Diagnostic of Carotid Stenosis: Systematic Review with ☸SAIMSARA.

Abstract: The aim of this paper is to systematically review and synthesize the diagnostic methodologies for carotid stenosis based on a structured extraction summary. The review utilises 187 studies with 62117 total participants (naïve ΣN). Duplex ultrasound (DUS) exhibits a median diagnostic accuracy of 83% (ranging from 66% to 94%) for carotid artery stenosis. This broad range in reported accuracy highlights the need for continued refinement and standardization in diagnostic practices. The heterogeneity of study designs and inconsistent reporting of diagnostic metrics represent the most significant limitation to synthesizing a unified understanding. Future efforts should focus on establishing standardized DUS protocols and rigorously validating novel biomarkers and advanced imaging techniques in large, prospective studies to improve diagnostic precision and patient outcomes.

Keywords: Carotid Stenosis; Diagnosis; Diagnostic Imaging; Biomarkers; Carotid Ultrasound; Magnetic Resonance Imaging

Review Stats

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- Scope: All fields
- Keyword Gate: Fuzzy (≥60% of required terms, minimum 2 terms matched in title/abstract)
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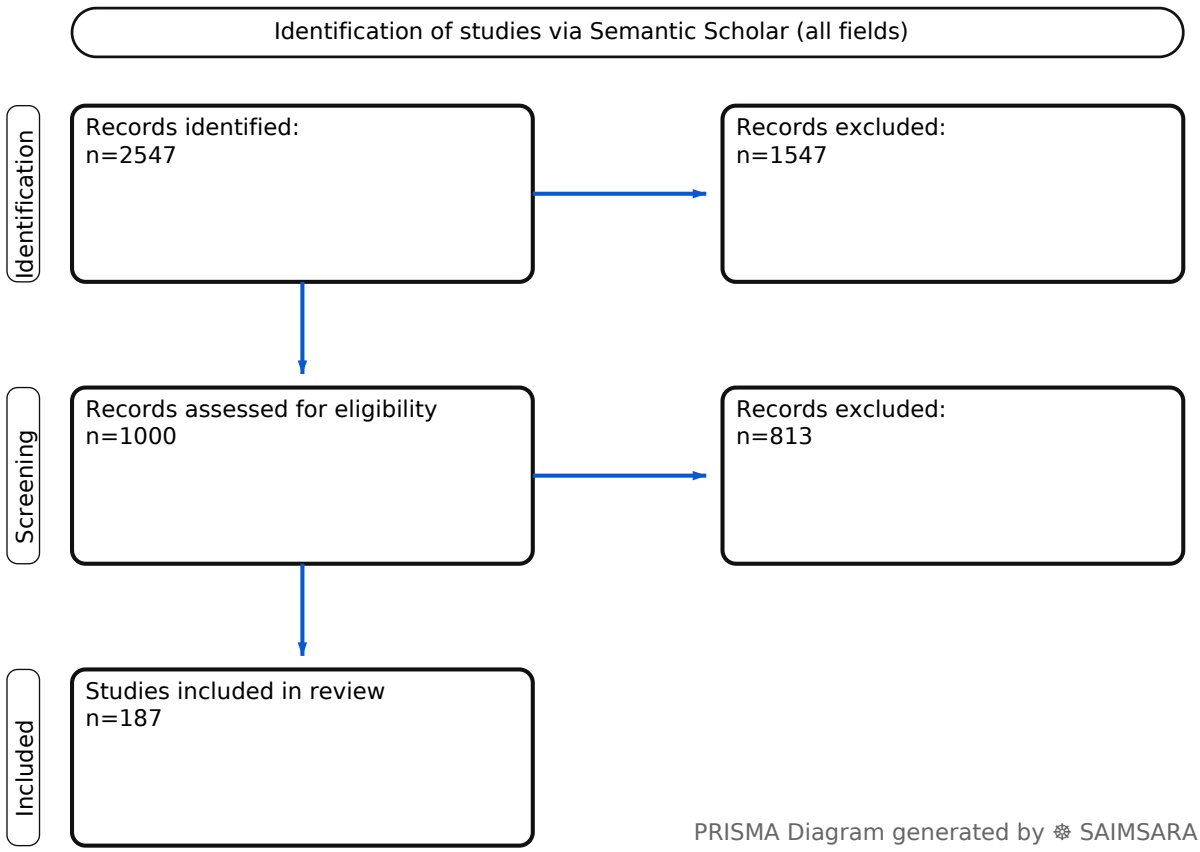
- Downloaded Abstracts/Papers: 1000
- Included original Abstracts/Papers: 187
- Total study participants (naïve ΣN): 62117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Records excluded:
n=1547
Screening
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Records excluded:
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Included
Studies included in review
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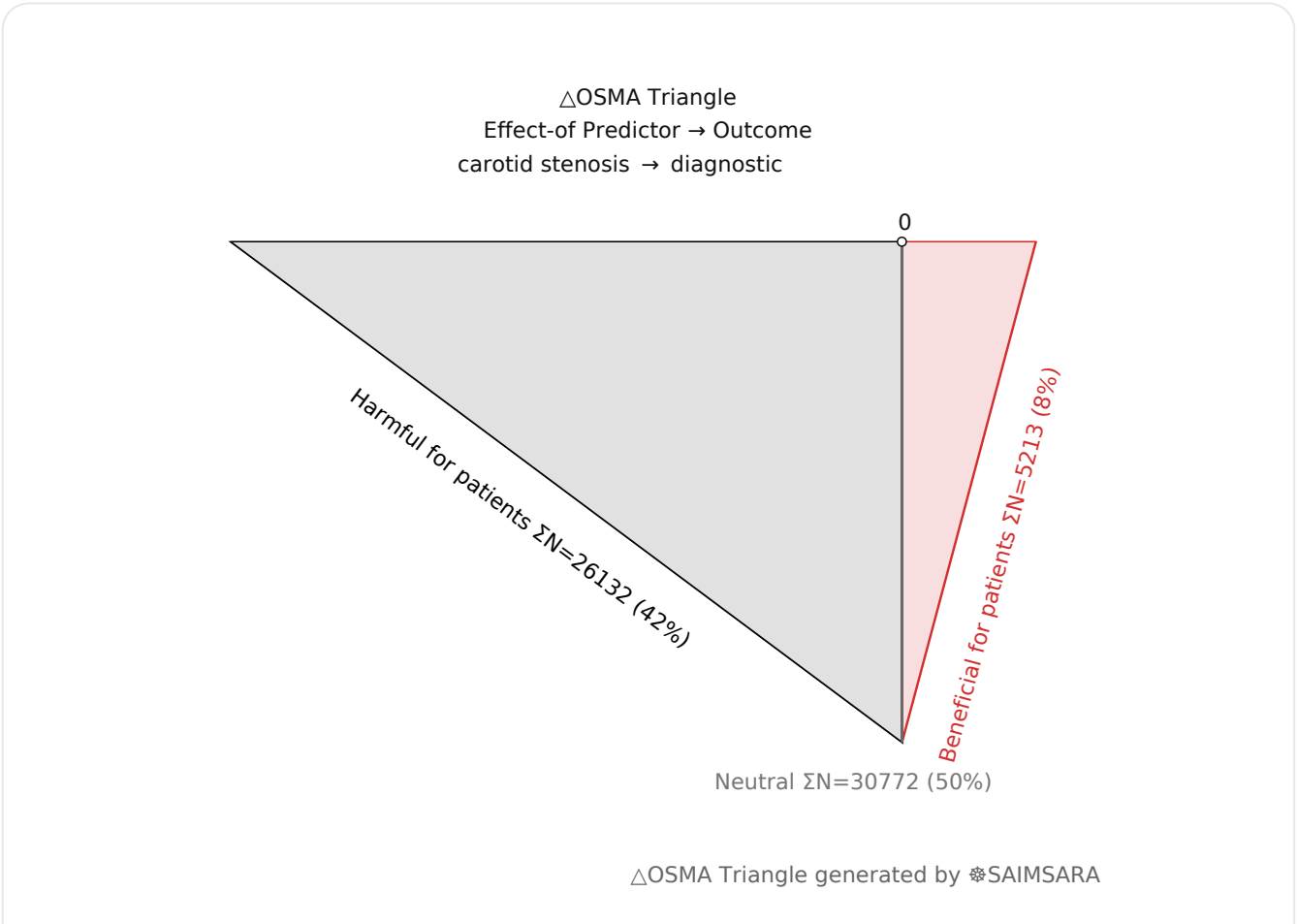
PRISMA Diagram generated by ☸ SAIMSARA


△OSMA Triangle
Effect-of Predictor → Outcome
carotid stenosis → diagnostic
0
Harmful for patients ΣN=26132 (42%)
Beneficial for patients ΣN=5213 (8%)
Neutral ΣN=30772 (50%)
△OSMA Triangle generated by ☸SAIMSARA

Outcome-Sentiment Meta-Analysis (OSMA): *(LLM-only)*

Frame: Effect-of Predictor → Outcome • *Source*: Semantic Scholar

Outcome: diagnostic Typical timepoints: 3-day, 2-day. Reported metrics: %, CI, p.

