

# Impact of Anatomical Variations in the Posterior Circle of Willis on Brain Infarction Patterns

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## Abstract-

**Background:** The link between anatomical variations in the circle of Willis and brain infarction is debated. This study examines how variations in the posterior part of the circle of Willis, as seen on MR angiography (MRA), relate to ischemic infarctions in different brain regions.

**Methods:** This cross-sectional study included consecutive patients undergoing brain MRI and MRA for suspected strokes. We analyzed the prevalence of anatomical variations, including the persistent fetal origin of the posterior cerebral artery (fPCA) and hypoplastic/aplastic posterior communicating artery (PCoA), and their association with infarctions in various brain regions.

**Results:** We enrolled 298 patients (155 men, 143 women; mean age 57±15) and divided them into two groups: those with infarctions (n=142) and those without (n=156). Persistent fetal origin of the posterior cerebral artery was found in 63 patients (21.1%), and 231 patients (77.5%) had hypoplastic/aplastic PCoA. There was no significant overall correlation between fPCA or PCoA hypoplasia/aplasia and the presence of infarction. However, thalamic infarctions were more frequent in patients with hypoplastic/aplastic PCoA (17/101, 16.8%) compared to those without this variation (1/41, 2.4%) (p=0.024). No significant difference in infarction frequency across brain territories was observed between patients with and without ipsilateral fPCA variations.

**Conclusions:** In patients with brain infarctions, an aplastic or hypoplastic ipsilateral PCoA is linked to a higher incidence of thalamic infarctions.

**Keywords:** Circle of Willis, MR angiogram, Posterior cerebral artery, Posterior communicating artery, Brain infarction.

## BACKGROUND

Stroke is a leading cause of disability and the second most common cause of death worldwide. Developing countries bear a significant burden, with 75% of all stroke deaths and 81% of disability-adjusted life years lost to stroke occurring in these regions. In India, a systematic review from 2010 reported an annual stroke incidence ranging from 23 to 103 per 100,000 people across various age groups. Key risk factors for stroke include age, sex, race, hypertension, diabetes, hyperlipidemia, diet, smoking, and alcohol consumption.

Arteriogenesis, a complex embryological process, can result in numerous anatomical variations. In cases of major cerebral arterial occlusion, collateral vessels are crucial for maintaining blood flow. The circle of Willis is the primary collateral system in the brain and exhibits numerous anatomical variations. Common variations include hypoplasia or aplasia of the posterior communicating arteries (PCoA) (34-68%), hypoplasia or aplasia of the A1 segment of the anterior cerebral artery (ACA) (4-10%), absence or fenestration of the anterior communicating artery (ACoA) (12-21%), persistent fetal origin of the posterior cerebral artery (fPCA) (4-26%), and infundibular dilatation or widening of the PCoA (7-15%).

Despite numerous studies on the anatomical variations of the circle of Willis, the relationship between these variations and the incidence of ischemic stroke remains unclear. Some research suggests that PCoA hypoplasia is linked to a higher incidence of ischemic stroke, particularly ipsilateral thalamic lacunar infarcts, even without internal carotid artery occlusion. Conversely, other studies indicate that a persistent fetal-type PCoA may enhance collateral circulation between the anterior and posterior circulations, potentially reducing stroke risk. Additionally, incomplete anterior or posterior circles of Willis are associated with a higher incidence of anterior circulation strokes. A recent meta-analysis found that individuals with any anatomical variation in the circle of Willis were 1.38 times more likely to experience ischemic stroke compared to those with a complete circle of Willis, suggesting a positive association between these variations and ischemic stroke.

This study aims to evaluate the relationship between anatomical variations in the posterior circle of Willis, as identified on MRA, and the occurrence of ischemic infarcts in different vascular territories.

## METHODS

### Patients

This retrospective cross-sectional study received approval from our institutional review board and adhered to the Helsinki Declaration. We included all consecutive patients who underwent brain MRI and MRA for suspected cerebrovascular accidents at maharajah's institute of medical sciences, nellimarla between March 20, 2022, and April 10, 2023. Patients with a history of head trauma, craniotomy or craniectomy, vasculitis, pregnancy, vascular malformations (including aneurysms or arteriovenous malformations), hemorrhagic infarction, significant stenosis or occlusion of the internal carotid artery, or significant stenosis or occlusion of the basilar artery or its major branches were excluded. We reviewed demographic data, presenting symptoms, and past medical history, including hypertension, diabetes, hyperlipidemia, heart disease, and smoking, from the patients' electronic medical records.

