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Association of descending thoracic aortic plaque with brain atrophy and white matter hyperintensities: The Framingham Heart Study

Hugo J. Aparicio [a, b, *], Rodica E. Petrea [a, b, c], Joseph M. Massaro [b, d], Warren J. Manning [b, e], Noriko Oyama-Manabe [e], Alexa S. Beiser [a, b, d], Carlos S. Kase [a, b, f], Ralph B. D'Agostino [b, d], Philip A. Wolf [a, b], Ramachandran S. Vasan [b, h], Charles DeCarli [i], Christopher J. O'Donnell [b, g, j], Sudha Seshadri [a, b]

[a] Department of Neurology, Boston University School of Medicine, 72 East Concord Street, C-3, Boston, MA 02118, USA
[b] National Heart, Lung, and Blood Institute's Framingham Study, 73 Mt. Wayte Avenue, Suite 2, Framingham, MA 01702, USA
[c] Department of Neurology, Creighton University School of Medicine, 601 North 30th Street, Suite 5300, Omaha, NE 68131, USA
[d] Department of Biostatistics, Boston University School of Public Health, Crosstown Building, 801Massachusetts Avenue, 3rd Floor, Boston, MA 02118, USA
[e] Departments of Medicine and Radiology, Beth Israel Deaconess Medical Center, 330 Brookline Ave, Boston, MA 02215, USA
[f] Department of Neurology, Emory University School of Medicine, 201 Dowman Drive, Atlanta, GA 30322, USA
[g] Department of Medicine, Massachusetts General Hospital, 55 Fruit St, Boston, MA 02215, USA
[h] Sections of Preventive Medicine and Cardiology, Boston University School of Medicine, Crosstown Building, 801 Massachusetts Avenue, 4th Floor, Boston, MA, USA
[i] Department of Neurology, School of Medicine, and Imaging of Dementia and Aging Laboratory, Center for Neuroscience, University of California-Davis, 1544 Newton Court, Davis, CA 95616, USA
[j] Cardiology Section, Boston Veterans Administration Healthcare, 150 S Huntington Ave, Boston, MA 02130, USA

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ABSTRACT

Background and aims: Aortic atherosclerosis is an aggregate marker of vascular risk factor exposure and has been associated with intracranial atherosclerosis and stroke. We hypothesized that atherosclerosis of the descending aorta (DAo) could be a risk marker for brain aging and injury.
Methods: We evaluated 1527 participants (mean age 59.9 years, 53.5% women) in the Framingham Offspring cohort who underwent both aortic and brain MRI. Participants were free of clinical stroke, dementia, or other neurological illness at the time of axial MRI of the thoracic and abdominal DAo and subsequent brain MRI. We related the prevalence and burden of aortic plaque to total cerebral brain volume (TCBV) and white matter hyperintensity volume (WMHV). An additional analysis compared incidence of stroke or TIA in participants with and without DAo plaques.
Results: Presence of thoracic DAo plaque (8%) was associated with decreased TCBV in sex-pooled analysis (−0.77, SE 0.25, $p = 0.002$, equivalent to 4.5 years of aging) and with increased WMHV only in men (0.26, SE 0.12, $p = 0.032$, equivalent to 6.5 years aging). We observed similar associations of DAo plaque burden with TCBV and WMHV. There were 43 strokes and 11 TIAs in prospective follow-up (median 7 years). Presence of DAo plaque was not associated with subsequent stroke or TIA.
Conclusions: In this cross-sectional community-based study, we found DAo plaque is associated with accelerated brain aging. These data underscore the potential implications of incidentally identified subclinical aortic atherosclerosis and question whether targeted intervention in these high risk individuals can modulate cognitive decline.

1. Introduction

Previous studies have linked the presence and burden of aortic atherosclerosis with cognitive impairment, magnetic resonance imaging (MRI) indices of brain aging and injury, and stroke [1–4]. Vascular injury to the brain can occur because of embolism from

* Corresponding author.Department of Neurology, Boston University School of Medicine, 72 East Concord Street, C-3, Boston, MA 02118, USA.
E-mail address: hugoa@bu.edu (H.J. Aparicio).

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atheroma in the aortic arch or may be related to a chronic disruption of central hemodynamics. The role of the latter mechanism is emphasized by investigations of aortic wall stiffness and the damaging effects of excessive pressure and flow in the cerebral microcirculation [5].

Aortic plaque may be a marker of overall atherosclerotic plaque burden [6], concomitant intracranial atherosclerotic disease [7], or systemic phenomena that can affect brain structure through neuronal loss. In the setting of large vessel atherosclerosis, cerebral damage may be mediated by elevated homocysteine levels or increased von Willebrand factor and hypercoagulability [8,9]. The severity of thoracic aortic intimal changes has been associated with both antioxidants and inflammatory markers in the serum, such as uric acid and high sensitive C-reactive protein [10], implicating chronic systemic oxidative and inflammatory processes, potentially damaging to the brain.

