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Dextran as an Adjunct in Carotid Endarterectomy: A Systematic Review and Meta-Analysis

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Background: Carotid endarterectomy (CEA) is a widely used surgical procedure to prevent stroke in patients with carotid artery stenosis. Dextran, an antithrombotic agent with antihemostatic properties, has been proposed as an adjunctive therapy to reduce thromboembolic complications during CEA. However, its effectiveness and safety remain controversial. This systematic review and meta-analysis aim to assess the incidence of thromboembolic and hemorrhagic complications in patients undergoing CEA with dextran administration.

Methods: A systematic search was conducted in MEDLINE, Scopus, and Web of Science for studies evaluating the postoperative effects of dextran in CEA patients. Random-effects meta-analysis was performed to estimate the pooled incidence of adverse events, and heterogeneity was assessed through meta-regression analysis. The quality of the included studies was evaluated using the National Heart, Lung, and Blood Institute Study Quality Assessment Tool for observational studies and the Cochrane Risk-of-Bias 2 tool for randomized controlled trials (RCTs).

Results: Ten studies, including a total of 149,540 patients, met the inclusion criteria. Of these, 9 were observational cohort studies (6 retrospective and 3 prospective), while one was an RCT. The meta-analytical incidence of stroke following CEA with dextran was 0.7% at 30 days post operatively (95% confidence interval, 0.3−1.1%), with moderate heterogeneity ($I^2 = 50.79\%$, $P = 0.002$). Meta-regression analysis indicated that geographic region significantly contributed to heterogeneity ($P = 0.010$), while other clinical covariates, such as diabetes, hypertension, and coronary artery disease, were not associated with significant variations in outcomes. Dextran

Conflicts of interest: The authors have no conflicts of interest to declare.

Funding: This research received no specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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Ann Vasc Surg 2025; 120: 246–259
https://doi.org/10.1016/j.avsg.2025.06.022

Manuscript received: March 24, 2025; manuscript accepted: June 15, 2025; published online: 27 June 2025

was primarily administered selectively to high-risk patients, with variations in dosing protocols across studies.
Conclusion: The use of dextran in CEA was associated with a low incidence of thromboembolic events. However, some heterogeneity among studies highlights the need for further large-scale RCTs to clarify its efficacy and safety. Given the potential risks of dextran, including hemorrhage and renal complications, individualized patient selection and standardized administration protocols are recommended.

INTRODUCTION

Carotid endarterectomy (CEA) is a surgical procedure commonly performed to reduce the risk of complications such as stroke or transient ischemic attack (TIA), which typically result from carotid artery stenosis. The procedure involves opening the blood vessel, after which the surgeon removes the plaque responsible for stenosis of the artery. Thromboembolic stroke is a major cause of morbidity and mortality in patients following CEA. The usage of transcranial Doppler (TCD) monitoring, followed by dextran administration, has been shown to reduce embolization rates.[1]

In medical practice, various adjuncts are used as supplements to anticoagulant therapy, such as polygeline (acting as plasma substitutes with anticoagulant properties),[2] gelatin-based colloid solutions (preventing clot formation),[3] and pentastarch or hydroxyethyl starch (plasma expanders with mild antithrombotic effects).[4,5]

The most commonly used, dextran, a complex branched glucan, has demonstrated antihemostatic properties, including the inhibition of platelet adhesion and aggregation, interference with fibrin polymerization, inhibition of erythrocyte aggregation, reduction of blood viscosity, and enhancement of fibrinolysis. Consequently, it has been theorized to lower the risk of complications associated with CEA and has traditionally been used, although the extent of its usage varies among surgeons.[1,6]

As a supportive treatment, dextran is used in combination with other anticoagulants. Its simultaneous use with heparin or low−molecular-weight heparin may enhance the anticoagulant effect of both by inhibiting platelet aggregation and prolonging clotting times. Dextran interacts with vitamin K antagonists and direct oral anticoagulants, amplifying their anticoagulant action. Dextran may also amplify the antiplatelet effect of aspirin. Using dextran during thrombolytics increased risk of hemorrhage. Concurrent use is avoided unless absolutely required.

Numerous reports have documented complications associated with dextran use, including hemorrhage, volume overload, allergic reactions, anaphylactic shock, thrombocytopenia, acute renal failure, and hemodilution.[7−9]

Hence, the impact of using dextran as an adjunct in CEA requires further investigation, as guidelines are not well established. The goal of this systematic review is to provide greater insight into the benefits and risks of dextran use in CEA.

MATERIALS AND METHODS

This systematic review was conducted in accordance with the Preferred Reporting Items for a Systematic Review and Meta-Analyses Statement and the Measurement Tool to Assess systematic reviews 2 critical appraisal tool.[10,11] Ethical approval from an institutional review board was not obtained due to the nature of this study. The review protocol has been registered at International Prospective Register of Systematic Reviews (reference: CRD42024593605).

Selection Criteria

The inclusion criteria encompassed all original studies conducted in humans, except for systematic reviews and case series with fewer than 15 patients that assessed the incidence of postoperative adverse events following CEA. No exclusion criteria were applied based on publication language or date.

Search Strategy

A systematic search was conducted in 3 databases—PubMed, Scopus, and Web of Science—in September 2024. The query and keywords are presented in Supplemental Table 1. In addition, the references of the included primary studies and relevant systematic reviews were screened to identify any further articles of potential interest.

