DOI: https://doi.org/10.54393/pjhs.v7i6.3889

PAKISTAN JOURNAL OF HEALTH SCIENCES
(LAHORE)
https://thejas.com.pk/index.php/pjhs
ISSN (E): 2790-9352, (P): 2790-9344
Volume 7, Issue 06 (June 2026)

Systematic Review

OPEN ACCESS

Anatomical Variations of the Circle of Willis and Their Clinical Significance: A Systematic Review

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ARTICLE INFO

Keywords:
Circle of Willis, Anatomical Variation, Collateral Circulation, Ischemic Stroke, Intracranial Aneurysm, Magnetic Resonance Angiography, Computed Tomography Angiography

How to Cite:
Ansari, H., Qayyum, M. A., Waheed, S. A., Bibi, H., Nawaz, A., & Ansar, T. (2026). Anatomical Variations of the Circle of Willis and Their Clinical Significance: A Systematic Review: Anatomical Variations of the Circle of Willis and Their Clinical Significance. Pakistan Journal of Health Sciences, 7(6), 164-171. https://doi.org/10.54393/pjhs.v7i6.3889

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Received Date: 26th January, 2026
1st Revision Received: 2nd March, 2026
Acceptance Date: 16th March, 2026
Published Date: 30th June, 2026

ABSTRACT

The Circle of Willis (CoW) is the principal intracranial collateral network connecting the anterior and posterior cerebral circulations. Anatomical variations of the CoW are common and may influence cerebral hemodynamics, collateral capacity, ischemic stroke outcomes, and aneurysm development. However, contemporary imaging-based evidence regarding their clinical significance has not been systematically synthesized. **Objectives:** To systematically review recent human imaging studies (2020–2025) evaluating anatomical variations of the Circle of Willis and their reported clinical associations. **Methods:** A systematic search of PubMed, Scopus, and the Cochrane Library was conducted following PRISMA 2020 guidelines. Original human studies assessing CoW anatomy using computed tomography angiography (CTA), magnetic resonance angiography (MRA), or conventional angiography were included. Data extracted included study design, population characteristics, imaging modality, prevalence of major variants, and clinical associations. Risk of bias was assessed using a qualitative domain-based approach. Due to methodological heterogeneity, findings were synthesized narratively. **Results:** Eighteen imaging-based studies were included. Incomplete CoW configurations and posterior communicating artery hypoplasia/aplasia were the most frequently reported variants, with incomplete configurations reported in 30–70% of participants. Several studies demonstrated associations between incomplete configurations and poorer ischemic stroke outcomes, vulnerable intracranial plaque features, and increased odds of intracranial aneurysm. Fetal-type posterior cerebral artery and A1 segment asymmetry were linked to distinct hemorrhagic and aneurysmal patterns. **Conclusions:** Anatomical variations of the Circle of Willis are highly prevalent and clinically relevant. Standardized reporting of CoW configuration may enhance cerebrovascular risk stratification and inform neurovascular decision-making.

INTRODUCTION

The Circle of Willis (CoW) is a polygonal arterial network located at the base of the brain that enables collateral circulation between the anterior and posterior cerebral circulations. This anatomical structure plays a critical role in maintaining cerebral perfusion during proximal arterial stenosis or occlusion [1]. Although traditionally described as a symmetrical and complete arterial ring, a complete Circle of Willis is found only in a minority of individuals, while segmental hypoplasia, aplasia, and asymmetry are common in both normal and diseased populations [2]. The physiological and clinical relevance of these anatomical variations is increasingly recognized. The presence or absence of communicating arteries influences collateral capacity, determines redistribution of cerebral blood flow, and may alter tissue vulnerability during acute ischemic events [3]. Experimental and clinical studies suggest that

DOI: https://doi.org/10.54393/pjhs.v7i6.3889

incomplete configurations may limit compensatory flow during large-vessel occlusion, contributing to larger infarct volumes and poorer functional outcomes. Conversely, well-developed communication pathways may provide protective collateral channels that preserve perfusion in critical regions [4]. Beyond ischemic stroke, variations in the Circle of Willis have also been implicated in the pathogenesis of intracranial aneurysms and hemorrhagic stroke. Asymmetries that alter flow dynamics, such as anterior cerebral artery A1 segment asymmetry or fetal-type posterior cerebral artery, may create focal hemodynamic stress at arterial bifurcations and perforator origins [5]. These altered flow states have been proposed as contributing factors in aneurysm formation, aneurysm progression, and specific hemorrhagic phenotypes involving deep or posterior circulation territories [6].

