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Comparison of Thromboembolic Complications After Carotid Artery Stenting with and without Using Protection Devices: A Systematic Review and Meta-Analysis Study

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Background: This study compared the rate of thromboembolic events during carotid angioplasty and stenting (CAS) with and without embolic protection devices (EPDs). We reviewed literature to find studies comparing embolic event rates during CAS with and without EPDs and conducted a meta-analysis to determine the safer approach.
Methods: The Embase, PubMed, and Web of Science databases were thoroughly searched following PRISMA guidelines. Each estimation was executed using random-effects models. The I^2 index was used to assess the heterogeneity among the studies. Egger and Begg's tests were applied to evaluate publication bias. Stata version 14.2 was used for statistical analysis.
Results: For 25% of patients, an EPD was used during CAS, and for 75% it was not. Of the patients undergoing CAS, the prevalences of hypertension, diabetes mellitus, coronary artery disease, and cigarette smoking were 81%, 37%, 39% and 43%, respectively. In total, of the patients included 52% were symptomatic and 48% were asymptomatic. The mortality rate reduced from 2% in the no-EPD subgroup to 1% in the EPD subgroup. The occurrence of all other complications was also reportedly higher in patients who did not receive an EPD, including major stroke and myocardial infarction, except for minor events, which were reported to be almost the same in both subgroups.
Conclusions: We found that the use of an EPD can help reduce the occurrence of thromboembolic complications of CAS, including myocardial infarction, major stroke, and death. Altogether, our results suggest that the benefits of using an EPD during CAS outweigh its risks.

Keywords: *Carotid Angioplasty; Carotid Artery Stenting; Protection Devices; Thromboembolic*

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INTRODUCTION

Stroke is a prominent cause of mortality and hospitalization in the United States [1]. Also, in developed countries, after cancer and cardiac-related fatalities, it is the third most significant cause of mortality [2]. Ischemic and hemorrhagic strokes are the most common types. According to population-based studies, internal carotid artery stenosis due to atherosclerosis is responsible for 15% to 20% of ischemic strokes [3,4]. In the United States, almost 500,000 new strokes occur each year; 20% to 30% of these occurrences are

caused by carotid artery disease [5]. The severity and symptomatic/asymptomatic nature of internal carotid artery atherosclerosis contribute to yearly stroke risk. Patients with asymptomatic stenosis (60–99%) had a 2–2.5% annual stroke risk, while symptomatic carotid stenosis (more than 70%) raises the chance of stroke by 10–15% per year [6–9].

Medical therapy is used to treat individuals with carotid artery disease to minimize emboli formation and regulate the progression of atherosclerosis. Revascularization should be considered in more severe cases [10,11]. In recent years, carotid artery angioplasty and carotid artery stenting have been developed as effective, minimally invasive methods for treating carotid stenosis. Carotid angioplasty and stenting (CAS) is a possible treatment in individuals with significant comorbidities for whom endarterectomy would be a high-risk procedure [5]. Regardless of advancements in stenting procedures and medical antiplatelet therapy, embolic neurologic events during CAS procedures are unavoidable [12,13]. The carotid artery's friable, ulcerated, and thrombotic material may embolize during the surgery [14–16].

Several protective methods are available to reduce the risk of thromboembolic complications [17]. Several cerebral protective devices have been manufactured to minimize the risk of pre-procedural problems [18]. Distal filters, proximal embolic protection devices (EPDs), particularly proximal balloon occlusion, and flow reversal devices are some of them [19–21]. The popularity of these gadgets has recently soared and they are now widely used in therapeutic settings [18]. Although cerebral protection devices minimize the risk of overt perioperative stroke during CAS, the chance of silent cerebral embolism is still considerable, and the risk varies depending on the type of protection utilized [22].

Much previous research has found no significant differences in embolic problems in CAS patients who received EPDs versus those who did not [23–25]. Some studies have shown that endovascular treatment of carotid artery stenosis without EPDs can yield acceptable outcomes in terms of safety and efficacy [5,18,26,27]. On the other hand, using EPDs during CAS has been shown in some studies to minimize embolic consequences [28,29]. Yusuf Inanc et al. reported that complication rates associated with embolization were as much as 5% lower when a protective device was used during stenting [30]. In the multicenter study by Scheinert et al. involving 120 patients, the combined 30-day endpoint of death and stroke was 2.5%, indicating that using an EPD during CAS may reduce the rate of embolic complications [31].

CAS has emerged as a highly effective treatment for carotid stenosis, but the risk of thromboembolic complications during this procedure remains a significant challenge. EPDs have been developed to address this issue, although the evidence supporting their efficacy has been inconsistent across studies. Given the critical need to minimize perioperative complications, our study takes a pivotal step in systematically reviewing the literature to evaluate the impact of EPDs on the rate of embolic events during CAS. Through a comprehensive meta-analysis, we aim to clarify whether the use of EPDs effectively reduces the incidence of serious complications such as myocardial infarction (MI), major stroke, and death. This analysis is crucial for guiding clinical decision-making and optimizing patient outcomes in carotid stenting procedures.

METHODS

Search Strategy

Systematic literature searches were thoroughly conducted in the PubMed, Scopus, Web of Science, Embase, and Google Scholar databases, following PRISMA guidelines. The keywords, keyword combinations, and mesh terms used in these databases were as follows: carotid artery stenting, CAS, carotid artery stenting with devices, embolic protection devices, embolic events, and stenting without protection. An independent investigator performed the search, and then, after removing duplicate articles, two other authors screened the articles based on title and abstract, and unrelated articles were excluded. Then they reviewed the remaining articles based on full text and included related articles in the study, and a third investigator resolved discrepancies. The literature lists of included studies were also manually reviewed to identify additional eligible articles.

Selection Criteria

This meta-analysis includes studies that met one or more of the following predefined criteria:

(1) randomized controlled trials (RCTs) or retrospective observational studies that compared embolic complications during carotid stenting with and without protective devices;
(2) studies published in English;
(3) studies that compare the EPD group with the control group;
(4) studies that evaluate embolic events during CAS.

