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The invariable and not asymmetric segments of the cerebral arterial network dampen the peak systolic pressures lowering development of aneurysms

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Abstract

Objective

The segments of cerebral basal arterial network (CBAN) dampen the peak pressure in blood flowing through these arteries, minimizing the chances of development of cerebral aneurysms. The objective of this research was to find the quantitative relationship of the variations of the components of the CBAN with the development of aneurysms.

Design and setting

This is an observational, quantitative, and retrospective research, which used Computed Tomography Angiography (CTA) images.

Participants

Cerebral CTA scans of 145 adult patients of both sexes were studied.

Main outcome measures

Diameters of segments of CBAN were measured in CTA images and the relative size of each vessel was calculated to standardise for differences in overall arterial sizes among patients. Relationships among sizes of CBAN components were analysed. Presence of aneurysms in different parts of CBAN was recorded.

Results

Forty-six aneurysms in right internal carotid artery (ICA) and middle cerebral artery (MCA) and 32 aneurysms in left ICA and MCA segments were noted in 42 and 30 patients, respectively. Aneurysms in anterior communicating artery complex (AcomAC) and vertebral-basilar (VB) arterial segments were seen in 27 and 8 patients respectively, while they were not detected in parts of posterior cerebral artery (PCA). The significant ($p<0.0001$) inverse relationships between sizes of posterior

communicating artery (PcomA) and the first segment of PCA on both sides indicated that blood inputs to the second part of PCA were similar. Differences in means of the index of arterial size variation for people with aneurysms (0.96) and without aneurysms (0.86) was significant ($p \leq 0.015$). Aneurysms in AcomAC, PCA and VB arteries were less and was proposed that it is due to dampening of peak systolic blood pressures.

Conclusion

Variation in segments of CBAN has been quantified. The peak pressure dampening mechanism in such arterial segments reduces the chances of development of aneurysms.

Key words

subarachnoid haemorrhage; aneurysm; stroke; hemodynamics; cerebral basal arterial network

Funding

None

Strengths and limitations of this study

The relationship of cerebral arterial variations to aneurysms has been observed, but not quantified.

This study presents quantitative evidence that the relative sizes and inter-arterial relationship of the components of the cerebral arterial network is associated with the development of cerebral aneurysms.

Follow up of such patients with variant segments of CBAN should be considered enabling aneurysms to be detected and treated at an early stage, prior to rupture.

Further prospective investigations of cerebral blood flow and the changes in the blood pressure in the presence of asymmetric and variant cerebral arteries would be helpful.

Introduction

Cerebral aneurysms are a common cause of haemorrhagic stroke. Diagnosis, management, prediction and prevention of aneurysms are challenging.[1] The middle cerebral artery (MCA) and anterior communicating artery complex (AcomAC) regions have been identified as the most common locations (>31%) for the occurrence of intracranial aneurysms.[2-5] However, the occurrence of more than two thirds of the total intracranial aneurysms has been reported in relation to internal carotid artery (ICA) territory.[6] Therefore, more than 80% of all cerebral aneurysms occur in ICA, MCA and AcomAC territories.[2-6] Pia and Fontana have described posterior cerebral artery (PCA) aneurysms, but the rate of prevalence of cerebral aneurysms in PCA and vertebrobasilar (VB) arterial components is the least.[7-9] The prevalence of intracranial aneurysms of various sizes ranged from 0.2 to 6.8 %, and approximately 6-10/100,000 people suffered from ruptured intracranial aneurysms per year.[4,10] These individuals had poor prognosis and more than a third of the mortalities occurred within a month of the illness.[4,10] Most of the ruptured aneurysms (85.6% cases) were reported to be symptomatic and were from the MCA and AcomAC territories.[4,5] Therefore, studying the relationship of relative sizes of cerebral arteries, sites of location of cerebral aneurysms and their relationship to the variant segments of CBAN would help to understand the risk factors, and maximise the management of strokes.

The blood flow to the cranial cavity through the four main incoming arteries is asynchronous.[11] The asynchronous blood pressure gradients in the incoming intracranial arteries combine via segments of the CBAN. This maintains a continuous, smooth blood flow through the arteries leaving the arterial network, thus minimises peaks in pressure and reduces the chances of development of cerebral aneurysms. [11,12] However, the blood flowing through the asymmetric and variant segments of CBAN, alters the hemodynamics and peaks in pressure and predisposes to the development of aneurysms in the associated "arterial complexes".[11,13] A relationship for the development of AcomAC aneurysms to the degree of asymmetry between left and right first segments of ACA (A1s) has been shown to occur.[14] The current study, investigated the relationship of locations of intracranial aneurysms to relative sizes of all arterial segments of CBAN and their individual variations. The concept that the mechanisms involved in dampening peak systolic pressures in arterial segments of CBAN, reduce the chances of the development of aneurysms in the ACA and PCA territories, justified the current investigation.

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Material and method

Patient and public involvement

The cerebral computed tomography angiography (CCTA) images used in this study were taken from patients who visited the RAH for a variety of reasons related to cranial pathologies and screening purposes. Personal information of patients recorded in the data system has not been included in this study. Human Research Ethics Board granted permission (approval number: H2014 -176) to access and use data from the Carestream data registry system (Vue RIS version 11.0.14.35).

Study design

Randomly selected CCTA images of 145 patients archived in the Carestream data registry system at Royal Adelaide Hospital (RAH), South Australia between January 2011 and December 2019, were used in the study (male = 67, female = 78, mean age = 60.9 years) (Supplementary file 1).The CCTA images with severe artefacts or from patients with severe cerebral vasospasm (i.e. diagnosed by radiologists) were excluded from the study. Missing arterial components or those not seen in the CCTA images (e.g. PcomA and proximal segment of ACA) were considered to have 0.1 mm diameter for the purpose of statistical analysis (Supplementary file 1). Components of CBAN in some CCTA were not visible, since the arteriography was not very clear, or the images were disrupted by the artefacts. In such situations, arterial measurements were not taken and included in the data. Therefore, the number of arterial components measured in CCTA varied to a moderate extent.

Data collection

The position, presence or absence of the aneurysms of any sizes were recorded from CCTA of 145 patients based on the diagnosis made by radiologists and clinicians. The position of aneurysms associated with the AcomAC, MCA, ICA, PCA and VB arterial regions were recorded. Some cases had multiple aneurysms. The internal diameters of intracranial segment of ICA at the level of anterior clinoid processes, the first segment of ACA (A1) at the mid-point, PcomAs at the mid-point, the proximal end of the first segment of MCA (M1), anterior communicating artery (AcomA) at the mid-point, the proximal end of the second part of ACA (A2), the first segment of PCA (P1) at the mid-point, the proximal segment of PCA (P2) at the level of dorsum sellae, the distal end of basilar artery just proximal to the origin of superior cerebellar artery (SCA), and

the distal vertebral arteries (AV) just proximal to the formation of basilar artery (BA) were measured at right angles to the longitudinal axis of arteries in each individual (Figure 1). The measured internal diameters (in millimetre, mm) were converted into the "relative sizes" of the vessels using the formula, "measured diameter of each vessel / the average size of all the CBAN components measured" (Supplementary file 1) and transferred into the SPSS v. 25 software, before the statistical analysis. The diameters of arteries were converted into "relative sizes" to neutralize the individual differences in sizes of CBAN components among patients.

The diameter of each artery was measured at the narrowest region of the selected site, perpendicular to the long axis of the vessel (Figure 1), to make the measurements consistent across all CCTA images. Furthermore, the CCTA arterial data taken from all the patients were divided into four groups (see below) in order to observe the relationship of aneurysms and the variation in the components of CBAN by analysing the average standard deviation (SD) of arterial sizes in each individual, average size of arteries and coefficients of variation of CBAN components as follows.

Group a: patients with multiple aneurysms (i.e. patients with two or more cerebral aneurysms), group b: patients with single cerebral aneurysm, group c: patients without aneurysms. Groups a and b were combined for some analyses to include all patients with aneurysms (Supplementary file 1).

Three variables characterising each patient's CBAN were constructed for the analysis of the variation of the sizes of all left and right segments of the CBAN (i.e. right and left ICA, first segment of MCA, A1, A2, P1, P2, AcomA, PcomA, and BA):

1. Average size (Av) of all CBAN arteries
2. Standard deviation (SD) of sizes of the same CBAN components
3. Coefficient of variation (CV) of CBAN segments = 100*SD/Av

The Av of CBAN, SD and CV of all components of CBAN were calculated to determine the degree of variation in the CBAN segments for each individual patient (Supplementary file 1)

The accuracy of the measurements was determined by repeating measurements in CCTA of 10 cases, a week after the first measurement (Table 1 and supplementary file 2). The relative technical error of the measurement (rTEM) was calculated and found to be within the statistically acceptable limits (i.e. ≤10%).

Figure 1 (about here)

Figure 1: Sites of arterial diameter measurement in cerebral angiography images. White lines perpendicular to the long axes of vessels show the measurement sites and white arrows depict the components of cerebral basal arterial network (CBAN). (a) = axial image showing the sites of measurement, (b) = coronal image showing the sites of measurement and location of aneurysms, (c) = coronal angiography showing the sites of vessel measurement, (d) = digital substraction angiography showing the sites of vessel measurement. ACA = anterior cerebral artery, MCA = middle cerebral artery, ICA = cranial component of internal carotid artery, PCA = posterior cerebral artery, A1 of ACA = the first segment of ACA, A2 of ACA = the second segment of ACA, AcomA = anterior communicating artery, PcomA = posterior communicating artery, M1 of MCA = the first segment of middle cerebral artery, P1 of PCA = first segment of PCA, P2 of PCA = second segment of PCA, BA = basilar artery, VA = vertebral artery, AcomACA= AcomA complex aneurysm, and MCAA = MCA aneurysm.

Table 1: The reliability of the measurements taken in Cerebral Computed Tomography Angiography (CCTA) images.

	rt VA	lft VA	BA	rt P2	lft P2	rt PcomA	lft PcomA	rt ICA	lft ICA	rt A2	lft A2	Acom A	rt M1	lft M1	rt P1	lft P1	rt A1	lft A1
TEM error	0.025	0.021	0.019	0.018	0.017	0.013	0.014	0.023	0.055	0.020	0.069	0.070	0.020	0.023	0.018	0.017	0.076	0.115
rTem (CV)	0.982	0.767	0.644	0.793	0.697	0.708	0.909	0.533	1.305	0.751	2.783	3.623	0.684	0.805	0.842	0.755	3.732	5.825
R reliability	0.998	0.999	0.999	0.997	0.996	0.999	0.999	0.998	0.988	0.998	0.948	0.971	0.998	0.998	0.999	0.998	0.991	0.982

Reliability, the coefficients of variation (CV) or the relative technical error of cerebral vessel internal diameter measurements (rTEM) and the technical error of measurements (TEM) are presented. Reliability is the correlation among the first measurements and the second measurements taken from the same artery, n = 10. rt = right, lft = left, dia = internal diameter, ACA = anterior cerebral artery, MCA = middle cerebral artery, ICA = cranial component of internal carotid artery, PCA = posterior cerebral artery, A1 = first segment of ACA, PcomA = posterior communicating artery, AcomA = anterior communicating artery, M1 = first segment of MCA, P1 = first segment of PCA, P2 = second segment of PCA, BA = basilar artery, and VA = vertebral artery (supplementary file 2).

Statistical analysis

This is a cross-sectional observational study. The data were analysed using excel data file and descriptive, parametric and non-parametric statistical methods, independent sample t – test, linear regression, and custom tables from Statistical Package for the Social Sciences (SPSS IBM, version 25) program. The p values less than 0.05 were considered statistically significant (Table 1, Table 2, Table 3, Supplementary files 1, 2, 3 and 4).

Findings

Statistically strong inverse relationships were found between relative sizes of ipsilateral PcomA, and P1 segments on the right and left sides (correlation coefficient = -0.600, p<0.0001 on right and correlation coefficient = -0.639, p<0.0001 on left respectively) (Table 2). The relative sizes of right and left PcomA were found to be inversely correlated with the relative size of basilar artery (correlation coefficient = -0.390, p = <0.0001 and -0.447, p = <0.0001 respectively) (Table 2 and Supplementary file 3). Furthermore, significant positive correlations were found between relative sizes of left and right cranial ICA, left and right first part of MCA (M1), left and right second part of ACA (A2), and left and right second part of PCA (P2) (p = <0.01) (Table 2 and supplementary file 3). The variation in the sizes of CBAN segments was found to be greater in people with aneurysms compared to those without aneurysms (SD, p≤0.015 and CV, p≤0.38)). The indices of variation in CBAN components in people with single and multiple aneurysms were insignificantly different (p ≥0.05) (Table 3 and Supplementary file 1).

Eighty-three patients out of 145 had cerebral aneurysms in various locations (Figure 1, Supplementary files 1 and 3). Some individuals had multiple aneurysms, thus a total of 113 aneurysms were found in the 83 patients (Figure 1, Supplementary files 3 and 4). Out of the total number of 113 aneurysms, 32 (28.31%), 14 (12.4%), 24 (21.24%) and 8 (7%) aneurysms were found in right MCA, right ICA, left MCA and left ICA regions respectively. Seventy-eight out of the 113 aneurysms in the 83 patients (i.e. 69% of the total) were in the right and left MCA and ICA regions (Supplementary files 1 and 3). Furthermore, 27 aneurysms (23.9% of the total) were in AcomAC regions, one in each of 27 patients (Figure 1 and Supplementary file 1). In addition, 8 aneurysms (7% of the total) were in the VB arterial regions (Supplementary file 1). Ten and 2 patients had bilateral MCA and ICA aneurysms respectively. Out of the 27 patients with AcomAC aneurysms, 19 of them had aneurysms only in the AcomAC regions. Eight patients with AcomAC aneurysms also had coexisting left MCA (n = 4), right MCA (n = 4), and right ICA (n = 4) aneurysms. Out of those eight patients with multiple coexisting aneurysms, one of them had aneurysms in AcomAC, right MCA and left MCA, while another had coexisting aneurysms in AcomAC, right ICA and right MCA. The third patient with AcomAC aneurysm also had coexisting aneurysms in right ICA and left MCA. Ten cases also had coexisting aneurysms in bilateral MCA territories (supplementary file 1). Out of eight patients with VB aneurysms, one, three, one, and one also had coexisting right ICA, right MCA, left ICA and left MCA aneurysms respectively. No aneurysms were detected at or distal to P2 segments of PCA (Figure 1, and supplementary file 1).

Table 2: Spearman's rho nonparametric correlation among the relative size of CBAN components.

Correlations - Spearman's rho

		RsBA	RsRt P2	RsLft P2	RsRtPcomA mid dia	RsLftPcomA mid dia	RsRt P1	RsLft P1
RsBA	**Correlation Coefficient**	**1.000**	**.169***	**-.017**	**-.390****	**-.447****	**.245***	**.293****
	Sig. (2-tailed)	.	.043	.839	.000	.000	.015	.003
	N	145	145	145	145	145	98	98
RsRt P2	**Correlation Coefficient**	**.169***	**1.000**	**.357****	**-.350****	**.286****	**.234***	**.168**
	Sig. (2-tailed)	.043	.	.000	.000	.000	.020	.098
	N	145	145	145	145	145	98	98
RsLft P2	**Correlation Coefficient**	**-.017**	**.357****	**1.000**	**-.206***	**-.140**	**.301****	**.191**
	Sig. (2-tailed)	.839	.000	.	.013	.093	.003	.059
	N	145	145	145	145	145	98	98
RsRtPcomA mid dia	**Correlation Coefficient**	**-.390****	**-.350****	**-.206***	**1.000**	**.456****	**-.600****	**-.388****
	Sig. (2-tailed)	.000	.000	.013	.	.000	.000	.000
	N	145	145	145	145	145	98	98
RsLftPcomA mid dia	**Correlation Coefficient**	**-.447****	**-.286****	**-.140**	**.456****	**1.000**	**-.315****	**-.639****
	Sig. (2-tailed)	.000	.000	.093	.000	.	.002	.000
	N	145	145	145	145	145	98	98
RsRtP1	**Correlation Coefficient**	**.245***	**.234***	**.301****	**-.600****	**.315****	**1.000**	**.352****
	Sig. (2-tailed)	.015	.020	.003	.000	.002	.	.000
	N	98	98	98	98	98	98	98
RsLft P1	**Correlation Coefficient**	**.293****	**.168**	**.191**	**-.388****	**.639****	**.352****	**1.000**
	Sig. (2-tailed)	.003	.098	.059	.000	.000	.000	.
	N	98	98	98	98	98	98	98

***. Correlation is significant at the 0.05 level (2-tailed), **. Correlation is significant at the 0.01 level (2-tailed).**

Cerebral basal arterial network = CBAN, Rs = relative size, Rt = right, Lft = left, PCA = posterior cerebral artery, PcomA = posterior communicating artery, BA = distal basilar artery, P2 = second part of PCA, PcomA = posterior communicating artery, P1 = first part of PCA, RsBA= relative size of distal basilar artery, RsRt P2 = relative size of right proximal P2, RsLft P2 = relative size of left proximal P2, RsRtPcomA mid dia = relative size of right PcomA at the mid-point, RsLftPcomA mid dia = relative size of left PcomA at mid-point, RsRt P1 = relative size of right P1 at mid-point, RsLft P1 = relative size of left P1 at mid-point.

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Table 3: Linear regression and independent sample t – test analysis of standard deviation (SD) of CBAN measurement, Coefficient of variation (CV), and an average size of CBAN in mm.

	Standard deviation of CBAN measurement (SD, mm) average (SD)	Coefficient of variation (CV) average (SD)	Size of CBAN (mm) average (SD)
Patients without cerebral aneurysms (n = 62)	0.86 (0.22)	34.9 (10.0)	2.50 (0.24)
Patients with one or multiple cerebral aneurysms (n = 83)	0.96 (0.23)	38.2 (9.1)	2.52 (0.26)
Significant (2- tailed, p value)	0.015	0.038	0.708

The table shows the variation in the components of CBAN in everyone in relation to the presence or absence of single or multiple aneurysms. CBAN = cerebral basal arterial network.

Discussion

The significant (i.e. SD, $p \leq 0.015$ and CV, $p \leq 0.038$) differences in the means of variation measures of segments of CBAN in people with aneurysms and without aneurysms suggest that the size of individual vessels of the CBAN differs within a person who had an aneurysm (Table 3 and Supplementary file 1). Furthermore, the analysis also confirmed that the occurrences of aneurysms did not depend on the average size of the segments of CBAN ($p \geq 0.70$) (Table 3). However, the overall variation in the size of individual segments of CBAN determined the probability of having the cerebral aneurysms (Table 3). Therefore, these statistically significant differences in the variation of segments of CBAN suggested that the minimally variant segments of CBAN served to best equalize the blood pressure preventing the development of cerebral aneurysms (Table 3). The majority of the cerebral aneurysms detected in the current study were in association with bilateral ICA and MCA (69%, chi-squared test, $p < 0.001$) (Supplementary files 1, 3 and 4). Similar distribution patterns of intracranial aneurysms have been described.[3,4,6,15] Aneurysms less than 3 mm in diameter could be missed in

commonly used CCTA imaging techniques.[16] The findings of the current study, on more than 4 mm in diameter sized ICA aneurysms compared well with Imaizumi and colleagues findings.[6] Approximately, 3% of the general population develop cerebral aneurysms and may not be diagnosed, until they enlarge sufficiently to cause symptoms or rupture.[17] However, more than 70 % of aneurysms detected by Imaizumi and colleagues[6] using advanced imaging technique were ≤3mm in diameter.[16] The current study, collected data from patients with complicated and ruptured aneurysmal cases, who were referred to the Neuro-interventional Centre in RAH for treatment. Imaizumi and colleagues[6] conducted the study on healthy and asymptomatic adults and detected the right ICA territory as the most common location (78%) for the development intracranial aneurysms. Almost 83% of the detected ICA aneurysms in the latter study were ≤3.9mm in diameter[6], thus individuals with these aneurysms would not have displayed aneurysm related symptoms. The chances for the rupture of an aneurysm is minimal, when the size is ≤4mm in diameter.[2,6] Most of the CCTA images with AcomAC aneurysms (19 cases) in the current study, had no other coexisting aneurysms located elsewhere in the intracranial regions (Supplementary file 1). The frequency of aneurysms was lower in AcomAC and PCA territories in comparison to the aneurysms found in the MCA and ICA territories in the current study and in a study published recently.[6]

The absence of aneurysms elsewhere in 19 out of 27 (i.e., 70.04%) AcomAC aneurysmal cases (Supplementary files 1 and 3) may indicate that the causes of aneurysms were not due to generalised weakness of the CBAN arterial wall, hypertension, smoking and familial reasons. Vrselja and colleagues suggested that the communicating arteries divert the blood flow and dampen the peaks in systolic pressure in the CBAN system to reduce the occurrence of aneurysms.[18] The chances of the development of AcomAC aneurysms have been predicted to be ≥80% when the asymmetric ratio between right and left A1 segments is 1.42 or more (i.e., larger diameter /smaller diameter).[14] Furthermore, the effect of fluctuating peak systolic pressure in causing aneurysms in AcomAC territories would be lower in the presence of symmetrical A1 arterial segments.[14] Therefore, these 19 cases of AcomAC aneurysms could have resulted from the altered haemodynamics caused by the asymmetry between right and left A1 segments.[14]

Fluctuation of peak systolic pressure may contribute to the occurrence and rupture of cerebral aneurysm.[19] In addition, the amount of blood flowing through MCA had been found to be increased in the presence of the hypoplastic or absent A1 segment or PcomA.[20] Therefore, the 8 cases of AcomAC aneurysms that cooccurred with aneurysms

elsewhere (i.e. AcomAC aneurysms cooccurred with right ICA, right MCA and left MCA regions) might have been associated with the presence of hypoplastic or absent A1 segments or PcomA (Supplementary file 1). These variations of A1 and PcomA segments would increase the resistance to the outflow of blood from the ICA, thus increase the flow and peak systolic pressure through the MCA. Therefore, the greater incidence (≥85% cases) of cerebral aneurysms found in the ICA and MCA territories, [3,4,15] might have been linked to the altered haemodynamic in the presence of variant segments of CBAN.[21-23] A significant amount of wall shear stress has been noticed on the stent placed next to the aneurysmal sac suggesting increased peaks in systolic pressure would result in the development of aneurysm.[24] This indicates that symmetrical A1 segment, and PcomA could act as the flow diverting segments of CBAN and reduce or dampen the peak systolic pressure in the ICA and MCA reducing the incidence of aneurysms in these regions. The PCA aneurysms are rare.[7,25] The i) significant positive correlations between right and left PcomA, ipsilateral P1 and P2 segments and BA with right and left P1 segments, and ii) inverse correlations between PcomA with ipsilateral and contralateral P1 segments and BA with right and left PcomA (Table 2 and supplementary file 3) help to balance and maintain optimal blood flow in P2 segments. Thus, the peak systolic pressure may not reach levels that could injure the arterial wall and cause aneurysms in the P2 segment and beyond.[26] This is particularly important, because the blood flow in P2 segment is maintained by two inversely correlated ($p \leq 0.01$) ipsilateral PcomA and P1 vessels (Table 2). Thus the prevalence of aneurysms in the P2 segment territory of PCA is zero or minimal (Supplementary file 1 and 3).[7] The peak systolic pressure of the blood flowing via the vertebral arteries would get dissipated in the basilar artery (which is also considered as a communicating artery [27]), and then in P1 before reaching the P2 segment. In a similar way, blood flowing from the ICA is dampened in PcomA before reaching the P2 segment, which ensures the less fluctuating peak systolic pressure distal to the P2 segment. Therefore, pressure dampening mechanisms could smoothen the arterial pressure distal to P2 segment and reduce the chances of developing aneurysms in PCA compared to ICA, MCA and AcomAC territories.

In vertebrate brain evolution, brainstem evolved first, whereas the telencephalon (specially the frontal lobes) was a later addition to the brain.[28] Therefore, the arterial supply in the brainstem and the posterior part of telencephalon had more time to be well established. The recently evolved large telencephalon is predominantly supplied by ICA.[29] The anterior part of CBAN evolved along with the telencephalon and has had less evolutionary time to develop, compared to the posterior segments.[28] Thus, the natural selection did not have adequate time to minimise the variations and asymmetries of the anterior segments of the CBAN. Furthermore, a larger blood volume has to flow

through the less evolved anterior segments of CBAN to meet the demand of the large telencephalon.[30] Therefore; the chances of development of aneurysms in the arteries supplied by the anterior segments of CBAN are higher compared to the posterior part. Asymmetry between antimere segments of CBAN could result from the mutations of genes involved in the development of cerebral arterial segments (e.g., development of hypoplastic right or left A1 segment of ACA) in the embryo. However, in some, the embryo has the ability to enlarge the collateral segment of the hypoplastic segment of CBAN and maintain adequate blood supply to the affected right or left side of the brain. Establishment of this compensatory blood flow also requires the enlargement of respective communicating arteries (i.e. anterior and posterior communicating arteries, or the basilar artery). Therefore, the brain develops normally and maintains normal function. However, the increase in blood flow in the enlarged arterial segments, could lead to the formation of aneurysms later in life. Asymmetry between antimere A1 is a good example. In these arterial segments, the risk of development of aneurysms in AcomAC is ≥80%, when the A1 asymmetry ratio remains ≥1.42.[14]

This study was not designed to examine the shape and characteristics of aneurysms, but the focus was on the relationship of the relative size of the blood vessels to the formation of aneurysms in different regions of the brain. Further investigations of cerebral blood flow and the changes in the blood pressure in the presence of asymmetric and variant arteries may help to understand the mechanisms involved in the development of aneurysms.

Conclusion

The first segments of anterior and posterior cerebral arteries, basilar and communicating arteries of cerebral basal arterial network (CBAN) help to reduce or dampen the peak systolic pressure and minimise the formation of aneurysms in the CBAN system. The hypoplastic or missing segments of CBAN increase the chance of development of aneurysms. The number of cerebral aneurysms varies with the ability of each arterial segment to dampen the peak systolic pressure. Patients who have asymmetric cerebral arterial segments and variant communicating arteries on a brain scans should be monitored regularly by follow up angiograms. This finding could be considered as one of the criteria for the screening of cerebral aneurysms.

Data sharing statement

Extra data is available by emailing Arjun.Burlakoti@unisa.edu.au

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None

Author contribution statement

Arjun Burlakoti- conceived the idea, designed the analysis, collected and analysed the data from CCTA, took pictures, recorded videos, contributed in conceptualization, prepared and drafted the manuscript.

Jaliya Kumaratilake- conceived the idea, contributed to the concept, helped in data interpretation, editing and the critical revision of the manuscript and approving the article.

Jamie Taylor- conceived the idea, contributed in collecting and interpreting the data, editing the manuscript, the critical revision of the manuscript and approving the article.

Maciej Henneberg- conceived the idea, helped in statistics, data analysis and interpretation, editing the manuscript, the critical revision of the manuscript and in approving the article.

Conflict of interest statements

There is no conflict of interest with any of the authors.

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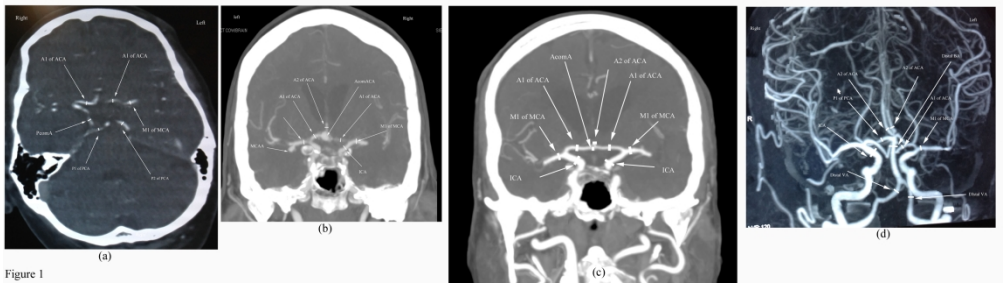
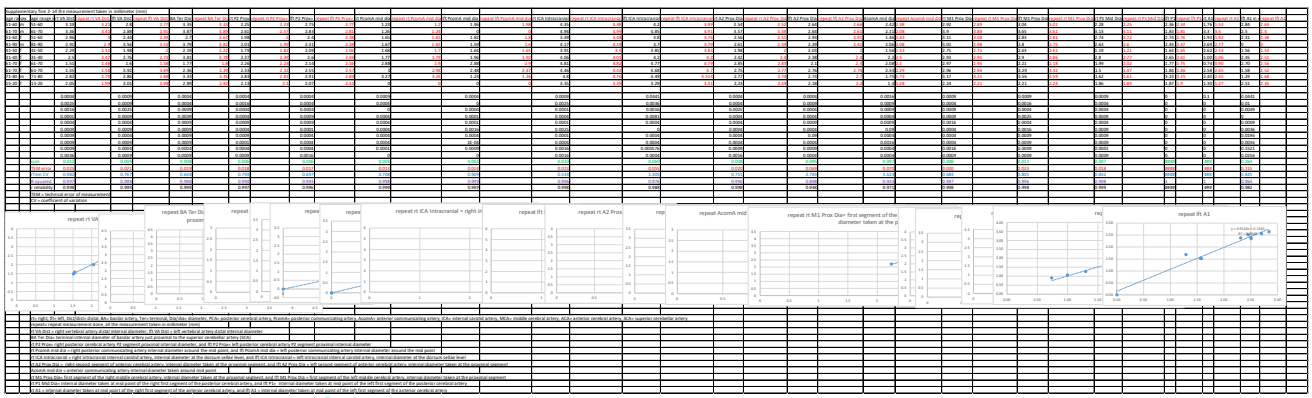


Figure 1: Sites of arterial diameter measurement in cerebral angiography images. White lines perpendicular to the long axes of vessels show the measurement sites and white arrows depict the components of cerebral basal arterial network (CBAN). (a) = axial image showing the sites of measurement, (b) = coronal image showing the sites of measurement and location of aneurysms, (c) = coronal angiography showing the sites of vessel measurement, (d) = digital substation angiography showing the sites of vessel measurement. ACA = anterior cerebral artery, MCA = middle cerebral artery, ICA = cranial component of internal carotid artery, PCA = posterior cerebral artery, A1 of ACA = the first segment of ACA, A2 of ACA = the second segment of ACA, AcomA = anterior communicating artery, PcomA = posterior communicating artery, M1 of MCA = the first segment of middle cerebral artery, P1 of PCA = first segment of PCA, P2 of PCA = second segment of PCA, BA = basilar artery, VA = vertebral artery, AcomACA= AcomA complex aneurysm, and MCAA = MCA aneurysm.

