

# BMJ Open Relationship between cerebral aneurysms and variations in cerebral basal arterial network: a morphometric cross-sectional study in Computed Tomography Angiograms from a neurointerventional unit

Arjun Burlakoti <sup>1,2</sup>, Jaliya Kumaratilake,<sup>3</sup> Jamie Taylor,<sup>4</sup> Maciej Henneberg<sup>5</sup>

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For numbered affiliations see end of article.

## Correspondence to

Arjun Burlakoti;  
[arjun.burlakoti@unisa.edu.au](mailto:arjun.burlakoti@unisa.edu.au)

## ABSTRACT

**Objective** Segments of cerebral basal arterial network (CBAN) dampen the peak pressure in blood flowing through these arteries, thus minimising 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 cerebral CT angiography (CCTA) images.

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

**Main outcome measures** Diameters of segments of CBAN were measured in CCTA 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 and vertebral-basilar 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 was quantified. The peak pressure dampening mechanism in such arterial segments reduces the chances of development of aneurysms.

## INTRODUCTION

Cerebral aneurysms are a common cause of haemorrhagic stroke. Diagnosis, management, prediction and prevention of

## Strengths and limitations of this study

- To the best of our knowledge, the standardisation of the sizes of the cerebral arteries is introduced for the first time.
- CT 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.

aneurysms are challenging.<sup>1</sup> 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.<sup>2–5</sup> 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.<sup>6</sup> Therefore, most of the cerebral aneurysms occur in ICA, MCA and AcomAC territories.<sup>2–6</sup> 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 has been reported to be the lowest.<sup>7–9</sup> 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.<sup>4 10</sup> Individuals with ruptured aneurysms had poor prognosis and more than a third of the mortalities occurred within the first month of the illness.<sup>4 10</sup> Most of the

ruptured aneurysms (85.6% cases) were reported to be symptomatic and they were in the MCA and AcomAC territories.<sup>45</sup> Therefore, studying the relationship of relative sizes of cerebral arteries, sites of location of cerebral aneurysms and their relationship to the variant segments of cerebral basal arterial network (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.<sup>11</sup> 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.<sup>11 12</sup> However, asymmetric and variant segments of the CBAN alter the haemodynamics and peaks in pressure of the blood flowing through them and predisposes the associated 'arterial complexes' to the development of aneurysms.<sup>11 13</sup> 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.<sup>14</sup> 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.

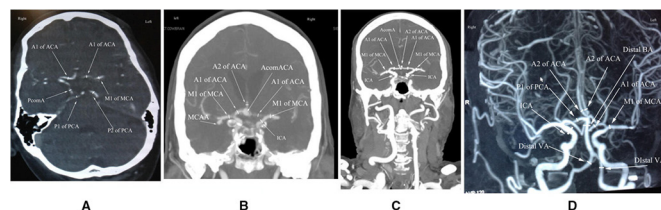
## MATERIAL AND METHOD

### Study design

Randomly selected cerebral CT angiography (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 18–100 years, male=67, female=78, mean age=60.9 years) (online supplemental file 1). The Carestream database file used in this study holds anonymised data of patients who on admission to the RAH, University of Adelaide, has 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.

The CCTA images with severe artefacts or from patients with severe cerebral vasospasm (ie, 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 (eg, P1, posterior communicating artery



**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; A1 of ACA, the first segment of ACA; A2 of ACA, the segment of ACA; AcomA, anterior communicating artery; AcomACA, AcomA complex aneurysm; BA, basilar artery; ICA, cranial component of internal carotid artery; MCA, middle cerebral artery; MCAA, MCA aneurysm; M1 of MCA, the first segment of middle cerebral artery; P1 of PCA, first segment of PCA; P2 of PCA, second segment of PCA; PCA, posterior cerebral artery; PcomA, posterior communicating artery; VA, vertebral artery.

and proximal segment of ACA) were considered to have 0.1 mm diameter for the purpose of statistical analysis (online supplemental file 1). The components of CBAN in some CCTA images were not visible due to artefacts and such cases were excluded. Therefore, the number of arterial components measured in CCTA images varied to a moderate extent. This, however, did not influence results of our statistical analyses (see Findings).