Also, the exclusion criteria for our study are as follows:

(1) studies in which the data are not clearly and accurately presented and that have no control groups;
(2) studies where authors could not provide additional quantitative data;
(3) incomplete data or unclear distinction between unprotected and protected CAS;
(4) high-risk bias studies or studies that reported irrelevant results.

Data Extraction

Two independent reviewers extracted the relevant data from the eligible studies. All disagreements were discussed, and the final decision was made through consensus with the third party. Then data extraction was carried out for the predefined variables listed below:

(First author, year of publication, country, sample size, patient characteristics (age, gender, smoking history, coronary artery disease, diabetes, hypertension, stenting with and without embolic protection, percentage of symptomatic and asymptomatic patients, number of minor embolic events, number of strokes, number of deaths (total and stroke-related), number of MI and follow-up duration)).

The ethics code of this study is IR.SBMU.RETECH.REC.1403.225.

Quality Assessment

The Newcastle–Ottawa Scale (NOS) was used in the present study to assess the quality of all selected articles [32]. This scale comprises eight elements for evaluating the quality of studies, such as "comparability," "outcome," and "selection." In addition, the Ottawa checklist was employed for cross-sectional studies. According to the standard of scoring in the NOS, cross-sectional studies can be classified as follows: low risk of bias (7–10), intermediate risk of bias (5–6), and high risk of bias (1–4) (Table 1).

Statistical Analysis

Stata version 14.2 (Stata Corp, College Station, TX, USA) was used to perform a meta-analysis (with metaprop command) and assess the pooled prevalence, along with the associated 95% confidence interval (CI) for the main complications in patients experiencing CAS with or without EPD. The heterogeneity of the included articles in this meta-analysis was measured by the heterogeneity index (I^2). If the heterogeneity was statistically significant ($P < 0.05$ and $I^2 > 50\%$), the random effects model was utilized to perform a meta-analysis; otherwise, the fixed-effect model was used. Meta-regression analyses were performed to assess the impact of the potential variables on discovering the source of heterogeneity. Moreover, Egger's test and Begg's funnel plot were used to evaluate the publication bias. A significant publication bias is considered to occur when $P < 0.05$.

RESULTS

Study Selection

In our initial search in the mentioned databases, 1,377 studies were identified. After removing 459 duplicate studies, we excluded 791 for irrelevant titles and abstracts. By reviewing the full text of the remaining 127 articles, 111 articles were excluded due to a lack of relevant information. Finally, 16 studies published from March 2002 until December 2021 met the eligibility criteria for final analysis (Figure 1).

Table 1 Newcastle–Ottawa quality assessment results for included studies.

	Selection				*Comparability*	*Outcome*			
Author	*1*	*2*	*3*	*4*	*1*	*1*	*2*	*Total Score*	*Risk of Bias*
Yabalak et al. [23]	*			**		**	*	6	Intermediate risk of bias
Dayama et al. [24]	*	*		**		**	*	7	Low risk of bias
Deharo et al. [33]	*	*		**		**		6	Intermediate risk of bias
Inanc et al. [30]	*	*		**		**		6	Intermediate risk of bias
Nazari et al. [34]	*	*	*	**	**	**	*	10	Low risk of bias
Garriboli et al. [26]	*	*		**		**		6	Intermediate risk of bias
Cremonesi et al. [35]	*	*		**		**		6	Intermediate risk of bias
Gray et al. [36]	*	*		**		**	*	7	Low risk of bias
Al mobarak et al. [37]	*	*		**		**		6	Intermediate risk of bias
Bastug et al. [3]	*	*		**		**		6	Intermediate risk of bias
Scheinert et al. [31]	*	*		**	**	**	*	9	Low risk of bias
Ghafari et al. [27]	*			**		**	*	6	Intermediate risk of bias
Mansour et al. [28]	*	*		**		**	*	7	Low risk of bias
Pandey et al. [5]	*			**		**	*	6	Intermediate risk of bias
Reimers et al. [29]	*	*		**		**	*	7	Low risk of bias
El-Sudany et al. [18]	*			**		**		5	Intermediate risk of bias

The overall score for the quality assessments for each study is represented by stars, with each star indicating the quality rating for the corresponding parameter.

