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REVIEW

Editor's Choice – An Updated Systematic Review and Meta-analysis of Outcomes Following Eversion vs. Conventional Carotid Endarterectomy in Randomised Controlled Trials and Observational Studies

Kosmas I. Paraskevas [a,*], **Vaux Robertson** [b], **Athanasios N. Saratzis** [b], **A. Ross Naylor** [b]

[a] Department of Vascular and Endovascular Surgery, Royal Free Hospital, Royal Free London NHS Foundation Trust, London, UK
[b] The Department of Vascular Surgery, Leicester Royal Infirmary, Leicester, UK

WHAT THIS PAPER ADDS
Using combined data from randomised controlled trials and observational studies, eversion carotid endarterectomy (eCEA) was superior to conventional CEA (cCEA) regarding peri-operative outcomes (death, stroke, death/stroke) and late (>50%) restenosis. However, when eCEA outcomes were compared with outcomes after patched CEA, there were no significant differences. This updated meta-analysis suggests that early and late outcomes following cCEA are similar to eCEA, provided the arteriotomy is patched.

Introduction: A 2011 meta-analysis comparing eversion (eCEA) with conventional (cCEA) carotid endarterectomy in 16,251 patients concluded that eCEA was associated with lower rates of peri-operative stroke and late occlusion compared with cCEA. However, randomised controlled trials (RCTs) showed no difference in outcomes. Since then, the literature contains outcome data on 49,500 patients undergoing eCEA or cCEA. An updated meta-analysis was performed to establish whether eCEA confers significant benefit over cCEA.
Methods: This was a systematic review of PubMed/Medline, Embase, and Cochrane databases for RCTs and observational studies (OSs) comparing eCEA with cCEA. A sensitivity analysis was also performed using data from OSs with a Newcastle-Ottawa score >5.
Results: There were 25 eligible studies (5 RCTs, 20 OSs) involving 49,500 CEAs (16,249 eCEAs; 33,251 cCEAs). RCT data: Compared with cCEA, eCEA did not confer significant reductions in 30 day stroke, death, death/stroke, death/stroke/MI, or neck haematoma. However, eCEA was associated with reduced late restenosis (OR 0.40; $p = .001$). OS data: eCEA was associated with significant reductions in 30 day death (OR 0.46; $p < .0001$), stroke (OR 0.58; $p < .0001$), death/stroke (OR 0.52; $p < .0001$), death/stroke/MI (OR 0.50; $p < .0001$), and late restenosis (OR 0.49; $p = .032$) compared with cCEA. RCT and OS data combined: eCEA was associated with significant reductions in 30 day death (OR 0.55; $p < .0001$), stroke (OR 0.63; $p = .004$), death/stroke (OR 0.58; $p < .0001$), and late restenosis (OR 0.45; $p = .004$) compared with cCEA. eCEA vs. patched cCEA (RCT and OS data): There were no differences between the two procedures except for neck haematoma, where eCEA was better than patched cCEA.
Conclusions: Using combined RCT and OS data, eCEA was superior to cCEA regarding peri-operative outcomes (stroke, death, death/stroke) and late restenosis, but was similar to patched CEA in both early and late outcomes. This updated meta-analysis suggests that early and late outcomes following cCEA are similar to eCEA, provided the arteriotomy is patched.

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INTRODUCTION

Eversion (eCEA) and conventional carotid endarterectomy (cCEA) are the commonest techniques for performing CEA. Arteriotomy closure following cCEA is achieved by either direct closure (dCEA) or by patch angioplasty (pCEA). The main advantage of eCEA is that no prosthetic material is used. However, eCEA is limited by an inability to insert a

* Corresponding author. Department of Vascular and Endovascular Surgery, Royal Free Hospital, Royal Free London NHS Foundation Trust, Pond Street, London NW3 2QG, UK.
E-mail address: paraskevask@hotmail.com (Kosmas I. Paraskevas).
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shunt until the plaque has been removed and by a significantly higher incidence of post-CEA hypertension.[1] On the other hand, dCEA is associated with higher rates of peri-operative stroke, peri-operative thrombosis and higher rates of late restenosis and late ipsilateral stroke compared with routine pCEA,[2,3] while pCEA is vulnerable to late prosthetic patch infection in about 1% of patients.[4]

Several randomised controlled trials (RCTs) and observational studies (OSs) have compared eCEA with cCEA with regard to short-term outcomes (30 day stroke, 30 day death/stroke, 30 day death/stroke/myocardial infarction [MI], cranial nerve injury [CNI], neck haematoma, and 30 day internal carotid artery [ICA] thrombosis) as well as late outcomes (late restenosis, late ipsilateral stroke). A 2001 Cochrane systematic review of five RCTs comparing eCEA ($n = 1303$) with cCEA ($n = 1286$) reported no significant differences in peri-operative stroke (1.4% vs. 2.0%), peri-operative death (0.6% vs. 0.7%), peri-operative stroke and/or death (1.7% vs. 2.6%), peri-operative MI (0.5% vs. 0.6%), CNI (3.8% vs. 5.6%), and long-term stroke (1.4% vs. 1.7%).[5] However, the meta-analysis suggested that eCEA was associated with significantly lower rates of restenosis >50%, compared with cCEA (2.5% vs. 5.2%, $p = .00036$).[5] However, when pCEA was compared with eCEA, there were no significant differences in late restenosis.[5]

