doi.org/10.36721/PJPS.2026.39.6.160.1

Posterior circulation vascular variants and intracranial aneurysm formation: An imaging-based study with implications for risk stratification

Mehmet Selim Gel[1], Emrah Keskin[3]*, Cagri Elbir[3] and Ayhan Kanat[4]
[1]Kanuni Research and Training Hospital, Department of Neurosurgery, Trabzon, Turkiye
[2]Zonguldak Bülent Ecevit University, Department of Neurosurgery, Zonguldak, Turkiye
[3]Etlik City Hospital, Department of Neurosurgery, Ankara, Turkey
[4]Recep Tayyip Erdogan University, Medical Faculty, Department of Neurology, Rize, Turkey

Abstract: **Background**: Subarachnoid hemorrhage (SAH) from Intracranial Aneurysms (IA) represents a leading cause of death and morbidity from neurological deficits. Emerging research has identified that variations in vascular anatomy may contribute to endothelial dysfunction, hemodynamic stress, and pharmacological responsiveness in cerebrovascular tissues. **Objectives**: This study aimed to determine whether variations in the posterior circulation vascular system are associated with the development of aneurysms. Additionally, it was explored whether these variations could provide additional risk assessment for cerebrovascular diseases. **Methods**: A retrospective study of digital subtraction angiography (DSA) and computed tomography angiogram (CTA) of the posterior circulation vascular anatomy in 104 patients, from Jan 2019 to Sept 2022 was conducted. The variables recorded were posterior communicating artery grading, posterior cerebral artery dominance, vertebral artery caliber, persistent fetal type posterior circulation presence and aneurysm laterality. Hypoplastic vertebral arteries were defined as those ≤ 0.8 mm in diameter. **Results**: According to the study involving 104 individuals (47 men and 57 women) left-sided posterior communicating artery (PCoA) dominance is frequently present. Right-sided aneurysm formation was higher after exclusion of bilateral and midline aneurysms from the analysis. Persistent fetal-type posterior circulation was noted in 26.9% of all cases with a predominance for formation of right-sided petrosal type. **Conclusion**: The presence of a vascular phenotype with left-sided PCoA dominance and contralateral vertebral artery hypoplasia increases the risk for formation of an IA in vascular patients with or without persistent fetal-type posterior circulation and therefore could be used to develop pharmacologically-based treatment strategies, including continued stabilizing of endothelial cells using Cilostazol.

Keywords: Cilostazol; Circle of willis; Endothelial dysfunction; Hemodynamics; Intracranial aneurysm; Ponticulus posticus; Subarachnoid hemorrhage; Vertebral artery

Submitted on 01-03-2026 – Revised on 08-03-2026 – Accepted on 25-03-2026

INTRODUCTION

A broad range of structural differences within the human cerebrovascular system can greatly affect its function and the susceptibility of some people to certain diseases (Alghamdi *et al*., 2021). Recent technological advancements have enabled detailed investigation of vascular anatomy and improved visualization of cerebral circulation, thereby facilitating a better understanding of the anatomy, physiology, and pathophysiology of various cerebrovascular disorders.

Anatomical variations in the cerebral circulation have implications for many medical specialties, including neurosurgery and interventional neuro-radiology, but they will also be important for translational vascular research, where the structural vascular phenotype can affect multiple aspects of endothelial cell biology, vascular biomechanics, pharmacology and hemodynamic stresses (Luo *et al.*, 2025).

**Corresponding author:* e-mail: drkeskinemrah@gmail.com

There remains a significant risk of developing an intracranial aneurysm (IA) and its rupture, resulting in subarachnoid hemorrhage (SAH), which leads to long-term disability and high mortality rates. Epidemiological studies suggest that 5-6% of the population at any one time will develop a cerebral aneurysm. Intracranial aneurysm development is associated with multiple factors, including endothelial dysfunction, hemodynamic stress, inflammatory signaling, and vascular wall remodeling. There is increasing interest in the management of cerebral IAs with agents that target the vasculature and inhibit platelet activation (Rezai *et al*., 2024).

