Carotid Disease and CEA: Systematic Review with ☸SAIMSARA.

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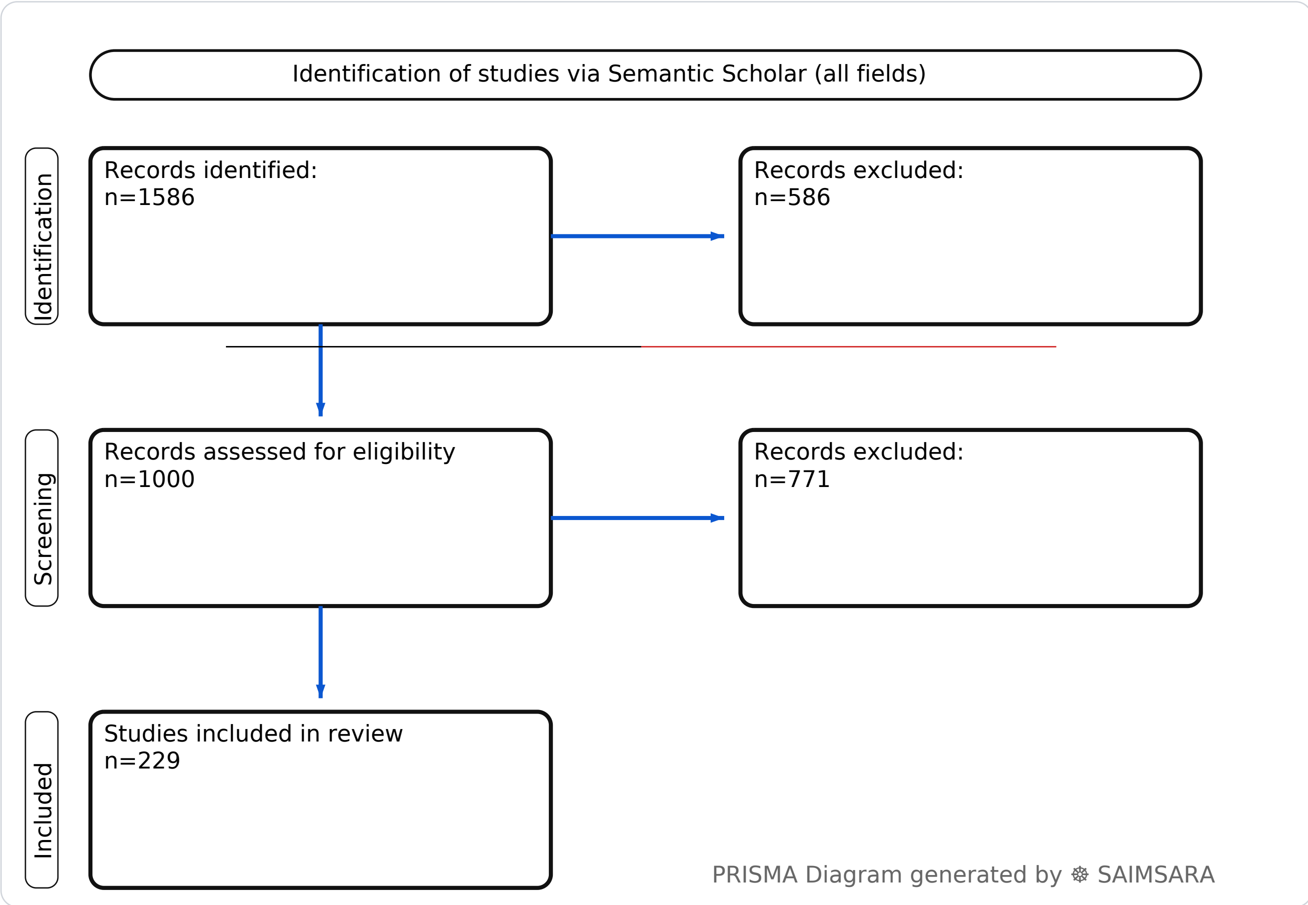
Abstract: The aim of this paper is to systematically review and synthesize the current academic landscape concerning carotid disease and carotid endarterectomy (CEA), focusing on diagnostic advancements, perioperative outcomes, comparative effectiveness of revascularization strategies, and long-term prognostic indicators. The review utilises 229 studies with 253324 total participants (naïve ΣN). The median 30-day stroke or death rate following carotid endarterectomy (CEA) was 1.65%, with a range from 0% to 4.2%, indicating that CEA is a generally safe and effective procedure for stroke prevention. This outcome is broadly generalizable to symptomatic and asymptomatic patients with significant carotid stenosis, though specific comorbidities and patient characteristics influence individual risk. The heterogeneity of study designs and inconsistent outcome reporting most significantly affects certainty in drawing broad comparative conclusions. Clinicians should consider individualized risk profiles, including plaque vulnerability and concomitant cardiovascular disease, when selecting revascularization strategies, and future research should focus on large-scale, standardized comparative trials.