Common endpoints: Common endpoints: complications, occlusion, functional.

Predictor: carotid stenosis — exposure/predictor. Doses/units seen: 81 mg, 1.2 mg. Typical comparator: controls, the control group and can, control, angiography….

- **1) Beneficial for patients** — diagnostic with carotid stenosis — [127], [128], [129], [130], [131], [132], [133], [134], [135], [138], [139], [140], [141], [142], [143], [145], [146], [148], [149], [150], [154], [158], [160], [161], [163], [169], [171], [173], [175] — ΣN=5213
- **2) Harmful for patients** — diagnostic with carotid stenosis — [165], [166], [179], [184], [185] — ΣN=26132
- **3) No clear effect** — diagnostic with carotid stenosis — [1], [2], [3], [4], [5], [6], [7], [8], [9], [10], [11], [12], [13], [14], [15], [16], [17], [18], [19], [20], [21], [22], [23], [24], [25], [26], [27], [28], [29], [30], [31], [32], [33], [34], [35], [36], [37], [38], [39], [40], [41], [42], [43], [44], [45], [46], [47], [48], [49], [50], [51], [52], [53], [54], [55], [56], [57], [58], [59], [60], [61], [62], [63], [64], [65], [66], [67], [68], [69], [70], [71], [72], [73], [74], [75], [76], [77], [78], [79], [80], [81], [82], [83], [84], [85], [86], [87], [88], [89], [90], [91], [92], [93], [94], [95], [96], [97], [98], [99], [100], [101], [102], [103], [104], [105], [106], [107], [108], [109], [110], [111], [112], [113], [114], [115], [116], [117], [118], [119], [120], [121], [122], [123], [124], [125], [126], [136], [137], [144], [147], [151], [152], [153], [155], [156], [157], [159], [162], [164], [167], [168], [170], [172], [174], [176], [177], [178], [180], [181], [182], [183], [186], [187] — ΣN=30772

1) Introduction

Carotid artery stenosis (CAS) is a significant contributor to cerebrovascular events, including acute ischemic stroke (AIS) and transient ischemic attacks (TIAs) [18, 45, 80, 161, 168]. Accurate and timely diagnosis of CAS is crucial for risk stratification and guiding therapeutic interventions to prevent severe neurological sequelae [119]. The diagnostic landscape for CAS is diverse, encompassing a range of imaging modalities, novel biochemical biomarkers, and advanced computational methods. This paper synthesizes current research on diagnostic approaches for carotid stenosis, highlighting their performance, emerging trends, and areas for future investigation.

2) Aim

The aim of this paper is to systematically review and synthesize the diagnostic methodologies for carotid stenosis based on a structured extraction summary.

3) Methods

Systematic review with multilayer AI research agent: keyword normalization, retrieval & structuring, and paper synthesis (see SAIMSARA About section for details).

- **Bias:** Qualitatively inferred from study design fields. The included studies exhibit a predominance of mixed and cohort designs, with a notable number of studies not specifying their design or directionality. Many studies were retrospective, and sample sizes varied significantly, ranging from single case reports to large population cohorts. The absence of specified population or setting in many extractions limits the assessment of generalizability and potential selection bias.

4) Results

4.1 Study characteristics:

The reviewed literature comprises a variety of study designs, predominantly mixed (combining retrospective and prospective elements or different methodologies), cohort, and cross-sectional studies. Populations investigated include patients with symptomatic or asymptomatic carotid artery stenosis (CAS), healthy controls, individuals with acute ischemic stroke (AIS) or TIA, and those with specific risk factors such as diabetes or hypercholesterolemia. Follow-up periods, when specified, ranged from 90 days to 7 years, though many studies did not report follow-up.

