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A systematic review of anatomical variations of the circle of willis: Implications for cerebrovascular risk, stroke patterns and neurosurgical planning

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Abstract

Background: The Circle of Willis (CoW) is the principal collateral arterial network at the base of the brain, yet fewer than half of individuals exhibit its textbook complete configuration. Anatomical variation of the CoW has been repeatedly implicated in cerebrovascular risk, stroke topography, and intracranial aneurysm formation, but the evidence remains scattered across heterogeneous case studies and primary research designs.

Methods: This scoping review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) framework. PubMed, Google Scholar, Taylor & Francis Online, Scopus, and ScienceDirect were searched for English-language case studies and primary research articles published between 2000 and 2026. Screening and eligibility assessment were conducted in duplicate against predefined inclusion and exclusion criteria.

Results: Forty-eight primary studies met inclusion criteria, comprising cadaveric dissections, magnetic resonance and computed tomography angiography cohorts, case-control investigations, and individual case reports. Pooled findings indicate that CoW variation occurs in approximately 50–70% of individuals, with posterior communicating artery hypoplasia/aplasia and anterior communicating artery anomalies being the most frequent configurations. Incomplete configurations were consistently associated with larger infarct volumes, altered stroke topography, and increased odds of anterior communicating and posterior communicating artery aneurysms.

Conclusion: CoW anatomical variation is common, clinically consequential, and population-dependent. Standardized preoperative angiographic characterization of the CoW is recommended to guide cerebrovascular risk stratification, stroke management, and neurosurgical or endovascular planning.

Keywords: Circle of willis, anatomical variation, cerebrovascular disease, stroke, intracranial aneurysm, neurosurgical planning, scoping review

Introduction

The Circle of Willis (CoW) is a ring-shaped anastomotic network of arteries located at the base of the brain that unites the anterior and posterior cerebral circulations and links the two cerebral hemispheres. Its principal physiological role is to provide immediate collateral blood flow whenever a parent vessel becomes stenotic, occluded, or otherwise compromised (Ravindran *et al*., 2022) [41]. Although the CoW is classically depicted in anatomy textbooks as a symmetrical heptagonal or hexagonal arrangement of the internal carotid, anterior cerebral, anterior communicating, posterior communicating, and posterior cerebral arteries, empirical studies dating back to Fawcett and Blachford's early twentieth-century dissections have repeatedly shown that this “typical” configuration is, in fact, the minority pattern (Ayre *et al*., 2022) [4].

Contemporary cadaveric and angiographic evidence indicates that anatomical variation of the CoW — including hypoplasia, aplasia, duplication, and fenestration of its constituent segments — is present in approximately half to more than two-thirds of the general population (Jones *et al*., 2021) [23]. These variations are not merely incidental findings; they have been mechanistically and epidemiologically linked to altered cerebral hemodynamics, differential susceptibility to ischemic stroke, and an elevated propensity for intracranial aneurysm formation at specific arterial junctions such as the anterior communicating artery (AComA) and posterior communicating artery (PComA) (Kayembe *et al*., 1984; Zhang *et al*., 2023) [26, 57].

From a clinical standpoint, awareness of CoW variability carries direct implications across three interconnected domains. First, in cerebrovascular risk assessment, an incomplete or asymmetric CoW may compromise the brain's capacity to compensate for large-vessel occlusive disease, thereby influencing which patients are more vulnerable to hemodynamically mediated ischemia (Silva *et al*., 2017; Casas-Vara *et al*., 2011) [9, 45]. Second, in stroke pattern analysis, the configuration of the CoW has been shown to shape infarct topography, lesion volume, and even atypical clinical presentations, as illustrated by case reports of bilateral embolic infarction attributable to dominant unilateral flow (Brownlee *et al*., 2006) [8]. Third, in neurosurgical and endovascular planning, precise preoperative characterization of CoW anatomy is essential for aneurysm clipping, coiling, bypass, and carotid revascularization procedures, since variant anatomy can alter surgical corridors, exposure, and the risk of iatrogenic injury (Ayre *et al*., 2022; Shah *et al*., 2019) [4, 43].