Keywords: Carotid Endarterectomy; Carotid Artery Disease; Carotid Stenosis; Stroke Prevention; Asymptomatic Carotid Disease; Symptomatic Carotid Disease; Carotid Artery Stenting; Vulnerable Plaque; Coronary Artery Disease; Perioperative Complications

Review Stats

- Generated: 2026-02-12 22:48:38 CET
- Plan: Pro (expanded craft tokens; source: Semantic Scholar)
- Source: Semantic Scholar
- Scope: All fields
- Keyword Gate: Fuzzy (≥60% of required terms, minimum 2 terms matched in title/abstract)
- Total Abstracts/Papers: 1586
- Downloaded Abstracts/Papers: 1000
- Included original Abstracts/Papers: 229
- Total study participants (naïve ΣN): 253324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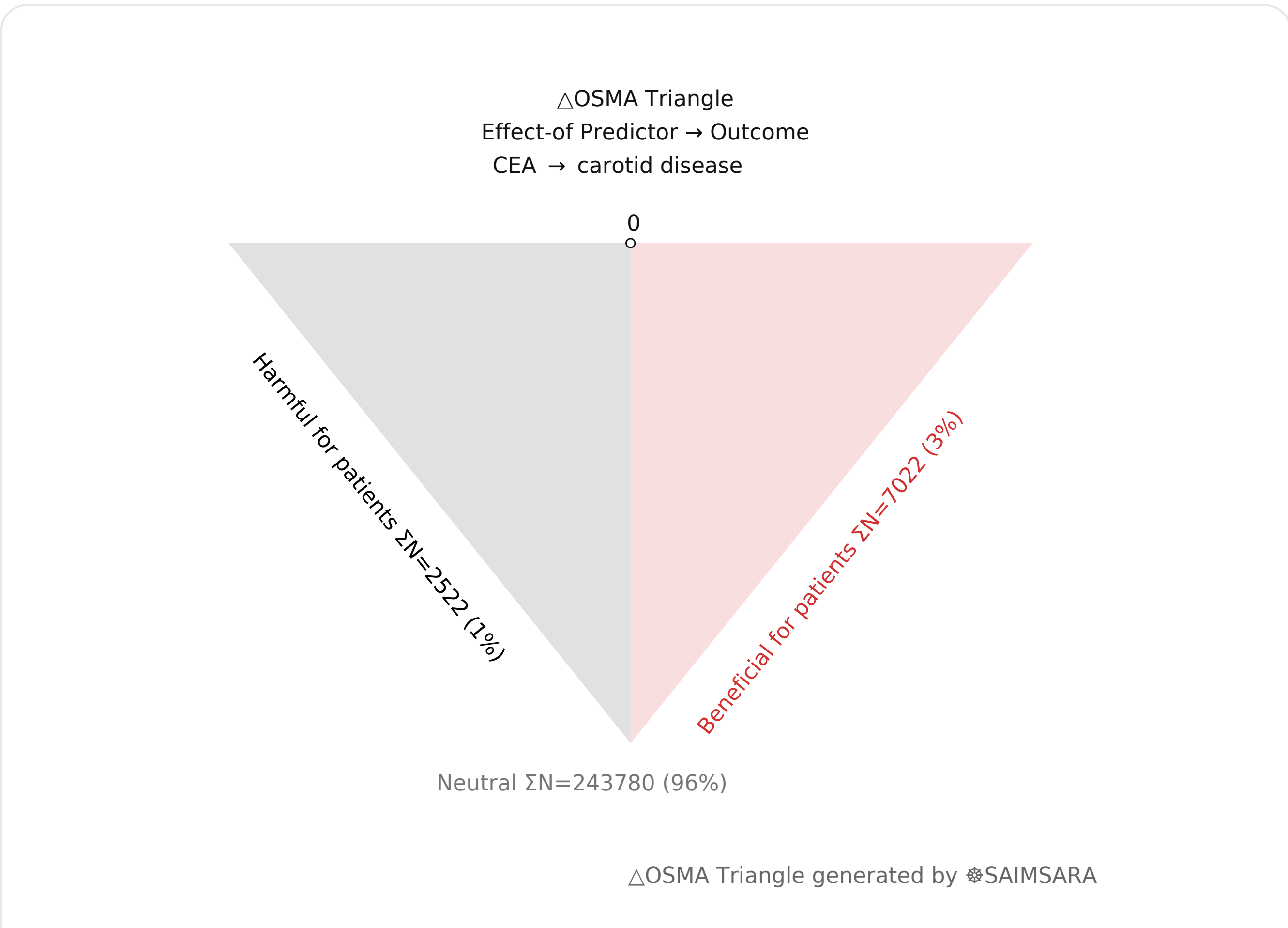
Identification
Records identified:
n=1586
Records excluded:
n=586
Screening
Records assessed for eligibility
n=1000
Records excluded:
n=771
Included
Studies included in review
n=229
PRISMA Diagram generated by ☸ SAIMSARA


