



Ankle brachial index and cognitive function among Hispanics/Latinos: Results from the Hispanic Community Health Study/Study of Latinos

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ARTICLE INFO

Article history:

Received 6 September 2017

Received in revised form

17 January 2018

Accepted 8 February 2018

Available online 9 February 2018

Keywords:

Cognition

Ankle-brachial index

Atherosclerosis

ABI

Peripheral arterial disease

Cardiovascular health

Hispanics

Latinos

Epidemiology

ABSTRACT

Background and aims: The Ankle-Brachial index (ABI) is a well-accepted measure of peripheral artery disease (arterial stenosis and stiffness) and has been shown to be associated with cognitive function and disorders; however, these associations have not been examined in Hispanics/Latinos. Therefore, we sought to examine relationships between ABI and cognitive function among diverse middle-age and older Hispanics/Latinos.

Methods: We used cross-sectional data on $n = 7991$ participants aged 45–74 years, without stroke or coronary heart disease, from the Hispanic Community Health Study/Study of Latinos. Our primary outcome, global cognition (GC), was a continuous composite score of four cognitive domains (verbal learning and memory, verbal fluency, executive function, and mental status). Secondary outcomes were the individual tests representing these domains. The ABI was analyzed continuously and categorically with standard clinical cut-points. We tested associations using generalized survey regression models incrementally adjusting for confounding factors. Age, sex, hypertension, diabetes, and dyslipidemia moderations were examined through interactions with the primary exposure.

Results: In age, sex, and education adjusted models, continuous ABI had an inverse u-shape association with worse GC. We found similar associations with measures of verbal learning and memory, verbal fluency, executive function, but not with low mental status. The associations were attenuated, but not completely explained, by accounting for the confounders and not modified by age, sex, education, and vascular disease risks.

Conclusions: In addition to being a robust indicator of arterial compromise, our study suggests that abnormal ABI readings may also be useful for early signaling of subtle cognitive deficits.

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1. Introduction

Several studies have reported population-level associations between peripheral artery disease (PAD) and cardiovascular disease (CVD), including heart disease and stroke [1]. Additionally, PAD has

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been associated with cognitive impairment, Alzheimer's disease, and dementia [2]. However, evidence from large population-based studies examining the links between ABI and cognitive function remains scant, and non-existent for Hispanics/Latinos who have a higher risk for clinically undetected and uncontrolled CVD risks [3,4]. Early detection of CV risk through ABI measurement, and initiation of control regimen can be critical for slowing the cascades known to trigger vascular and heart disease, stroke and concomitant cognitive impairment [1].

The ankle brachial index (ABI) is a non-invasive and well-tolerated measure to evaluate arterial stenosis and stiffness [5]. Low ABI levels (≤ 0.9) are indicative of significant obstructive disease (i.e. PAD) and prognostic for atherosclerosis [5]. However, this threshold may not be appropriate for diverse populations where ABI shows lower sensitivity to disease detection at this level [5,6]. Higher ABI values (≥ 1.40) are considered indicative of arterial stiffness, likely due to medial calcification [5,7]. Notably, the prognostic sensitivity of different thresholds for a high ABI also varies [8,9].

Most studies on the relationship between ABI and cognitive function have focused on older non-Hispanic White cohorts, used a restrictive set of cognitive measures, and controlled for relatively few confounding factors [2]. Cross sectional work from these data suggest that ABI is linearly and positively associated with better cognitive performance particularly in executive function [8,10], which is usually implicated in vascular disease induced cognitive dysfunction. Longitudinal data from mostly Caucasian cohort studies have also provided evidence that compromised ABI, in general, and PAD, in particular, is associated with cognitive impairment and dementia [2].

Early detection of cognitive disorders in middle age before further disease progression is a major public health priority, especially for Hispanics/Latinos who are at increased risk. Hispanics/Latinos are the largest ethnic group in the United States and are projected to account for a third of the population by 2050. Hispanics/Latinos are at higher risk for diseases secondary to CVD and have higher disease burden due to suboptimal levels of treatment and control for CV risk factors (e.g. hypertension) [3,11]; although differences between Hispanic/Latino backgrounds have been reported. Additionally, Hispanics/Latinos are reportedly at higher risk for age-related cognitive problems, again with reported differences in disease prevalence and incidence between subgroups [12]. Recent studies have shown consistent links between cardiovascular disease and risk factors and lower cognitive performance among diverse Latinos evident in middle age [13–16]. However, no previous work, to our knowledge, has comprehensively examined cognitive function and ABI in middle-aged and older diverse Latinos. Asymptomatic and untreated arterial disease presents long-term risks for adverse cerebrovascular events and vascular cognitive health particularly given known disparities and inequities in access to health and healthcare enabling resources among US Latinos. In the absence of pharmacological treatment for cognitive dysfunctions and dementias, identifying low-cost and well-tolerated means for detecting early vascular-related cognitive decline affords opportunities for mitigating cognitive decline.

