Eur J Vasc Endovasc Surg (2023) 65, 467–473

Editor's Choice – Nationwide Outcome Analysis of Primary Carotid Endarterectomy in Symptomatic Patients Depending on Closure Technique and Patch Type

Magnus Jonsson [a,b,*], **Kimberley Hammar** [c], **Malin Lindberg** [a], **Annika Lundström** [c], **Mikael A. Franko** [d], **Ann-Charlotte Laska** [c], **Per Wester** [c,e], **Kevin Mani** [f]

[a] Department of Molecular Medicine and Surgery, Karolinska Institute, Stockholm, Sweden
[b] Department of Vascular Surgery, Karolinska University Hospital, Stockholm, Sweden
[c] Department of Clinical Sciences, Danderyd Hospital, Division of Neurology, Karolinska Institute, Stockholm, Sweden
[d] Department of Clinical Science and Education, Södersjukhuset, Karolinska Institute, Stockholm, Sweden
[e] Department of Public Health and Clinical Medicine, Umeå University, Umeå, Sweden
[f] Section of Vascular Surgery, Department of Surgical Sciences, Uppsala University, Uppsala, Sweden

WHAT THIS PAPER ADDS

Closure of the arteriotomy for carotid endarterectomy is controversial. Previous randomised controlled trials have shown the benefit of routine patch closure over routine primary closure; however, many surgeons still prefer selective patch closure to minimise carotid clamp time and avoid using prosthetic material. The present study shows that primary closure should be avoided and that endarterectomy should be performed with either routine patch closure or using the eversion technique. The study also shows that the long term durability of different patch materials is equivalent, and that bovine pericardium and eversion have a lower risk of late infections.

Objective: Current European guidelines recommend both eversion carotid endarterectomy (CEA) and conventional CEA with routine patch closure, rather than routine primary closure. Polyester and polytetrafluoroethylene (PTFE) have been used as patch material for a long time. More recently, bovine pericardium has been used; however, there are few studies comparing long term results between bovine pericardium and other patch types. The aim of this study was to investigate the short and long term results after CEA depending on surgical technique and patch material.

Methods: A registry based study on all primary CEAs ($n = 9\ 205$) performed for symptomatic carotid artery stenosis in Sweden from July 2008 to December 2019, cross linked with data from the Swedish stroke registry, Riksstroke, and chart review for evaluation of any events occurring during follow up. The primary endpoint was ipsilateral stroke < 30 days. Secondary endpoints included re-operations due to neck haematoma and < 30 day ipsilateral stroke, > 30 day ipsilateral stroke, all stroke > 30 days, and all cause mortality.

Results: 2 495 patients underwent eversion CEA and 6 710 conventional CEA for symptomatic carotid stenosis. The most commonly used patch material was Dacron ($n = 3\ 921$), followed by PTFE ($n = 588$) and bovine pericardium ($n = 413$). A total of 1 788 patients underwent conventional CEA with primary closure. Two hundred and seventy-three patients (3.0%) had a stroke < 30 days. Primary closure was associated with an increased risk of ipsilateral stroke and stroke or death <30 days: odds ratio 1.7 (95% confidence interval [CI] 1.2 – 2.4, $p = .002$); and 1.5 (95% CI 1.2 – 2.0), respectively. During follow up (median 4.2 years), 592 patients had any form of stroke and 1 492 died. There was no significant difference in long term risk of ipsilateral stroke, all stroke, or death depending on surgical technique or patch material.

Conclusion: There was an increased risk of ipsilateral stroke < 30 days in patients operated on with primary closure compared with eversion CEA and patch angioplasty. There was no difference between primary closure, different patch types, or eversion after the peri-operative phase.

Keywords: Bovine pericardium, Carotid endarterectomy, Carotid stenosis, Direct suture, Eversion, Patch
Article history: Received 8 April 2022, Accepted 29 December 2022, Available online 2 January 2023

* Corresponding author. Department of Vascular Surgery, Norrbacka S3:01, Karolinska University Hospital, 71 76 Stockholm, Sweden.
E-mail address: Magnus.jonsson@sll.se (Magnus Jonsson).

https://doi.org/10.1016/j.ejvs.2022.12.033

INTRODUCTION

There are several methods of performing carotid endarterectomy (CEA), each with its advantages and disadvantages. The most commonly used techniques for CEA are eversion and conventional endarterectomy.