△OSMA Triangle
Effect-of Predictor → Outcome
CEA → carotid disease
0
Harmful for patients ΣN=2522 (1%)
Beneficial for patients ΣN=7022 (3%)
Neutral ΣN=243780 (96%)
△OSMA Triangle generated by ☸SAIMSARA

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

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

Outcome: carotid disease Typical timepoints: peri/post-op, 30-day. Reported metrics: %, CI, p.

Common endpoints: Common endpoints: complications, mortality, functional.

Predictor: CEA — procedure/intervention. Routes seen: iv. Typical comparator: cas, cea, cea. cas might be as safe as, best medical therapy….

- **1) Beneficial for patients** — carotid disease with CEA — [51], [109], [187], [199] — ΣN=7022
- **2) Harmful for patients** — carotid disease with CEA — [61], [64], [73], [198] — ΣN=2522
- **3) No clear effect** — carotid disease with CEA — [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], [52], [53], [54], [55], [56], [57], [58], [59], [60], [62], [63], [65], [66], [67], [68], [69], [70], [71], [72], [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], [110], [111], [112], [113], [114], [115], [116], [117], [118], [119], [120], [121], [122], [123], [124], [125], [126], [127], [128], [129], [130], [131], [132], [133], [134], [135], [136], [137], [138], [139], [140], [141], [142], [143], [144], [145], [146], [147], [148], [149], [150], [151], [152], [153], [154], [155], [156], [157], [158], [159], [160], [161], [162], [163], [164], [165], [166], [167], [168], [169], [170], [171], [172], [173], [174], [175], [176], [177], [178], [179], [180], [181], [182], [183], [184], [185], [186], [188], [189], [190], [191], [192], [193], [194], [195], [196], [197], [200], [201], [202], [203], [204], [205], [206], [207], [208], [209], [210], [211], [212], [213], [214], [215], [216], [217], [218], [219], [220], [221], [222], [223], [224], [225], [226], [227], [228], [229] — ΣN=243780

1) Introduction

Carotid artery disease, primarily characterized by atherosclerotic stenosis of the extracranial carotid arteries, represents a significant risk factor for ischemic stroke. Carotid endarterectomy (CEA) is a well-established surgical intervention aimed at preventing stroke by removing atherosclerotic plaque from the carotid artery [12, 31]. The management of carotid disease involves complex considerations, including patient symptomatology, degree of stenosis, presence of vulnerable plaque, and co-existing comorbidities such as coronary artery disease (CAD) [6, 10, 25]. Recent advancements in imaging, artificial intelligence (AI), and alternative revascularization techniques like carotid artery stenting (CAS) and transcarotid artery revascularization (TCAR) have further diversified treatment paradigms, necessitating a comprehensive understanding of their comparative efficacy, safety, and long-term outcomes [2, 15, 55]. This paper synthesizes current evidence on carotid disease and CEA, encompassing diagnostic approaches, perioperative risks, treatment comparisons, and prognostic factors.

2) Aim

The aim of this paper is to systematically review and synthesize the current academic landscape concerning carotid disease and carotid endarterectomy (CEA), focusing on diagnostic advancements, perioperative outcomes, comparative effectiveness of revascularization strategies, and long-term prognostic indicators.