4.2 Main numerical result aligned to the query:

Diagnostic accuracy for duplex ultrasound (DUS) in detecting carotid artery stenosis varied across studies, with a median accuracy of 83% [8, 83] and a range from 66% [83] to 94% [108]. For specific stenosis ranges, DUS showed an accuracy of 69% for 50-94% stenosis and 84% for 70-94% stenosis of the internal carotid artery (ICA) [14]. Other reported DUS accuracies included 74.5% for peak systolic velocity (PSV) ≥ 125 cm/sec, 85.2% for PSV ≥ 180 cm/sec, and 87.4% for ICA/CCA PSV ratio ≥ 2.0 for ≥50% ICA stenosis [8].

4.3 Topic synthesis:

- **MicroRNA (miRNA) Biomarkers:** Multiple miRNAs demonstrate high diagnostic accuracy for CAS and predictive value for cerebral ischemic events (CIEs). Serum miR-125a showed an AUC of 0.931 for distinguishing CAS patients [3], miR-206 had an AUC of 0.939 (sensitivity 86.70%, specificity 86.14%) for asymptomatic CAS [9], and miR-455-5p achieved an AUC of

0.927 for early diagnosis of CAS [34]. Other promising miRNAs include miR-486-5p [6], miR-637 [7], miR-9-5p [11], miR-19a-3p [13], miR-186-5p [15], miR-106b-5p [16], miR-92a [17], miR-532-5p [22], miR-361-5p [27], miR-27b [28], miR-28-5p [38], miR-375-3p [40], miR-503-5p [46], miR-483-5p (AUC 0.910) [37], miR-145 and miR-210 [122], and miR-638 (AUC 0.66-0.85) [133].

- **Advanced Imaging Modalities:** Beyond DUS, various imaging techniques offer high diagnostic performance. Contrast-enhanced magnetic resonance angiography (CE MRA) demonstrated pooled sensitivity of 94.3% and specificity of 93.0% for severe carotid stenosis [49], and higher sensitivity and specificity than color Doppler ultrasound (CDUS) for diagnosis of CAS [50]. Computed tomography angiography (CTA) showed high accuracy (69-84%) for 50-94% stenosis [14, 72], and multidetector-row CTA (MDCTA) had 93.75% sensitivity and 98.59% specificity for ulcerated plaques [102]. Three-dimensional (3D) cardiovascular magnetic resonance (CMR) vessel wall imaging (VWI) achieved AUCs of 0.998 for >50% stenosis and 0.999 for >70% stenosis [59].
- **Plaque Vulnerability and Characterization:** Assessing plaque characteristics is critical for risk stratification. Downstream wall shear stress (WSSdown) showed high diagnostic efficacy (AUC 0.96, sensitivity 93.7%, specificity 87.5%) in differentiating vulnerable from stable plaques [12]. Multimodal ultrasound nomograms combining plaque surface morphology, intraplaque neovascularization (IPN), and stenosis degree had an AUC of 0.85 for ischemic vascular event (IVE) risk stratification [31]. Contrast-enhanced ultrasound (CEUS) demonstrated 89.2% sensitivity and 80.0% specificity for vulnerable plaques [57]. A radiomics model incorporating stenosis degree achieved AUCs of 0.959 (training) and 0.942 (testing) for differentiating vulnerable from stable plaques [130].
- **Hemodynamic Parameters and Flow Dynamics:** Hemodynamic measurements provide insights into stenosis severity and cerebral perfusion. The internal carotid artery-cerebral blood flow (ICA-CBF) ratio on PC-MRI was 90% sensitive and 99% specific for near-occlusion, with AUCs of 0.98–0.99 [4]. Distal PSV < 50 cm/s was 63% sensitive and 94% specific for separating near-occlusion from conventional stenosis [140]. The first harmonic ratio (FHR) was significantly higher in patients with intracranial internal carotid artery stenosis (IICAS) and showed superior diagnostic performance for early diagnosis compared to traditional hemodynamic indices [131].
- **Other Blood Biomarkers:** Beyond miRNAs, other circulating markers show diagnostic promise. Combined zinc, chrome, and copper concentrations yielded an AUC of 0.935 (sensitivity 95%, specificity 82.4%) for carotid artery disease [29]. Serum Lp-PLA2 level had an AUC of 0.938 for moderate to severe artery stenosis or occlusion (sensitivity 79.6%, specificity 95.2%) [80]. HCG11 was enriched in CAS patients' serum, serving as a possible biomarker with an AUC of 0.930 [171]. Raised serum RMST levels were found in CAS patients, predicting occurrence and outcomes [5].