Eversion uses no prosthetic material and shortens the clamp time but makes the operation more technically demanding if there is a need for shunt use. A Cochrane analysis showed significantly less re-stenosis and occlusion in eversion, and a non-significant trend in favour of eversion technique with respect to cranial nerve injuries.[1] In a cohort study with 1 737 CEA cases the type of closure affected neither the peri-operative nor the long term risk of stroke after CEA.[2] A meta-analysis demonstrated that eversion is associated with an increased risk of post-operative hypertension.[3]

Arteriotomy closure in conventional endarterectomy could either be direct (primary closure) or with a patch (patch closure). Primary closure uses no prosthetic material and shortens the clamp time compared with patch closure. However, a Cochrane review found that patch closure was associated with a decreased risk of peri-operative ipsilateral stroke and arterial occlusion, and also with decreased re-stenosis during follow up.[4] However, small sample sizes and significant loss to follow up have made these results uncertain. A recently published systematic review found no difference in stroke rates between direct suture and patch closure in cohort studies.[5]

Selective patch use has not been studied in randomised controlled trials but is often applied in clinical practice.[6]

There are several available patch types on the market. Dacron, vein and polytetrafluoroethylene (PTFE) have been used for a long time, and in more recent years, bovine pericardium has been used. Bovine pericardium may have the advantage of greater resistance to late infections and smaller haematomas than other patch types, but there are few long term follow up studies comparing bovine pericardium with other patch materials.

Furthermore, a large cohort trial showed that eversion and conventional CEA are equally effective provided that conventional CEA is performed with patch angioplasty.[7]

Current European guidelines recommend both eversion CEA and conventional CEA with routine patch closure, rather than routine primary closure;[8] however, many surgeons prefer selective patching and there remains much controversy about the relative benefits of the different surgical techniques and patches for CEA. The aim of this study was to evaluate the short and long term outcomes after CEA based on surgical technique and patch types.

MATERIALS AND METHODS

Data on all primary carotid procedures for symptomatic stenosis performed in Sweden, prospectively registered in the Swedish National Registry for Vascular Surgery, Swedvasc, between July 2008 and December 2019, were obtained and used for this retrospective cohort study analysis. Records were excluded for patients treated with carotid artery stenting (CAS), redo (ipsilateral) procedures, secondary (contralateral) procedures, and carotid procedures for other indications than symptomatic carotid stenosis (e.g., asymptomatic carotid stenosis, dissections, aneurysms, trauma, and before coronary artery bypass grafting). The study was approved by the ethics committee (EPN dnr 2017/1223-31 and EPN dnr 2021-04167).

Clinical data and risk factors were retrieved from the Swedvasc registry as well as 30 day outcome events. Follow up at 30 days includes clinical examination by a vascular surgeon or neurologist, depending on local practice. As has been described earlier, the Swedvasc registry has a very high external and internal validity for carotid procedures.[9] Since every person in Sweden has a unique 12 digit identification number, cross linking between Swedvasc and other registries is possible. Data from Swedvasc were cross linked to the Swedish population registry to obtain information on survival with 100% accuracy for all Swedish individuals. The Swedish Stroke Register (Riksstroke) is a quality registry where all hospitals in Sweden report ischaemic and haemorrhagic strokes. Riksstroke covers approximately 96% of all strokes.[10] The identified cohort from Swedvasc with procedures performed between 1 July 2008 and 30 September 2017 was cross matched against the Riksstroke registry for evaluation of any stroke occurring beyond 30 days during follow up. Charts were obtained for all patients with a stroke more than 30 days after the operation to determine the brain territory affected.

Outcome and definitions

The primary endpoint was ipsilateral stroke $<$ 30 days. Secondary endpoints were any stroke or death $<$ 30 days, acute myocardial infarction (AMI) $<$ 30 days, re-operation due to neck haematoma, myocardial infarction $<$ 30 days, ipsilateral stroke $>$ 30 days, any stroke $>$ 30 days, all cause mortality, and risk of re-operation.