3) Methods

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

- **Bias:** The included studies exhibit a range of designs, from prospective randomized controlled trials (RCTs) [17, 19, 35, 64, 208] and prospective cohort studies [1, 5, 10, 76, 81, 107, 119, 120, 142, 145, 183, 184, 185, 194, 224] to retrospective cohort studies [4, 8, 32, 37, 39, 41, 42, 45, 63, 67, 68, 69, 72, 73, 74, 75, 77, 82, 85, 86, 87, 89, 93, 94, 96, 98, 101, 102, 104, 105, 106, 110, 121, 122, 125, 126, 128, 129, 130, 132, 133, 134, 137, 138, 139, 140, 143, 150, 152, 153, 154, 159, 161, 164, 168, 169, 170, 171, 172, 173, 174, 175, 179, 182, 185, 186, 187, 188, 189, 191, 192, 193, 198, 199, 200, 201, 203, 204, 205, 209, 210, 213, 215, 216, 218, 219, 222, 223, 225, 228, 229], case series [9] and case reports [22, 23, 26, 136, 214], and cross-sectional studies [83, 190]. Many studies are retrospective, which inherently limits the ability to control for confounding variables and establish causality. Reporting heterogeneity in outcomes and patient populations across studies also introduces variability.

4) Results

4.1 Study characteristics:

The evidence base comprises a diverse array of study designs, including prospective and retrospective cohort studies, randomized controlled trials (RCTs), case-control studies, case series, and case reports. Populations frequently include patients undergoing CEA for symptomatic or asymptomatic carotid stenosis, often with concomitant coronary artery disease (CAD) or other multimorbidities. Studies also focus on specific subgroups such as elderly patients, those with vulnerable plaques, or those undergoing alternative revascularization procedures. Follow-up periods vary widely, ranging from immediate perioperative outcomes (30-day) to long-term assessments spanning several years.

4.2 Main numerical result aligned to the query:

The median 30-day stroke or death rate following carotid endarterectomy (CEA) was 1.65%, with a range from 0% to 4.2% [137, 160, 172, 176, 209, 216, 228].

4.3 Topic synthesis:

- **Vulnerable Plaque Identification and AI:** Imaging techniques like duplex ultrasound (DU) and AI-based models show high positive predictive value (PPV) for identifying vulnerable plaque (VP) and >50% stenosis, with AI accuracy increasing from 0.73 to 0.94 in identifying VP [1]. Noninvasive prediction models based on IL-6 and TSHI [43], or multimodal vascular ultrasound parameters and clinical risk factors [211], demonstrate high diagnostic efficacy (AUC 0.959) for VP. Contrast-enhanced ultrasound (CEUS) also shows 86.8% accuracy for vulnerable plaques, correlating with CD147 and MMP-9 [178].
- **Perioperative Complications and Risk Factors:** Perioperative major adverse cardiac events (MACE) and non-MACE rates for CEA range from 15.8% to 18.8% in CAD patients [4], with MACE occurring in 4.3% of patients overall [47]. Preoperative white matter hyperintensities and lacunes are independently associated with postoperative cerebral hyperperfusion (CH) [11], and intraoperative systolic blood pressure drop >44 mmHg is linked to postoperative cerebrovascular accident (POCVA) [13]. Elevated lipoprotein (a) levels are associated with increased 30-day MACE risk (HR 2.05) [77]. Preoperative anxiety (HADS-A score >6) is associated with higher intra- and postoperative neurological events [76].
- **Comparison of Revascularization Strategies (CEA vs CAS vs TCAR):** CEA is generally considered the first-line treatment for symptomatic patients with >50% and asymptomatic patients with >60% carotid stenosis [31]. While some studies show comparable perioperative stroke or death rates between CEA, CAS, and TCAR [71, 152, 172], others indicate CEA may be associated with lower odds of post-procedural stroke compared to CAS (OR 0.17) [8], fewer new acute ischemic brain lesions (14.2% CEA vs 47.6% CAS) [51], and a higher stroke-free survival rate (100% CEA vs 93.5% CAS at 12 months) [91]. Covert strokes are 3.75 times lower after CEA (10%) than CAS (38%) [170].
- **Concomitant Carotid and Coronary Artery Disease (CABG+CEA):** Simultaneous carotid endarterectomy (CEA) and coronary artery bypass grafting (CABG) can be performed with acceptable morbidity and mortality rates [67, 72, 106, 125, 222], though some studies

report higher immediate complications and prolonged ventilation compared to staged procedures [40, 93]. Preoperative coronary revascularization is associated with lower odds of perioperative MACE and non-MACE in CAD patients undergoing CEA [4]. Severe left ventricular (LV) dysfunction is a significant risk factor for perioperative myocardial infarction (MI) during CEA in high-risk CAD patients [10].