- **Artificial Intelligence and Machine Learning:** Computational methods are enhancing diagnostic accuracy. Deep convolutional neural networks achieved peak test metric performance accuracies of 98.37% and 97.26% in classifying sonographic images for carotid stenosis [33]. The RUSBoost algorithm improved performance for early detection of cardiovascular disease with an accuracy of 90.1% [19]. A video-based motion analysis (VMA) system showed excellent diagnostic performance (AUC=0.914, sensitivity 87%, specificity 87%) for screening CAS [127].
- **Risk Factors and Prevalence:** Carotid stenosis is associated with various risk factors and has a notable prevalence in specific populations. The prevalence of CAS ≥ 50% in acute ischemic stroke (AIS) patients was 18.7% [18]. In a rural Chinese population, the overall prevalence of asymptomatic ICA stenosis (AICAS) was 7.6%, increasing with age [148]. Type 2 diabetes mellitus (T2DM) and smoking significantly increased the possibility of carotid stenosis development [36]. Hypertension and hyperlipidemia showed positive correlation with stenosis [86].

5) Discussion

5.1 Principal finding:

The central finding of this review is that duplex ultrasound (DUS) exhibits a median diagnostic accuracy of 83% (ranging from 66% to 94%) for carotid artery stenosis [8, 83, 108], positioning it as a widely utilized, albeit variable, diagnostic tool.

5.2 Clinical implications:

- **Initial Screening Tool:** DUS remains a valuable initial screening tool for carotid stenosis due to its non-invasive nature and generally good diagnostic accuracy [108, 143].
- **Enhanced Diagnostic Criteria:** Refining DUS criteria, such as adjusting PSV thresholds (e.g., ≥180 cm/sec or ICA/CCA PSV ratio ≥ 2.0 for ≥50% stenosis) [8, 23], can improve accuracy and reduce overestimation.
- **Multimodal Imaging for Vulnerability:** For comprehensive risk stratification, particularly for vulnerable plaques, advanced imaging like CEUS, MRI, and CTA should be considered, as they offer superior characterization of plaque morphology and components compared to DUS alone [1, 12, 57, 59].
- **Biomarker Integration:** Emerging miRNA and other blood biomarkers (e.g., miR-125a, Lp-PLA2, HCG11) with high AUCs could complement imaging by identifying high-risk patients or asymptomatic CAS, potentially guiding earlier intervention [3, 80, 171].
- **AI-Assisted Diagnostics:** The integration of AI/machine learning into image analysis holds promise for improving diagnostic performance and efficiency, particularly in classifying

sonographic images and hemodynamic parameters [19, 33, 127].

5.3 Research implications / key gaps:

- **Standardized DUS Criteria:** Further research is needed to establish universally accepted and harmonized duplex ultrasonography criteria for carotid stenosis across different laboratories and populations [51, 65].
- **Validation of Novel Biomarkers:** Large-scale, prospective cohort studies are required to validate the diagnostic and prognostic value of promising miRNA and other blood biomarkers in diverse patient populations [3, 9, 29].
- **Comparative Effectiveness of Imaging:** Head-to-head comparative studies are needed to determine the optimal sequence and combination of imaging modalities (e.g., DUS, CTA, MRA, CEUS) for different stages and clinical presentations of carotid stenosis [53, 64].
- **Plaque Vulnerability Phenotyping:** Research should focus on developing and validating non-invasive methods for comprehensive phenotyping of vulnerable plaques, integrating imaging, hemodynamic, and molecular biomarkers [12, 31, 81].
- **AI Model Generalizability:** Future studies should focus on validating AI-based diagnostic models in larger, more diverse datasets to ensure their generalizability and robustness in real-world clinical settings [33, 127].

5.4 Limitations:

- **Heterogeneous Study Designs** — The variability in study designs (mixed, cohort, cross-sectional) and lack of specified directionality in many studies limit the ability to draw definitive causal conclusions or perform robust meta-analysis.
- **Inconsistent Reporting of Metrics** — Diverse metrics, units, and stenosis thresholds for diagnostic performance (e.g., sensitivity, specificity, accuracy, AUC) hinder direct quantitative comparison across all studies.
- **Limited Population Detail** — Many studies did not specify population characteristics or settings, making it difficult to assess the generalizability of findings to broader patient groups.
- **Varied Gold Standards** — Different reference standards (e.g., angiography, histopathology) were used across studies, which can influence reported diagnostic accuracies.
- **Lack of Long-term Follow-up** — While some studies included follow-up, many did not, particularly for novel biomarkers, limiting the understanding of long-term prognostic value.