Continuous data with symmetrical distribution are presented with mean $\pm$ standard deviation (SD) and skewed data with median and interquartile range (IQR). Peri-operative results were analysed by mixed logistic regression using GEE (generalised estimating equation) adjusted for demographics, shunt use, and risk factor profile with random operating centre effect. Since the study extended over 11 years and practices have changed over time, this was also adjusted for.

Time to ipsilateral stroke, all stroke, and death were analysed by Cox regression adjusted for demographics and risk factor profile (age, sex, smoking, hypertension, diabetes, pulmonary disease, renal insufficiency, ischaemic heart disease, qualifying neurological event and degree of carotid stenosis). Data were imputed by creating a new "missing" category for all missing values in covariables.

RESULTS

In total, 9 205 patients were included, all treated for symptomatic carotid stenosis. Baseline characteristics are presented in Table 1. The mean age was 72.5 $\pm$ SD 8.2

Table 1. Baseline characteristic of 9 205 patients undergoing carotid endarterectomy (CEA) for symptomatic carotid artery stenosis in Sweden from 2008 to 2019

Variable	Eversion CEA (n = 2 495)	Primary closure (n = 1 788)	Dacron (n = 3 921)	PTFE (n = 588)	Bovine pericardium (n = 413)	p value
Age − y	73.2 ± 8.2	73.1 ± 7.6	71.7 ± 8.3	73.0 ± 8.5	73.2 ± 8.2	<.001
Male sex	65.7	74.6	65.5	61.9	64.9	<.001
Current smoker	19.7	18.4	21.1	23.6	23.5	<.001
Hypertension	72.2	82.9	77.6	79.8	83.8	<.001
Diabetes	19.5	22.2	19.6	21.2	23.0	<.001
Pulmonary disease	10.5	10.8	9.5	10.4	9.4	<.001
Renal insufficiency	7.5	7.2	6.9	8.6	8.4	.85
Dialysis	1.0	1.0	0.8	1.0	0.5	<.001
Ischaemic heart disease	27.9	31.8	28.8	30.1	31.7	<.001
Qualifying neurological event						.050
Amaurosis fugax	19.8	19.2	20.4	17.2	14.3	
TIA	40.6	38.8	38.6	42.6	44.5	
Minor stroke	35.7	37	36.6	35.2	37.3	
Major stroke	2.2	2.5	2.6	3.6	1.7	
Crescendo TIA	1.7	2.5	1.8	1.4	2.2	
Ipsilateral degree of stenosis − NASCET						<.001
<50%	8.7	5.0	5.4	5.4	5.6	
50−69%	25.4	32.3	28 7	27.7	16.9	
70−99%	65.9	62.7	65.9	66.9	77.5	
Contralateral degree of stenosis − NASCET						<.001
<50%	79.6	75.1	74.6	74.9	71.4	
50−69%	9.5	12.5	12.5	10.5	11.4	
70−99%	7.7	7.7	8.1	9.5	12.6	
Occlusion	3.2	4.6	4.8	5.1	4.4	
Pre-operative thrombolysis	8.5	12.7	11.4	17.7	10.9	.002
Time between qualifying event and surgery − d	8 (9)	8 (10)	7 (9)	9 (10)	7 (6)	.35
Shunt use	7.2	20.1	31.0	36.7	40.2	<.001

Data are presented as mean ± standard deviation, %, or median (IQR). PTFE = polytetrafluoroethylene; TIA = transient ischaemic attack; NASCET = North American symptomatic carotid endarterectomy trial; IQR = Interquartile range.

years, 32.9% were female, and 20.3% had diabetes. The majority had transient ischaemic attack (TIA) or minor stroke as the qualifying neurological event; only 19.5% presented with amaurosis fugax. Of the patients, 11.2% had undergone pre-operative thrombolysis. There were 4.3% with contralateral carotid occlusion, and 65.8% of the patients had an ipsilateral stenosis of 70 − 99% (measured according to North American Symptomatic Carotid Endarterectomy Trial criteria). Average time from qualifying neurological event to operation was eight days (IQR 9), and 76.6% of the patients were operated on within 14 days from the index neurological event.