Study Selection and Data Extraction

After duplicates removal, 2 authors (DSV and JRN) independently selected studies. Any disagreements were resolved through the intervention of a third author (APN). First, studies were screened by title and abstract, and those remaining were assessed to full-text eligibility. Exclusion criteria included

patients undergoing synchronous cardiac surgery, carotid stenting, or carotid reintervention. Efforts were made to contact authors to obtain full texts that were not publicly available. The selected studies were carefully reviewed to avoid duplicate populations.

Data from included studies were independently extracted by 2 authors (DSV and JRN) using a standardized form. Extracted data included the year of publication, country and center of recruitment, study design, recruitment period, number of participants undergoing CEA, participants' age and gender, prevalence of cardiovascular comorbidities, and carotid symptomatic status (Tables I and II). In addition, information on patients' pre-operative characteristics and 30-day postoperative outcomes was extracted (Tables III and IV). By contrast, evidence regarding long-term outcomes was scarce and not readily accessible (Table V).

Assessment of Study Quality

For qualitative assessment, the Cochrane Risk-of-Bias 2 tool was used for randomized clinical trials, while the National Heart, Lung, and Blood Institute (NHLBI) Study Quality Assessment Tool was applied for observational cohort and cross-sectional studies (2013). Two authors (DSV and JRN) independently conducted the assessment, and any disagreements were resolved by consensus following a third-party review (APN).

Quantitative Synthesis

A random-effects meta-analysis (using the restricted maximum likelihood method) of log-transformed proportions was conducted to calculate the meta-analytical pooled incidence of stroke among participants. Pooled estimates and 95% confidence intervals (95% CIs) were back-transformed into their original scale to easier interpretation. Heterogeneity was assessed using the Q-Cochran P value and the I^2 statistic, a P-value < 0.10 and an $I^2 \geq 50\%$ were considered indicative of substantial heterogeneity. Sources of heterogeneity were explored through leave-one-out sensitivity analysis and univariable meta-regression models. Assessed covariates included the publication year, participants' mean age, percentage of male participants, and prevalence of arterial hypertension (HTA), dyslipidaemia, diabetes, or coronary artery disease (CAD). Other factors included the percentage of symptomatic patients and proportion of patients using antiplatelet drugs.

Subgroup analyses were conducted to separately evaluate studies in which participants underwent general anesthesia versus regional anesthesia. The potential for publication bias was assessed using funnel plots.

All statistical analysis was performed using Open Meta®.

RESULTS

Search Results

After the database search and duplicate removal, a total of 135 studies were screened. Following title and abstract screening, 114 studies were excluded. Twenty-one studies proceeded to full-text assessment, during which 10 studies were excluded, and 1 study could not be retrieved (Fig. 1).

Comprehensive reasons for exclusion during full-text assessment included: multiple articles from the same patient population ($N = 6$), incorrect patient population ($N = 1$), irrelevant outcome ($N = 3$), and unavailable full text despite contacting the respective author ($N = 1$). Thus, a total of 10 published articles were included in this systematic review.[1,6–9,12–16]

Description of Studies

Nine of the 10 studies were observational cohorts' studies—6 retrospective and 3 prospective. The remaining study was a randomized controlled trial (RCT). The included studies were conducted across 3 different countries spanning 3 continents—2 from North America,[7,8] 6 from Europe,[1,9,13–16] and 2 studies from Oceania.[6,12] A total of 149,540 patients were assessed, with study sample sizes ranging from 19 participants[1] to 140,893 participants[8] The mean participant age was 70 years, and 60.1% ($n = 89{,}909$) were male.

Demographics and comorbidities of the included study population are presented in Table II.

Main Findings and Meta-Analysis

The meta-analytical incidence of stroke after CEA with dextran was 0.7% at 30 days postoperatively (Fig. 2) [95% CI: 0.3−1.1%], with moderate heterogeneity observed ($I^2 = 50.79\%$ $P = 0.002$), indicating tolerable variability among the included studies.

In all leave-one-out sensitivity analyses and univariable meta-regression models, substantial heterogeneity persisted. Data on hemorrhagic complications were inconsistently reported across

Table I. Study characteristics

Author	Journal	Pub. year	Study design	Study center	Recruitment period	Sample size	Grade evaluation	No. CEA
Saedon M et al.	Stroke	2013	Cohort	University Hospitals Coventry and Warwickshire NHS Trust	2000–2010	Spontaneous resolution: 54, tirofiban: 40, dextran: 34 ($n = 128$)	★★☆☆	Spontaneous resolution: 54, tirofiban: 40, dextran: 34 ($n = 128$)
Moore, JM et al.	Annals of Vascular Surgery	2023	Retrospective cohort	VQI	2008–2022	Dextran: 9935/no dextran: 130,958 ($n = 140,893$)	★★☆☆	140,893
Farber, A et al.	Journal of Vascular Surgery	2013	Retrospective Cohort	VSGNE	2003–2010	Dextran: 334/no dextran: 6,307 ($n = 6,641$)	★★☆☆	6,641
Levi, CR et al.	Annals of Neurology	2001	RCT	Austin and Repatriation Medical Center and Warringal Private Hospital	N/A	Dextran: 72/no dextran: 69 ($n = 141$)	★★★☆	141
Dunne, VG et al.	Journal of Clinical Neuroscience	2001	Retrospective cohort	Royal Prince Alfred Hospital	1996–1999	30	★★☆☆	32
Sharpe, RY et al.	Eur J Vasc Endovasc Surg	2010	Prospective audit	Leicester Royal Infirmary	2006–2009	297	★★☆☆	297
Sharpe, RY et al.	Eur J Vasc Endovasc Surg	2009	Prospective audit	Leicester Royal Infirmary	1995–2006	821	★★☆☆	821
Lennard, NS et al.	The British Journal of Surgery	2003	Prospective cohort	Coventry and Warwickshire University Hospitals	1998–2001	19	★★☆☆	19
Naylor, AR et al.	Journal of Vascular Surgery	2000	Prospective audit	Leicester Royal Infirmary	1995–1999	500	★★☆☆	500
Robless, PA et al.	Platelets	2002	Prospective cohort	St Mary's Hospital	N/A	40	★★☆☆	40

CEA, carotid endarterectomy; RA, regional anesthesia; NA, information not available; VQI, Vascular Quality Initiative; VSGNE, Vascular Surgery Group of New England.