Despite the accumulation of primary research and case reports on this topic, the evidence remains dispersed across anatomical, radiological, and neurosurgical literature, employing heterogeneous classification systems, hypoplasia thresholds, and population samples. No comprehensive scoping synthesis has systematically mapped case studies and primary research specifically addressing the intersection of CoW variation with cerebrovascular risk, stroke patterning, and neurosurgical planning across the 2000–2026 period. This review therefore aims to (a) characterize the prevalence and typology of CoW anatomical variations reported in the primary literature, (b) synthesize their documented associations with cerebrovascular risk and stroke patterns, and (c) delineate their implications for neurosurgical and endovascular planning.

Methods

1. Protocol and Reporting Framework

This review was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) checklist (Tricco *et al*., 2018) [48]. The PRISMA-ScR framework was selected because the objective of this review was to map the breadth and characteristics of available case studies and primary research on CoW anatomical variation, rather than to pool effect sizes across a narrowly defined clinical outcome, consistent with the scoping review methodology described by Arksey and O'Malley and later refined by the Joanna Briggs Institute.

2. Eligibility Criteria

Eligibility was defined using a Population–Concept–Context (PCC) framework appropriate for scoping reviews.

- **Population:** Human subjects (cadaveric specimens, living patients, or imaging cohorts) of any age or sex.
- **Concept:** Anatomical variation(s) of the Circle of Willis, including hypoplasia, aplasia, duplication, fenestration, azygos configuration, and fetal-type posterior cerebral artery, and their reported associations with cerebrovascular risk, stroke pattern, or neurosurgical/endovascular planning.
- **Context:** Any clinical, radiological, cadaveric, or surgical setting, without geographic restriction.

Only case studies (single case reports and case series) and primary research articles (cross-sectional, cohort, case-control, and cadaveric observational studies) were eligible. Secondary literature such as narrative reviews, systematic reviews, meta-analyses, editorials, and conference abstracts without extractable primary data were excluded, except where cited contextually in the introduction or discussion. Eligible articles were required to be published in English between January 2000 and 2026 inclusive, and to report original anatomical or clinical data on the CoW. Animal studies, purely computational/simulation studies without anatomical validation, and articles for which full text could not be retrieved were excluded.

3. Information Sources and Search Strategy

A structured search was conducted across five databases: PubMed, Google Scholar, Taylor & Francis Online, Scopus, and ScienceDirect. The search strategy combined controlled vocabulary and free-text terms for the anatomical concept (“circle of Willis” OR “cerebral arterial circle” OR “circle of Willis anatomical variation” OR “CoW variant”) with terms for the clinical concepts of interest (“stroke” OR “cerebrovascular” OR “aneurysm” OR “neurosurgical planning” OR “collateral circulation”). Boolean operators (AND/OR) and database-specific filters were applied to restrict results to human studies, English language, and the 2000–2026 publication window. Reference lists of eligible articles were also hand-searched to identify additional relevant case studies.

4. Study Selection

All records retrieved from the five databases were exported and de-duplicated. Two reviewers independently screened titles and abstracts against the eligibility criteria, followed by full-text assessment of potentially eligible articles. Disagreements were resolved by discussion and, where necessary, consultation with a third party. The study selection process is summarized in the PRISMA-ScR flow diagram below.

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Identification: Records identified through database searching (PubMed = 612; Google Scholar = 940; Scopus = 578; ScienceDirect = 401; Taylor & Francis = 233) — Total n = 2,764
Records after duplicates removed (n = 1,987)
Records screened by title/abstract (n = 1,987) — Records excluded (n = 1,724): not case study/primary research, non-CoW focus, animal studies, non-English, outside 2000–2026 window
Full-text articles assessed for eligibility (n = 263) — Full-text articles excluded (n = 215): reviews/meta-analyses without new primary data, conference abstracts only, insufficient anatomical detail, duplicate cohort reporting
Studies included in the scoping review (n = 48) — Case reports/case series (n = 19); Cross-sectional/cohort imaging or cadaveric studies (n = 25); Case-control studies (n = 4)

Table 1: PRISMA-ScR flow diagram of study identification, screening, eligibility assessment, and inclusion.

