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*Original Article*

The Neuroradiology Journal
2024, Vol. 37(3) 304–313
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DOI: 10.1177/19714009231224429
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# Association of brain arterial diameters with demographic and anatomical factors in a multi-national pooled analysis of cohort studies

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## Abstract

**Background and Purpose:** Brain arterial diameters are markers of cerebrovascular disease. Demographic and anatomical factors may influence arterial diameters. We hypothesize that age, sex, height, total cranial volume (TCV), and persistent fetal posterior cerebral artery (fPCA) correlate with brain arterial diameters across populations.

**Methods:** Participants had a time-of-flight MRA from nine international cohorts. Arterial diameters of the cavernous internal carotid arteries (ICA), middle cerebral arteries (MCA), and basilar artery (BA) were measured using LAVA software. Regression models assessed the association between exposures and brain arterial diameters.

**Results:** We included 6,518 participants (mean age: 70 ± 9 years; 41% men). Unilateral fPCA was present in 13.2% and bilateral in 3.2%. Larger ICA, MCA, and BA diameters correlated with older age (Weighted average [WA] per 10 years: 0.18 mm, 0.11 mm, and 0.12 mm), male sex (WA: 0.24 mm, 0.13 mm, and 0.21 mm), and TCV (WA: for one TCV standard deviation: 0.24 mm, 0.29 mm, and 0.18 mm). Unilateral and bilateral fPCAs showed a positive correlation with ICA diameters (WA: 0.39 mm and 0.73 mm) and negative correlation with BA diameters (WA: −0.88 mm and −1.73 mm). Regression models including age, sex, TCV, and fPCA explained on average 15%, 13%, and 25% of the ICA, MCA, and BA diameter interindividual variation, respectively. Using height instead of TCV as a surrogate of head size decreased the R-squared by 3% on average.

**Conclusion:** Brain arterial diameters correlated with age, sex, TCV, and fPCA. These factors should be considered when defining abnormal diameter cutoffs across populations.

## Keywords

Arterial diameters, carotid artery, middle cerebral artery, basilar artery, fetal posterior cerebral artery, cohort studies

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## Introduction

Abnormal brain arterial diameters are associated with a higher risk of vascular events and death.[1] For example, reduced brain arterial diameters due to intracranial atherosclerosis are a well-characterized form of large-artery disease in which stroke risk is linked to the degree of luminal stenosis caused by the atherosclerotic plaque.[2] Moreover, larger brain arterial diameters—the extreme phenotype of which is known as dolichoectasia—are an increasingly recognized marker of vascular-related morbidity and mortality.[1,3–5] In contrast to intracranial atherosclerosis, where standardized methods exist to establish arterial stenosis and its severity,[6] there is no unified criteria to determine pathological brain arterial dilation. Previous proposed definitions for abnormal brain dilation (or dolichoectasia) were based on diameters distribution from relatively small study populations,[7–9] focused on individuals with stroke,[10,11] or assessed arterial diameters only in the posterior circulation.[7,12] Importantly, these definitions have not considered demographic and anatomical characteristics that may influence arterial dimensions within the normal spectrum.

The heterogeneity of brain arterial diameters is evidence of an interplay between innate individual factors and adaptive physiological processes, as well as aberrant vascular remodeling in response to pathological conditions leading to extremes of very small or very large diameters. Larger brain arterial diameters are associated with aging,[3,4,13] suggesting an age-related arterial remodeling process that may be further affected by the duration of exposure to vascular risk factors. Sex is another plausible determinant of brain arterial diameters as evidenced by a higher frequency of dolichoectasia in men compared to women when fixed diameter cutoffs are used for diagnosis.[10,11,14,15] The latter may be related to different body size dimensions between men and women, particularly head size. One study demonstrated that women had relative larger brain arterial diameters when the analysis was adjusted for total cranial volume (TCV).[16] Finally, Circle of Willis (CoW) configuration, especially the degree of communication between the anterior and posterior circulation (i.e., presence of persistent fetal posterior cerebral artery [fPCA]), is associated with variations in brain arterial diameters, a consequence of flow diversion leading to adaptive vascular remodeling.[3,17,18]

The lack of large-scale population- or community-based studies that examined these factors raises the question of whether these associations are generalizable and relevant to define abnormal brain arterial dilation. The objective of our analysis is to test the hypothesis that demographics (age and sex) and anatomical (head size and presence of fPCA) factors correlate with brain arterial diameters across a multi-national pool of cohort studies, and to evaluate to what extent these factors underlie interindividual variations. The overall study goal is to provide normative data that would inform future research on the factors to be considered when defining abnormal brain arterial phenotypes.

## Methods

This cross-sectional study used data from nine cohort studies across the United States, Singapore, Venezuela, Ecuador, and South Africa (Figure 1). Cohort studies included were the Atherosclerosis Risk in Communities (ARIC) study,[19] Northern Manhattan Study (NOMAS),[9,13] Washington Heights/Inwood Columbia Aging Project (WHICAP),[20] Framingham Heart Study,[21] Epidemiology of Dementia in Singapore (EDIS),[22] the Harmonization study,[23] Maracaibo Aging Study,[24] the Atahualpa Project,[11] and the Health and Aging in Africa: Longitudinal Study of an INDEPTH Community in South Africa dementia sub-study (HAALSI-Dementia).[25] Population characteristics of each cohort study are summarized in Table 1. The analytical sample comprised participants who had available time-of-flight MRA. Data were analyzed between May 2022 and March 2023. All participating cohorts have local ethics approval with appropriate data sharing agreements, which enable current study analysis. We followed the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) reporting guidelines for cohort studies.

A prespecified and harmonized imaging analysis protocol was applied to obtain cross-sectional arterial diameters in 13 intracranial arterial segments at the base of the skull using commercially available software (LAVA, Leiden University Medical Center, The Netherlands, build date October 19th, 2018) previously validated by our group and others (Figure 2).[5,13,26] For each individual, we calculated the average diameter in millimeters (mm) for the ascending portion of the cavernous internal carotid arteries (ICA), the intracranial portion of the vertebral arteries (V4 segment), and the basilar artery (BA). For the middle cerebral arteries (MCA), the anterior cerebral arteries (ACA), and the posterior cerebral arteries (PCA), we only used the most proximal average diameter (first 1 mm) given the highly variable length of these arterial segments. The correlation between the most proximal average diameter (first 1 mm) and the whole segment average of the studied arterial segments is shown in the supplemental material (Table 1S). We measured the posterior communicating arteries from their origin in the ICA until the meeting point with the PCA-P1 segment. For this analysis, we focused on the averaged diameters of the ICA, MCA, and BA due to their relatively constant presence despite CoW anatomical heterogeneity across populations.