In 2011, an updated systematic review reported early and late outcomes following 8530 eCEAs and 7721 cCEAs.[6] This meta-analysis now included data from 7 RCTs and 15 OSs and reported that eCEA was associated with significant reductions in peri-operative stroke (OR 0.46; 95% CI 0.35—0.62; $p < .001$) and peri-operative death (OR 0.49; 95% CI 0.34—0.69; $p < .001$) compared with cCEA.[6] In addition, patients undergoing eCEA had significantly lower rates of late ICA occlusion (OR 0.48; 95% CI 0.25—0.90; $p = .02$) and late mortality (OR 0.76; 95% CI 0.61—0.94; $p = .001$).[6] Interestingly, with the exception of late ICA occlusion, each of these statistically significant differences were maintained in a further analysis comparing eCEA with pCEA.[6]

Since the 2011 meta-analysis was published,[6] the literature now contains outcome data on 49,500 patients undergoing either eCEA or cCEA. Given the discordance between the findings of the 2001 and 2011 meta-analyses (especially that eCEA may be safer than pCEA), a further meta-analysis was undertaken to determine whether eCEA conferred significant benefit over cCEA. If true, this would support preferential use of eCEA in an increasing majority of patients.

MATERIALS AND METHODS

A systematic review was conducted according to the recommendations of the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement (Fig. 1).[7] PubMed/Medline, Embase, and the Cochrane databases were independently searched by two investigators (KIP, VR) from December 30, 2010 (end of study inclusion of the previous meta-analysis)[6] until February 1, 2017 to identify studies comparing short (30 day) and late outcomes following eCEA and cCEA. Only those studies reporting outcome data for both eCEA and cCEA were included. If there was any disagreement between the two investigators, this was resolved either by consensus discussion or via referral to a third party (ARN). Data abstraction was performed independently and the results were subsequently compared between investigators.

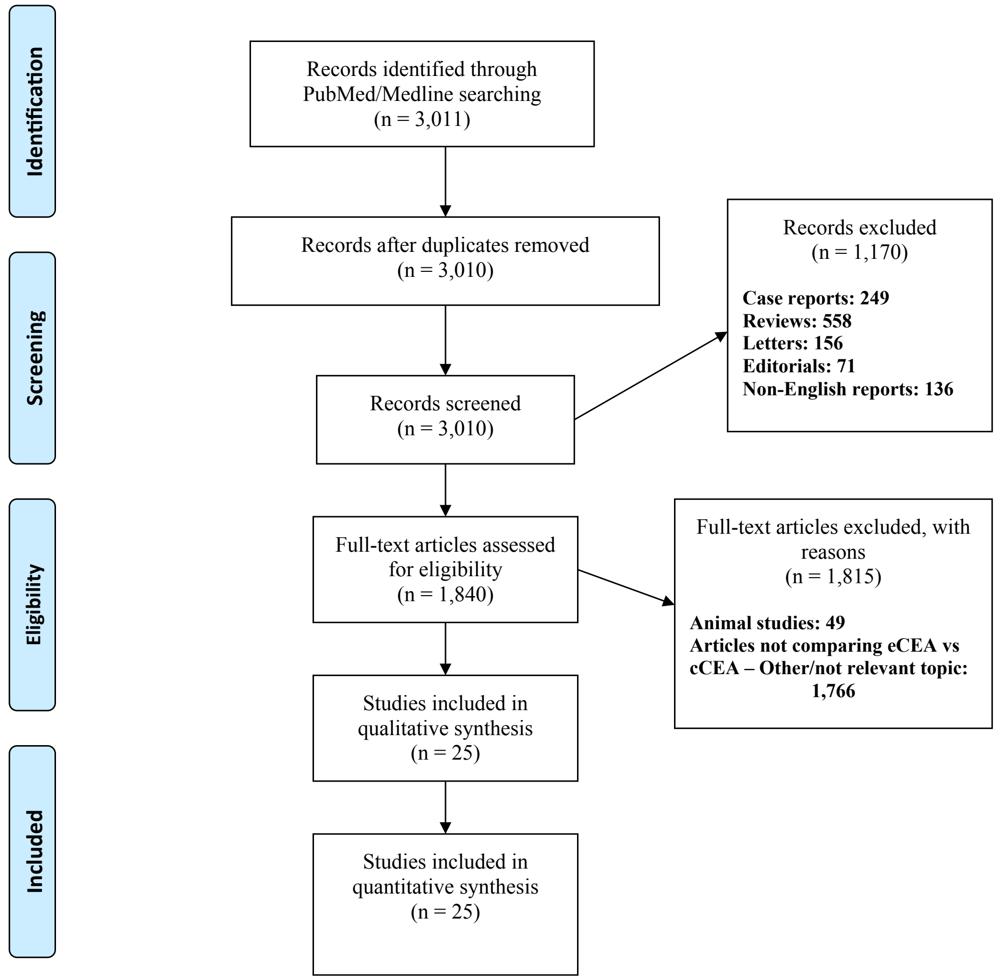
By use of the mesh term “carotid endarterectomy” and application of a filter “from 2010/12/30 to 2017/02/01,” a total of 3011 reports was identified. The abstracts were read to identify studies comparing outcomes after eCEA and cCEA. Only English language reports were considered.