5. Data Charting Process and Items

A standardized data-charting form was used to extract the following items from each included study: author(s) and year of publication, country/population studied, study design (case study, cadaveric, cross-sectional, cohort, or case-control), imaging or dissection modality, sample size, CoW variant(s) reported, prevalence or case-specific findings, and reported clinical association(s) with cerebrovascular risk, stroke pattern, or neurosurgical/endovascular planning. Data charting was performed independently by both reviewers and cross-checked for consistency.

6. Synthesis of Results

Given the heterogeneity of study designs, hypoplasia thresholds, and outcome definitions across the included literature, results were synthesized narratively and descriptively rather than through formal meta-analytic pooling, consistent with standard scoping review practice. Where multiple primary studies reported comparable quantitative prevalence estimates, these were tabulated to illustrate the range of reported frequencies across populations and imaging modalities.

Results

1. Characteristics of Included Studies

A total of 2,764 records were identified across the five databases (PubMed = 612; Google Scholar = 940; Scopus = 578; ScienceDirect = 401; Taylor & Francis = 233). After removal of duplicates, 1,987 unique records underwent title/abstract screening, of which 263 proceeded to full-text review. Forty-eight studies satisfied all eligibility criteria and were included in the final synthesis, comprising 25 cross-sectional or cohort imaging/cadaveric studies, 19 case reports or case series, and 4 case-control studies. Included studies originated from a broad range of populations, including Sri Lankan, Chinese, Polish, Ethiopian, Nepalese, Trinidadian, South African, and North American cohorts, reflecting substantial geographic and ethnic diversity in the evidence base.

2. Prevalence and Typology of Circle of Willis Variation

Across the included primary research, the reported prevalence of a "complete" or classic CoW configuration varied markedly, from as low as 16.6% in a South Indian tertiary hospital cohort to approximately 46.7% in an Egyptian sample and 69.57% in a Malawian cadaveric series, underscoring pronounced inter-population heterogeneity (Berghout *et al*., 2023) [6]. A frequently cited meta-analytic estimate placed the pooled prevalence of any CoW variation at 68.22% ± 14.32% across the literature (Jones *et al*., 2021) [23], while other large single-center MRA series reported a complete CoW in as few as 24.3% of subjects (Berghout *et al*., 2023) [6].

The posterior segment of the CoW was consistently reported as the more variable portion relative to the anterior segment. Multiple studies identified hypoplasia or aplasia of the posterior communicating artery — unilateral or bilateral — as the single most common variant, occurring in approximately 20–70% of samples depending on the diagnostic threshold applied (Jones *et al*., 2021; De Silva *et al*., 2009) [13, 23]. In the anterior segment, anomalies of the anterior communicating artery, including duplication (up to 18% prevalence), fenestration (up to 21%), and the rare azygos anterior cerebral artery configuration (approximately 1–2% prevalence), were the most frequently documented findings (Ghaffari *et al*., 2024) [17]. A recent North American cadaveric study similarly reported a higher variation rate in the anterior CoW (84%) compared with the posterior CoW (72%), a reversal of the pattern seen in several Asian cohorts and illustrating that the anterior-versus-posterior variability ratio itself differs by population (Prasad *et al*., 2025) [37].

Rare but clinically significant variants were also documented in individual case reports, including a duplicated posterior cerebral artery described as a "true fetal PCA" (Coulier, 2018) [11], a carotid–anterior cerebral artery anastomosis with an infraoptic ACA course (Sanchez van Kammen *et al*., 2023; Yurt *et al*., 2008) [42, 55], and dual fenestration of the A1 segment combined with an azygos A2 configuration. These case reports, although individually rare, consistently emphasized the co-occurrence of unusual CoW anatomy with aneurysm formation or altered hemodynamics in the same arterial territory.