To assess the overall arterial diameter status of each individual, we calculated the global Brain Arterial Remodeling (BAR) score by transforming each measured arterial segment into a normal distribution using the Blom method.[27] This transformation allows for an equal weighting of otherwise inherently larger arterial segments (i.e., the ICA is expected to be larger than the MCA or PCA). If an arterial segment was visible but too small to be reconstructed in the 3D projections, we assigned it (arbitrarily) the value of the smallest measured diameters for that segment minus 10%. If an arterial segment was absent, we coded it as zero but this segment was not considered in the denominator for calculating the BAR score.

We used the TCV as provided by each cohort. Because of the variability of methods to calculate TCV in each cohort, we transformed TCV into a standardized normal distribution in each cohort using the Blom method. Presence of fPCA was determined when the diameter of the posterior communicating artery was greater than the ipsilateral PCA-P1 diameter. Fetal posterior cerebral artery presence was categorized as absent, unilateral, or bilateral. Finally,

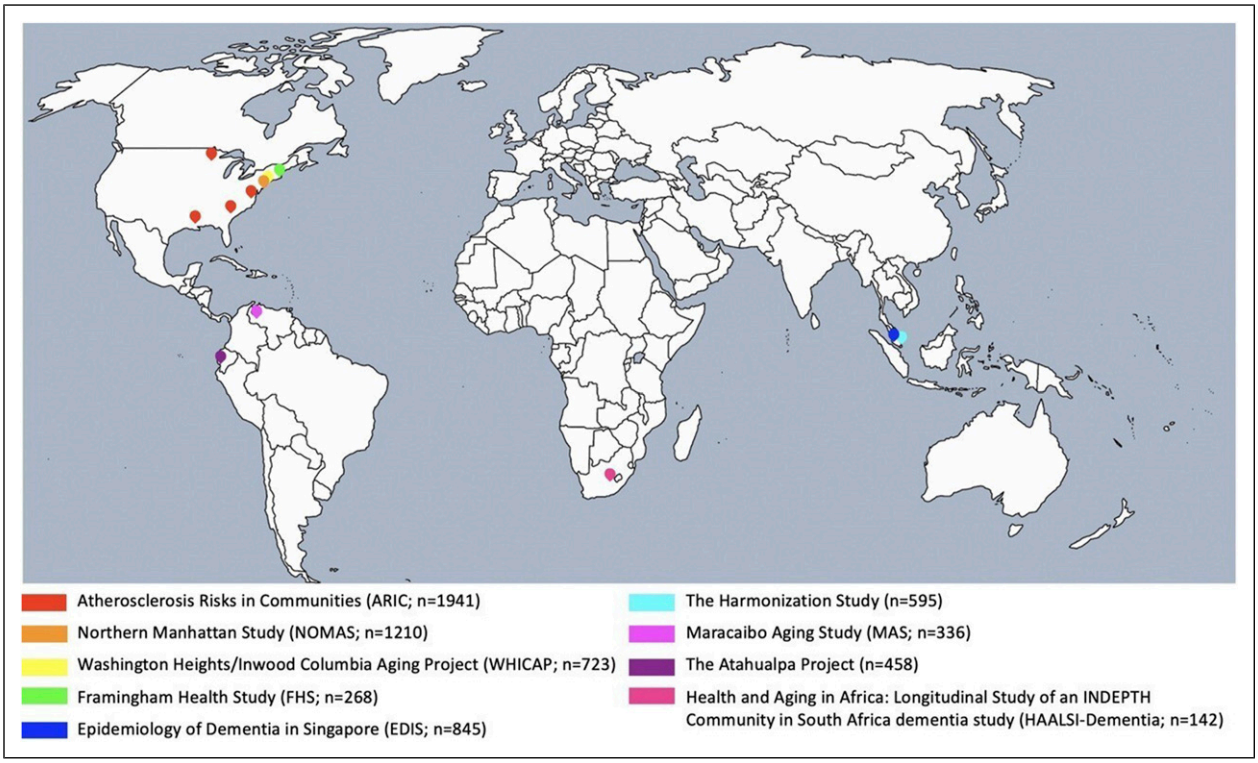



**Figure 1.** Geographic location of cohort studies included in this analysis.

participants' ages were ascertained at the time of MRA and baseline study enrollment information provided participants' sex and height in centimeters.

Summary descriptive statistics were used to present means ± standard deviations (SD) for continuous variables and percentages for categorical variables. To examine the correlation between exposure variables and brain arterial diameters across cohorts, we employed cohort-specific linear regression models. We included age, sex, TCV, and fetal posterior cerebral artery (fPCA) as independent variables, while ICA, MCA, and BA diameters served as the dependent variables in their respective models. For the overall BAR score, linear regression models were adjusted for age, sex, and TCV. We also fitted similar regression models using height instead of TCV to investigate whether height was a suitable surrogate for head size. We conducted a meta-analysis on the outcomes of each model to derive weighted averages for each correlation. Linear regression models were also used to calculate the R-squared ($R^2$) to examine the extent of interindividual variability in brain arterial diameters explained by the factors included in each model. Analyses were conducted using SAS version 9.4 (SAS Institute; Cary, NC). A two-sided $p$ value <.05 was considered statistically significant.

## Results

The analytical sample included 6,518 participants (mean age 70 ± 9 years; 41% men). Overall, the mean height was 159 ± 10 cm, unilateral fPCA was found in 13.2%, of participants and bilateral fPCAs in 3.2%. The mean diameters ranged from 4.00–4.43 mm for the ICA, 2.22–2.80 mm for the MCA, and 2.52–3.00 mm for the BA. Distribution of the collected covariates stratified by cohort study are shown in Table 2.