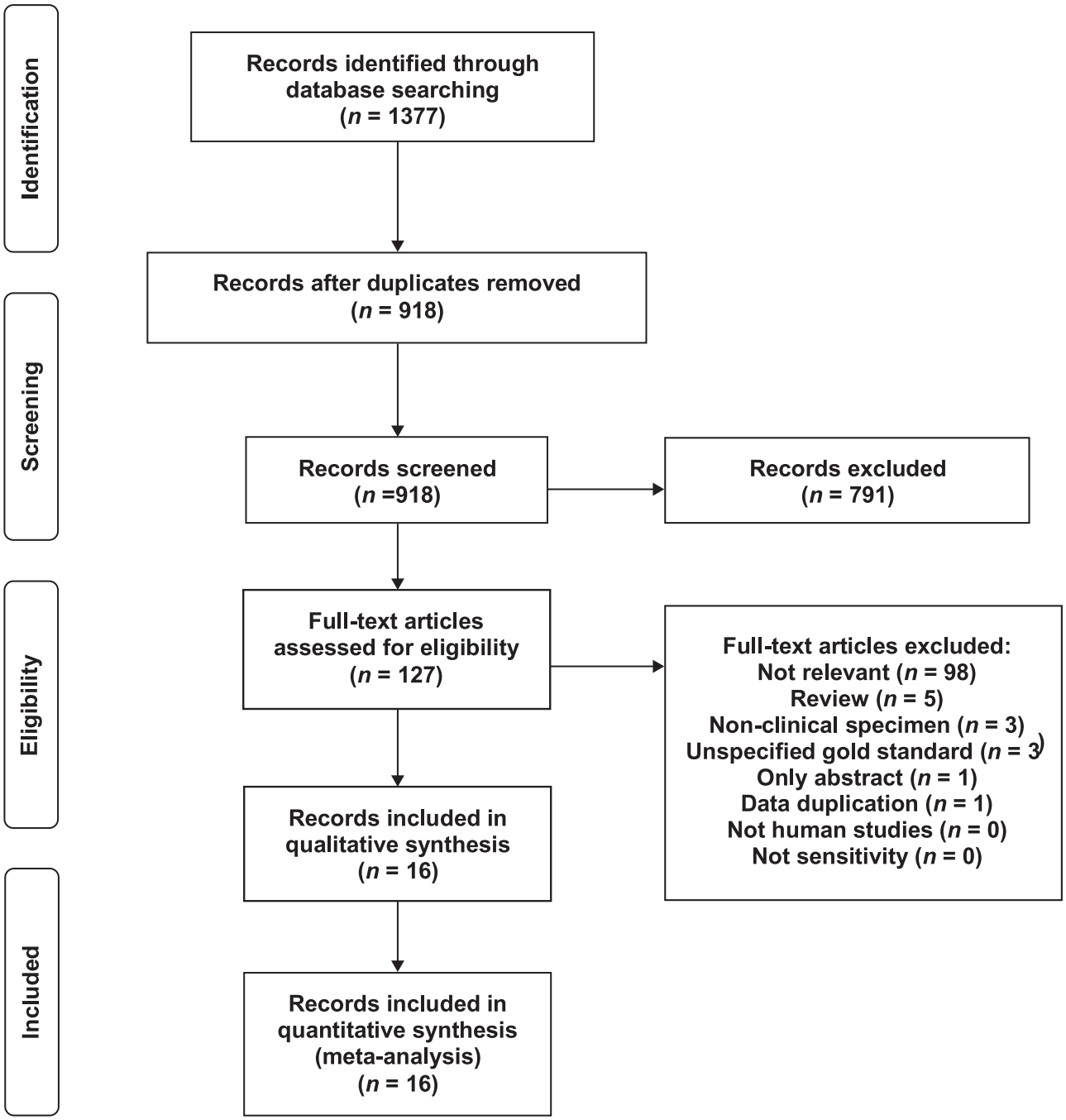

Figure 1 The process of study selection.

Demographic Characteristics of Included Studies

After merging all the extracted data, our study covered 3,875 patients, 1,171 (30%) female (95% CI: 26–34; I^2 = 85.0%) [3,5,18,23,24,26–31,33–37]. Of the participants, for 2,923 EPDs were used during CAS and for 952 they were not. Based on the average age reported in the articles, the mean age of patients was 70.05 (95% CI: 68.55–71.54; I^2 = 93.7%). Furthermore, the full-text reviewed studies were primarily conducted in Europe (*N* = 13) (Table 2).

Risk Factors, Complications, and Outcomes

Based on the primary analysis, the assessment of risk factors revealed hypertension, diabetes mellitus, coronary artery disease, and cigarette smoking with 81% (95% CI: 0.76–0.86; I^2 = 89.83%), 37% (95% CI: 0.31–0.43; I^2 = 89.90%), 39% (95% CI: 0.28–0.50; I^2 = 94.65%), and 43% (95% CI: 0.30–0.57; I^2 = 96.69%) prevalences, respectively (Figure 2). Among the patients who underwent CAS, the total death rate was measured to be 1% (95% CI: 0.01–0.01; I^2 = 0.00%) (Figure 3). After

Table 2 Baseline characteristics of the included studies. The articles have been examined and compared from the point of view of demographics, comorbidities, complications and outcomes.

					Demographics			*Comorbidities*				*Complications and Outcomes*			
Author	*Country*	*Year*	*Embolic Protection Devices*	*Sample Size (N)*	*Mean Age (SD)*	*Female (%)*	*Symptomatic (%)*	*Hypertension (%)*	*Coronary Artery Disease (%)*	*Diabetes mellitus (%)*	*Smoking (%)*	*Major Stroke (%)*	*Minor Events (%)*	*MI (%)*	*Total death (%)*
Al mobarak et al. [37]	Ireland	2002	EPD	162	68 (8)	13	48	80	54	31		0	1.2	0	1.2
Cremonesi et al. [35]	Italy	2003	EPD	442	73 (8)	21	57					0.2	0.9	0	0
Reimers et al. [29]	Italy	2004	EPD	753	70 (8)	36	28	77.2	62.9	20.8		0.8	2	0.4	0.5
Pandey et al. [5]	USA	2007	No-EPD	94	68 (10)	45	63	68.9	33	31	32.9	1.9		1.9	1.9
Mansour et al. [28]	Germany	2011	No-EPD	133	71 (10)	23	68	72.1	21.8	24.8		2.2	0.7	0	4.5
Dayama et al. [24]	Germany	2017	EPD	200	68 (11)	23	0					3.5		1.5	0.5
Dayama et al. [24]	Germany	2017	No-EPD	57	69 (9)	35	0					7		1.8	1.8
Scheinert et al. [31]	Germany	2017	EPD	120	75 (8)	28	12	88.3	43.3	34.2	47.5	2	0	0.8	0
Gray et al. [36]	USA	2017	EPD	250	75 (10)	30	15	94.4		34.8	72.4	0.4	2.4	0.4	0.8
Inanc et al. [30]	Turkey	2018	No-EPD	171	67 (14)	36		65.4	33.9	38.5	56	0	5.8	0	0
De Haro et al. [33]	Spain	2018	EPD	21	73 (7)	23	100	0.01	33.3	66.7	43	0	0	0	4.7
Garriboli et al. [26]	Italy	2018	No-EPD	77	77	22	0	61	20	22		1.3	0	0	0
Ghaffari et al. [27]	Iran	2020	No-EPD	36	65 (11)	44	75	61.1	11.1	13.9	8.3	5.6	0	0	2.8
El-Sudany et al. [18]	Egypt	2021	No-EPD	91	63 (10)	37	100	82.4	25.3	65.9	37.4	0	1	0	0
Yabalak et al. [23]	Turkey	2021	EPD	35	69 (9)	23	86	65.7	37.1	57.7		2.9	0	2.9	2.9
Yabalak et al. [23]	Turkey	2021	No-EPD	16	70 (9)	25	81	0.01	56.3	50		0	12	0	0
Nazari et al. [34]	USA	2021	No-EPD	277		31	51	80.5		33.9	28.5	6.5		2.5	2.2
Nazari et al. [34]	USA	2021	EPD	923		33	46	84.4		34.3	27.2	2.1		2.1	1.1
Bastug et al. [3]	Turkey	2021	EPD	17	76 (7)	24	100	0.01	88.2	82.3	88.2	5.8	0	0	0

Embolic protection device (EPD); myocardial infraction (MI).