The outcomes/endpoints that were compared between the two techniques included: (i) 30 day stroke; (ii) 30 day death; (iii) 30 day MI; (iv) 30 day stroke/death; (v) 30 day stroke/death/MI; (vi) 30 day neck haematoma; (vii) 30 day CNI; and (vii) late >50% restenosis.

Statistical analyses

Statistical analyses were performed using the R package for Microsoft Windows (version 3.0). Random and fixed effects meta-analyses were performed using the proportions of patients who experienced the outcome of interest in each case, as described above (stroke — 30 day or late, >50% restenosis, death, MI, neck haematoma). ORs with 95% CI were calculated for each study included in the final synthesis to assess the association between each type of carotid intervention and subsequent outcomes. Results from the various studies were combined in a stepwise manner: initially ORs were combined for both RCTs and OSs; subsequently, data were analysed separately for RCTs and OSs. For those studies where one arm reported no post-operative events but another arm reported at least one event, a fixed factor of 0.5 was added to cells of the study results with zero events to calculate an appropriate OR and allow synthesis. This type of continuity correction is a well established approach to incorporate zero event studies and 0.5 is the commonest choice of correction factor. ORs were then combined using meta-analysis (fixed and random effects models, where appropriate). Inter-study heterogeneity was analysed using the I^2 statistic in all analyses. This describes the percentage of total variation across studies because of heterogeneity, rather than chance or random error and is a recognised method of quantifying heterogeneity in literature synthesis. An I^2 value $\geq$ 50% reflects significant heterogeneity owing to real differences in study populations, protocols, interventions, and outcomes. Based on the result of the I^2 statistic, a fixed effects model was used to combine studies if I^2 was <50% and a random effects model if I^2 was $\geq$50%. A p value $< .05$ was considered to be statistically significant.

To minimise bias through the inclusion of poorer quality OSs, a sensitivity analysis was also performed which used data from OSs in which the Newcastle-Ottawa score (NOS) was >5 (i.e. studies deemed better quality methodologically). Given the nature of the studies included in the



*Of these 520 non-English reports, 147 were in German, 108 in Chinese, 120 in Japanese, 57 in Russian, 38 in French, 37 in Spanish and 13 in other language (e.g. Croatian, Bulgarian)

Figure 1. PRISMA 2009 flow diagram.

literature synthesis (OSs combined with RCTs), the significant heterogeneity in most of these series (as reflected by the I^2 statistics in most instances), and the significant differences in terms of the size/effect among the observational cohorts, weighted proportions were reported for all analyses.

RESULTS

The systematic review

By use of the mesh term "carotid endarterectomy" and application of a filter "from 2010/12/30 to 2017/02/01," a total of 3011 reports were identified. After duplicate publications were excluded, 3010 reports were screened, after which 1170 studies were excluded (reasons for exclusion are given in Fig. 1). A total of 1840 articles were subsequently assessed for eligibility, following which 1815 articles were excluded (Fig. 1). This left 25 papers for qualitative and quantitative synthesis (Table 1).[8–32]

Of the 25 papers, 5 were RCTs[14,15,18,26,30] while the remaining 20[8–13,16,17,19–25,27–29,31,32] were OSs. A total of 49,500 CEA procedures were included, with 16,249 patients undergoing eCEA and 33,251 patients undergoing cCEA. Some studies included patch closure CEAs only[9,13–16,19,21,22,25,27,30,31] or primary closure CEA only.[24] Others included both pCEA and dCEA,[8,17,18,20,23,26,29,32] while some did not specify how the arteriotomy was closed.[10–12,28] Finally some studies did not specifically differentiate outcomes between pCEA and dCEA.[10–12,17,18,26,28,29,32] An assessment of the methodological quality of the included studies using the Cochrane risk of bias assessment tool for the RCTs and the NOS for the OSs is presented in Tables 2 and 3, respectively.

RCT data only

Table 4 summarises the main outcome analyses for when eCEA was compared with cCEA in RCT data only. Compared with cCEA, eCEA did not confer significant reductions in (i) 30 day stroke, (ii) 30 day death, (iii) 30 day death/stroke, (iv) 30 day MI, (v) 30 day death/stroke/MI, (vi) CNI, and (vii) neck haematoma. However, eCEA was associated with a

Table 1. List of the studies included in the meta-analysis with the short and long-term outcomes investigated.