Supplementary file 1:

Supplementary file 2:



Supplementary file 3

Abbreviations and full forms

- All the measurements were taken in millimetre (mm)
- SCA = superior cerebellar artery
- rt or Rt = right, lft or Lft = left, ter = terminal, dia = diameter, dis = distal, m = male, f = female, Rs = relative size,
- stDev = standard deviation, CV = coefficient of variation, Aver = average
- ACA = anterior cerebral artery, PCA = posterior cerebral artery, A1 = first segment of ACA, A2= second part of ACA, P2 = second segment of PCA, P1 = first segment of PCA
- ICA = internal carotid artery, MCA = middle cerebral artery, M1 = first segment of MCA, PcomA = posterior communicating artery, AcomA = anterior communicating artery
- VA or va = vertebral artery, ba or BA = basilar artery, VB Aneu = vertebro basilar aneurysm, Aneu Els = elsewhere aneurysm
- ba ter dia = diameter measured just proximal to the origin of superior cerebellar artery
- AcomAC = Anterior communicating artery complex
- AcomAC aneurysm= Aneurysm positioned at Anterior communicating artery complex (AcomAC) region, y = present, and n = absent
- Aneurysm elsewhere= Aneurysm positioned elsewhere (other than AcomAC region), y = present, and n = absent
- CBAN = cerebral basal arterial network,
- VB Aneu = vertebro basilar aneurysm, rt= right, lft= left, Dist/dist = distal, BA= basilar artery, Ter= terminal, Dia/dia= diameter
- PCA= posterior cerebral artery, PcomA= posterior communicating artery, AcomA= anterior communicating artery, ICA= internal carotid artery, MCA= middle cerebral artery, ACA= anterior cerebral artery, and SCA= superior cerebellar artery

Frequency Table

Sex

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	f	78	53.8	53.8	53.8
	m	67	46.2	46.2	100.0
	Total	145	100.0	100.0	

AcomAC An = aneurysms at AcomAC junction, y=yes and n=no

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	n	118	81.4	81.4	81.4
	y	27	18.6	18.6	100.0
	Total	145	100.0	100.0	

rt ICA Aneurysm

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	n	131	90.3	90.3	90.3
	y	14	9.7	9.7	100.0
	Total	145	100.0	100.0	

rt MCA Aneurysm

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	n	113	77.9	77.9	77.9
	y	32	22.1	22.1	100.0
	Total	145	100.0	100.0	

lft ICA Aneurysm

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	n	137	94.5	94.5	94.5
	y	8	5.5	5.5	100.0
	Total	145	100.0	100.0	

lft MCA Aneurysm

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	**n**	121	83.4	83.4	83.4
	y	24	16.6	16.6	100.0
	Total	145	100.0	100.0	

vertebro basilar aneurysm

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	**n**	137	94.5	94.5	94.5
	y	8	5.5	5.5	100.0
	Total	145	100.0	100.0	

Spearman's rho Correlations

Correlations

			RsRtVA dis = relative size of right vertebral artery distal internal diameter	RsLftVA dis = relative size left vertebral artery distal internal diameter	RsBA= relative size of terminal basilar artery just proximal to SCA	RsRt P2 = relative size of proximal right 2nd part of posterior cerebral artery (P2) internal diameter	RsLft P2 = relative size of proximal left 2nd part of posterior cerebral artery (P2) internal diameter	RsRtPcoA mid dia = relative size of right posterior communicating artery external diameter around the mid-point	RsLftPcoA mid dia = relative size of left posterior communicating artery external diameter around the mid-point	RsRt IntCA = relative size of right internal carotid arterial internal diameter at the dorsum sellae level
Spearman's rho	RsRtVA dis = relative size of right vertebral artery distal internal diameter	Correlation Coefficient	1.000	-.235**	.172*	.044	-.129	-.108	-.059	-.011
		Sig. (2-tailed)	.	.005	.039	.597	.122	.196	.478	.894
		N	145	145	145	145	145	145	145	145
	RsLftVA dis = relative size left vertebral artery distal internal diameter	Correlation Coefficient	-.235**	1.000	.337**	.070	.078	-.379**	-.389**	.050
		Sig. (2-tailed)	.005	.	.000	.401	.351	.000	.000	.550
		N	145	145	145	145	145	145	145	145
	RsBA= relative size of terminal basilar artery proximal to SCA	Correlation Coefficient	.172*	.337**	1.000	.169*	-.017	-.390**	-.447**	-.062
		Sig. (2-tailed)	.039	.000	.	.043	.839	.000	.000	.460
		N	145	145	145	145	145	145	145	145
	RsRt P2 = relative size of proximal right 2nd part of posterior cerebral artery (P2) internal diameter	Correlation Coefficient	.044	.070	.169*	1.000	.357**	-.350**	-.286**	-.066
		Sig. (2-tailed)	.597	.401	.043	.	.000	.000	.000	.431
		N	145	145	145	145	145	145	145	145
	RsLft P2 = relative size of	Correlation Coefficient	-.129	.078	-.017	.357**	1.000	-.206*	-.140	-.150

	proximal left	Sig. (2-tailed)	.122	.351	.839	.000	.	.013	.093	.072
	2nd part of	N	145	145	145	145	145	145	145	145
	posterior									
	cerebral artery									
	(P2) internal									
	diameter									
	RsRtPcomA mid	Correlation	-.108	-.379**	-.390**	-.350**	-.206*	1.000	.456**	-.170*
	dia = relative	Coefficient								
	size of right	Sig. (2-tailed)	.196	.000	.000	.000	.013	.	.000	.041
	posterior	N	145	145	145	145	145	145	145	145
	communicating									
	artery internal									
	diameter around									
	the mid point									
	RsLftPcomA	Correlation	-.059	-.389**	-.447**	-.286**	-.140	.456**	1.000	-.277**
	mid dia =	Coefficient								
	relative size of	Sig. (2-tailed)	.478	.000	.000	.000	.093	.000	.	.001
	left posterior	N	145	145	145	145	145	145	145	145
	communicating									
	artery internal									
	diameter around									
	the mid point									
	RsRt IntCA =	Correlation	-.011	.050	-.062	-.066	-.150	-.170*	-.277**	1.000
	relative size of	Coefficient								
	right internal	Sig. (2-tailed)	.894	.550	.460	.431	.072	.041	.001	.
	carotid arterial	N	145	145	145	145	145	145	145	145
	internal diameter									
	at the dorsum									
	sellae level									
	RsLft IntCA =	Correlation	-.018	-.014	.002	.198*	-.132	-.225**	-.160	.462**
	relative size of	Coefficient								
	left internal	Sig. (2-tailed)	.826	.868	.981	.017	.114	.006	.055	.000
	carotid arterial	N	145	145	145	145	145	145	145	145
	internal diameter									
	at the dorsum									
	sellae level									
	RsRt A2 =	Correlation	-.162	.114	-.152	-.074	-.170*	.002	-.068	-.016
	relative size of	Coefficient								
	proximal right	Sig. (2-tailed)	.052	.173	.069	.380	.041	.979	.417	.847
	2nd part of	N	145	145	145	145	145	145	145	145
	anterior cerebral									
	artery (A2)									
	internal diameter									

RsLft A2 = relative size of proximal left 2nd part of anterior cerebral artery (A2) internal diameter	Correlation Coefficient	-.181*	.162	.006	-.014	-.031	-.154	-.230**	.034
	Sig. (2-tailed)	.029	.051	.941	.865	.713	.065	.005	.684
	N	145	145	145	145	145	145	145	145
RsAComA mid dia = relative size of anterior communicating artery internal diameter around mid-point	Correlation Coefficient	-.264**	-.061	-.059	-.184*	-.086	.151	.112	-.221*
	Sig. (2-tailed)	.003	.492	.508	.037	.335	.088	.209	.012
	N	128	128	128	128	128	128	128	128
RsRt M1 = relative size of proximal right 1st part of middle cerebral artery (M1) internal diameter	Correlation Coefficient	-.185*	-.074	-.040	.206*	.165*	-.203*	-.205*	.126
	Sig. (2-tailed)	.026	.376	.636	.013	.047	.014	.013	.131
	N	145	145	145	145	145	145	145	145
RsLft M1 = relative size of proximal left 1st part of middle cerebral artery (M1) internal diameter	Correlation Coefficient	-.139	.023	-.026	.194*	.021	-.296**	-.198*	.155
	Sig. (2-tailed)	.096	.782	.756	.019	.805	.000	.017	.062
	N	145	145	145	145	145	145	145	145
RsRt P1 = relative size of proximal right first segment of posterior cerebral artery (PCA) internal diameter taken at mid-point	Correlation Coefficient	.107	.152	.245*	.234*	.301**	-.600**	-.315**	-.164
	Sig. (2-tailed)	.295	.134	.015	.020	.003	.000	.002	.107
	N	98	98	98	98	98	98	98	98
RsLft P1 = relative size of proximal left	Correlation Coefficient	.015	.290**	.293**	.168	.191	-.388**	-.639**	.060
	Sig. (2-tailed)	.883	.004	.003	.098	.059	.000	.000	.554

	first segment of posterior cerebral artery (PCA) internal diameter taken at mid-point	N	98	98	98	98	98	98	98	98
	RsRt A1 = relative size of proximal right	Correlation Coefficient	-.115	-.029	-.008	.060	.222**	-.326**	-.043	-.037
		Sig. (2-tailed)	.169	.729	.922	.470	.007	.000	.604	.655
	1st part of anterior cerebral artery (A1) internal diameter	N	145	145	145	145	145	145	145	145
	RsLft A1 = relative size of proximal left 1st part of anterior cerebral artery (A1) internal diameter	Correlation Coefficient	-.176*	-.087	.026	.088	.044	-.143	-.233**	.048
		Sig. (2-tailed)	.034	.300	.754	.290	.599	.086	.005	.568
		N	145	145	145	145	145	145	145	145

Correlations

			RsLft IntCA = relative size of left internal carotid arterial internal diameter at the dorsum sellae level	RsRt A2 = relative size of proximal right 2nd part of anterior cerebral artery (A2) internal diameter	RsLft A2 = relative size of proximal left 2nd part of anterior cerebral artery (A2) internal diameter	RsACom A mid dia = relative size of anterior communicating artery internal diameter around mid-point	RsRt M1 = relative size of proximal right 1st part of middle cerebral artery (M1) internal diameter	RsLft M1 = relative size of proximal left 1st part of middle cerebral artery (M1) internal diameter	RsRt P1 = relative size of proximal right 1st part of posterior cerebral artery (P1) internal diameter taken at midpoint	RsLft P1 = relative size of proximal left 1st part of posterior cerebral artery (P1) internal diameter taken at midpoint
Spearman's rho	RsRtVA dis = relative size of right vertebral artery distal internal diameter	Correlation Coefficient	-.018	-.162	-.181*	-.264**	-.185*	-.139	.107	.015
		Sig. (2-tailed)	.826	.052	.029	.003	.026	.096	.295	.883
		N	145	145	145	128	145	145	98	98
	RsLftVA dis = relative size left	Correlation Coefficient	-.014	.114	.162	-.061	-.074	.023	.152	.290**

vertebral artery distal internal diameter	Sig. (2-tailed)	.868	.173	.051	.492	.376	.782	.134	.004
	N	145	145	145	128	145	145	98	98
RsBA= relative size of terminal basilar artery, proximal to the origin of SCA	Correlation Coefficient	.002	-.152	.006	-.059	-.040	-.026	.245*	.293**
	Sig. (2-tailed)	.981	.069	.941	.508	.636	.756	.015	.003
	N	145	145	145	128	145	145	98	98
RsRt P2 = relative size of proximal right 2nd part of posterior cerebral artery (P2) internal diameter	Correlation Coefficient	.198*	-.074	-.014	-.184*	.206*	.194*	.234*	.168
	Sig. (2-tailed)	.017	.380	.865	.037	.013	.019	.020	.098
	N	145	145	145	128	145	145	98	98
RsLft P2 = relative size of proximal left 2nd part of posterior cerebral artery (P2) internal diameter	Correlation Coefficient	-.132	-.170*	-.031	-.086	.165*	.021	.301**	.191
	Sig. (2-tailed)	.114	.041	.713	.335	.047	.805	.003	.059
	N	145	145	145	128	145	145	98	98
RsRtPcomA mid dia = relative size of right posterior communicating artery internal diameter around the mid point	Correlation Coefficient	-.225**	.002	-.154	.151	-.203*	-.296**	-.600**	-.388**
	Sig. (2-tailed)	.006	.979	.065	.088	.014	.000	.000	.000
	N	145	145	145	128	145	145	98	98
RsLftPcomA mid dia = relative size of left posterior communicating artery internal diameter around the mid point	Correlation Coefficient	-.160	-.068	-.230**	.112	-.205*	-.198*	-.315**	-.639**
	Sig. (2-tailed)	.055	.417	.005	.209	.013	.017	.002	.000
	N	145	145	145	128	145	145	98	98
RsRt IntCA = relative size of right internal	Correlation Coefficient	.462**	-.016	.034	-.221*	.126	.155	-.164	.060
	Sig. (2-tailed)	.000	.847	.684	.012	.131	.062	.107	.554

	carotid arterial internal diameter at the dorsum sellae level	N	145	145	145	128	145	145	98	98
	RsLft IntCA = relative size of left internal carotid arterial internal diameter at the dorsum sellae level	Correlation Coefficient	1.000	-.139	-.024	-.435**	.100	.218**	-.088	-.052
		Sig. (2-tailed)	.	.094	.776	.000	.231	.008	.387	.612
		N	145	145	145	128	145	145	98	98
	RsRt A2 = relative size of proximal right 2nd part of anterior cerebral artery (A2) internal diameter	Correlation Coefficient	-.139	1.000	.579**	.173	-.071	-.030	-.134	-.156
		Sig. (2-tailed)	.094	.	.000	.051	.393	.720	.188	.126
		N	145	145	145	128	145	145	98	98
	RsLft A2 = relative size of proximal left 2nd part of anterior cerebral artery (A2) internal diameter	Correlation Coefficient	-.024	.579**	1.000	-.009	-.041	.061	-.054	.017
		Sig. (2-tailed)	.776	.000	.	.917	.624	.465	.598	.867
		N	145	145	145	128	145	145	98	98
	RsAComA mid dia = relative size of anterior communicating artery internal diameter around mid-point	Correlation Coefficient	-.435**	.173	-.009	1.000	-.050	-.178*	-.159	-.237*
		Sig. (2-tailed)	.000	.051	.917	.	.578	.045	.156	.033
		N	128	128	128	128	128	128	81	81
	RsRt M1 = relative size of proximal right 1st part of middle cerebral artery (M1) internal diameter	Correlation Coefficient	.100	-.071	-.041	-.050	1.000	.521**	.060	.012
		Sig. (2-tailed)	.231	.393	.624	.578	.	.000	.558	.910
		N	145	145	145	128	145	145	98	98
	RsLft M1 = relative size of proximal left 1st	Correlation Coefficient	.218**	-.030	.061	-.178*	.521**	1.000	.031	.114
		Sig. (2-tailed)	.008	.720	.465	.045	.000	.	.764	.262

	part of middle cerebral artery (M1) internal diameter	N	145	145	145	128	145	145	98	98
	RsRt P1 = relative size of proximal right 1st part of posterior cerebral artery (P1) internal diameter taken at midpoint	Correlation Coefficient	-.088	-.134	-.054	-.159	.060	.031	1.000	.352**
		Sig. (2-tailed)	.387	.188	.598	.156	.558	.764	.	.000
		N	98	98	98	81	98	98	98	98
	RsLft P1 = relative size of proximal left 1st part of posterior cerebral artery (P1) internal diameter taken at midpoint	Correlation Coefficient	-.052	-.156	.017	-.237*	.012	.114	.352**	1.000
		Sig. (2-tailed)	.612	.126	.867	.033	.910	.262	.000	.
		N	98	98	98	81	98	98	98	98
	RsRt A1 = relative size of proximal right 1st part of anterior cerebral artery (A1) internal diameter	Correlation Coefficient	-.056	.026	.071	-.200*	.180*	.137	.164	.053
		Sig. (2-tailed)	.501	.755	.397	.024	.031	.101	.106	.605
		N	145	145	145	128	145	145	98	98
	RsLft A1 = relative size of proximal left 1st part of anterior cerebral artery (A1) internal diameter	Correlation Coefficient	.248**	-.073	.129	-.143	.164*	.102	.029	.222*
		Sig. (2-tailed)	.003	.383	.121	.107	.049	.221	.777	.028
		N	145	145	145	128	145	145	98	98

Correlations

		RsRt A1 = relative size of proximal right 1st part of anterior cerebral artery (A1) internal diameter	RsLft A1 = relative size of proximal left 1st part of anterior cerebral artery (A1) internal diameter
RsRt A1 = relative size of proximal right 1st part of anterior cerebral artery (A1) internal diameter	Correlation Coefficient	1.000	.222*
	Sig. (2-tailed)	.	.028
	N	98	98
RsLft A1 = relative size of proximal left 1st part of anterior cerebral artery (A1) internal diameter	Correlation Coefficient	.222*	1.000
	Sig. (2-tailed)	.028	.
	N	98	98

Spearman's rho	RsRtVA dis = relative size of right vertebral artery distal internal diameter	Correlation Coefficient	-.115	-.176*
		Sig. (2-tailed)	.169	.034
		N	145	145
	RsLftVA dis = relative size left vertebral artery distal internal diameter	Correlation Coefficient	-.029	-.087
		Sig. (2-tailed)	.729	.300
		N	145	145
	RsBA= relative size of terminal basilar artery, internal diameter measured proximal to the SCA	Correlation Coefficient	-.008	.026
		Sig. (2-tailed)	.922	.754
		N	145	145
	RsRt P2 = relative size of proximal right 2nd part of posterior cerebral artery (P2) internal diameter	Correlation Coefficient	.060	.088
		Sig. (2-tailed)	.470	.290
		N	145	145
	RsLft P2 = relative size of proximal left 2nd part of posterior cerebral artery (P2) internal diameter	Correlation Coefficient	.222**	.044
		Sig. (2-tailed)	.007	.599
		N	145	145
	RsRtPcomA mid dia = relative size of right posterior communicating artery internal diameter at the mid point	Correlation Coefficient	-.326**	-.143
		Sig. (2-tailed)	.000	.086
		N	145	145
	RsLftPcomA mid dia = relative size of left posterior communicating artery internal diameter at the mid point	Correlation Coefficient	-.043	-.233**
		Sig. (2-tailed)	.604	.005
		N	145	145
	RsRt IntCA = relative size of right internal carotid arterial internal diameter at the dorsum sellae level	Correlation Coefficient	-.037	.048
		Sig. (2-tailed)	.655	.568
		N	145	145
	RsLft IntCA = relative size of left internal carotid arterial internal diameter at the dorsum sellae level	Correlation Coefficient	-.056	.248**
		Sig. (2-tailed)	.501	.003
		N	145	145
	RsRt A2 = relative size of proximal right 2nd part of anterior cerebral artery (A2) internal diameter	Correlation Coefficient	.026	-.073
		Sig. (2-tailed)	.755	.383
		N	145	145
	RsLft A2 = relative size of proximal left 2nd part of anterior cerebral artery (A2) internal diameter	Correlation Coefficient	.071	.129
		Sig. (2-tailed)	.397	.121
		N	145	145
	RsAComA mid dia = relative size of anterior communicating artery internal diameter around mid point	Correlation Coefficient	-.200*	-.143
		Sig. (2-tailed)	.024	.107
		N	128	128
	RsRt M1 = relative size of proximal right 1st part of middle	Correlation Coefficient	.180*	.164*
		Sig. (2-tailed)	.031	.049

cerebral artery (M1) internal diameter	N	145	145
RsLft M1 = relative size of proximal left 1st part of middle cerebral artery (M1) internal diameter	Correlation Coefficient	.137	.102
	Sig. (2-tailed)	.101	.221
	N	145	145
RsRt P1 = relative size of proximal right first segment of posterior cerebral artery (PCA) internal diameter taken at mid-point	Correlation Coefficient	.164	.029
	Sig. (2-tailed)	.106	.777
	N	98	98
RsLft P1 = relative size of proximal left first segment of posterior cerebral artery (PCA) internal diameter taken at mid-point	Correlation Coefficient	.053	.222*
	Sig. (2-tailed)	.605	.028
	N	98	98
RsRt A1 = relative size of proximal right 1st part of anterior cerebral artery (A1) internal diameter	Correlation Coefficient	1.000	.106
	Sig. (2-tailed)	.	.204
	N	145	145
RsLft A1 = relative size of proximal left 1st part of anterior cerebral artery (A1) internal diameter	Correlation Coefficient	.106	1.000
	Sig. (2-tailed)	.204	.
	N	145	145

**. Correlation is significant at the 0.01 level (2-tailed).

*. Correlation is significant at the 0.05 level (2-tailed).

Supplementary file 4:

Supplementary file 4 - please refer to the supplementary file 1 as well																
Total CTA cases	CTA cases (patients) with aneurysm	Cases (patients) with single aneurysm	Cases (patients) with no aneurysm	Cases (patients) with multiple aneurysm	AcomAC aneurysm	Total rt ICA aneurysm	Total rt MCA aneurysm	Total Pt ICA aneurysm	Total Pt MCA aneurysm	Total VB aneurysm	Total number of aneurysms in all cases	Total aneurysms in left and right ICA and MCA region	Aneurysms other than right and left ICA and MCA regions	Number of AcomAC aneurysm	Number of left and right PCA aneurysm
165	83	56	82	27	27	16	32	8	24	8	113	78	35	27	0
ACA = anterior cerebral artery, PCA = posterior cerebral artery, A1 = first segment of ACA, P2 = second segment of PCA, P1 = first segment of PCA																
CTA = cerebral computed tomography angiography,																
Chi squared test, p≤0.001																
ICA = cranial segment of internal carotid artery, MCA = middle cerebral artery, PcomA = posterior communicating artery, AcomA = anterior communicating artery																
AcomAC aneurysm= Aneurysm positioned at anterior communicating artery complex (AcomAC) region																
78 out of 113 number of aneurysms were located in the ICA and MCA territories (i.e. 69% of the total aneurysms occurred in ICA an MCA regions), Chi squared test, p≤0.001)																
r or Rt = right, l or Lft = left																

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2 and 3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5
Bias	9	Describe any efforts to address potential sources of bias	*5 and 6*
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5 and 8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	5
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	5
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	5
		(b) Indicate number of participants with missing data for each variable of interest	
Outcome data	15*	Report numbers of outcome events or summary measures	10
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9, 10, and 11
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	11
Discussion			
Key results	18	Summarise key results with reference to study objectives	11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14
Generalisability	21	Discuss the generalisability (external validity) of the study results	13 and 14
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	15

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Prevalence of cerebral aneurysms is related to anatomical variations in cerebral basal arterial network: Investigation of cerebral Computed Tomography Angiography in a neurointerventional unit

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Prevalence of cerebral aneurysms is related to anatomical variations in cerebral basal arterial network: Investigation of cerebral Computed Tomography Angiography in a neurointerventional unit

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Abstract

Objective

The segments of cerebral basal arterial network (CBAN) dampen the peak pressure in blood flowing through these arteries, minimizing the chances of development of cerebral aneurysms. The objective of this research was to find the relationship of intracranial aneurysms to variations of the components of the CBAN.

Design and setting

This is an observational, quantitative, and retrospective research, which used Computed Tomography Angiography (CTA) images.

Participants

Cerebral CTA scans of 145 adult patients of both sexes were studied.

Main outcome measures

Diameters of segments of CBAN were measured in cerebral CTA images and the relative size of each vessel was calculated to standardise for differences in overall arterial sizes among patients. Relationships among sizes of CBAN components were analysed. Presence of aneurysms in different parts of the CBAN was recorded.

Results

Forty-six aneurysms in right internal carotid artery (ICA) and middle cerebral artery (MCA) and 32 aneurysms in left ICA and MCA segments were noted in 42 and 30 patients, respectively. Aneurysms in anterior communicating artery complex (AcomAC) and vertebral-basilar (VB) arterial segments were seen in 27 and 8 patients respectively, while they were not detected in parts of posterior cerebral artery (PCA). The significant ($p<0.0001$) inverse relationships between sizes of posterior communicating artery (PcomA) and the first segment of PCA on both sides indicated that blood inputs to the second part of PCA were similar. Differences in means of the index of arterial size variation for people with aneurysms (0.96) and without aneurysms (0.86) was significant ($p<0.015$). Aneurysms in AcomAC, PCA and VB arteries were less and was proposed that it is due to dampening of peak systolic blood pressures.

Conclusion

Variation in segments of CBAN has been quantified. The peak pressure dampening mechanism in such arterial segments reduces the chances of development of aneurysms.

Key words

subarachnoid haemorrhage; aneurysm; stroke; hemodynamics; cerebral basal arterial network

Funding

None

Strengths and limitations of this study

The relationship of cerebral arterial variations to aneurysms has been quantified for the first time.

A method for standardising size of individual cerebral arteries in relation to the total size of the cerebral arterial system has been introduced.

Parametric and non-parametric statistical methods were used.

Patients from neurointerventional unit are not a random representation of the general population.

A cross-sectional, not a longitudinal study.

Introduction

Cerebral aneurysms are a common cause of haemorrhagic stroke. Diagnosis, management, prediction and prevention of aneurysms are challenging.[1] The middle cerebral artery (MCA) and anterior communicating artery complex (AcomAC) regions have been identified as the most common locations for the occurrence of intracranial aneurysms.[2-5] However, the occurrence of more than two thirds of the total intracranial aneurysms has been reported in relation to internal carotid artery (ICA) territory.[6] Therefore, most of the cerebral aneurysms occur in ICA, MCA and AcomAC territories.[2-6] Pia and Fontana have described posterior cerebral artery (PCA) aneurysms, but the rate of prevalence of cerebral aneurysms in PCA and vertebrobasilar (VB) arterial components is the least.[7-9] The prevalence of intracranial aneurysms of various sizes ranged from 0.2 to 6.8 %, and approximately 6-10/100,000 people suffered from ruptured intracranial aneurysms per year.[4,10] These individuals had poor prognosis and more than a third of the mortalities occurred within a month of the illness.[4,10] Most of the ruptured aneurysms (85.6% cases) were reported to be symptomatic and were from the MCA and AcomAC territories.[4,5] Therefore, studying the relationship of relative sizes of cerebral arteries, sites of location

of cerebral aneurysms and their relationship to the variant segments of CBAN would help to understand the risk factors, and maximise the management of strokes.

The blood flow to the cranial cavity through the four main incoming arteries is asynchronous.[11] The asynchronous blood pressure gradients in the incoming intracranial arteries combine via segments of the CBAN. This maintains a continuous, smooth blood flow through the arteries leaving the arterial network, thus minimises peaks in pressure and reduces the chances of development of cerebral aneurysms. [11,12] However, the blood flowing through the asymmetric and variant segments of CBAN, alters the hemodynamics and peaks in pressure and predisposes to the development of aneurysms in the associated "arterial complexes".[11,13] A relationship for the development of AcomAC aneurysms to the degree of asymmetry between left and right first segments of ACA (A1s) has been shown to occur.[14] The current study, investigated the relationship of locations of intracranial aneurysms to relative sizes of all arterial segments of CBAN and their individual variations. The concept that the mechanisms involved in dampening peak systolic pressures in arterial segments of CBAN, reduce the chances of the development of aneurysms in the ACA and PCA territories, justified the current investigation.

Material and method

Patient and public involvement

The cerebral computed tomography angiography (CCTA) images used in this study were taken from patients who visited the Royal Adelaide Hospital (RAH) for a variety of reasons related to cranial pathologies and screening purposes. Personal information of patients recorded in the data system has not been included in this study. Human Research Ethics Board granted permission (approval number: H2014 -176) to access and use data from the Carestream data registry system (Vue RIS version 11.0.14.35).

Study design

Randomly selected CCTA images of 145 patients archived in the Carestream data registry system at RAH, South Australia between January 2011 and December 2019, were used in the study (age range 18 to 100 years, male = 67, female = 78, mean age = 60.9 years) (Supplementary file 1).The CCTA images with severe artefacts or from patients with severe cerebral vasospasm (i.e. diagnosed by radiologists) were excluded from the study. Missing arterial components or those not seen in the CCTA images (e.g. PcomA and proximal segment of ACA) were considered to have 0.1 mm diameter for the purpose of statistical analysis (Supplementary file 1). The

components of CBAN in some CCTA were not visible due to artefacts and such cases were excluded. Therefore, the number of arterial components measured in CCTA varied to a moderate extent.

Data collection

The position, presence or absence of aneurysms of any sizes were recorded from CCTA of 145 patients based on the diagnosis made by radiologists and clinicians. The position of aneurysms associated with the AcomAC, MCA, ICA, PCA and VB arterial regions were recorded. Some cases had multiple aneurysms. The internal diameters of intracranial segment of ICA at the level of anterior clinoid processes, the first segment of ACA (A1) at the mid-point, PcomAs at the mid-point, the proximal end of the first segment of MCA (M1), anterior communicating artery (AcomA) at the mid-point, the proximal end of the second part of ACA (A2), the first segment of PCA (P1) at the mid-point, the proximal segment of PCA (P2) at the level of dorsum sellae, the distal end of basilar artery just proximal to the origin of superior cerebellar artery (SCA), and the distal vertebral arteries (AV) just proximal to the formation of basilar artery (BA) were measured at right angles to the longitudinal axis of arteries in each individual (Figure 1). The measured internal diameters (in millimetre, mm) were converted into the "relative sizes" of the vessels using the formula, "measured diameter of each vessel / the average size of all the CBAN components measured" (Supplementary file 1) and transferred into the SPSS v. 25 software, before the statistical analysis. The diameters of arteries were converted into "relative sizes" to neutralize the individual differences in sizes of CBAN components among patients.

The diameter of each artery was measured at the narrowest region of the selected site, perpendicular to the long axis of the vessel (Figure 1), to make the measurements consistent across all CCTA images. Furthermore, the CCTA arterial data taken from all the patients were divided into two groups (see below) in order to observe the relationship of aneurysms to the variation in the components of CBAN. This was achieved by analysing the average standard deviation (SD) of arterial sizes in each individual, and coefficients of variation of CBAN components.

Group a: patients with one and more than one cerebral aneurysms; group b: patients without cerebral aneurysm (see columns number 44 to 53 in Supplementary file 1).

Three variables (shown below) characterising each patient's CBAN were constructed for the analysis of the variation of the sizes of all left and right segments of the CBAN (i.e. left and right ICA, first segment of MCA, A1, A2, P1, P2, AcomA, PcomA, and BA):

1. Average sizes (Av) of all CBAN arteries
2. Standard deviation (SD) of sizes of the same CBAN components
3. Coefficient of variation (CV) of CBAN segments = 100*SD/Av

The average size of CBAN, SD and CV of all components of CBAN were calculated to determine the degree of variation in the CBAN segments for each individual patient (columns 23 to 25 in Supplementary file 1)

The accuracy of the measurements was determined by repeating measurements in CCTA of 10 cases, a week after the first measurement (Table 1 and Supplementary file 2). The relative technical error of the measurement (rTEM) was calculated and found to be within the statistically acceptable limits (i.e., ≤10%).

Figure 1 (about here)

Figure 1: Sites of arterial diameter measurement in cerebral angiography images. White lines perpendicular to the long axes of vessels show the measurement sites and white arrows depict the components of cerebral basal arterial network (CBAN). (a) = axial image showing the sites of measurement, (b) = coronal image showing the sites of measurement and location of aneurysms, (c) = coronal angiography showing the sites of vessel measurement, (d) = digital subtraction angiography showing the sites of vessel measurement. ACA = anterior cerebral artery, MCA = middle cerebral artery, ICA = cranial component of internal carotid artery, PCA = posterior cerebral artery, A1 of ACA = the first segment of ACA, A2 of ACA = the second segment of ACA, AcomA = anterior communicating artery, PcomA = posterior communicating artery, M1 of MCA = the first segment of middle cerebral artery, P1 of PCA = first segment of PCA, P2 of PCA = second segment of PCA, BA = basilar artery, VA = vertebral artery, AcomACA= AcomA complex aneurysm, and MCAA = MCA aneurysm.