- **Cognitive Outcomes and Cerebral Hemodynamics:** CEA can significantly improve cognitive function, cerebral blood flow, energy metabolism, and white matter integrity in patients with carotid artery stenosis (CAS)-induced cognitive impairment [14, 50, 109]. Cerebral hemodynamics are altered by carotid artery disease and improve after CEA [53, 58, 139]. However, preoperative white matter lesions influence brain connectivity [190], and normal BMI in older patients with cardiovascular disease may be a risk factor for postoperative cerebral dysfunction [220].
- **Patient Selection and Risk Stratification:** Age, comorbidities (e.g., CAD, chronic kidney disease, diabetes, heart failure, peripheral artery disease, COPD), and inflammatory biomarkers are crucial for risk stratification [21, 37, 42, 68, 69, 82, 84, 103, 118, 171, 175, 177, 179, 183, 185, 197, 198, 209, 216]. Elderly patients (>80 years) undergoing CEA or CAS have higher mortality but comparable subsequent vascular events to younger patients [41, 133, 134, 188]. Machine learning models (e.g., XGBoost) can accurately predict 30-day outcomes after CEA (AUC 0.91) [47].
- **Surgical Techniques and Anesthesia:** CEA under local anesthesia is safe [27, 89, 99], and regional anesthesia is associated with decreased risk of postoperative pneumonia and reduced need for transfusions compared to general anesthesia [182]. Primary closure and patch angioplasty show equivalent complication rates and restenosis at 5 years in selected CEA cases [57]. Modified eversion technique reduces patchplasty and restenosis [117].
- **Plaque Characteristics and Pathophysiology:** Vulnerable plaque features, including plaque hemorrhage (PH) [75, 121], inflammation (e.g., CCR2 cellular content, enlarged pericarotid lymph nodes, specific ceramides, miR-155, TNK1) [25, 29, 63, 70, 116, 147, 148, 155, 157, 196, 197, 221, 226], and specific molecular signatures (e.g., albumin, CRP, monocyte percentage, CXCL9) [21, 43], are associated with symptomatic disease and adverse outcomes. Women are less likely to have plaque hemorrhage and have longer time to recurrent ischemic events than men [121, 224].
- **Long-term Outcomes and Restenosis:** Carotid interventions (CEA or CAS) provide durable long-term outcomes [45, 125, 137, 186]. Wall Shear Stress (WSS) topological skeleton features are associated with long-term restenosis after CEA [66]. Dual antiplatelet therapy (DAPT) following CEA is associated with lower rates of late restenosis compared to single antiplatelet therapy (SAPT) [85].

5) Discussion

5.1 Principal finding:

The median 30-day stroke or death rate following carotid endarterectomy (CEA) was 1.65%, with a range from 0% to 4.2% [137, 160, 172, 176, 209, 216, 228], indicating that CEA is a procedure with generally low perioperative morbidity and mortality.

5.2 Clinical implications:

- **Patient Selection Refinement:** Preoperative assessment should integrate advanced imaging for vulnerable plaque identification [1, 178, 211], along with comprehensive risk stratification considering comorbidities like CAD, diabetes, and chronic kidney disease [4, 10, 82, 185, 198].
- **Anesthesia and Surgical Technique:** Regional anesthesia for CEA may offer advantages over general anesthesia in reducing postoperative complications like pneumonia and transfusion needs [182]. Standardized techniques like eversion endarterectomy or patch angioplasty demonstrate good safety and efficacy [57, 87, 117].
- **Postoperative Monitoring:** Close monitoring of cerebral hemodynamics and blood pressure is critical to mitigate risks of cerebral hyperperfusion syndrome and POCVA [11, 13, 184, 189].
- **Antiplatelet Therapy:** Dual antiplatelet therapy (DAPT) may be beneficial for reducing late restenosis after CEA compared to single antiplatelet therapy (SAPT) [85].
- **Concomitant Disease Management:** For patients with concomitant carotid and coronary artery disease, the choice between simultaneous or staged procedures remains complex, with both approaches showing acceptable outcomes but varying complication profiles [40, 73, 90, 93].

5.3 Research implications / key gaps:

- **Long-term Cognitive Outcomes:** Further prospective studies are needed to compare the long-term cognitive impact of CEA versus CAS/TCAR in various patient subgroups [2, 14, 28].
- **Standardized Biomarker Panels:** Research should focus on validating and integrating novel inflammatory and genetic biomarkers into routine clinical risk prediction models for perioperative and long-term adverse events [43, 44, 63, 68, 179].
- **AI Model Validation:** Large-scale, external validation of AI models for vulnerable plaque identification and outcome prediction is essential to confirm their generalizability and clinical utility [1, 3, 47, 211].
- **Optimal Management of Non-Stenotic Disease:** High-quality evidence is needed to define the role of CEA in symptomatic non-stenotic carotid artery disease, particularly

regarding long-term stroke prevention [9, 223].