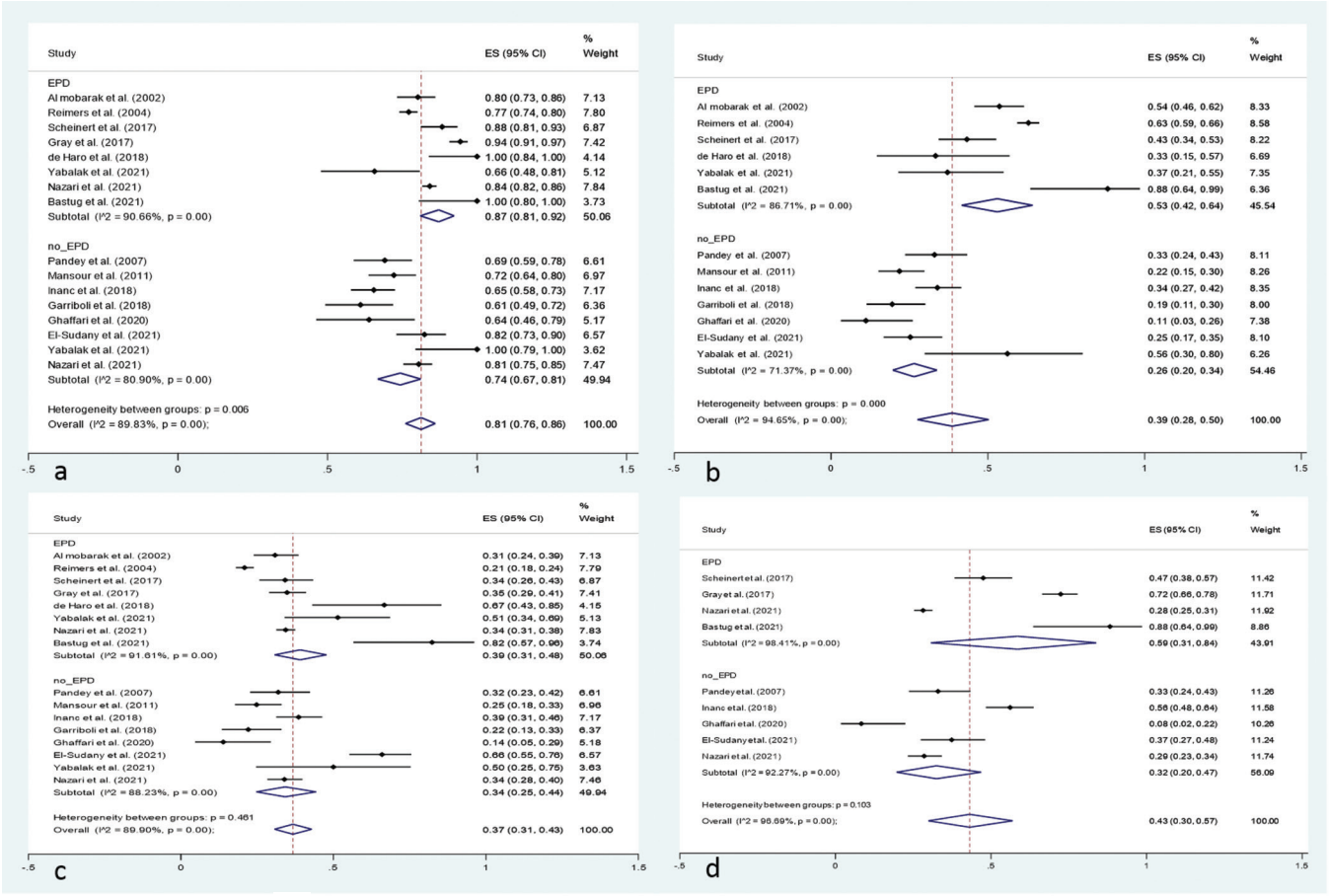

Figure 2 The prevalence of risk factors. Forest plot of the prevalence of hypertension (**a**), coronary artery disease (**b**), diabetes mellitus (**c**), and cigarette smoking (**d**) in patients who underwent carotid angioplasty and stenting (CAS). Each square shows the effect estimate of individual studies with their 95% CI. The size of the squares is proportional to the weight of each study in the meta-analysis. In this plot, studies are shown in the order of publication date and first author's names (based on a random-effects model). Effect size (ES).

eliminating three studies, 52% of included patients were symptomatic (95% CI: 0.41–0.64; I^2 = 98.0%), and by eliminating six studies, 48% of patients were asymptomatic (95% CI: 0.36–0.60; I^2 = 98%) (Figure 4). The prevalence of minor events in the study population of the articles included was about 2% (95% CI: 0.01–0.03; I^2 = 52.83%). Moreover, the prevalence of MI and major stroke was 1% (95% CI: 0.00–0.02; I^2 = 56.68%) and 2% (95% CI: 0.01–0.03; I^2 = 73.44%), respectively (Figure 5).

Meta-Regression

Since the heterogeneity in assessing the effects of using EPD in CAS was high, we used a meta-regression to determine the potential sources of heterogeneity. The results of the meta-regression analyses indicate that the association of death with either mean age or comorbidities, duration, smoking, being female, and symptoms of recently experienced cerebral vascular accidents was not statistically significant. Moreover, major adverse cardiovascular and cerebral events were not significantly related to the mentioned content in both groups. However, there was an exception, where we found that the prevalence of coronary artery disease as a risk factor was correlated with a higher mortality rate.