Regression models showed that older age, male sex, and larger TCV were positively correlated with brain arterial diameters across cohort studies (Table 3). The average diameter difference per 10 years of age was 0.18 mm for the ICA, 0.11 mm for the MCA, and 0.12 mm for the BA. The average diameter difference for male sex was 0.28 mm for the ICA, 0.13 mm for the MCA, and 0.21 mm for the BA. The average diameter difference per each TCV standard deviation was 0.24 mm for the ICA, 0.29 mm for the MCA, and 0.18 mm for the BA. The presence of fPCA was associated with larger ICA diameters, smaller BA diameters, and had no significant correlation with MCA diameters. On average, the ICA diameters were 0.39 mm larger with unilateral fPCA and 0.73 mm larger with bilateral fPCA, whereas the BA diameter was 0.88 mm smaller with unilateral fPCA and 1.73 mm smaller with bilateral fPCA (Table 3). Regression models fitted for age, sex, TCV, and presence of fPCA explained on average 15.4% of ICA diameter variability, 12.9% of MCA diameter variability, and 25.4% of BA diameter variability.

When regression models included height instead of TCV as a surrogate of head size, height mostly showed a positive correlation with brain arterial diameters. However, the significance between height and brain arterial diameters was inconsistent (Table 4). The weighted average variability explained by regression models using height instead of TCV was 12.1% for ICA diameter, 8.1% for MCA diameter, and 23.7% for BA diameter.

The overall BAR score also showed a positive correlation with age, male sex and TCV. Regression models fitted for age, sex, and TCV explained 19.5% of BAR score variability on average (Table 3), whereas when height was used instead

**Table 1.** Population characteristics of the cohort studies included in the analysis.

| Cohort study | Population characteristics | Location | MRA acquisition period | Analytical sample | MR brand | MR strength | MR eco time | MR frequency encoding |
|---|---|---|---|---|---|---|---|---|
| Atherosclerosis Risk in Communities (ARIC) | Randomly selected individuals aged 45–65 years from one of four US communities | Four US communities: Washington County, Maryland; Forsyth County, North Carolina; Minneapolis, Minnesota; and Jackson, Mississippi. | 2011–2013 | 1941 | Siemens | 3 | 3.7 | 320 |
| Northern Manhattan Study (NOMAS) | Population-based sample of Northern Manhattan residents ages >50 years who lived in a house with a telephone and had no history of clinical stroke | Northern Manhattan, New York, US | 2003–2008 | 1210 | Philips | 1.5 | 2.7 | 63.9 |
| Washington Heights Inwood Community Aging Project (WHICAP) | Medicare beneficiaries aged >65 years without diagnosis of dementia | Northern Manhattan, New York, US | 2005–2007 | 723 | Phillips GE 3 | 3 | 3.4 | 512 |
| Framingham Heart study (FHS) | Stroke- and dementia-free individuals who attended the Framingham Heart study offspring cohort on the 7th examination cycle | Framingham, Massachusetts, US | 1999–2005 | 268 | GE, Philips, Siemens, Toshiba | 1.5, 3 | 1.7-7 | 123-512 |
| Epidemiology of Dementia in Singapore (EDIS) | Population-based community-dwelling adults aged ≥60 years of Chinese, Malays and Indians background who screened positive for cognitive impairment | Singapore, Singapore | 2010–2012 | 845 | Siemens | 1.5 | 3.4 | 123.3 |
| The Harmonization Study | Consecutive first-visit patients ≥50 years old attending an academic memory clinic | Singapore, Singapore | 2009–2015 | 595 | Siemens | 3 | 3.4 | 123.3 |
| Maracaibo Aging Study (MAS) | Population-based community-dwelling adults ≥55 years old identified by means of door-to-door survey | Maracaibo, Venezuela | 1998 and 2010 | 336 | GE | 1.5 | 4.2 | 63.9 |
| The Atahualpa Project | Population-based community-dwelling, non-disabled adults aged ≥60 years, of Amerindian ancestry, identified by means of yearly door-to-door surveys | Atahualpa, Ecuador | 2012–2017 | 458 | BIOLAB | 1.5 | 6.9 | 192 |
| Health and aging in Africa: Longitudinal Study of an INDEPTH Community in South Africa dementia sub-study (HAALSI-Dementia) | Population-based random sample of adults aged ≥50 years from a rural community | Agincourt, South Africa | 2014–2015 | 142 | GE | 1.5 | 2.9 | 320 |