Table II. Populations demographics and risk factors

Author	Mean age	Male	Arterial hypertension	Dyslipidemia	Diabetes mellitus	Smoking history	CAD	Carotid territory symptoms
Moore, JM et al.	Dextran: 71/no dextran: 70.7	Dextran: 5,947 (4.2%)/no dextran: 79,527 (56.4%) ($n = 85,474$) (61%)	Dextran: 8,834 (6.3%)/no dextran: 116,968 (82.5%) ($n = 125,802$) (89.2%)	N/A	Dextran: 3,057 (2.2%)/no dextran: 41,281 (29.3%) ($n = 44,338$) (31.5%)	Dextran: 2515 (1.8%)/no dextran: 33,778 (24%) ($n = 36,293$) (25.8%)	Dextran: 2542 (1.8%)/no dextran: 34,034 (24.2%) ($n = 36,576$) (26%)	Dextran: 2447 (1.7%)/no dextran: 38,055 (27%) ($n = 40,052$) (28.4%)
Farber, A et al.	Dextran: 70/no dextran: 70	Dextran: 217 (3.3%)/no dextran: 3,784 (57%) ($n = 4,001$) (60.2%)	Dextran: 274 (4.1%)/no dextran: 5,550 (83.6%) ($n = 5,824$) (87.7%)	N/A	Dextran: 104 (1.6%)/no dextran: 1955 (29.4%) ($n = 2059$) (31%)	Dextran: 264 (4.0%)/no dextran: 5,046 (76%) ($n = 5,310$) (80%)	Dextran: 94 (1.4%)/no dextran: 2081 (31.3%) ($n = 2175$) (32.8%)	1660 (25%) symptomatic
Levi, CR et al.	Dextran: 69/no dextran: 69.5	Dextran: 50 (35.4%)/no dextran: 52 (36.9%) ($n = 102$) (72.3%)	N/A	N/A	Dextran: 8 (5.7%) /no dextran: 10 (7.1%) ($n = 18$) (12.8%)	Dextran: 13 (9.2%)/no dextran: 8 (5.7%) ($n = 21$) (14.9%)	Dextran: 28 (19.9%)/no dextran: 32 (22.7%) ($n = 60$) (42.6%)	N/A
Saedon M et al.	Spontaneous resolution: 71/ tirofiban: 74/ dextran: 69	Spontaneous resolution: 36 (28.1%)/ tirofiban: 27 (21.1%)/ dextran: 22 (17.2%) ($n = 85$) (66.4%)	Spontaneous resolution: 47 (36.7%)/ tirofiban: 31 (24.2%)/ dextran: 27 (21.1%) ($n = 105$) (82%)	N/A	Spontaneous resolution: 16 (12.5%)/ tirofiban: 10 (7.8%)/ dextran: 6 (4.7%) ($n = 32$) (25%)	Spontaneous resolution: 12 (9.4%)/ tirofiban: 13 (10.2%)/ dextran: 9 (7%) ($n = 34$) (26.6%)	Spontaneous resolution: 24 (18.8%)/ tirofiban: 14 (11%)/dextran: 14 (11%) ($n = 52$) (40.6%)	N/A
Dunne, VG et al.	64	22 (68.8%)	22 (68.8%)	20 (62.5%)	8 (25%)	11 (34.8%)	18 (56.2%)	15 TIA (46.9%), 6 amaurosis fugax (18.8%), 8 stroke (25%) ($n = 29$) (90.6%)
Sharpe, RY et al.	69	204 (68.7%)	N/A	N/A	N/A	N/A	N/A	253 (84.9%) symptomatic
Sharpe, RY et al.	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A

Lennard NS et al.	38–86	13 (68.4%)	N/A	N/A	1 (5.3%)		8 (42.1%)	N/A
Naylor AR et al.	N/A	N/A	310 (62%)	N/A	74 (14.8%)	N/A	123 (24.6%)	421 (84.2%)
Robless, PA et al.	68	30 (75%)	25 (62.5%)	12 (30%)	10 (25%)	16 (40%)	13 (32.5%)	36 (90%)

CEA, carotid endarterectomy; NA, information not available; CAD, coronary artery disease.

studies. Furthermore, TIA were very infrequent and with low report rates across studies.

Regarding the meta-regression analysis, the following covariates showed no significant association with outcomes: gender, diabetes mellitus, HTA, CAD, smoking, and symptomatic carotid stenosis. These findings suggest that these clinical factors did not significantly influence the proportion of adverse events across studies. Detailed results are presented in Supplementary Figure 1.

Meta-Regression by Continent

The meta-regression analysis identified a statistically significant association between continent and the proportion of adverse events ($P = 0.010$).

The adjusted model yielded an intercept coefficient of 0.004 (95% CI: 0.001−0.007, $P = 0.009$), suggesting regional variations in the reported incidence of events.