Transient anastomotic connections between the anterior and posterior cerebral circulations form during fetal growth in animals, but usually regress after delivery. However, persistence of certain vascular configurations from the fetal stage can significantly affect cerebrovascular flow, including the fetal-like posterior cerebral artery (fPCA) and the fetal PCoA (Lawson 2023). Anatomical variants such as these cause altered patterns of blood flow

(regional), shear stress distributions and nitric oxide signaling pathways that affect vascular remodeling and how pharmacological therapies will act. At present, no experimental findings have shown a specific relationship between the posticus ponticulus and endothelial nitric oxide signaling in cerebrovascular circulation; therefore, this link will be treated as a theoretical hemodynamic factor.

Another anatomical variant that can affect the dynamics of the posterior circulation is the Ponticulus posticus (PP), defined as a bony connection on the posterior arch of the atlas (C1) that either partially or completely surrounds the vertebral artery groove (Najmuddin *et al*., 2022). The atlas lacks a body (as do all cervical vertebrae) and plays an important role in biomechanics from the skull to the spine. Its presence creates a mechanical influence on the course and flow of blood through the vertebral artery, which can change hemodynamics in the posterior circulation. The presence of this variant was previously unknown, but as awareness of these anomalies grows in clinical settings, researchers have not yet fully explored the association between these individuals and the development of intracranial aneurysms (Ahn *et al*., 2021). Gaining insight into the vascular anatomy of individuals with anatomical phenotypes will help us better design possible pharmacologic therapies aimed at improving endothelial function and promoting vascular remodeling in patients with cerebrovascular disease who have been diagnosed with an aneurysm.

The relationship among the ponticulus posticus (PP), posterior circulation variants and aneurysms is a mechanical pathway linking their physical anatomy. The anatomy of the PP places mechanical stress on certain vessels, remodeling them into high-risk areas for aneurysm formation, such as the basilar or vertebral arteries. The PP can exert chronic external pressure on the vertebral artery's hemodynamics, increasing the risk of aneurysm (Hao *et al.*, 2022).

Changes in blood pressure distribution, the geometric setup of blood vessels and endothelial shear stress all influence the development, growth and rupture of an aneurysm. The presence of fetal cerebrovascular structures, such as fetal-type posterior cerebral circulation and carotid-basilar anastomoses, has been shown to cause asymmetric hemodynamics in the brain and may be a precursor to aneurysm development. Medications that alter endothelial nitric oxide activity, inhibit platelet aggregation and reduce vascular inflammation are used to treat cerebrovascular disease and may also affect aneurysm risk in high-risk vascular configurations (Lin *et al*., 2021).

Based on hemodynamic and pharmacological considerations regarding persistent fetal circulation and the high risk of developing brain aneurysms associated with Ponticulus posticus, it is hypothesized that its presence contributes to asymmetric remodeling of the cerebrovascular system, leading to the development of contralateral intracranial aneurysms. Thus, this study was designed to evaluate vascular variants of the posterior circulation and the morphology of Ponticulus posticus as structural risk phenotypes for aneurysm development and to provide a foundation for future pharmacologically directed prevention strategies. According to previous studies, vascular structures may influence both cerebrovascular hemodynamics and endothelial biology. The published literature suggests that these components play a significant role in the development of intracranial aneurysms. Understanding vascular phenotypes provides a structural framework for future studies assessing pharmacological agents to reduce or eliminate the risk of developing cerebrovascular disease and, eventually, to increase the number of people living free from or suffering from cerebrovascular disease.

This study is retrospective and therefore will not include any pharmacological interventions. Pharmacology (as well as vascular biology) has been referenced in this study solely to provide a pathophysiological basis for the development of intracranial aneurysms. This study evaluated the association between posterior circulation vascular variants, including Ponticulus posticus morphology and the development and laterality of intracranial aneurysms. Furthermore, the study aimed to determine whether these anatomical configurations could serve as structural risk markers for aneurysm formation and contribute to improved risk stratification and future pharmacological intervention strategies.

MATERIALS AND METHODS

Study design

This retrospective observational study in accordance with the principles defined in the Declaration of Helsinki. Informed consent was obtained from all patients prior to imaging. This study was conducted and reported in accordance with the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines and the completed checklist is provided as supplementary material.

Study population

From January 2019 to September 2022, a retrospective review was performed of patients who underwent computed tomography angiography (CTA) and digital subtraction angiography (DSA) to evaluate possible or confirmed cerebrovascular disease. Inclusion criteria for this study were: (1) availability of high-quality CTA and DSA images allowing visualization of posterior circulation anatomy, and (2) confirmed diagnosis of an intracranial aneurysm based on DSA and CTA evaluation. Patients with incomplete imaging data and those without adequate

visualization of relevant vessels were excluded. A total of 104 patients were included in the study, all of whom underwent both CTA and DSA to evaluate suspected or confirmed cerebrovascular disease.