- **Comparative Effectiveness in Specific Subgroups:** More RCTs are required to compare CEA, CAS, and TCAR outcomes in underrepresented or high-risk populations, such as women, octogenarians, or patients with specific plaque characteristics [41, 80, 121, 173, 224].

5.4 Limitations:

- **Heterogeneity of Study Designs** — The diverse range of study designs (RCTs, cohorts, case reports) limits the ability to draw definitive, generalizable conclusions due to varying levels of evidence and potential for bias.
- **Inconsistent Outcome Reporting** — Variability in definitions and reporting of perioperative complications (e.g., stroke, death, MACE) across studies complicates direct comparisons and meta-analysis.
- **Lack of Direct Comparisons** — Many studies compare CEA to CAS or TCAR, but direct head-to-head randomized controlled trials for all permutations and patient subgroups are still limited.
- **Focus on Short-Term Outcomes** — A significant portion of the literature emphasizes 30-day perioperative outcomes, potentially underrepresenting the long-term efficacy and safety profiles of interventions.
- **Selection Bias in Observational Studies** — Retrospective and observational studies are prone to selection bias, as patient characteristics often influence the choice between CEA and alternative treatments.

5.5 Future directions:

- **Large-Scale RCTs** — Conduct large-scale, pragmatic RCTs comparing CEA, CAS, and TCAR in diverse patient populations, including asymptomatic and symptomatic subgroups.
- **Standardized Outcome Definitions** — Develop and adopt standardized definitions for perioperative and long-term outcomes to facilitate more robust comparative effectiveness research.
- **AI-Driven Risk Stratification** — Further develop and validate AI models for personalized risk assessment, integrating multimodal imaging, clinical data, and biomarkers.
- **Biomarker-Guided Therapy** — Investigate the utility of novel biomarkers (e.g., inflammatory markers, genetic profiles) to guide patient selection and optimize antiplatelet or medical therapies post-CEA.

- **Longitudinal Cognitive Studies** — Implement long-term prospective studies to thoroughly evaluate the cognitive impact of different carotid revascularization strategies.

6) Conclusion

The median 30-day stroke or death rate following carotid endarterectomy (CEA) was 1.65%, with a range from 0% to 4.2% [137, 160, 172, 176, 209, 216, 228], indicating that CEA is a generally safe and effective procedure for stroke prevention. This outcome is broadly generalizable to symptomatic and asymptomatic patients with significant carotid stenosis, though specific comorbidities and patient characteristics influence individual risk. The heterogeneity of study designs and inconsistent outcome reporting most significantly affects certainty in drawing broad comparative conclusions. Clinicians should consider individualized risk profiles, including plaque vulnerability and concomitant cardiovascular disease, when selecting revascularization strategies, and future research should focus on large-scale, standardized comparative trials.

References

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Figure 1. Publication-year distribution of included originals