The omnibus P value for the model was 0.010, confirming that the continent significantly contributed to the observed heterogeneity among the included studies. North America presented a single study with an increased stroke rate compared to the remaining.[8]

Dextran Administration Approaches

Dextran administration across studies was primarily selective, targeting high-risk patients undergoing CEA.[7] Most protocols utilized TCD to identify patients with significant embolization (e.g., > 25 emboli in 10 min or > 50 per hr) or severe stenosis. An example of this is Lennard et al.,[1] who administered preoperative dextran 40−19 patients with crescendo (unstable) TIAs and ≥ 70% stenosis. As such across the selective-protocol studies, high risk was most commonly defined by a heavy intra- or postoperative microembolic load (microembolic signals [MES]) on TCD (> 25 MES/10 min or > 50 MES/h)[9,12–16] critical stenosis (≥ 70%),[1,13,15,16] unstable neurological symptoms such as crescendo TIAs,[1] or the presence of intraluminal thrombus/intimal flap.[13] Dextran was administered intraoperatively or postoperatively, often as a bolus followed by infusion. A notable exception was observed in the study by Farber et al.,[7] where dextran was administered to 5% of patients without specific embolization criteria, reflecting a less selective approach.

Studies Quality

The risk of bias in the selected articles is displayed in Figures 3 and 4. The risk of bias for each observational cohort is individually shown in Figure 2A,

Table III. Preoperative characteristics

Author	Ipsilateral stenosis	Contralateral stenosis	Antiplatelet therapy	Anticoagulation	General anesthesia	Regional anesthesia	Intraoperative anticoagulation protocol	Dextran administered
Moore, JM et al.	Dextran: 4,864/no dextran: 58,957	N/A	Aspirin: Dextran: 8,144/no dextran: 109,736// inhibitor P2Y12: dextran: 3,027/ no dextran: 46,335	N/A	Dextran: 9569/no dextran: 120,856 ($n = 130,425$)	N/A	N/A	Dextran was administered. A total of 7.1% of patients rec
Farber, A et al.	N/A	N/A	Dextran: 291/no dextran: 5,676 ($n = 5,967$)	N/A	Dextran: 248/no dextran: 5,613 ($n = 5,838$)	N/A	N/A	Dextran was administered ($n = 33$)
Levi, CR et al.	N/A	N/A	N/A	N/A	N/A	N/A	Heparinization (UFH)	N/A
Saedon M et al.	N/A	N/A	N/A	N/A	N/A	N/A	N/A	Dextran as well as tirofiban was administered and reported by
Dunne, VG et al.	N/A	13	30	N/A	32	N/A	N/A	Dextran 40 was administered in patients w $\geq$50
Sharpe, RY et al.	241 > 70%	29	N/A	N/A	297	N/A	N/A	Patients with increased postoperative emb received de
Sharpe, RY et al.	N/A	N/A	N/A	N/A	821	N/A	N/A	Patients with increased post-operative emb received de
Lennard NS et al.	N/A	N/A	N/A	N/A	1	18	Heparinization (UFH)	Dextran infusion was given to patients with TCD or 2 or more TIA in 30 days. 20 mL b
Naylor AR et al.	317 (>70%)	88	N/A	N/A	125	N/A	Heparinization (UFH)	Dextran was given selectively to high postemboli per hour during
Robless, PA et al.	N/A	N/A	N/A	N/A	40	N/A	N/A	Patients with > 50 signs of embolization (HIT)

CEA, carotid endarterectomy; NA, information not available; TCD, transcranial Doppler; TIA, transient ischemic attack; UFH, unfractionated heparin; HIT, high intensity transient signals.

Table IV. Postoperative outcomes in the first month

Author	Stroke	Stroke/death	Death	MI	MACE	MACE definition	Postoperative adverse events
Moore, JM et al.	Dextran: 85/no dextran: 1175 ($n = 1260$)	Dextran: 105/no dextran: 1419 ($n = 1524$)	Dextran: 23/no dextran: 349 ($n = 372$)	Dextran: 61/ no dextran: 463 ($n = 524$)	Dextran: 160/no dextran: 1817 ($n = 1977$)	MI, CHF, dysrhythmia	N/A
Farber, A et al.	N/A	Dextran: 4/no dextran: 63 ($n = 67$)	N/A	Dextran: 8/no dextran: 63 ($n = 71$)	N/A	N/A	N/A
Levi, CR et al.	N/A	N/A	N/A	N/A	N/A	N/A	7 patients with wound hematoma
Saedon M et al.	Spontaneous resolution: 0/ Tirofiban: 1/ Dextran: 0 ($n = 1$)	N/A	N/A	Spontaneous resolution: 1/ Tirofiban: 1/ Dextran: 2 ($n = 4$)	N/A	N/A	N/A
Dunne, VG et al.	8	N/A	N/A	N/A	N/A	N/A	N/A
Sharpe, RY et al.	3	3	0	N/A	N/A	N/A	N/A
Sharpe, RY et al.	N/A	21	N/A	N/A	N/A	N/A	N/A
Lennard NS et al.	1	N/A	N/A	N/A	N/A	N/A	N/A
Naylor AR et al.	4	11	6	N/A	N/A	N/A	N/A
Robless, PA et al.	2	2	0	0	N/A	N/A	N/A

CEA, carotid endarterectomy; CHF, congestive heart failure; MACE, major adverse cardiovascular events; MI, myocardial infarction; NA, information not available.