Although imaging-based studies evaluating Circle of Willis variations have increased substantially in recent years, the available evidence remains heterogeneous in terms of study design, imaging modality, operational definitions of anatomical variants, and reporting of clinical outcomes. Most studies are single-center and referral-based, limiting generalizability. Furthermore, despite advances in computed tomography angiography (CTA) and high-resolution magnetic resonance angiography (MRA) that have enhanced visualization of intracranial arterial anatomy, a contemporary synthesis of recent evidence is lacking. Therefore, this systematic review was conducted to synthesize recent human imaging studies (2020–2025) evaluating anatomical variations of the Circle of Willis and their clinical significance. This review aims to summarize the prevalence of major CoW variants and examine their reported associations with ischemic stroke outcomes, intracranial aneurysms, and hemorrhagic cerebrovascular disease.

METHODS

This systematic review aimed to assess anatomical variations of the Circle of Willis (CoW) and their clinical implications in human populations. The review was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines. The methodological framework, including objectives, eligibility criteria, search strategy, and data synthesis approach, was predefined before conducting the review to enhance transparency and reproducibility. Although a structured protocol was developed a priori, it was not prospectively registered in an international database (e.g., PROSPERO), which is acknowledged as a limitation. An electronic literature search was conducted in three major databases: PubMed, Scopus, and the Cochrane Library. The search included studies published between January 2020 and December 2025. Both controlled vocabulary and free-text terms were used to maximize search sensitivity. The primary PubMed search strategy was: ("Circle of Willis" OR "cerebral arterial circle") AND (variation OR variant OR anomaly OR hypoplasia OR aplasia OR "incomplete circle") AND (angiography OR "computed tomography angiography" OR CTA OR "magnetic resonance angiography" OR MRA). Equivalent search strategies were adapted for Scopus and the Cochrane Library. In addition, the reference lists of all included studies were manually screened to identify any potentially eligible articles not captured in the electronic search. Studies were selected based on predefined inclusion and exclusion criteria. Eligible studies were original human research published between 2020 and 2025 that evaluated anatomical variations of the Circle of Willis using imaging modalities such as computed tomography angiography (CTA), magnetic resonance angiography (MRA), or conventional angiography. Studies were required to report either the prevalence of CoW variants or their clinical associations with cerebrovascular outcomes. Animal studies, case reports, narrative reviews, systematic reviews, meta-analyses, pilot studies, conference abstracts without full text, and studies that did not report Circle of Willis configuration were excluded. All identified records were imported into reference management software, and duplicates were removed before screening. Titles and abstracts were independently screened by two reviewers according to predefined eligibility criteria. Full-text articles of potentially relevant studies were subsequently retrieved and independently assessed for eligibility by the same two reviewers. Disagreements at any stage were resolved through discussion and consensus. Formal inter-rater agreement statistics (e.g., kappa coefficient) were not calculated, which is acknowledged as a methodological limitation. The study selection process followed the PRISMA 2020 framework. A total of 515 records were identified through database searching. After the removal of records before screening, 350 records underwent title and abstract screening. Fifty-three full-text articles were assessed for eligibility, and 18 studies were ultimately included in the qualitative synthesis. Flow diagram illustrating the identification, screening, eligibility assessment, and inclusion of studies in this systematic review. A total of 515 records were identified from PubMed (n=210), Scopus (n=185), and Cochrane Library (n=120). After removal of 165 records before screening (duplicates and other exclusions), 350 records were screened. Out of these, 285 were excluded at the title and abstract level. Sixty-five full-text reports were sought for retrieval, of which 12 were not retrieved. Fifty-three full-text articles were assessed for eligibility, and 35 were excluded based on predefined criteria. Ultimately, 18 studies were included in the qualitative synthesis (Figure 1).