### Data collection

The position, presence or absence of aneurysms of any sizes were recorded from CCTA images 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 was 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 (BA) just proximal to the origin of superior cerebellar artery and the distal vertebral arteries (VA) just proximal to the formation of BA were measured at right angles to the longitudinal axis of arteries in each individual (figure 1). The measured internal diameters (mm) of each individual 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' (columns

24–39 in online supplemental file 1) and transferred into the SPSS V.25 software, before the statistical analysis. The diameters of arteries were converted into ‘relative sizes’ to neutralise the individual differences in sizes of CBAN components among patients.

The internal diameters of the components of CBAN in CCTA images 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 online supplemental file 1).

The accuracy of the measurements was determined by repeating measurements in CCTA images of 10 cases, a week after the first measurement (table 1 and online supplemental file 2). The relative technical error of the measurement was calculated and found to be within the statistically acceptable limits (ie, ≤10%).

The average size (Avg), SD and coefficient of variation (CV) of all components of CBAN (ie, left and right ICA, first segment of MCA, A1, A2, P1, P2, AcomA, PcomA and BA) were calculated. 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 all the arteries of this individual’s CBAN. Averages of such relative values obviously were close to 1.00, while SD are a measure of each individual’s CBAN variation, which was insensitive to its overall size (online supplemental 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  $\chi^2$  tests from Statistical Package for the Social Sciences (SPSS IBM, V.25) programme. The p values less than 0.05 were considered statistically significant, but exact p values were also quoted as calculated.

### Patient and public involvement

According to the conditions of the ethics permit, the access was given 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. Experiences

**Table 1** The reliability of the measurements taken in cerebral CT angiography (CCTA) images

	rt VA	lft VA	BA	rt P2	lft P2	rt PcomA	lft PcomA	rt ICA	lft ICA	rt A2	lft A2	AcomA	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.

A1, first segment of ACA; ACA, anterior cerebral artery; AcomA, anterior communicating artery; BA, basilar artery; dia, internal diameter; ICA, cranial component of internal carotid artery; lft, left; M1, first segment of MCA; MCA, middle cerebral artery; P1, first segment of PCA; P2, second segment of PCA; PcomA, posterior communicating artery; rt, right; VA, vertebral artery.

**Table 2** Spearman's rho non-parametric correlations among the relative size of components of CBAN, p = significance (2-tailed)

Correlations: Spearman's rho								
		BA	Rt P2	Lft P2	Rt PcomA mid dia	Lft PcomA mid dia	Rt P1	Lft P1
BA	rho	<b>1.00</b>	<b>0.17*</b> p=0.045	-0.02	<b>-0.39**</b>	<b>-0.45**</b>	<b>0.25*</b> p=0.015	<b>0.29**</b> p=0.003
	N	145	145	145	145	145	98	98
Rt P2	rho	<b>0.17*</b> p=0.043	<b>1.00</b>	<b>0.36**</b> p<0.001	<b>-0.35**</b>	<b>-0.29**</b>	<b>0.23*</b> p=0.020	0.17
	N	145	145	145	145	145	98	98
Lft P2	rho	-0.02	<b>0.36**</b> p<0.001	<b>1.00</b>	<b>-0.21*</b>	-0.14	<b>0.30**</b> p=0.003	0.19
	N	145	145	145	145	145	98	98
RtPcomA mid dia	rho	<b>-0.39**</b>	<b>-0.35**</b>	<b>-0.21*</b>	<b>1.00</b>	<b>0.46**</b> p<0.001	<b>-0.60**</b>	<b>-0.39**</b>
	N	145	145	145	145	145	98	98
LftPcomA mid dia	rho	<b>-0.45**</b>	<b>-0.29**</b>	-0.14	<b>0.46**</b>	<b>1.00</b>	<b>-0.32**</b>	<b>-0.64**</b>
	N	145	145	145	145	145	98	98
RtP1	rho	<b>0.25*</b> p=0.015	<b>0.23*</b> p=0.020	<b>0.30**</b> p=0.003	<b>-0.60**</b>	<b>-0.32**</b>	<b>1.00</b>	<b>0.35**</b> p<0.001
	N	98	98	98	98	98	98	98
Lft P1	rho	<b>0.29**</b> p=0.003	0.17	0.19	<b>-0.39**</b> p<0.001	<b>-0.64**</b>	<b>0.35**</b> p<0.001	<b>1.00</b>
	N	98	98	98	98	98	98	98

