Original Article

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Anatomy Section

Age and Sex-related Anatomical Variation in Vessel Diameters of Circle of Willis in Patients of Subarachnoid Haemorrhage using Digital Subtraction Angiography: A Retrospective Descriptive Study

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ABSTRACT

Introduction: Subarachnoid Haemorrhage (SAH) is a distinct form of stroke characterised by bleeding in the subarachnoid space. The incidence of SAH is influenced by various factors, including age, gender, and geographic location.

Aim: To evaluate age and sex-related anatomical variation in vessel diameters of the Circle of Willis (CoW) in patients with SAH in Eastern India.

Materials and Methods: A retrospective descriptive analysis was conducted on patients with ruptured intracranial aneurysms who were admitted to the Institute of Neurosciences in Kolkata and diagnosed with SAH using brain computed tomography between January 2014 and September 2015. Digital Subtraction Angiography (DSA) was performed on 50 patients, aged 15 to 70 years. The vessel diameters of CoW components were measured using specialised software. Statistical analysis using the Mann-Whitney test was conducted to assess differences in vessel diameters based on age and sex.

Results: The results showed that older patients (≤40 years) had larger vessel diameters compared to younger patients (<40 years) in most segments of the CoW, indicating possible age-related atherosclerotic changes. Among female patients, the younger age group exhibited a significantly larger mean vessel diameter of 1.67 mm in the Anterior Cerebral Artery (ACA) (A1) segment of the left-side compared to the older age group with a mean vessel diameter of 1.32 mm in the same segment (p-value=0.045). In general, males had larger vessel diameters than females, except in specific segments.

Conclusion: The knowledge gained from this research can contribute to improve the accuracy and effectiveness of interventions, such as endovascular coiling or surgical clipping, and ultimately optimising patient outcomes.

Keywords: Cerebral artery, Hypoplastic vessels, Morphometric variation, Neuroimaging

INTRODUCTION

Subarachnoid Haemorrhage (SAH) is distinct from other forms of stroke due to its risk factors, demographics, and treatment. It involves bleeding in the subarachnoid space between the arachnoid mater and pia mater of the brain coverings, caused by factors such as aneurysmal rupture, trauma, or bleeding disorders. The incidence of SAH is influenced by several factors, including age, gender, race, and geographical location. The most common cause of SAH is the rupture of a cerebral aneurysm, and individuals with a family history of SAH, smoking, hypertension, and heavy alcohol consumption are at increased risk [1]. SAH is often clustered with other stroke subtypes, making its unique epidemiology less apparent. Unlike other types of strokes, the population-based incidence of SAH has remained stable over the last three decades at approximately 10 per 100,000 per year, accounting for 6-8% of all strokes in Western populations [2,3]. However, a study conducted on the Kashmiri population suggests a higher incidence rate of 13 per 100,000 in that population [4]. SAH is a catastrophic event with a mortality rate of 25% to 50%, and nearly 50% of survivors experience permanent disability [5]. Unlike other stroke subcategories, SAH affects younger people and women more than men, and has a higher early case fatality rate, making it a medical emergency [6].

Intracranial berry aneurysms, also known as a saccular aneurysms, are sac-like out-pouchings in a cerebral blood vessels that can resemble berries. They occur in 1-2% of the population and account for about 80-85% of non-traumatic SAH cases [7]. Approximately 75% of aneurysms are found in the Circle of Willis (CoW), which is where the main cerebral arteries bifurcate and connect [8]. The CoW is a large arterial anastomosis that unites the internal carotid and vertebrobasilar systems. It is located in the subarachnoid space within the interpeduncular cistern and surrounds the optic chiasma and infundibulum. The CoW consists of the Anterior Cerebral Arteries (ACA A1 segment) anteriorly, which are derived from the Internal Carotid Arteries (ICA) and connected by the small Anterior Communicating Artery (ACom). Posteriorly, the two Posterior Cerebral Arteries (PCA P1 segment), formed by the division of the Basilar artery, are joined to the ipsilateral ICA by a Posterior Communicating Artery (PCom) [9].