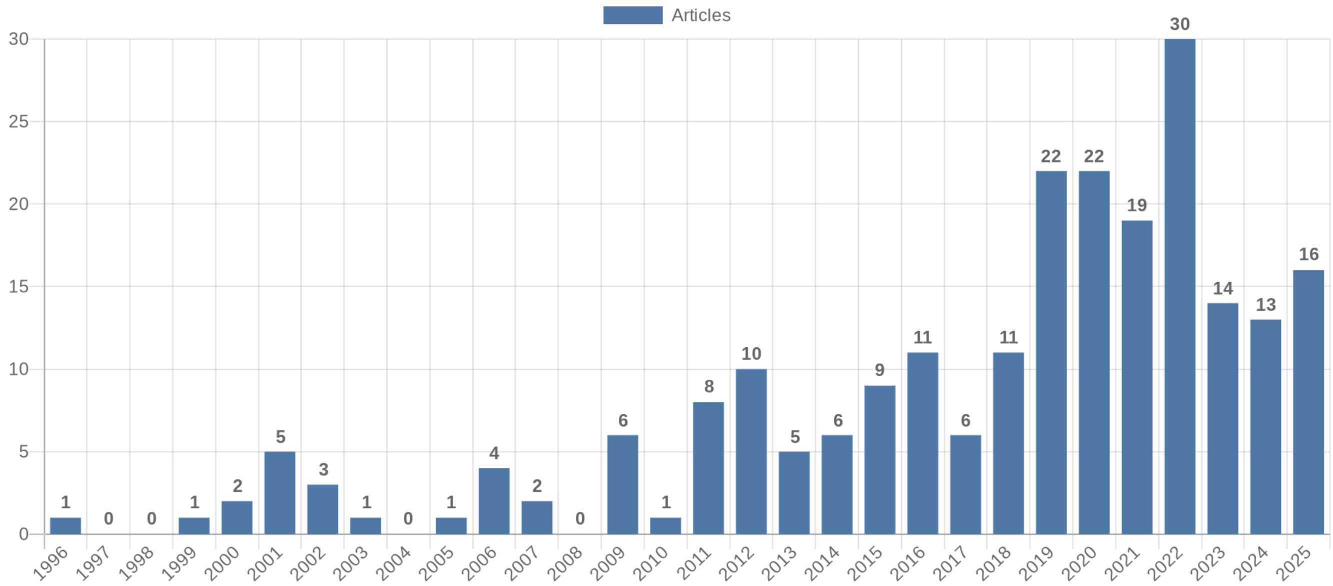

Figure 2. Study-design distribution of included originals

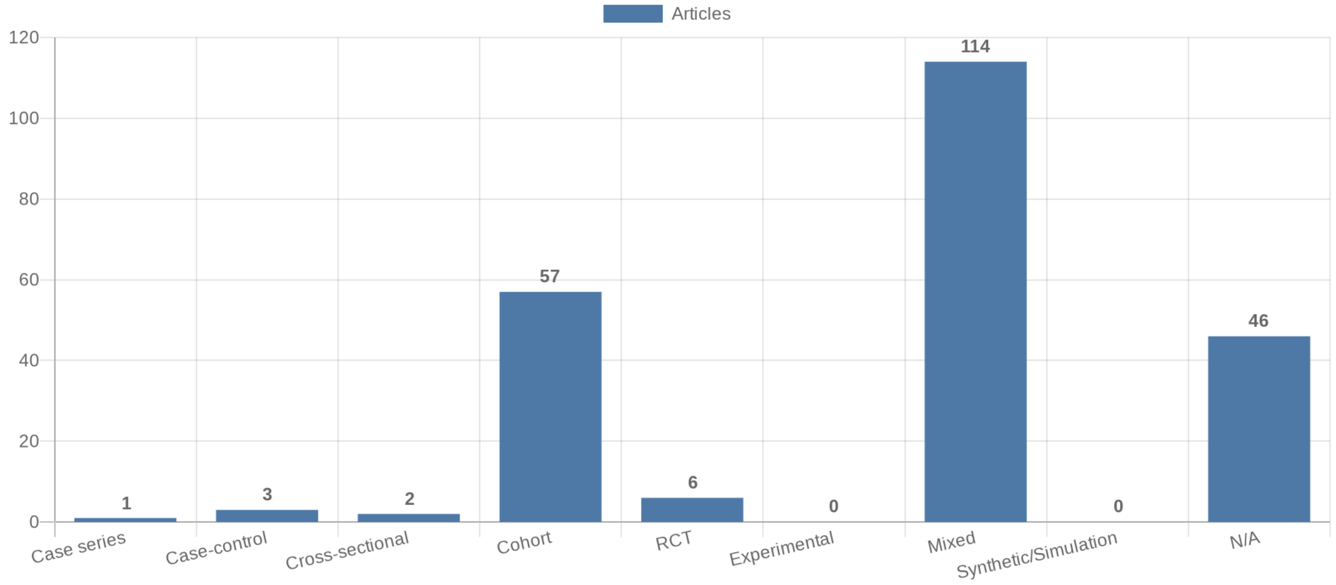

Figure 3. Study-type (directionality) distribution of included originals