Few investigations have associated descending aortic plaque of the thorax or abdomen to brain changes or injury [11,12]. Blood flow in the descending aorta is separate from cervical and cerebral circulation, thus plaques in the descending aorta may serve as more specific markers of generalized atherosclerosis or microvascular damage, relative to ascending aortic plaques. Additionally, aortic atherosclerosis may not be fully correlated with results of other non-invasive measures of subclinical atherosclerosis, such as coronary artery calcification and carotid intima-media thickness by ultrasound [13].

We sought to evaluate the cross-sectional association between descending aorta (DAo) plaque prevalence and burden and total cerebral brain volume (TCBV) and white matter hyperintensity volume (WMHV). In additional analysis, we studied the prospective relation of DAo plaque prevalence to incidence of stroke in a community-based sample.

2. Patients and methods

2.1. Study population

The Framingham Offspring cohort was recruited in 1971 and comprises 5124 participants who have been evaluated nine times. Non-simultaneous brain MRI and cardiovascular magnetic resonance (CMR) imaging were performed during and after the seventh ('baseline') examination cycle (1998–2001) between 1999 and 2005. Persons with clinical stroke, dementia or other neurological conditions that could affect brain MRI measures were excluded. Participants with a history of atrial fibrillation were excluded as well as those with a prosthetic valve. Of the 2219 participants with available brain MRI data, 1576 had attended the baseline examination and had undergone CMR; 49 were excluded because of missing data on education and other risk factors, yielding a study sample of 1527 for the present investigation. The median length of time between brain MRI and cardiac MRI was 3.7 years (Q1 3.0, Q3 4.6). The Institutional Review Boards of Boston University Medical Center and Beth Israel Deaconess Medical Center approved the study protocol and written informed consent was obtained from all study participants.

2.2. Baseline examinations

Educational achievement was dichotomized at high school graduation. Body mass index (BMI) was the ratio of measured weight in kilograms to the square of height in meters (kg/m^2). Serum total cholesterol, high-density lipoprotein cholesterol levels, and triglycerides were measured at the baseline exam. We determined whether lipid lowering therapy was used. Plasma total homocysteine levels were measured at the prior exam (1995–1998) using high-performance liquid chromatography with fluorescence detection.

Information on vascular risk factors was collected at the baseline exam, including the components of the Framingham Stroke Risk Profile (FSRP), which has been described and validated for predicting stroke risk [14]. The FSRP risk factors include systolic blood pressure, use of antihypertensive therapy, diabetes mellitus (defined as a fasting blood glucose of ≥126 mg/dL, a previous diagnosis of diabetes, or using hypoglycemic medication or insulin), current smoking status, atrial fibrillation, and previous cardiovascular disease including diagnoses of coronary heart disease, heart failure, or peripheral vascular disease.

Carotid intima-media thickness (IMT) was measured using carotid ultrasound studies, acquired following a standard protocol [15]. during the sixth examination cycle (1995–1998). Methods for ultrasound imaging of the carotid arteries, and measurement of IMT, are described in a previous report [16]. Coronary artery calcium score (CAC) was calculated in participants who underwent a non-contrast cardiac multidetector computed tomography (MDCT) scan during the seventh examination cycle (1998–2001). MDCT protocols and methods for calculation of Agatston Score for prevalence of coronary artery calcium are previously described [17,18].

2.3. Cardiovascular Magnetic Resonance (CMR)

CMR acquisition, measurement techniques, and inter-rater reliability of aortic plaque measurement have been described previously [19]. Briefly, a commercial 1.5T whole-body CMR system (Gyroscan ACS-NT or Achieva, Philips Medical Systems) was used to perform thoraco-abdominal aortic CMR. Approximately thirty-six transverse slices were obtained; this included twelve 10-mm thick slices, with a 10-mm gap, spanning the aortic arch and thoracic DAo and twenty-four 5-mm thick slices spanning the abdominal DAo to the origin of the common iliac arteries. Atherosclerotic plaque was defined as a characteristic luminal protrusion of ≥1 mm in radial thickness that could be distinguished from the minimal residual blood signal (Fig. 1) by a single blinded observer (NO-M). DAo plaques were divided according to their location into thoracic or abdominal plaques, above and under the diaphragm. For plaque prevalence, participants were dichotomized by presence or absence of plaque. Plaque burden was defined as the percent of axial slices demonstrating plaque.

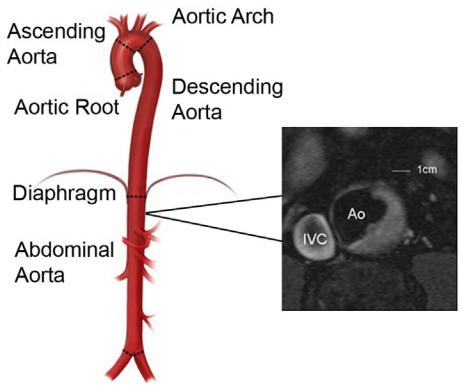

Fig. 1. Transverse cardiovascular magnetic resonance image of the abdominal aorta and an aortic plaque, from a Framingham Offspring Cohort participant.
IVC, inferior vena cava; Ao, aorta. Illustration adapted from www.mountsinai.org with permission from Dr. Allan Stewart. Copyright 2016, Icahn School of Medicine at Mount Sinai.

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