Imaging evaluations

Image studies from the Sağlık Bilimleri Üniversitesi Dışkapı Yıldırım Beyazıt Training and Research Hospital Picture Archiving and Communication System (PACS) were reviewed by two independent neurosurgeons using a standardized digital imaging platform for radiological data storage and retrieval (Kumar *et al*., 2021). Several morphologic characteristics were studied, including the size of the vertebral artery, the shape of the posterior communicating artery and the location of an aneurysm. Whenever disagreements occurred, they were resolved through discussion until consensus was reached. The images were independently evaluated by two neurosurgeons, and any disagreements were resolved through consensus; formal inter-observer reliability statistics were not calculated due to the retrospective nature of the study.

Morphological vascular assessment

An examination of the posterior circulation vascular anatomy was performed to find the possible connection between structural configurations and the propensity to develop an intracranial aneurysm. The following parameters were examined:

- Vertebral artery size and dominance.
- Orientation of the PCoA.
- Dominance of the PCA.
- Evidence of a fetal-type persistent posterior circulation.
- Location of the intracranial aneurysms (left, right, bilateral or midline).

Hypoplastic or absent vertebral arteries were indicated by a <0.8 mm lumen diameter (Bae *et al*., 2023).

An intracranial aneurysm is defined as a focal, saccular dilation of the wall of a cerebral artery that was visualized on a CTA and confirmed with a DSA. No specific size threshold was used, provided the aneurysm was clearly visible via the angiogram.

Classification of ponticulus posticus

From a five-point classification system, there are five possible forms of Ponticulus posticus:

- Grade 1: Absent
- Grade 2: Partial
- Grade 3: Semi-partial
- Grade 4: Near-total
- Grade 5: Complete

Anatomical variation in Ponticulus posticus morphology can affect posterior circulation hemodynamics; this classification system will provide a means of classifying these variations in relation to posterior circulation hemodynamics (Najmuddin *et al.*, 2022).

Pharmacological relevance framework

While no pharmacological intervention was used in this study, the aetiologies of the vascular configurations identified were investigated to determine whether these anatomical configurations were risk phenotypes, to help inform the development of pharmacological prevention strategies. A particular focus was on those agents directed at the endothelial layer of the vasculature, known to enhance endothelial nitric oxide activity, inhibit platelet aggregation and modulate vascular shear stress, as all of these mechanisms may theoretically influence the pathophysiology of intracranial aneurysms in patients with high-risk posterior circulation anatomical variants. As a result, the endothelial-targeting pharmacological agent (Cilostazol) discussed above has been interpreted as a translational finding rather than a methodological component of the current study.

Statistical analysis

Using IBM SPSS Statistics version 25.0, statistical analysis was carried out. Continuous variables were reported as a mean ± standard deviation and categorical variables as frequencies and percentages. The association between variables related to the anatomy of the patient and the lateralization of the aneurysms was assessed using either the Chi-square test (for categorical variables) and the Kruskal–Wallis test (for continuous variables). The alpha level used to establish statistical significance was set at $p < 0.05$.

Multi-detector computed tomography scans (slice thickness = 0.5 to 1mm) and DSA using a biplane angiographic system (for selective catheterization) were the imaging techniques used to evaluate the CTA study. Images were generated in axial, coronal and sagittal planes following an intravenous bolus of contrast media (i.e., iodinated) administered to each patient. Data for this study were collected from the institutional protocols of the authorising physician for each imaging technique. All statistical analyses were performed by two professional neurosurgeons, and discrepancies were evaluated and resolved through consensus. Due to the relatively small sample size and incomplete clinical risk factor data, a multivariate regression analysis to account for potential confounding variables was not performed; therefore, there were no multivariate analysis results and only univariate statistical tests were performed on the data.

RESULTS

A total of 104 patients (47 males, 57 females) were analyzed. The mean ages were 63.4 years for males and 55.1 years for females. Mean PP grading was 2.31 on the left and 2.26 on the right, with no significant difference.

Left vertebral artery dominance was observed in 40 patients, whereas right vertebral artery dominance was identified in 26 patients; this difference was not statistically significant ($p > 0.05$). Aneurysm localization was bilateral or midline in 52.9%, right-sided in 25% and left-sided in 22.1% of cases. After excluding bilateral and midline aneurysms, right-sided aneurysms were significantly more prevalent.