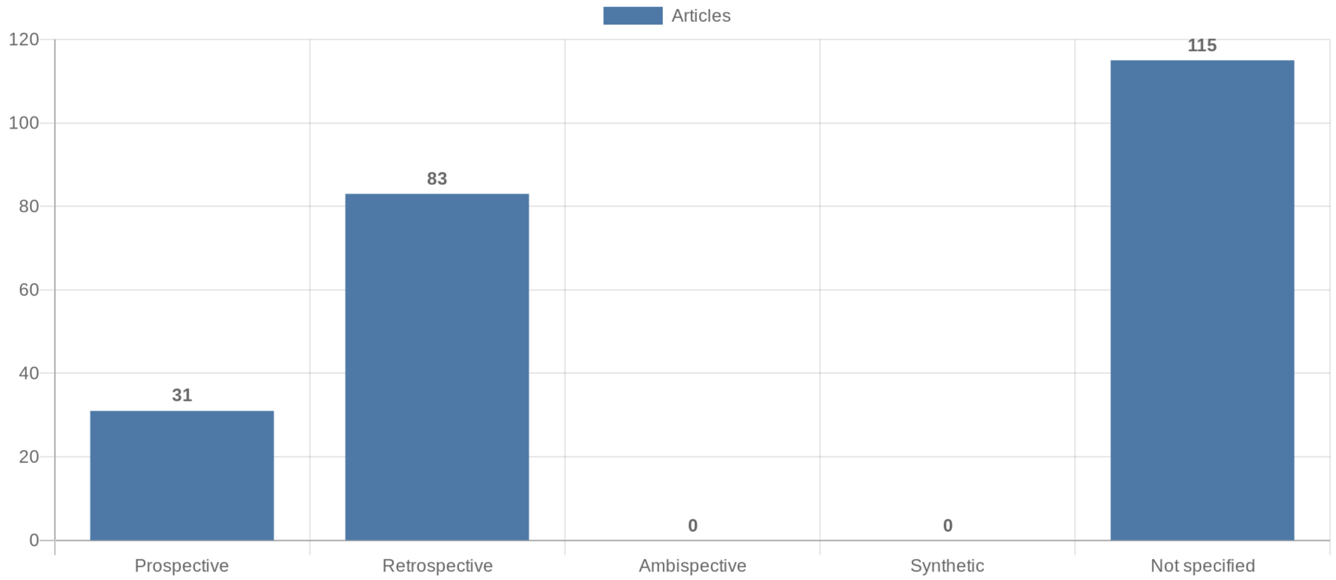

Figure 4. Main extracted research topics

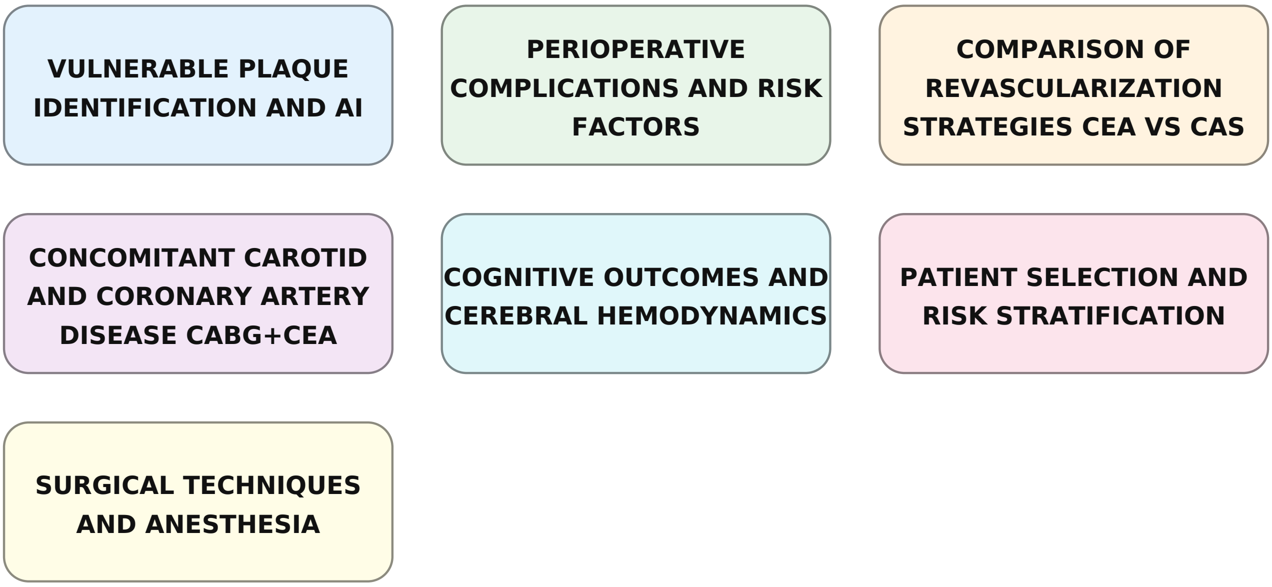

Figure 5. Limitations of current studies (topics)

Figure 6. Future research directions (topics)