DOI: https://doi.org/10.54393/pjhs.v7i6.3889

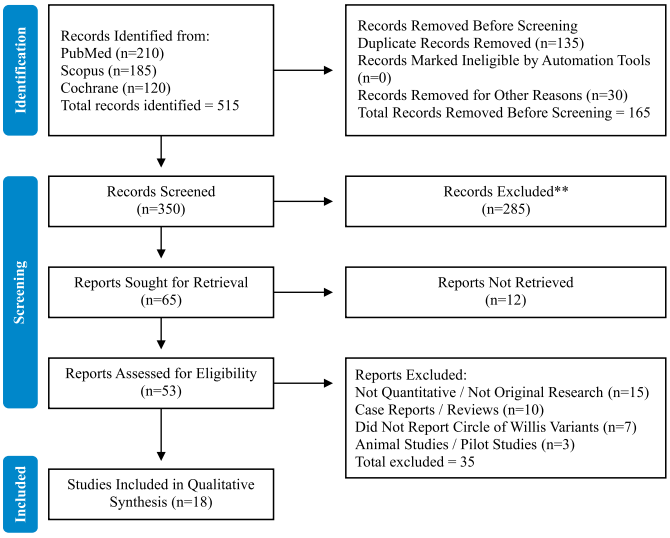

Figure 1: Study Selection Process

Data extraction was performed using a standardized data extraction form. Extracted variables included first author and year of publication, study design, sample size, characteristics of the study population, imaging modality and protocol, definitions of anatomical variants, prevalence of major CoW variants, reported clinical associations, and effect estimates such as odds ratios where available. Data extraction was conducted independently by two reviewers, and discrepancies were resolved through consensus to ensure data accuracy and completeness. Standardized definitions of "incomplete Circle of Willis" and "hypoplasia" were not uniformly applied across included studies. Diameter thresholds used to define hypoplasia and criteria for completeness varied between studies, contributing to methodological heterogeneity. This variability was documented during data extraction and considered during qualitative synthesis. Risk of bias was assessed using a qualitative domain-based approach tailored to observational imaging studies. Three principal domains were evaluated: selection bias (population representativeness), measurement bias (imaging protocol standardization and clarity of variant definitions), and control of confounding (use of multivariable or adjusted analyses when reporting associations). Formal risk-of-bias tools designed for randomized controlled trials were not applicable because the majority of included studies were cross-sectional or observational imaging studies. Each study was categorized as having low, moderate, or low–moderate overall risk of bias. Due to substantial heterogeneity in study design, imaging modalities, operational definitions of anatomical variants, outcome measures, and population characteristics, a quantitative meta-analysis was not performed. The decision to refrain from pooled statistical synthesis was based on methodological variability that precluded meaningful statistical aggregation. Instead, prevalence ranges and reported associations were summarized descriptively. A structured qualitative narrative synthesis was conducted to compare patterns of anatomical variation and reported clinical associations across studies.

RESULTS

A total of 18 original human imaging studies published between 2020 and 2025 were included in the qualitative synthesis. Across studies, Circle of Willis (CoW) anatomy was assessed predominantly using CTA and MRA in symptomatic, referral-based, or population cohorts. The study summarizes the characteristics of the 18 included studies (2020–2025), including design, population, imaging modality, reported variants, and clinical relevance. Most studies were cross-sectional or observational and mainly included symptomatic or referred cerebrovascular populations, with sample sizes ranging from 85 to >1,000 participants. CTA and MRA were the most frequently used modalities, reflecting modern imaging-based evaluation of CoW variants (Table 1).

Table 1: Characteristics of Included Studies (2020–2025) on Anatomical Variations of the Circle of Willis and Their Clinical Significance

Sr. No.	References	Design / Population	Modality	Key CoW Findings	Clinical Significance Reported
1	[7]	Cross-sectional; suspected cerebrovascular pathology (n=95)	CTA	Variants in 55%; PCoA hypoplasia common; fetal PCA present	Variants noted as important for aneurysm/vascular planning
2	[8]	Retrospective; symptomatic patients (n=231)	3T MRA	PCoA hypoplasia and fetal-type PCA documented	Highlights the prognostic/diagnostic relevance of posterior variants
3	[9]	Large observational; ischemic stroke vs controls (>1000 stroke)	Imaging-based CoW assessment	Higher variant prevalence in the stroke cohort	Examined severity/in-hospital prognosis associations
4	[10]	Cross-sectional; CTA dataset (n=255)	CTA	CoW variants characterized alongside stenosis patterns	Linked variants with cerebral/cervical stenosis patterns (plus automated analysis)
5	[11]	Cross-sectional; children vs adults	MRA	CoW morphometric differences by age group	Developmental anatomy implications for flow/collateral interpretation
6	[12]	Cross-sectional; suspected cerebrovascular disease (n=102)	64-MSCT angiography	Anterior and posterior pattern classifications: ACoA/PCoA aplasia/hypoplasia patterns	Relevance for endovascular planning in their cohort