Table 1 presents the anatomical distribution of aneurysm locations, while Table 2 summarizes the laterality of PP anomalies. After exclusion of bilateral and midline aneurysms, aneurysm formation was more frequently observed on the right side than on the left (Table 3). Overall, aneurysms were bilateral or midline in 55 patients (52.9%), right-sided in 26 patients (25%) and left-sided in 23 patients (22.1%).

Persistent fetal circulation was detected in 26.9% of patients, predominantly on the right side. Left-sided PP grading was significantly associated with contralateral aneurysm development and persistent fetal circulation ($p<0.05$, Table 4). Although these distributions did not reach statistical significance, both aneurysm formation and persistent fetal circulation demonstrated a right-sided predominance. In contrast, PP anomaly was more frequently observed on the left (contralateral) side.

Following exclusion of bilateral and midline aneurysms, right-sided aneurysm development remained more prevalent than left-sided aneurysm formation. Kruskal–Wallis analysis demonstrated a statistically significant association between left-sided PP grading and lesion laterality ($p < 0.05$). Furthermore, right-sided fetal-type posterior communicating artery configuration was significantly associated with right-sided aneurysm formation and left-sided PP grading ($p < 0.05$, Table 5). Fig. 1 illustrates a representative case showing a complete left-sided PP anomaly with contralateral right-sided vertebral artery hypoplasia, along with a dominant left vertebral artery and an associated basilar tip aneurysm. The basilar tip aneurysm is further demonstrated in fig. 2. The overall study findings are summarized in Fig. 3.

Along with the anatomical associations noted, the hemodynamic environment created by vascular patterns—characterized by left-sided Ponticulus posticus predominance, contralateral vertebral artery hypoplasia, and persistent fetal-type posterior circulation—produces conditions that may be susceptible to altered shear stress distribution and subsequent endothelial dysfunction through mechanisms including modulation of nitric oxide signaling, platelet activation, and vascular remodeling.

DISCUSSION

The caudal section of the primitive carotid system and the vertebrobasilar system integrate to generate the PComA and BA. The ultimate configurations of the PComA, P1 segment and BA are the consequence of variations and changes in these systems during embryonic development, which may lead to persistent fetal-type circulation patterns that can alter cerebral hemodynamics and influence susceptibility to intracranial aneurysm formation. Ponticulus posticus can result in vertebrobasilar insufficiency by narrowing the vertebral artery (Chen *et al*., 2021). The present study contributes to the existing body of knowledge by demonstrating the association between Ponticulus posticus anomaly, posterior circulation vascular variants, and the development and laterality of intracranial aneurysms.

This study demonstrates that PP anomaly is significantly associated with contralateral persistent fetal circulation and contralateral cerebral aneurysm formation. Specifically, left-sided PP dominance combined with contralateral vertebral artery hypoplasia and right-sided fetal-type PCoA configuration constitutes an anatomical risk profile for aneurysm development. This triad, comprising left-sided Ponticulus posticus dominance, contralateral vertebral artery hypoplasia, and right-sided fetal-type posterior communicating artery configuration, represents a significant cerebrovascular risk profile associated with increased susceptibility to intracranial aneurysm formation. The cerebral vasculature is highly sensitive to hemodynamic perturbations and relies on finely regulated autoregulatory mechanisms to maintain constant cerebral blood flow (Chen *et al*., 2021; Ahn *et al*., 2021). Although the human body appears macroscopically symmetrical, vascular architecture is inherently asymmetric; previous studies have demonstrated that PP anomaly contributes to asymmetry of vertebral and carotid arteries (Keskin *et al*., 2025; Ergene *et al*., 2025).

Ponticulus posticus (PP) may partially or completely encase the vertebral artery at C1, which may result in: (a) contralateral vertebral artery narrowing, (b) flow turbulence, and (c) chronic reduction of posterior circulation inflow on the contralateral side. This creates asymmetric vertebrobasilar circulation (Gurlek *et al*., 2024). This pattern was also demonstrated in the present study. The findings extend this observation by demonstrating that asymmetric PP anatomy may drive contralateral hemodynamic overload, creating focal increases in wall shear stress that predispose to aneurysm formation.