Study (year)	Total	eCEA	cCEA	Death	Stroke	MI	Death/stroke	Death/stroke/MI	Mean follow-up (months)	Restenosis	Cranial nerve injury	Neck Haematoma
Ballotta[14] (1999)[a]	336	169	167p	√	√	√	√	√	34 (1–69)[b]	√	√	√
Ballotta[15] (2000)[a]	136	68	68p	√	√	NM	√	NM	40 (6–69)[b]	√	√	√
Brothers[16] (2005)	200	100	100p	√	√	√	√	√	36	√	NM	NM
Cao[17] (1997)	514	274	118p; 122dc	√	√	NM	√	NM	28 (12–54)[b]	√	NM	NM
Cao[18] (1998)[a]	1353	678	256p; 419dc	√	√	√	√	√	33 (12–55)[b]	√	√	√
Crawford[19] (2007)	290	135	155 p	√	√	√	√	√	55 (12–140)[b]	√	√	√
Economopoulos[20] (1999)	190	33	142p; 15dc	√	√	√	√	√	16 (0–48)[b]	√	√	√
Entz[21] (1997)	1454	739	715p	√	√	NM	√	NM	36	NM	NM	NM
Green[22] (2000)	274	107	167p	√	√	NM	√	NM	12	√	NM	√
Katras[23] (2001)	322	118	107p; 97dc	√	√	√	√	√	23 (6–42)[b]	√	√	√
Kieny[24] (1993)	368	212	156dc	NM	NM	NM	NM	NM	44	√	NM	NM
Littooy[25] (2004)	189	64	125p	√	√	NM	√	NM	17 (3–42)[b]	√	√	NM
Markovic[26] (2008)[a]	201	103	77p; 21dc	√	√	√	√	√	38 (24–52)[b]	√	√	NM
Peiper[27] (1999)	863	475	388p	√	√	NM	√	NM	31	√	√	√
Radak[28] (2000)	2806	2124	682	√	√	√	√	√	56 (6–92)[b]	√	√	√
Shah[29] (1998)	2723	2249	73p; 401dc	√	√	√	√	√	18 (1–52)[b]	√	√	√
Vanmaele[30] (1994)[a]	200	102	98p	√	√	NM	√	√	12 ± 0.8[c]	√	√	NM
Winkler[31] (2006)	116	51	65p	√	√	NM	√	NM	18 (6–42)[b]	NM	NM	NM
Wistrand[32] (2010)	171	73	65p; 33dc	√	√	√	√	√	76	NM	NM	√
Ben Ahmed[13] (2015)	560	220	340p	√	NM	NM	NM	NM	NM	NM	NM	√
Demirel[9] (2012)	516	206	310p	√	√	√	√	√	24	NM	√	√
Lee[10] (2014)	120	57	63	√	√	√	√	√	29.4 ± 23.5[c]	√	√	NM
Menyhei[8] (2011)	15,698	5349	6226p; 4123dc	√	√	NM	√	NM	NM	NM	√	NM
Schneider[12] (2015)	19,520	2365	17,155	NM	√	√	NM	NM	12	NM	√	√
Yasa[11] (2014)	380	178	202	√	√	√	√	√	26 (14–38)[b]	√	√	√
Total	49,500	16,249	33,251									

eCEA = eversion carotid endarterectomy; cCEA = conventional carotid endarterectomy; MI = myocardial infarction; p = patch; dc = direct closure; √ = data included; NM = not mentioned.

[a] RCT.

[b] Results presented as mean (range).

[c] Results presented as mean ± standard deviation.

Table 2. Assessment of the methodological quality of the included randomised controlled trials using the Cochrane risk of bias assessment tool.

Reference (year)	Random sequence generation	Allocation concealment	Binding of participant/ personnel	Binding of outcome assessment	Incomplete outcome data
Vanmaele et al[30] (1994)	Low	High	High	Low	High
Cao et al[18] (1998)	Low	High	High	Low	Low
Ballotta et al[14] (1999)	Low	High	High	Low	Low
Ballotta et al[15] (2000)	Low	High	High	Low	High
Markovic et al[26] (2008)	Low	High	High	Low	High

Table 3. Assessment of the methodological quality of the included observational studies using the Newcastle-Ottawa score.

Study (year)	Selection (maximum 4 stars)	Comparability (maximum 2 stars)	Outcome (maximum 3 stars)	Total Newcastle-Ottawa score
Kieny et al[24] (1993)	2	1	1	4
Cao et al[17] (1997)	3	2	1	6
Entz et al[21] (1997)	2	1	1	4
Shah et al[29] (1998)	3	2	2	7
Economopoulos et al[20] (1999)	3	2	3	8
Peiper et al[27] (1999)	2	1	1	4
Radak et al[28] (2000)	3	2	2	7
Green et al[22] (2000)	3	2	1	6
Katras et al[23] (2001)	3	2	2	7
Littooy et al[25] (2004)	3	1	2	6
Brothers[16] (2005)	3	2	1	6
Winkler et al[31] (2006)	2	1	1	4
Crawford et al[19] (2007)	3	2	3	8
Wistrand et al[32] (2010)	2	2	2	6
Menyhei et al[8] (2011)	4	1	2	7
Demirel et al[9] (2012)	3	2	1	6
Lee and Suh[10] (2014)	3	2	2	7
Yasa et al[11] (2014)	3	2	3	8
Schneider et al[12] (2015)	2	1	1	4
Ben Ahmed et al[13] (2015)	2	1	1	4

Table 4. Comparison of 30 day outcomes between eversion carotid endarterectomy (eCEA) vs. conventional carotid endarterectomy (cCEA)[a] using randomised controlled trial (RCT) data only.