### Imaging Protocol

Scans were performed using a 1.5-T Philips ingenia. The examination was conducted without intravenous contrast and included echo-planar T1-weighted images (TR: 591 ms, TE: 15 ms, spatial resolution: 6.2 mm, FoV: 230 mm x 230 mm), T2-weighted images (TR: 4048 ms, TE: 90 ms, spatial resolution: 6.2 mm, FoV: 230 mm x 230 mm), FLAIR, and diffusion-weighted images (DWI). For evaluating the circle of Willis, images were obtained in three slabs, each containing 30 slices, using a 3-dimensional time-of-flight MRA technique (TR: 22 ms, TE: 7 ms, number of acquisitions: 2; flip angle: 17°; 1 mm slice thickness with a 0.5 mm overlap; matrix size: 256 x 160, FOV: 200 mm x 200 mm). MRA images were reconstructed in transverse oblique planes using a maximum intensity projection algorithm.

### Definitions

The following variations in the posterior aspect of the circle of Willis on MRA were recorded: partial or complete fetal origin of the posterior cerebral artery (pfPCA and cfPCA) and aplasia or hypoplasia of the PCoA. CfPCA was defined as the absence of the P1 segment with the PCA originating entirely from the internal carotid artery (ICA). PfPCA was defined as an existing P1 segment with a diameter equal to or smaller than the PCoA.

Due to the limited resolution of MRA, differentiating between PCoA hypoplasia (<1 mm in diameter) and aplasia (absence of PCoA) was challenging. Therefore, we considered hypoplasia and aplasia together, defined as a PCoA diameter of <1 mm or non-visualization of the PCoA.

In cases of infarction, the affected side, vascular territory, and age of the infarct (acute/subacute versus chronic) were recorded based on MRI findings and clinical history. Areas of restricted diffusion (bright signal on DWI with corresponding low ADC values) were qualitatively determined by consensus of the reviewing radiologists and considered acute/subacute infarcts. Areas of encephalomalacia or gliosis without associated restricted diffusion and with volume loss were considered chronic infarcts. In cases with simultaneous acute and chronic infarcts, the territory with the acute infarct was considered. The vascular distribution of infarcts was categorized into anterior, posterior, thalamus, and watershed areas, following the methodology of previous studies. For unilateral anatomical variations, if the variation was on the same side as the infarct, it was labelled as "ipsilateral anatomical variation." In cases of bilateral anatomical variations, the variation on the side with the infarction was counted and reclassified as "ipsilateral."

### Statistical Analysis

The results were expressed as mean  $\pm$  standard deviation (SD) for quantitative variables, and as absolute frequencies and percentages for categorical variables. Categorical variables were compared using the Chi-square test or Fisher's exact test when more than 20% of cells had an expected count of less than 5. Quantitative variables were compared using the Student's t-test for parametric data and the Mann-Whitney U test for nonparametric data. Statistical analysis was conducted using SPSS version 21.0 for Windows (SPSS Inc., Chicago, IL). A p-value of 0.05 or less was considered statistically significant.

## RESULTS

A total of 298 cases were included in the study, divided into two groups: those with infarction (n=142) and those without infarction (n=156). The infarction group had a higher mean age and higher rates of hypertension, diabetes mellitus, and ischemic heart disease, as detailed in Table 1.

Within the infarction group, 46.5% had right-sided infarcts, while 53.5% had left-sided infarcts. Acute or subacute infarcts were observed in 90.1% of the patients, whereas chronic infarcts were present in 9.9% as the sole type of infarct.

**Table 1: Distribution of Cerebrovascular Risk Factors in Patients With and Without Infarction**

Parameter	With Infarction (n=142)	Without Infarction (n=156)	p-value
Male gender	80 (56.3%)	75 (48.1%)	0.154
Mean age (years)	63.36 ± 12.82	52.61 ± 16.30	<0.001
Hypertension	103 (72.5%)	76 (48.7%)	<0.001
Diabetes mellitus	57 (40.1%)	35 (22.4%)	0.001
Hyperlipidemia	14 (9.9%)	13 (8.3%)	0.647
Smoking	23 (16.2%)	13 (8.3%)	0.038
Ischemic heart disease	41 (28.9%)	25 (16.0%)	0.008

**Interpretation**

- The proportion of male patients did not significantly differ between the groups (p=0.154).
- Patients with infarction were significantly older on average than those without infarction (p<0.001).
- Hypertension, diabetes mellitus, smoking, and ischemic heart disease were significantly more prevalent in patients with infarction (p<0.001, p=0.001, p=0.038, and p=0.008, respectively).
- There was no significant difference in the prevalence of hyperlipidemia between the two groups (p=0.647).