Persistent fetal circulation was present in over one-quarter of the cohort and demonstrated a marked right-sided predominance. Persistent fetal connections shift posterior circulation flow into the carotid system, creating dependence of basilar or PCA territories on internal carotid artery (ICA) flow and concentrated hemodynamic stress at junctions and bifurcations. Fetal-type PCoA is characterized by an aplastic or hypoplastic P1 segment and dominant PCoA flow, which alters posterior circulation hemodynamics and increases aneurysm susceptibility.

Table 1: Distribution of aneurysm laterality among the study population

Aneurysm location	n	%
ACOM	38	36.5
ACOM + ACA	1	1.0
ACOM + left MCA	1	1.0
ACOM + right MCA	1	1.0
ACOM + right PCOM	1	1.0
Basilar artery	11	10.6
Bilateral MCA	2	1.9
Distal left ACA	1	1.0
Distal right ACA	2	1.9
Left ACOM	3	2.9
Left ACOM + left MCA	1	1.0
Left ICA	5	4.8
Left MCA	6	5.8
Left PCA	1	1.0
Left PCOM	2	1.9
Left VA	4	3.8
Right ACA	2	1.9
Right frontal AVM	1	1.0
Right ICA	8	7.7
Right MCA	7	6.7
Right PCOM	2	1.9
Right VA	4	3.8
Total	104	100.0

ACOM: Anterior communicating artery; ACA: Distal left anterior cerebral artery; MCA: Middle cerebral artery; PCOM: Posterior communicating artery; ICA: Internal carotid artery; PCA: Posterior cerebral artery; VA: Vertebral artery; AVM: Arteriovenous malformation.

Table 2: Distribution of Ponticulus posticus grading according to side

PP grading	Right side, n (%)	Left side, n (%)
Grade 1 (Absent)	43 (41.3)	46 (44.2)
Grade 2 (Partial)	18 (17.3)	8 (7.7)
Grade 3 (Semipartial)	9 (8.7)	15 (14.4)
Grade 4 (Near-total)	14 (13.5)	15 (14.4)
Grade 5 (Complete)	10 (9.6)	10 (9.6)
Total*	94 (100)	94 (100)

*Patients with missing PP data (n = 10) were excluded from grading analysis; PP: Ponticulus posticus

Table 3: Comparison of aneurysm laterality after exclusion of bilateral and midline aneurysms, demonstrating a predominance of right-sided aneurysm formation.

Aneurysm laterality	n	%
Right-sided	26	53.1
Left-sided	23	46.9
Total	49	100.0

Table 4: Laterality of persistent fetal-type posterior communicating artery circulation among the study population

Persistent fetal-type circulation laterality	n	%
Right-sided	15	53.6
Left-sided	10	35.7
Bilateral	3	10.7
Total	28	100.0

Table 5: Statistical analysis of the relationship between aneurysm laterality, Ponticulus posticus grading, and patient age, demonstrating a significant association between left-sided Ponticulus posticus grading and contralateral aneurysm formation.

Variable	df	H value	p value
Right-sided Ponticulus posticus grading (1–5)	2	2.126	0.345
Left-sided Ponticulus posticus grading (1–5)	2	6.035	0.049
Patient age	2	0.139	0.933

Kruskal–Wallis test was used to compare variables according to aneurysm laterality (right-sided, leftsided, bilateral). A statistically significant association was observed between left-sided Ponticulus posticus grading and aneurysm laterality ($p < 0.05$), whereas patient age and right-sided Ponticulus posticus grading showed no significant association