5.5 Future directions:

- **Standardized DUS Protocols** — Develop and implement standardized duplex ultrasound protocols and interpretation criteria.
- **Biomarker Prospective Trials** — Conduct large, prospective trials to validate novel miRNA and blood biomarkers.
- **Multimodality Imaging Pathways** — Establish evidence-based clinical pathways for multimodal imaging in carotid stenosis.
- **AI Diagnostic Tool Development** — Develop and validate AI-powered tools for automated plaque characterization and stenosis detection.
- **Clinical Outcome Integration** — Integrate diagnostic findings with long-term clinical outcomes in comprehensive registries.

6) Conclusion

Duplex ultrasound (DUS) exhibits a median diagnostic accuracy of 83% (ranging from 66% to 94%) for carotid artery stenosis [8, 83, 108]. This broad range in reported accuracy highlights the need for continued refinement and standardization in diagnostic practices. The heterogeneity of study designs and inconsistent reporting of diagnostic metrics represent the most significant limitation to synthesizing a unified understanding. Future efforts should focus on establishing standardized DUS protocols and rigorously validating novel biomarkers and advanced imaging techniques in large, prospective studies to improve diagnostic precision and patient outcomes.

References

SAIMSARA Session Index — session.json

Figure 1. Publication-year distribution of included originals

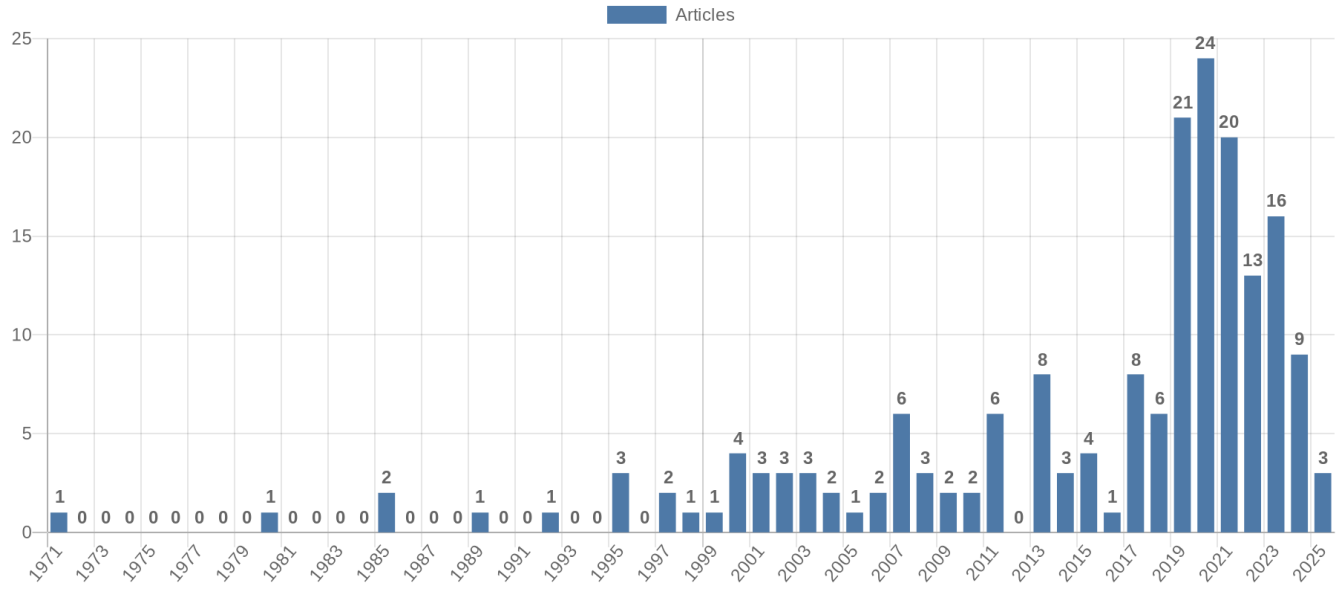


Figure 2. Study-design distribution of included originals

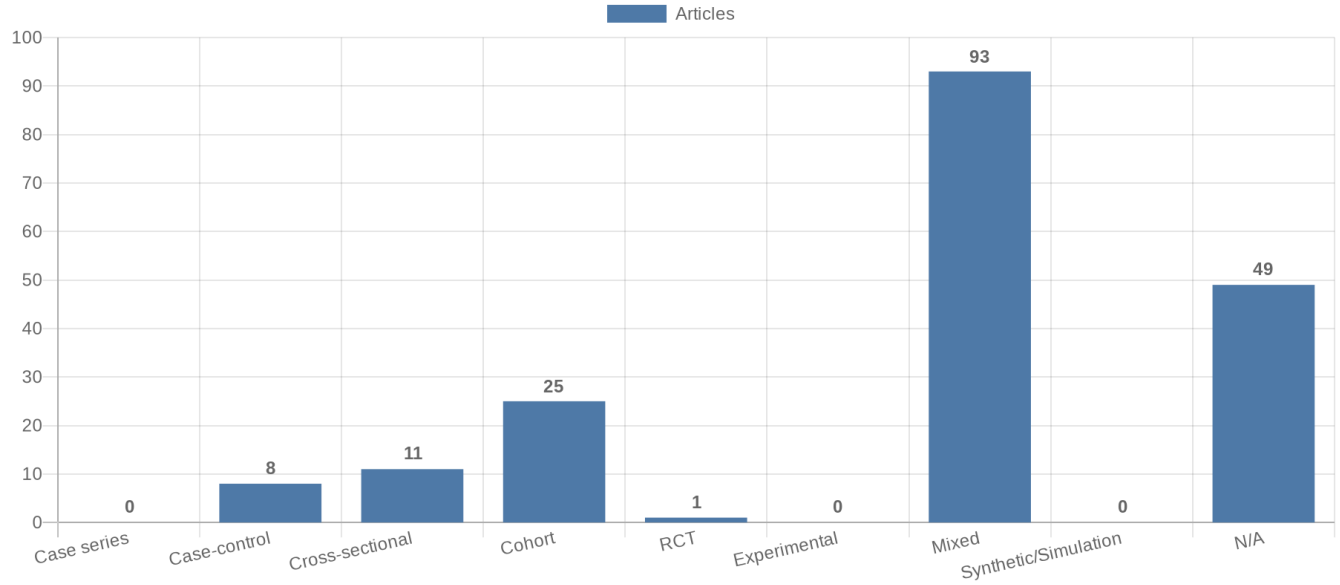


Figure 3. Study-type (directionality) distribution of included originals

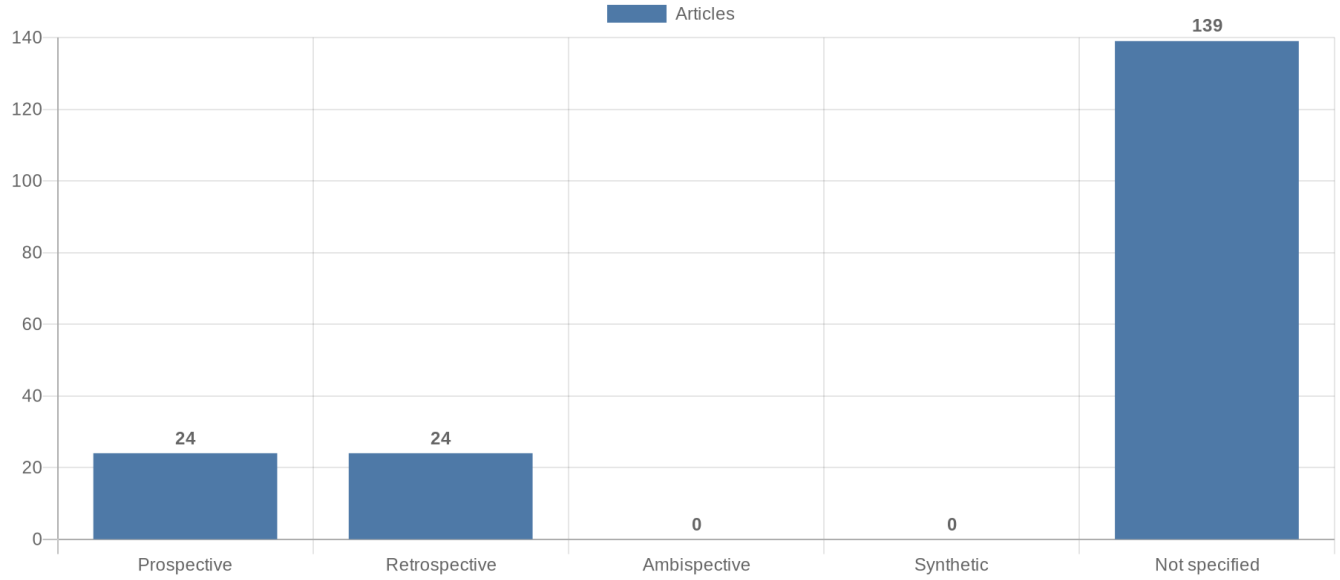


Figure 4. Main extracted research topics

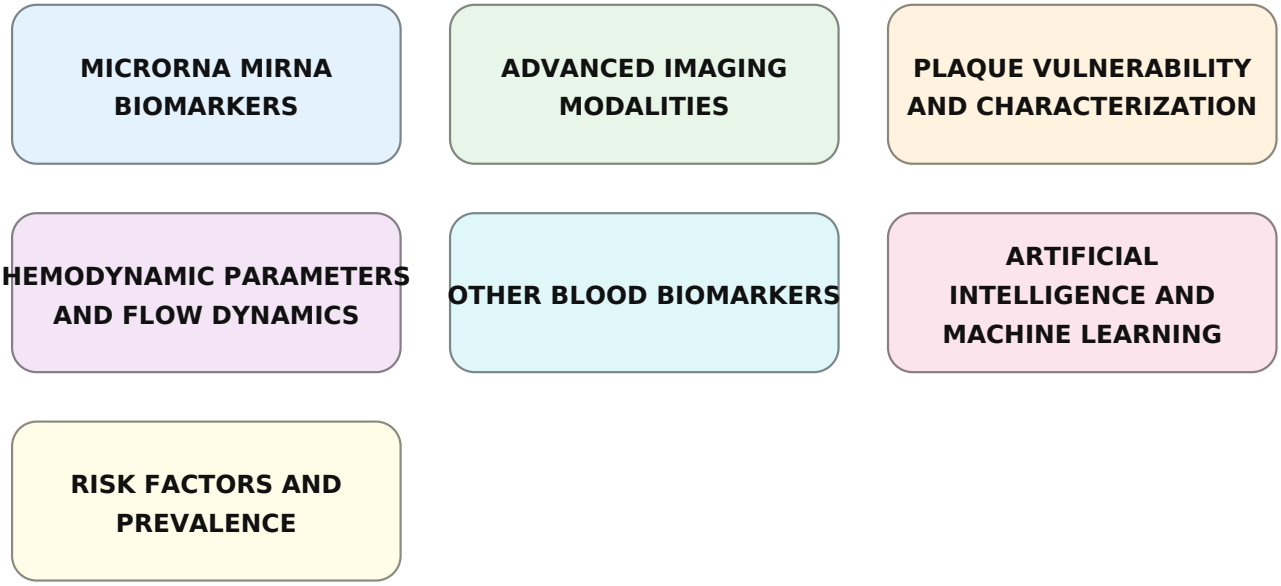


Figure 5. Limitations of current studies (topics)

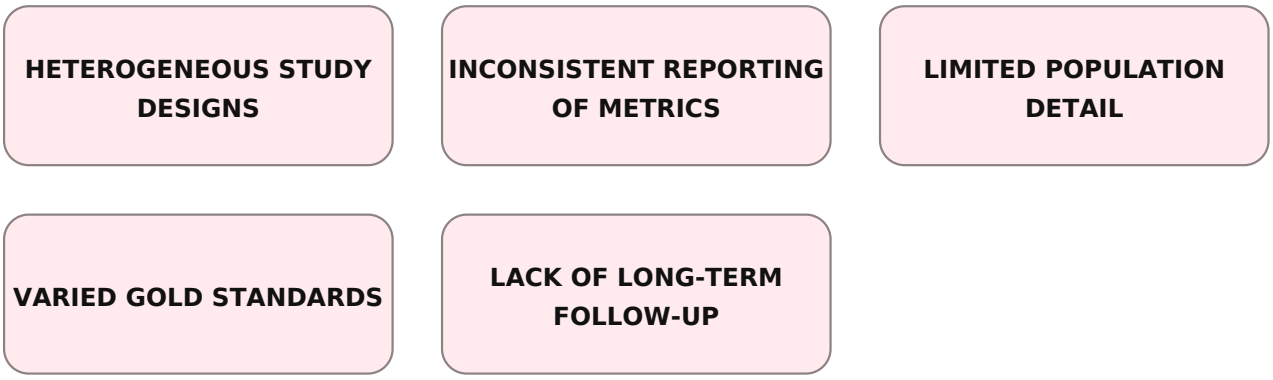


Figure 6. Future research directions (topics)