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Table 1: The reliability of the measurements taken in Cerebral Computed Tomography Angiography (CCTA) images.

	rt VA	lft VA	BA	rt P2	lft P2	rt PcomA	lft PcomA	rt ICA	lft ICA	rt A2	lft A2	Aco mA	rt M1	lft M1	rt P1	lft P1	rt A1	lft A1
TEM error	0.025	0.021	0.019	0.018	0.017	0.013	0.014	0.023	0.055	0.020	0.069	0.070	0.020	0.023	0.018	0.017	0.076	0.115
rTem (CV)	0.982	0.767	0.644	0.793	0.697	0.708	0.909	0.533	1.305	0.751	2.783	3.623	0.684	0.805	0.842	0.755	3.732	5.825
R reliability	0.998	0.999	0.999	0.997	0.996	0.999	0.999	0.998	0.988	0.998	0.948	0.971	0.998	0.998	0.999	0.998	0.991	0.982

Reliability, the coefficients of variation (CV) or the relative technical error of cerebral vessel internal diameter measurements (rTEM) and the technical error of measurements (TEM) are presented. Reliability is the correlation among the first measurements and the second measurements taken from the same artery, n = 10. rt = right, lft = left, dia = internal diameter, ACA = anterior cerebral artery, MCA = middle cerebral artery, ICA = cranial component of internal carotid artery, PCA = posterior cerebral artery, A1 = first segment of ACA, PcomA = posterior communicating artery, AcomA = anterior communicating artery, M1 = first segment of MCA, P1 = first segment of PCA, P2 = second segment of PCA, BA = basilar artery, and VA = vertebral artery (Supplementary file 2).

Statistical analysis

This is a cross-sectional observational study. The data were analysed using excel data file and descriptive, parametric and non-parametric statistical methods, independent sample t – test, linear regression, logistic regression, and custom tables from Statistical Package for the Social Sciences (SPSS IBM, version 25) program. The p values less than 0.05 were considered statistically significant (Table 1, Table 2, Table 3, Table 4, Supplementary files 1, 2, 3 and 4).

Findings

The majority of the cerebral aneurysms detected in the current study were in association with bilateral ICA and MCA (columns number 45 to 53 in Supplementary file 1, pages 2-4 in Supplementary file 3, Supplementary file 4, Supplementary table 1 and 2). Statistically strong inverse relationships were found between relative sizes of ipsilateral PcomA, and P1 segments on the right and left sides (Table 2). The relative sizes of right and left PcomA were found to be inversely correlated with the relative size of basilar artery (Table 2 and Supplementary file 3). Furthermore, significant positive correlations were found between relative sizes of left and right cranial ICA, left and right first part of MCA (M1), left and right second part of ACA (A2), and left and right second part of PCA (P2) (Table 2, Supplementary table 1 and page number 4 to 8 in Supplementary file 3). The differences in averages of standard deviation (std. Dev) and Coefficient of variation (CV) analysed by means of logistic regression and independent sample t – test in groups with or without aneurysms were statistically significant (Table 3 and 4). The variation in the sizes of CBAN segments was found to be greater in people with aneurysms compared to those without aneurysms (Table 3, Table 4, and column number 23 to 25 in Supplementary file 1).

Eighty-three patients out of 145 had cerebral aneurysms in various locations (Supplementary tables 1 and 2, columns number 45 to 53 in Supplementary files 1, page 2 in Supplementary files 3). Some individuals had multiple aneurysms, thus a total of 113 aneurysms were found in the 83 patients (Supplementary table 1 and 2, columns number 45 to 53 in Supplementary file 1, and Supplementary file 4). Out of the total number of 113 aneurysms, 32 (28.31%), 14 (12.4%), 24 (21.24%) and 8 (7%) aneurysms were found in right MCA, right ICA, left MCA and left ICA regions respectively. Seventy-eight out of the 113 aneurysms in the 83 patients (i.e. 69% of the total) were in the right and left MCA and ICA regions (Supplementary table 1, columns number 45 to 53 in Supplementary file 1 and page 2 to 4 in Supplementary file 3). Furthermore, 27 aneurysms (23.9% of the total) were in AcomAC regions, one in each of 27 patients (Supplementary table 1 and columns number 45 to 53 in Supplementary file 1). In addition, 8 aneurysms (7% of the total) were located in the VB arterial regions (Supplementary table 1). Ten and 2 patients had bilateral MCA and ICA aneurysms respectively (Supplementary table 1). Out of the 27 patients with AcomAC aneurysms, 19 of them had aneurysms only in the AcomAC regions (Supplementary table 1). Eight patients with AcomAC aneurysms also had coexisting left MCA (n = 4), right MCA (n = 4), and right ICA (n = 4) aneurysms. Out of those eight patients with multiple coexisting aneurysms, one of them had aneurysms in AcomAC, right MCA and left MCA, while another had coexisting aneurysms in AcomAC, right ICA and right MCA (Supplementary table 1). The third patient with

AcomAC aneurysm also had coexisting aneurysms in right ICA and left MCA (Supplementary table 1). Ten cases also had coexisting aneurysms in bilateral MCA territories (Supplementary table 1 and columns 45 to 53 in Supplementary file 1). Out of eight patients with VB aneurysms, one, three, one, and one also had coexisting right ICA, right MCA, left ICA and left MCA aneurysms respectively. No aneurysms were detected at or distal to P2 segments of PCA (column 45 to 53 in Supplementary file 1, Supplementary table 1 and 2).

Table 2: Spearman's rho nonparametric correlation among the relative size of CBAN components.

Correlations - Spearman's rho

		RsBA	RsRt P2	RsLft P2	RsRtPcomA mid dia	RsLftPcomA mid dia	RsRt P1	RsLft P1
RsBA	**Correlation Coefficient**	**1.000**	**.169***	**-.017**	**-.390****	**-.447****	**.245***	**.293****
	Sig. (2-tailed)	.	<.043	.839	<.000	<.000	<.015	<.003
	N	145	145	145	145	145	98	98
RsRt P2	**Correlation Coefficient**	**.169***	**1.000**	**.357****	**-.350****	**-.286****	**.234***	**.168**
	Sig. (2-tailed)	<.043	.	<.000	<.000	<.000	<.020	.098
	N	145	145	145	145	145	98	98
RsLft P2	**Correlation Coefficient**	**-.017**	**.357****	**1.000**	**-.206***	**-.140**	**.301****	**.191**
	Sig. (2-tailed)	.839	<.000	.	<.013	.093	<.003	.059
	N	145	145	145	145	145	98	98
RsRtPcomA mid dia	**Correlation Coefficient**	**-.390****	**-.350****	**-.206***	**1.000**	**.456****	**-.600****	**-.388****
	Sig. (2-tailed)	<.000	<.000	<.013	.	<.000	<.000	<.000
	N	145	145	145	145	145	98	98
RsLftPcomA mid dia	**Correlation Coefficient**	**-.447****	**-.286****	**-.140**	**.456****	**1.000**	**-.315****	**-.639****
	Sig. (2-tailed)	<.000	<.000	.093	<.000	.	<.002	<.000
	N	145	145	145	145	145	98	98

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RsRtP1	**Correlation Coefficient**	**.245***	**.234***	**.301****	**-.600****	**-.315****	**1.000**	**.352****
	Sig. (2-tailed)	<.015	<.020	<.003	<.000	<.002	.	<.000
	N	98	98	98	98	98	98	98
RsLft P1	**Correlation Coefficient**	**.293****	**.168**	**.191**	**-.388****	**-.639****	**.352****	**1.000**
	Sig. (2-tailed)	<.003	.098	.059	<.000	<.000	<.000	.
	N	98	98	98	98	98	98	98

***. Correlation is significant at the <0.05 level (2-tailed), **. Correlation is significant at the <0.01 level (2-tailed).**

Cerebral basal arterial network = CBAN, Rs = relative size, Rt = right, Lft = left, PCA = posterior cerebral artery, PcomA = posterior communicating artery, BA = distal basilar artery, P2 = second part of PCA, PcomA = posterior communicating artery, P1 = first part of PCA, RsBA= relative size of distal basilar artery, RsRt P2 = relative size of right proximal P2, RsLft P2 = relative size of left proximal P2, RsRtPcomA mid dia = relative size of right PcomA at the mid-point, RsLftPcomA mid dia = relative size of left PcomA at mid-point, RsRt P1 = relative size of right P1 at mid-point, RsLft P1 = relative size of left P1 at mid-point.

Table 3: Comparison of average SD and CV of cerebral basal arterial network (CBAN) measurement in patients with and without cerebral aneurysms (Independent sample t – test). Analysis of standard deviation (SD) of CBAN measurement, Coefficient of variation (CV), and an average size of CBAN in mm.

	Standard deviation of CBAN measurement (SD, mm) average (SD)	**Coefficient of variation (CV) average (SD)**	**Size of CBAN (mm) average (SD)**
Patients without cerebral aneurysms (n = 62)	0.86 (0.22)	34.9 (10.0)	2.50 (0.24)
Patients with one or multiple cerebral aneurysms (n = 83)	0.96 (0.23)	38.2 (9.1)	2.52 (0.26)
Significant (2- tailed, p value)	0.015	0.038	0.708

The table 3 shows the variation in the components of CBAN in everyone in relation to the presence or absence of aneurysms. CBAN = cerebral basal arterial network.

Table 4: Comparison of average standard deviation (std. Dev) and Coefficient of variation (CV) of cerebral basal arterial network (CBAN) measurement in patients with and without cerebral aneurysms (using a logistic regression model for the presence of cerebral aneurysms).

Variables	B	Constant	p
CV	0.037	-1.071	<0.040
Std. Dev	1.822	-1.368	<0.017

Cerebral aneurysms = CV. 0.037-1.071, significant $p<0.040$

Cerebral aneurysms = std. Dev. 1.822-1.368, significant $p<0.017$

Discussion

The significant differences in the means of variation measures of segments of CBAN in people with aneurysms and without aneurysms suggest that the size of individual vessels of the CBAN differs within a person who had an aneurysm (Table 3 and 4 and columns number 23 to 26 in Supplementary file 1). Furthermore, the analysis also confirmed that the occurrences of aneurysms did not depend on the average size of the segments of CBAN (columns number 23 to 26 in Supplementary file 1 and Table 3). However, the overall variation in the size of individual segments of CBAN determined the probability of having the cerebral aneurysms (Table 3). Therefore, these statistically significant differences in the variation of segments of CBAN suggested that the minimally variant segments of CBAN served to best equalize the blood pressure preventing the development of cerebral aneurysms (Table 3). Similar distribution patterns of intracranial aneurysms have been described in the literatures.[3,4,6,15] Aneurysms less than 3 mm in diameter could be missed in commonly used CCTA imaging techniques.[16] The findings of the current study, on more than 4 mm in diameter sized ICA aneurysms compared well with Imaizumi and colleagues findings.[6] Approximately, 3% of the general population develop cerebral aneurysms and may not be diagnosed, until they enlarge sufficiently to cause symptoms or rupture.[17] However, more than 70 % of aneurysms detected by Imaizumi and colleagues[6] using advanced imaging technique were ≤3mm in diameter.[16] The current study, collected data from patients with complicated and ruptured aneurysmal cases, who were referred to the Neuro-interventional Centre in RAH for treatment. Imaizumi and colleagues[6]

conducted the study on healthy and asymptomatic adults and detected the right ICA territory as the most common location (78%) for the development intracranial aneurysms. Almost 83% of the detected ICA aneurysms in the latter study were ≤3.9mm in diameter[6], thus individuals with these aneurysms would not have displayed aneurysm related symptoms. The chances for the rupture of an aneurysm is minimal, when the size is ≤4mm in diameter.[2,6] Most of the CCTA images with AcomAC aneurysms (19 cases) in the current study, had no other coexisting aneurysms located elsewhere in the intracranial regions (Supplementary file 1). The frequency of aneurysms was lower in AcomAC and PCA territories in comparison to the aneurysms found in the MCA and ICA territories in the current study and in a study published recently.[6]

The absence of aneurysms elsewhere in 19 out of 27 (i.e., 70.04%) AcomAC aneurysmal cases (Supplementary files 1 and 3) may indicate that the causes of aneurysms were not due to generalised weakness of the CBAN arterial wall, hypertension, smoking and familial reasons. Vrselja and colleagues suggested that the communicating arteries divert the blood flow and dampen the peaks in systolic pressure in the CBAN system to reduce the occurrence of aneurysms.[18] The chances of the development of AcomAC aneurysms have been predicted to be ≥80% when the asymmetric ratio between right and left A1 segments is 1.42 or more (i.e., larger diameter /smaller diameter).[14] Furthermore, the effect of fluctuating peak systolic pressure in causing aneurysms in AcomAC territories would be lower in the presence of symmetrical A1 arterial segments.[14] Therefore, these 19 cases of AcomAC aneurysms could have resulted from the altered haemodynamics caused by the asymmetry between right and left A1 segments.[14]

Fluctuation of peak systolic pressure may contribute to the occurrence and rupture of cerebral aneurysm.[19] In addition, the amount of blood flowing through a MCA had been found to be increased in the presence of the hypoplastic or absent A1 segment or PcomA on that side of CBAN.[20] Therefore, the 8 cases of AcomAC aneurysms that cooccurred with aneurysms elsewhere (i.e. AcomAC aneurysms cooccurred with right ICA, right MCA and left MCA regions) might have been associated with the presence of hypoplastic or absent A1 segments or PcomA (Supplementary file 1). These variations of A1 and PcomA segments would increase the resistance to the outflow of blood from the ICA, thus increase the flow and peak systolic pressure through the MCA. Therefore, the greater incidence (≥85% cases) of cerebral aneurysms found in the ICA and MCA territories, [3,4,15] could be linked to the altered haemodynamic in the presence of variant segments of CBAN.[21-23] A significant amount of wall shear stress has been noticed on the stent placed next to the aneurysmal sac suggesting increased peaks in systolic pressure would result in the development of aneurysm.[24] This indicates that symmetrical A1 segments, and PcomA could act as the flow diverting segments of CBAN and reduce or

dampen the peak systolic pressure in the ICA and MCA reducing the incidence of aneurysms in these regions. The PCA aneurysms are rare.[7,25] The i) significant positive correlations between right and left PcomA, ipsilateral P1 and P2 segments and BA with right and left P1 segments, and ii) inverse correlations between PcomA with ipsilateral and contralateral P1 segments and BA with right and left PcomA (Table 2 and supplementary file 3) indicate that these arterial segments help to balance and maintain optimal blood flow in P2 segments. Thus, the peak systolic pressures may not reach levels that could injure the arterial wall and cause aneurysms in P2 segment and beyond.[26] This is particularly important, because the blood flow in P2 segment is maintained by two inversely correlated ($p \leq 0.01$) ipsilateral PcomA and P1 vessels (Table 2). Thus the prevalence of aneurysms in the P2 segment territory of PCA is zero or minimal (Supplementary file 1 and 3).[7] The peak systolic pressures of the blood flowing via the vertebral arteries would get dissipated in the basilar artery (which is also considered as a communicating artery [27]), and then in P1 before reaching the P2 segment. In a similar way, blood flowing from the ICA is dampened in PcomA before reaching the P2 segments, which ensures the less fluctuating peak systolic pressures in P2 and distal to the P2 segments. Therefore, pressure dampening mechanisms could smoothen the arterial pressure distal to P2 segments and reduce the chances of developing aneurysms in PCA compared to ICA, MCA and AcomAC territories.

In vertebrate brain evolution, brainstem evolved first, whereas the telencephalon (specially the frontal lobes) was a later addition to the brain.[28] Therefore, the arterial supply in the brainstem and the posterior part of telencephalon had more time to be well established. The recently evolved large telencephalon is predominantly supplied by ICA.[29] The anterior part of CBAN evolved along with the telencephalon and has had less evolutionary time to develop, compared to the posterior segments.[28] Thus, the natural selection did not have adequate time to minimise the variations and asymmetries of the anterior segments of the CBAN. Furthermore, a larger blood volume has to flow through the less evolved anterior segments of CBAN to meet the demand of the large telencephalon.[30] Therefore; the chances of development of aneurysms in the arteries supplied by the anterior segments of CBAN are higher compared to the posterior part. Asymmetry between antimere segments of CBAN could result from the mutations of genes involved in the development of cerebral arterial segments (e.g., development of hypoplastic right or left A1 segment of ACA) in the embryo. However, in some, the embryo has the ability to enlarge the collateral segment of a hypoplastic segment of CBAN and maintain adequate blood supply to the affected right or left side of the brain. Establishment of this compensatory blood flow also requires the enlargement of respective communicating arteries (i.e. anterior and posterior communicating arteries, or the basilar artery). Therefore, the brain develops normally and maintains normal

function. However, the increase in blood flow in the enlarged arterial segments, could lead to the formation of aneurysms later in life. Asymmetry between antimere A1 is a good example. In these arterial segments, the risk of development of aneurysms in AcomAC is ≥80%, when the A1 asymmetry ratio remains ≥1.42.[14]

This study was not designed to examine the shape and characteristics of aneurysms, but the focus was on the relationship of the relative size of the blood vessels to the formation of aneurysms in different regions of the brain. Further investigations of cerebral blood flow and the changes in the blood pressure in the presence of asymmetric and variant arteries may help to understand the mechanisms involved in the development of aneurysms. Limitations: The data for this study were obtained from the cases treated at a highly specialised neurointerventional centre, thus the prevalence rate of cerebral aneurysms was higher compared to the general population. It is unethical to expose general population to CTA related radiation purely for research purposes. This study is a pure cross-sectional study, since the repeated CTA from the same patient could not be obtained at different time points. The timeframe of the current study did not allow us to follow up the patients and continue as a longitudinal study.

Conclusion

The number of cerebral aneurysms vary with the sizes of arteries constituting the cerebral basal arterial network. Variation of those arteries is said to affect hemodynamics, thus predisposing to aneurysms. Patients who have asymmetric and variant cerebral arterial segments and communicating arteries in CBAN should be monitored regularly. This finding could be considered as one of the criteria for screening the cerebral aneurysms.

Data sharing statement

Extra data is available by emailing to Arjun.Burlakoti@unisa.edu.au

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None

Author contribution statement

Arjun Burlakoti- conceived the idea, designed the analysis, collected and analysed the data from CCTA, took pictures, recorded videos, contributed in conceptualization, prepared and drafted the manuscript.

Jaliya Kumaratilake- conceived the idea, contributed to the concept, helped in data interpretation, editing and the critical revision of the manuscript and approving the article.

Jamie Taylor- conceived the idea, contributed in collecting and interpreting the data, editing the manuscript, the critical revision of the manuscript and approving the article.

Maciej Henneberg- conceived the idea, helped in statistics, data analysis and interpretation, editing the manuscript, the critical revision of the manuscript and in approving the article.

Conflict of interest statements

There is no conflict of interest with any of the authors.

Ethical Approval Statement

The University of Adelaide, Human Research Ethics Board granted permission to access and use data for this research project (Ethics Approval Number: H2014 -176).

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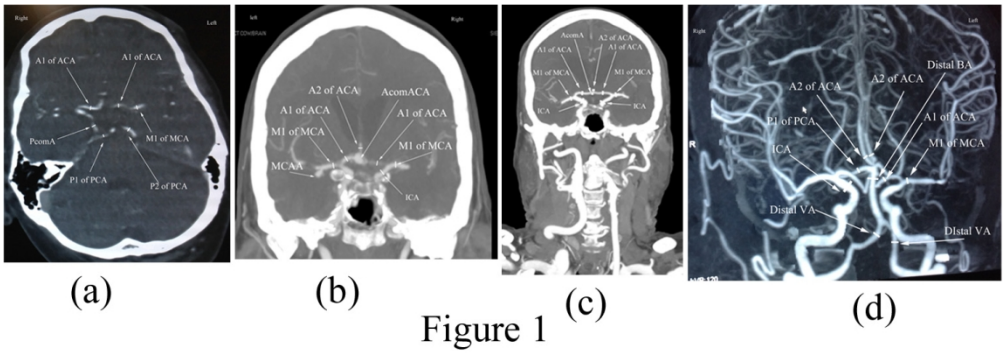


Figure 1

Figure 1: Sites of arterial diameter measurement in cerebral angiography images.
White lines perpendicular to the long axes of vessels show the measurement sites and white arrows depict the components of cerebral basal arterial network (CBAN). (a) = axial image showing the sites of measurement, (b) = coronal image showing the sites of measurement and location of aneurysms, (c) = coronal angiography showing the sites of vessel measurement, (d) = digital subtraction angiography showing the sites of vessel measurement. ACA = anterior cerebral artery, MCA = middle cerebral artery, ICA = cranial component of internal carotid artery, PCA = posterior cerebral artery, A1 of ACA = the first segment of ACA, A2 of ACA = the second segment of ACA, AcomA = anterior communicating artery, PcomA = posterior communicating artery, M1 of MCA = the first segment of middle cerebral artery, P1 of PCA = first segment of PCA, P2 of PCA = second segment of PCA, BA = basilar artery, VA = vertebral artery, AcomACA= AcomA complex aneurysm, and MCAA = MCA aneurysm.

128x45mm (300 x 300 DPI)

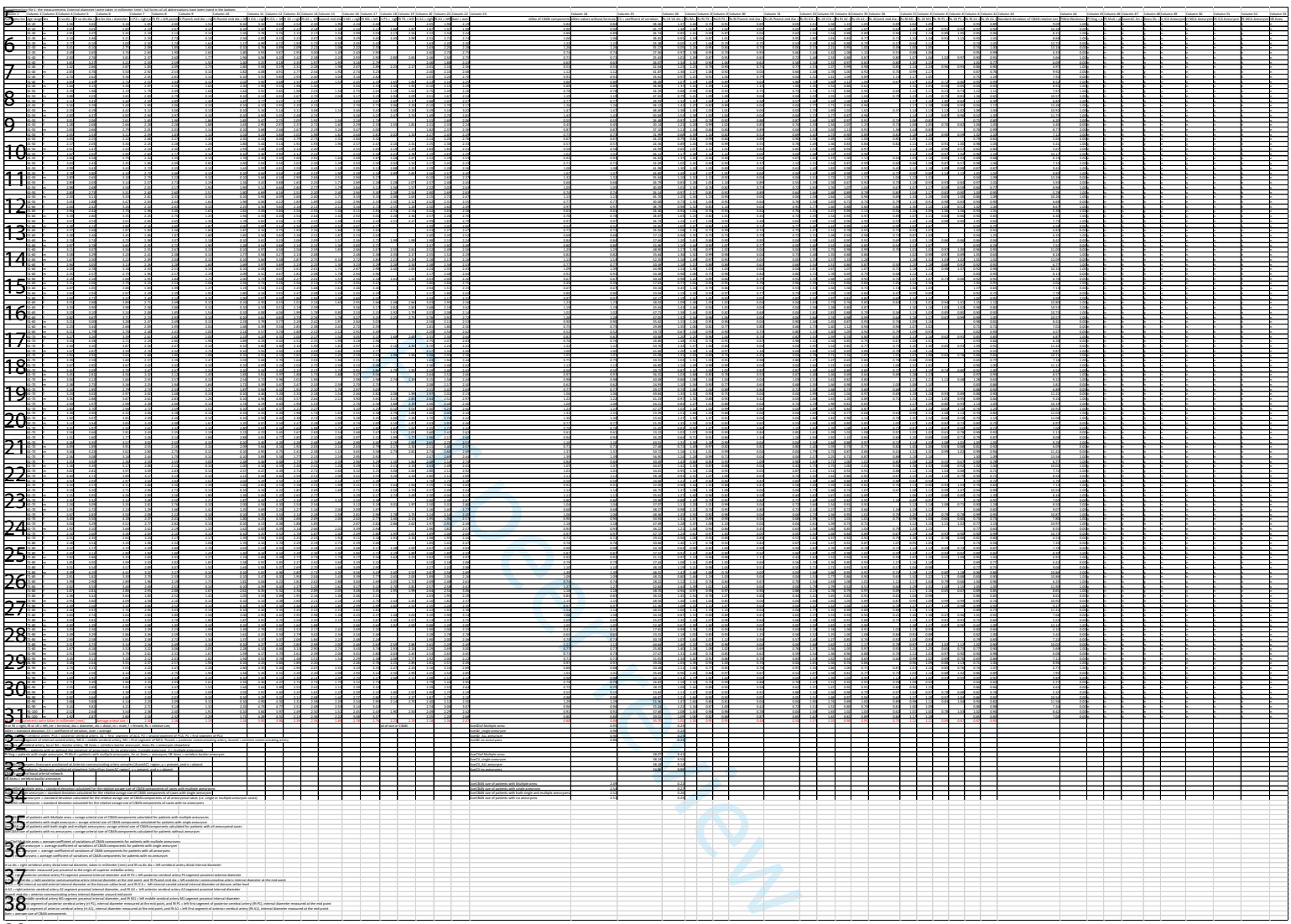
Supplementary Table 1: Anatomical locations of intracranial cerebral aneurysms in the current Cerebral Computed Tomography Angiography scans study (n = 145, age range = 18 to 100 years, female = 79, male = 67). Total 113 aneurysms were recorded in 83 patients. rt = right, lft = left, AcomAC = anterior communicating artery complex, MCA= middle cerebral artery, ICA = internal carotid artery, y = aneurysms present, n = aneurysms absent, MCA = middle cerebral artery, PCA = posterior cerebral artery, VBA = vertebra basilar arteries. P1 = first segment of PCA, and P2 = second segment of PCA.

		Aneurysms at AcomAC		rt ICA Aneurysm		rt MCA Aneurysm		lft ICA Aneurysm		lft MCA Aneurysm		Vertebro basilar aneurysm		PCA aneurysm
		n	y	n	y	n	y	n	y	n	y	n	y	n
		Count	Count	Count	Count	Count	Count	Count	Count	Count	Count	Count	Count	Count
Aneurysms at AcomAC	**n**	118	0	108	10	90	28	110	8	98	20	110	8	118
	y	0	27	23	4	23	4	27	0	23	4	27	0	27
rt ICA Aneurysm	**n**	108	23	131	0	102	29	125	6	108	23	124	7	131
	y	10	4	0	14	11	3	12	2	13	1	13	1	14
rt MCA Aneurysm	**n**	90	23	102	11	113	0	105	8	99	14	108	5	113
	y	28	4	29	3	0	32	32	0	22	10	29	3	32
lft ICA Aneurysm	**n**	110	27	125	12	105	32	137	0	115	22	130	7	137
	y	8	0	6	2	8	0	0	8	6	2	7	1	8
lft MCA Aneurysm	**n**	98	23	108	13	99	22	115	6	121	0	114	7	121
	y	20	4	23	1	14	10	22	2	0	24	23	1	24
Vertebro basilar aneurysm	**n**	110	27	124	13	108	29	130	7	114	23	137	0	137
	y	8	0	7	1	5	3	7	1	7	1	0	8	8
PCA aneurysm	**n**	118	27	131	14	113	32	137	8	121	24	137	8	145

Supplementary Table 2: Average relative sizes of cerebral arteries and aanatomical locations of cerebral aneurysms in the current Cerebral Computed Tomography Angiography scans studies (total cases, n = 145, age range = 18 to 100 years, female = 79, male = 67). Total 113 aneurysms were recorded in 83 patients. VBA = vertebra basilar arteries; ACA = anterior cerebral artery, AcomAC = anterior communicating artery complex; A1 = first segment of ACA; P2 of PCA = second part of PCA; ICA = internal carotid arterial; A2 of ACA = second part of ACA, and M1 of MCA= first part of MCA.