The 9 205 patients operated on with CEA during the study period were divided according to type of endarterectomy: eversion (n = 2 495) or conventional (n = 6 710), and the latter group were subdivided depending on type of patch or primary closure. Dacron was most frequently used as patch material (n = 3 921) followed by PTFE (n = 588). Bovine pericardium was introduced in Sweden in 2013, and, as described in Supplementary Fig. S1, has become more frequently used over time. Currently, 24.0% of the patches used are from bovine pericardium. Primary closure was used in 19.4% of the patients (n = 1 788), equivalent to 26.6% of the conventional CEAs. Only two of 23 centres used primary closure in more than 50% of conventional CEAs.

Peri-operative results < 30 days from operation

As described in Table 1, there were multiple small and large differences in patient characteristics between the groups. A larger proportion of men were treated with primary closure, 74.6%, compared with 65.7% in the eversion group, 65.5% in the Dacron group, 61.9% in the PTFE group, and 64.9% in the bovine pericardium group (p < .001). Diabetes and contralateral occlusion were less prevalent in patients treated with eversion, and amaurosis fugax was less frequently the qualifying event in patients treated with bovine pericardium. There was greater shunt use in the groups using patch than eversion and primary closure, ranging from 40.2% in the bovine pericardium group, 36.7% in the PTFE group, 31.0% in the Dacron group, 20.1% in the primary closure group, and 7.2% in the eversion group (p < .001).

Major complications. Stroke < 30 days and stroke or death < 30 days for the whole cohort was 3.0% (95% CI 2.6 − 3.3) and 3.4% (95% CI 3.0 − 3.8), respectively, as shown in Table 2. Other complications that occurred within 30 days were death 0.8%, AMI 1.1%, cranial nerve injuries 4.3%, re-operation due to haematoma 3.3%, intracerebral haemorrhage 0.5%, and hyperperfusion syndrome 0.4% (Table 3).

In a risk factor adjusted analysis, primary closure was associated with a significantly increased risk of ipsilateral

Table 2. Odds ratio (OR) with corresponding 95% confidence interval (CI) for stroke or death within 30 days from carotid endarterectomy for symptomatic carotid artery stenosis in 9 205 patients in Sweden from 2008 to 2019

	Ipsilateral stroke		Any stroke		Ipsilateral stroke or death		Any stroke or AMI	
	OR (95% CI)	*p* value	OR (95% CI)	*p* value	OR (95% CI)	*p* value	OR (95% CI)	*p* value
Dacron	Ref		Ref		Ref		REF	
Primary closure	1.7 (1.2–2.4)	0.002	1.5 (1.1–2.1)	0.011	1.7 (1.2–2.2)	0.001	1.3 (1.0–1.7)	.039
PTFE	1.3 (0.7–2.5)	0.41	1.4 (0.8–2.6)	0.23	1.4 (0.8–2.5)	0.29	1.3 (0.8–2.2)	.36
Bovine pericardium	0.8 (0.3–2.3)	0.61	1.0 (0.7–1.6)	0.84	0.9 (0.5–1.6)	0.71	0.6 (0.6–1.8)	.85
Eversion	1.5 (0.9–2.6)	0.15	1.4 (0.9–2.3)	0.15	1.4 (0.9–2.4)	0.14	1.3 (0.9–1.8)	.15

PTFE = polytetrafluoroethylene; AMI = acute myocardial infarction.