Table V. Other outcomes

Author	Other outcomes	Long-term outcomes	Long-term follow-up time	Long-term MI	Long-term stroke	Long-term MACE	Long-term all-cause mortality
Moore, JM et al.	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Farber, A et al.	N/A	N/A	1 year	N/A	Dextran: 0.4% No Dextran: 0,8%	N/A	2.5% (167) dextran vs. 3.2% (202) no dextran
Levi, CR et al.	Reduction in embolic signals	N/A	N/A	N/A	N/A	N/A	N/A
Saedon M et al.	N/A	N/A	N/A	Dextran: 2 Tirofiban: 1	Dextran: 1 Tirofiban: 1	N/A	N/A
Dunne, VG et al.	Dextran 40 reduced embolic loads	N/A	N/A	N/A	N/A	N/A	N/A
Sharpe, RY et al.	Dextran reduced embolic signals	N/A	N/A	N/A	N/A	N/A	N/A
Sharpe, RY et al.	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Lennard NS et al.	Dextran controlled emboli and symptoms preoperatively	N/A	N/A	N/A	N/A	N/A	N/A
Naylor AR et al.	Reduction of embolic signals	N/A	N/A	N/A	N/A	N/A	N/A
Robless, PA et al.	N/A	N/A	N/A	N/A	N/A	N/A	N/A

MACE, major adverse cardiac effects; MI, myocardial infarction.

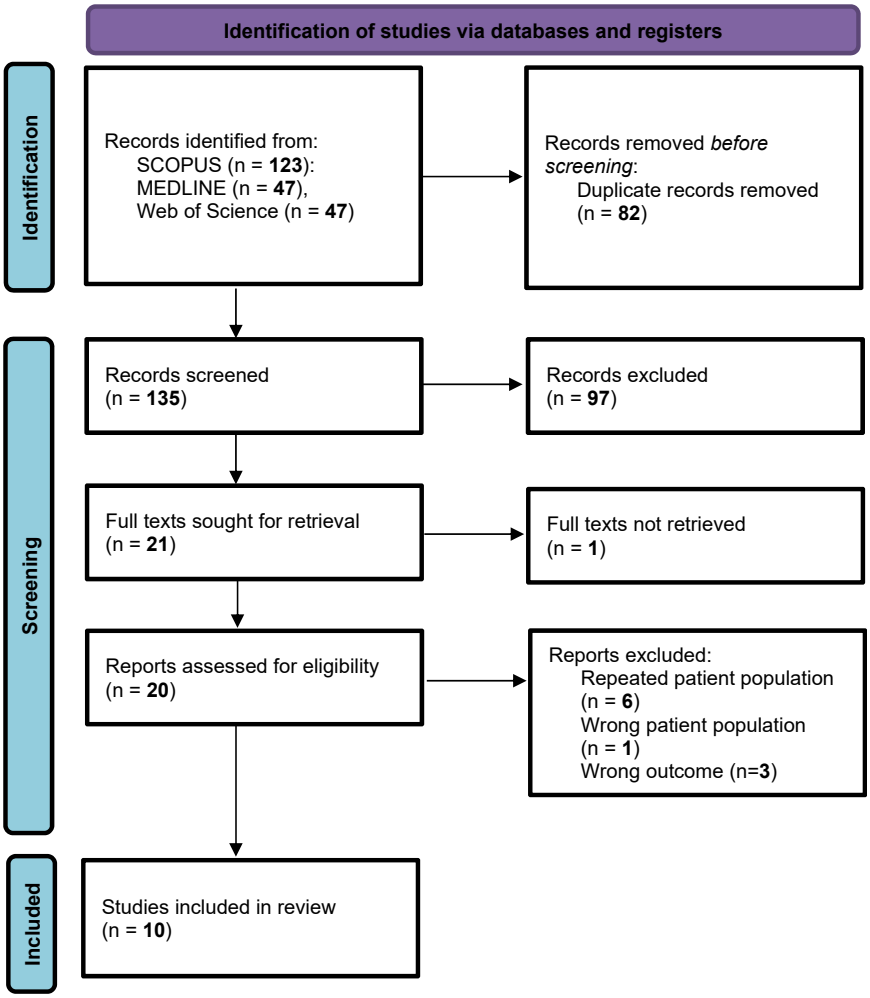

Fig. 1. PRISMA flow chart illustrating the number of records included and excluded at various screening and reviewing steps, leading to final list of records for data extraction and meta-analysis. PRISMA, Preferred Reporting Items for a Systematic Review and Meta-Analyses.

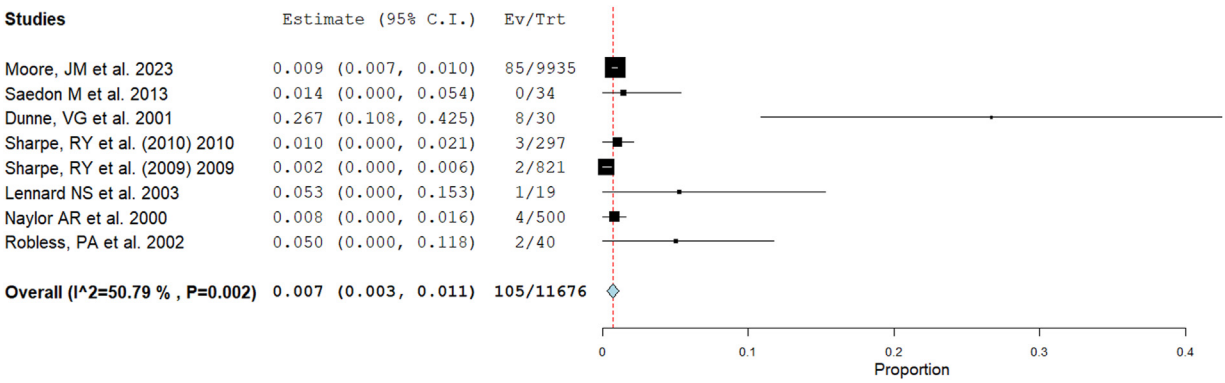

Fig. 2. Forest plot of adverse event proportions across studies. Squares represent study estimates (size ∝ weight), horizontal lines show 95% CIs, and the diamond indicates the pooled estimate. The red dashed line marks the overall proportion ($I^2 = 50.79\%$, $P = 0.002$). CIs, confidence intervals.