	Aneurysms		Average relative artery size (internal diameter)		Average artery size in mm (internal diameter)	
	Right	**Left**	**Right**	**Left**	**Right**	**Left**
A1 of ACA	27 aneurysms in AcomAC		0.87	0.95	2.36	2.47
ICA	14	8	1.57	1.55	3.9	3.86
M 1 of MCA	32	24	1.12	1.11	2.78	2.76
P2 of PCA	0	0	0.95	0.95	2.36	2.36
A2 of ACA	0	0	0.96	0.95	2.39	2.36
VBA aneurysms		8				

Supplementary file 1:



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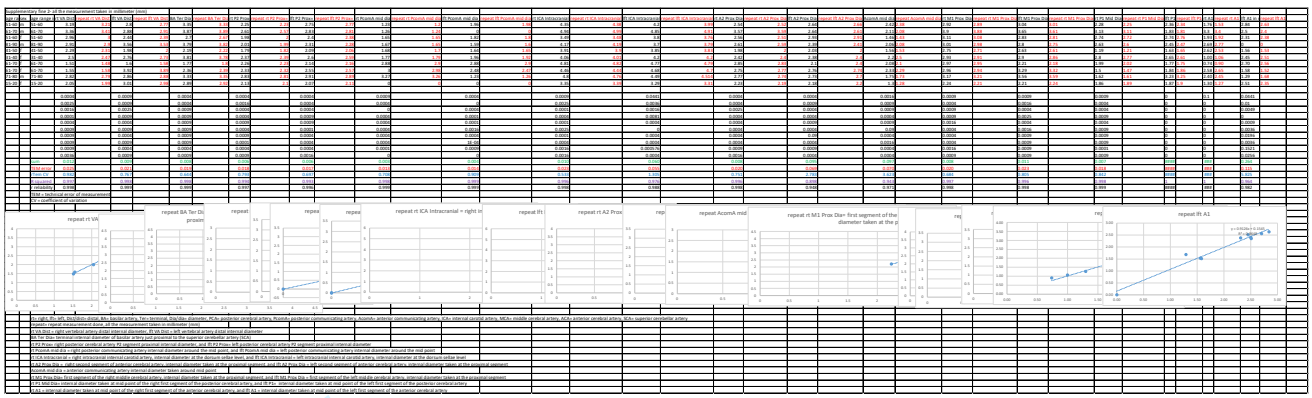

Supplementary file 3

Abbreviations and full forms

- All the measurements were taken in millimetre (mm)
- SCA = superior cerebellar artery
- rt or Rt = right, lft or Lft = left, ter = terminal, dia = diameter, dis = distal, m = male, f = female, Rs = relative size,
- stDev = standard deviation, CV = coefficient of variation, Aver = average
- ACA = anterior cerebral artery, PCA = posterior cerebral artery, A1 = first segment of ACA, A2= second part of ACA, P2 = second segment of PCA, P1 = first segment of PCA
- ICA = internal carotid artery, MCA = middle cerebral artery, M1 = first segment of MCA, PcomA = posterior communicating artery, AcomA = anterior communicating artery
- VA or va = vertebral artery, ba or BA = basilar artery, VB Aneu = vertebro basilar aneurysm, Aneu Els = elsewhere aneurysm
- ba ter dia = diameter measured just proximal to the origin of superior cerebellar artery
- AcomAC = Anterior communicating artery complex
- AcomAC aneurysm= Aneurysm positioned at Anterior communicating artery complex (AcomAC) region, y = present, and n = absent
- Aneurysm elsewhere= Aneurysm positioned elsewhere (other than AcomAC region), y = present, and n = absent
- CBAN = cerebral basal arterial network,
- VB Aneu = vertebro basilar aneurysm, rt= right, lft= left, Dist/dist = distal, BA= basilar artery, Ter= terminal, Dia/dia= diameter
- PCA= posterior cerebral artery, PcomA= posterior communicating artery, AcomA= anterior communicating artery, ICA= internal carotid artery, MCA= middle cerebral artery, ACA= anterior cerebral artery, and SCA= superior cerebellar artery

Frequency Table

Sex

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	f	78	53.8	53.8	53.8
	m	67	46.2	46.2	100.0
	Total	145	100.0	100.0	

AcomAC An = aneurysms at AcomAC junction, y=yes and n=no

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	n	118	81.4	81.4	81.4
	y	27	18.6	18.6	100.0
	Total	145	100.0	100.0	

rt ICA Aneurysm

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	n	131	90.3	90.3	90.3
	y	14	9.7	9.7	100.0
	Total	145	100.0	100.0	

rt MCA Aneurysm

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	n	113	77.9	77.9	77.9
	y	32	22.1	22.1	100.0
	Total	145	100.0	100.0	

lft ICA Aneurysm

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	n	137	94.5	94.5	94.5
	y	8	5.5	5.5	100.0
	Total	145	100.0	100.0	

lft MCA Aneurysm

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	**n**	121	83.4	83.4	83.4
	y	24	16.6	16.6	100.0
	Total	145	100.0	100.0	

vertebro basilar aneurysm

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	**n**	137	94.5	94.5	94.5
	y	8	5.5	5.5	100.0
	Total	145	100.0	100.0	

Spearman's rho Correlations

Correlations

			RsRtVA dis = relative size of right vertebral artery distal internal diameter	RsLftVA dis = relative size left vertebral artery distal internal diameter	RsBA= relative size of terminal basilar artery just proximal to SCA	RsRt P2 = relative size of proximal right 2nd part of posterior cerebral artery (P2) internal diameter	RsLft P2 = relative size of proximal left 2nd part of posterior cerebral artery (P2) internal diameter	RsRtPcoA mid dia = relative size of right posterior communicating artery external diameter around the mid-point	RsLftPcoA mid dia = relative size of left posterior communicating artery external diameter around the mid-point	RsRt IntCA = relative size of right internal carotid arterial internal diameter at the dorsum sellae level
Spearman's rho	RsRtVA dis = relative size of right vertebral artery distal internal diameter	Correlation Coefficient	1.000	-.235**	.172*	.044	-.129	-.108	-.059	-.011
		Sig. (2-tailed)	.	.005	.039	.597	.122	.196	.478	.894
		N	145	145	145	145	145	145	145	145
	RsLftVA dis = relative size left vertebral artery distal internal diameter	Correlation Coefficient	-.235**	1.000	.337**	.070	.078	-.379**	-.389**	.050
		Sig. (2-tailed)	.005	.	.000	.401	.351	.000	.000	.550
		N	145	145	145	145	145	145	145	145
	RsBA= relative size of terminal basilar artery proximal to SCA	Correlation Coefficient	.172*	.337**	1.000	.169*	-.017	-.390**	-.447**	-.062
		Sig. (2-tailed)	.039	.000	.	.043	.839	.000	.000	.460
		N	145	145	145	145	145	145	145	145
	RsRt P2 = relative size of proximal right 2nd part of posterior cerebral artery (P2) internal diameter	Correlation Coefficient	.044	.070	.169*	1.000	.357**	-.350**	-.286**	-.066
		Sig. (2-tailed)	.597	.401	.043	.	.000	.000	.000	.431
		N	145	145	145	145	145	145	145	145
	RsLft P2 = relative size of	Correlation Coefficient	-.129	.078	-.017	.357**	1.000	-.206*	-.140	-.150

	proximal left	Sig. (2-tailed)	.122	.351	.839	.000	.	.013	.093	.072
	2nd part of	N	145	145	145	145	145	145	145	145
	posterior									
	cerebral artery									
	(P2) internal									
	diameter									
	RsRtPcomA mid	Correlation	-.108	-.379**	-.390**	-.350**	-.206*	1.000	.456**	-.170*
	dia = relative	Coefficient								
	size of right	Sig. (2-tailed)	.196	.000	.000	.000	.013	.	.000	.041
	posterior	N	145	145	145	145	145	145	145	145
	communicating									
	artery internal									
	diameter around									
	the mid point									
	RsLftPcomA	Correlation	-.059	-.389**	-.447**	-.286**	-.140	.456**	1.000	-.277**
	mid dia =	Coefficient								
	relative size of	Sig. (2-tailed)	.478	.000	.000	.000	.093	.000	.	.001
	left posterior	N	145	145	145	145	145	145	145	145
	communicating									
	artery internal									
	diameter around									
	the mid point									
	RsRt IntCA =	Correlation	-.011	.050	-.062	-.066	-.150	-.170*	-.277**	1.000
	relative size of	Coefficient								
	right internal	Sig. (2-tailed)	.894	.550	.460	.431	.072	.041	.001	.
	carotid arterial	N	145	145	145	145	145	145	145	145
	internal diameter									
	at the dorsum									
	sellae level									
	RsLft IntCA =	Correlation	-.018	-.014	.002	.198*	-.132	-.225**	-.160	.462**
	relative size of	Coefficient								
	left internal	Sig. (2-tailed)	.826	.868	.981	.017	.114	.006	.055	.000
	carotid arterial	N	145	145	145	145	145	145	145	145
	internal diameter									
	at the dorsum									
	sellae level									
	RsRt A2 =	Correlation	-.162	.114	-.152	-.074	-.170*	.002	-.068	-.016
	relative size of	Coefficient								
	proximal right	Sig. (2-tailed)	.052	.173	.069	.380	.041	.979	.417	.847
	2nd part of	N	145	145	145	145	145	145	145	145
	anterior cerebral									
	artery (A2)									
	internal diameter									

RsLft A2 = relative size of proximal left 2nd part of anterior cerebral artery (A2) internal diameter	Correlation Coefficient	-.181*	.162	.006	-.014	-.031	-.154	-.230**	.034
	Sig. (2-tailed)	.029	.051	.941	.865	.713	.065	.005	.684
	N	145	145	145	145	145	145	145	145
RsAComA mid dia = relative size of anterior communicating artery internal diameter around mid-point	Correlation Coefficient	-.264**	-.061	-.059	-.184*	-.086	.151	.112	-.221*
	Sig. (2-tailed)	.003	.492	.508	.037	.335	.088	.209	.012
	N	128	128	128	128	128	128	128	128
RsRt M1 = relative size of proximal right 1st part of middle cerebral artery (M1) internal diameter	Correlation Coefficient	-.185*	-.074	-.040	.206*	.165*	-.203*	-.205*	.126
	Sig. (2-tailed)	.026	.376	.636	.013	.047	.014	.013	.131
	N	145	145	145	145	145	145	145	145
RsLft M1 = relative size of proximal left 1st part of middle cerebral artery (M1) internal diameter	Correlation Coefficient	-.139	.023	-.026	.194*	.021	-.296**	-.198*	.155
	Sig. (2-tailed)	.096	.782	.756	.019	.805	.000	.017	.062
	N	145	145	145	145	145	145	145	145
RsRt P1 = relative size of proximal right first segment of posterior cerebral artery (PCA) internal diameter taken at mid-point	Correlation Coefficient	.107	.152	.245*	.234*	.301**	-.600**	-.315**	-.164
	Sig. (2-tailed)	.295	.134	.015	.020	.003	.000	.002	.107
	N	98	98	98	98	98	98	98	98
RsLft P1 = relative size of proximal left	Correlation Coefficient	.015	.290**	.293**	.168	.191	-.388**	-.639**	.060
	Sig. (2-tailed)	.883	.004	.003	.098	.059	.000	.000	.554

	first segment of posterior cerebral artery (PCA) internal diameter taken at mid-point	N	98	98	98	98	98	98	98	98
	RsRt A1 = relative size of proximal right	Correlation Coefficient	-.115	-.029	-.008	.060	.222**	-.326**	-.043	-.037
		Sig. (2-tailed)	.169	.729	.922	.470	.007	.000	.604	.655
	1st part of anterior cerebral artery (A1) internal diameter	N	145	145	145	145	145	145	145	145
	RsLft A1 = relative size of proximal left 1st part of anterior cerebral artery (A1) internal diameter	Correlation Coefficient	-.176*	-.087	.026	.088	.044	-.143	-.233**	.048
		Sig. (2-tailed)	.034	.300	.754	.290	.599	.086	.005	.568
		N	145	145	145	145	145	145	145	145

Correlations

			RsLft IntCA = relative size of left internal carotid arterial internal diameter at the dorsum sellae level	RsRt A2 = relative size of proximal right 2nd part of anterior cerebral artery (A2) internal diameter	RsLft A2 = relative size of proximal left 2nd part of anterior cerebral artery (A2) internal diameter	RsACom A mid dia = relative size of anterior communicating artery internal diameter around mid-point	RsRt M1 = relative size of proximal right 1st part of middle cerebral artery (M1) internal diameter	RsLft M1 = relative size of proximal left 1st part of middle cerebral artery (M1) internal diameter	RsRt P1 = relative size of proximal right 1st part of posterior cerebral artery (P1) internal diameter taken at midpoint	RsLft P1 = relative size of proximal left 1st part of posterior cerebral artery (P1) internal diameter taken at midpoint
Spearman's rho	RsRtVA dis = relative size of right vertebral artery distal internal diameter	Correlation Coefficient	-.018	-.162	-.181*	-.264**	-.185*	-.139	.107	.015
		Sig. (2-tailed)	.826	.052	.029	.003	.026	.096	.295	.883
		N	145	145	145	128	145	145	98	98
	RsLftVA dis = relative size left	Correlation Coefficient	-.014	.114	.162	-.061	-.074	.023	.152	.290**

vertebral artery distal internal diameter	Sig. (2-tailed)	.868	.173	.051	.492	.376	.782	.134	.004
	N	145	145	145	128	145	145	98	98
RsBA= relative size of terminal basilar artery, proximal to the origin of SCA	Correlation Coefficient	.002	-.152	.006	-.059	-.040	-.026	.245*	.293**
	Sig. (2-tailed)	.981	.069	.941	.508	.636	.756	.015	.003
	N	145	145	145	128	145	145	98	98
RsRt P2 = relative size of proximal right 2nd part of posterior cerebral artery (P2) internal diameter	Correlation Coefficient	.198*	-.074	-.014	-.184*	.206*	.194*	.234*	.168
	Sig. (2-tailed)	.017	.380	.865	.037	.013	.019	.020	.098
	N	145	145	145	128	145	145	98	98
RsLft P2 = relative size of proximal left 2nd part of posterior cerebral artery (P2) internal diameter	Correlation Coefficient	-.132	-.170*	-.031	-.086	.165*	.021	.301**	.191
	Sig. (2-tailed)	.114	.041	.713	.335	.047	.805	.003	.059
	N	145	145	145	128	145	145	98	98
RsRtPcomA mid dia = relative size of right posterior communicating artery internal diameter around the mid point	Correlation Coefficient	-.225**	.002	-.154	.151	-.203*	-.296**	-.600**	-.388**
	Sig. (2-tailed)	.006	.979	.065	.088	.014	.000	.000	.000
	N	145	145	145	128	145	145	98	98
RsLftPcomA mid dia = relative size of left posterior communicating artery internal diameter around the mid point	Correlation Coefficient	-.160	-.068	-.230**	.112	-.205*	-.198*	-.315**	-.639**
	Sig. (2-tailed)	.055	.417	.005	.209	.013	.017	.002	.000
	N	145	145	145	128	145	145	98	98
RsRt IntCA = relative size of right internal	Correlation Coefficient	.462**	-.016	.034	-.221*	.126	.155	-.164	.060
	Sig. (2-tailed)	.000	.847	.684	.012	.131	.062	.107	.554

	carotid arterial internal diameter at the dorsum sellae level	N	145	145	145	128	145	145	98	98
	RsLft IntCA = relative size of left internal carotid arterial internal diameter at the dorsum sellae level	Correlation Coefficient	1.000	-.139	-.024	-.435**	.100	.218**	-.088	-.052
		Sig. (2-tailed)	.	.094	.776	.000	.231	.008	.387	.612
		N	145	145	145	128	145	145	98	98
	RsRt A2 = relative size of proximal right 2nd part of anterior cerebral artery (A2) internal diameter	Correlation Coefficient	-.139	1.000	.579**	.173	-.071	-.030	-.134	-.156
		Sig. (2-tailed)	.094	.	.000	.051	.393	.720	.188	.126
		N	145	145	145	128	145	145	98	98
	RsLft A2 = relative size of proximal left 2nd part of anterior cerebral artery (A2) internal diameter	Correlation Coefficient	-.024	.579**	1.000	-.009	-.041	.061	-.054	.017
		Sig. (2-tailed)	.776	.000	.	.917	.624	.465	.598	.867
		N	145	145	145	128	145	145	98	98
	RsAComA mid dia = relative size of anterior communicating artery internal diameter around mid-point	Correlation Coefficient	-.435**	.173	-.009	1.000	-.050	-.178*	-.159	-.237*
		Sig. (2-tailed)	.000	.051	.917	.	.578	.045	.156	.033
		N	128	128	128	128	128	128	81	81
	RsRt M1 = relative size of proximal right 1st part of middle cerebral artery (M1) internal diameter	Correlation Coefficient	.100	-.071	-.041	-.050	1.000	.521**	.060	.012
		Sig. (2-tailed)	.231	.393	.624	.578	.	.000	.558	.910
		N	145	145	145	128	145	145	98	98
	RsLft M1 = relative size of proximal left 1st	Correlation Coefficient	.218**	-.030	.061	-.178*	.521**	1.000	.031	.114
		Sig. (2-tailed)	.008	.720	.465	.045	.000	.	.764	.262

	part of middle cerebral artery (M1) internal diameter	N	145	145	145	128	145	145	98	98
	RsRt P1 = relative size of proximal right 1st part of posterior cerebral artery (P1) internal diameter taken at midpoint	Correlation Coefficient	-.088	-.134	-.054	-.159	.060	.031	1.000	.352**
		Sig. (2-tailed)	.387	.188	.598	.156	.558	.764	.	.000
		N	98	98	98	81	98	98	98	98
	RsLft P1 = relative size of proximal left 1st part of posterior cerebral artery (P1) internal diameter taken at midpoint	Correlation Coefficient	-.052	-.156	.017	-.237*	.012	.114	.352**	1.000
		Sig. (2-tailed)	.612	.126	.867	.033	.910	.262	.000	.
		N	98	98	98	81	98	98	98	98
	RsRt A1 = relative size of proximal right 1st part of anterior cerebral artery (A1) internal diameter	Correlation Coefficient	-.056	.026	.071	-.200*	.180*	.137	.164	.053
		Sig. (2-tailed)	.501	.755	.397	.024	.031	.101	.106	.605
		N	145	145	145	128	145	145	98	98
	RsLft A1 = relative size of proximal left 1st part of anterior cerebral artery (A1) internal diameter	Correlation Coefficient	.248**	-.073	.129	-.143	.164*	.102	.029	.222*
		Sig. (2-tailed)	.003	.383	.121	.107	.049	.221	.777	.028
		N	145	145	145	128	145	145	98	98

Correlations

		RsRt A1 = relative size of proximal right 1st part of anterior cerebral artery (A1) internal diameter	RsLft A1 = relative size of proximal left 1st part of anterior cerebral artery (A1) internal diameter
RsRt A1 = relative size of proximal right 1st part of anterior cerebral artery (A1) internal diameter	Correlation Coefficient	1.000	.222*
	Sig. (2-tailed)	.	.028
	N	98	98
RsLft A1 = relative size of proximal left 1st part of anterior cerebral artery (A1) internal diameter	Correlation Coefficient	.222*	1.000
	Sig. (2-tailed)	.028	.
	N	98	98

Spearman's rho	RsRtVA dis = relative size of right vertebral artery distal internal diameter	Correlation Coefficient	-.115	-.176*
		Sig. (2-tailed)	.169	.034
		N	145	145
	RsLftVA dis = relative size left vertebral artery distal internal diameter	Correlation Coefficient	-.029	-.087
		Sig. (2-tailed)	.729	.300
		N	145	145
	RsBA= relative size of terminal basilar artery, internal diameter measured proximal to the SCA	Correlation Coefficient	-.008	.026
		Sig. (2-tailed)	.922	.754
		N	145	145
	RsRt P2 = relative size of proximal right 2nd part of posterior cerebral artery (P2) internal diameter	Correlation Coefficient	.060	.088
		Sig. (2-tailed)	.470	.290
		N	145	145
	RsLft P2 = relative size of proximal left 2nd part of posterior cerebral artery (P2) internal diameter	Correlation Coefficient	.222**	.044
		Sig. (2-tailed)	.007	.599
		N	145	145
	RsRtPcomA mid dia = relative size of right posterior communicating artery internal diameter at the mid point	Correlation Coefficient	-.326**	-.143
		Sig. (2-tailed)	.000	.086
		N	145	145
	RsLftPcomA mid dia = relative size of left posterior communicating artery internal diameter at the mid point	Correlation Coefficient	-.043	-.233**
		Sig. (2-tailed)	.604	.005
		N	145	145
	RsRt IntCA = relative size of right internal carotid arterial internal diameter at the dorsum sellae level	Correlation Coefficient	-.037	.048
		Sig. (2-tailed)	.655	.568
		N	145	145
	RsLft IntCA = relative size of left internal carotid arterial internal diameter at the dorsum sellae level	Correlation Coefficient	-.056	.248**
		Sig. (2-tailed)	.501	.003
		N	145	145
	RsRt A2 = relative size of proximal right 2nd part of anterior cerebral artery (A2) internal diameter	Correlation Coefficient	.026	-.073
		Sig. (2-tailed)	.755	.383
		N	145	145
	RsLft A2 = relative size of proximal left 2nd part of anterior cerebral artery (A2) internal diameter	Correlation Coefficient	.071	.129
		Sig. (2-tailed)	.397	.121
		N	145	145
	RsAComA mid dia = relative size of anterior communicating artery internal diameter around mid point	Correlation Coefficient	-.200*	-.143
		Sig. (2-tailed)	.024	.107
		N	128	128
	RsRt M1 = relative size of proximal right 1st part of middle	Correlation Coefficient	.180*	.164*
		Sig. (2-tailed)	.031	.049

cerebral artery (M1) internal diameter	N	145	145
RsLft M1 = relative size of proximal left 1st part of middle cerebral artery (M1) internal diameter	Correlation Coefficient	.137	.102
	Sig. (2-tailed)	.101	.221
	N	145	145
RsRt P1 = relative size of proximal right first segment of posterior cerebral artery (PCA) internal diameter taken at mid-point	Correlation Coefficient	.164	.029
	Sig. (2-tailed)	.106	.777
	N	98	98
RsLft P1 = relative size of proximal left first segment of posterior cerebral artery (PCA) internal diameter taken at mid-point	Correlation Coefficient	.053	.222*
	Sig. (2-tailed)	.605	.028
	N	98	98
RsRt A1 = relative size of proximal right 1st part of anterior cerebral artery (A1) internal diameter	Correlation Coefficient	1.000	.106
	Sig. (2-tailed)	.	.204
	N	145	145
RsLft A1 = relative size of proximal left 1st part of anterior cerebral artery (A1) internal diameter	Correlation Coefficient	.106	1.000
	Sig. (2-tailed)	.204	.
	N	145	145

**. Correlation is significant at the 0.01 level (2-tailed).

*. Correlation is significant at the 0.05 level (2-tailed).

Supplementary file 4:

Supplementary file 4 - please refer to the supplementary file 1 as well																
Total CTA cases	CTA cases (patients) with aneurysm	Cases (patients) with single aneurysm	Cases (patients) with no aneurysm	Cases (patients) with multiple aneurysm	AcomAC aneurysm	Total rt ICA aneurysm	Total rt MCA aneurysm	Total Pt ICA aneurysm	Total Pt MCA aneurysm	Total VB aneurysm	Total number of aneurysms in all cases	Total aneurysms in left and right ICA and MCA region	Aneurysms other than right and left ICA and MCA regions	Number of AcomAC aneurysm	Number of left and right PCA aneurysm
165	83	56	82	27	27	16	32	8	24	8	113	78	35	27	0
ACA = anterior cerebral artery, PCA = posterior cerebral artery, A1 = first segment of ACA, P2 = second segment of PCA, P1 = first segment of PCA																
CTA = cerebral computed tomography angiography,																
Chi squared test, p≤0.001																
ICA = cranial segment of internal carotid artery, MCA = middle cerebral artery, PcomA = posterior communicating artery, AcomA = anterior communicating artery																
AcomAC aneurysm= Aneurysm positioned at anterior communicating artery complex (AcomAC) region																
78 out of 113 number of aneurysms were located in the ICA and MCA territories (i.e. 69% of the total aneurysms occurred in ICA an MCA regions), Chi squared test, p≤0.001)																
r or Rt = right, l or Lft = left																

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2 and 3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5
Bias	9	Describe any efforts to address potential sources of bias	*5 and 6*
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5 and 8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	5
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	5
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	5
		(b) Indicate number of participants with missing data for each variable of interest	
Outcome data	15*	Report numbers of outcome events or summary measures	10
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9, 10, and 11
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	11
Discussion			
Key results	18	Summarise key results with reference to study objectives	11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14
Generalisability	21	Discuss the generalisability (external validity) of the study results	13 and 14
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	15

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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The relationship between cerebral aneurysms and variations in cerebral basal arterial network: a morphometric cross-sectional study in Computed Tomography Angiograms from a neurointerventional unit

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The relationship between cerebral aneurysms and variations in cerebral basal arterial network: a morphometric cross-sectional study in Computed Tomography Angiograms from a neurointerventional unit

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Abstract

Objective

The segments of cerebral basal arterial network (CBAN) dampen the peak pressure in blood flowing through these arteries, thus minimizing the chances of development of cerebral aneurysms. The objective of this research was to find the relationship of occurrence of intracranial aneurysms to variations of the components of the CBAN.

Design and setting

This is an observational, quantitative, and retrospective research, which used Computed Tomography Angiography (CTA) images.

Participants

Cerebral CTA of 145 adult patients of both sexes were studied.

Main outcome measures

Diameters of segments of CBAN were measured in cerebral CTA and the relative size of each vessel was calculated to standardise for differences in overall arterial sizes among patients. Relationships among sizes of CBAN components were analysed. Presence of aneurysms in different parts of the CBAN was recorded.

Results

Forty-six aneurysms in right internal carotid artery (ICA) and middle cerebral artery (MCA) and 32 aneurysms in left ICA and MCA segments were noted in 42 and 30 patients, respectively. Aneurysms in anterior communicating artery complex (AcomAC) and vertebral-basilar (VB) arterial segments were seen in 27 and 8 patients respectively, while they were not detected in parts of posterior cerebral artery (PCA). The significant ($p<0.001$) inverse relationships between sizes of posterior communicating artery and the first segment of PCA on both sides indicated that blood inputs to the second part of PCA were similar. Difference in means of the index of arterial size variation for people with aneurysms [mean 0.96, SD 0.23] and without aneurysms [mean 0.86), SD 0.22] was significant ($p = 0.015$). This may have been the result of better dampening of peak systolic blood pressures.

Conclusion

Variation in segments of CBAN were quantified. The peak pressure dampening mechanism in such arterial segments reduces the chances of development of aneurysms.

Key words

subarachnoid haemorrhage; aneurysm; stroke; hemodynamics; cerebral basal arterial network

Funding

None

Strengths and limitations of this study

First morphometric quantification of the variations of the components of cerebral basal arterial network.

A method for standardising the size of individual cerebral arteries in relation to the total size of the cerebral arterial system has been introduced.

Parametric and non-parametric statistical methods were used.

Patients from the neurointerventional unit are not a random representation of the general population.

A cross-sectional, not a longitudinal study.

Introduction

Cerebral aneurysms are a common cause of haemorrhagic stroke. Diagnosis, management, prediction and prevention of aneurysms are challenging.[1] The middle cerebral artery (MCA) and anterior communicating artery complex (AcomAC) regions have been identified as the most common locations for the occurrence of intracranial aneurysms.[2-5] Contrary to these, the occurrence of more than two thirds of the total intracranial aneurysms has been reported in relation to internal carotid artery (ICA) territory.[6] Therefore, most of the cerebral aneurysms occur in ICA, MCA and AcomAC territories. 2-6 Pia and Fontana have observed posterior cerebral artery (PCA) aneurysms, but the rate of prevalence of cerebral aneurysms in PCA and vertebrobasilar (VB) arterial components have been reported to be the lowest.[7-9] The prevalence rate of intracranial aneurysms ranged from 0.2 to 6.8 %, and approximately 6-10/100,000 people suffered from ruptured intracranial aneurysms per year and the size of such ruptured aneurysms varied.[4,10] Individuals with ruptured aneurysms had poor prognosis and more than a third of the mortalities occurred within the first month of the illness.[4,10] Most of the ruptured aneurysms (85.6% cases) were reported to be symptomatic and they were in the MCA and AcomAC territories.[4,5] Therefore, studying the relationship of relative sizes of cerebral arteries, sites of location

of cerebral aneurysms and their relationship to the variant segments of CBAN would help to understand the risk factors, and maximise the management of strokes.

The blood flow to the cranial cavity through the four main incoming arteries is asynchronous.[11] The asynchronous blood pressure gradients in the incoming intracranial arteries combine via segments of the CBAN. This helps to maintain a continuous, smooth blood flow through the arteries that are leaving the arterial network, thus minimises peaks in pressure and reduces the chances of development of cerebral aneurysms.[11,12] However, asymmetric and variant segments of the CBAN alter the hemodynamics and peaks in pressure of the blood flowing through them and predisposes the associated "arterial complexes" to the development of aneurysms.[11,13] A relationship for the development of AcomAC aneurysms to the degree of asymmetry between left and right first segments of ACA (A1s) has been shown to occur.[14] The current study, investigated the relationship of locations of intracranial aneurysms to the relative sizes of all arterial segments of CBAN and their individual variations. The concept that the mechanisms involved in dampening peak systolic pressures in arterial segments of CBAN, reduce the chances of the development of aneurysms in the ACA and PCA territories, justified the current investigation.

Material and method

Study design

Randomly selected CCTA images of 145 patients archived in the Carestream data registry system at RAH, South Australia between January 2011 and December 2019, were used in the study (age range 18 to 100 years, male = 67, female = 78, mean age = 60.9 years) (Supplementary file 1). The cerebral computed tomography angiography (CCTA) images with severe artefacts or from patients with severe cerebral vasospasm (i.e., diagnosed by radiologists) were excluded from the study. The CCTA images used in this study were taken from patients who visited the Royal Adelaide Hospital (RAH) for a variety of reasons related to cranial pathologies and screening purposes. Personal information of patients recorded in the data system has not been included in this study.

Missing arterial components or those not seen in the CCTA images (e.g., P1, posterior communicating artery and proximal segment of ACA) were considered to have 0.1 mm diameter for the purpose of statistical analysis (Supplementary file 1). The components of CBAN in some CCTA were not visible due to artefacts and such cases were excluded. Therefore, the number of arterial components measured in CCTA varied to a moderate extent. This, however, did not influence results of our statistical analyses (see Results). Human Research Ethics

Committee, Office of Research Ethics, Compliance and Integrity, Faculty of Health Sciences, University of Adelaide granted permission (approval number: H2014 -176) to access and use anonymised data from the Carestream data registry system (Vue RIS version 11.0.14.35).

Data collection

The position, presence or absence of aneurysms of any sizes were recorded from CCTA of 145 patients based on the diagnosis made by radiologists and clinicians. The position of aneurysms associated with the AcomAC, MCA, ICA, PCA and VB arterial regions were recorded. Some cases had multiple aneurysms. The internal diameters of intracranial segment of ICA at the level of anterior clinoid processes, the first segment of ACA (A1) at the mid-point, posterior communicating artery (PcomA) at the mid-point, the proximal end of the first segment of MCA (M1), anterior communicating artery (AcomA) at the mid-point, the proximal end of the second part of ACA (A2), the first segment of PCA (P1) at the mid-point, the proximal segment of PCA (P2) at the level of dorsum sellae, the distal end of basilar artery just proximal to the origin of superior cerebellar artery (SCA), and the distal vertebral arteries (AV) just proximal to the formation of basilar artery (BA) were measured at right angles to the longitudinal axis of arteries in each individual (Figure 1). The measured internal diameters (in millimetre, mm) were converted into the "relative sizes" of the vessels using the formula, "measured diameter of each vessel / the average size of all the CBAN components measured" (column 24 to 39 in Supplementary file 1) and transferred into the SPSS v. 25 software, before the statistical analysis. The diameters of arteries were converted into "relative sizes" to neutralize the individual differences in sizes of CBAN components among patients.

The internal diameters of the components of CBAN in CCTA were measured using image J software programme (Ij153-win-java8.zip, https://wsr.imagej.net). The diameter of each artery was measured at the narrowest region of the selected site, perpendicular to the long axis of the vessel (Figure 1), to make the measurements consistent across all CCTA images. Furthermore, the CCTA arterial data taken from all the patients were divided into two groups (see below) in order to observe the relationship of aneurysms to the variation in the components of CBAN. Group a: patients with one and more than one cerebral aneurysm; group b: patients without cerebral aneurysms (see column number 41 in Supplementary file 1).

The accuracy of the measurements was determined by repeating measurements in CCTA of 10 cases, a week after the first measurement (Table 1 and Supplementary file 2). The relative technical error of the measurement (rTEM) was calculated and found to be within the statistically acceptable limits (i.e., ≤10%).

Figure 1 (about here)

Figure 1: Sites of arterial diameter measurement in cerebral angiography images. White lines perpendicular to the long axes of vessels show the measurement sites and white arrows depict the components of cerebral basal arterial network (CBAN). (a) = axial image showing the sites of measurement, (b) = coronal image showing the sites of measurement and location of aneurysms, (c) = coronal angiography showing the sites of vessel measurement, (d) = digital subtraction angiography showing the sites of vessel measurement. ACA = anterior cerebral artery, MCA = middle cerebral artery, ICA = cranial component of internal carotid artery, PCA = posterior cerebral artery, A1 of ACA = the first segment of ACA, A2 of ACA = the second segment of ACA, AcomA = anterior communicating artery, PcomA = posterior communicating artery, M1 of MCA = the first segment of middle cerebral artery, P1 of PCA = first segment of PCA, P2 of PCA = second segment of PCA, BA = basilar artery, VA = vertebral artery, AcomACA= AcomA complex aneurysm, and MCAA = MCA aneurysm.

Table 1: The reliability of the measurements taken in Cerebral Computed Tomography Angiography (CCTA) images.

	rt VA	lft VA	BA	rt P2	lft P2	rt PcomA	lft PcomA	rt ICA	lft ICA	rt A2	lft A2	Acom A	rt M1	lft M1	rt P1	lft P1	rt A1	lft A1
TEM	0.025	0.021	0.019	0.018	0.017	0.013	0.014	0.023	0.055	0.020	0.069	0.070	0.020	0.023	0.018	0.017	0.076	0.115
error																		
rTem	0.982	0.767	0.644	0.793	0.697	0.708	0.909	0.533	1.305	0.751	2.783	3.623	0.684	0.805	0.842	0.755	3.732	5.825
(CV)																		
R	0.998	0.999	0.999	0.997	0.996	0.999	0.999	0.998	0.988	0.998	0.948	0.971	0.998	0.998	0.999	0.998	0.991	0.982
reliabilit																		
y																		

Reliability, the coefficients of variation (CV) or the relative technical error of cerebral vessel internal diameter measurements (rTEM) and the technical error of measurements (TEM) are presented. Reliability is the correlation among the first measurements and the second measurements taken from the same artery, n = 10. rt = right, lft = left, dia = internal diameter, ACA = anterior cerebral artery, MCA = middle cerebral artery, ICA =

cranial component of internal carotid artery, PCA = posterior cerebral artery, A1 = first segment of ACA, PcomA = posterior communicating artery, AcomA = anterior communicating artery, M1 = first segment of MCA, P1 = first segment of PCA, P2 = second segment of PCA, BA = basilar artery, and VA = vertebral artery (Supplementary file 2).