Table 3. Odds ratio (OR) with corresponding 95% confidence interval (CI) for other major complications within 30 days from carotid endarterectomy for symptomatic carotid artery stenosis in 9 205 patients in Sweden from 2008 to 2019

	Death	AMI	Cranial nerve injury	Re-operation for neck haematoma	Intracerebral haemorrhage	Hyperperfusion syndrome
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Dacron	Ref	Ref	Ref	Ref	Ref	Ref
Primary closure	1.4 (1.0–2.1)	0.7 (0.4–1.2)	1.1 (0.6–2.1)	0.9 (0.7–1.2)	0.9 (0.4–2.1)	1.1 (0.6–2.1)
PTFE	1.3 (0.7–2.5)	0.7 (0.3–1.6)	0.7 (0.4–1.0)	0.8 (0.5–1.5)	0.7 (0.1–3.6)	1.5 (0.4–5.0)
Bovine pericardium	1.2 (0.8–2.3)	0.7 (0.1–3.6)	0.2 (0.05–1.1)	0.8 (0.4–1.7)	2.1 (1.2–3.8)	0.7 (0.1–3.5)
Eversion	1.2 (0.8–1.9)	0.9 (0.5–1.5)	0.5 (0.3–0.8)	1.0 (0.8–1.2)	1.2 (0.6–2.6)	2.7 (0.9–7.6)

PTFE = polytetrafluoroethylene; AMI = acute myocardial infarction.

stroke (odds ratio [OR] 1.7; 95% CI 1.2—2.4; $p = .002$), and any stroke or death < 30 days (OR 1.5; 95% CI 1.2 — 2.0) compared with Dacron patch closure. Post-operative intracerebral haemorrhage < 30 days was more common in the bovine pericardium group (OR 2.1; 95% CI 1.2 — 3.8) than in the Dacron group. When comparing primary closure with all patches combined, there was a highly significant increased risk of ipsilateral stroke (OR 1.6; 95% CI 1.2 — 2.2; $p = .002$) (Supplementary Table S1). There were no significant differences between various types of patches or eversion with respect to any stroke or death. There were no significant differences between the groups with respect to death, AMI, nor re-operation due to neck wound haematoma.

When comparing eversion with all patches, eversion was not associated with an increased risk of ipsilateral stroke > 30 days (OR 1.5; 95% CI 0.9 — 2.2; $p = .14$), but there was a borderline significantly increased risk of hyperperfusion syndrome (OR 2.5; 95% CI 1.0 — 6.5; $p = .052$).

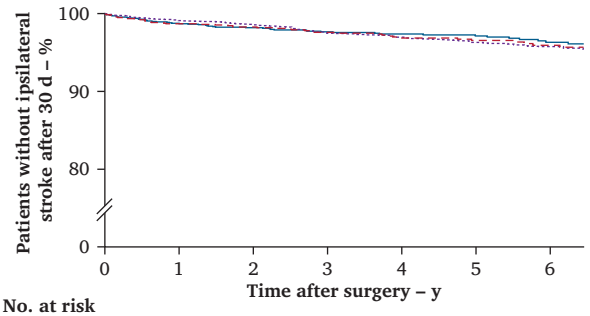
Long term outcome

Patients operated on between 1 June 2008 and 30 September 2017 ($n = 7\ 694$) and surviving 30 days were followed until censoring for end point (ipsilateral stroke, any stroke, or death) or until study end. Median follow up time was 4.2 years, equivalent to a total follow up of 32 084

Table 4. Cox regression analysis of complication rate >30 days after surgery depending on carotid endarterectomy technique for symptomatic carotid artery stenosis in 9 205 patients in Sweden from 2008 to 2019

	Crude		Age and sex adjusted		Multivariable adjusted	
	HR (95% CI)	*p* value	HR (95% CI)	*p* value	HR (95% CI)	*p* value
Ipsilateral stroke after 30 d						
Eversion — ref						
Primary closure	1.12 (0.74–1.68)	.60	1.17 (0.78–1.77)	.44	1.13 (0.74–1.72)	.56
Patch closure	1.17 (0.84–1.64)	.35	1.23 (0.88–1.72)	.22	1.21 (0.86–1.70)	.27
All stroke after 30 d						
Eversion — ref						
Primary closure	1.18 (0.93–1.51)	.18	1.21 (0.95–1.55)	.12	1.18 (0.92–1.52)	.19
Patch closure	1.09 (0.89–1.34)	.41	1.16 (0.94–1.42)	.17	1.15 (0.94–1.42)	.18
All cause mortality after 30 d						
Eversion — ref						
Primary closure	0.92 (0.79–1.07)	.30	0.98 (0.84–1.14)	.79	0.94 (0.80–1.09)	.41
Patch closure	0.87 (0.77–0.98)	.025	0.98 (0.87–1.11)	.74	0.98 (0.86–1.11)	.72

HR= hazard ratio; CI = confidence interval.