\*Correlation is significant at p=0.05 level (two-tailed).

†Correlation is significant at p=0.01 (two-tailed).

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

shared and 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 SD of the relative sizes of components of CBAN in 81 individuals who 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 online supplemental 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 BA (table 2 and online supplemental

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, online supplemental table 2 and page numbers 4–8 in online supplemental file 3).

The variation in the sizes of CBAN segments was found to be greater in people with aneurysms compared with 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 (online supplemental tables 2 and 3, pages 2–4 in online supplemental files 3 and 4). Eighty-three patients out of 145 had cerebral aneurysms in various locations (online supplemental tables 2 and 3 and page 2 in online supplemental file 3). Some individuals had multiple aneurysms, thus a total of 113 aneurysms were found in the 83 patients (online supplemental tables 2 and 3, and online supplemental

**Table 3** Comparison of average size, 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)

	SD of CBAN measurement (SD, mm)	Coefficient of variation (CV)	Size of CBAN (mm)	SD of relative size of CBAN	Coefficient of variation (CV) of Relative size
	Average (SD)	Average (SD)	Average (SD)	Average (SD)	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 (two-tailed, p-value)	0.015	0.038	0.708	0.036	0.033

CBAN, cerebral basal arterial network.

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 (ie, 69% of the total) were in the right and left MCA and ICA regions (online supplemental table 2, and pages 2–4 in online supplemental file 3). Furthermore, 27 aneurysms (23.9% of the total) were in AcomAC regions, one in each of 27 patients (online supplemental table 2). In addition, eight aneurysms (7% of the total) were located in the VB arterial regions (online supplemental table 2). Ten and two patients had bilateral MCA and ICA aneurysms, respectively (online supplemental table 2). Out of the 27 patients with AcomAC aneurysms, 19 of them had aneurysms only in the AcomAC regions (online supplemental 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 (online supplemental table 2). The third patient with AcomAC aneurysm also had coexisting aneurysms in right ICA and left MCA (online supplemental table 2). Ten cases also had coexisting aneurysms in bilateral MCA territories (online supplemental 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 (online supplemental tables 2 and 3).

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

Standard deviation and coefficient of variation (CV) were 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 two in online supplemental file 1 and page two in online supplemental file 3). A logistic regression analysis, where age and CV were included together as independent variables, indicated that both variables had a significant effect on the probability of the occurrence of aneurysms (ie, 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 SD or CVs alone.

**Table 4** Results of logistic regression analysis relating presence of aneurysms to CV and SD

Variables	B	Constant	P value	EXP (B)	Sensitivity	Specificity
SD	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 SD	3.983	-1.142	0.035	53.684	80.7	27.4
Relative size CV	0.039	-1.136	0.033	1.040	80.7	27.4

SD calculated as the SD of the relative diameter of all the components of CBAN in an individual, and CV calculated as 100×SD divided by the average relative size of all the components of CBAN in an individual; significant at the p≤0.05. CBAN, cerebral basal arterial network; CV, coefficient of variation.