The functional aspect of the CoW was postulated by Thomas Willis nearly 400 years ago, suggesting that it serves as a compensatory mechanism in cases of ICA or vertebral artery occlusion or stenosis [10,11]. However, an alternative perspective on the evolutionary purpose of the CoW challenges this notion and suggests a passive energy (pressure) dissipating system from high-pressure regions to low-pressure regions. The communicating arteries within the CoW are often observed to be too small or hypoplastic in the majority of individuals. This mechanism helps prevent damage to the delicate cranial microvasculature and preserves the integrity of the blood-brain barrier, safeguarding the cranial microvasculature [12]. Therefore, accurate evaluation of the morphometric anatomy of this region is crucial, especially in the context of SAH. Previous studies have been conducted using cadaver dissection, CT or MR angiography, but there is a lack of DSA-guided studies in the scientific arena. Currently, intra-arterial DSA is considered the gold standard diagnostic method for detecting cerebral aneurysms, with a sensitivity of 89% and a specificity of 100% [13]. DSA is an effective method for evaluation of cerebral aneurysms and designing treatment plans before surgery in SAH patients. This study utilised DSA to evaluate the morphology of the CoW in the setting of SAH, providing important data on the eastern Indian population that can be used by neuro-interventionists to design a suitable treatment plans.

MATERIALS AND METHODS

This retrospective descriptive analysis focused on patients with ruptured intracranial aneurysms who were admitted to the Institute of Neurosciences in Kolkata, West Bengal, India, and diagnosed with Subarachnoid Haemorrhage (SAH) using brain computed tomography between January 2014 and September 2015. The study received approval from the institutional ethical committee of Medical College, Kolkata.

Inclusion criteria: The study included SAH patients aged 15 to 70 years who voluntarily gave consent to participate.

Exclusion criteria: Traumatic SAH patients were excluded from the study.

Procedure

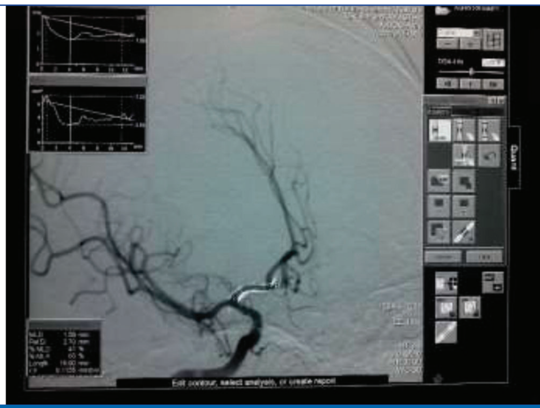
Digital Subtraction Angiography (DSA) was conducted using a Siemens-Artis-Zee single-plane flat-panel cerebral angiography machine with 3D rotation capability. Patients were brought to the procedure room, and consent to perform DSA was obtained from the patient and/or their relatives. The angiography was performed under local anaesthesia in the presence of an anaesthesiologist. Mild sedation was administered when necessary. The procedure involved puncturing the femoral artery using the Seldinger technique. A 5Fr Glide Catheter (TERUMO) was placed in the right and left Internal Carotid Artery (ICA) and basilar artery for imaging using contrast agents such as Omnipaque (350 mg/100 mL) or Visipaque (320 mg/100 mL). DSA was performed at a rate of two frames per second. Images were taken for each artery in antero-posterior (matrix 1440×1440), right and left lateral (matrix 1920×1920), and oblique (matrix 1024×1024) views.

Images were captured for all four vessels of the bilateral ICA and vertebral artery in different views. Vessel caliber was assessed computationally using a CF value of 0.1155. If an aneurysm was found, 3D rotation was used to examine the territory. At the end of the procedure, the angiograms were analysed at a workstation using 3D reconstruction.