The average size (Avg), standard deviation (SD) and coefficient of variation (CV) of all components of CBAN (i.e., left, and right ICA, first segment of MCA, A1, A2, P1, P2, AcomA, PcomA, and BA) were calculated for each individual. In order to avoid the influence of differences in sizes of individual CBANs, the relative sizes of each vessel of each individual were calculated by dividing its size by the average size of this individual's CBAN. Averages of such relative values obviously were close to 1.00, while standard deviations are a measure of each individual's CBAN variation, which was insensitive to its overall size (Supplementary file 1).

Statistical analysis

This is a cross-sectional observational study. The data were analysed using Excel data file and descriptive, parametric and non-parametric statistical methods, independent sample t – test, linear regression, logistic regression, and custom tables from Statistical Package for the Social Sciences (SPSS IBM, version 25) program. The p values less than 0.05 were considered statistically significant, but we quote also exact p values as calculated.

Patient and public involvement

The Carestream database file used in this study holds anonymised data of patients who upon admission to the Royal Adelaide Hospital, University of Adelaide have expressed their consent to use their clinical information for research purposes. The hospital does not supply informed consent documents to the researcher, in order to protect the anonymity of patients. This procedure was approved by the ethics permit (Ethics Approval Number: H2014 -176), under which the study has been conducted. Families, patients, clinical and academic staff from the University of Adelaide have been encouraged to base research on anonymised data. Patients and families who visit the hospital for clinical follow ups will be informed about the findings of the study. The findings will be disseminated to the parties involved via a series of public presentations. All the parties involved, will be requested to share their experiences during the presentation seminar and be encouraged to email the authors for further enquiries. The experience shared and the suggestions received from the parties involved, will be respected and the privacy will be maintained.

Findings

Comparing averages of individual averages and averages of individual standard deviations (Std. Dev.) of the relative sizes of components of CBAN of 81 individuals that had complete data with 64 of those who had missing measurements for P1 segment or AcomA, or both, showed no significant differences. Therefore, all further analyses were based on a joint sample of 145 individuals, since these data were not sensitive to missing values (see Supplementary table 1).

Correlations between relative sizes of various components of the CBAN, though often were statistically significant, were not strong (Table 2), indicating that the individual components' sizes varied in the same individual. Statistically significant inverse relationships were found between relative sizes of ipsilateral PcomA, and P1 segments on the right and left sides (Table 2). The relative sizes of right and left PcomA were found to be inversely correlated with the relative size of basilar artery (Table 2 and Supplementary file 3). Furthermore, significant positive correlations were found between relative sizes of left and right cranial ICA, left and right first part of MCA (M1), left and right second part of ACA (A2), and left and right second part of PCA (P2) (Table 2, Supplementary table 2 and page number 4 to 8 in Supplementary file 3).

The variation in the sizes of CBAN segments was found to be greater in people with aneurysms compared to those without aneurysms (Table 3). The probability of the occurrence of aneurysms was linked significantly to variations in measurements of individual segments of CBAN, as analysed by the logistic regression (Table 4).

The majority of the cerebral aneurysms detected in the current study were in association with bilateral ICA and MCA (Supplementary tables 2 and 3, pages 2 - 4 in Supplementary file 3, and Supplementary file 4). Eighty-three patients out of 145 had cerebral aneurysms in various locations (Supplementary tables 2 and 3 and page 2 in Supplementary files 3). Some individuals had multiple aneurysms, thus a total of 113 aneurysms were found in the 83 patients (Supplementary table 2 and 3, and Supplementary file 4). Out of the total number of 113 aneurysms, 32 (28.31%), 14 (12.4%), 24 (21.24%) and 8 (7%) aneurysms were found in right MCA, right ICA, left MCA and left ICA regions respectively. Seventy-eight out of the 113 aneurysms in the 83 patients (i.e., 69% of the total) were in the right and left MCA and ICA regions (Supplementary table 2, and page 2 to 4 in Supplementary file 3). Furthermore, 27 aneurysms (23.9% of the total) were in AcomAC regions, one in each of 27 patients (Supplementary table 2). In addition, 8 aneurysms (7% of the total) were located in the VB arterial regions (Supplementary table 2). Ten and 2 patients had bilateral MCA and ICA aneurysms respectively (Supplementary table 2). Out of the 27 patients with AcomAC aneurysms, 19 of them had aneurysms only in

the AcomAC regions (Supplementary table 2). Eight patients with AcomAC aneurysms also had coexisting left MCA (n = 4), right MCA (n = 4), and right ICA (n = 4) aneurysms. Out of those eight patients with multiple coexisting aneurysms, one of them had aneurysms in AcomAC, right MCA and left MCA, while another had coexisting aneurysms in AcomAC, right ICA and right MCA (Supplementary table 2). The third patient with AcomAC aneurysm also had coexisting aneurysms in right ICA and left MCA (Supplementary table 2). Ten cases also had coexisting aneurysms in bilateral MCA territories (Supplementary table 2). Out of eight patients with VB aneurysms, one, three, one, and one also had coexisting right ICA, right MCA, left ICA and left MCA aneurysms respectively. No aneurysms were detected at or distal to P2 segments of PCA (Supplementary table 2 and 3).

Table 2: Spearman's rho nonparametric correlations among the relative size of components of CBAN.

Correlations - Spearman's rho

		BA	Rt P2	Lft P2	Rt PcomA mid dia	Lft PcomA mid dia	Rt P1	Lft P1
BA	**rho**	**1.00**	**.17***	**-.02**	**-.39****	**-.45****	**.25***	**.29****
	N	145	145	145	145	145	98	98
Rt P2	**rho**	**.17***	**1.00**	**.36****	**-.35****	**-.29****	**.23***	**.17**
	N	145	145	145	145	145	98	98
Lft P2	**rho**	**-.02**	**.36****	**1.00**	**-.21***	**-.14**	**.30****	**.19**
	N	145	145	145	145	145	98	98
RtPcomA mid dia	**rho**	**-.39****	**-.35****	**-.21***	**1.00**	**.46****	**-.60****	**-.39****
	N	145	145	145	145	145	98	98
LftPcomA mid dia	**rho**	**-.45****	**-.29****	**-.14**	**.46****	**1.00**	**-.32****	**-.64****
	N	145	145	145	145	145	98	98
RtP1	**rho**	**.25***	**.23***	**.30****	**-.60****	**-.32****	**1.00**	**.35****
	N	98	98	98	98	98	98	98
Lft P1	**rho**	**.29****	**.17**	**.19**	**-.39****	**-.64****	**.35****	**1.00**
	N	98	98	98	98	98	98	98

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***. Correlation is significant at p = 0.05 level (2-tailed), **. Correlation is significant at p = 0.01 (2-tailed).**

Cerebral basal arterial network = CBAN, Rt = right, Lft = left, PCA = posterior cerebral artery, PcomA = posterior communicating artery, BA = distal basilar artery, P2 = second part of PCA, PcomA = posterior communicating artery, P1 = first part of PCA, BA= relative size of distal basilar artery, Rt P2 = relative size of right proximal P2, Lft P2 = relative size of left proximal P2, RtPcomA mid dia = relative size of right PcomA at the mid-point, LftPcomA mid dia = relative size of left PcomA at mid-point, Rt P1 = relative size of right P1 at mid-point, Lft P1 = relative size of left P1 at mid-point.

Table 3: Comparison of average size, standard deviation (SD) and Coefficient of Variation (CV) of size of CBAN, both absolute and relative, in patients with and without cerebral aneurysms (Independent sample t – test). CBAN = cerebral basal arterial network.

	Standard deviation of CBAN measurement (SD, mm) average (SD)	Coefficient of variation (CV) average (SD)	Size of CBAN (mm) average (SD)	Standard deviation of Relative size of CBAN average (SD)	Coefficient of variation (CV) of Relative size average (SD)
Patients without cerebral aneurysms (n = 62)	0.86 (0.22)	34.9 (10.0)	2.51 (0.25)	0.34 (0.10)	34.73 (9.77)
Patients with one or multiple cerebral aneurysms (n = 83)	0.96 (0.23)	38.2 (9.2)	2.52 (0.26)	0.38 (0.09)	38.18 (9.15)
Significant (2- tailed, p value)	0.015	0.038	0.708	0.036	0.033

The table 3 shows variations in components of CBAN in individuals in relation to the presence or absence of aneurysms. Variations were significantly greater in patients with aneurysms, though there was no difference in the average size of arteries in their CBAN.

Table 4: Results of logistic regression analysis relating presence of aneurysms to CV and Std. Dev.

Cerebral Basal Arterial Network = CBAN,

standard deviation = std. Dev., calculated as the standard deviation of the relative diameter of all the components of CBAN in an individual, and Coefficient of Variation = CV, calculated as 100* Std. Dev divided by the average relative size of all the components of CBAN in an individual; significant at the $p \leq 0.05$

Variables	B	Constant	p-value	EXP (B)	Sensitivity	Specificity
Std. Dev.	1.822	-1.368	0.017	6.182	78.3	33.9
CV	0.037	-1.071	0.040	1.038	81.9	27.4
Relative size Std. Dev	3.983	-1.142	0.035	53.684	80.7	27.4
Relative size CV.	.039	-1.136	0.033	1.040	80.7	27.4

Both standard deviation (Std.Dev.) and Coefficient of Variation (CV) calculated directly from the components of CBAN measured in mm and the relative size of the components of CBAN measurement, provided significant logistic result with sensitivity approximately 80% and specificity 30% (Table 4). Age of the patients in the current study, ranged from 18 to 100 years (mean = 50.9, SD =15.8) (column 2 in Supplementary file 1 and page 2 in Supplementary file 3). A logistic regression analysis, where age and coefficient of variation were included together as independent variables, indicated that both variables had a significant effect on the probability of the occurrence of aneurysms (i.e., for age: B = -0.034, p = 0.005; for CV: B = 0.038, p = 0.041), but sensitivity remained at 81.9 %, not different from sensitivities produced by standard deviations or CVs alone.

Discussion

The significant differences in the variation of segments of CBAN in people with aneurysms and without aneurysms suggest that the size of individual vessels of the CBAN varies more within a person who has an aneurysm (Table 3 and Table 4). Furthermore, the analysis also confirmed that the occurrences of aneurysms did not depend on the average size of the segments of CBAN (Table 3), but the overall variation in the size of individual segments of CBAN determined the probability of having the cerebral aneurysms (Table 3). Therefore, these statistically significant differences in the variation of segments of CBAN suggests that the correctly formed (minimally variant) segments of CBAN served to best equalize the blood pressure peaks preventing the development of cerebral aneurysms (Table 3).

Aneurysms less than 3 mm in diameter could be missed in commonly used CCTA imaging techniques.[15] The findings of the current study, on more than 4 mm in diameter sized ICA aneurysms compared well with Imaizumi and colleagues findings.[6] Approximately, 3% of the general population develop cerebral aneurysms and may not be diagnosed, until they enlarge sufficiently to cause symptoms or rupture.[16] However, more than 70 % of aneurysms detected by Imaizumi and colleagues[6] using advanced imaging technique were ≤3mm in diameter.[16] The current study, collected data from patients with complicated and ruptured aneurysmal cases, who were referred to the Neuro-interventional Centre in RAH for treatment. Imaizumi and colleagues[6] conducted the study on healthy and asymptomatic adults and detected the right ICA territory as the most common location (78%) for the development intracranial aneurysms. Almost 83% of the detected ICA aneurysms in the latter study were ≤3.9mm in diameter[6], thus individuals with aneurysms of these sizes would not have been diagnosed and included in the current collection. The chances for the rupture of an aneurysm is minimal, when the size is ≤4mm in diameter.[2,6] Most of the CCTA images with AcomAC aneurysms (19 cases) in the current study, had no other coexisting aneurysms located elsewhere in the intracranial regions (Supplementary file 1). The frequency of aneurysms was lower in AcomAC and PCA territories in comparison to the aneurysms found in the MCA and ICA territories in the current study and in a study published recently.[6] Similar distribution patterns of intracranial aneurysms have been described in the literatures.[3,4,6,17] The absence of aneurysms elsewhere in 19 out of 27 (i.e., 70.04%) AcomAC aneurysmal cases (Supplementary files 1 and 3) may indicate that the causes of aneurysms were not due to generalised weakness of the CBAN arterial wall, hypertension, smoking and familial reasons. Vrselja and colleagues suggested that the communicating arteries divert the blood flow and dampen the peaks in systolic pressure in the CBAN system to reduce the occurrence of aneurysms.[18] The chances of the development of AcomAC aneurysms have been predicted to be ≥80% when the asymmetric ratio between right and left A1 segments is 1.42 or more (i.e., larger diameter /smaller diameter).[14] Furthermore, the effect of fluctuating peak systolic pressure in causing aneurysms in AcomAC territories would be lower in the presence of symmetrical A1 arterial segments.[14] Therefore, these 19 cases of AcomAC aneurysms could have resulted from the altered haemodynamics caused by the asymmetry between right and left A1 segments.[14]

Fluctuations of peak systolic pressures may contribute to the occurrence and rupture of cerebral aneurysm.[19] In addition, the amount of blood flowing through a MCA had been found to be increased in the presence of the hypoplastic or absent A1 segment or PcomA on that side of CBAN.[20] Therefore, the 8 cases of AcomAC aneurysms that cooccurred with aneurysms elsewhere (i.e. AcomAC aneurysms cooccurred with right ICA,

right MCA and left MCA regions) might have been associated with the presence of hypoplastic or absent A1 segments or PcomA (Supplementary file 1). These variations of A1 and PcomA segments would increase the resistance to the outflow of blood from the ICA, thus increase the flow and peak systolic pressures through the MCA. Therefore, the greater incidence (≥85% cases) of cerebral aneurysms found in the ICA and MCA territories,[3,4,17] could be linked to the altered haemodynamic in the presence of variant segments in the anterior part of CBAN.[21-23] A significant amount of wall shear stress has been noticed on a stent placed next to the aneurysmal sac, suggesting increased peaks in systolic pressure would result in the development of aneurysm.[24] This indicates that symmetrical A1 segments, and PcomA could act as the flow diverting segments of CBAN, which reduce or dampen the peak systolic pressures in the ICA and MCA reducing the incidence of aneurysms in these regions. The PCA aneurysms are rare.[7,25] The i) significant positive correlations between right and left PcomA, ipsilateral P1 and P2 segments and BA with right and left P1 segments, and ii) inverse correlations between PcomA with ipsilateral and contralateral P1 segments and BA with right and left PcomA (Table 2 and supplementary file 3) indicate that these arterial segments help to balance and maintain optimal blood flow in P2 segments. Thus, the peak systolic pressures may not reach levels that could injure the arterial wall and cause aneurysms in P2 segment and beyond.[26] This is particularly important, because the blood flow in P2 segment is maintained by two inversely correlated ($p = 0.01$) ipsilateral PcomA and P1 vessels (Table 2). Thus, the prevalence of aneurysms in the P2 segment territory of PCA is zero or minimal (Supplementary file 1 and 3). The peak systolic pressures of the blood flowing via the vertebral arteries would get dissipated in the basilar artery (which is also considered as a communicating artery[27]), and then in P1 before reaching the P2 segment. In a similar way, blood flowing from the ICA is dampened in PcomA before reaching the P2 segments, which ensures the less fluctuating peak systolic pressures in P2 and distal to the P2 segments. Therefore, pressure dampening mechanisms could smoothen the arterial pressure distal to P2 segments and reduce the chances of developing aneurysms in PCA compared to ICA, MCA and AcomAC territories.

In vertebrate brain evolution, brainstem evolved first, whereas the telencephalon (specially the frontal lobes) was a later addition to the brain.[28] Therefore, the arterial supply to the brainstem and the posterior part of the telencephalon had more time to be well established. The recently evolved large telencephalon is predominantly supplied by ICA.[29] The anterior part of CBAN evolved along with the telencephalon and has had less evolutionary time to develop, compared to the posterior segments.[28] Thus, the natural selection did not have adequate time to minimise the variations and asymmetries of the anterior segments of the CBAN. Furthermore, a larger blood volume has to flow through the less evolved anterior segments of CBAN to meet the demands of

the large telencephalon.[30] Therefore; the chances of development of aneurysms in the arteries supplied by the anterior segments of CBAN are higher compared to the posterior part. Asymmetry between antimere segments of CBAN could result from the mutations of genes involved in the development of cerebral arterial segments (e.g., development of hypoplastic right or left A1 segment of ACA) in the embryo. However, in some, the embryo has the ability to enlarge the collateral segment of a hypoplastic segment of CBAN and maintain adequate blood supply to the affected right or left side of the brain. Establishment of this compensatory blood flow also requires the enlargement of respective communicating arteries (i.e., anterior and posterior communicating arteries, or the basilar artery). Therefore, the adult brains investigated in this study (i.e., those with variations in the respective segments of the CBAN) developed normally and maintained normal function. However, the increase in blood flow in the enlarged arterial segments, could lead to the formation of aneurysms later in life. Asymmetry between antimere A1 is a good example. In these arterial segments, the risk of development of aneurysms in AcomAC is ≥80%, when the A1 asymmetry ratio remains ≥1.42.[14]

This study was not designed to examine the shape and characteristics of aneurysms, but the focus was on the relationship of the relative size of the blood vessels to the formation of aneurysms in different regions of the brain. Further investigations of cerebral blood flow and the changes in the blood pressure in the presence of asymmetric and variant arteries may help to understand the mechanisms involved in the development of aneurysms.

Limitations: The data for this study were obtained from the cases treated at a highly specialised neurointerventional centre, thus the prevalence rate of cerebral aneurysms was higher compared to the general population. It is unethical to expose general population to CTA related radiation purely for research purposes. This study is a pure cross-sectional study, since the repeated CTA from the same patient could not be obtained at different time points. The timeframe of the current study did not allow us to follow up the patients and continue as a longitudinal study. The lack of hemodynamic, patients history of smoking and blood pressure data are limitations of this study.

Conclusion

The occurrence of cerebral aneurysms varies with the variation of sizes of arteries constituting the cerebral basal arterial network. Variation of those arteries is said to affect hemodynamics, thus predisposing the associated vessels to aneurysms. Patients who have asymmetric and variant cerebral arterial segments in CBAN, should be

monitored regularly. This finding could be considered as one of the criteria for screening the cerebral aneurysms.

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Data sharing statement

Extra data is available by emailing to Arjun.Burlakoti@unisa.edu.au

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Author contribution statement

Arjun Burlakoti- conceived the idea, designed the analysis, collected and analysed the data from CCTA, took pictures, recorded videos, contributed in conceptualization, prepared and drafted the manuscript.

Jaliya Kumaratilake- conceived the idea, contributed to the concept, helped in data interpretation, editing and the critical revision of the manuscript and approving the article.

Jamie Taylor- conceived the idea, contributed in collecting and interpreting the data, editing the manuscript, the critical revision of the manuscript and approving the article.

Maciej Henneberg- conceived the idea, helped in statistics, data analysis and interpretation, editing the manuscript, the critical revision of the manuscript and in approving the article.

Competing interests

None declared. All authors have nothing to disclose.

Ethical Approval Statement

The University of Adelaide, Human Research Ethics Board granted permission to access and use data for this research project (Ethics Approval Number: H2014 -176).

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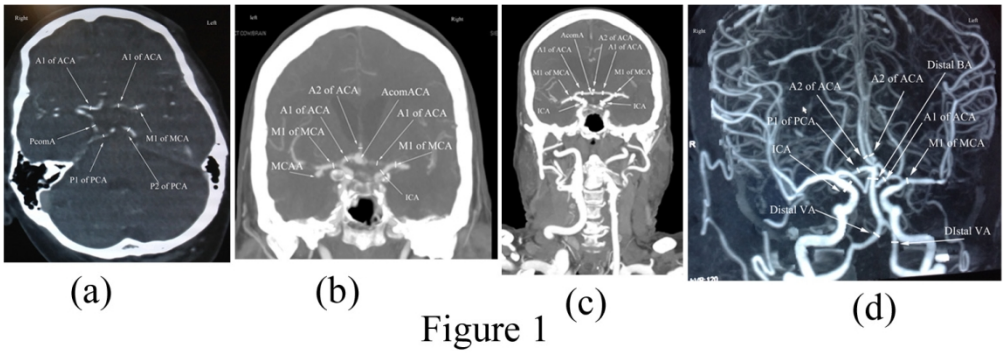


Figure 1

Figure 1: Sites of arterial diameter measurement in cerebral angiography images.
White lines perpendicular to the long axes of vessels show the measurement sites and white arrows depict the components of cerebral basal arterial network (CBAN). (a) = axial image showing the sites of measurement, (b) = coronal image showing the sites of measurement and location of aneurysms, (c) = coronal angiography showing the sites of vessel measurement, (d) = digital subtraction angiography showing the sites of vessel measurement. ACA = anterior cerebral artery, MCA = middle cerebral artery, ICA = cranial component of internal carotid artery, PCA = posterior cerebral artery, A1 of ACA = the first segment of ACA, A2 of ACA = the second segment of ACA, AcomA = anterior communicating artery, PcomA = posterior communicating artery, M1 of MCA = the first segment of middle cerebral artery, P1 of PCA = first segment of PCA, P2 of PCA = second segment of PCA, BA = basilar artery, VA = vertebral artery, AcomACA= AcomA complex aneurysm, and MCAA = MCA aneurysm.

128x45mm (300 x 300 DPI)

Supplementary Table 1: Comparing averages of individual averages and averages of individual standard deviations of the relative sizes of components of CBAN of 81 individuals that have complete data with 64 of those who had missing measurements of P1, or AcomA measurements.

	Individual averages	Individual Std. Dev.
Average	0.99661246	0.34829138
Std. Dev.	0.02189848	0.10008849
Count (N)	64	64
Average	0.9959641	0.36482336
Std. Dev.	0.01402553	0.08525546
Count (N)	81	81

CBAN = cerebral basal arterial network, P1 = first segment of posterior cerebral artery, AcomA = anterior communicating artery, Std. Dev. = standard deviations. Averages: 0.9960 for N=81 (Std. Dev. = 0.0140) and 0.9966 for N=64 (Std. Dev. = 0.0219), t = 0.20; Standard deviations: 0.3648 for N=81 (Std. Dev. = 0.0853) and 0.3483 for N=64 (Std. Dev. =0.1000), t = 1.07.

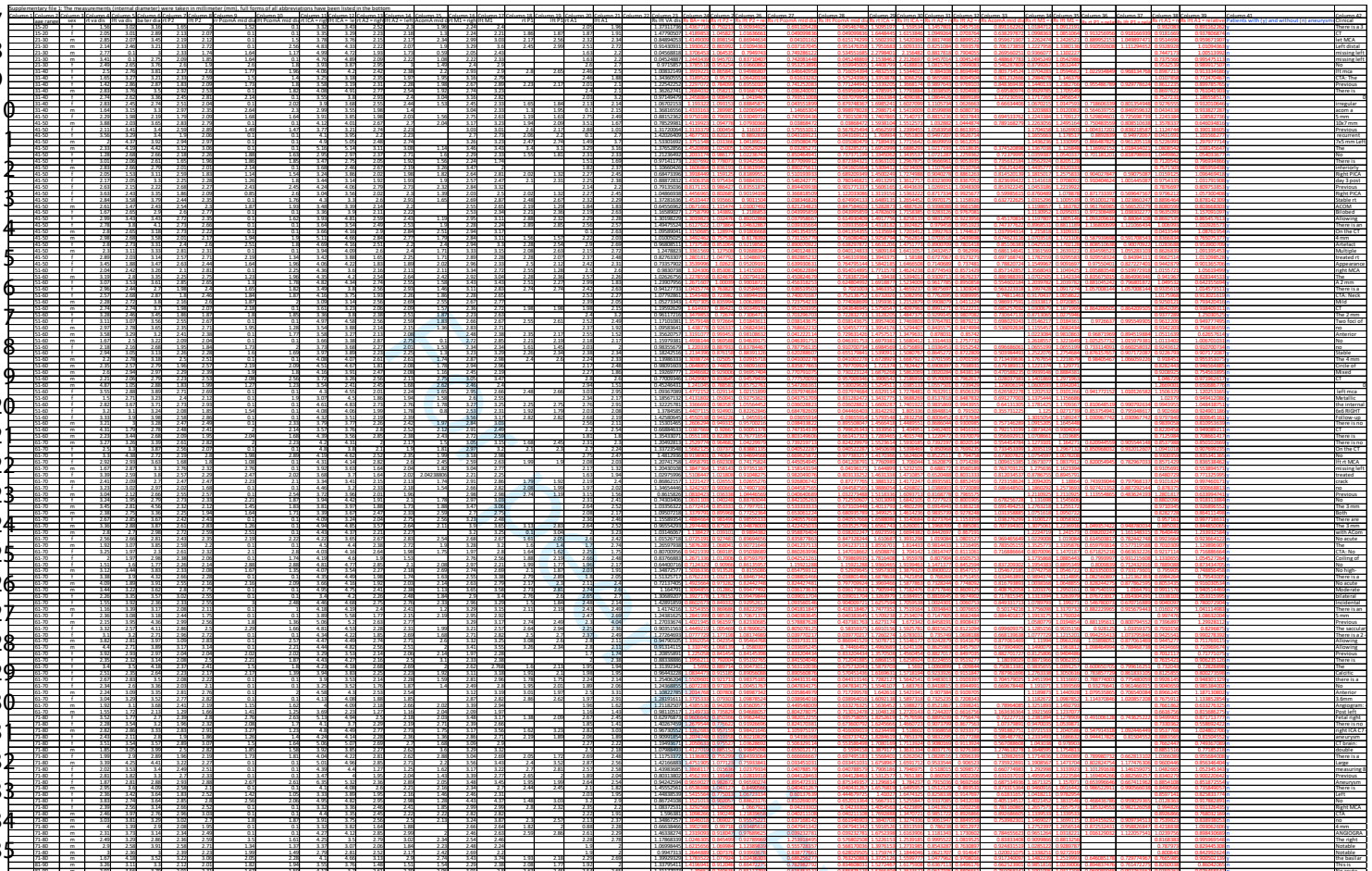
Supplementary Table 2: Anatomical locations of intracranial cerebral aneurysms in the current Cerebral Computed Tomography Angiography scans study (n = 145, age range = 18 to 100 years, female = 79, male = 67). Total 113 aneurysms were recorded in 83 patients. rt = right, lft = left, AcomAC = anterior communicating artery complex, MCA= middle cerebral artery, ICA = internal carotid artery, y = aneurysms present, n = aneurysms absent, MCA = middle cerebral artery, PCA = posterior cerebral artery, VBA = vertebra basilar arteries. P1 = first segment of PCA, and P2 = second segment of PCA.

		Aneurysms at AcomAC		rt ICA Aneurysm		rt MCA Aneurysm		lft ICA Aneurysm		lft MCA Aneurysm		Vertebro basilar aneurysm		PCA aneurysm
		n	y	n	y	n	y	n	y	n	y	n	y	n
		Count	Count	Count	Count	Count	Count	Count	Count	Count	Count	Count	Count	Count
Aneurysms at AcomAC	**n**	118	0	108	10	90	28	110	8	98	20	110	8	118
	y	0	27	23	4	23	4	27	0	23	4	27	0	27
rt ICA Aneurysm	**n**	108	23	131	0	102	29	125	6	108	23	124	7	131
	y	10	4	0	14	11	3	12	2	13	1	13	1	14
rt MCA Aneurysm	**n**	90	23	102	11	113	0	105	8	99	14	108	5	113
	y	28	4	29	3	0	32	32	0	22	10	29	3	32
lft ICA Aneurysm	**n**	110	27	125	12	105	32	137	0	115	22	130	7	137
	y	8	0	6	2	8	0	0	8	6	2	7	1	8
lft MCA Aneurysm	**n**	98	23	108	13	99	22	115	6	121	0	114	7	121
	y	20	4	23	1	14	10	22	2	0	24	23	1	24
Vertebro basilar aneurysm	**n**	110	27	124	13	108	29	130	7	114	23	137	0	137
	y	8	0	7	1	5	3	7	1	7	1	0	8	8
PCA aneurysm	**n**	118	27	131	14	113	32	137	8	121	24	137	8	145

Supplementary Table 3: Average relative sizes of cerebral arteries and aanatomical locations of cerebral aneurysms in the current Cerebral Computed Tomography Angiography scans studies (total cases, n = 145, age range = 18 to 100 years, female = 79, male = 67). Total 113 aneurysms were recorded in 83 patients. VBA = vertebra basilar arteries; ACA = anterior cerebral artery, AcomAC = anterior communicating artery complex; A1 = first segment of ACA; P2 of PCA = second part of PCA; ICA = internal carotid arterial; A2 of ACA = second part of ACA, and M1 of MCA= first part of MCA.