## 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 (tables 3 and 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 equalise 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.<sup>15</sup> The findings of the current study, on more than 4 mm in diameter sized ICA aneurysms compared well with Imaizumi and colleagues findings.<sup>6</sup> Approximately, 3% of the general population develop cerebral aneurysms and may not be diagnosed, until they enlarge sufficiently to cause symptoms or rupture.<sup>16</sup> However, more than 70% of aneurysms detected by Imaizumi and colleagues<sup>6</sup> using advanced imaging technique were  $\leq 3$  mm in diameter.<sup>16</sup> 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<sup>6</sup> conducted the study on healthy and asymptomatic adults and detected the right ICA territory as the most common location (78%) for the development of intracranial aneurysms. Almost 83% of the detected ICA aneurysms in the latter study were  $\leq 3.9$  mm in diameter,<sup>6</sup> 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 are minimal, when the size is  $\leq 4$  mm in diameter.<sup>2,6</sup> 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 (online supplemental 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.<sup>6</sup> Similar distribution patterns of intracranial aneurysms have been described in the literatures.<sup>3,4,6,17</sup> The absence of aneurysms elsewhere in 19 out of 27 (ie, 70.04%) AcomAC aneurysmal cases (online supplemental 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.<sup>11</sup> The chances of the development of AcomAC aneurysms have been predicted to be  $\geq 80\%$  when the asymmetric ratio between right and left

A1 segments is 1.42 or more (ie, larger diameter/smaller diameter).<sup>14</sup> 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.<sup>14</sup> Therefore, these 19 cases of AcomAC aneurysms could have resulted from the altered haemodynamics caused by the asymmetry between right and left A1 segments.<sup>14</sup>

Fluctuations of peak systolic pressures may contribute to the occurrence and rupture of cerebral aneurysm.<sup>18</sup> 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 the CBAN.<sup>19</sup> Therefore, the eight cases of AcomAC aneurysms that cooccurred with aneurysms elsewhere (ie, 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 (online supplemental 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 ( $\geq 85\%$  cases) of cerebral aneurysms found in the ICA and MCA territories<sup>3,4,17</sup> could be linked to the altered haemodynamics in the presence of variant segments in the anterior part of CBAN.<sup>20-22</sup> 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.<sup>23</sup> 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.<sup>7,24</sup> 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 online supplemental 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.<sup>25</sup> 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 (online supplemental files 1 and 3). The peak systolic pressures of the blood flowing via the VAs would get dissipated in the BA (which is also considered as a communicating artery),<sup>12</sup> 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 with 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.<sup>26</sup> 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.<sup>27</sup> The anterior part of CBAN evolved along with the telencephalon and has had less evolutionary time to develop, compared with the posterior segments.<sup>26</sup> 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.<sup>28</sup> Therefore, the chances of development of aneurysms in the arteries supplied by the anterior segments of CBAN are higher compared with the posterior part. Asymmetry between antimeres segments of CBAN could result from the mutations of genes involved in the development of cerebral arterial segments (eg, 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 (ie, AcomA, PcomA or the BA). Therefore, the adult brains investigated in this study (ie, 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 antimeres of A1 is a good example. In these arterial segments, the risk of development of aneurysms in AcomAC is  $\geq 80\%$ , when the A1 asymmetry ratio reaches  $\geq 1.420$ .<sup>14</sup>

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 with 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 haemodynamics, 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 CBAN. Variation of those arteries is said to affect haemodynamics, 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.

#### Author affiliations

<sup>1</sup>School of Health Sciences, University of South Australia, Adelaide, South Australia, Australia

<sup>2</sup>UniSA Allied Health and Human Performance, University of South Australia, Adelaide, South Australia, Australia

<sup>3</sup>Anatomy and Pathology, The University of Adelaide Adelaide Medical School, Adelaide, South Australia, Australia

<sup>4</sup>South Australia Medical Imaging, Royal Adelaide Hospital, Adelaide, South Australia, Australia

<sup>5</sup>Institute of Evolutionary Medicine, University of Zurich, Zurich, Switzerland

**Twitter** Arjun Burlakoti @draburlakoti

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#### ORCID iD

Arjun Burlakoti <http://orcid.org/0000-0001-9317-6352>

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