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7	[13]	Cross-sectional; large clinical sample (n=867)	MRA	Detailed variant prevalence; incomplete CoW frequent	Collateral-pathway implications emphasized
8	[14]	Observational; stroke patients	Imaging-based CoW completeness	Incomplete CoW common (1/3)	An incomplete CoW is associated with worse functional outcome (adjusted)
9	[15]	Cross-sectional; clinical referrals (n=264)	MRA	Variation frequencies reported	Emphasized clinical importance for neurovascular procedures
10	[16]	Prospective cross-sectional; tertiary MRA cohort (n=152)	MRA	Complete CoW 24%; posterior variants common (PCoA aplasia)	Links discussed with future cerebrovascular risk and demographics
11	[17]	Observational association; ICAS/AIS focus	Vascular imaging	Incomplete CoW phenotypes categorized	Incomplete CoW associated with vulnerable plaque features and AIS
12	[18]	Population study (Tromsø)	Imaging-based CoW variants	Incomplete CoW variants defined	An incomplete CoW is associated with higher odds of intracranial aneurysm
13	[19]	Observational; anterior circulation ischemic stroke	CoW communicating artery presence	Presence/absence of communicating arteries assessed	Communicating arteries associated with higher functional recovery rates
14	[20]	Retrospective; cerebral angiography/MRA images (n=85)	Angiography/ MRA	Age/sex differences in completeness and vessel diameters	Highlights demographic influences relevant to interpretation/planning
15	[21]	Observational: hypertensive thalamic hemorrhage	Imaging-defined fetal PCA	Fetal-type PCA presence assessed	Reported association between fetal PCA and hemorrhage-related phenotype
16	[22]	Cross-sectional; archived CT brain images (n=200)	CT-based vascular assessment	Posterior/anterior communicating segment variants	Emphasized implications for cerebrovascular risk/interpretation
17	[23]	Retrospective cross-sectional (n=384)	3T MRA	Patterns and prevalence of CoW variants	Clinical relevance framed around cerebrovascular health
18	[24]	Association study: aneurysm vs control	CTA	A1 dysplasia/variation analyzed	A1 variation associated with MCA aneurysm occurrence/rupture indicators

The results summarize the most frequently reported CoW variants and the clinical associations described across included studies. The most commonly reported variants were posterior communicating artery (PCoA) hypoplasia/aplasia and incomplete Circle of Willis configurations. Across studies, incomplete configurations were reported in approximately 30–70% of participants, depending on the study population and operational definitions. Several studies reported associations between incomplete configurations and poorer ischemic stroke outcomes, vulnerable intracranial plaque features, or increased odds of intracranial aneurysm (Table 2).

Table 2: Major Patterns of Circle of Willis Variations and Their Reported Clinical Associations in Included Studies

Variant / Configuration	References	Typical Prevalence / Description	Main Clinical Associations Reported
Posterior communicating artery (PCoA) hypoplasia/aplasia	[16, 22]	Most frequent posterior variant; often unilateral or bilateral	Reduced collateral capacity: relevance for stroke prognosis and endovascular planning
Incomplete Circle of Willis (any segment absent/hypoplastic)	[13, 17]	Reported in 30–70%, depending on the definition and population	Worse functional outcome after stroke; higher odds of intracranial aneurysm; vulnerable plaque features
Fetal-type posterior cerebral artery (fetal PCA)	[7, 8]	Present in a substantial minority; usually unilateral	Associated with hemorrhagic phenotype; important for posterior circulation flow patterns
Anterior cerebral artery A1 segment asymmetry/dysplasia	[17, 24]	Variable frequency; often unilateral	Associated with the middle cerebral artery aneurysm occurrence and altered flow distribution
Absence or hypoplasia of the anterior communicating artery (ACoA)	[12, 13]	Less frequent than PCoA variants	Impaired anterior collateral circulation; relevance for procedural planning
Age-related morphological differences	[11, 20]	Children show different calibers and configurations than adults	Developmental and demographic influence on collateral interpretation
Presence of complete communicating pathways	[19]	Minority of patients with a fully complete Circle of Willis	Higher rates of functional recovery after anterior circulation stroke

The study outlines the methodological distribution of included studies by imaging modality, study design, and study population. MRA was the most frequently used modality, particularly in prevalence-focused studies, whereas CTA was more commonly used in studies examining acute stroke and aneurysm-related outcomes. Cross-sectional designs predominated, while a smaller subset of studies assessed clinical associations with stroke outcomes, aneurysm presence, or hemorrhagic phenotypes (Table 3).