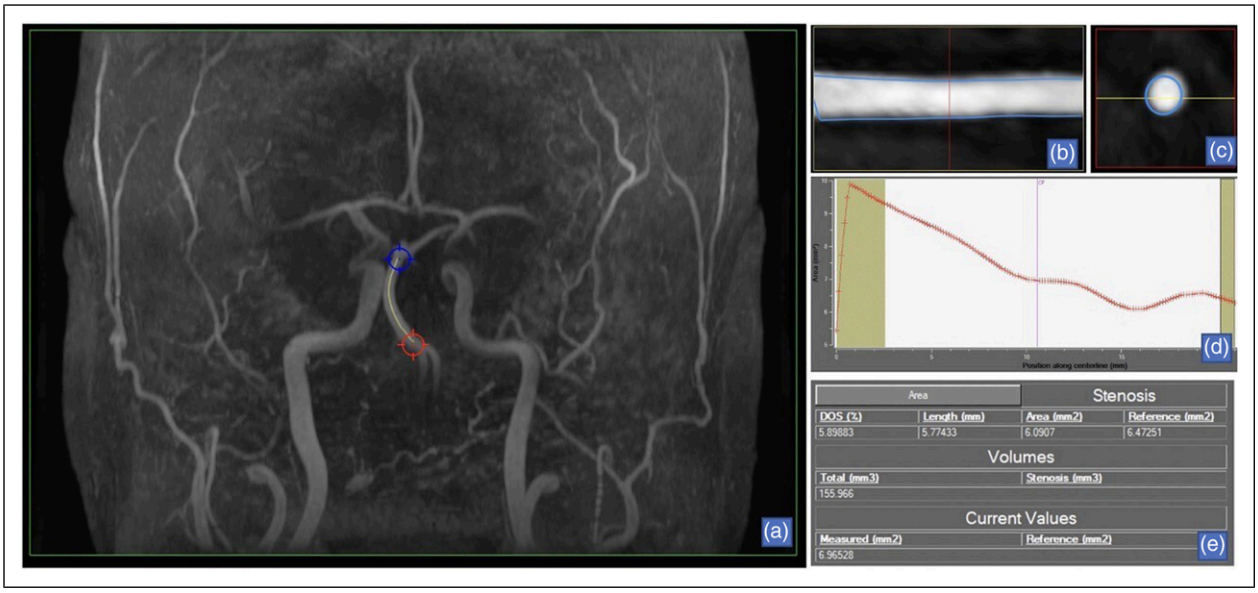



**Figure 2.** LKEB LAVA measures the arterial diameters several times across a segment by using a technique called multiplanar reformatted (MPR) imaging. MPR allows the user to create cross-sectional views of the blood vessels at any orientation and at any point along the vessel's centerline. The user selects a segment of the blood vessel to analyze (a). The MRA image data for the selected segment is reformatted into a 3D volume, with the centerline of the vessel as the axis of rotation (b). The user can then create cross-sectional views of the vessel at any point along the centerline using the MPR tool (c). The arterial diameter is measured on each cross-sectional view, providing multiple measurements of the diameter across the selected segment (d). The measured diameters are then used to calculate average, maximum, and minimum diameters, as well as diameter variations along the segment (e).

of TCV as a surrogate of head size, variability explained by the regression models decreased to 13.1% (Table 4).

## Discussion

Larger brain arterial diameters are a risk marker for stroke,[3,5] vascular events,[1,3,5] cognitive impairment,[28] and mortality,[1,4,5] whereas the extreme phenotype of brain arterial dilation (dolichoectasia) is recognized as a direct etiology for cerebrovascular disorders such as ischemic stroke, intracerebral hemorrhage, and brain tissue compression syndromes.[29] Understanding the association of demographic and anatomical characteristics with brain arterial diameters is critical to discriminate expected brain arterial diameters variability within the normal spectrum from the abnormal widening of brain arteries in response to pathological processes. Furthermore, recognizing the variability in brain arterial diameters is key in the selection of devices and procedural strategies for neuro-endovascular interventions,[30,31] as well as potentially influential for clinical outcomes and procedures success.[32,33] In this context, our analysis across a large pool of community-dwelling individuals participating in cohort studies from different geographic locations provide robust evidence on the influence of age, sex, head size, and presence of fPCA on brain arterial diameters. Overall, models adjusted for these covariates explained nearly 20% of interindividual variation in the diameters of major intracranial arteries, thus supporting that these factors should be considered when establishing diameters cutoffs to define abnormal brain arterial phenotypes such as dolichoectasia.

We found that every decade of aging, the ICA diameters were approximately 0.2 mm larger, while the MCA and BA diameters were 0.1 mm larger. Blood flow is a potent determinant of arterial diameters in physiological and pathological conditions.[34] Living longer increases the duration of exposure to blood flow and therefore age-related brain arterial dilation might result from chronic blood flow wear and tear on the arterial wall. In addition to flow, other age-related processes such as collagen accumulation and elastin fibers loss in the arterial wall can cause arterial stiffness, which in turn may lead to increased arterial diameters.[35] Also, age-related buildup of fatty plaques within arteries (i.e., atherosclerosis) can cause arterial narrowing and stenosis, which can result in compensatory larger diameters in unaffected arterial segments that provide collateral flow.[36] Our study also confirms that men have larger brain arterial diameters compared to women irrespective of body size. On average, ICA and BA diameters in men were 0.2 mm larger, whereas MCA diameters were 0.1 mm larger. Differences in sex hormones could play also a role in determining arterial diameters. For example, testosterone, the predominant male sex hormone, has been implicated in promoting vascular remodeling and increasing arterial diameter.[37] Conversely, estrogen, the primary female sex hormone, may have a protective effect preserving arterial elasticity and potentially limiting arterial dilation.[38]

The main determinant of arterial diameters is the size of territory to be supplied, a consequence of a primordial coupling between demand and supply in living organisms. In our study, larger head size—as determined by TCV—correlated with larger brain arterial diameters. An individual's height also demonstrated a positive correlation with brain arterial diameters, although the correlation was weaker when compared to TCV. In the case of the aorta, body surface area and not height or weight, account better for diameter variability.[39] Therefore, TCV is an ideal parameter for adjusting brain arterial diameter values, particularly in the

**Table 2.** Covariates collected from each cohort study along with ICA, MCA, and BA diameters distribution in the cohort studies included in the analysis.