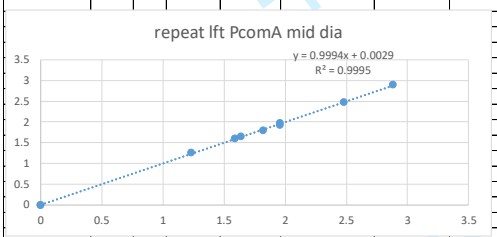
	Aneurysms		Average relative artery size (internal diameter)		Average artery size in mm (internal diameter)	
	Right	**Left**	**Right**	**Left**	**Right**	**Left**
A1 of ACA	27 aneurysms in AcomAC		0.87	0.95	2.36	2.47
ICA	14	8	1.57	1.55	3.9	3.86
M 1 of MCA	32	24	1.12	1.11	2.78	2.76
P2 of PCA	0	0	0.95	0.95	2.36	2.36
A2 of ACA	0	0	0.96	0.95	2.39	2.36
VBA aneurysms		8				

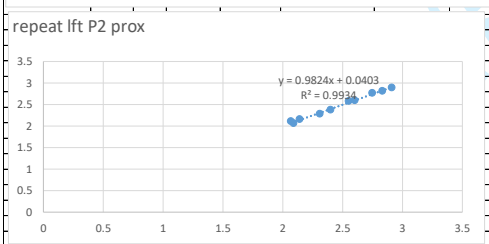
Supplementary file 1:

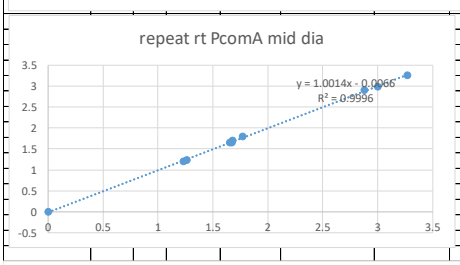


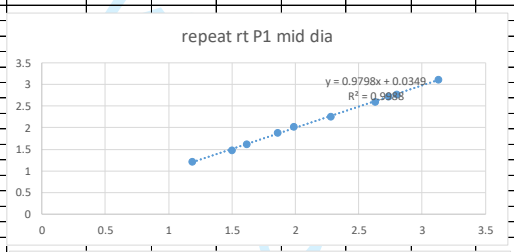
Supplementary file 2:

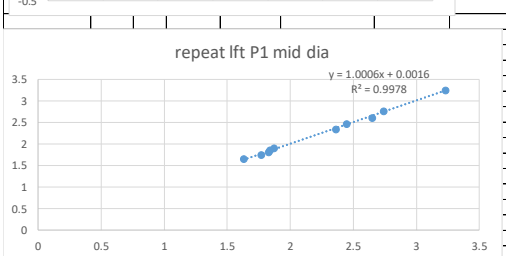
Supplementary file 2: reliability															
Sites of internal diameter r	➔	➔		rt P2 prox d	repeat rt P2 prox d	lft P2 prox dia	repeat lft P2	rt PcomA mid d	repeat rt Pco	lft PcomA m	repeat lft Pco	rt P1 mid dia	repeat rt P1	lft P1 mid dia	repeat lft P1 mid dia
				2.25	2.23	2.75	2.77	1.23	1.2	1.96	1.98	2.28	2.25	2.36	2.34
				2.61	2.57	2.83	2.81	1.26	1.24	0	0	3.13	3.11	1.83	1.81
				1.98	2	2.4	2.38	1.65	1.65	1.82	1.8	2.74	2.72	2.74	2.76
				2.01	1.99	2.31	2.28	1.67	1.65	1.59	1.6	2.63	2.6	2.45	2.47
				1.79	1.82	2.09	2.06	1.68	1.7	1.64	1.65	1.19	1.21	1.63	1.65
				2.37	2.39	2.6	2.59	1.77	1.79	1.96	1.92	2.8	2.77	2.65	2.61
				2.26	2.23	2.14	2.16	2.88	2.9	2.88	2.9	1.99	2.02	1.77	1.75
				2.33	2.32	2.55	2.57	3	2.98	2.48	2.47	1.5	1.47	1.84	1.86
				2.83	2.81	2.91	2.89	3.27	3.26	1.23	1.26	1.62	1.61	3.23	3.25
				2.13	2.1	2.07	2.11	0	0	0	0	1.86	1.89	1.87	1.9
				0.0004		0.0004		0.0009		0.0004		0.0009		0.0004	
				0.0016		0.0004		0.0004		0		0.0004		0.0004	
				0.0004		0.0004		0		0.0004		0.0004		0.0004	
				0.0004		0.0009		0.0004		0.0001		0.0009		0.0004	
				0.0009		0.0009		0.0004		0.0001		0.0004		0.0004	
				0.0004		0.0001		0.0004		0.0016		0.0009		0.0016	
				0.0009		0.0004		0.0004		0.0004		0.0009		0.0004	
				0.0001		0.0004		0.0004		1E-04		0.0009		0.0004	
				0.0004		0.0004		0.0001		0.0009		0.0001		0.0004	
				0.0009		0.0016		0		0		0.0009		0.0009	
			Sum	0.006		0.006		0.003		0.004		0.007		0.006	
		TEM		0.018		0.017		0.013		0.014		0.018		0.017	
		rTEM	CV	0.793		0.697		0.708		0.909		0.842		0.755	
			R- Square	0.995		0.993		1.000		1.000		0.999		0.998	
			r reliability	0.997		0.997		1.000		1.000		0.999		0.999	

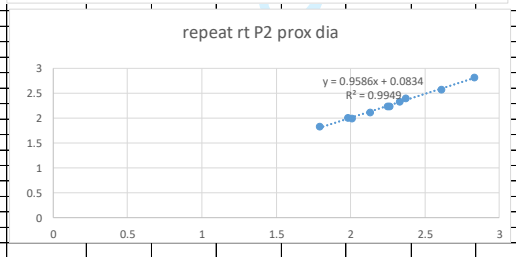












Abbreviations
PCA= posterior cerebral artery, ACA= anterior cerebral artery, MCA= middle cerebral artery, ICA= intracranial pat of internal carotid artery
P1= proximal segment of PCA, P2= ssecond segment of PCA, A1= proximal segment of ACA, A2= second segment of ACA
rt= right, lft= left, PcomA= posterior communicating artery, prox= proximal, mid dia= diameter in the middle
prox= proximal, dia= diameter
TEM= technical error of measurement
rTEM= relative TEM
CV= coefficient of variation
R squared= coefficient of determination
r= coefficient of correlation or reliability

Supplementary file 3

Abbreviations and full forms

- All the measurements were taken in millimetre (mm)
- SCA = superior cerebellar artery
- rt or Rt = right, lft or Lft = left, ter = terminal, dia = diameter, dis = distal, m = male, f = female, Rs = relative size,
- stDev = standard deviation, CV = coefficient of variation, Aver = average
- ACA = anterior cerebral artery, PCA = posterior cerebral artery, A1 = first segment of ACA, A2= second part of ACA, P2 = second segment of PCA, P1 = first segment of PCA
- ICA = internal carotid artery, MCA = middle cerebral artery, M1 = first segment of MCA, PcomA = posterior communicating artery, AcomA = anterior communicating artery
- VA or va = vertebral artery, ba or BA = basilar artery, VB Aneu = vertebro basilar aneurysm, Aneu Els = elsewhere aneurysm
- ba ter dia = diameter measured just proximal to the origin of superior cerebellar artery
- AcomAC = Anterior communicating artery complex
- AcomAC aneurysm= Aneurysm positioned at Anterior communicating artery complex (AcomAC) region, y = present, and n = absent
- Aneurysm elsewhere= Aneurysm positioned elsewhere (other than AcomAC region), y = present, and n = absent
- CBAN = cerebral basal arterial network,
- VB Aneu = vertebro basilar aneurysm, rt= right, lft= left, Dist/dist = distal, BA= basilar artery, Ter= terminal, Dia/dia= diameter
- PCA= posterior cerebral artery, PcomA= posterior communicating artery, AcomA= anterior communicating artery, ICA= internal carotid artery, MCA= middle cerebral artery, ACA= anterior cerebral artery, and SCA= superior cerebellar artery

Descriptive Statistics

	N	Minimum	Maximum	Mean	Std. Deviation
Age in years	145	18	100	60.87	15.799
Valid N (listwise)	145				

Frequency Table

Sex

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	f	78	53.8	53.8	53.8
	m	67	46.2	46.2	100.0
	Total	145	100.0	100.0	

AcomAC An = aneurysms at AcomAC junction, y=yes and n=no

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	n	118	81.4	81.4	81.4
	y	27	18.6	18.6	100.0
	Total	145	100.0	100.0	

rt ICA Aneurysm

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	n	131	90.3	90.3	90.3
	y	14	9.7	9.7	100.0
	Total	145	100.0	100.0	

rt MCA Aneurysm

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	n	113	77.9	77.9	77.9

	y	32	22.1	22.1	100.0
	Total	145	100.0	100.0	

lft ICA Aneurysm

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	n	137	94.5	94.5	94.5
	y	8	5.5	5.5	100.0
	Total	145	100.0	100.0	

lft MCA Aneurysm

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	**n**	121	83.4	83.4	83.4
	y	24	16.6	16.6	100.0
	Total	145	100.0	100.0	

vertebro basilar aneurysm

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	**n**	137	94.5	94.5	94.5
	y	8	5.5	5.5	100.0
	Total	145	100.0	100.0	

Spearman's rho Correlations

Correlations

			RsRtVA dis = relative size of right vertebral artery distal internal diameter	RsLftVA dis = relative size left vertebral artery distal internal diameter	RsBA= relative size of terminal basilar artery just proximal to SCA	RsRt P2 = relative size of proximal right 2nd part of posterior cerebral artery (P2) internal diameter	RsLft P2 = relative size of proximal left 2nd part of posterior cerebral artery (P2) internal diameter	RsRtPcoA mid dia = relative size of right posterior communicating artery external diameter around the mid-point	RsLftPcoA mid dia = relative size of left posterior communicating artery external diameter around the mid-point	RsRt IntCA = relative size of right internal carotid arterial internal diameter at the dorsum sellae level
Spearman's rho	RsRtVA dis = relative size of right vertebral artery distal internal diameter	Correlation Coefficient	1.000	-.235**	.172*	.044	-.129	-.108	-.059	-.011
		Sig. (2-tailed)	.	.005	.039	.597	.122	.196	.478	.894
		N	145	145	145	145	145	145	145	145
	RsLftVA dis = relative size left vertebral artery distal internal diameter	Correlation Coefficient	-.235**	1.000	.337**	.070	.078	-.379**	-.389**	.050
		Sig. (2-tailed)	.005	.	.000	.401	.351	.000	.000	.550
		N	145	145	145	145	145	145	145	145
	RsBA= relative size of terminal basilar artery proximal to SCA	Correlation Coefficient	.172*	.337**	1.000	.169*	-.017	-.390**	-.447**	-.062
		Sig. (2-tailed)	.039	.000	.	.043	.839	.000	.000	.460
		N	145	145	145	145	145	145	145	145
	RsRt P2 = relative size of proximal right	Correlation Coefficient	.044	.070	.169*	1.000	.357**	-.350**	-.286**	-.066
		Sig. (2-tailed)	.597	.401	.043	.	.000	.000	.000	.431

	2nd part of posterior cerebral artery (P2) internal diameter	N	145	145	145	145	145	145	145	145
	RsLft P2 = relative size of proximal left	Correlation Coefficient	-.129	.078	-.017	.357**	1.000	-.206*	-.140	-.150
		Sig. (2-tailed)	.122	.351	.839	.000	.	.013	.093	.072
	2nd part of posterior cerebral artery (P2) internal diameter	N	145	145	145	145	145	145	145	145
	RsRtPcomA mid dia = relative size of right posterior communicating artery internal diameter around the mid point	Correlation Coefficient	-.108	-.379**	-.390**	-.350**	-.206*	1.000	.456**	-.170*
		Sig. (2-tailed)	.196	.000	.000	.000	.013	.	.000	.041
		N	145	145	145	145	145	145	145	145
	RsLftPcomA mid dia = relative size of left posterior communicating artery internal diameter around the mid point	Correlation Coefficient	-.059	-.389**	-.447**	-.286**	-.140	.456**	1.000	-.277**
		Sig. (2-tailed)	.478	.000	.000	.000	.093	.000	.	.001
		N	145	145	145	145	145	145	145	145
	RsRt IntCA = relative size of right internal carotid arterial internal diameter at the dorsum sellae level	Correlation Coefficient	-.011	.050	-.062	-.066	-.150	-.170*	-.277**	1.000
		Sig. (2-tailed)	.894	.550	.460	.431	.072	.041	.001	.
		N	145	145	145	145	145	145	145	145
	RsLft IntCA = relative size of left internal carotid arterial internal diameter at the dorsum sellae level	Correlation Coefficient	-.018	-.014	.002	.198*	-.132	-.225**	-.160	.462**
		Sig. (2-tailed)	.826	.868	.981	.017	.114	.006	.055	.000
		N	145	145	145	145	145	145	145	145

	RsRt A2 = relative size of proximal right 2nd part of anterior cerebral artery (A2) internal diameter	Correlation Coefficient	-.162	.114	-.152	-.074	-.170*	.002	-.068	-.016
		Sig. (2-tailed)	.052	.173	.069	.380	.041	.979	.417	.847
		N	145	145	145	145	145	145	145	145
	RsLft A2 = relative size of proximal left 2nd part of anterior cerebral artery (A2) internal diameter	Correlation Coefficient	-.181*	.162	.006	-.014	-.031	-.154	-.230**	.034
		Sig. (2-tailed)	.029	.051	.941	.865	.713	.065	.005	.684
		N	145	145	145	145	145	145	145	145
	RsAComA mid dia = relative size of anterior communicating artery internal diameter around mid-point	Correlation Coefficient	-.264**	-.061	-.059	-.184*	-.086	.151	.112	-.221*
		Sig. (2-tailed)	.003	.492	.508	.037	.335	.088	.209	.012
		N	128	128	128	128	128	128	128	128
	RsRt M1 = relative size of proximal right 1st part of middle cerebral artery (M1) internal diameter	Correlation Coefficient	-.185*	-.074	-.040	.206*	.165*	-.203*	-.205*	.126
		Sig. (2-tailed)	.026	.376	.636	.013	.047	.014	.013	.131
		N	145	145	145	145	145	145	145	145
	RsLft M1 = relative size of proximal left 1st part of middle cerebral artery (M1) internal diameter	Correlation Coefficient	-.139	.023	-.026	.194*	.021	-.296**	-.198*	.155
		Sig. (2-tailed)	.096	.782	.756	.019	.805	.000	.017	.062
		N	145	145	145	145	145	145	145	145
	RsRt P1 = relative size of proximal right	Correlation Coefficient	.107	.152	.245*	.234*	.301**	-.600**	-.315**	-.164
		Sig. (2-tailed)	.295	.134	.015	.020	.003	.000	.002	.107

	first segment of posterior cerebral artery (PCA) internal diameter taken at mid-point	N	98	98	98	98	98	98	98	98
	RsLft P1 = relative size of proximal left	Correlation Coefficient	.015	.290**	.293**	.168	.191	-.388**	-.639**	.060
		Sig. (2-tailed)	.883	.004	.003	.098	.059	.000	.000	.554
	first segment of posterior cerebral artery (PCA) internal diameter taken at mid-point	N	98	98	98	98	98	98	98	98
	RsRt A1 = relative size of proximal right	Correlation Coefficient	-.115	-.029	-.008	.060	.222**	-.326**	-.043	-.037
		Sig. (2-tailed)	.169	.729	.922	.470	.007	.000	.604	.655
	1st part of anterior cerebral artery (A1) internal diameter	N	145	145	145	145	145	145	145	145
	RsLft A1 = relative size of proximal left 1st part of anterior cerebral artery (A1) internal diameter	Correlation Coefficient	-.176*	-.087	.026	.088	.044	-.143	-.233**	.048
		Sig. (2-tailed)	.034	.300	.754	.290	.599	.086	.005	.568
		N	145	145	145	145	145	145	145	145

Correlations

			RsLft IntCA = relative size of left internal carotid arterial internal diameter at the dorsum sellae level	RsRt A2 = relative size of proximal right 2nd part of anterior cerebral artery (A2) internal diameter	RsLft A2 = relative size of proximal left 2nd part of anterior cerebral artery (A2) internal diameter	RsACom A mid dia = relative size of anterior communicating artery internal diameter around mid-point	RsRt M1 = relative size of proximal right 1st part of middle cerebral artery (M1) internal diameter	RsLft M1 = relative size of proximal left 1st part of middle cerebral artery (M1) internal diameter	RsRt P1 = relative size of proximal right 1st part of posterior cerebral artery (P1) internal diameter taken at midpoint	RsLft P1 = relative size of proximal left 1st part of posterior cerebral artery (P1) internal diameter taken at midpoint
Spearman's rho	RsRtVA dis = relative size of right vertebral artery distal internal diameter	Correlation Coefficient	-.018	-.162	-.181*	-.264**	-.185*	-.139	.107	.015
		Sig. (2-tailed)	.826	.052	.029	.003	.026	.096	.295	.883
		N	145	145	145	128	145	145	98	98
	RsLftVA dis = relative size left vertebral artery distal internal diameter	Correlation Coefficient	-.014	.114	.162	-.061	-.074	.023	.152	.290**
		Sig. (2-tailed)	.868	.173	.051	.492	.376	.782	.134	.004
		N	145	145	145	128	145	145	98	98
	RsBA= relative size of terminal basilar artery, proximal to the origin of SCA	Correlation Coefficient	.002	-.152	.006	-.059	-.040	-.026	.245*	.293**
		Sig. (2-tailed)	.981	.069	.941	.508	.636	.756	.015	.003
		N	145	145	145	128	145	145	98	98
	RsRt P2 = relative size of proximal right 2nd part of posterior cerebral artery (P2) internal diameter	Correlation Coefficient	.198*	-.074	-.014	-.184*	.206*	.194*	.234*	.168
		Sig. (2-tailed)	.017	.380	.865	.037	.013	.019	.020	.098
		N	145	145	145	128	145	145	98	98
	RsLft P2 = relative size of proximal left	Correlation Coefficient	-.132	-.170*	-.031	-.086	.165*	.021	.301**	.191
		Sig. (2-tailed)	.114	.041	.713	.335	.047	.805	.003	.059

	2nd part of posterior cerebral artery (P2) internal diameter	N	145	145	145	128	145	145	98	98
	RsRtPcomA mid dia = relative	Correlation Coefficient	-.225**	.002	-.154	.151	-.203*	-.296**	-.600**	-.388**
	size of right	Sig. (2-tailed)	.006	.979	.065	.088	.014	.000	.000	.000
	posterior communicating artery internal diameter around the mid point	N	145	145	145	128	145	145	98	98
	RsLftPcomA mid dia =	Correlation Coefficient	-.160	-.068	-.230**	.112	-.205*	-.198*	-.315**	-.639**
	relative size of	Sig. (2-tailed)	.055	.417	.005	.209	.013	.017	.002	.000
	left posterior communicating artery internal diameter around the mid point	N	145	145	145	128	145	145	98	98
	RsRt IntCA = relative size of	Correlation Coefficient	.462**	-.016	.034	-.221*	.126	.155	-.164	.060
	right internal	Sig. (2-tailed)	.000	.847	.684	.012	.131	.062	.107	.554
	carotid arterial internal diameter at the dorsum sellae level	N	145	145	145	128	145	145	98	98
	RsLft IntCA = relative size of	Correlation Coefficient	1.000	-.139	-.024	-.435**	.100	.218**	-.088	-.052
	left internal	Sig. (2-tailed)	.	.094	.776	.000	.231	.008	.387	.612
	carotid arterial internal diameter at the dorsum sellae level	N	145	145	145	128	145	145	98	98
	RsRt A2 = relative size of	Correlation Coefficient	-.139	1.000	.579**	.173	-.071	-.030	-.134	-.156
	proximal right	Sig. (2-tailed)	.094	.	.000	.051	.393	.720	.188	.126
	2nd part of anterior cerebral artery (A2) internal diameter	N	145	145	145	128	145	145	98	98

	RsLft A2 = relative size of proximal left 2nd part of anterior cerebral artery (A2) internal diameter	Correlation Coefficient	-.024	.579**	1.000	-.009	-.041	.061	-.054	.017
		Sig. (2-tailed)	.776	.000	.	.917	.624	.465	.598	.867
		N	145	145	145	128	145	145	98	98
	RsACom A mid dia = relative size of anterior communicating artery internal diameter around mid-point	Correlation Coefficient	-.435**	.173	-.009	1.000	-.050	-.178*	-.159	-.237*
		Sig. (2-tailed)	.000	.051	.917	.	.578	.045	.156	.033
		N	128	128	128	128	128	128	81	81
	RsRt M1 = relative size of proximal right 1st part of middle cerebral artery (M1) internal diameter	Correlation Coefficient	.100	-.071	-.041	-.050	1.000	.521**	.060	.012
		Sig. (2-tailed)	.231	.393	.624	.578	.	.000	.558	.910
		N	145	145	145	128	145	145	98	98
	RsLft M1 = relative size of proximal left 1st part of middle cerebral artery (M1) internal diameter	Correlation Coefficient	.218**	-.030	.061	-.178*	.521**	1.000	.031	.114
		Sig. (2-tailed)	.008	.720	.465	.045	.000	.	.764	.262
		N	145	145	145	128	145	145	98	98
	RsRt P1 = relative size of proximal right 1st part of posterior cerebral artery (P1) internal diameter taken at midpoint	Correlation Coefficient	-.088	-.134	-.054	-.159	.060	.031	1.000	.352**
		Sig. (2-tailed)	.387	.188	.598	.156	.558	.764	.	.000
		N	98	98	98	81	98	98	98	98
	RsLft P1 = relative size of proximal left 1st	Correlation Coefficient	-.052	-.156	.017	-.237*	.012	.114	.352**	1.000
		Sig. (2-tailed)	.612	.126	.867	.033	.910	.262	.000	.

	part of posterior cerebral artery (P1) internal diameter taken at midpoint	N	98	98	98	81	98	98	98	98
	RsRt A1 = relative size of proximal right	Correlation Coefficient	-.056	.026	.071	-.200*	.180*	.137	.164	.053
		Sig. (2-tailed)	.501	.755	.397	.024	.031	.101	.106	.605
	1st part of anterior cerebral artery (A1) internal diameter	N	145	145	145	128	145	145	98	98
	RsLft A1 = relative size of proximal left 1st part of anterior cerebral artery (A1) internal diameter	Correlation Coefficient	.248**	-.073	.129	-.143	.164*	.102	.029	.222*
		Sig. (2-tailed)	.003	.383	.121	.107	.049	.221	.777	.028
		N	145	145	145	128	145	145	98	98

Correlations

			RsRt A1 = relative size of proximal right 1st part of anterior cerebral artery (A1) internal diameter	RsLft A1 = relative size of proximal left 1st part of anterior cerebral artery (A1) internal diameter
Spearman's rho	RsRtVA dis = relative size of right vertebral artery distal internal diameter	Correlation Coefficient	-.115	-.176*
		Sig. (2-tailed)	.169	.034
		N	145	145
	RsLftVA dis = relative size left vertebral artery distal internal diameter	Correlation Coefficient	-.029	-.087
		Sig. (2-tailed)	.729	.300
		N	145	145
	RsBA= relative size of terminal basilar artery, internal diameter measured proximal to the SCA	Correlation Coefficient	-.008	.026
		Sig. (2-tailed)	.922	.754
		N	145	145
	RsRt P2 = relative size of proximal right 2nd part of posterior cerebral artery (P2) internal diameter	Correlation Coefficient	.060	.088
		Sig. (2-tailed)	.470	.290
		N	145	145
	RsLft P2 = relative size of proximal left 2nd part of posterior cerebral artery (P2) internal diameter	Correlation Coefficient	.222**	.044
		Sig. (2-tailed)	.007	.599
		N	145	145

RsRtPcomA mid dia = relative size of right posterior communicating artery internal diameter at the mid point	Correlation Coefficient	-.326**	-.143
	Sig. (2-tailed)	.000	.086
	N	145	145
RsLftPcomA mid dia = relative size of left posterior communicating artery internal diameter at the mid point	Correlation Coefficient	-.043	-.233**
	Sig. (2-tailed)	.604	.005
	N	145	145
RsRt IntCA = relative size of right internal carotid arterial internal diameter at the dorsum sellae level	Correlation Coefficient	-.037	.048
	Sig. (2-tailed)	.655	.568
	N	145	145
RsLft IntCA = relative size of left internal carotid arterial internal diameter at the dorsum sellae level	Correlation Coefficient	-.056	.248**
	Sig. (2-tailed)	.501	.003
	N	145	145
RsRt A2 = relative size of proximal right 2nd part of anterior cerebral artery (A2) internal diameter	Correlation Coefficient	.026	-.073
	Sig. (2-tailed)	.755	.383
	N	145	145
RsLft A2 = relative size of proximal left 2nd part of anterior cerebral artery (A2) internal diameter	Correlation Coefficient	.071	.129
	Sig. (2-tailed)	.397	.121
	N	145	145
RsAComA mid dia = relative size of anterior communicating artery internal diameter around mid point	Correlation Coefficient	-.200*	-.143
	Sig. (2-tailed)	.024	.107
	N	128	128
RsRt M1 = relative size of proximal right 1st part of middle cerebral artery (M1) internal diameter	Correlation Coefficient	.180*	.164*
	Sig. (2-tailed)	.031	.049
	N	145	145
RsLft M1 = relative size of proximal left 1st part of middle cerebral artery (M1) internal diameter	Correlation Coefficient	.137	.102
	Sig. (2-tailed)	.101	.221
	N	145	145
RsRt P1 = relative size of proximal right first segment of posterior cerebral artery (PCA) internal diameter taken at mid-point	Correlation Coefficient	.164	.029
	Sig. (2-tailed)	.106	.777
	N	98	98
RsLft P1 = relative size of proximal left first segment of posterior cerebral artery (PCA) internal diameter taken at mid-point	Correlation Coefficient	.053	.222*
	Sig. (2-tailed)	.605	.028
	N	98	98
RsRt A1 = relative size of proximal right 1st part of anterior cerebral	Correlation Coefficient	1.000	.106
	Sig. (2-tailed)	.	.204

artery (A1) internal diameter	N	145	145
RsLft A1 = relative size of	Correlation Coefficient	.106	1.000
proximal left 1st part of anterior	Sig. (2-tailed)	.204	.
cerebral artery (A1) internal	N	145	145
diameter			

**. Correlation is significant at the 0.01 level (2-tailed).

*. Correlation is significant at the 0.05 level (2-tailed).

Supplementary file 4:

Supplementary file 4 - please refer to the supplementary file 1 as well																
Total CTA cases	CTA cases (patients) with	cases (patients) with single aneurysm	cases (patients) with no aneurysm	cases (patients) with multiple aneurysm	AcomAC aneurysm	total rt ICA aneurysm	total rt MCA aneurysm	total lft ICA aneurysm	total lft MCA aneurysm	total VB aneurysm	total number of aneurysms in all cases	total aneurysms in left and right ICA and MCA region	aneurysms other than right and left ICA and MCA regions	number of AcomAC aneurysm	number of left and right PCA aneurysm
165	83	56	62	27	27	16	32	8	24	8	113	78	35	27	0
ACA = anterior cerebral artery, PCA = posterior cerebral artery, A1 = first segment of ACA, P2 = second segment of PCA, P1 = first segment of PCA																
CTA = cerebral computed tomography angiography,																
Chi squared test, p≤0.001																
ICA = cranial segment of internal carotid artery, MCA = middle cerebral artery, AcomA = anterior communicating artery																
AcomAC aneurysm= Aneurysm positioned at anterior communicating artery complex (AcomAC) region																
78 out of 113 number of aneurysms were located in the ICA and MCA territories (i.e. 69% of the total aneurysms occurred in ICA an MCA regions), Chi squared test, p≤0.001)																
r or Rt = right, lft or Lft = left																

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2 and 3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5
Bias	9	Describe any efforts to address potential sources of bias	*5 and 6*
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5 and 8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	5
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	5
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	5
		(b) Indicate number of participants with missing data for each variable of interest	
Outcome data	15*	Report numbers of outcome events or summary measures	10
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9, 10, and 11
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	11
Discussion			
Key results	18	Summarise key results with reference to study objectives	11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14
Generalisability	21	Discuss the generalisability (external validity) of the study results	13 and 14
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	15

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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The relationship between cerebral aneurysms and variations in cerebral basal arterial network: a morphometric cross-sectional study in Computed Tomography Angiograms from a neurointerventional unit

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The relationship between cerebral aneurysms and variations in cerebral basal arterial network: a morphometric cross-sectional study in Computed Tomography Angiograms from a neurointerventional unit

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Abstract

Objective

The segments of cerebral basal arterial network (CBAN) dampen the peak pressure in blood flowing through these arteries, thus minimizing the chances of development of cerebral aneurysms. The objective of this research was to find the relationship of occurrence of intracranial aneurysms to variations of the components of the CBAN.

Design and setting

This is an observational, quantitative, and retrospective research, which used Computed Tomography Angiography (CTA) images.

Participants

Cerebral CTA of 145 adult patients of both sexes were studied.

Main outcome measures

Diameters of segments of CBAN were measured in cerebral CTA and the relative size of each vessel was calculated to standardise for differences in overall arterial sizes among patients. Relationships among sizes of CBAN components were analysed. Presence of aneurysms in different parts of the CBAN was recorded.

Results

Forty-six aneurysms in right internal carotid artery (ICA) and middle cerebral artery (MCA) and 32 aneurysms in left ICA and MCA segments were noted in 42 and 30 patients, respectively. Aneurysms in anterior communicating artery complex (AcomAC) and vertebral-basilar (VB) arterial segments were seen in 27 and 8 patients respectively, while they were not detected in parts of posterior cerebral artery (PCA). The significant ($p<0.001$) inverse relationships between sizes of posterior communicating artery and the first segment of PCA on both sides indicated that blood inputs to the second part of PCA were similar. Difference in means of the index of arterial size variation for people with aneurysms [mean 0.96, SD 0.23] and without aneurysms [mean 0.86), SD 0.22] was significant ($p = 0.015$).

Conclusion

Variation in segments of CBAN were quantified. The peak pressure dampening mechanism in such arterial segments reduces the chances of development of aneurysms.

Key words

subarachnoid haemorrhage; aneurysm; stroke; hemodynamics; cerebral basal arterial network

Funding

None

Strengths and limitations of this study

To our knowledge, the standardization of the sizes of the cerebral arteries is introduced for the first time.

Computed Tomography Angiography images of brains of patients from the neurointerventional unit used to obtain diameters of major cerebral arteries.

Parametric and non-parametric statistical methods were used.

Patients from the neurointerventional unit are not a random representation of the general population.

A cross-sectional, not a longitudinal study.

Introduction

Cerebral aneurysms are a common cause of haemorrhagic stroke. Diagnosis, management, prediction and prevention of aneurysms are challenging.[1] The middle cerebral artery (MCA) and anterior communicating artery complex (AcomAC) regions have been identified as the most common locations for the occurrence of intracranial aneurysms.[2-5] Contrary to these, the occurrence of more than two thirds of the total intracranial aneurysms has been reported in relation to internal carotid artery (ICA) territory.[6] Therefore, most of the cerebral aneurysms occur in ICA, MCA and AcomAC territories. 2-6 Pia and Fontana have observed posterior cerebral artery (PCA) aneurysms, but the rate of prevalence of cerebral aneurysms in PCA and vertebrobasilar (VB) arterial components have been reported to be the lowest.[7-9] The prevalence rate of intracranial aneurysms ranged from 0.2 to 6.8 %, and approximately 6-10/100,000 people suffered from ruptured intracranial aneurysms per year and the size of such ruptured aneurysms varied.[4,10] Individuals with ruptured aneurysms had poor prognosis and more than a third of the mortalities occurred within the first month of the illness.[4,10] Most of the ruptured aneurysms (85.6% cases) were reported to be symptomatic and they were in the MCA and AcomAC territories.[4,5] Therefore, studying the relationship of relative sizes of cerebral arteries, sites of location

of cerebral aneurysms and their relationship to the variant segments of CBAN would help to understand the risk factors, and maximise the management of strokes.

The blood flow to the cranial cavity through the four main incoming arteries is asynchronous.[11] The asynchronous blood pressure gradients in the incoming intracranial arteries combine via segments of the CBAN. This helps to maintain a continuous, smooth blood flow through the arteries that are leaving the arterial network, thus minimises peaks in pressure and reduces the chances of development of cerebral aneurysms.[11,12] However, asymmetric and variant segments of the CBAN alter the hemodynamics and peaks in pressure of the blood flowing through them and predisposes the associated "arterial complexes" to the development of aneurysms.[11,13] A relationship for the development of AcomAC aneurysms to the degree of asymmetry between left and right first segments of ACA (A1s) has been shown to occur.[14] The current study, investigated the relationship of locations of intracranial aneurysms to the relative sizes of all arterial segments of CBAN and their individual variations. The concept that the mechanisms involved in dampening peak systolic pressures in arterial segments of CBAN, reduce the chances of the development of aneurysms in the ACA and PCA territories, justified the current investigation.