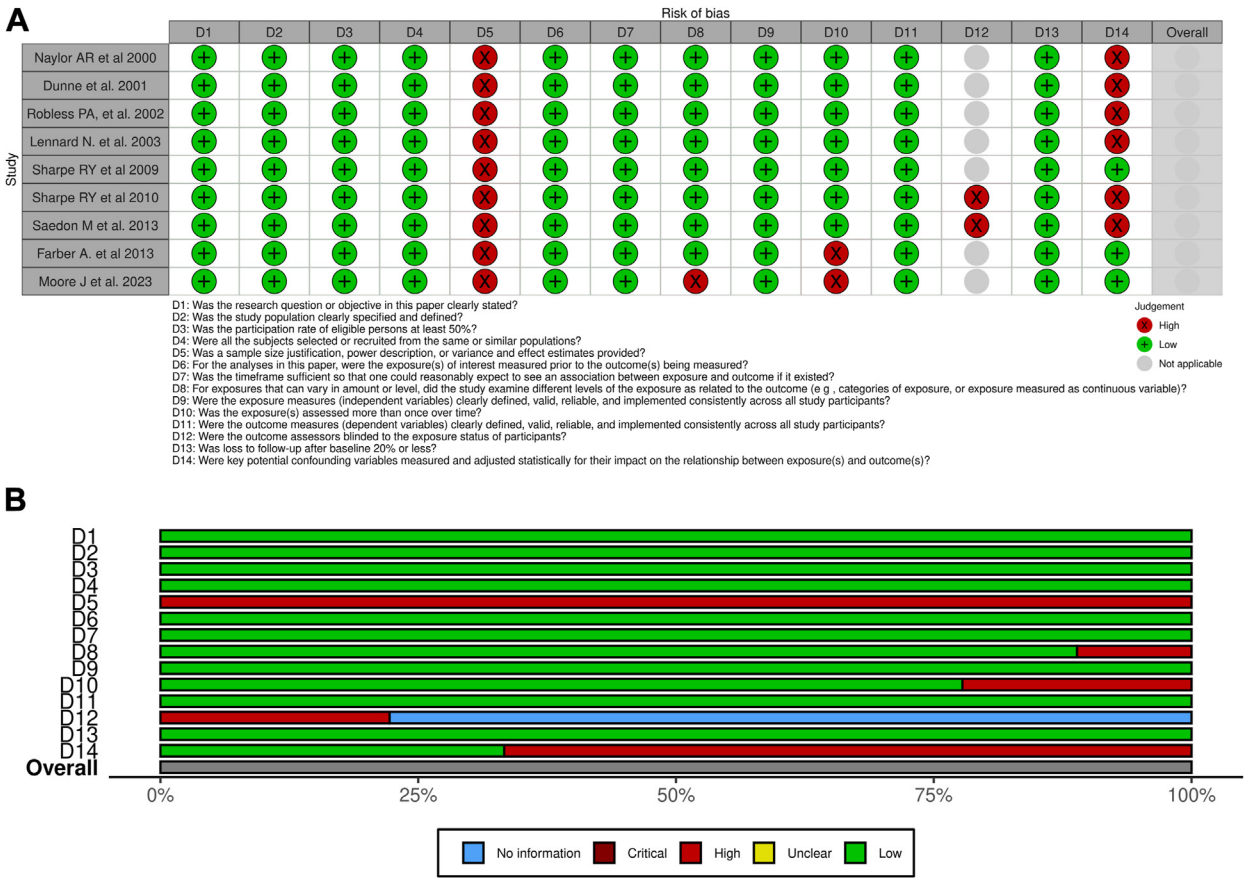

Fig. 3. (A) Risk of bias for each observational cohort individually, using NHLBI Study Quality Assessment Tool. **(B)** Overall judgment of bias for each evaluated item regarding observational cohorts, using NHLBI Study Quality Assessment Tool. NHBL, National Heart, Lung, and Blood Institute.

while the risk of bias for the RCT is displayed in Figure 3A. The overall judgment per evaluated item regarding observational cohorts is presented in Figure 2B, whereas that for the RCT is shown in Figure 3B.

All studies included in this review exhibited an overall low risk of bias—both cohorts and RCT. The items most frequently associated with high risk of bias among observational cohorts included sample size justification and statistical adjustment for confounding factors. For the RCT, high or unclear risk patterns were noted in essential domains such as allocation concealment and outcome measurement.

DISCUSSION

This systematic review and meta-analysis demonstrated that dextran administration during CEA was associated with a low incidence of stroke (0.7%), with moderate heterogeneity among included studies. The findings suggest that dextran may be beneficial in reducing thromboembolic events; however, significant variability in study methodologies and patient selection criteria limits definitive conclusions.