Outcome	Total number of patients		Weighted proportions		OR (95% CI)	p	I^2
	eCEA	cCEA	eCEA	cCEA			
30 day stroke	1157	1249	1.72%	2.67%	0.57 (0.31—1.04)	.07	45.3%
30 day death	1157	1249	1.11%	1.70%	0.75 (0.34—1.70)	.50	38.1%
MI	1089	1181	0.79%	0.69%	1.13 (0.39—3.25)	.81	0%
30 day stroke/death	1157	1249	2.66%	4.32%	0.37 (0.11—1.28)	.12	65.9%
30 day stroke/death/MI	1089	1181	3.32%	5.62%	0.51 (0.18—1.46)	.21	68.5%
Recurrent stenosis	951	939	1.98%	4.54%	0.40 (0.23—0.69)	**.001**	**0%**
Cranial nerve injury	1157	1249	3.89%	6.66%	0.68 (0.45—1.01)	.06	49.5%
Neck haematoma	952	1053	3.88%	6.19%	0.69 (0.27—1.77)	.44	66.7%

MI = myocardial infarction.
All significant p values are marked in bold.
[a] Conventional CEA included patients undergoing either primary closure or patch closure of the arteriotomy.

significant reduction in late >50% restenosis, but not late ipsilateral stroke.

OS data only

Table 5 summarises the main outcome analyses for when eCEA was compared with cCEA in OS data. Compared with cCEA, eCEA was associated with significant reductions in (i) 30 day ipsilateral stroke, (ii) 30 day death, (iii) 30 day death/stroke, (iv) 30 day death/stroke/MI, and (v) late >50% restenosis. There were no differences in 30 day rates of MI, CNI, or neck haematoma. A sensitivity analysis (using only OSs with a NOS >5) showed similar findings (Table 5).

RCT and OS data combined

Table 6 summarises the main outcome analyses for when eCEA was compared with cCEA in combined RCT and OS data. Compared with cCEA, eCEA was associated with significant reductions in (i) 30 day ipsilateral stroke, (ii) 30 day

Table 5. Comparison of outcomes between eversion CEA (eCEA) vs. conventional CEA (cCEA)[a] using data derived from observational studies only.

Outcome	Total meta-analysis							Sensitivity analysis (involving only those observational studies with NOS>5)[b]				
	Weighted proportions		Total number of patients		OR (95% CI)	p	I^2	Weighted proportions		OR (95% CI)[b]	p	I^2
	eCEA	cCEA	eCEA	cCEA				eCEA	cCEA			
30 day stroke	1.18%	2.14%	11,067	9203	0.58 (0.49—0.71)	**<.0001**	1.5%	1.56%	3.03%	0.62 (0.51—0.75)	**<.0001**	38.6%
30 day death	0.83%	1.49%	11,067	9203	0.46 (0.32—0.67)	**<.0001**	0%	0.83%	1.30%	0.57 (0.42—0.76)	**.0002**	0%
MI	0.91%	0.89%	5273	2445	1.01 (0.71—1.44)	.94	0%	0.90%	0.89%	1.09 (0.61—1.94)	.78	0%
30 day stroke/death	2.26%	4.32%	11,067	9203	0.52 (0.44—0.61)	**<.0001**	0%	2.36%	4.21%	0.59 (0.50—0.70)	**<.0001**	39.6%
30 day stroke/death/MI	2.62%	4.78%	5273	2445	0.50 (0.38—0.67)	**<.0001**	0%	3.17%	4.69%	0.69 (0.53—0.90)	**.007**	46.7%
Recurrent stenosis	2.34%	4.68%	5439	2569	0.49 (0.25—0.94)	**.032**	77.9%	2.77%	4.31%	0.63 (0.30—1.33)	.22	78%
Cranial nerve injury	2.52%	4.08%	10,513	8598	0.76 (0.37—1.56)	.46	93%	1.97%	3.22%	0.71 (0.29—1.78)	.47	88.6%
Neck haematoma	2.70%	2.04%	5116	2282	1.25 (0.82—1.90)	.31	49.2%	3.80%	2.56%	1.34 (0.95—1.90)	.10	27.6%

NOS = Newcastle Ottawa scale; eCEA = eversion carotid endarterectomy; cCEA = conventional carotid endarterectomy; MI = myocardial infarction.

All significant p values are marked in bold.

[a] Conventional CEA included patients undergoing either primary closure or patch closure of the arteriotomy.

[b] Sensitivity analysis (which included only those observational studies with a NOS score >5). See Methods for details.

Table 6. Comparison of outcomes between eversion CEA (eCEA) vs. conventional CEA (cCEA)[a] using combined data from randomised controlled trials and observational studies.