Material and method

Study design

Randomly selected CCTA images of 145 patients archived in the Carestream data registry system at Royal Adelaide Hospital (RAH), South Australia between January 2011 and December 2019, were used in the study (age range 18 to 100 years, male = 67, female = 78, mean age = 60.9 years) (Supplementary file 1). The Carestream database file used in this study holds anonymised data of patients who upon admission to the RAH, University of Adelaide have expressed their consent to use their clinical information for research purposes. The hospital does not supply informed consent documents to the researcher, in order to protect the anonymity of patients. Human Research Ethics Committee, Office of Research Ethics, Compliance and Integrity, Faculty of Health Sciences, University of Adelaide granted permission (approval number: H2014 -176) to access and use anonymised data from the Carestream data registry system (Vue RIS version 11.0.14.35).

The cerebral computed tomography angiography (CCTA) images with severe artefacts or from patients with severe cerebral vasospasm (i.e., diagnosed by radiologists) were excluded from the study. The CCTA images used in this study were taken from patients who visited the RAH for a variety of reasons related to cranial

pathologies and screening purposes. Personal information of patients recorded in the data system has not been included in this study.

Missing arterial components or those not seen in the CCTA images (e.g., P1, posterior communicating artery and proximal segment of ACA) were considered to have 0.1 mm diameter for the purpose of statistical analysis (Supplementary file 1). The components of CBAN in some CCTA were not visible due to artefacts and such cases were excluded. Therefore, the number of arterial components measured in CCTA varied to a moderate extent. This, however, did not influence results of our statistical analyses (see Results).

Data collection

The position, presence or absence of aneurysms of any sizes were recorded from CCTA of 145 patients based on the diagnosis made by radiologists and clinicians. The position of aneurysms associated with the AcomAC, MCA, ICA, PCA and VB arterial regions were recorded. Some cases had multiple aneurysms. The internal diameters of intracranial segment of ICA at the level of anterior clinoid processes, the first segment of ACA (A1) at the mid-point, posterior communicating artery (PcomA) at the mid-point, the proximal end of the first segment of MCA (M1), anterior communicating artery (AcomA) at the mid-point, the proximal end of the second part of ACA (A2), the first segment of PCA (P1) at the mid-point, the proximal segment of PCA (P2) at the level of dorsum sellae, the distal end of basilar artery just proximal to the origin of superior cerebellar artery (SCA), and the distal vertebral arteries (AV) just proximal to the formation of basilar artery (BA) were measured at right angles to the longitudinal axis of arteries in each individual (Figure 1). The measured internal diameters (in millimetre, mm) were converted into the "relative sizes" of the vessels using the formula, "measured diameter of each vessel / the average size of all the CBAN components measured" (column 24 to 39 in Supplementary file 1) and transferred into the SPSS v. 25 software, before the statistical analysis. The diameters of arteries were converted into "relative sizes" to neutralize the individual differences in sizes of CBAN components among patients.

The internal diameters of the components of CBAN in CCTA were measured using image J software programme (Ij153-win-java8.zip, https://wsr.imagej.net). The diameter of each artery was measured at the narrowest region of the selected site, perpendicular to the long axis of the vessel (Figure 1), to make the measurements consistent across all CCTA images. Furthermore, the CCTA arterial data taken from all the patients were divided into two groups (see below) in order to observe the relationship of aneurysms to the

variation in the components of CBAN. Group a: patients with one and more than one cerebral aneurysm; group b: patients without cerebral aneurysms (see column number 41 in Supplementary file 1).

The accuracy of the measurements was determined by repeating measurements in CCTA of 10 cases, a week after the first measurement (Table 1 and Supplementary file 2). The relative technical error of the measurement (rTEM) was calculated and found to be within the statistically acceptable limits (i.e., ≤10%).

Figure 1 (about here)

Figure 1: Sites of arterial diameter measurement in cerebral angiography images. White lines perpendicular to the long axes of vessels show the measurement sites and white arrows depict the components of cerebral basal arterial network (CBAN). (a) = axial image showing the sites of measurement, (b) = coronal image showing the sites of measurement and location of aneurysms, (c) = coronal angiography showing the sites of vessel measurement, (d) = digital subtraction angiography showing the sites of vessel measurement. ACA = anterior cerebral artery, MCA = middle cerebral artery, ICA = cranial component of internal carotid artery, PCA = posterior cerebral artery, A1 of ACA = the first segment of ACA, A2 of ACA = the second segment of ACA, AcomA = anterior communicating artery, PcomA = posterior communicating artery, M1 of MCA = the first segment of middle cerebral artery, P1 of PCA = first segment of PCA, P2 of PCA = second segment of PCA, BA = basilar artery, VA = vertebral artery, AcomACA= AcomA complex aneurysm, and MCAA = MCA aneurysm.

Table 1: The reliability of the measurements taken in Cerebral Computed Tomography Angiography (CCTA) images.

	rt VA	lft VA	BA	rt P2	lft P2	rt PcomA	lft PcomA	rt ICA	lft ICA	rt A2	lft A2	Aco mA	rt M1	lft M1	rt P1	lft P1	rt A1	lft A1
TEM	0.025	0.021	0.019	0.018	0.017	0.013	0.014	0.023	0.055	0.020	0.069	0.070	0.020	0.023	0.018	0.017	0.076	0.115
rTem (CV)	0.982	0.767	0.644	0.793	0.697	0.708	0.909	0.533	1.305	0.751	2.783	3.623	0.684	0.805	0.842	0.755	3.732	5.825
rt reliabilit y	0.998	0.999	0.999	0.997	0.996	0.999	0.999	0.998	0.988	0.998	0.948	0.971	0.998	0.998	0.999	0.998	0.991	0.982

Reliability, the coefficients of variation (CV) or the relative technical error of cerebral vessel internal diameter measurements (rTEM) and the technical error of measurements (TEM) are presented. Reliability is the correlation among the first measurements and the second measurements taken from the same artery, n = 10. rt = right, lft = left, dia = internal diameter, ACA = anterior cerebral artery, MCA = middle cerebral artery, ICA = cranial component of internal carotid artery, PCA = posterior cerebral artery, A1 = first segment of ACA, PcomA = posterior communicating artery, AcomA = anterior communicating artery, M1 = first segment of MCA, P1 = first segment of PCA, P2 = second segment of PCA, BA = basilar artery, and VA = vertebral artery (Supplementary file 2).

The average size (Avg), standard deviation (SD) and coefficient of variation (CV) of all components of CBAN (i.e., left, and right ICA, first segment of MCA, A1, A2, P1, P2, AcomA, PcomA, and BA) were calculated for each individual. In order to avoid the influence of differences in sizes of individual CBANs, the relative sizes of each vessel of each individual were calculated by dividing its size by the average size of this individual's CBAN. Averages of such relative values obviously were close to 1.00, while standard deviations are a measure of each individual's CBAN variation, which was insensitive to its overall size (Supplementary file 1).

Statistical analysis

This is a cross-sectional observational study. The data were analysed using Excel data file and descriptive, parametric and non-parametric statistical methods, independent sample t – test, linear regression, logistic regression, and Chi squared tests from Statistical Package for the Social Sciences (SPSS IBM, version 25) program. The p values less than 0.05 were considered statistically significant, but we quote also exact p values as calculated.

Patient and public involvement

According to the conditions of our ethics permit, we were given the access to the retrospective anonymised data, thus it was impossible for us to involve patients for planning and running of this project. However, once published, the findings will be communicated to the public via a series of public seminars and information in the media. Patients and families who visit the hospital for clinical follow ups will be informed about the findings of the study. All the parties involved, will be requested to share their experiences during follow ups and seminars and be encouraged to email the authors for further enquiries. The experience shared and the suggestions received from the parties involved, will be respected and the privacy will be maintained.

Findings

Comparing averages of individual averages and averages of individual standard deviations (Std. Dev.) of the relative sizes of components of CBAN of 81 individuals that had complete data with 64 of those who had missing measurements for P1 segment or AcomA, or both, showed no significant differences. Therefore, all further analyses were based on a joint sample of 145 individuals, since these data were not sensitive to missing values (see Supplementary table 1).

Correlations between relative sizes of various components of the CBAN, though often were statistically significant, were not strong (Table 2), indicating that the individual components' sizes varied in the same individual. Statistically significant inverse relationships were found between relative sizes of ipsilateral PcomA, and P1 segments on the right and left sides (Table 2). The relative sizes of right and left PcomA were found to be inversely correlated with the relative size of basilar artery (Table 2 and Supplementary file 3). Furthermore, significant positive correlations were found between relative sizes of left and right cranial ICA, left and right first part of MCA (M1), left and right second part of ACA (A2), and left and right second part of PCA (P2) (Table 2, Supplementary table 2 and page number 4 to 8 in Supplementary file 3).

The variation in the sizes of CBAN segments was found to be greater in people with aneurysms compared to those without aneurysms (Table 3). The probability of the occurrence of aneurysms was linked significantly to variations in measurements of individual segments of CBAN, as analysed by the logistic regression (Table 4).

The majority of the cerebral aneurysms detected in the current study were in association with bilateral ICA and MCA (Supplementary tables 2 and 3, pages 2 - 4 in Supplementary file 3, and Supplementary file 4). Eighty-three patients out of 145 had cerebral aneurysms in various locations (Supplementary tables 2 and 3 and page 2 in Supplementary files 3). Some individuals had multiple aneurysms, thus a total of 113 aneurysms were found in the 83 patients (Supplementary table 2 and 3, and Supplementary file 4). Out of the total number of 113 aneurysms, 32 (28.31%), 14 (12.4%), 24 (21.24%) and 8 (7%) aneurysms were found in right MCA, right ICA, left MCA and left ICA regions respectively. Seventy-eight out of the 113 aneurysms in the 83 patients (i.e., 69% of the total) were in the right and left MCA and ICA regions (Supplementary table 2, and page 2 to 4 in Supplementary file 3). Furthermore, 27 aneurysms (23.9% of the total) were in AcomAC regions, one in each of 27 patients (Supplementary table 2). In addition, 8 aneurysms (7% of the total) were located in the VB arterial regions (Supplementary table 2). Ten and 2 patients had bilateral MCA and ICA aneurysms respectively (Supplementary table 2). Out of the 27 patients with AcomAC aneurysms, 19 of them had aneurysms only in

the AcomAC regions (Supplementary table 2). Eight patients with AcomAC aneurysms also had coexisting left MCA (n = 4), right MCA (n = 4), and right ICA (n = 4) aneurysms. Out of those eight patients with multiple coexisting aneurysms, one of them had aneurysms in AcomAC, right MCA and left MCA, while another had coexisting aneurysms in AcomAC, right ICA and right MCA (Supplementary table 2). The third patient with AcomAC aneurysm also had coexisting aneurysms in right ICA and left MCA (Supplementary table 2). Ten cases also had coexisting aneurysms in bilateral MCA territories (Supplementary table 2). Out of eight patients with VB aneurysms, one, three, one, and one also had coexisting right ICA, right MCA, left ICA and left MCA aneurysms respectively. No aneurysms were detected at or distal to P2 segments of PCA (Supplementary table 2 and 3).

Table 2: Spearman's rho nonparametric correlations among the relative size of components of CBAN.

Correlations - Spearman's rho

		BA	Rt P2	Lft P2	Rt PcomA mid dia	Lft PcomA mid dia	Rt P1	Lft P1
BA	**rho**	**1.00**	**.17***	**-.02**	**-.39****	**-.45****	**.25***	**.29****
	N	145	145	145	145	145	98	98
Rt P2	**rho**	**.17***	**1.00**	**.36****	**-.35****	**-.29****	**.23***	**.17**
	N	145	145	145	145	145	98	98
Lft P2	**rho**	**-.02**	**.36****	**1.00**	**-.21***	**-.14**	**.30****	**.19**
	N	145	145	145	145	145	98	98
RtPcomA mid dia	**rho**	**-.39****	**-.35****	**-.21***	**1.00**	**.46****	**-.60****	**-.39****
	N	145	145	145	145	145	98	98
LftPcomA mid dia	**rho**	**-.45****	**-.29****	**-.14**	**.46****	**1.00**	**-.32****	**-.64****
	N	145	145	145	145	145	98	98
RtP1	**rho**	**.25***	**.23***	**.30****	**-.60****	**-.32****	**1.00**	**.35****
	N	98	98	98	98	98	98	98
Lft P1	**rho**	**.29****	**.17**	**.19**	**-.39****	**-.64****	**.35****	**1.00**
	N	98	98	98	98	98	98	98

***. Correlation is significant at p = 0.05 level (2-tailed), **. Correlation is significant at p = 0.01 (2-tailed).**

Cerebral basal arterial network = CBAN, Rt = right, Lft = left, PCA = posterior cerebral artery, PcomA = posterior communicating artery, BA = distal basilar artery, P2 = second part of PCA, PcomA = posterior communicating artery, P1 = first part of PCA, BA= relative size of distal basilar artery, Rt P2 = relative size of right proximal P2, Lft P2 = relative size of left proximal P2, RtPcomA mid dia = relative size of right PcomA at the mid-point, LftPcomA mid dia = relative size of left PcomA at mid-point, Rt P1 = relative size of right P1 at mid-point, Lft P1 = relative size of left P1 at mid-point.

Table 3: Comparison of average size, standard deviation (SD) and Coefficient of Variation (CV) of size of CBAN, both absolute and relative, in patients with and without cerebral aneurysms (Independent sample t – test). CBAN = cerebral basal arterial network.

	Standard deviation of CBAN measurement (SD, mm) average (SD)	Coefficient of variation (CV) average (SD)	Size of CBAN (mm) average (SD)	Standard deviation of Relative size of CBAN average (SD)	Coefficient of variation (CV) of Relative size average (SD)
Patients without cerebral aneurysms (n = 62)	0.86 (0.22)	34.9 (10.0)	2.51 (0.25)	0.34 (0.10)	34.73 (9.77)
Patients with one or multiple cerebral aneurysms (n = 83)	0.96 (0.23)	38.2 (9.2)	2.52 (0.26)	0.38 (0.09)	38.18 (9.15)
Significant (2- tailed, p value)	0.015	0.038	0.708	0.036	0.033

The table 3 shows variations in components of CBAN in individuals in relation to the presence or absence of aneurysms. Variations were significantly greater in patients with aneurysms, though there was no difference in the average size of arteries in their CBAN.

Table 4: Results of logistic regression analysis relating presence of aneurysms to CV and Std. Dev.

Cerebral Basal Arterial Network = CBAN,

standard deviation = std. Dev., calculated as the standard deviation of the relative diameter of all the components of CBAN in an individual, and Coefficient of Variation = CV, calculated as 100* Std. Dev divided by the average relative size of all the components of CBAN in an individual; significant at the $p \leq 0.05$

Variables	B	Constant	p-value	EXP (B)	Sensitivity	Specificity
Std. Dev.	1.822	-1.368	0.017	6.182	78.3	33.9
CV	0.037	-1.071	0.040	1.038	81.9	27.4
Relative size Std. Dev	3.983	-1.142	0.035	53.684	80.7	27.4
Relative size CV.	.039	-1.136	0.033	1.040	80.7	27.4

Both standard deviation (Std.Dev.) and Coefficient of Variation (CV) calculated directly from the components of CBAN measured in mm and the relative size of the components of CBAN measurement, provided significant logistic result with sensitivity approximately 80% and specificity 30% (Table 4). Age of the patients in the current study, ranged from 18 to 100 years (mean = 50.9, SD =15.8) (column 2 in Supplementary file 1 and page 2 in Supplementary file 3). A logistic regression analysis, where age and coefficient of variation were included together as independent variables, indicated that both variables had a significant effect on the probability of the occurrence of aneurysms (i.e., for age: B = -0.034, p = 0.005; for CV: B = 0.038, p = 0.041), but sensitivity remained at 81.9 %, not different from sensitivities produced by standard deviations or CVs alone.

Discussion

The significant differences in the variation of segments of CBAN in people with aneurysms and without aneurysms suggest that the size of individual vessels of the CBAN varies more within a person who has an aneurysm (Table 3 and Table 4). Furthermore, the analysis also confirmed that the occurrences of aneurysms did not depend on the average size of the segments of CBAN (Table 3), but the overall variation in the size of individual segments of CBAN determined the probability of having the cerebral aneurysms (Table 3). Therefore, these statistically significant differences in the variation of segments of CBAN suggests that the correctly formed (minimally variant) segments of CBAN served to best equalize the blood pressure peaks preventing the development of cerebral aneurysms (Table 3).

Aneurysms less than 3 mm in diameter could be missed in commonly used CCTA imaging techniques.[15] The findings of the current study, on more than 4 mm in diameter sized ICA aneurysms compared well with

Imaizumi and colleagues findings.[6] Approximately, 3% of the general population develop cerebral aneurysms and may not be diagnosed, until they enlarge sufficiently to cause symptoms or rupture.[16] However, more than 70 % of aneurysms detected by Imaizumi and colleagues[6] using advanced imaging technique were ≤3mm in diameter.[16] The current study, collected data from patients with complicated and ruptured aneurysmal cases, who were referred to the Neuro-interventional Centre in RAH for treatment. Imaizumi and colleagues[6] conducted the study on healthy and asymptomatic adults and detected the right ICA territory as the most common location (78%) for the development intracranial aneurysms. Almost 83% of the detected ICA aneurysms in the latter study were ≤3.9mm in diameter[6], thus individuals with aneurysms of these sizes would not have been diagnosed and included in the current collection. The chances for the rupture of an aneurysm is minimal, when the size is ≤4mm in diameter.[2,6] Most of the CCTA images with AcomAC aneurysms (19 cases) in the current study, had no other coexisting aneurysms located elsewhere in the intracranial regions (Supplementary file 1). The frequency of aneurysms was lower in AcomAC and PCA territories in comparison to the aneurysms found in the MCA and ICA territories in the current study and in a study published recently.[6] Similar distribution patterns of intracranial aneurysms have been described in the literatures.[3,4,6,17] The absence of aneurysms elsewhere in 19 out of 27 (i.e., 70.04%) AcomAC aneurysmal cases (Supplementary files 1 and 3) may indicate that the causes of aneurysms were not due to generalised weakness of the CBAN arterial wall, hypertension, smoking and familial reasons. Vrselja and colleagues suggested that the communicating arteries divert the blood flow and dampen the peaks in systolic pressure in the CBAN system to reduce the occurrence of aneurysms.[18] The chances of the development of AcomAC aneurysms have been predicted to be ≥80% when the asymmetric ratio between right and left A1 segments is 1.42 or more (i.e., larger diameter /smaller diameter).[14] Furthermore, the effect of fluctuating peak systolic pressure in causing aneurysms in AcomAC territories would be lower in the presence of symmetrical A1 arterial segments.[14] Therefore, these 19 cases of AcomAC aneurysms could have resulted from the altered haemodynamics caused by the asymmetry between right and left A1 segments.[14]

Fluctuations of peak systolic pressures may contribute to the occurrence and rupture of cerebral aneurysm.[19] In addition, the amount of blood flowing through a MCA had been found to be increased in the presence of the hypoplastic or absent A1 segment or PcomA on that side of CBAN.[20] Therefore, the 8 cases of AcomAC aneurysms that cooccurred with aneurysms elsewhere (i.e. AcomAC aneurysms cooccurred with right ICA, right MCA and left MCA regions) might have been associated with the presence of hypoplastic or absent A1 segments or PcomA (Supplementary file 1). These variations of A1 and PcomA segments would increase the

resistance to the outflow of blood from the ICA, thus increase the flow and peak systolic pressures through the MCA. Therefore, the greater incidence (≥85% cases) of cerebral aneurysms found in the ICA and MCA territories,[3,4,17] could be linked to the altered haemodynamic in the presence of variant segments in the anterior part of CBAN.[21-23] A significant amount of wall shear stress has been noticed on a stent placed next to the aneurysmal sac, suggesting increased peaks in systolic pressure would result in the development of aneurysm.[24] This indicates that symmetrical A1 segments, and PcomA could act as the flow diverting segments of CBAN, which reduce or dampen the peak systolic pressures in the ICA and MCA reducing the incidence of aneurysms in these regions. The PCA aneurysms are rare.[7,25] The i) significant positive correlations between right and left PcomA, ipsilateral P1 and P2 segments and BA with right and left P1 segments, and ii) inverse correlations between PcomA with ipsilateral and contralateral P1 segments and BA with right and left PcomA (Table 2 and supplementary file 3) indicate that these arterial segments help to balance and maintain optimal blood flow in P2 segments. Thus, the peak systolic pressures may not reach levels that could injure the arterial wall and cause aneurysms in P2 segment and beyond.[26] This is particularly important, because the blood flow in P2 segment is maintained by two inversely correlated ($p = 0.01$) ipsilateral PcomA and P1 vessels (Table 2). Thus, the prevalence of aneurysms in the P2 segment territory of PCA is zero or minimal (Supplementary file 1 and 3). The peak systolic pressures of the blood flowing via the vertebral arteries would get dissipated in the basilar artery (which is also considered as a communicating artery[27]), and then in P1 before reaching the P2 segment. In a similar way, blood flowing from the ICA is dampened in PcomA before reaching the P2 segments, which ensures the less fluctuating peak systolic pressures in P2 and distal to the P2 segments. Therefore, pressure dampening mechanisms could smoothen the arterial pressure distal to P2 segments and reduce the chances of developing aneurysms in PCA compared to ICA, MCA and AcomAC territories.

In vertebrate brain evolution, brainstem evolved first, whereas the telencephalon (specially the frontal lobes) was a later addition to the brain.[28] Therefore, the arterial supply to the brainstem and the posterior part of the telencephalon had more time to be well established. The recently evolved large telencephalon is predominantly supplied by ICA.[29] The anterior part of CBAN evolved along with the telencephalon and has had less evolutionary time to develop, compared to the posterior segments.[28] Thus, the natural selection did not have adequate time to minimise the variations and asymmetries of the anterior segments of the CBAN. Furthermore, a larger blood volume has to flow through the less evolved anterior segments of CBAN to meet the demands of the large telencephalon.[30] Therefore; the chances of development of aneurysms in the arteries supplied by the anterior segments of CBAN are higher compared to the posterior part. Asymmetry between antimere segments

of CBAN could result from the mutations of genes involved in the development of cerebral arterial segments (e.g., development of hypoplastic right or left A1 segment of ACA) in the embryo. However, in some, the embryo has the ability to enlarge the collateral segment of a hypoplastic segment of CBAN and maintain adequate blood supply to the affected right or left side of the brain. Establishment of this compensatory blood flow also requires the enlargement of respective communicating arteries (i.e., anterior and posterior communicating arteries, or the basilar artery). Therefore, the adult brains investigated in this study (i.e., those with variations in the respective segments of the CBAN) developed normally and maintained normal function. However, the increase in blood flow in the enlarged arterial segments, could lead to the formation of aneurysms later in life. Asymmetry between antimere A1 is a good example. In these arterial segments, the risk of development of aneurysms in AcomAC is ≥80%, when the A1 asymmetry ratio remains ≥1.42.[14]

This study was not designed to examine the shape and characteristics of aneurysms, but the focus was on the relationship of the relative size of the blood vessels to the formation of aneurysms in different regions of the brain. Further investigations of cerebral blood flow and the changes in the blood pressure in the presence of asymmetric and variant arteries may help to understand the mechanisms involved in the development of aneurysms.

Limitations: The data for this study were obtained from the cases treated at a highly specialised neurointerventional centre, thus the prevalence rate of cerebral aneurysms was higher compared to the general population. It is unethical to expose general population to CTA related radiation purely for research purposes. This study is a pure cross-sectional study, since the repeated CTA from the same patient could not be obtained at different time points. The timeframe of the current study did not allow us to follow up the patients and continue as a longitudinal study. The lack of hemodynamic, patients history of smoking and blood pressure data are limitations of this study.

Conclusion

The occurrence of cerebral aneurysms varies with the variation of sizes of arteries constituting the cerebral basal arterial network. Variation of those arteries is said to affect hemodynamics, thus predisposing the associated vessels to aneurysms. Patients who have asymmetric and variant cerebral arterial segments in CBAN, should be monitored regularly. This finding could be considered as one of the criteria for screening the cerebral aneurysms.

Data sharing statement

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Extra data is available by emailing to Arjun.Burlakoti@unisa.edu.au

Funding

None

Author contribution statement

Arjun Burlakoti- conceived the idea, designed the analysis, collected and analysed the data from CCTA, took pictures, recorded videos, contributed in conceptualization, prepared and drafted the manuscript.

Jaliya Kumaratilake- conceived the idea, contributed to the concept, helped in data interpretation, editing and the critical revision of the manuscript and approving the article.

Jamie Taylor- conceived the idea, contributed in collecting and interpreting the data, editing the manuscript, the critical revision of the manuscript and approving the article.

Maciej Henneberg- conceived the idea, helped in statistics, data analysis and interpretation, editing the manuscript, the critical revision of the manuscript and in approving the article.

Competing interests

None declared. All authors have nothing to disclose.

Ethical Approval Statement

The University of Adelaide, Human Research Ethics Board granted permission to access and use data for this research project (Ethics Approval Number: H2014 -176).

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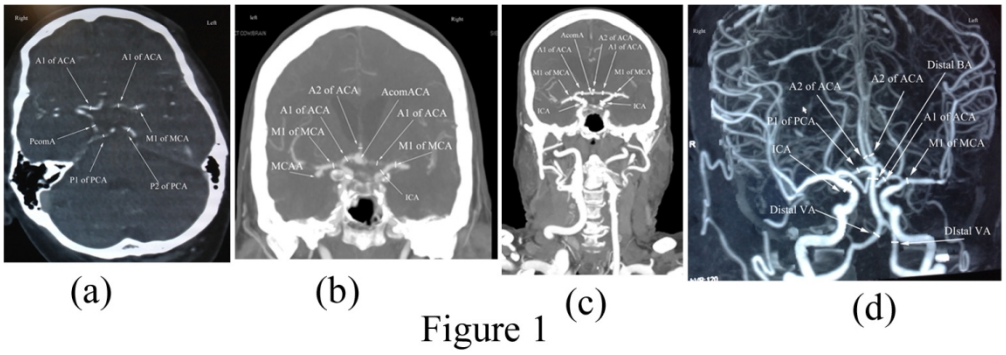


Figure 1

Figure 1: Sites of arterial diameter measurement in cerebral angiography images.
White lines perpendicular to the long axes of vessels show the measurement sites and white arrows depict the components of cerebral basal arterial network (CBAN). (a) = axial image showing the sites of measurement, (b) = coronal image showing the sites of measurement and location of aneurysms, (c) = coronal angiography showing the sites of vessel measurement, (d) = digital subtraction angiography showing the sites of vessel measurement. ACA = anterior cerebral artery, MCA = middle cerebral artery, ICA = cranial component of internal carotid artery, PCA = posterior cerebral artery, A1 of ACA = the first segment of ACA, A2 of ACA = the second segment of ACA, AcomA = anterior communicating artery, PcomA = posterior communicating artery, M1 of MCA = the first segment of middle cerebral artery, P1 of PCA = first segment of PCA, P2 of PCA = second segment of PCA, BA = basilar artery, VA = vertebral artery, AcomACA= AcomA complex aneurysm, and MCAA = MCA aneurysm.

128x45mm (300 x 300 DPI)

Supplementary Table 1: Comparing averages of individual averages and averages of individual standard deviations of the relative sizes of components of CBAN of 81 individuals that have complete data with 64 of those who had missing measurements of P1, or AcomA measurements.

	Individual averages	Individual Std. Dev.
Average	0.99661246	0.34829138
Std. Dev.	0.02189848	0.10008849
Count (N)	64	64
Average	0.9959641	0.36482336
Std. Dev.	0.01402553	0.08525546
Count (N)	81	81

CBAN = cerebral basal arterial network, P1 = first segment of posterior cerebral artery, AcomA = anterior communicating artery, Std. Dev. = standard deviations. Averages: 0.9960 for N=81 (Std. Dev. = 0.0140) and 0.9966 for N=64 (Std. Dev. = 0.0219), t = 0.20; Standard deviations: 0.3648 for N=81 (Std. Dev. = 0.0853) and 0.3483 for N=64 (Std. Dev. =0.1000), t = 1.07.

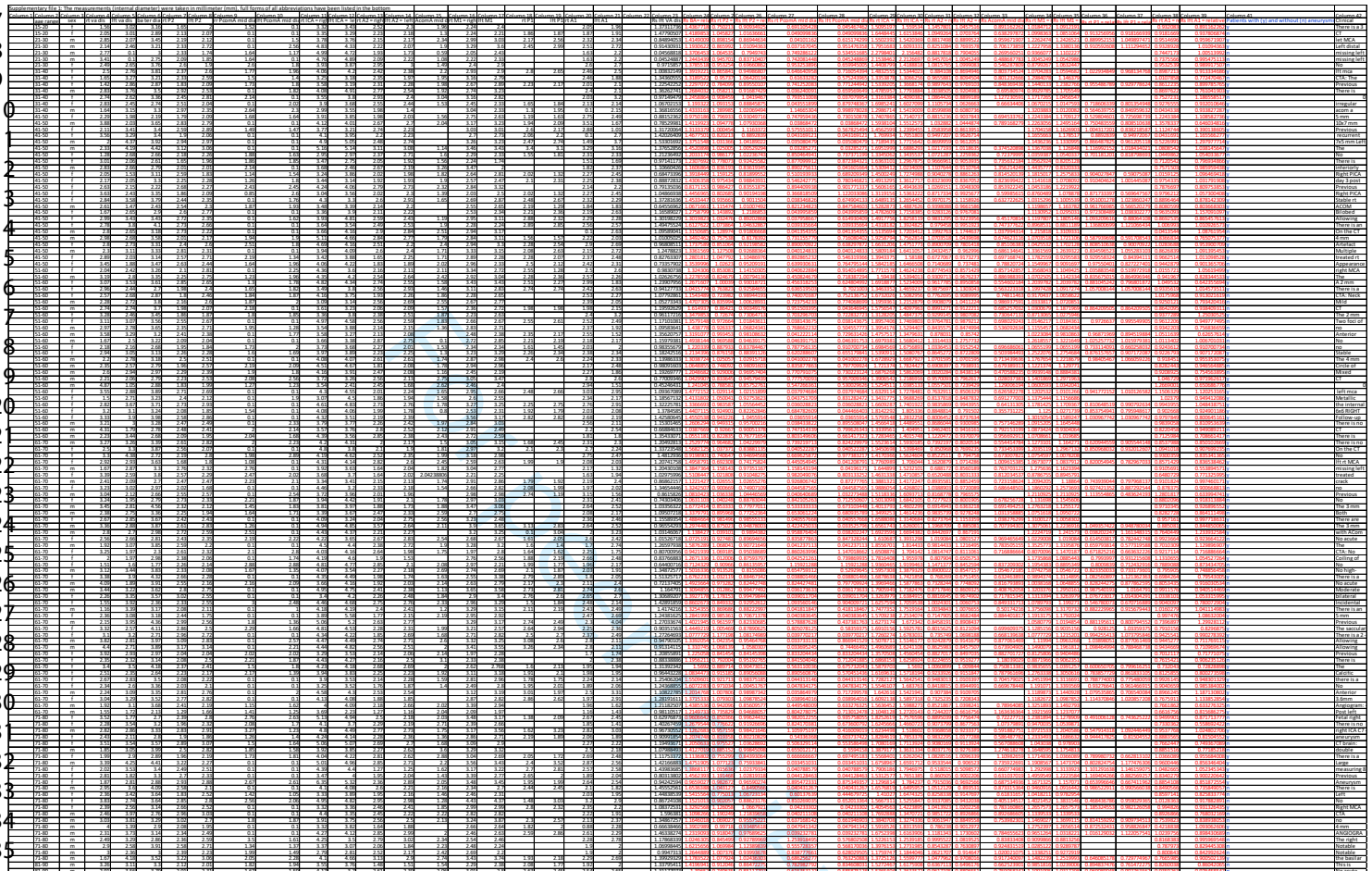
Supplementary Table 2: Anatomical locations of intracranial cerebral aneurysms in the current Cerebral Computed Tomography Angiography scans study (n = 145, age range = 18 to 100 years, female = 79, male = 67). Total 113 aneurysms were recorded in 83 patients. rt = right, lft = left, AcomAC = anterior communicating artery complex, MCA= middle cerebral artery, ICA = internal carotid artery, y = aneurysms present, n = aneurysms absent, MCA = middle cerebral artery, PCA = posterior cerebral artery, VBA = vertebra basilar arteries. P1 = first segment of PCA, and P2 = second segment of PCA.