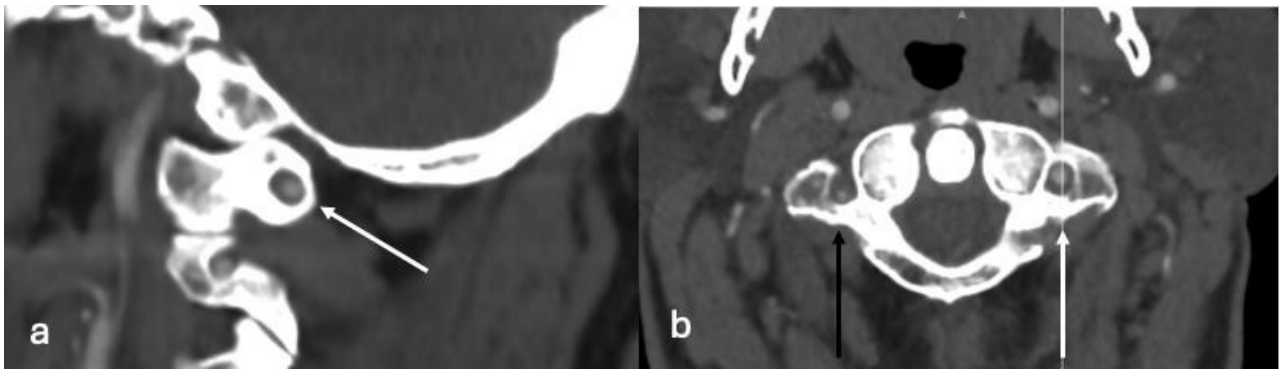

Fig. 1: (a, b) Computed tomography images demonstrating a complete left-sided Ponticulus posticus anomaly (white arrows); (b) Contralateral right-sided vertebral artery hypoplasia (black arrow).

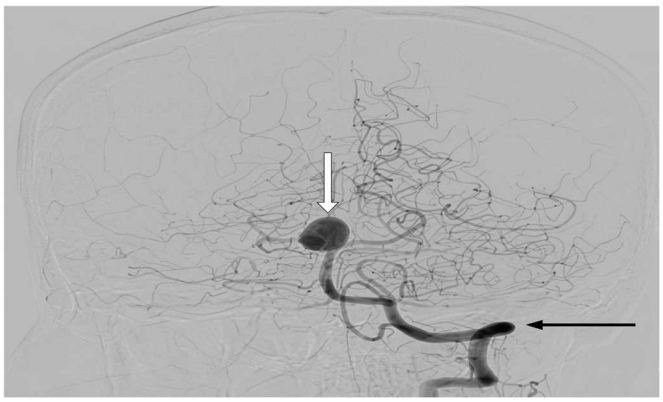

Fig. 2: Angiographic image demonstrating a dominant left vertebral artery (black arrow) associated with a basilar tip aneurysm (white arrow).

Computational fluid dynamics demonstrates that higher "fetalization" (bigger PCoA relative to P1) significantly reduces basilar contribution while increasing wall shear stress and oscillatory shear index in PCoA, P1 and ACoA segments—conditions associated with aneurysm onset and growth. Fetal-type PCoA may lead to aneurysm formation and unfavorable outcomes following aneurysmal subarachnoid hemorrhage (Wada *et al*., 2021). The data indicate that left-sided PP anomaly may indirectly promote contralateral fetal-type circulation by impairing vertebrobasilar inflow, thereby forcing compensatory remodeling of the PCoA. This remodeling increases local wall shear stress and may explain the preferential development of right-sided aneurysms observed in the cohort.

It is clear that aneurysm formation is multifactorial and involves multiple pathogenic mechanisms (Gurlek *et al*., 2024). Aneurysm development is multifactorial and driven by chronic endothelial stress, inflammation and arterial wall remodeling. Aberrant hemodynamics are a critical initiating factor, particularly in anatomically predisposed regions. Wall shear stress is a principal determinant of endothelial injury and vascular remodeling. Larger-caliber fetal-type PCoA vessels carry greater flow volumes, thereby amplifying shear stress at bifurcation points. In this