| | ARIC | NOMAS | WHICAP | FHS | EDIS | Harmonization | MAS | Atahualpa | HAALSI-Dementia |
|---|---|---|---|---|---|---|---|---|---|
| Age in years, mean (SD) | 76.9 (5.3) | 70.6 (8.9) | 76.4 (6.3) | 72.6 (11.6) | 70.2 (6.62) | 73.5 (7.9) | 58.9 (12.6) | 64.9 (11.2) | 68.31 (10.7) |
| Men, *n* (%) | 722 (39.8) | 510 (39.5) | 260 (36.0) | 105 (43.9) | 462 (47.8) | 268 (44.8) | 83 (24.1) | 202 (43.2) | 55 (38.7) |
| TCV ($cm^3$) | | | | | | | | | |
| Mean (SD) | 1381.9 (156.6) | 1156.5 (121.8) | 1469.8 (182.5) | 1261 (159.2) | 1237.2 (5168.9) | 1355.8 (164.6) | 1093.5 (114) | 1644.4 (286.3) | 1605.9 (301.5) |
| Median (IQR) | 1367.8 (222.6) | 1147.2 (170.2) | 1447.9 (237.2) | 1236.5 (177.6) | 1055.9 (152.5) | 1340.3 (229.6) | 1083.4 (143.1) | 1628 (383.2) | 1595.9 (431.1) |
| Height (cm) | | | | | | | | | |
| Mean (SD) | 165 (9.6) | 163.7 (9.7) | 161.9 (10) | 165.7 (10.1) | 157.5 (9.5) | 157.3 (8.5) | 157.6 (8.4) | 148.7 (8.9) | 157 (28.3) |
| Median (IQR) | 164 (14) | 162.6 (12.7) | 161.5 (15) | 165.1 (14) | 157 (14.5) | 156.6 (11) | 157 (12.5) | 147 (14) | 161 (14) |
| Brain arterial diameters | | | | | | | | | |
| Average of both internal carotid arteries | | | | | | | | | |
| Mean | 4.43 | 4.27 | 4.32 | 4.35 | 4.43 | 4.31 | 4.21 | 4.00 | 4.26 |
| SD | 0.51 | 0.56 | 0.50 | 0.59 | 0.56 | 0.61 | 0.55 | 0.55 | 0.53 |
| Minimum | 1.90 | 1.62 | 2.61 | 1.63 | 1.43 | 1.51 | 2.29 | 1.49 | 1.89 |
| Maximum | 6.79 | 6.45 | 6.29 | 5.89 | 6.02 | 5.91 | 5.72 | 5.64 | 5.73 |
| <2 SD | 3.41 | 3.16 | 3.32 | 3.17 | 3.31 | 3.09 | 3.12 | 2.89 | 3.20 |
| >2 SD | 5.45 | 5.39 | 5.32 | 5.53 | 5.55 | 5.53 | 5.30 | 5.10 | 5.31 |
| Average of both middle cerebral arteries | | | | | | | | | |
| Mean | 2.57 | 2.72 | 2.65 | 2.71 | 2.52 | 2.52 | 2.22 | 2.39 | 2.80 |
| SD | 0.33 | 0.26 | 0.35 | 0.33 | 0.33 | 0.36 | 0.31 | 0.25 | 0.57 |
| Minimum | 1.38 | 1.81 | 1.90 | 1.79 | 1.39 | 1.43 | 1.61 | 1.77 | 1.84 |
| Maximum | 3.99 | 3.84 | 4.14 | 3.79 | 3.78 | 4.04 | 3.46 | 3.08 | 4.65 |
| <2 SD | 1.91 | 2.20 | 1.95 | 2.05 | 1.86 | 1.80 | 1.60 | 1.89 | 1.66 |
| >2 SD | 3.23 | 3.24 | 3.35 | 3.37 | 3.18 | 3.24 | 2.84 | 2.89 | 3.94 |
| Basilar artery | | | | | | | | | |
| Mean | 3.00 | 2.77 | 2.78 | 2.91 | 2.86 | 2.89 | 2.66 | 2.54 | 2.52 |
| SD | 0.54 | 0.51 | 0.54 | 0.59 | 0.51 | 0.59 | 0.42 | 0.37 | 0.51 |
| Minimum | 1.05 | 1.36 | 1.06 | 1.40 | 1.40 | 1.45 | 1.64 | 1.50 | 1.36 |
| Maximum | 5.29 | 5.54 | 5.68 | 5.89 | 4.78 | 5.23 | 4.23 | 3.88 | 3.52 |
| <2 SD | 1.92 | 1.75 | 1.71 | 1.73 | 1.83 | 1.70 | 1.83 | 1.79 | 1.50 |
| >2 SD | 4.08 | 3.79 | 3.86 | 4.09 | 3.88 | 4.08 | 3.50 | 3.29 | 3.53 |

Abbreviations: ARIC Atherosclerosis Risk in Communities, EDIS Epidemiology of Dementia in Singapore, FHS Framingham Heart Study, HAALSI Health and Aging in Africa: Longitudinal Study of an INDEPTH Community in South Africa dementia sub-study, IQR interquartile range, MAS Maracaibo Aging Study, NOMAS Northern Manhattan Study, SD standard deviation, WHICAP Washington Heights Inwood Community Aging Project.

research setting. However, as TCV measurement requires specialized software, height could be considered a suitable alternative in routine clinical practice. Finally, our study confirmed the significant influence of the CoW configuration on brain arterial diameters as a result of redistribution of collateral blood flow. We specifically focused on the presence of persistent fPCA as being the most common CoW anatomical variant shifting blood flow from the anterior to the posterior cerebral circulation.[17,18] The presence of unilateral and bilateral persistent fPCA resulted in an average increase of 0.4 mm and 0.7 mm of ICA diameters, respectively, while BA diameters showed an average decrease of 0.9 mm and 1.7 mm, respectively. It is important to note that, although the association between CoW configuration and arterial diameters is believed to be a benign compensatory phenomenon, it is still unknown whether brain arterial diameter variations in response to CoW variants have clinical implications, including increased risk of stroke.[40]

The present study has several strengths. First, we conducted a harmonized analysis of MRAs using automated software, ensuring consistency and minimizing potential measurement biases. Furthermore, our study included a large and diverse population, encompassing individuals with various ethnic and environmental backgrounds. This broad sample allowed us to gather baseline data through well-designed population-based cohort studies. However, it is important to acknowledge certain study limitations. Different MRI technologies across cohort studies may have introduced biases in diameter measurements. The analyzed population primarily consisted of older adults, with the lower age cutoff ranging from 40 to 65 years across the included cohort studies. Consequently, the generalizability of our findings to younger populations, where vascular remodeling processes might be at earlier stages, is limited. Additionally, our analysis focused on the presence of persistent fPCA due to its high prevalence and its direct influence on the studied arterial

**Table 3.** Linear regression models adjusted for age, sex, total cranial volume and presence of fetal posterior cerebral artery stratified by cohort study.