3. Associations with Cerebrovascular Risk and Stroke Patterns

A substantial subset of the included primary studies examined the relationship between CoW configuration and ischemic cerebrovascular events. A case-control study using transcranial color-coded duplex ultrasonography found that a nonfunctional anterior collateral pathway was present in 33% of ischemic stroke patients compared with only 6% of controls, corresponding to an odds ratio of 7.33 for stroke among patients with collateral-deficient anterior circulation (Silva *et al*., 2017) [45]. Similarly, multidetector CT angiography studies of patients undergoing carotid endarterectomy demonstrated a significantly higher prevalence of CoW variants (97%) and a compromised collateral network (81%) compared with controls, with internal carotid artery stenosis emerging as an independent predictor of CoW morphology (Qiu *et al*., 2022) [38].

Beyond binary presence/absence of stroke, several primary studies linked CoW configuration to stroke topography and severity. Casas-Vara *et al*. (2011) [9] reported a correlation between the structural integrity of the CoW and the severity of initial noncardiac cerebral infarction, while a systematic synthesis of primary outcome studies found that patients with a fully developed contralateral A1 segment and anterior communicating artery achieved more favorable outcomes following distal internal carotid artery occlusion, and that clinical outcomes were significantly better when only a single arterial territory, rather than two or more, was affected (Tandel *et al*., 2022) [47]. A case report further illustrated how CoW asymmetry can produce an atypical stroke presentation — bilateral artery-to-artery embolic infarction masquerading as a cervical spinal cord lesion following trauma — highlighting the diagnostic relevance of CoW variation beyond purely statistical associations (Brownlee *et al*., 2006) [8].

In the posterior circulation, primary research has additionally examined the interaction between vertebral artery hypoplasia and fetal-type posterior CoW configuration. A recent retrospective study found that the fetal-type configuration appeared protective in individuals with concurrent vertebral artery hypoplasia but was associated with increased ischemic vulnerability among individuals with otherwise normal vertebral arteries, indicating that the clinical significance of a given CoW variant cannot be interpreted in isolation from co-existing vascular anatomy (Ranade *et al*., 2020) [40].

4. Associations with Intracranial Aneurysm Formation

The relationship between CoW variation and intracranial aneurysm development was the most extensively documented theme among the included primary research and case studies. Foundational work by Kayembe *et al*. (1984) [26] established a significant correlation between asymmetric A1 segments and AComA aneurysms, and between asymmetric posterior communicating arteries and internal carotid artery–PComA junction aneurysms, in a comparative case series of 44 aneurysmal circles. This early hemodynamic hypothesis — that variant anatomy elevates wall shear stress at specific arterial junctions — has since been substantiated by larger contemporary cohorts.

A large observational case-control study using time-of-flight MRA in 1,021 aneurysm patients and 1,052 controls confirmed that CoW arterial diameters, anatomical variants, and bifurcation angles were significantly associated with both the presence and the specific location of intracranial aneurysms (Groenheide *et al*., 2026) [18]. A systematic synthesis of primary studies similarly concluded that hypoplastic or aplastic A1 segments and fetal-type posterior cerebral arteries were commonly observed in patients with AComA and PComA aneurysms, respectively, although the evidence linking these variants specifically to aneurysm rupture (as opposed to formation) remained less consistent across studies (Zhang *et al*., 2023) [57].

Family-based primary research has extended this evidence toward a potential genetic contribution: in two independent cohorts of families with intracranial aneurysms, incomplete posterior communicating artery configuration showed significantly higher concordance within families than between unrelated families, suggesting heritability of this specific CoW variant (Merckel *et al*., 2018) [33]. Complementary genetic association research identified a moyamoya-related RNF213 gene variant as being linked to specific CoW configurations in patients with cerebrovascular disease, further supporting a biological, rather than purely mechanical, contribution to variant CoW anatomy (Eto *et al*., 2021) [16]. Newer primary work has also extended the anatomical-hemodynamic hypothesis beyond the classic AComA/PComA sites to middle cerebral artery aneurysms, reporting that A1 segment variation independently altered blood flow distribution and shifted the site of hemodynamic impact along the parent vessel (Yang *et al*., 2025) [54].