Subgroup Analysis

The results of subgroup analysis showed that the patients who received EPD during CAS were mostly asymptomatic [symptomatic: 41% (95% CI: 27–55; I^2 = 98.4%); asymptomatic: 59% (95% CI: 45–73; I^2 = 98.4%)], whereas in patients with no-EPD it was the opposite [symptomatic: 68% (95% CI: 56–80; I^2 = 86.1%); asymptomatic: 32% (95% CI: 21–44; I^2 = 85.0%)]. The mortality rate reduced from 2% (95% CI: 0.01–0.04; I^2 = 0.00%) in the no-EPD subgroup to 1% (95% CI: 0.00–0.01; I^2 = 0.00%) among the EPD subgroup. The occurrence of all other complications was also reportedly higher in patients who did not receive EPD, including major stroke [EPD subgroup: 1% (95% CI: 0.00–0.02; I^2 = 65.23%); no-EPD subgroup: 4% (95%CI:

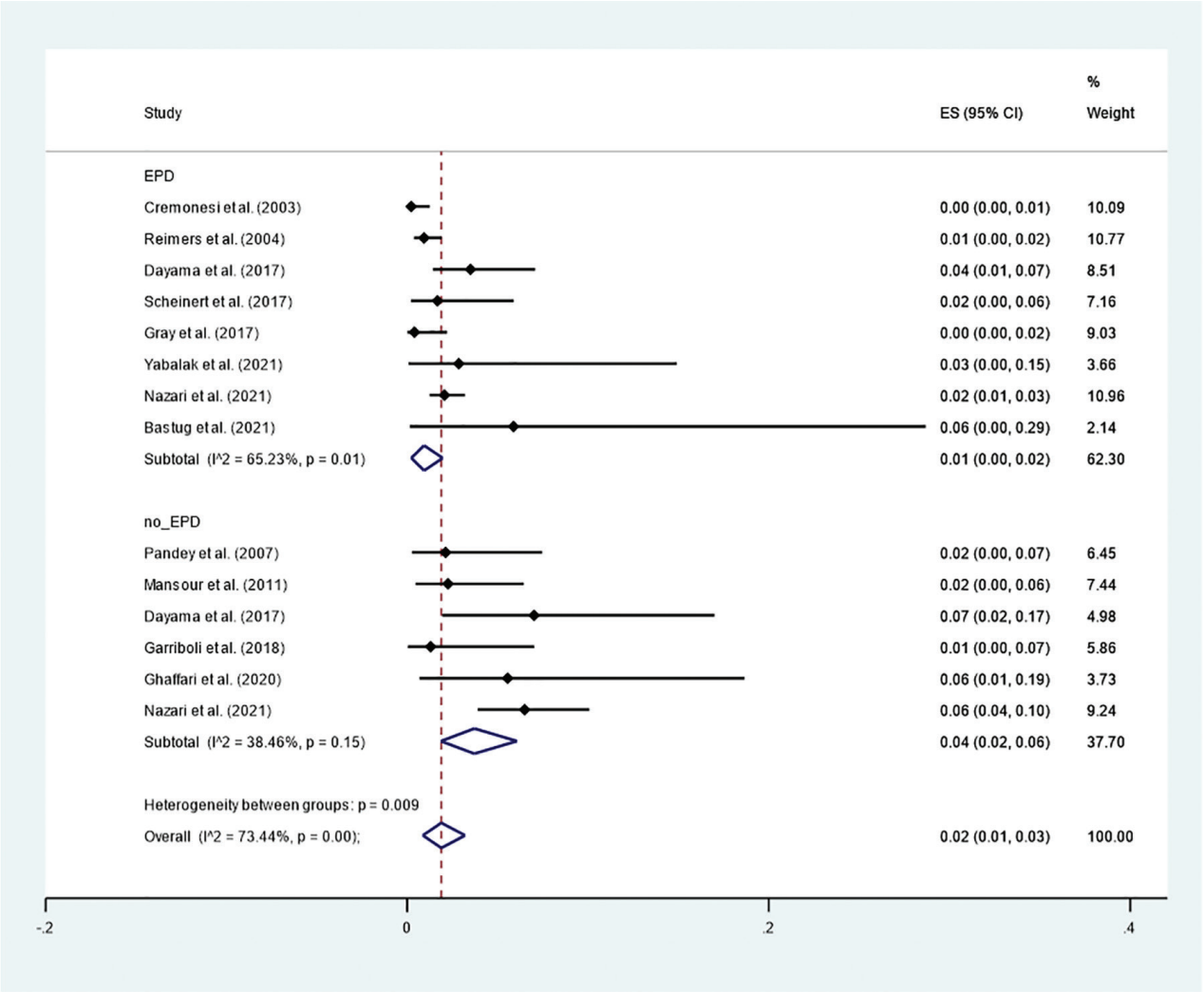

Figure 3 Forest plot of the prevalence of total death in patients who underwent CAS. Each square shows effect estimates of individual studies with their 95% CI. The size of the squares is proportional to the weight of each study in the meta-analysis. In this plot, studies are shown in the order of publication date and first author's names (based on a fixed-effects model). Effect size (ES).

0.02–0.06; I^2 = 38.46%)] and MI [EPD subgroup: 1% (95% CI: 0.00–0.02; I^2 = 62.16%); no-EPD subgroup: 2% (95% CI: 0.01–0.04; I^2 = 0.00%)], except for minor events [EPD subgroup: 2% (95% CI: 0.01–0.03; I^2 = 21.12%); no-EPD subgroup: 2% (95% CI: 0.01–0.03; I^2 = 0.00%)], which were reported to be almost identical in both subgroups (Table 3).

Publication Bias

Figure 6 demonstrates Begg's and Egger's funnel plots for relevant studies. Considering that there were no significant symmetries in Begg's (P = 0.047) and Egger's (P = 0.003) test results, it can be concluded that there was publication bias among the included studies. Also the risk of bias assessment was based on several criteria, including selection bias, comparability of study groups, and outcome reporting. Out of the total studies, six were classified as having a low risk of bias, indicated by higher total scores (7 to 10), suggesting a more robust methodological quality. Conversely, studies with intermediate risk of bias, scoring between 5 and 6, may have potential limitations that could influence the reliability of their findings. This distribution highlights the importance of considering bias when interpreting the study outcomes and their implications for broader application.