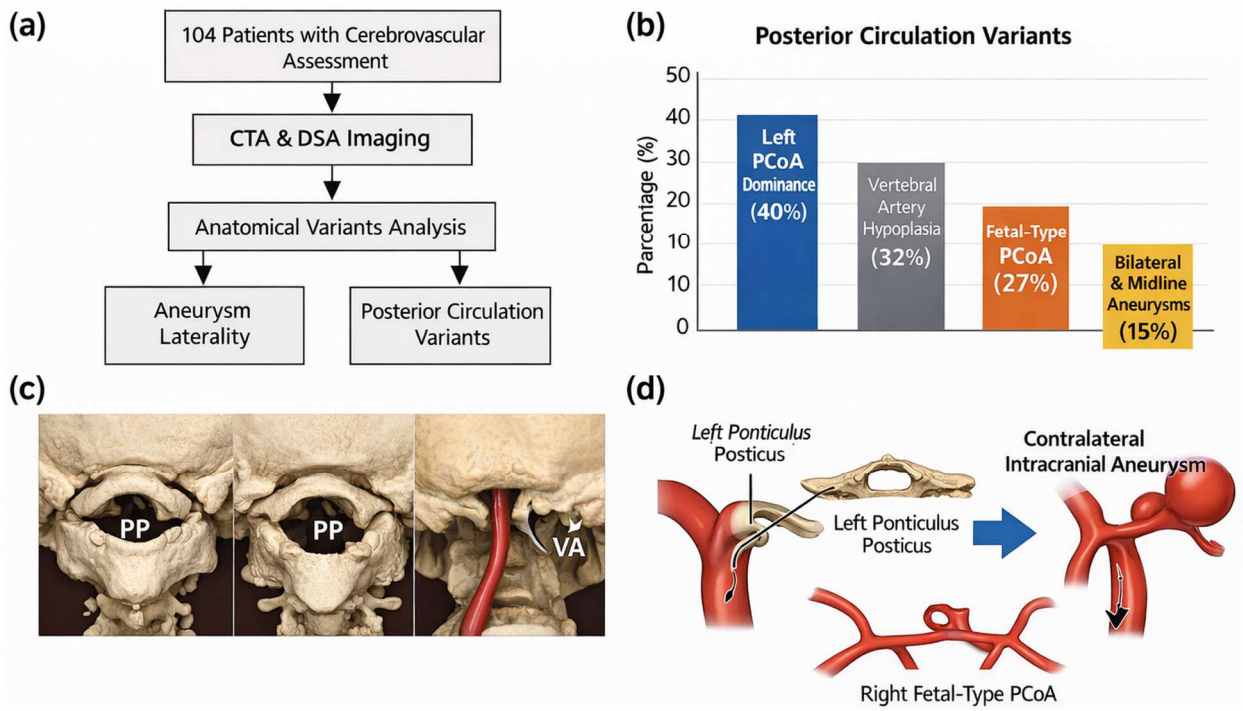

Fig. 3: (a) Flowchart illustrating the study design and patient selection process; (b) Distribution of posterior circulation vascular variants; (c) Representative imaging of Ponticulus posticus morphology and vertebral artery variations; (d) Schematic representation of the association between Ponticulus posticus anomaly, persistent fetal-type posterior circulation and contralateral intracranial aneurysm formation. PP: Ponticulus posticus; PCoA: posterior communicating artery.

study, contralateral vertebral artery hypoplasia, combined with PP-related vertebrobasilar flow restriction, likely increased the hemodynamic burden on fetal-type PCoA channels, thereby promoting aneurysm formation in the contralateral anterior and posterior circulation territories. Aneurysm sites are presented in Table 1.

Aneurysmal SAH remains a leading cause of cerebrovascular mortality (Cruzalegui-Bazán *et al*., 2024). A statistically significant association was observed between left-sided PP grading and contralateral aneurysm laterality. This supports the hypothesis that asymmetric developmental anatomy contributes to focal aneurysm susceptibility through chronic hemodynamic imbalance. Right-sided aneurysm predominance in the cohort further suggests that vascular asymmetry may act in a directional manner, with unilateral anatomical restriction generating contralateral vascular overload.

These findings have important clinical implications for neurosurgeons and interventional neuroradiologists. Identification of PP anomaly on routine cervical or cranial CT imaging should prompt careful evaluation of contralateral vertebral artery caliber and fetal-type circulation (Naderi-Meshkin *et al*., 2024). Patients exhibiting this anatomical triad may represent a high-risk subgroup requiring intensified aneurysm surveillance and earlier intervention strategies.

This study provides clinical evidence of a real anatomical-hemodynamic relationship between PP anomaly and the development of intracranial aneurysms. The findings provide a mechanistic framework linking embryologic vascular persistence, cervical vertebral anomalies and intracranial aneurysm formation. PP is not just a benign bony variant. It changes vertebral artery geometry, lumen diameter and flow direction and therefore alters posterior circulation hemodynamics. This creates a cascade that can directly promote aneurysm formation. Larger multicenter prospective studies incorporating computational fluid dynamics and multivariate modeling are required to validate PP anomaly as an independent predictive factor for aneurysm development. No pharmacological therapy has been studied in this cohort; however, the anatomical patterns support the justification for future studies evaluating whether the typical clinical dosing of the concerned drugs may affect endothelial function and the risk of developing aneurysms in patients with identified high-risk posterior circulation variants.