Individually, rare-variant case reports reinforced this pattern: a duplicated AComA was documented alongside localized atherosclerosis affecting collateral flow capacity (Tritsch *et al*., 2024) [49], and an infraoptic carotid–ACA anastomosis was associated with a ruptured AComA aneurysm that required careful preoperative angiographic characterization prior to successful surgical clipping (Yurt *et al*., 2008) [55].

5. Implications for Neurosurgical and Endovascular Planning

Multiple primary studies and case reports emphasized that awareness of CoW variant anatomy directly informs neurosurgical decision-making. Ayre *et al*. (2022) [4] proposed a standardized classification and coding system explicitly intended to reduce the risk of surgical misinterpretation during aneurysm clipping, endovascular coiling, and internal carotid artery ligation, noting that variation — particularly hypoplasia and duplication — may affect surgical approach, aneurysm exposure, and the accuracy of clip or coil placement. Cadaveric case series from Indian and South African institutions similarly concluded that preoperative MR or CT angiographic evaluation is strongly advisable for any patient undergoing neurovascular intervention, given the high population prevalence of non-classical configurations (Shah *et al*., 2019; Rai *et al*., 2018) [39, 43].

Simulation-based primary research has translated these anatomical findings into surgical training tools: additive-manufactured, anatomically accurate CoW aneurysm simulators have been developed and validated to prepare neurosurgical trainees for the technical demands of aneurysm clipping in the context of variant anatomy, including scenarios simulating intraoperative aneurysm leakage (Domanasiewicz & Guze, 2025) [15]. Collectively, the included evidence supports the position that systematic, standardized preoperative characterization of CoW anatomy — rather than reliance on the assumption of a classic, symmetrical configuration — should be considered a routine component of neurovascular surgical planning.

6. Scoping Overview of Included Primary Studies and Case Studies

Table 2 presents a scoping summary of representative case studies and primary research articles included in this review, selected to illustrate the breadth of study designs, populations, and clinical themes synthesized above. Full citation details for all included and cited sources appear in the reference list.

Table 2: Scoping Summary of Representative Case Studies and Primary Research on Circle of Willis Anatomical Variation

Author (Year)	DOI	Title	Note (Relevance)
De Silva *et al*. (2009) [13]	10.4103/0972-2327.56314	Prevalence of typical circle of Willis and the variation in the anterior communicating artery: A study of a Sri Lankan population	Cadaveric primary study (n=225); establishes baseline hypoplasia and AComA variant rates relevant to regional comparison.
Jones *et al*. (2021) [23]	10.1002/ca.23662	Anatomical variations of the circle of Willis and their prevalence, with a focus on the posterior communicating artery: A literature review and meta-analysis	Pooled prevalence estimate (68.22%) used as the review's principal quantitative benchmark for overall variation rate.
Ayre *et al*. (2022) [4]	10.1111/joa.13616	A new classification system for the anatomical variations of the human circle of Willis: A systematic review	Proposes a standardized coding classification; directly informs neurosurgical planning and reporting terminology.
Krabbe-Hartkamp *et al*. (1998) [29]	10.1148/radiology.207.1.9530305	Circle of Willis: Morphologic variation on three-dimensional time-of-flight MR angiograms	Foundational large-sample (n=1,004) MRA primary study defining classic vs. incomplete configurations.
Kayembe *et al*. (1984) [26]	10.1161/01.STR.15.5.846	Cerebral aneurysms and variations in the circle of Willis	Landmark case-control primary study linking A1/AComA asymmetry to aneurysm formation.
Silva *et al*. (2017) [45] / Case-control	PMID 12865604	Absent collateral function of the circle of Willis as risk factor for ischemic stroke	Case-control TCCD study showing nonfunctional collateral pathways increase stroke risk (OR 7.33).
Brownlee *et al*. (2006) [8]	10.1186/1752-1947-1-45	Circle of Willis variation in a complex stroke presentation: A case report	Case report illustrating atypical stroke presentation (pseudo-cervical cord lesion) from CoW asymmetry.
Merckel *et al*. (2018) [33]	10.1371/journal.pone.0191493	Heritability of circle of Willis variations in families with intracranial aneurysms	Family-based cohort study suggesting genetic heritability of PComA incompleteness relevant to risk stratification.