DISCUSSION

This systematic review and meta-analysis compared the rate of probable embolic events during CAS with and without EPD. We found that the application of an EPD

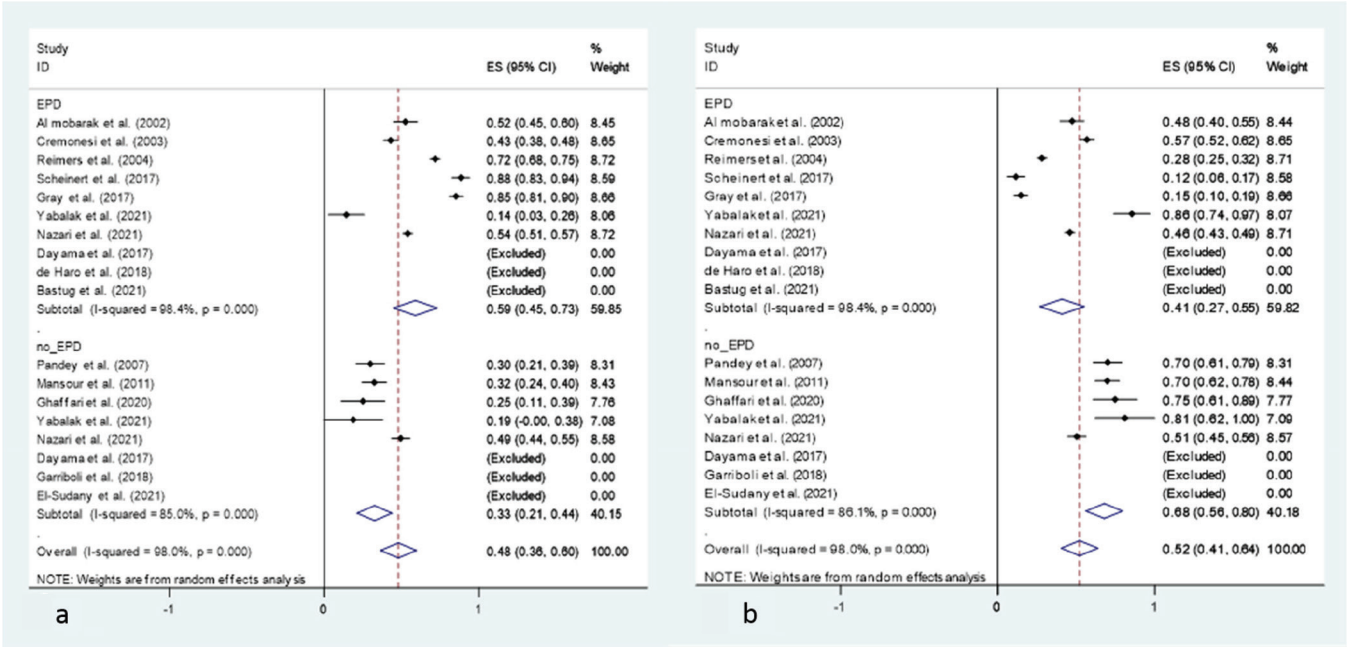

Figure 4 Prevalence of asymptomatic and symptomatic patients undergoing CAS. Forest plot of the prevalence of asymptomatic patients (**a**) and symptomatic (**b**) patients who underwent CAS. Each square shows the effect estimate of individual studies with their 95% CI. The size of the squares is proportional to the weight of each study in the meta-analysis. In this plot, studies are shown in the order of publication date and first author's names (based on a random-effects model). Effect size (ES).

during CAS can help with reducing the occurrence of thromboembolic complications of CAS, including MI, major stroke, and death.

CAS is a less invasive treatment method than carotid endarterectomy (CEA) and is usually recommended for surgical candidates with worse conditions [38]. In a meta-analysis, Sardar et al. showed that minor intraoperative stroke rates during CAS are higher than CEA [39]. Therefore, this increased risk of stroke in patients undergoing endovascular interventions for carotid artery disorders necessitates the use of a protective device during surgery. However, patients are not entirely protected by EPDs against these thromboembolic complications. Also, the placement of such devices is inherently risky. One possible risk is the long operation duration, which increases the chance of thromboembolism.

Previous studies have provided reasons and probable mechanisms for why EPDs fail to prevent the dislodgement of microemboli. In a survey conducted in the Netherlands, Vos et al. determined the presence of macro emboli, isolated microemboli, micro embolic showers, and distal thrombus with the transcranial Doppler ultrasound in two groups of patients who underwent CAS with and without EPD [40]. In their study, the number of microemboli in the group with an EPD was higher than in the group without an EPD. They explained that by capturing macro emboli, the EPD filter causes macro embolies to disintegrate and generate more microemboli. Moreover, according to the laboratory data they reported, there is still a potential space for embolic particles between the device and the vascular wall after EPD deployment. The results of a study by Pandey et al. [5] in the United States showed that there is no additional risk associated with placing an EPD during CAS, which is in line with the results of other studies, including those of Coward et al. [41], Cremonesi et al. [35], Gray et al. [42], Mas et al. [43], and White et al. [44].

In a meta-analysis by Cho et al. in 2018, including 25 articles, using an EPD was significantly associated with a lower occurrence of stroke after CAS ($P = 0.001$). The prevalence of cerebrovascular events in protected and unprotected CAS was 2.0% and 3.4%, respectively [45]. Our results are almost similar to their findings. At the same time, we also included the latest studies (over 70% of studies are after 2017), a larger sample size, subgroup analysis, and more complications (major stroke, minor events, MI, and total death) and comorbidities (hypertension, coronary artery disease, diabetes mellitus, and smoking).

