table 1).

Polytherapy for hypertension was common in both groups. Of the 72 participants on an ACEI, 42 (58.3%) received a second medication for hypertension or a diuretic, and in the No ACEI group, 107 (51.2%) received a second medication for hypertension or a diuretic. Monotherapy for hypertension in this sample was not common: 30 (10.7%)

**Table 1**Baseline Characteristics in Older Adults With Hypertension on ACEIs and Not on ACEIs

Baseline Characteristic	ACEI,	No ACEI,	P
	n=72	n=209	
Age, y, mean, SD	$76.0 \pm 6.5$	77.2 ± 6.9	.131
Women, n (%)	38 (53)	124 (61)	.337
Educational level, y	$14.7\pm3.3$	$14.1\pm2.7$	.092
Congestive heart failure, n (%)	3 (4.2)	4 (1.9)	.381
Diabetes, n (%)	23 (31.9)	43 (20.5)	.081
Myocardial infarction, n (%)	10 (13.7)	13 (6.2)	.080
Chronic obstructive pulmonary	9 (12.5)	17 (8.6)	.351
disease, n (%)			
Stroke, n (%)	5 (6.9)	15 (7.2)	1.000
Depression, n (%)	7 (9.7)	19 (9.1)	1.000
Osteoarthritis	39 (54.2)	101 (48.3)	.404
Antiplatelet agents,*n (%)	14 (19.4)	42 (20)	.866
Nonsteroidal anti-inflammatory	1 (1.4)	11 (5.3)	.194
drugs, n (%)			
Antihypertensives, n (%)			
ARBs	1 (1.4)	63 (30)	.000
Beta blockers	23 (31.9)	64 (30.1)	1.000
Calcium channel blockers	14 (19.4)	64 (30.6)	.069
Alpha 1 antagonists	2 (2.8)	6 (2.9)	1.000
Diuretics, n (%)			
Loop	9 (12.5)	12 (5.7)	.118
Thiazide	10 (13.9)	10 (4.8)	.018
Potassium sparing	0 (0)	3 (1.4)	.569
HMGCoA reductase inhibitors, n (%)	39 (54.2)	95 (45.5)	.346
Systolic blood pressure, mm Hg	$132.0\pm12.5$	$131.5\pm14.0$	.996
Diastolic blood pressure, mm Hg	$77.6\pm7.8$	$77.5\pm7.9$	.944
Knee extensor strength, kg	$31.7\pm15.0$	$35.1\pm71.7$	.902
Falls within the past year, n (%)	16 (22.2)	36 (17.2)	.384
Body mass index, kg/m <sup>2</sup> , mean, SD	$30.5\pm6.2$	$29.5\pm6.8$	.284

<sup>\*</sup>Antiplatelet agents: aspirin, clopidogrel, aspirin/dipyridamole, Cilostazol.

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