Outcome	Total meta-analysis							Sensitivity analysis (involving only those observational studies with NOS>5)[b]				
	Total number of patients		Weighted proportions		OR (95% CI)	p	I^2	Weighted proportions		OR (95% CI)[b]	p	I^2
	eCEA	cCEA	eCEA	cCEA				eCEA	cCEA			
30 day stroke	15,817	28,632	1.38%	2.33%	0.63 (0.46—0.86)	**.004**	40.7%	1.49%	2.99%	0.61 (0.51—0.86)	**<.0001**	36.1%
30 day death	13,672	11,817	0.86%	1.52%	0.55 (0.43—0.72)	**<.0001**	0%	0.86%	1.36%	0.60 (0.45—0.79)	**<.0001**	0.0%
MI	8690	20,638	0.95%	0.91%	1.04 (0.75—1.45)	.82	0%	0.89%	0.84%	1.09 (0.66—1.82)	.72	0%
30 day stroke/death	13,452	11,477	2.35%	4.3%	0.58 (0.50—0.67)	**<.0001**	48.3%	2.37%	4.22%	0.59 (0.42—0.82)	**<.0001**	48.3%
30 day stroke/death/MI	6325	3483	3.19%	4.74%	0.68 (0.45—1.02)	.065	50.9%	2.27%	5.01%	0.33 (0.13—0.86)	.17	32.5%
Recurrent stenosis	7246	4219	2.02%	4.71%	0.45 (0.26—0.78)	**.004**	72.5%	2.01%	4.15%	0.53 (0.29—0.95)	**.033**	72.5%
Cranial nerve injury	14,473	27,247	2.77%	4.82%	0.69 (0.40—1.22)	.205	90.4%	2.31%	4.29%	0.63 (0.32—1.24)	.178	86.3%
Neck haematoma	9091	21,075	3.04%	2.49%	1.27 (1.01—1.58)	.037	43.2%	3.30%	2.97%	1.13 (0.86—1.49)	.037	44.3%

eCEA = eversion carotid endarterectomy; cCEA = conventional carotid endarterectomy; NOS = Newcastle Ottawa scale; MI = myocardial infarction.

All significant p values are marked in bold.

[a] Conventional CEA included patients undergoing either primary closure or patch closure of the arteriotomy.

[b] Sensitivity analysis (which included only those observational studies with a NOS score >5). See Methods for details.

death, (iii) 30 day death/stroke, (iv) neck haematoma, and (v) late >50% restenosis. There were no differences in 30 day MI, 30 day death/stroke/MI, or CNI. A sensitivity analysis (using only OSs with a NOS >5) showed similar findings (Table 6).

Eversion CEA vs. patched CEA in RCTs and OSs

Table 7 summarises the main outcome analyses for when eCEA was compared with outcomes in patients undergoing patched CEA in combined RCT and OS data. Compared with pCEA, eCEA was not associated with significant reductions in (i) 30 day death, (ii) 30 day stroke, (iii) 30 day MI, (iv) 30 day death/stroke, (v) CNI, (vi) neck haematoma, or (vii) late >50 restenosis. On the other hand, eCEA was associated with lower rates of 30 day stroke/death/MI, but because of small numbers, the statistical analysis did not produce reliable outcomes. eCEA was associated with lower rates of neck haematoma compared with pCEA. A sensitivity analysis (using only OSs with a NOS >5) showed similar findings (Table 7). Furthermore, eCEA was now associated with lower rates of CNI compared with pCEA.

DISCUSSION

There are several methods of performing CEA, each with their own inherent advantages and disadvantages. In the first meta-analysis of RCT outcomes in 2001, there were no significant differences between cCEA and eCEA, except for a higher rate of late restenosis (>50%) following cCEA, although this disappeared when pCEA was compared with eCEA (i.e. having excluded dCEA patients).[5] By 2011, however, an updated meta-analysis (involving a much larger cohort of patients from mainly non-randomised studies)

Table 7. Comparison of 30 day outcomes between eversion CEA (eCEA) vs. patched CEA (pCEA) using data from randomised controlled trials and observational studies.

Outcome	Total meta-analysis							Sensitivity analysis (involving only those observational studies with NOS>5)[a]				
	Total number of patients		Weighted proportions		OR (95% CI)	p	I^2	Weighted proportions		OR (95% CI)[a]	p	I^2
	eCEA	pCEA	eCEA	pCEA				eCEA	pCEA			
30 day stroke	7565	8584	1.38%	1.93%	0.71 (0.37—1.36)	.30	58.7%	1.41%	1.85%	0.81 (0.39—1.68)	.57	48.3%
30 day death	7785	8924	0.86%	1.12%	0.64 (0.35—1.18)	.15	68.7%	0.73%	0.77%	0.95 (0.64—1.42)	.90	0%
MI	371	365	0.77%	0.89%	0.98 (0.17—5.69)	.98	0%	0.77%	0.89%	0.98 (0.17—5.69)	.98	0%
30 day stroke/death	7565	8584	2.35%	3.31%	0.64 (0.35—1.18)	.15	71.3%	2.14%	3.44%	0.57 (0.28—1.18)	.13	71.8%
30 day stroke/death/MI	371	365	3.19%	5.42%	—[b]	—[b]	—[b]	3.19%	5.42%	—[b]	—[b]	—[b]
Recurrent stenosis	1220	1268	2.02%	6.21%	0.68 (0.24—1.95)	.47	84.6%	5.15%	5.46%	0.84 (0.27—2.66)	.77	79.9%
Cranial nerve injury	6227	7072	4.82%	7.18%	0.50 (0.20—1.28)	.15	89.9%	2.32%	6.19%	0.37 (0.19—0.74)	**.005**	91%
Neck haematoma	932	963	3.04%	3.62%	0.53 (0.30—0.95)	**.03**	0%	4.78%	10.25%	0.43 (0.20—0.90)	**.02**	0.0%