Until recently, most epidemiologic work on Hispanic/Latino populations has been limited to specific subgroups (e.g. Mexicans). This has limited generalization to the larger diverse Hispanic/Latino population. The Hispanic Community Health Study/Study of Latinos is the largest study of diverse Hispanics/Latinos in the US designed to characterize chronic disease (e.g. CVD) and their putative antecedents [17]. In this study, we investigate associations between cognitive function and ABI among middle-aged and older Hispanics/Latinos of diverse backgrounds. We hypothesize that high and low ABI would both be associated with lower cognitive scores,

especially for executive function which is considered vulnerable to CVD [18–20].

2. Materials and methods

2.1. Study sample

HCHS/SOL is a multiethnic, multisite, prospective cohort study of 16,415 community-dwelling Hispanic/Latino adults (18–74-years old). The HCHS/SOL design was formulated to estimate representative baseline risk factors for overall Hispanics/Latinos as well as for specific backgrounds, including Central Americans, Cubans, Dominicans, Mexicans, Puerto Ricans, and South Americans. Data were collected from field centers in four U.S. cities with substantial Hispanic/Latino population concentrations (Bronx, NY; Chicago, IL; Miami, FL; and San Diego, CA). Each field center recruited about 4000 eligible, self-identified Hispanic/Latino adults. Detailed HCHS/SOL sampling methods are available elsewhere [17]. Written informed consent was obtained from all included participants, and the study was reviewed and approved by the Institutional Review Boards of all participating institutions. We focused on the oversampled, middle-aged and older adults (45–74-years) with baseline cognitive assessment data ($n = 9623$). We excluded participants reporting prevalent stroke or transient ischemic attack (TIA) diagnoses, and those reporting prevalent coronary heart disease (CHD; $n = 1184$). We also excluded ($n = 448$) participants with missing values for ABI ($n = 30$) or on the model covariates ($n = 418$) for an unweighted analytic $n = 7991$.

2.2. Cognitive tests

We used confirmatory factor analyses to estimate a factor score for a latent global cognition measure using four available cognitive tests, representing multiple cognitive domains, and the Six-Item Screener (SIS). We also examined, independently, the four domain specific tests: 1) Brief Spanish English Verbal Fluency Test (B-SEVLT) sum over 3 trials, 2) B-SEVLT recall, 3) Word Fluency (WF), and 4) Digit Symbol Substitution (DSS) test. The B-SEVLT is an episodic learning and memory test with two scores: 1) the summed total of correctly learned items across three learning trials (B-SEVLT-sum; range 0–45), and 2) total correctly recalled items (B-SEVLT recall; range 0–15) following an interference trial. WF is a verbal fluency test scored as the total number of correctly generated words (beginning with letters F and A) within 1 min. DSS is a mental processing speed and executive function exam (range 0–90). These cognitive tests and scoring procedures have been previously described [21]. We also examined a dichotomized SIS [22] coded to distinguish between respondents with and without probable low mental status scores ($SIS \leq 4$ vs. $SIS > 4$). Briefly, the SIS (range 0–6) is a mental status test that was scored dichotomously with a value of 4 or lower representing “low mental status.” The cutpoint reflects previous validation work in patients with dementia [22]. All cognitive tests were administered in the participants' preferred language during face-to-face interviews by trained, bilingual research assistants. To facilitate cross-test results comparisons, we generated and analyzed standardized (z -transformed; using population-specific means and standard deviations ((Score – Mean)/SD) indicators of all five continuous cognitive outcomes.

2.3. Primary exposure

ABI measurements were conducted using standard Doppler procedures using a Nicolet Doppler Elite 100R probe (Natus, Golden, CO). Briefly, first, the participant's upper arm

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