No. at risk

Eversion	1 923	1 646	1 428	1 182	925	720	516
Primary	1 477	1 296	1 109	922	756	596	418
Patch	3 900	3 409	2 883	2 366	1 864	1 449	1 018

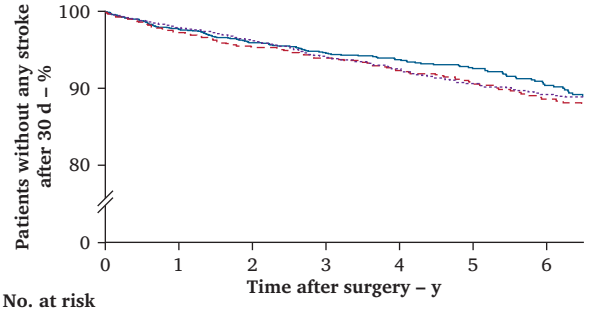
Figure 1. Cumulative Kaplan–Meier estimate of risk of ipsilateral stroke after 30 days in patients treated with carotid endarterectomy with eversion (solid line), patch closure (dotted line), or primary closure (dashed line) for symptomatic carotid artery stenosis. Note the adapted scale for y-axis.

person years. During follow up, 592 patients (7.7%) had a stroke and 1 492 died (19.4%).

In the long term follow up, there was no significant difference with respect to ipsilateral stroke after 30 days, all stroke after 30 days, or all cause mortality between patients operated on with eversion, primary closure, or patch closure (Table 4) after multivariable adjustment. Additionally, there was no difference in various patch types with respect to ipsilateral stroke, all stroke, or all cause mortality after the peri-operative period (Supplementary Table S2).

Kaplan–Meier plots of the risks of ipsilateral stroke, all stroke, and death are shown in Figures 1, 2, and 3, respectively, for primary closure, eversion, and patch closure.

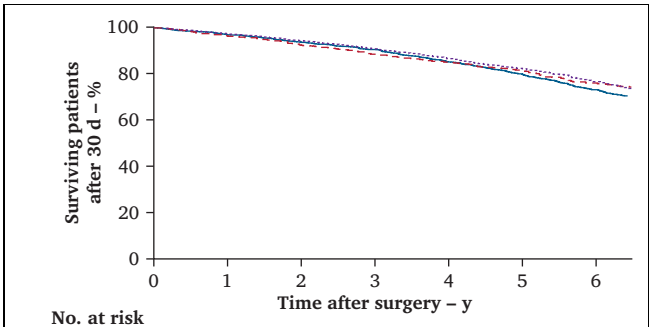
Besides re-operation due to surgical site bleeding and acute re-operations in the first 30 days, 61 patients (0.66%) were re-operated on the ipsilateral side during follow up. The main reasons for re-operation were deep infection (n = 21) or re-stenosis (n = 40). Time from primary operation



No. at risk

Eversion	1 923	1 629	1 400	1 147	903	697	493
Primary	1 477	1 278	1 081	891	723	563	389
Patch	3 901	3 372	2 826	2 292	1 789	1 383	959

Figure 2. Cumulative Kaplan–Meier estimate of risk of all stroke after 30 days in patients treated with carotid endarterectomy with eversion (solid line), patch closure (dotted line) or primary closure (dashed line) for symptomatic carotid artery stenosis. Note the adapted scale for y-axis.



No. at risk

Eversion	1 923	1 666	1 451	1 207	946	740	528
Primary	1 477	1 309	1 124	940	775	614	434
Patch	3 900	3 433	2 920	2 415	1 911	1 492	1 053

Figure 3. Cumulative Kaplan–Meier estimate of all cause mortality after 30 days in patients treated with carotid endarterectomy with eversion (solid line), patch closure (dotted line), or primary closure (dashed line) for symptomatic carotid artery stenosis.

was a median 15 months (range 1 — 116). No patients operated on with bovine pericardium or eversion required re-operation for infection.