**Territorial Distribution of Ischemic Infarct in Patients with fPCA**

Among the study participants, 63 patients (21.1%) had a fetal-type posterior cerebral artery (fPCA), with 48 (16.1%) exhibiting complete fetal-type PCA (cfPCA) and 16 (5.3%) having partial fetal-type PCA (pfPCA). One patient had cfPCA on one side and pfPCA on the other. Of those with cfPCA, 27 (56.2%) were right-sided, 16 (33.3%) were left-sided, and 4 (8.3%) were bilateral. Among those with pfPCA, 9 (56.2%) were right-sided, 4 (31.2%) were left-sided, and 2 (12.5%) were bilateral. Seven cases with bilateral fPCA were excluded from the analysis. In the remaining cases with unilateral fPCA, 11 patients had ipsilateral infarcts. No significant association was found between fPCA and infarcts.

In patients with infarction, a subgroup analysis comparing those with and without fPCA showed no significant difference in infarct territories as detailed in Table 2. When comparing patients with versus without ipsilateral fPCA, anterior circulation infarcts (ACA and MCA) occurred in 6/11 (54.4%) versus 77/127 (60.6%) patients; posterior circulation infarcts (basilar artery, superior cerebellar artery, PCA, and posterior inferior cerebellar artery) in 3/11 (27.2%) versus 23/127 (18.1%) patients; thalamic infarcts in 1/11 (9.1%) versus 17/127 (13.4%) patients; and watershed territory infarcts in 1/11 (9.1%) versus 10/127 (7.9%) patients. No significant relationship was found between fPCA and clinical risk factors for cerebrovascular disease (including male gender, diabetes, hypertension, hyperlipidemia, smoking, and ischemic heart disease) in patients with infarction.

**Territorial Distribution of Ischemic Infarction in Patients with PCoA Hypoplasia/Aplasia**

A total of 231 patients (77.5%) had PCoA hypoplasia or aplasia, with 35 (11.7%) on the right side, 38 (12.7%) on the left side, and 158 (53.2%) bilaterally. In cases with infarction and bilateral PCoA hypoplasia/aplasia, the anatomical variation ipsilateral to the infarct was used for comparison to those without infarction. The frequency of ipsilateral PCoA hypoplasia/aplasia in patients with infarction was 101/142 (71.1%), compared to 116/156 (74.4%) in those without infarction, showing no significant difference (p=0.531).

Comparing patients with versus without ipsilateral PCoA hypoplasia/aplasia (Table 3), anterior circulation territory infarcts (ACA and MCA) occurred in 57/101 (56.4%) versus 30/41 (73.2%) patients; posterior circulation territory infarcts (basilar artery, superior cerebellar artery, PCA, and posterior inferior cerebellar artery) in 17/101 (16.8%) versus 9/41 (22.0%) patients; thalamic infarcts in 17/101 (16.8%) versus 1/41 (2.4%) patients; and watershed territory infarcts in 10/101 (9.9%) versus 1/41 (2.4%) patients. A statistically significant difference was found only for thalamic infarcts (p=0.024).

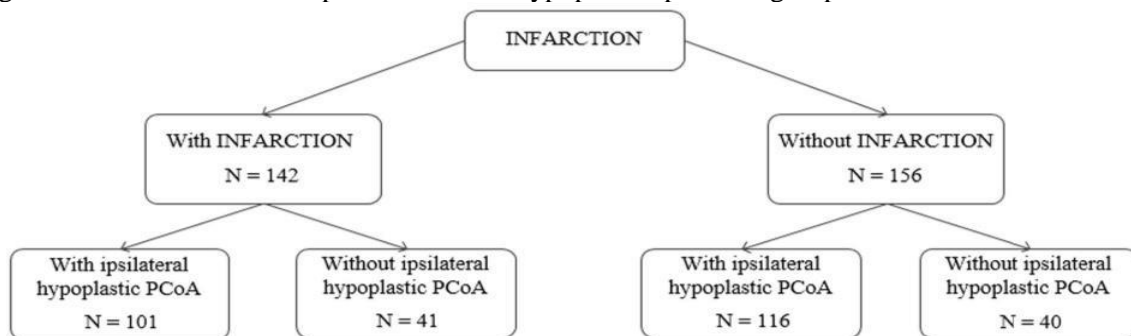
To account for potentially confounding clinical risk factors, the relationship between PCoA hypoplasia/aplasia and clinical risk factors was analyzed, revealing no significant correlation.