Garg et al. compared the total incidence of stroke within 30 postoperative days between protected and unprotected CAS by pooling the data from 24 studies. Their findings indicated that protected CAS reduced stroke with a relative risk of 0.59 (95% CI: 0.47–0.73) compared with unprotected CAS [46]. A 4.7% (95% CI: 4.1–5.2) reduction in the risk of stroke after CAS was also reported by Touzé et al. [47]. By comparing long-term side effects between symptomatic and asymptomatic patients who underwent

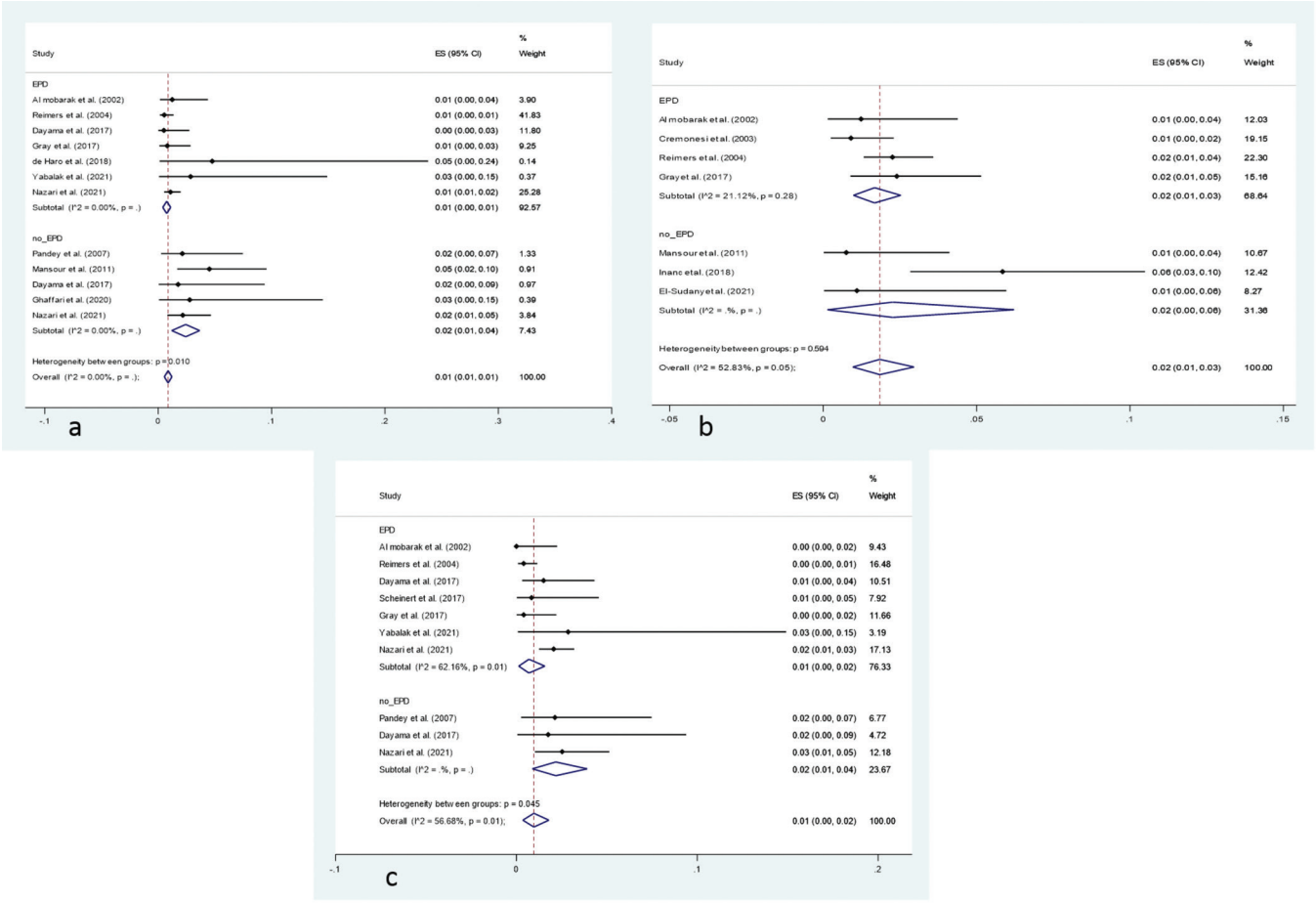

Figure 5 Prevalence of major stroke, minor events, and MI in patients undergoing CAS. Forest plot of the prevalence of major stroke (**a**), minor events (**b**), and MI (**c**) in patients who underwent CAS. Each square shows the effect estimate of individual studies with their 95% CI. The size of the squares is proportional to the weight of each study in the meta-analysis. In this plot, studies are shown in the order of publication date and first author's names (based on a random-effects model). Effect size (ES).

CAS, Kosowski et al. concluded that there was no statistically significant difference in stroke and death between the groups [48].

The filter deployed through the lesion during the procedure is at a higher risk of causing embolic events than other methods, such as proximal occlusion or flow reversal systems. This increased risk occurs because the filter may capture debris that dislodges from the lesion itself. Therefore, a proximal EPD can be more effective in preventing strokes during CAS, as it reduces the likelihood of embolic material travelling to the brain. Giri et al. compared the clinical outcome of events between distal and proximal protective devices during CAS, but the results were not significant based on the type of device (P = 0.07). However, proximal protective devices had higher rates of symptomatic lesion status [49]. Moreover, Zhan et al. revealed that stroke or death was not statistically different between groups that used filter (1.8%) and distal occlusion (2.3%) EPDs (odds ratio 1.04, P = 0.958) [50]. Furthermore, prospective trials are needed to compare the specificity and efficacy of the protective device with larger sample sizes and generalizable information.

Our analysis showed no significant association between cardiovascular risk factors and long-term complications. This can be attributed to the small sample size of the included studies, the shorter follow-up period, or the longer follow-up not being reported. However, according to our meta-regression analysis, the higher prevalence of cardiovascular disease was correlated with a higher mortality rate. This result can be justified by higher base-rate mortality in these patients and their higher susceptibility to endothelial injuries [51,52].

The study of the Paraskevas KI, referred to as The Carotid Revascularization Endarterectomy versus Stenting Trial (CREST), has been used to support the equivalence of CAS and CEA in the treatment of carotid stenosis in patients with symptoms or without symptoms. According to CREST data, there was no difference in outcome between CAS and CEA. However, subsequent subgroup analyses showed that CAS was associated with higher rates of stroke and mortality in symptomatic

Table 3 Statistical analysis of the reviewed studies. The studies were analyzed in terms of risk factors and, finally, in terms of the rate of major stroke, minor events, MI, and total death.