| | Age | Sex | TCV | fPCA | | |
|---|---|---|---|---|---|---|
| | (10 years) | (Male) | (Z-score) | Unilateral | Bilateral | R-squared |
| ICA | | | | | | |
| ARIC | 0.20 (0.04) * | 0.20 (0.06) * | 0.27 (0.03) * | 0.44 (0.07) * | 0.68 (0.17) * | 0.159 |
| NOMAS | 0.22 (0.03) * | 0.25 (0.07) * | 0.32 (0.03) * | 0.38 (0.08) * | 0.46 (0.12) * | 0.207 |
| WHICAP | 0.31 (0.06) * | 0.33 (0.10) * | 0.23 (0.05) * | 0.29 (0.24) | 0.98 (0.64) | 0.158 |
| FHS | 0.23 (0.06) * | 0.32 (0.16) * | 0.13 (0.09) | 0.31 (0.18) | 1.67 (0.69) * | 0.127 |
| EDIS | 0.08 (0.05) | −0.01 (0.08) * | 0.23 (0.04) * | 0.36 (0.08) * | 0.47 (0.14) * | 0.079 |
| Harmonization | 0.04 (0.05) | 0.21 (0.10) * | 0.24 (0.05) * | 0.30 (0.10) * | 0.85 (0.23) * | 0.125 |
| MAS | 0.21 (0.04) * | 0.42 (0.14) * | 0.08 (0.06) | 0.70 (0.16) * | 1.16 (0.41) * | 0.187 |
| Atahualpa | 0.17 (0.04) * | 0.47 (0.10) * | 0.14 (0.05) * | 0.26 (0.13) * | 0.82 (0.38) * | 0.147 |
| HAALSI-Dementia | 0.09 (0.06) | 0.40 (0.15) * | 0.10 (0.07) | 0.35 (0.26) | 0.41 (0.22) | 0.218 |
| Weighted average | 0.18 (0.04) | 0.24 (0.08) | 0.24 (0.04) | 0.39 (0.11) | 0.73 (0.26) | 0.154 |
| MCA | | | | | | |
| ARIC | 0.09 (0.04) * | 0.10 (0.06) | 0.37 (0.03) * | −0.02 (0.07) | −0.18 (0.17) | 0.168 |
| NOMAS | 0.15 (0.03) * | 0.12 (0.07) | 0.32 (0.03) * | −0.02 (0.09) | 0.04 (0.13) | 0.134 |
| WHICAP | 0.06 (0.06) | 0.18 (0.10) | 0.29 (0.05) * | 0.31 (0.24) | 0.08 (0.64) | 0.130 |
| FHS | 0.14 (0.06) * | 0.11 (0.17) | 0.16 (0.09) | −0.09 (0.19) | 0.63 (0.72) | 0.054 |
| EDIS | 0.13 (0.05) * | 0.03 (0.08) | 0.30 (0.04) * | 0.03 (0.08) | −0.00 (0.14) | 0.100 |
| Harmonization | 0.01 (0.05) | 0.18 (0.10) | 0.19 (0.05) * | −0.16 (0.11) | −0.13 (0.24) | 0.069 |
| MAS | 0.17 (0.04) * | 0.35 (0.13) * | 0.14 (0.06) * | 0.06 (0.15) | 0.54 (0.40) | 0.137 |
| Atahualpa | 0.19 (0.04) * | 0.24 (0.10) * | 0.20 (0.05) * | −0.08 (0.13) | 0.63 (0.39) | 0.119 |
| HAALSI-Dementia | 0.02 (0.06) | 0.01 (0.14) | 0.11 (0.07) | 0.75 (0.24) * | 0.36 (0.20) | 0.134 |
| Weighted average | 0.11 (0.04) | 0.13 (0.08) | 0.29 (0.04) | 0.03 (0.11) | 0.06 (0.27) | 0.129 |
| BA | | | | | | |
| ARIC | 0.01 (0.04) * | 0.14 (0.05) * | 0.23 (0.03) * | −1.03 (0.06) * | −2.02 (0.16) * | 0.252 |
| NOMAS | 0.14 (0.03) * | 0.16 (0.06) * | 0.20 (0.03) * | −0.86 (0.07) * | −1.67 (0.12) * | 0.276 |
| WHICAP | 0.24 (0.07) * | 0.20 (0.10) | 0.23 (0.05) * | −0.54 (0.25) * | −1.08 (0.67) | 0.123 |
| FHS | 0.12 (0.05) * | 0.12 (0.15) | 0.23 (0.08) * | −0.97 (0.17) * | −1.00 (0.65) | 0.216 |
| EDIS | 0.09 (0.04) * | 0.28 (0.06) * | 0.11 (0.03) * | −0.97 (0.07) * | −1.99 (0.11) * | 0.403 |
| Harmonization | 0.03 (0.05) | 0.234 (0.09) * | 0.15 (0.04) * | −1.01 (0.09) * | −1.92 (0.21) * | 0.295 |
| MAS | 0.16 (0.04) * | 0.43 (0.14) * | 0.10 (0.06) | −0.68 (0.16) * | −1.18 (0.41) * | 0.189 |
| Atahualpa | 0.16 (0.04) * | 0.37 (0.10) * | 0.11 (0.05) * | −0.61 (0.13) * | −1.73 (0.38) * | 0.159 |
| HAALSI-Dementia | 0.15 (0.09) | 0.13 (0.23) | 0.09 (0.12) | −0.54 (0.40) | −1.65 (0.33) * | 0.269 |
| Weighted average | 0.12 (0.04) | 0.21 (0.08) | 0.18 (0.04) | −0.88 (0.11) | −1.73 (0.26) | 0.254 |
| BAR score | | | | | | |
| ARIC | 0.09 (0.01) * | 0.08 (0.03) * | 0.17 (0.02) * | – | – | 0.180 |
| NOMAS | 0.09 (0.03) * | 0.18 (0.05) * | 0.20 (0.02) * | – | – | 0.268 |
| WHICAP | 0.11 (0.03) * | 0.20 (0.08) * | 0.13 (0.04) * | – | – | 0.182 |
| FHS | 0.07 (0.03) * | 0.12 (0.04) * | 0.16 (0.02) * | – | – | 0.151 |
| EDIS | 0.06 (0.02) * | 0.18 (0.04) * | 0.08 (0.02) * | – | – | 0.137 |
| Harmonization | 0.07 (0.02) * | 0.14 (0.03) * | 0.18 (0.01) * | – | – | 0.230 |
| MAS | 0.08 (0.02) * | 0.30 (0.07) * | 0.07 (0.03) * | – | – | 0.172 |
| Atahualpa | 0.01 (0.03) | 0.15 (0.05) * | 0.18 (0.03) * | – | – | 0.179 |
| HAALSI-Dementia | 0.01 (0.04) | 0.08 (0.10) | 0.08 (0.05) | – | – | 0.070 |
| Weighted average | 0.07 (0.02) | 0.14 (0.04) | 0.16 (0.02) | – | – | 0.195 |