**Table 2: Involvement of Different Territories in Groups with and without fPCA Variation**

Infarcted Vascular Territory	With Ipsilateral fPCA (n=11)	Without Ipsilateral fPCA (n=127)
Hemispheric Stroke		
- Anterior	6 (54.4%)	77 (60.6%)
- Posterior	3 (27.2%)	23 (18.1%)
Thalamus	1 (9.1%)	17 (13.4%)
Watershed	1 (9.1%)	10 (7.9%)

**Interpretation**

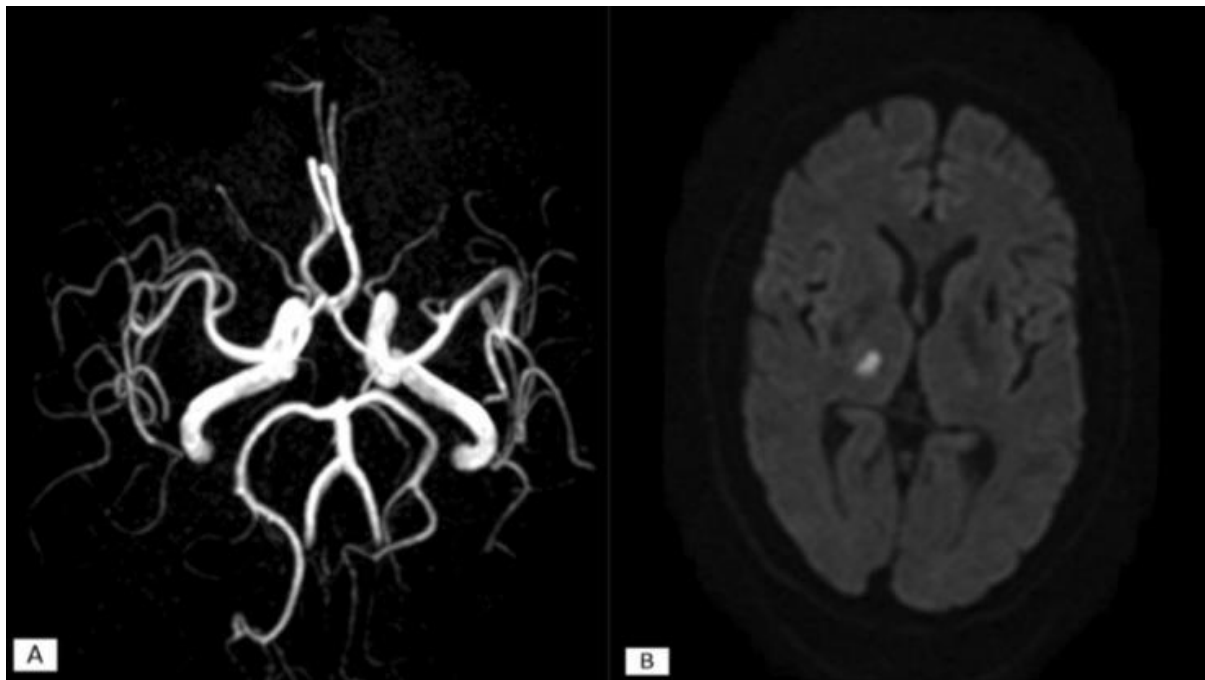
- Patients with ipsilateral fPCA had slightly lower percentages of anterior and posterior hemisphere infarctions compared to those without ipsilateral fPCA.
- Thalamic infarctions were slightly more common in patients without ipsilateral fPCA.
- The occurrence of watershed infarctions was similar between the two groups.