Data	*Variable*	*Number of Studies*	*Embolic Protection Device*	*Number of Patients*	*ES (95% CI)*	*I^2 (%)*
Demographic data	Mean age	13	EPD		71.80 (70.01–73.58)	94.7
			No-EPD		67.59 (65.38–69.80)	84.2
	Female	16	EPD	860	27% (22–33)	90.3
			No-EPD	311	33% (27–38)	64.3
	Symptomatic	15	EPD	1,086	41% (27–55)	98.4
			No-EPD	430	68% (56–80)	86.1
Comorbidities	Hypertension	14	EPD	1,891	87% (81–92)	90.66
			No-EPD	657	74% (67–81)	80.90
	Coronary artery disease	12	EPD	648	53% (42–64)	86.71
			No-EPD	169	26% (20–34)	71.37
	Diabetes mellitus	14	EPD	698	39% (31–48)	91.61
			No-EPD	313	34% (25–44)	88.23
	Smoking	9	EPD	513	59% (31–84)	98.41
			No-EPD	243	32% (20–47)	96.69
Complications and outcomes	Major stroke	16	EPD	38	1% (0–2)	65.23
			No-EPD	30	4% (2–6)	38.46
	Minor events	12	EPD	29	2% (1–3)	21.12
			No-EPD	12	2% (1–3)	0.0
	MI	14	EPD	28	1% (0–2)	62.16
			No-EPD	10	2% (1–4)	0.0
	Total death	16	EPD	21	1% (0–1)	0.0
			No-EPD	16	2% (1–4)	0.0

Embolic protection device (EPD); myocardial infraction (MI); effect size (ES).

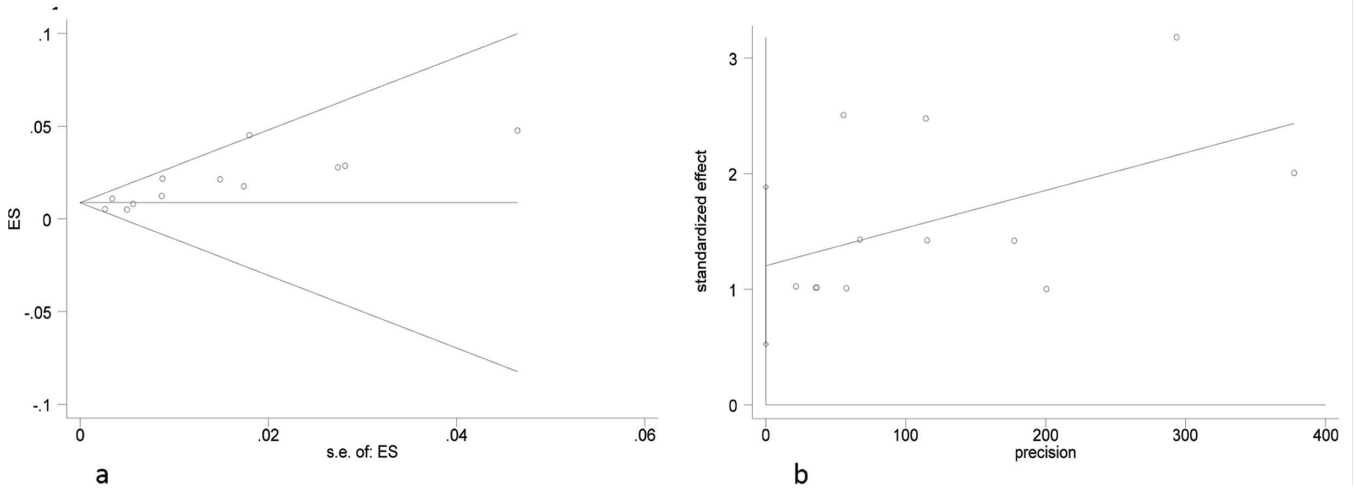

Figure 6 Publication bias. Begg's (**a**) and Egger's (**b**) funnel plots.

patients, women, and patients over 65 years of age compared with CEA. Thus, these data show that CEA and CAS are not equivalent, and CAS, until now, has a higher risk of stroke and death rates compared with CEA. Of course, it is worth mentioning that CREST used CAS technology and indications that are now expired [53].

This study had some limitations. A few studies reported data on other variables that a meta-analysis could not be performed on due to the small number of studies. Also, some studies had a high risk of bias. These factors can lead to limitations on the scope of research or the sample size. Also, some studies compare different types of devices, which leads to heterogeneity in our analysis, and non-English studies could not be included in our study.

Future research will expand the sample size, incorporate long-term outcomes, and evaluate emerging technologies in carotid artery stenting. Additionally,

cost-effectiveness and subgroup analyses, along with a potential randomized controlled trial, will be prioritized to enhance evidence quality and clinical practice.

CONCLUSION

In this systematic review and meta-analysis, we compared the rate of probable embolic events during CAS with and without using EPD. We found that the use of an EPD can help reduce the occurrence of perioperative complications of CAS, including MI, major stroke, and death. According to our meta-regression analysis, the prevalence of coronary artery disease as a risk factor was correlated with a higher mortality rate. Our results also showed that the patients who received an EPD during CAS were mostly asymptomatic, while in patients with no EPD usage, it was the opposite. Altogether, our results suggest that the benefits of using an EPD during CAS outweigh the risks of CAS.

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Conflict of Interest

The authors declare that they have no conflicts of interest.

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Availability of data, code and other materials

The datasets, analysis code, and any additional materials used in this study are available from the corresponding author upon reasonable request. Any proprietary software or data not freely available will be provided under appropriate agreements or licenses.

Registration and Protocol Information

No formal protocol was prepared prior to the study. As such, there were no amendments to any registration or protocol information. All procedures and methodologies were developed in accordance with standard systematic review practices.

Ethics Statement

(1) All the authors mentioned in the manuscript have agreed to authorship, read and approved the manuscript, and given consent for submission and subsequent publication of the manuscript.
(2) The authors declare that they have read and abided by the JEVTM statement of ethical standards including rules of informed consent and ethical committee approval as stated in the article.

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