DISCUSSION

This nationwide cohort, including 9 205 symptomatic carotid patients with long term follow up, underlines the variation in surgical techniques used for CEA in Sweden, with up to 20% of patients being operated on with primary closure without patch, and increasing use of bovine pericardium over recent years. Interestingly, the analysis shows that primary closure of the carotid artery after endarterectomy was associated with an increased risk of ipsilateral stroke within 30 days from the procedure compared with patch closure with Dacron, but no difference between primary closure or patch closure or eversion after the peri-operative phase. This is similar to what has been demonstrated for CEA *vs*. carotid artery stenting,[11] and underlines the importance of optimising the peri-operative period. Also in a cohort study on mainly asymptomatic patients, they found a similar low stroke rate, after the peri-operative phase, in patients treated with primary closure, patch closure, or eversion.[12]

In a Cochrane analysis from 2009, patch angioplasty was associated with a decreased risk of ipsilateral stroke within 30 days.[4] A subgroup analysis of patients randomised to CEA in the International Carotid Stenting Study also showed an increased rate of re-stenosis in patients operated on with primary closure compared with patch angioplasty or eversion CEA.[13] Similar results were shown in a large retrospective cohort study of 14 636 patients undergoing CEA, with higher rates of restenosis and post-operative stroke or TIA after primary closure compared with patch angioplasty.[14] However, a large cohort study revealed that it was possible to achieve results with primary closure similar to patch closure,[2] although the patients operated on with primary closure had more experienced surgeons and were more likely to be non-smokers than patients operated on with patch angioplasty or eversion CEA. In the current study, background data

indicated that there is a selection in patients with primary closure: 74.6% were men compared with 65.7% with eversion and 65.0% with patch closure. Possibly primary closure has been used in men with a larger diameter internal carotid artery (ICA). Also, the fact that only two of 23 vascular centres used primary closure in more than 50% of conventional CEAs, indicating a widespread use of selective primary closure. Interestingly, a shunt was used 62% more often in patients with patch closure than primary closure. While the analysis of peri-operative stroke and death was performed with adjustment for patient demographics and risk factors, peri-operative use of shunt was not included in the adjustment, and may therefore contribute to this difference in outcome.

Bovine pericardium has become more popular over time, and currently more than a quarter of all patches used during CEA in Sweden are from bovine pericardium. Bovine pericardium has some theoretical advantages over synthetic patch materials, with less risk of patch infections and possibly less bleeding. One randomised controlled trial showed less suture line bleeding when using a bovine pericardial patch compared with Dacron.[15] Additionally, a recently published cohort study indicated a lower risk of returns to the operating theatre with a bovine pericardial patch than with other synthetic patch materials.[16] In the present study, bovine pericardium had no benefit with respect to stroke or death compared with Dacron, and there was no difference in risk of re-operation due to haematoma. However, the current dataset did not include data on dual antiplatelet therapy (DAPT) prior to surgery. A causal relationship with intracerebral haemorrhage is unlikely, and more possible that bovine pericardium is used more frequently when patients are on DAPT due to its superiority in haemostasis compared with other patch types, and this may also explain why bovine pericardium was associated with an increased rate of intracerebral haemorrhage, although the numbers were low.

There was a borderline increased risk of ipsilateral stroke $<$ 30 days in patients operated on with eversion compared with patched CEA. This contrasts with a meta-analysis of randomised and observational studies.[17] One can only speculate the reasons for these results, but shunt use is technically demanding when performing eversion, and in the present study, with only symptomatic patients, there might have been an underuse of shunting in patients treated with eversion technique.

In the present study, eversion was also associated with an increased risk of hyperperfusion syndrome. The CIs were large, so there may be a statistical type 1 error, but, on the other hand, eversion increases the risk of post-operative hypertension,[3] so there might be a causal relationship.