The primary finding of this study—the low incidence of stroke associated with dextran use—supports its potential as an adjunct therapy during CEA. While dextran can decrease embolic signals detected via TCD, studies show it fails to significantly lower stroke rates and is associated with severe complications such as anaphylaxis, hemorrhage, myocardial infarction, congestive heart failure (CHF), renal failure, and prolonged hospital stays.[7,8] In contrast, dual antiplatelet therapy (DAPT), combining aspirin and clopidogrel, has proven more effective in reducing postoperative embolization and stroke risk without the adverse

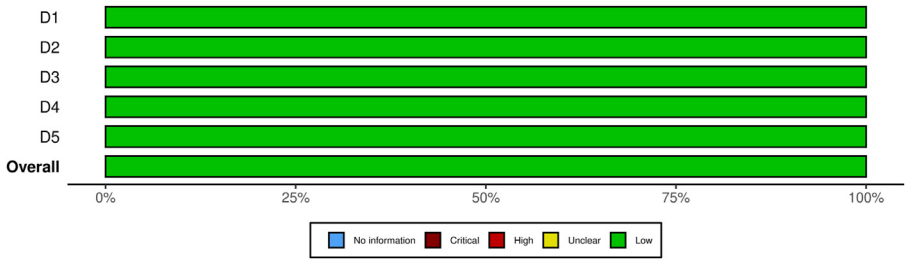

Fig. 4. Risk of bias for each RCT individually, using RoB2 evaluation tool. RCT, randomized controlled trial; Rob2; risk-of-bias 2 tool.

cardiac effects linked to dextran. A study demonstrated that preoperative DAPT reduced high-rate embolization to 0.4%, compared to 3.2% in historical controls using dextran[15]

For asymptomatic patients undergoing CEA, the risks associated with dextran administration may outweigh its benefits. DAPT provides a safer alternative, minimizing complications while maintaining efficacy in stroke prevention. This highlights a shift away from dextran in favor of therapies with better safety profiles and comparable or superior outcomes.

Dextran exerts its protective effects through multiple physiological mechanisms that contribute to the reduction of thromboembolic events during CEA. As a branched polysaccharide, dextran interferes with coagulation by inhibiting platelet aggregation and adhesion, reducing blood viscosity, and enhancing fibrinolysis. These effects collectively prevent the formation of microthrombi, which are a major cause of perioperative stroke. In addition, dextran's ability to interfere with fibrin polymerization further contributes to its antithrombotic profile.[7,8] Another key aspect of dextran's protective mechanism is its role in improving blood flow properties. By reducing erythrocyte aggregation and increasing capillary perfusion, dextran helps maintain adequate cerebral oxygenation and prevents hypoperfusion-related ischemic events. Furthermore, dextran has been shown to decrease endothelial activation and reduce inflammatory responses, which may play a role in limiting vascular complications following CEA.[1,6,7]

A key observation from this review is the variability in dextran administration protocols across studies. Most studies employed a selective approach, administering dextran only to high-risk patients identified via TCD monitoring, particularly those exhibiting high embolization rates. The high-risk definition varied across studies. In most, high-risk was defined by intraoperative TCD evidence of heavy embolization as previously mentioned ($>$ 25 emboli in 10 min or $>$ 50 per hr), or by critical carotid stenosis, but some protocols also included patients with unstable neurological symptoms as candidates for dextran—most notably the series by Lennard et al.—as well as the presence of luminal thrombus or intimal flap.[1,13] Some studies, such as Farber et al.,[7] reported a nonselective approach, administering dextran to a broader patient population without stringent embolization criteria. These discrepancies in dextran administration highlight the lack of standardized guidelines, making direct comparisons challenging. The impact of dextran may therefore be contingent upon specific patient selection strategies.

Meta-regression analysis revealed that the continent in which the study was conducted significantly influenced the incidence of adverse events ($P = 0.010$). This finding suggests that regional variations in perioperative management, patient selection criteria, and institutional practices may contribute to heterogeneity in outcomes. Studies from Europe tended to report lower adverse event rates, potentially reflecting more stringent patient selection and perioperative monitoring protocols. Conversely, studies from North America and Oceania exhibited higher variability in outcomes, which may be attributed to differing dextran administration strategies and institutional guidelines. These regional discrepancies further emphasize the necessity of establishing universal, evidence-based recommendations for dextran use in CEA.

Other findings, such as the lack of significant associations between patient comorbidities (e.g., diabetes, HTA, CAD) and stroke incidence, suggest that dextran's benefits may be independent of traditional cardiovascular risk factors. However, the significant regional variations identified through meta-regression underscore the influence of

institutional practices and geographical differences in patient management.

Multiple studies have examined the potential side effects of dextran in patients undergoing CEA. While some publications have not reported significant complications, others have noted important adverse events. For instance, Levi et al.[6] observed 7 wound hematomas in patients who received dextran, and both Farber et al. and Moore et al.[7,8] found associations between dextran use and an increased risk of perioperative cardiovascular complications, such as myocardial infarction and CHF. Although the exact mechanism underlying these complications may stem from dextran's antihemostatic and plasma volume—expanding properties, these findings underscore the possible importance of careful risk—benefit assessment and support the use of selective administration protocols—particularly in high—cardiovascular risk patients. It is noteworthy that none of the studies specifically reported increased renal complications.[7,8] The absence of reported renal complications could suggest that current protocols for dextran administration during CEA may be relatively safe for renal function. Some studies mention the specific heparin protocol, which consists of the administration of unfractionated heparin prior to carotid artery clamping.[1,6,12,13]

This study has several limitations. The heterogeneity in study designs, dextran administration protocols, and patient selection criteria complicates direct comparisons. In addition, most included studies were observational, with some risk of bias due to inadequate statistical adjustments and sample size limitations. Furthermore, hemorrhagic complications were not consistently reported among studies, limiting our possibility of drawing conclusions about bleeding risk. On another note, information on patients' preoperative antiplatelet or anticoagulant use was often not provided, making it difficult to assess the influence of prior antithrombotic therapy on outcomes. Aside from that, TIA were not uniformly reported across included studies. Only one study explicitly documented TIA outcomes post-CEA—that study being Saedon et al.,[9] who reported 5 patients sustaining a postoperative TIA despite receiving dextran 40. Most other studies did not separately report TIA incidences, and therefore this remains a limitation.