**Fig. 1** Number of cases with ipsilateral PCoA hypoplasia/aplasia in groups with and without infarction**Table 3: Involvement of Different Territories in Groups with and without Ipsilateral Hypoplastic PCoA Variation**

Infarcted Vascular Territory	With Ipsilateral Hypoplasia/Aplasia (n=101)	Without Ipsilateral Hypoplasia/Aplasia (n=41)
Hemispheric Stroke		
- Anterior	57 (56.4%)	30 (73.2%)
- ACA	3 (2.9%)	4 (9.8%)
- MCA	54 (53.5%)	26 (63.4%)
- Posterior	17 (16.8%)	9 (21.9%)
- PCA	6 (5.94%)	2 (4.9%)
- SCA/Basilar/PICA	11 (10.9%)	7 (17.0%)
Thalamus*	17 (16.8%) *	1 (2.4%)
Watershed	10 (9.9%)	1 (2.4%)

**Interpretation**

- Patients with ipsilateral PCoA hypoplasia/aplasia had slightly lower percentages of anterior hemisphere infarctions compared to those without ipsilateral PCoA hypoplasia/aplasia.
- Thalamic infarctions were significantly more common in patients with ipsilateral PCoA hypoplasia/aplasia (p=0.024).
- The occurrence of posterior hemisphere and watershed infarctions did not show significant differences between the two groups.



**Fig. 2** Axial Maximal Intensity Projection (MIP) reconstructed MRA image (A) demonstrates right PCoA hypoplasia/aplasia. Corresponding diffusion-weighted image (B) depicts an acute right thalamic infarct.

## DISCUSSION

The relationship between anatomical variations in the circle of Willis and the occurrence of infarcts in different vascular territories has been a topic of debate. Numerous previous studies have suggested that such variations, whether anatomical or pathological, may be associated with a higher incidence of brain infarction. In our study, we evaluated anatomical variations in the posterior aspect of the circle of Willis using MRI and MRA findings and explored their relationship with infarcts in various vascular territories.

Consistent with previous findings, patients with infarcts in our study tended to be older and had a higher prevalence of hypertension, diabetes, smoking, and heart diseases.

We observed that 21.1% of our patients had fetal-type posterior cerebral artery (fPCA), while 77.5% had hypoplastic or aplastic posterior communicating artery (PCoA). The reported prevalence of fPCA and PCoA hypoplasia/aplasia in the literature varies widely. Different criteria for defining hypoplasia, such as luminal diameter thresholds, may contribute to this variability.

Our results did not demonstrate a statistically significant association between complete or partial fPCA and infarcts in different vascular territories. Previous studies have provided conflicting reports on the association between fPCA and an increased risk of infarcts. While some studies did not find an elevated risk with fPCA, others observed higher rates of ischemic infarcts in partial fPCA cases.

Similarly, we found no significant association between PCoA variation and an increased risk of brain infarcts overall. However, in subgroup analysis, we noted a significantly higher incidence of infarcts in the thalamic territory among patients with ipsilateral PCoA hypoplasia/aplasia compared to those without. This finding is consistent with previous studies that have linked PCoA hypoplasia to an elevated risk of ischemic stroke, particularly involving arteries penetrating the thalamus.

The thalamus receives blood supply from a complex arterial network, with some branches originating from the proximal PCA. Thus, in patients with normal PCoA, occlusion of one of these branches may not lead to infarcts due to collateral circulation. However, in individuals with PCoA hypoplasia/aplasia, occlusion of these branches may result in tissue ischemia and infarction. PCoA hypoplasia/aplasia may weaken segmental collaterals, increasing the risk of thalamic infarcts.

In conclusion, while our study did not find a significant overall association between fPCA or PCoA variation and brain infarcts, subgroup analysis revealed a significant association between ipsilateral PCoA hypoplasia/aplasia and thalamic infarcts. These findings underscore the importance of considering anatomical variations in the circle of Willis when assessing stroke risk, particularly in specific vascular territories like the thalamus. Our study possesses inherent limitations. The resolution of our Time-of-Flight Magnetic Resonance Angiography (TOF MRA) with 1.5 Tesla MRI may be limited, potentially resulting in the non-visualization of the posterior communicating artery (PCoA) when it is exceedingly narrow. However, we combined hypoplasia and aplasia criteria, defining them as a

vessel diameter of less than 1 mm or absence, to mitigate this issue. Despite these criteria, there is a possibility of misinterpretation in cases of potential thromboembolic occlusion or narrowing of the vessel, although this occurrence is claimed to be of very low incidence. Other limitations include the retrospective design, small sample size, and the limited number of patients with simultaneous A1 and PCoA hypoplasia/aplasia, which restricts our ability to draw conclusions about their combined effects.

**In conclusion, our findings suggest that the absence or hypoplasia of the ipsilateral posterior communicating artery (PCoA) may be linked to a higher incidence of thalamic infarcts.**

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