Abbreviations: ARIC Atherosclerosis Risk in Communities, BA basilar artery, BAR Brain Arterial Remodeling, EDIS Epidemiology of Dementia in Singapore, FHS Framingham Heart Study, fPCA fetal posterior cerebral artery, HAALSI Health and Aging in Africa: Longitudinal Study of an INDEPTH Community in South Africa dementia sub-study, ICA internal carotid artery, MAS Maracaibo Aging Study, MCA middle cerebral artery, NOMAS Northern Manhattan Study, TCV total cranial volume, WHICAP Washington Heights Inwood Community Aging Project.

segments. We recognize that other CoW variants, such as ACA-A1 segment hypoplasia, MCA branching patterns, or dominant vertebral artery presence, may also impact brain arterial diameters through similar principles of flow distribution.[13] Due to the variability and potential interactions of these additional CoW variants, it was not practical to incorporate them into our analysis. Finally, we did not consider exposure to vascular risk factors such as hypertension, hyperlipidemia, and smoking, which are known to affect brain arterial diameters.[10,11] Our study purpose was to specifically investigate non-modifiable factors that contribute to brain arterial diameters, rather than focusing on pathological conditions that affect vascular health. Future studies will seek to examine potential interactions between vascular risk factors and the factors analyzed in this study to determine their influence on brain arterial diameters.

**Table 4.** Linear regression models adjusted for age, sex, height, and presence of fetal posterior cerebral artery stratified by cohort study.

| | Age | Sex | Height | fPCA | | |
|---|---|---|---|---|---|---|
| | (per 10 years) | (Male) | (cm) | Unilateral | Bilateral | R-squared |
| ICA | | | | | | |
| ARIC | 0.34 (0.07) * | 0.29 (0.10) * | 0.02 (0.01) * | 0.49 (0.11) * | 0.71 (0.27) * | 0.119 |
| NOMAS | 0.22 (0.03) * | 0.43 (0.08) * | 0.02 (0.00) * | 0.37 (0.08) * | 0.41 (0.13) * | 0.155 |
| WHICAP | 0.31 (0.06) * | 0.48 (0.09) * | 0.01 (0.01) | 0.29 (0.14) * | 0.26 (0.22) | 0.111 |
| FHS | 0.27 (0.06) * | 0.47 (0.19) * | 0.00 (0.01) | 0.40 (0.20) * | 1.58 (0.68) * | 0.15 |
| EDIS | 0.08 (0.05) | 0.14 (0.10) | 0.01 (0.01) | 0.35 (0.09) * | 0.42 (0.14) * | 0.04 |
| Harmonization | 0.04 (0.05) | 0.23 (0.12) | 0.02 (0.01) * | 0.33 (0.11) * | 0.88 (0.24) * | 0.094 |
| MAS | 0.22 (0.04) * | 0.20 (0.16) | 0.03 (0.01) * | 0.72 (0.16) * | 1.13 (0.41) * | 0.149 |
| Atahualpa | 0.17 (0.04) * | 0.43 (0.15) * | 0.01 (0.01) | 0.26 (0.13) * | 0.81 (0.39) * | 0.137 |
| HAALSI-Dementia | 0.16 (0.08) | 0.41 (0.18) | 0.00 (0.00) | 0.18 (0.30) | 0.88 (0.33) | 0.161 |
| Weighted average | 0.22 (0.05) | 0.35 (0.12) | 0.01 (0.01) | 0.39 (0.12) | 0.63 (0.25) | 0.121 |
| MCA | | | | | | |
| ARIC | 0.22 (0.07) * | 0.36 (0.10) * | 0.01 (0.01) * | −0.01 (0.11) | −0.16 (0.26) | 0.085 |
| NOMAS | 0.13 (0.03) * | 0.42 (0.08) * | 0.01 (0.00) | −0.03 (0.08) | −0.02 (0.13) | 0.074 |
| WHICAP | 0.09 (0.06) | 0.45 (0.10) * | 0.01 (0.01) | −0.25 (0.14) | −0.59 (0.22) | 0.088 |
| FHS | 0.18 (0.06) * | 0.21 (0.20) | 0.00 (0.01) | −0.09 (0.21) | 0.48 (0.73) | 0.045 |
| EDIS | 0.12 (0.05) * | 0.36 (0.10) * | −0.00 (0.01) | 0.03 (0.09) | −0.08 (0.14) | 0.034 |
| Harmonization | 0.01 (0.06) | 0.23 (0.12) | 0.01 (0.01) * | −0.13 (0.11) | −0.10 (0.24) | 0.046 |
| MAS | 0.18 (0.04) * | 0.44 (0.26) * | 0.01 (0.01) | 0.08 (0.16) | 0.51 (0.41) | 0.127 |
| Atahualpa | 0.18 (0.04) * | 0.35 (0.15) * | 0.01 (0.01) | −0.07 (0.13) | 0.65 (0.40) | 0.084 |
| HAALSI-Dementia | 0.13 (0.08) | 0.01 (0.18) | 0.00 (0.00) | 0.63 (0.29) | 0.20 (0.31) | 0.059 |
| Weighted average | 0.15 (0.05) | 0.37 (0.18) | 0.01 (0.01) | −0.02 (0.12) | −0.05 (0.25) | 0.081 |
| BA | | | | | | |
| ARIC | 0.12 (0.06) | 0.33 (0.09) * | 0.01 (0.01) | −1.06 (0.10) * | −2.06 (0.24) * | 0.227 |
| NOMAS | 0.11 (0.03) * | 0.46 (0.07) * | −0.00 (0.00) | −0.87 (0.07) * | −1.71 (0.12) * | 0.253 |
| WHICAP | 0.21 (0.06) * | 0.45 (0.09) * | −0.00 (0.00) | −0.65 (0.13) * | −1.61 (0.22) * | 0.155 |
| FHS | 0.13 (0.06) * | 0.66 (0.18) * | −0.02 (0.01) | −0.88 (0.18) * | −1.23 (0.64) | 0.202 |
| EDIS | 0.09 (0.04) * | 0.35 (0.08) * | 0.00 (0.00) | −0.96 (0.07) * | −2.02 (0.11) * | 0.393 |
| Harmonization | 0.01 (0.05) | 0.18 (0.10) * | 0.02 (0.01) * | −0.99 (0.10) * | −1.89 (0.21) * | 0.289 |
| MAS | 0.18 (0.04) * | 0.55 (0.16) * | 0.00 (0.01) | −0.71 (0.16) * | −1.77 (0.41) * | 0.125 |
| Atahualpa | 0.17 (0.04) * | 0.33 (0.14) * | 0.01 (0.01) | −0.60 (0.13) * | −1.74 (0.38) * | 0.152 |
| HAALSI-Dementia | 0.06 (0.07) | 0.11 (0.17) | 0.00 (0.00) | −0.43 (0.26) | −1.69 (0.28) * | 0.226 |
| Weighted average | 0.12 (0.04) | 0.38 (0.10) | 0.00 (0.01) | −0.89 (0.11) | −1.85 (0.24) | 0.237 |
| BAR score | | | | | | |
| ARIC | 0.08 (0.01) * | 0.26 (0.04) * | 0.00 (0.00) | – | – | 0.105 |
| NOMAS | 0.09 (0.03) * | 0.38 (0.05) * | 0.00 (0.00) | – | – | 0.162 |
| WHICAP | 0.13 (0.03) * | 0.34 (0.09) * | 0.00 (0.01) | – | – | 0.174 |
| FHS | 0.07 (0.03) * | 0.28 (0.05) * | 0.00 (0.00) | – | – | 0.081 |
| EDIS | 0.07 (0.02) * | 0.15 (0.06) * | 0.01 (0.00) * | – | – | 0.120 |
| Harmonization | 0.13 (0.03) * | 0.22 (0.05) * | 0.01 (0.00) * | – | – | 0.151 |
| MAS | 0.10 (0.02) * | 0.28 (0.08) * | 0.01 (0.00) * | – | – | 0.178 |
| Atahualpa | 0.01 (0.02) | 0.20 (0.06) * | 0.01 (0.00) * | – | – | 0.109 |
| HAALSI-Dementia | 0.01 (0.04) | 0.15 (0.08) | 0.00 (0.00) | – | – | 0.035 |
| Weighted average | 0.08 (0.02) | 0.26 (0.05) | 0.01 (0.00) | – | – | 0.131 |