eCEA = eversion carotid endarterectomy; pCEA = patched carotid endarterectomy; NOS = Newcastle Ottawa scale; MI = myocardial infarction.

[a] Sensitivity analysis (which included only those observational studies with a NOS score >5). See Methods for details.

[b] The small number of patients with available data meant that calculations were deemed inaccurate.

now suggested that eCEA conferred significant benefits relating to 30 day death, 30 day stroke, 30 day death/stroke, as well as lower rates of restenosis and late ipsilateral stroke. More importantly, these differences remained statistically significant when eCEA was compared with pCEA.[6]

The current meta-analysis benefits from having three times the number of patients that were included in the 2011 meta-analysis.[6] If its findings corroborated the 2011 findings (especially if eCEA was superior to pCEA), this would constitute compelling evidence for preferentially performing eCEA over either dCEA or pCEA.

As was observed with the 2011 meta-analysis,[6] combined RCT and OS data involving >49,000 patients in the 2017 updated meta-analysis suggested that eCEA conferred significant benefits over cCEA in terms of 30 day (reduced mortality, reduced death/stroke) and late outcomes (lower rates of restenosis). However, when the analysis was solely confined to RCTs, the findings were almost identical to those of the 2001 meta-analysis.[5] In short, eCEA conferred no significant benefit in terms of 30 day risk, although eCEA was associated with a significantly lower rate of late restenosis.[5] However, these findings are not unexpected as only one further RCT was added to the literature between 2002 and 2017.[26]

So how should the findings of the 2017 meta-analysis influence contemporary clinical practice? Before concluding that eCEA is preferable to cCEA, the key message still appears to be the importance of stratifying for whether cCEA patients underwent primary arteriotomy closure or patch angioplasty. A meta-analysis of 10 RCTs (2157 patients), which compared routine patching versus routine primary closure, observed that routine patching was associated with significant reductions in 30 day ipsilateral stroke, compared with routine primary closure (patch 1.5% vs. 4.5% for primary closure; OR 0.2; 95% CI 0.1—0.6; $p = .001$), along with significant reductions in 30 day ICA thrombosis (0.5% pCEA vs. 3.1% for dCEA; OR 0.18; 95% CI 0.16—0.76; $p = .0011$).[2] In addition, routine patching was associated with significantly lower rates of late restenosis (4.3% pCEA vs. 13.8% dCEA; OR 0.24; 95% CI 0.17—0.34; $p < .01$), as well as significant reductions in late ipsilateral stroke (1.6% pCEA vs. 4.8% dCEA; OR 0.32; 95% CI 0.16—0.63; $p = .001$).[2]

When data from RCTs and OSs were combined in the current meta-analysis and then stratified for whether the conventional CEA patient underwent either primary closure or patch angioplasty, all of the significant benefits apparently conferred by eCEA disappeared (Table 7). Compared with pCEA, eCEA was now not associated with significant reductions in (i) 30 day death, (ii) 30 day death/stroke, or (iii) late >50% restenosis. Accordingly, the data from the updated 2017 meta-analysis suggest that patients undergoing cCEA have very similar 30 day outcomes as well as late outcomes to patients undergoing eCEA, provided the arteriotomy is patched.

The present meta-analysis does have limitations. Ideally, dCEA should be compared separately with pCEA and with eCEA. However, some studies did not differentiate outcomes between dCEA and pCEA patients.[10—12,17,18,26,28,29,32] In addition, in some of the studies that included pCEA only, there was inconsistency in the type of patch used (prosthetic vs. autologous vein).[8,12] The quality of some OSs was low (NOS <5).[12,13,21,24,27,31] However, a sensitivity analysis (which excluded OSs with a NOS <5) did not observe any changes in the principle findings that had been reported for the cohort as a whole (30 day stroke, 30 day death, 30 day MI, 30 day stroke/death, 30 day stroke/death/MI, and late >50% restenosis). The percentage of symptomatic/asymptomatic patients and the time from the occurrence of the cerebrovascular event to CEA varied both within, as well as between studies. In addition, the majority of studies did not use a randomisation protocol for the selection of eCEA or pCEA. The potential for overlap between two studies from the same centre[14,15] is recognised. Cao et al published two consecutive series on outcomes after cCEA and eCEA, but there was no overlap in terms of patient recruitment.[17,18] By contrast, Ballotta published two sequential studies on eCEA and cCEA, where a small number of patients ($n = 26$) were common to both cohorts.[14,15] Finally, three studies[23,29,30] reported >60% (instead of >50%) restenosis rates, while another reported restenosis rates >80%.[20] The results of the present meta-analysis are in agreement with the 2017 European Society for Vascular Surgery (ESVS) guidelines for the management of atherosclerotic carotid and vertebral artery disease,[33] which suggested that eCEA provides equivalent outcomes to cCEA provided the arteriotomy is closed with a patch.