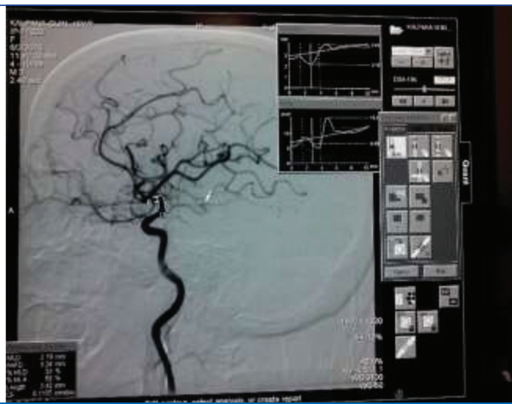
The DSA images were accessed and analysed through the Picture Archiving and Communication System (PACS). The course and caliber of vessels in the Circle of Willis (CoW) were assessed, including the Anterior Cerebral Artery (ACA) A1 segment [Table/Fig-1], ICA [Table/Fig-2], Posterior Cerebral Artery (PCA) P1 segment, and Posterior Communicating Artery (PCom). Vessel diameters were measured. The detailed anatomy of the anterior communicating artery was not studied unless an aneurysm was present in that location, in which case its shape and diameter were measured after 3D reconstruction. Treatment decisions were based on these findings.

STATISTICAL ANALYSIS

The data collected during the study were entered into an excel sheet and subjected to statistical analysis using Statistical Package for Social Sciences (SPSS) software version 22.0. Categorical variables were presented as the number and percentage of patients. Continuous variables were expressed as mean, median, and standard deviation, and comparisons between groups were made using the Mann-Whitney U test and t-test. A significance level of 5% (alpha level ≤0.05) was considered statistically significant.



[Table/Fig-1]: Oblique view showing A1 segment of ACA & bifurcation of ICA.



[Table/Fig-2]: Lateral view showing ICA.

RESULTS

A total of 50 patients (31 males and 19 females), ranging in age from 15 to 70 years with a mean age of 52.5 years, were included in this study. Among the selected cases, nine patients (5 males and 4 females) were below 40 years of age, while the remaining 41 patients (26 males and 15 females) were above 40 years of age. The bilateral mean vessel diameter with standard deviation of the Internal Carotid Artery (ICA) at its bifurcation, bilateral Anterior Cerebral Artery (ACA) A1 segment, Posterior Cerebral Artery (PCA) P1 segment, and Posterior Communicating Artery (PCom) were observed [Table/Fig-3]. A total of nine observations among vessel segments were suggested to be hypoplastic and not visible with angiography. At the level of the Circle of Willis (CoW), it was noted that the centripetal vessels (right and left ICA) had larger diameters than the rest.

Vessels of CoW	Minimum (mm)	Maximum (mm)	Mean (mm)	Std. Deviation (mm)
Age (years)	15.00	79.00	52.52	12.98
ACA (A1)-right-side	0.40	2.26	1.57	0.38
ICA-right-side	1.14	6.34	3.01	0.83
PCOM-right-side	0.40	1.70	0.90	0.36
PCA (P1)-right-side	0.40	2.61	1.44	0.45
ACA (A1)-left-side	0.40	2.07	1.48	0.37
ICA-left-side	2.02	4.93	3.03	0.62
PCOM-left-side	0.40	1.64	0.94	0.31
PCA (P1)-left-side	0.40	2.94	1.47	0.45

[Table/Fig-3]: Morphometric analysis of vessels of CoW in all age and gender groups with mean and standard deviation done with Mann-Whitney test.

It was observed that the mean vessel diameter increased with age, with subjects above 40 years showing larger mean diameters compared to those below 40 years, except for the left PCA P1 segment, left ACA A1 segment, and right PCom, which had larger mean diameters, although the difference was not statistically significant [Table/Fig-4].

A larger mean diameter was noted in males compared to females, except in the left and right PCom where the mean diameter was higher in females, although the difference was not statistically significant [Table/Fig-5].

Analysis of vessels CoW	Age (years)				p-value
	<=40		>40		
	Mean (mm)	Std. Deviation (mm)	Mean (mm)	Std. Deviation (mm)	
ACA (a1)-right-side	1.52	0.38	1.58	0.38	0.686
ICA-right-side	2.69	0.45	3.09	0.88	0.120
PCOM-right-side	0.96	0.41	0.89	0.36	0.649
PCA (p1)-right-side	1.36	0.23	1.46	0.49	0.283
ACA (a1)-left-side	1.65	0.34	1.44	0.36	0.096
ICA-left-side	2.73	0.58	3.10	0.61	0.086
PCOM-left-side	0.88	0.34	0.95	0.31	0.464
PCA (p1)-left-side	1.53	0.29	1.46	0.48	0.920

[Table/Fig-4]: Morphometric analysis of vessels of CoW in two age groups i.e., >40 and ≤40 years with statistical significance done with t-test.