Zhang *et al*. (2023) [57]	10.3389/fneur.2023.1091361	Anatomical variations in the circle of Willis and the formation and rupture of intracranial aneurysms: A systematic review and meta-analysis	Meta-analysis quantifying hypoplastic A1/fetal-PCA association with AComA/PComA aneurysms.
Groenheide *et al*. (2026) [18]	10.3174/ajnr. A 9428	Anatomical variations of the circle of Willis and their association with intracranial aneurysm presence and location	Large case-control MRA cohort (n=2,073) confirming CoW variant-aneurysm location relationship.
Rai *et al*. (2018) [39]	N/A (WNS)	Morphologic variations in the circle of Willis as a risk factor for aneurysm rupture in the anterior and posterior communicating arteries	Primary case series correlating variant morphology with rupture likelihood at AComA/PComA sites.
Yang *et al*. (2025) [54]	PMC11936263	Association of middle cerebral artery aneurysms and variation of the A1 segment	Primary imaging study extending CoW-aneurysm hemodynamic hypothesis to MCA aneurysms.
Tritsch *et al*. (2024) [49]	10.7759/cureus.53321	Examining atherosclerosis patterns in the circle of Willis: A case study of duplicated anterior communicating artery	Case study of a rare AComA duplication with coexisting atherosclerosis affecting collateral capacity.
Yurt *et al*. (2008) [55]	10.4137/CCRep.S918	A rare embryologic variation: Anterior communicating artery aneurysm associated with carotid-anterior cerebral artery anastomosis	Rare-variant case report with direct surgical/clipping decision-making implications.
Coulier (2018) [11]	10.5334/jbsr.1502	Duplication of the posterior cerebral artery (PCA) or “true fetal PCA”: An extremely rare variant	Case report of an exceedingly rare posterior variant discovered incidentally during TIA workup.
Ghaffari *et al*. (2024) [17]	10.7759/cureus.69528	Morphometric and clinical analysis of the azygos anterior cerebral artery: Insights from a cadaveric case report study	Cadaveric case report quantifying azygos ACA incidence (1.1%) and its bilateral infarction risk.
Sanchez van Kammen *et al*. (2023)	10.1016/j.inat.2023.101740	Left anterior cerebral artery arising from a right internal carotid artery: A rare case of carotid-ACA anastomosis	Rare embryological anomaly case report with fenestration; relevant to preoperative vascular mapping.
Xu *et al*. (2020)	10.1155/2020/3067679	MRA study on variation of the circle of Willis in healthy Chinese male adults	Large primary MRA cohort (n>1,000) establishing sex- and ethnicity-specific variant frequencies.
Li *et al*. (2011)	10.1016/j.jocn.2010.07.137	A multidetector CT angiography study of variations in the circle of Willis in a Chinese population	Primary CTA study proposing 1 mm hypoplasia threshold widely adopted in later literature.
Klimek-Piotrowska *et al*. (2016) [28]	10.5603/FM. a2015.0134	Configurations of the circle of Willis: A computed tomography angiography-based study on a Polish population	Population-specific CTA primary study used for cross-ethnic comparison of complete-circle prevalence.
Iqbal (2013) [21]	10.7860/JCDR/2013/6580.3563	A comprehensive study of the anatomical variations of the circle of Willis in adult human brains	Cadaveric dissection primary study cataloguing multiple co-occurring anterior and posterior variants.
Gunnal *et al*. (2014) [19]	10.1155/2014/687281	Anatomical variations of the circulus arteriosus in cadaveric human brains	Widely cited cadaveric case series informing classification of hypoplasia and duplication patterns.
Qiu *et al*. (2022) [38]	10.1007/s00330-021-08095-5	Multidetector CT angiography of the circle of Willis: Association of its variants with carotid artery disease and brain ischemia	Case-control CTA study linking CoW compromise to ischemia severity in carotid endarterectomy candidates.
Berghout *et al*. (2023) [6]	N/A (J Neurol)	Variations in intracranial arterial anatomy of the circle of Willis and their association with arteriosclerosis in patients with ischemic cerebrovascular disease	Primary cohort study connecting arteriosclerotic burden to incomplete CoW configuration.
Ranade *et al*. (2020 [40]/2026)	N/A (Front Neurol)	Interaction between vertebral artery hypoplasia and circle of Willis variants in posterior circulation stroke and TIA	Retrospective primary study on fetal-type PCA interacting with vertebral hypoplasia in posterior strokes.
Eto *et al*. (2021) [16]	10.3389/fnagi.2021.681743	RNF213 p. R4810K variant determines anatomical variations of the circle of Willis in cerebrovascular disease	Genetic association primary study linking a moyamoya-related variant to CoW configuration.
Kirtiraj & Deopujari (2025) [27]	10.1186/s12883-025-04082-y	Association of circle of Willis variants with stroke and aneurysm: Insights from a tertiary hospital in Ethiopia	Cross-sectional CTA primary study from an underrepresented African cohort correlating variants with disease.
Shah *et al*. (2019) [43] / Munshi *et al*. (2025)	N/A (EJCM)	A cross-sectional study on the variations of the circle of Willis in human cadavers and its clinical significance	Cadaveric case series emphasizing pedagogical and preoperative planning value for neurosurgeons.
Prasad *et al*. (2025) [37]	10.1016/j.tria.2025.100365	Circle of Willis variations and features in an American Midwestern cadaver population	Recent North American cadaveric primary study reporting anterior (84%) vs. posterior (72%) variant rates.
Poudel *et al*. (2025) [36]	N/A (JNHRC)	Prevalence and patterns of circle of Willis variants in a civil service hospital: A	Recent high-resolution 3T MRA primary study from Nepal expanding South Asian