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Table 3: Distribution of Imaging Modalities, Study Designs, and Study Populations in Included Studies (2020–2025)

Category	Subgroup	References	Key Observations
Imaging Modality	Computed tomography angiography (CTA / CT-based)	[7, 22]	CTA was mainly used in acute stroke and aneurysm-focused studies, allowing detailed segmental assessment
	Magnetic resonance angiography (MRA)	[8, 11]	MRA was the most frequently used modality, particularly in prevalence and population-based studies
	Mixed/conventional angiography	[20]	Used for detailed morphometric and anatomical evaluation
Study Design	Cross-sectional prevalence studies	[7, 15]	Predominant design: focused on describing frequency and patterns of Circle of Willis variants
	Observational association studies	[18, 19]	Explored associations with stroke outcome, aneurysm risk, plaque vulnerability, and hemorrhagic phenotypes
	Prospective imaging cohort	[16]	Provided standardized imaging protocol and demographic analysis
Study Population	Symptomatic cerebrovascular patients	[23, 24]	Majority of studies involved clinically relevant stroke or vascular disease populations
	General / referred imaging population	[15, 16]	Used primarily for prevalence estimates of Circle of Willis variants
	Pediatric/developmental population	[11]	Only study specifically addressing developmental differences

The results present the domain-based qualitative risk-of-bias assessment across the included studies. Most studies were judged to have a moderate overall risk of bias, primarily due to referral-based sampling and limited population representativeness. Measurement bias was generally low in studies using standardized CTA or high-field MRA protocols, whereas confounding control varied across association studies depending on whether multivariable adjustment was performed (Table 4).

Table 4: Risk of Bias Assessment of Included Studies Using a Domain-Based Qualitative Approach

References	Selection Bias (Population Representativeness)	Measurement Bias (Imaging and Definitions)	Confounding Control	Overall Risk of Bias
[7]	Moderate (single-center, symptomatic cohort)	Low (standard CTA protocol)	Not applicable	Moderate
[8]	Moderate (referred clinical population)	Low (3T MRA, clear definitions)	Not applicable	Moderate
[9]	Moderate	Low	Moderate (adjusted analyses)	Moderate
[10]	Moderate	Low	Low (multivariable + automated model)	Low–Moderate
[11]	Low (healthy controls included)	Low	Not applicable	Low
[12]	Moderate	Moderate (mixed CT definitions)	Not applicable	Moderate
[13]	Moderate	Low (standard MRA protocol)	Not applicable	Moderate
[14]	Moderate	Low	Low (multivariable outcome model)	Low–Moderate
[15]	Moderate	Moderate	Not applicable	Moderate
[16]	Moderate	Low	Not applicable	Moderate
[17]	Moderate	Low	Low (adjusted plaque analysis)	Low–Moderate
[18]	Low (population-based cohort)	Low	Low (multivariable model)	Low
[19]	Moderate	Low	Low (adjusted functional outcome model)	Low–Moderate
[20]	Moderate	Low	Not applicable	Moderate
[21]	Moderate	Low	Low (adjusted hemorrhage model)	Low–Moderate
[22]	Moderate	Moderate	Not applicable	Moderate
[23]	Moderate	Low	Not applicable	Moderate
[24]	Moderate	Low	Low (case–control adjustment)	Low–Moderate

DISCUSSION

The present systematic review synthesizes contemporary imaging-based evidence (2020–2025) regarding anatomical variations of the Circle of Willis (CoW) and their clinical relevance. Across included studies, incomplete CoW configurations and posterior communicating artery (PCoA) hypoplasia/aplasia emerged as the most frequently reported variants, whereas a fully complete arterial circle was consistently observed in a minority of individuals. This finding is consistent with recent large imaging cohorts demonstrating that incomplete configurations represent the predominant anatomical pattern in adult populations [25, 26]. Beyond prevalence, this review demonstrates that CoW configuration has meaningful implications for collateral flow and ischemic vulnerability. Incomplete configurations and absent communicating segments may limit compensatory redistribution of blood flow during large-vessel occlusion, potentially contributing to larger infarct volumes and poorer functional recovery. Recent