Analysis of CoW	Sex				p-value
	Female		Male		
	Mean (mm)	Std. Deviation (mm)	Mean (mm)	Std. Deviation (mm)	
ACA(A1)-right-side	1.53	0.45	1.59	0.34	0.529
ICA-right-side	2.91	1.11	3.07	0.63	0.184
PCOM-right-side	1.02	0.40	0.83	0.32	0.131
PCA (P1)-right-side	1.26	0.52	1.56	0.37	0.089
ACA (A1)-left-side	1.39	0.36	1.54	0.37	0.159
ICA-left-side	3.04	0.67	3.02	0.60	0.984
PCOM-left-side	1.00	0.26	0.90	0.33	0.215
PCA (P1)-left-side	1.41	0.47	1.51	0.44	0.303

[Table/Fig-5]: Morphometric analysis of vessels of CoW among two gender group with statistical significance done with Mann-Whitney test.

Variables were also compared in sub-analysis among the age groups (≤40 years and >40 years) along with individual gender groups [Table/Fig-6]. In the female population, it was found that the vessel diameters in the older age group were greater than those in the younger age group, except for the right and left PCA P1 segments and left ACA A1 segment, although only the difference in the left ACA (A1) segment was statistically significant. Data analysis in male subjects in the two age groups suggested larger mean diameters of the right PCom, left ACA (A1), and left PCA (P1) in the younger age group, although the data was not statistically significant.

DISCUSSION

The incidence of Subarachnoid Haemorrhage (SAH) is higher in women compared to men, with a ratio of 2 to 1. The highest incidence of SAH is observed in individuals aged 50 to 60 years [14,15]. A study conducted by Linn FHH et al., on patients with spontaneous SAH revealed that it primarily occurs between the ages of 40 and 60, although it can affect individuals from childhood to old age. Additionally, the study found that SAH is approximately 1.6 times more common in women than men [16]. Sadasivam AS et al., observed a relatively higher occurrence of SAH in females compared to males, with a male-to-female ratio of 1.3:1 and a median age of 55 years in the South Indian population [17]. The present study found more cases of spontaneous SAH in men than women within the age groups of 15 to 79 years.

At the Circle of Willis (CoW), the most common variation is a hypoplastic posterior communicating artery, while other structural variations include duplicated or missing communicating arteries [18]. El Barhoun EN et al., in their MR angiography-guided study considered a diameter smaller than 0.8 mm as a non-detectable vessel, either absent or hypoplastic[19]. Similarly, Karatas A et al., in their cadaveric study defined an artery with a diameter smaller than 1 mm as hypoplastic [20].

In terms of age, a consistent trend was observed, indicating an increase in vessel diameter in the older age group (>40 years) compared to the younger age group (≤40 years), likely due to atherosclerotic changes associated with age. Chen HW et al., in their study found no statistically significant difference in mean vessel diameter among each age group in normal subjects, except for the observation that older subjects had a smaller caliber in the left A1 segment compared to younger subjects [21]. In a study conducted by Maaly MA and Ismail AA using 3D TOF-MR angiography, statistically significant data suggested that in older individuals, the diameters of centripetal vessels were larger than those of centrifugal vessels. They also found that males had increased vessel diameters compared to females, except for the Posterior Communicating Artery (PCO), which was slightly larger in females than in males, and the difference was statistically significant in healthy individuals [22].