		retrospective cross-sectional study using 3T MRA	regional data.
Casas-Vara *et al*. (2011) [9]	N/A (JSCVD)	Correlation between the integrity of the circle of Willis and the severity of initial noncardiac cerebral infarction and clinical prognosis	Primary clinical study linking CoW integrity to infarct severity and short-term prognosis.
Tandel *et al*. (2022) [47]	10.3390/jcm11247482	Circle of Willis configuration and thrombus localization impact on ischemic stroke patient outcomes: A systematic review	Synthesizes primary outcome studies on how CoW completeness affects thrombolysis/thrombectomy results.

Note: DOI entries marked "N/A" indicate that a Digital Object Identifier was not available in the source database at the time of review; the full bibliographic citation is provided in the reference list.

Discussion

This scoping review mapped 48 case studies and primary research articles published between 2000 and 2026 addressing anatomical variation of the Circle of Willis and its implications for cerebrovascular risk, stroke patterning, and neurosurgical planning. Three principal observations emerge from this synthesis. First, CoW variation is the anatomical norm rather than the exception, with complete configurations reported in well under half of most sampled populations, and with substantial variability in reported prevalence attributable to differences in imaging modality, hypoplasia thresholds, and population ethnicity (Jones *et al*., 2021; Berghout *et al*., 2023) [6, 23]. Second, the accumulated primary evidence consistently, though not universally, supports a mechanistic link between incomplete or asymmetric CoW segments and both ischemic stroke vulnerability and intracranial aneurysm formation, mediated primarily through altered collateral capacity and localized hemodynamic stress (Silva *et al*., 2017; Kayembe *et al*., 1984; Zhang *et al*., 2023) [26, 45, 57]. Third, this anatomical variability carries direct and actionable implications for neurosurgical and endovascular practice, motivating calls for standardized classification systems and routine preoperative angiographic characterization (Ayre *et al*., 2022) [4].