		Aneurysms at AcomAC		rt ICA Aneurysm		rt MCA Aneurysm		lft ICA Aneurysm		lft MCA Aneurysm		Vertebro basilar aneurysm		PCA aneurysm
		n	y	n	y	n	y	n	y	n	y	n	y	n
		Count	Count	Count	Count	Count	Count	Count	Count	Count	Count	Count	Count	Count
Aneurysms at AcomAC	**n**	118	0	108	10	90	28	110	8	98	20	110	8	118
	y	0	27	23	4	23	4	27	0	23	4	27	0	27
rt ICA Aneurysm	**n**	108	23	131	0	102	29	125	6	108	23	124	7	131
	y	10	4	0	14	11	3	12	2	13	1	13	1	14
rt MCA Aneurysm	**n**	90	23	102	11	113	0	105	8	99	14	108	5	113
	y	28	4	29	3	0	32	32	0	22	10	29	3	32
lft ICA Aneurysm	**n**	110	27	125	12	105	32	137	0	115	22	130	7	137
	y	8	0	6	2	8	0	0	8	6	2	7	1	8
lft MCA Aneurysm	**n**	98	23	108	13	99	22	115	6	121	0	114	7	121
	y	20	4	23	1	14	10	22	2	0	24	23	1	24
Vertebro basilar aneurysm	**n**	110	27	124	13	108	29	130	7	114	23	137	0	137
	y	8	0	7	1	5	3	7	1	7	1	0	8	8
PCA aneurysm	**n**	118	27	131	14	113	32	137	8	121	24	137	8	145

Supplementary Table 3: Average relative sizes of cerebral arteries and aanatomical locations of cerebral aneurysms in the current Cerebral Computed Tomography Angiography scans studies (total cases, n = 145, age range = 18 to 100 years, female = 79, male = 67). Total 113 aneurysms were recorded in 83 patients. VBA = vertebra basilar arteries; ACA = anterior cerebral artery, AcomAC = anterior communicating artery complex; A1 = first segment of ACA; P2 of PCA = second part of PCA; ICA = internal carotid arterial; A2 of ACA = second part of ACA, and M1 of MCA= first part of MCA.

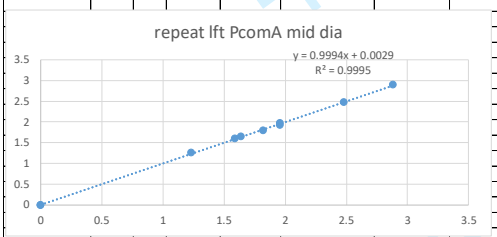
	Aneurysms		Average relative artery size (internal diameter)		Average artery size in mm (internal diameter)	
	Right	**Left**	**Right**	**Left**	**Right**	**Left**
A1 of ACA	27 aneurysms in AcomAC		0.87	0.95	2.36	2.47
ICA	14	8	1.57	1.55	3.9	3.86
M 1 of MCA	32	24	1.12	1.11	2.78	2.76
P2 of PCA	0	0	0.95	0.95	2.36	2.36
A2 of ACA	0	0	0.96	0.95	2.39	2.36
VBA aneurysms		8				

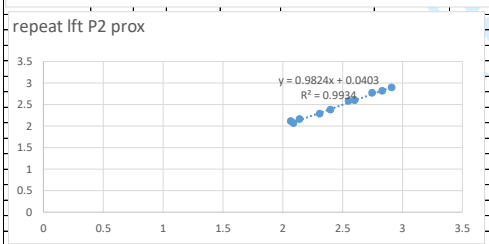
Supplementary file 1:

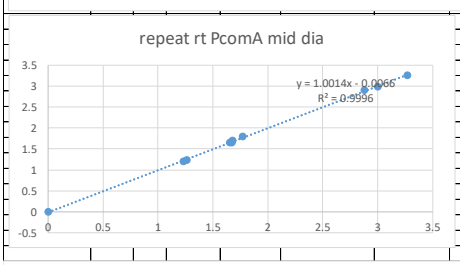


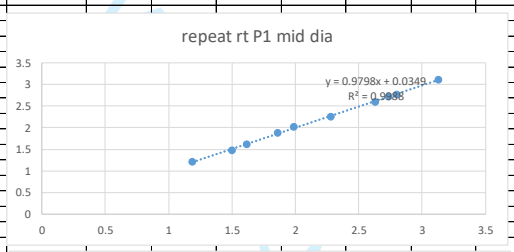
Supplementary file 2:

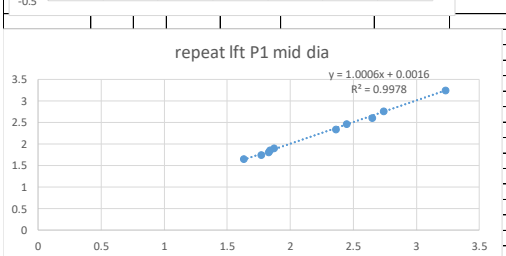
Supplementary file 2: reliability															
Sites of internal diameter r	➔	➔		rt P2 prox d	repeat rt P2 prox d	lft P2 prox dia	repeat lft P2	rt PcomA mid d	repeat rt Pco	lft PcomA m	repeat lft Pco	rt P1 mid dia	repeat rt P1	lft P1 mid dia	repeat lft P1 mid dia
				2.25	2.23	2.75	2.77	1.23	1.2	1.96	1.98	2.28	2.25	2.36	2.34
				2.61	2.57	2.83	2.81	1.26	1.24	0	0	3.13	3.11	1.83	1.81
				1.98	2	2.4	2.38	1.65	1.65	1.82	1.8	2.74	2.72	2.74	2.76
				2.01	1.99	2.31	2.28	1.67	1.65	1.59	1.6	2.63	2.6	2.45	2.47
				1.79	1.82	2.09	2.06	1.68	1.7	1.64	1.65	1.19	1.21	1.63	1.65
				2.37	2.39	2.6	2.59	1.77	1.79	1.96	1.92	2.8	2.77	2.65	2.61
				2.26	2.23	2.14	2.16	2.88	2.9	2.88	2.9	1.99	2.02	1.77	1.75
				2.33	2.32	2.55	2.57	3	2.98	2.48	2.47	1.5	1.47	1.84	1.86
				2.83	2.81	2.91	2.89	3.27	3.26	1.23	1.26	1.62	1.61	3.23	3.25
				2.13	2.1	2.07	2.11	0	0	0	0	1.86	1.89	1.87	1.9
				0.0004		0.0004		0.0009		0.0004		0.0009		0.0004	
				0.0016		0.0004		0.0004		0		0.0004		0.0004	
				0.0004		0.0004		0		0.0004		0.0004		0.0004	
				0.0004		0.0009		0.0004		0.0001		0.0009		0.0004	
				0.0009		0.0009		0.0004		0.0001		0.0004		0.0004	
				0.0004		0.0001		0.0004		0.0016		0.0009		0.0016	
				0.0009		0.0004		0.0004		0.0004		0.0009		0.0004	
				0.0001		0.0004		0.0004		1E-04		0.0009		0.0004	
				0.0004		0.0004		0.0001		0.0009		0.0001		0.0004	
				0.0009		0.0016		0		0		0.0009		0.0009	
			Sum	0.006		0.006		0.003		0.004		0.007		0.006	
		TEM		0.018		0.017		0.013		0.014		0.018		0.017	
		rTEM	CV	0.793		0.697		0.708		0.909		0.842		0.755	
			R- Square	0.995		0.993		1.000		1.000		0.999		0.998	
			r reliability	0.997		0.997		1.000		1.000		0.999		0.999	

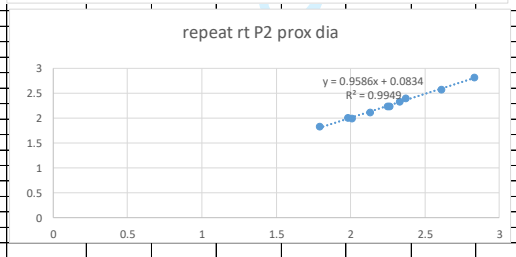












Abbreviations
PCA= posterior cerebral artery, ACA= anterior cerebral artery, MCA= middle cerebral artery, ICA= intracranial pat of internal carotid artery
P1= proximal segment of PCA, P2= ssecond segment of PCA, A1= proximal segment of ACA, A2= second segment of ACA
rt= right, lft= left, PcomA= posterior communicating artery, prox= proximal, mid dia= diameter in the middle
prox= proximal, dia= diameter
TEM= technical error of measurement
rTEM= relative TEM
CV= coefficient of variation
R squared= coefficient of determination
r= coefficient of correlation or reliability

Supplementary file 3

Abbreviations and full forms

- All the measurements were taken in millimetre (mm)
- SCA = superior cerebellar artery
- rt or Rt = right, lft or Lft = left, ter = terminal, dia = diameter, dis = distal, m = male, f = female, Rs = relative size,
- stDev = standard deviation, CV = coefficient of variation, Aver = average
- ACA = anterior cerebral artery, PCA = posterior cerebral artery, A1 = first segment of ACA, A2= second part of ACA, P2 = second segment of PCA, P1 = first segment of PCA
- ICA = internal carotid artery, MCA = middle cerebral artery, M1 = first segment of MCA, PcomA = posterior communicating artery, AcomA = anterior communicating artery
- VA or va = vertebral artery, ba or BA = basilar artery, VB Aneu = vertebro basilar aneurysm, Aneu Els = elsewhere aneurysm
- ba ter dia = diameter measured just proximal to the origin of superior cerebellar artery
- AcomAC = Anterior communicating artery complex
- AcomAC aneurysm= Aneurysm positioned at Anterior communicating artery complex (AcomAC) region, y = present, and n = absent
- Aneurysm elsewhere= Aneurysm positioned elsewhere (other than AcomAC region), y = present, and n = absent
- CBAN = cerebral basal arterial network,
- VB Aneu = vertebro basilar aneurysm, rt= right, lft= left, Dist/dist = distal, BA= basilar artery, Ter= terminal, Dia/dia= diameter
- PCA= posterior cerebral artery, PcomA= posterior communicating artery, AcomA= anterior communicating artery, ICA= internal carotid artery, MCA= middle cerebral artery, ACA= anterior cerebral artery, and SCA= superior cerebellar artery

Descriptive Statistics

	N	Minimum	Maximum	Mean	Std. Deviation
Age in years	145	18	100	60.87	15.799
Valid N (listwise)	145				

Frequency Table

Sex

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	f	78	53.8	53.8	53.8
	m	67	46.2	46.2	100.0
	Total	145	100.0	100.0	

AcomAC An = aneurysms at AcomAC junction, y=yes and n=no

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	n	118	81.4	81.4	81.4
	y	27	18.6	18.6	100.0
	Total	145	100.0	100.0	

rt ICA Aneurysm

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	n	131	90.3	90.3	90.3
	y	14	9.7	9.7	100.0
	Total	145	100.0	100.0	

rt MCA Aneurysm

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	n	113	77.9	77.9	77.9

	y	32	22.1	22.1	100.0
	Total	145	100.0	100.0	

lft ICA Aneurysm

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	n	137	94.5	94.5	94.5
	y	8	5.5	5.5	100.0
	Total	145	100.0	100.0	

lft MCA Aneurysm

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	**n**	121	83.4	83.4	83.4
	y	24	16.6	16.6	100.0
	Total	145	100.0	100.0	

vertebro basilar aneurysm

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	**n**	137	94.5	94.5	94.5
	y	8	5.5	5.5	100.0
	Total	145	100.0	100.0	

Spearman's rho Correlations

Correlations

			RsRtVA dis = relative size of right vertebral artery distal internal diameter	RsLftVA dis = relative size left vertebral artery distal internal diameter	RsBA= relative size of terminal basilar artery just proximal to SCA	RsRt P2 = relative size of proximal right 2nd part of posterior cerebral artery (P2) internal diameter	RsLft P2 = relative size of proximal left 2nd part of posterior cerebral artery (P2) internal diameter	RsRtPcoA mid dia = relative size of right posterior communicating artery external diameter around the mid-point	RsLftPcoA mid dia = relative size of left posterior communicating artery external diameter around the mid-point	RsRt IntCA = relative size of right internal carotid arterial internal diameter at the dorsum sellae level
Spearman's rho	RsRtVA dis = relative size of right vertebral artery distal internal diameter	Correlation Coefficient	1.000	-.235**	.172*	.044	-.129	-.108	-.059	-.011
		Sig. (2-tailed)	.	.005	.039	.597	.122	.196	.478	.894
		N	145	145	145	145	145	145	145	145
	RsLftVA dis = relative size left vertebral artery distal internal diameter	Correlation Coefficient	-.235**	1.000	.337**	.070	.078	-.379**	-.389**	.050
		Sig. (2-tailed)	.005	.	.000	.401	.351	.000	.000	.550
		N	145	145	145	145	145	145	145	145
	RsBA= relative size of terminal basilar artery proximal to SCA	Correlation Coefficient	.172*	.337**	1.000	.169*	-.017	-.390**	-.447**	-.062
		Sig. (2-tailed)	.039	.000	.	.043	.839	.000	.000	.460
		N	145	145	145	145	145	145	145	145
	RsRt P2 = relative size of proximal right	Correlation Coefficient	.044	.070	.169*	1.000	.357**	-.350**	-.286**	-.066
		Sig. (2-tailed)	.597	.401	.043	.	.000	.000	.000	.431

	2nd part of posterior cerebral artery (P2) internal diameter	N	145	145	145	145	145	145	145	145
	RsLft P2 = relative size of proximal left	Correlation Coefficient	-.129	.078	-.017	.357**	1.000	-.206*	-.140	-.150
		Sig. (2-tailed)	.122	.351	.839	.000	.	.013	.093	.072
	2nd part of posterior cerebral artery (P2) internal diameter	N	145	145	145	145	145	145	145	145
	RsRtPcomA mid dia = relative size of right posterior communicating artery internal diameter around the mid point	Correlation Coefficient	-.108	-.379**	-.390**	-.350**	-.206*	1.000	.456**	-.170*
		Sig. (2-tailed)	.196	.000	.000	.000	.013	.	.000	.041
		N	145	145	145	145	145	145	145	145
	RsLftPcomA mid dia = relative size of left posterior communicating artery internal diameter around the mid point	Correlation Coefficient	-.059	-.389**	-.447**	-.286**	-.140	.456**	1.000	-.277**
		Sig. (2-tailed)	.478	.000	.000	.000	.093	.000	.	.001
		N	145	145	145	145	145	145	145	145
	RsRt IntCA = relative size of right internal carotid arterial internal diameter at the dorsum sellae level	Correlation Coefficient	-.011	.050	-.062	-.066	-.150	-.170*	-.277**	1.000
		Sig. (2-tailed)	.894	.550	.460	.431	.072	.041	.001	.
		N	145	145	145	145	145	145	145	145
	RsLft IntCA = relative size of left internal carotid arterial internal diameter at the dorsum sellae level	Correlation Coefficient	-.018	-.014	.002	.198*	-.132	-.225**	-.160	.462**
		Sig. (2-tailed)	.826	.868	.981	.017	.114	.006	.055	.000
		N	145	145	145	145	145	145	145	145

	RsRt A2 = relative size of proximal right 2nd part of anterior cerebral artery (A2) internal diameter	Correlation Coefficient	-.162	.114	-.152	-.074	-.170*	.002	-.068	-.016
		Sig. (2-tailed)	.052	.173	.069	.380	.041	.979	.417	.847
		N	145	145	145	145	145	145	145	145
	RsLft A2 = relative size of proximal left 2nd part of anterior cerebral artery (A2) internal diameter	Correlation Coefficient	-.181*	.162	.006	-.014	-.031	-.154	-.230**	.034
		Sig. (2-tailed)	.029	.051	.941	.865	.713	.065	.005	.684
		N	145	145	145	145	145	145	145	145
	RsAComA mid dia = relative size of anterior communicating artery internal diameter around mid-point	Correlation Coefficient	-.264**	-.061	-.059	-.184*	-.086	.151	.112	-.221*
		Sig. (2-tailed)	.003	.492	.508	.037	.335	.088	.209	.012
		N	128	128	128	128	128	128	128	128
	RsRt M1 = relative size of proximal right 1st part of middle cerebral artery (M1) internal diameter	Correlation Coefficient	-.185*	-.074	-.040	.206*	.165*	-.203*	-.205*	.126
		Sig. (2-tailed)	.026	.376	.636	.013	.047	.014	.013	.131
		N	145	145	145	145	145	145	145	145
	RsLft M1 = relative size of proximal left 1st part of middle cerebral artery (M1) internal diameter	Correlation Coefficient	-.139	.023	-.026	.194*	.021	-.296**	-.198*	.155
		Sig. (2-tailed)	.096	.782	.756	.019	.805	.000	.017	.062
		N	145	145	145	145	145	145	145	145
	RsRt P1 = relative size of proximal right	Correlation Coefficient	.107	.152	.245*	.234*	.301**	-.600**	-.315**	-.164
		Sig. (2-tailed)	.295	.134	.015	.020	.003	.000	.002	.107

	first segment of posterior cerebral artery (PCA) internal diameter taken at mid-point	N	98	98	98	98	98	98	98	98
	RsLft P1 = relative size of proximal left	Correlation Coefficient	.015	.290**	.293**	.168	.191	-.388**	-.639**	.060
		Sig. (2-tailed)	.883	.004	.003	.098	.059	.000	.000	.554
	first segment of posterior cerebral artery (PCA) internal diameter taken at mid-point	N	98	98	98	98	98	98	98	98
	RsRt A1 = relative size of proximal right	Correlation Coefficient	-.115	-.029	-.008	.060	.222**	-.326**	-.043	-.037
		Sig. (2-tailed)	.169	.729	.922	.470	.007	.000	.604	.655
	1st part of anterior cerebral artery (A1) internal diameter	N	145	145	145	145	145	145	145	145
	RsLft A1 = relative size of proximal left 1st part of anterior cerebral artery (A1) internal diameter	Correlation Coefficient	-.176*	-.087	.026	.088	.044	-.143	-.233**	.048
		Sig. (2-tailed)	.034	.300	.754	.290	.599	.086	.005	.568
		N	145	145	145	145	145	145	145	145

Correlations

			RsLft IntCA = relative size of left internal carotid arterial internal diameter at the dorsum sellae level	RsRt A2 = relative size of proximal right 2nd part of anterior cerebral artery (A2) internal diameter	RsLft A2 = relative size of proximal left 2nd part of anterior cerebral artery (A2) internal diameter	RsACom A mid dia = relative size of anterior communicating artery internal diameter around mid-point	RsRt M1 = relative size of proximal right 1st part of middle cerebral artery (M1) internal diameter	RsLft M1 = relative size of proximal left 1st part of middle cerebral artery (M1) internal diameter	RsRt P1 = relative size of proximal right 1st part of posterior cerebral artery (P1) internal diameter taken at midpoint	RsLft P1 = relative size of proximal left 1st part of posterior cerebral artery (P1) internal diameter taken at midpoint
Spearman's rho	RsRtVA dis = relative size of right vertebral artery distal internal diameter	Correlation Coefficient	-.018	-.162	-.181*	-.264**	-.185*	-.139	.107	.015
		Sig. (2-tailed)	.826	.052	.029	.003	.026	.096	.295	.883
		N	145	145	145	128	145	145	98	98
	RsLftVA dis = relative size left vertebral artery distal internal diameter	Correlation Coefficient	-.014	.114	.162	-.061	-.074	.023	.152	.290**
		Sig. (2-tailed)	.868	.173	.051	.492	.376	.782	.134	.004
		N	145	145	145	128	145	145	98	98
	RsBA= relative size of terminal basilar artery, proximal to the origin of SCA	Correlation Coefficient	.002	-.152	.006	-.059	-.040	-.026	.245*	.293**
		Sig. (2-tailed)	.981	.069	.941	.508	.636	.756	.015	.003
		N	145	145	145	128	145	145	98	98
	RsRt P2 = relative size of proximal right 2nd part of posterior cerebral artery (P2) internal diameter	Correlation Coefficient	.198*	-.074	-.014	-.184*	.206*	.194*	.234*	.168
		Sig. (2-tailed)	.017	.380	.865	.037	.013	.019	.020	.098
		N	145	145	145	128	145	145	98	98
	RsLft P2 = relative size of proximal left	Correlation Coefficient	-.132	-.170*	-.031	-.086	.165*	.021	.301**	.191
		Sig. (2-tailed)	.114	.041	.713	.335	.047	.805	.003	.059

	2nd part of posterior cerebral artery (P2) internal diameter	N	145	145	145	128	145	145	98	98
	RsRtPcomA mid dia = relative	Correlation Coefficient	-.225**	.002	-.154	.151	-.203*	-.296**	-.600**	-.388**
	size of right	Sig. (2-tailed)	.006	.979	.065	.088	.014	.000	.000	.000
	posterior communicating artery internal diameter around the mid point	N	145	145	145	128	145	145	98	98
	RsLftPcomA mid dia =	Correlation Coefficient	-.160	-.068	-.230**	.112	-.205*	-.198*	-.315**	-.639**
	relative size of	Sig. (2-tailed)	.055	.417	.005	.209	.013	.017	.002	.000
	left posterior communicating artery internal diameter around the mid point	N	145	145	145	128	145	145	98	98
	RsRt IntCA = relative size of	Correlation Coefficient	.462**	-.016	.034	-.221*	.126	.155	-.164	.060
	right internal	Sig. (2-tailed)	.000	.847	.684	.012	.131	.062	.107	.554
	carotid arterial internal diameter at the dorsum sellae level	N	145	145	145	128	145	145	98	98
	RsLft IntCA = relative size of	Correlation Coefficient	1.000	-.139	-.024	-.435**	.100	.218**	-.088	-.052
	left internal	Sig. (2-tailed)	.	.094	.776	.000	.231	.008	.387	.612
	carotid arterial internal diameter at the dorsum sellae level	N	145	145	145	128	145	145	98	98
	RsRt A2 = relative size of	Correlation Coefficient	-.139	1.000	.579**	.173	-.071	-.030	-.134	-.156
	proximal right	Sig. (2-tailed)	.094	.	.000	.051	.393	.720	.188	.126
	2nd part of anterior cerebral artery (A2) internal diameter	N	145	145	145	128	145	145	98	98

	RsLft A2 = relative size of proximal left 2nd part of anterior cerebral artery (A2) internal diameter	Correlation Coefficient	-.024	.579**	1.000	-.009	-.041	.061	-.054	.017
		Sig. (2-tailed)	.776	.000	.	.917	.624	.465	.598	.867
		N	145	145	145	128	145	145	98	98
	RsACom A mid dia = relative size of anterior communicating artery internal diameter around mid-point	Correlation Coefficient	-.435**	.173	-.009	1.000	-.050	-.178*	-.159	-.237*
		Sig. (2-tailed)	.000	.051	.917	.	.578	.045	.156	.033
		N	128	128	128	128	128	128	81	81
	RsRt M1 = relative size of proximal right 1st part of middle cerebral artery (M1) internal diameter	Correlation Coefficient	.100	-.071	-.041	-.050	1.000	.521**	.060	.012
		Sig. (2-tailed)	.231	.393	.624	.578	.	.000	.558	.910
		N	145	145	145	128	145	145	98	98
	RsLft M1 = relative size of proximal left 1st part of middle cerebral artery (M1) internal diameter	Correlation Coefficient	.218**	-.030	.061	-.178*	.521**	1.000	.031	.114
		Sig. (2-tailed)	.008	.720	.465	.045	.000	.	.764	.262
		N	145	145	145	128	145	145	98	98
	RsRt P1 = relative size of proximal right 1st part of posterior cerebral artery (P1) internal diameter taken at midpoint	Correlation Coefficient	-.088	-.134	-.054	-.159	.060	.031	1.000	.352**
		Sig. (2-tailed)	.387	.188	.598	.156	.558	.764	.	.000
		N	98	98	98	81	98	98	98	98
	RsLft P1 = relative size of proximal left 1st	Correlation Coefficient	-.052	-.156	.017	-.237*	.012	.114	.352**	1.000
		Sig. (2-tailed)	.612	.126	.867	.033	.910	.262	.000	.

	part of posterior cerebral artery (P1) internal diameter taken at midpoint	N	98	98	98	81	98	98	98	98
	RsRt A1 = relative size of proximal right	Correlation Coefficient	-.056	.026	.071	-.200*	.180*	.137	.164	.053
		Sig. (2-tailed)	.501	.755	.397	.024	.031	.101	.106	.605
	1st part of anterior cerebral artery (A1) internal diameter	N	145	145	145	128	145	145	98	98
	RsLft A1 = relative size of proximal left 1st part of anterior cerebral artery (A1) internal diameter	Correlation Coefficient	.248**	-.073	.129	-.143	.164*	.102	.029	.222*
		Sig. (2-tailed)	.003	.383	.121	.107	.049	.221	.777	.028
		N	145	145	145	128	145	145	98	98

Correlations

			RsRt A1 = relative size of proximal right 1st part of anterior cerebral artery (A1) internal diameter	RsLft A1 = relative size of proximal left 1st part of anterior cerebral artery (A1) internal diameter
Spearman's rho	RsRtVA dis = relative size of right vertebral artery distal internal diameter	Correlation Coefficient	-.115	-.176*
		Sig. (2-tailed)	.169	.034
		N	145	145
	RsLftVA dis = relative size left vertebral artery distal internal diameter	Correlation Coefficient	-.029	-.087
		Sig. (2-tailed)	.729	.300
		N	145	145
	RsBA= relative size of terminal basilar artery, internal diameter measured proximal to the SCA	Correlation Coefficient	-.008	.026
		Sig. (2-tailed)	.922	.754
		N	145	145
	RsRt P2 = relative size of proximal right 2nd part of posterior cerebral artery (P2) internal diameter	Correlation Coefficient	.060	.088
		Sig. (2-tailed)	.470	.290
		N	145	145
	RsLft P2 = relative size of proximal left 2nd part of posterior cerebral artery (P2) internal diameter	Correlation Coefficient	.222**	.044
		Sig. (2-tailed)	.007	.599
		N	145	145

RsRtPcomA mid dia = relative size of right posterior communicating artery internal diameter at the mid point	Correlation Coefficient	-.326**	-.143
	Sig. (2-tailed)	.000	.086
	N	145	145
RsLftPcomA mid dia = relative size of left posterior communicating artery internal diameter at the mid point	Correlation Coefficient	-.043	-.233**
	Sig. (2-tailed)	.604	.005
	N	145	145
RsRt IntCA = relative size of right internal carotid arterial internal diameter at the dorsum sellae level	Correlation Coefficient	-.037	.048
	Sig. (2-tailed)	.655	.568
	N	145	145
RsLft IntCA = relative size of left internal carotid arterial internal diameter at the dorsum sellae level	Correlation Coefficient	-.056	.248**
	Sig. (2-tailed)	.501	.003
	N	145	145
RsRt A2 = relative size of proximal right 2nd part of anterior cerebral artery (A2) internal diameter	Correlation Coefficient	.026	-.073
	Sig. (2-tailed)	.755	.383
	N	145	145
RsLft A2 = relative size of proximal left 2nd part of anterior cerebral artery (A2) internal diameter	Correlation Coefficient	.071	.129
	Sig. (2-tailed)	.397	.121
	N	145	145
RsAComA mid dia = relative size of anterior communicating artery internal diameter around mid point	Correlation Coefficient	-.200*	-.143
	Sig. (2-tailed)	.024	.107
	N	128	128
RsRt M1 = relative size of proximal right 1st part of middle cerebral artery (M1) internal diameter	Correlation Coefficient	.180*	.164*
	Sig. (2-tailed)	.031	.049
	N	145	145
RsLft M1 = relative size of proximal left 1st part of middle cerebral artery (M1) internal diameter	Correlation Coefficient	.137	.102
	Sig. (2-tailed)	.101	.221
	N	145	145
RsRt P1 = relative size of proximal right first segment of posterior cerebral artery (PCA) internal diameter taken at mid-point	Correlation Coefficient	.164	.029
	Sig. (2-tailed)	.106	.777
	N	98	98
RsLft P1 = relative size of proximal left first segment of posterior cerebral artery (PCA) internal diameter taken at mid-point	Correlation Coefficient	.053	.222*
	Sig. (2-tailed)	.605	.028
	N	98	98
RsRt A1 = relative size of proximal right 1st part of anterior cerebral	Correlation Coefficient	1.000	.106
	Sig. (2-tailed)	.	.204

artery (A1) internal diameter	N	145	145
RsLft A1 = relative size of	Correlation Coefficient	.106	1.000
proximal left 1st part of anterior	Sig. (2-tailed)	.204	.
cerebral artery (A1) internal	N	145	145
diameter			

**. Correlation is significant at the 0.01 level (2-tailed).

*. Correlation is significant at the 0.05 level (2-tailed).

Supplementary file 4:

Supplementary file 4 - please refer to the supplementary file 1 as well																
Total CTA cases	CTA cases (patients) with	cases (patients) with single aneurysm	cases (patients) with no aneurysm	cases (patients) with multiple aneurysm	AcomAC aneurysm	total rt ICA aneurysm	total rt MCA aneurysm	total lft ICA aneurysm	total lft MCA aneurysm	total VB aneurysm	total number of aneurysms in all cases	total aneurysms in left and right ICA and MCA region	aneurysms other than right and left ICA and MCA regions	number of AcomAC aneurysm	number of left and right PCA aneurysm
165	83	56	62	27	27	16	32	8	24	8	113	78	35	27	0
ACA = anterior cerebral artery, PCA = posterior cerebral artery, A1 = first segment of ACA, P2 = second segment of PCA, P1 = first segment of PCA																
CTA = cerebral computed tomography angiography,																
Chi squared test, p≤0.001																
ICA = cranial segment of internal carotid artery, MCA = middle cerebral artery, AcomA = anterior communicating artery																
AcomAC aneurysm= Aneurysm positioned at anterior communicating artery complex (AcomAC) region																
78 out of 113 number of aneurysms were located in the ICA and MCA territories (i.e. 69% of the total aneurysms occurred in ICA an MCA regions), Chi squared test, p≤0.001)																
r or Rt = right, lft or Lft = left																

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2 and 3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5
Bias	9	Describe any efforts to address potential sources of bias	*5 and 6*
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5 and 8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	5
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	5
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	5
		(b) Indicate number of participants with missing data for each variable of interest	
Outcome data	15*	Report numbers of outcome events or summary measures	10
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9, 10, and 11
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	11
Discussion			
Key results	18	Summarise key results with reference to study objectives	11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14
Generalisability	21	Discuss the generalisability (external validity) of the study results	13 and 14
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	15

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.