Regarding sex-related differences, it was found that in SAH patients, males generally exhibited larger mean vessel diameters compared to females, except for the left and right PCOM and left ICA, where the mean diameter was greater in females. Hafez KA et al., also found that the mean diameters of male vessels were larger than those of female vessels, except for the PCO which was larger in females with a mean diameter of 1.2 mm compared to males with 1.1 mm [23]. This study utilised Digital Subtraction Angiography (DSA), a highly sensitive test, to categorise vessels measuring =0.4 mm in diameter as functional and visible, while vessels <0.4 mm were considered hypoplastic. This approach is supported by a study conducted by Krabbe-Hartkamp MJ et al., which observed that functional completeness in an anatomically complete CoW was identified in less than half of the population due to narrow communicating arteries with diameters <0.4 mm, hindering proper blood flow [24]. They presented that larger mean diameters were observed in men, particularly in the ICA, basilar artery, middle cerebral artery, pre-communicating segment of the posterior cerebral artery, and

Sex			ACA (A1)-right-side (mm)	ICA-right-side (mm)	PCOM-right-side (mm)	PCA (P1)-right-side (mm)	ACA (A1)-left-side (mm)	ICA-left-side (mm)	PCOM-left-side (mm)	PCA (P1)-left-side (mm)
Female	≤40 yr	Mean	1.42	2.55	0.97	1.37	1.67	2.65	1.00	1.46
		SD	0.45	0.29	0.41	0.30	0.31	0.34	0.41	0.09
	>40 yr	Mean	1.56	3.01	1.04	1.23	1.32	3.15	1.00	1.40
		SD	0.46	1.23	0.41	0.57	0.34	0.70	0.23	0.53
		p-value	0.484	0.230	0.841	0.689	0.045	0.133	0.689	0.617
Male	≤40 yr	Mean	1.59	2.80	0.95	1.36	1.64	2.80	0.80	1.58
		SD	0.34	0.56	0.45	0.20	0.40	0.76	0.30	0.39
	>40 yr	Mean	1.59	3.13	0.80	1.60	1.51	3.07	0.92	1.50
		SD	0.34	0.63	0.30	0.39	0.36	0.57	0.34	0.45
		p-value	0.809	0.295	0.519	0.107	0.452	0.320	0.468	0.957
		Significance	NS	NS	NS	NS	NS	NS	NS	NS

[Table/Fig-6]: Morphometric analysis of vessels of CoW among each age group within individual gender groups done with Mann-Whitney test.

anterior communicating artery, except for the PCO which tended to be larger in women [24].

During the analysis of the female population, the current study revealed that the younger age group exhibited significantly larger vessel diameters in the A1 segment of the left ACA compared to the older age group, suggesting that either SAH or female gender in the Eastern Indian population may be the reason for this difference, and further research is needed in this aspect. In other segments, vessel diameter tended to be higher in the older age group than the younger age group, except for the right and left PCA P1 segments, although statistically not significant. Conversely, in the male population, we observed a trend towards larger mean diameters in the younger age group for the right PCOM, left A1 ACA, and left PCA (P1). However, statistical significance was not achieved in these segments, suggesting that the observed differences may be due to chance or require a larger sample size for confirmation.

Limitation(s)

The study is based on a relatively small sample size of 50 patients with a retrospective design, which can introduce bias and limitations related to data accuracy, completeness, and availability. It relies on DSA for vessel diameter measurements, which can be influenced by factors such as the degree of vessel contraction or dilation at the time of imaging. The study primarily focuses on age and sex-related differences in vessel diameters. Other demographic and clinical factors, such as co-morbidities, genetics, and lifestyle factors, as well as potential ethnic or genetic variations in vessel diameters, were not considered here. Longitudinal data with a larger sample size would have provided more robust and generalisable results and could provide insights into how vessel diameters change over time and their relevance to SAH risk.

CONCLUSION(S)

The results revealed larger vessel diameters in the older age group (>40 years) compared to the younger age group (≤40 years), which may be due to atherosclerotic changes noted with age. Statistical significance was achieved for the left ACA A1 segment of CoW in female subjects, where the mean diameter is higher in the younger age group. Males generally exhibited larger mean diameters than females, except in a few specific segments. The knowledge gained from this study can be utilised by neuro-interventionists in designing personalised treatment plans for individual SAH patients, taking into account the anatomical variations in vessel diameters. This information may aid in improving the accuracy and effectiveness of interventions, such as endovascular coiling or surgical clipping, to prevent re-bleeding and optimise patient outcomes. Further research with larger sample sizes is needed to confirm and expand upon these observations.

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