In conclusion, this updated systematic review and meta-analysis reporting outcomes in nearly 50,000 CEA procedures has shown that eCEA was associated with similar outcomes to cCEA, provided the arteriotomy was closed with a patch.

CONFLICT OF INTEREST

None.

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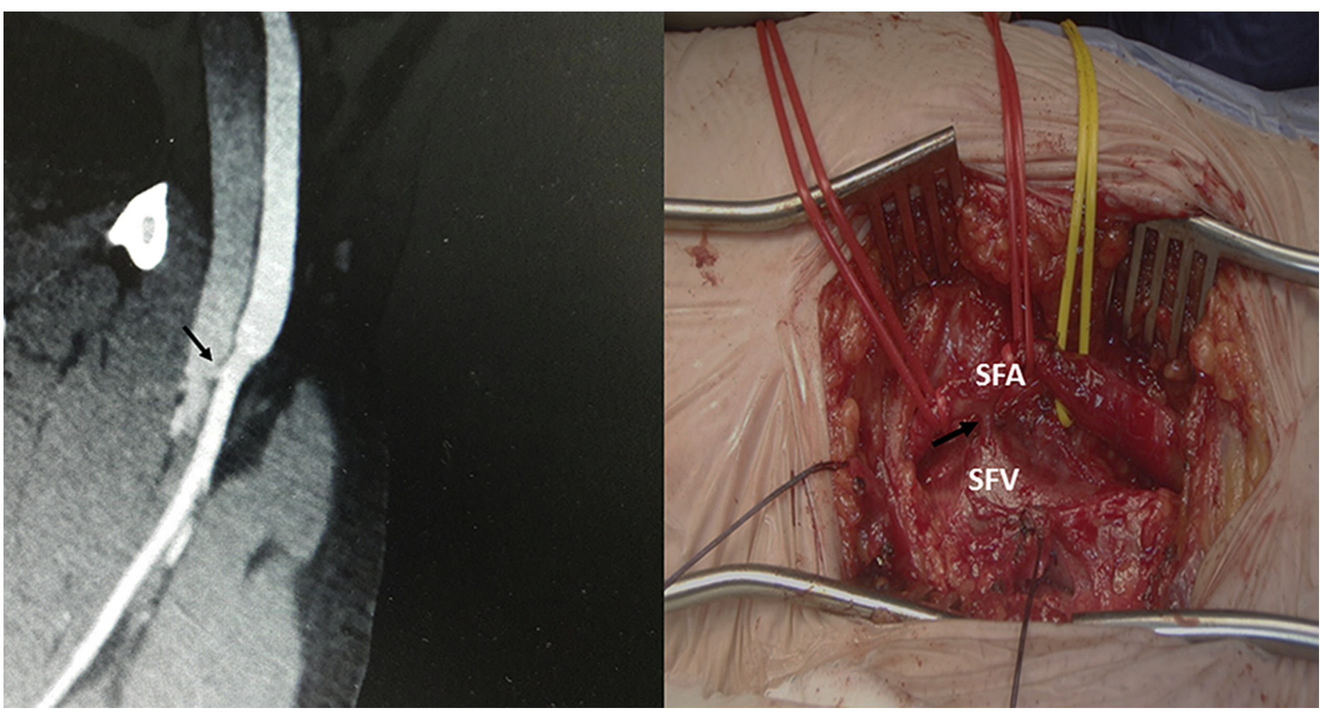
COUP D'OEIL

Secondary Varicose Veins — An Uncommon Way to Present

Amber Dhillon [b], **Sriram Rajagopalan** [a,*]
[a] Royal Stoke University Hospital, Stoke on Trent, UK
[b] Keele Medical School, UK



A 37 year old male attended with right sided great saphenous vein (GSV) varicosity. Duplex scan suggested arterial waveforms in the superficial femoral vein (SFV) with communication to superficial femoral artery (SFA) and an incompetent GSV. Patient history and records excluded previous groin interventions or injections. Computed tomography angiography confirmed the presence of an arteriovenous fistula (AVF). Surgical exploration revealed normal tissue planes with a 4 mm long AVF between SFA and SFV. Secondary varicose veins caused by isolated groin AVF are rare but need distinction before intervention. Duplex scan in varicose vein practice is integral to identifying these uncommon, yet treatment changing, scenarios.

* Corresponding author. Vascular secretariat, Parish Building (A block), Royal Stoke University Hospital, Stoke on Trent ST46QG, UK.
E-mail address: surgeryram@doctors.org.uk (Sriram Rajagopalan).

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