Abbreviations: ARIC Atherosclerosis Risk in Communities, BA basilar artery, BAR Brain Arterial Remodeling, EDIS Epidemiology of Dementia in Singapore, FHS Framingham Heart Study, fPCA fetal posterior cerebral artery, HAALSI Health and Aging in Africa: Longitudinal Study of an INDEPTH Community in South Africa dementia sub-study, ICA internal carotid artery, MAS Maracaibo Aging Study, MCA middle cerebral artery, NOMAS Northern Manhattan Study, WHICAP Washington Heights Inwood Community Aging Project.

In summary, our study contributes valuable normative data on brain arterial diameters across diverse populations, shedding light on the impact of age, sex, head size, and the presence of persistent fPCA. These findings hold significant implications for the diagnosis and epidemiological analysis of abnormal brain arterial phenotypes. By considering the influence of the studied factors, we caution against the use of fixed universal arterial cutoffs, which may introduce errors and incorrectly attribute pathological significance to larger diameters that are actually physiological. Study results underscore the importance of incorporating our findings into future clinical studies that aim to define appropriate thresholds of arterial dilation associated with cerebrovascular risk.

## Acknowledgments

The authors thank the staff and participants of the ARIC study for their important contributions.

## Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

## Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This investigation was supported by National Institutes of Health grant R01 AG057709. The Atherosclerosis Risk in Communities (ARIC) Study is carried out as a collaborative study supported by National Heart, Lung, and Blood Institute contracts (75N92022D00001, 75N92022D00002, 75N92022D00003, 75N92022D00004, 75N92022D00005). The ARIC Neurocognitive Study is supported by U01HL096812, U01HL096814, U01HL096899, U01HL096902, and U01HL096917 from the NIH (NHLBI, NINDS, NIA and NIDCD). Funding was also supported by R01AG054491, R01HL087641, RO1HL105930, and R01HL086694; National Human Genome Research Institute contract U01HG004402; and National Institutes of Health contract HHSN268200625226C. Infrastructure was partly supported by Grant Number UL1RR025005, a component of the National Institutes of Health and NIH Roadmap for Medical Research. The Northern Manhattan Study (NOMAS) was supported by National Institutes of Health (R01 AG066162, R01 NS36286, R01 NS29993). The Washington Heights–Inwood Columbia Aging Project (WHICAP) was supported by National Institutes of Health (R01 AG072474, R01 AG037212, RF1 AG054023). The Atahualpa Project was supported by Universidad Espíritu Santo – Ecuador. The Epidemiology of Dementia in Singapore (EIDS) study was supported by the National Medical Research Council, Singapore (NMRC/CG/NUHS/2010 [Grant no: R-184-006-184-511]). The Harmonization study was supported by U01 AG052409. The Framingham Heart Study (FHS) was supported by National Heart, Lung and Blood Institute contracts (N01 HC25195, HHSN268201500001I, 75N92019D00031) with additional support from National Institutes of Health grants (R01 AG047645, R01 HL131029) and an American Heart Association Award (15GPSGC24800006). HAALSI-Dementia is a collaboration between Harvard Center for Population and Development Studies from the Harvard T.H. Chan School of Public Health, and MRC/Wits Rural Public Health and Health Transitions Research Unit from the School of Public Health at the University of the Witwatersrand in South Africa and is supported by the National Institute on Aging [5R01AG054066]. The MRC/Wits Rural Public Health and Health Transitions Research Unit and Agincourt Health and Socio- Demographic Surveillance System, a node of the South African Population Research Infrastructure Network (SAPRIN), have been supported by the National Department of Science and Innovation (grants 058893/Z/99/ A), the University of the Witwatersrand (069683/Z/02/Z), the Medical Research Council, South Africa (085477/Z/08/Z), and by the Welcome Trust, UK (085477/B/08/Z). The Maracaibo Aging Study was supported by the Gene-Environment Interaction in Cognition in Venezuela Families project founded by the National Institute on Aging National Institutes of Health under Award Numbers R01AG036469, AG056609, and 1 R03AG054186-01.

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## Supplemental Material

Supplemental material for this article is available online

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