Future research should focus on large-scale, well-designed RCTs to establish standardized protocols for dextran use in CEA and clarify its risk—benefit profile. Until then, clinicians should weigh its potential benefits against the associated risks and consider selective administration based on individual patient profiles.

CONCLUSIONS

This systematic review and meta-analysis provide insight into the role of dextran as an adjunct in CEA. The findings suggest that dextran administration is associated with a very low incidence of stroke and may offer protective benefits in high-risk patients. However, concerns regarding variations in dosing protocols warrant caution in its widespread use.

This study highlights the need for further research to mitigate intraoperative stroke risk. Future large-scale RCTs should focus on defining optimal dextran dosage, evaluating short-term safety, and assessing its overall impact on patient outcomes. Until robust evidence is available, dextran should be used selectively, with careful consideration of individual patient risk factors to balance its benefits and risks effectively.

CREDIT AUTHORSHIP CONTRIBUTION STATEMENT

Duarte Silva-Vieira: Writing — review & editing, Writing — original draft, Validation, Supervision, Project administration, Funding acquisition, Formal analysis, Conceptualization. **António Pereira-Neves:** Writing — review & editing, Validation, Supervision, Software, Methodology, Data curation. **Hipolito Nzwalo:** Writing — review & editing, Validation, Supervision, Resources, Investigation. **Piotr Myrcha:** Writing — review & editing, Writing — original draft, Visualization, Supervision, Methodology, Formal analysis, Data curation, Conceptualization. **João Rocha Neves:** Writing — review & editing, Writing — original draft, Visualization, Validation, Supervision, Software, Project administration, Methodology, Data curation, Conceptualization.

The authors have no acknowledgments to declare.

SUPPLEMENTARY DATA

Supplementary data related to this article can be found at https://doi.org/10.1016/j.avsg.2025.06.022.

REFERENCES

1. Lennard NS, Vijayasekar C, Tiivas C, et al. Control of emboli in patients with recurrent or crescendo transient ischaemic attacks using preoperative transcranial Doppler-directed Dextran therapy. Br J Surg 2003;90:166—70.

2. Singh A, Ali S, Shetty R. Effectiveness and safety of polygeline in patients with hypovolemia due to trauma. J Emerg Trauma Shock 2017;10:116–20.
3. Charlesworth M, Shelton CL. Should intravenous gelatins have a role in contemporary peri-operative and critical care? Anaesthesia 2020;75:266–9.
4. Golparvar M, Saghaei M, Hamidi H, et al. Comparative evaluation of the effects of hydroxyethyl starch on coagulation state of patients during brain tumor surgeries in comparison to crystalloids by thromboelastography. J Res Med Sci 2014;19:8–12.
5. Van der Linden P, Ickx BE. The effects of colloid solutions on hemostasis. Can J Anaesth 2006;53:S30–9.
6. Levi CR, Stork JL, Chambers BR, et al. Dextran reduces embolic signals after carotid endarterectomy. Ann Neurol 2001;50:544–7.
7. Farber A, Tan TW, Rybin D, et al. Intraoperative use of dextran is associated with cardiac complications after carotid endarterectomy. J Vasc Surg 2013;57:635–41.
8. Moore JM, Garg K, Laskowski IA, et al. Intraoperative infusion of dextran confers No additional benefit after carotid endarterectomy but is associated with increased perioperative major adverse cardiac events. Ann Vasc Surg 2023;97:8–17.
9. Saedon M, Singer DR, Pang R, et al. Registry report on kinetics of rescue antiplatelet treatment to abolish cerebral microemboli after carotid endarterectomy. Stroke 2013;44:230–3.
10. McInnes MDF, Moher D, Thombs BD, et al. Preferred reporting items for a systematic review and meta-analysis of diagnostic test accuracy studies: the PRISMA-DTA statement. JAMA 2018;319:388–96.
11. Shea BJ, Reeves BC, Wells G, et al. Amstar 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. BMJ 2017;358:j4008.
12. Dunne VG, Besser M, Ma WJ. Transcranial Doppler in carotid endarterectomy. J Clin Neurosci 2001;8:140–5.
13. Naylor AR, Hayes PD, Allroggen H, et al. Reducing the risk of carotid surgery: a 7-year audit of the role of monitoring and quality control assessment. J Vasc Surg 2000;32:750–9.
14. Robless PA, Tegos TJ, Okonko D, et al. Platelet activation during carotid endarterectomy and the antiplatelet effect of Dextran 40. Platelets 2002;13:231–9.
15. Sharpe RY, Dennis MJ, Nasim A, et al. Dual antiplatelet therapy prior to carotid endarterectomy reduces post-operative embolisation and thromboembolic events: post-operative transcranial Doppler monitoring is now unnecessary. Eur J Vasc Endovasc Surg 2010;40:162–7.
16. Sharpe RY, Walker J, Bown MJ, et al. Identifying the high-risk patient with clinically relevant embolisation after carotid endarterectomy. Eur J Vasc Endovasc Surg 2009;37:1–7.