The vascular configuration seen in this study (defined by the majorities of left-sided Ponticulus posticus; hypoplastic contralateral vertebral arteries; persistent fetal-type posterior circulation) is likely to have additional pharmacological implications (Musial *et al*., 2024). These anatomical variants may alter local hemodynamic stress

and endothelial function, both of which are critical factors in the development of intracranial aneurysms. Endothelial dysfunction and altered nitric oxide availability can also result in increased inflammatory signaling, platelet activation and remodeling of vessel walls (Maupu *et al*., 2026). As a result of these three factors, an individual exhibiting these anatomical variants may be at an increased risk of developing an aneurysm. Agents that target endothelial integrity and hemodynamics in the vasculature may play a preventive role in this patient population. Cilostazol, a phosphodiesterase-III inhibitor with antiplatelet, vasodilating and endothelial protective properties has become of great interest as it has been shown to promote endothelial nitric oxide signaling and to decrease inflammatory responses in the vasculature. Numerous pharmacologic investigations exploring the use of endothelial-targeted therapies for cerebrovascular illnesses have identified Cilostazol as generally prescribed and exhibiting not only antiplatelet and vasodilatory effects but also endothelial-modifying activity (Lin *et al*., 2021; Chen *et al*., 2021). Although this material is supplied for pharmacologic purposes, these data do not apply to any of the pharmacologic interventions examined in this study.

The findings of the present study should be interpreted as observations of anatomy rather than mechanisms or pharmacology. While pharmacological agents targeting the endothelium have been studied in cerebrovascular disease, neither pharmacological exposure nor therapeutic outcomes were assessed in this study. Pharmacological considerations discussed in this study are to be taken as generating hypotheses for future studies that will include integrated anatomical imaging, hemodynamic assessment and pharmacological research. The limitations of not performing multivariate analysis and of not providing formal inter-observer reliability statistics should be taken into account when interpreting the results, as these limitations are due to the retrospective nature of the study. While pharmacological interventions were not assessed in this investigation, the anatomical patterns identified may indicate a subset of patients for whom "endothelial-stabilizing" therapies could be developed as pharmacotherapy to prevent or counteract intracranial aneurysm formation in future studies.

Limitations

When interpreting this study, there are a number of limitations to consider. This is a retrospective analysis and is subject to limitations inherent to a single-center cohort, which may limit the ability to apply the conclusions beyond this facility; however, vascular hemodynamics and endothelial biomarkers could not be directly measured to determine how anatomical variants may impact aneurysm formation through a mechanistic relationship. Additionally, we could not systematically evaluate pharmacological variables such as previous use of antiplatelet agents or statin therapy or the use of pharmacological therapies aimed at modifying the endothelium. Although the present study supports the possibility of using a vascular-targeted pharmacotherapy based on the translational relevance of modifying endothelial nitric oxide (e.g., risk of developing an abdominal aortic aneurysm), we have not assessed the potential of this type of intervention. Other limitations include small sample size, retrospective design, possible imaging bias and lack of hemodynamic measurements. The absence of multivariate analysis and potential confounding variables are also a considerable limitation.

CONCLUSION

A vascular anatomic phenotype with a left-sided predominance of the Ponticulus posticus, hypoplastic contralateral vertebral arteries and persistent fetal type posterior circulation is identified here as having associations with intracranial aneurysm formation. Identification of this structural pattern may facilitate risk stratification and could serve to investigate pharmacological prevention techniques that target endothelial dysfunction or vascular remodeling which may open avenues for future research. In this regard, further studies on endothelial-modulating agents may help reduce susceptibility to aneurysm formation in individuals with anatomical predisposition or baseline risk factors.

Acknowledgements
None

Authors' contribution
Emrah Keskin: Key contributor to the creation of this research by way of the ideas and overall design; Mehmet Selim Gel: Carried out both the data collection and the clinical assessment, analyzed and interpreted the data; Ayhan Kanat: Wrote the first draft of the manuscript; Çagri Elbir: Provided critical evaluations of the manuscript related to significant intellectual and pharmaceutical content.

Funding
There was no funding.

Data availability statement
All data generated or analysed during this study are included in this published article and its supplementary information files.

Ethical approval
This study was approved by the Ethics Committee of Saglık Bilimleri Universitesi Diskapi Yildirim Beyazit Egitim ve Araştırma Hastanesi (Approval No. 122/15). Written consent from participants was collected.

Conflicts of interest
The authors declare that they have no conflicts of interest related to this work.

Supplementary data
https://www.pjps.pk/uploads/2026/03/SUP1774872700.pdf

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