The population-dependent nature of CoW prevalence estimates observed across the included studies — ranging from roughly 16% to nearly 70% for a complete configuration — is a recurring source of interpretive difficulty in this literature. This variability likely reflects genuine ethnic and geographic differences in vascular anatomy, as suggested by comparative cadaveric studies (De Silva *et al*., 2009) [13], but is compounded by methodological heterogeneity, including inconsistent hypoplasia diameter thresholds (ranging from 0.5 mm to 1 mm across studies) and differences between cadaveric dissection and *in vivo* angiographic detection sensitivity (Prasad *et al*., 2025) [37]. Future primary research would benefit from harmonized diagnostic criteria to permit more direct cross-population comparison.

The evidence linking CoW variation to intracranial aneurysm formation was both the most abundant and the most mechanistically coherent theme identified in this review, spanning classic case-control comparisons (Kayembe *et al*., 1984) [26], large modern cohort studies (Groenheide *et al*., 2026) [18], family-based heritability research (Merckel *et al*., 2018) [33], and genetic association studies (Eto *et al*., 2021) [16]. By contrast, the relationship between CoW variation and aneurysm rupture, as opposed to formation, remained less consistently supported, suggesting that variant anatomy may function primarily as a predisposing structural factor rather than a direct trigger for rupture (Zhang *et al*., 2023) [57]. This distinction has practical relevance for clinical counseling, as the presence of a variant CoW configuration alone should not be over-interpreted as an imminent rupture risk factor without corroborating aneurysm-specific features.

Findings regarding stroke pattern and severity similarly reinforce the clinical utility of CoW characterization, particularly in the context of large-vessel occlusive disease, carotid stenosis, and thrombectomy candidacy (Tandel *et al*., 2022; Casas-Vara *et al*., 2011) [9, 47]. The illustrative case report of a bilateral embolic stroke masquerading as a cervical cord lesion (Brownlee *et al*., 2006) [8] underscores that CoW variation can shape not only outcome severity but also diagnostic reasoning at the bedside, reinforcing the pedagogical value emphasized by several of the included cadaveric case series (Shah *et al*., 2019) [43].

From a translational perspective, this review supports the continued development and adoption of standardized CoW classification systems (Ayre *et al*., 2022) [4] and reinforces the practical recommendation, echoed across multiple primary studies, that preoperative MR or CT angiographic mapping of CoW anatomy be incorporated into routine planning for aneurysm clipping, coiling, bypass, and carotid revascularization procedures. Simulation-based training incorporating anatomically variant CoW models further represents a promising avenue for preparing neurosurgical trainees for the technical variability they are statistically likely to encounter in practice (Domanasiewicz & Guze, 2025) [15].

1. Limitations

Several limitations should be considered when interpreting this review. As a scoping review, no formal quality appraisal or risk-of-bias assessment was performed on individual included studies, consistent with PRISMA-ScR methodology, meaning that the strength of individual associations should be interpreted cautiously. The restriction to English-language publications may have excluded relevant primary research published in other languages, particularly from regions with substantial anatomical variation data. Additionally, the heterogeneity in hypoplasia thresholds and classification systems across included studies precluded formal quantitative pooling, limiting this review to a narrative and descriptive synthesis.

2. Implications for Future Research

Future primary research would benefit from three developments identified through this synthesis: adoption of a single, widely endorsed CoW classification and hypoplasia-threshold system to enable cross-study comparability; larger prospective cohorts examining the relationship between specific CoW variants and aneurysm rupture (rather than formation alone); and expanded case-based and cohort data from underrepresented populations, including Southeast Asian cohorts, to clarify the extent to which the anatomical and clinical patterns summarized here generalize across ethnic groups.

Conclusion

Anatomical variation of the Circle of Willis is common, heterogeneous across populations, and clinically consequential. The primary literature and case studies synthesized in this scoping review consistently indicate that incomplete or asymmetric CoW configurations compromise collateral capacity, influence stroke topography and severity, and are mechanistically associated with intracranial aneurysm formation at characteristic arterial junctions. These findings collectively support the routine incorporation of standardized preoperative CoW characterization into cerebrovascular risk assessment, stroke management, and neurosurgical or endovascular planning, and highlight the need for harmonized classification systems and expanded population-specific research to strengthen this evidence base.

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