DOI: https://doi.org/10.54393/pjhs.v7i6.3889

systematic and imaging-based studies have similarly reported that preserved collateral anatomy is associated with improved functional outcomes after ischemic stroke [27]. These findings support the hypothesis that structural collateral anatomy directly influences hemodynamic resilience in acute ischemic events. In the context of mechanical thrombectomy, preserved communicating pathways may enhance procedural efficacy by maintaining perfusion to distal territories, as suggested by contemporary endovascular outcome studies [28]. The relationship between CoW variants and intracranial aneurysm formation is also highlighted in this synthesis. Anterior cerebral artery (A1) segment asymmetry appears to alter flow dominance within the anterior communicating complex, potentially increasing focal wall shear stress and aneurysm susceptibility. Hemodynamic modeling studies have demonstrated that altered flow patterns within asymmetric anterior circulation segments may predispose to aneurysm development [29]. Similarly, clinical imaging studies have reported associations between anterior circulation dominance and aneurysm characteristics [30]. These findings suggest that CoW morphology may influence aneurysm biology through flow redistribution rather than acting as a purely incidental anatomical variant. Posterior circulation variants, particularly fetal-type posterior cerebral artery (fetal PCA), were also associated with distinct clinical phenotypes. Fetal PCA shifts perfusion dependency toward the internal carotid system, which may modify posterior circulation hemodynamics. Recent studies have reported associations between fetal PCA configuration and specific hemorrhagic or posterior circulation stroke patterns [31, 32]. Although the exact causal mechanisms remain incompletely defined, consistent associations across imaging cohorts indicate potential prognostic relevance. Age- and sex-related morphological differences were observed in selected studies. Developmental variation in CoW anatomy suggests that collateral capacity may not be static across the lifespan. Population-based anatomical studies have demonstrated that vessel caliber and completeness vary with age and sex [33, 34]. Pediatric and adult configurations differ in vessel morphology, which may partly explain heterogeneity in cerebrovascular risk profiles. Importantly, methodological heterogeneity across studies must be considered when interpreting prevalence ranges. Operational definitions of "incomplete CoW" and "hypoplasia" varied substantially, and imaging modality (CTA vs. MRA) may influence detection rates of small-caliber segments. Prior imaging comparison studies have shown imperfect agreement between modalities in detecting small communicating arteries [35]. Such variability limits direct quantitative comparison across cohorts and underscores the need for standardized definitions.

This review has several limitations. First, the majority of included studies were single-center and referral-based, raising the possibility of spectrum bias and limiting generalizability to broader populations. Second, heterogeneity in imaging protocols and variant definitions precluded quantitative meta-analysis and limited pooled prevalence estimation. Third, formal inter-rater agreement statistics were not calculated during screening, and standardized risk-of-bias tools specific to observational imaging studies are lacking. Fourth, because most included studies were cross-sectional, causal inference between anatomical configuration and clinical outcomes remains limited. Future research should prioritize large-scale, multicenter population-based studies using harmonized definitions of CoW completeness and hypoplasia. Standardized imaging acquisition protocols and consensus-based reporting frameworks would improve comparability across studies. Prospective longitudinal designs are needed to clarify causal relationships between CoW morphology and cerebrovascular outcomes. Furthermore, integration of computational flow modeling with clinical outcome data may provide mechanistic insight into how specific configurations influence hemodynamic stress and stroke vulnerability.

CONCLUSIONS

This systematic review demonstrates that anatomical variations of the Circle of Willis, particularly incomplete configurations and posterior communicating artery hypoplasia or aplasia, are common findings in contemporary imaging cohorts. Evidence suggests that these variants are associated with altered collateral capacity, ischemic stroke outcomes, aneurysm susceptibility, and distinct hemorrhagic phenotypes. Standardized and routine reporting of CoW configuration in neurovascular imaging may enhance risk stratification, inform procedural planning, and improve individualized clinical decision-making. Future harmonized, population-based, and longitudinal investigations are required to refine prognostic models and clarify the mechanistic pathways linking vascular anatomy with cerebrovascular disease.

Authors' Contribution

Conceptualization: HA
Methodology: MAQ, SAW, AN, TA
Formal analysis: SAW, AN, TA
Writing and Drafting: HA, MAQ, HB, AN, TA
Review and Editing: HA, MAQ, SAW, HB, AN, TA

All authors approved the final manuscript and take responsibility for the integrity of the work

DOI: https://doi.org/10.54393/pjhs.v7i6.3889

Conflicts of Interest

All the authors declare no conflict of interest.

Source of Funding

The authors received no financial support for the research, authorship and/or publication of this article.

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