The patients were followed for up to nine years after surgery, with a median 4.2 years. There were no differences between eversion and conventional CEA, nor primary closure *vs.* patch closure beyond 30 days from operation with respect to ipsilateral stroke, all stroke, or death. All different patches seemed to be effective at preventing new stroke and none of them was found to be superior to another.

There was a very low incidence of re-operations after the peri-operative period. Less than 1% were re-operated on, mainly due to symptomatic re-stenosis or late patch infection. No infections were found in the eversion group nor in primary operation with bovine pericardium group. One patient with primary closure was operated on for late deep infection. Even though there was no information about the number of medically treated infections, this finding strengthens the theoretical advantage of lower risk of late infections with the bovine pericardium or eversion technique.

The results of the current study should be interpreted within the context of the strengths and limitations associated with retrospective analysis of prospectively collected registry data. The high validity of the Swedvasc registry, with almost 100% coverage for all carotid procedures performed in Sweden, and the possibility for cross linkage of data based on unique personal identifiers to assess long term survival and stroke outcome result in high generalisability and low loss to follow up in this study. However, considering that the study assesses carotid procedures performed over 10 years in Sweden, changes in practice over time may be a confounder affecting results for factors not captured by the registry. This may include changes in medical management of patients prior to surgery, including pre-operative thrombolysis or antiplatelet therapy, as well as changes in peri-procedural routines, such as use of different techniques for cerebral monitoring during carotid surgery. Also, the Swedvasc registry did not include data on arteriotomy length, width of ICA, type of anaesthesia, and intracerebral vessel network, so these variables were not corrected for. The multivariable analyses in the study included patient demographics and risk factors to mitigate the risk of results being affected by differences in patient selection for various techniques, but the risk of presence of residual confounders especially related to the above mentioned time related factors cannot be excluded.

Perhaps the main takeaway from the current study is that primary closure during CEA is associated with an increased risk of post-procedural stroke and should not be used. While it has previously been shown that routine primary closure increases the risk of an ipsilateral neurological event, the current report underlines that selective primary closure remains common practice by some surgeons. Further educational efforts to move towards routine patch closure or eversion endarterectomy among all carotid surgeons is warranted.

Conclusions

In this nationwide cohort study, including all CEAs performed for symptomatic carotid stenosis, primary closure was associated with an increased risk of ipsilateral stroke compared with patch closure and eversion. The use of a bovine pericardial patch increased over time, and there was no difference in outcome between primary closure, different patch

types, or eversion after the peri-operative period. Bovine pericardium and eversion have a lower risk of late infections.

CONFLICT OF INTEREST STATEMENT AND FUNDING

None.

ACKNOWLEDGEMENTS

The Swedvasc steering committee: Lena Blomgren, Mari Holsti, Magnus Jonsson, Kevin Mani, Kristian Smidfelt, Joachim Starck, Talha Butt, and Catharina Cicek

APPENDIX A. SUPPLEMENTARY DATA

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejvs.2022.12.033.

REFERENCES

1 Cao PG, de Rango P, Zannetti S, Giordano G, Ricci S, Celani MG. Eversion versus conventional carotid endarterectomy for preventing stroke. *Cochrane Database Syst Rev* 2001;**2000**:CD001921.
2 Avgerinos ED, Chaer RA, Naddaf A, El-Shazly OM, Marone L, Makaroun MS. Primary closure after carotid endarterectomy is not inferior to other closure techniques. *J Vasc Surg* 2016;**64**:678–83.
3 Demirel S, Goossen K, Bruijnen H, Probst P, Böckler D. Systematic review and meta-analysis of postcarotid endarterectomy hypertension after eversion versus conventional carotid endarterectomy. *J Vasc Surg* 2017;**65**:868–82.
4 Rerkasem K, Rothwell PM. Patch angioplasty versus primary closure for carotid endarterectomy. *Cochrane Database Syst Rev* 2009;**2009**:CD000160.
5 Huizing E, Vos CG, van den Akker PJ, Schreve MA, de Borst GJ, Ünlü Ç. A systematic review of patch angioplasty versus primary closure for carotid endarterectomy. *J Vasc Surg* 2019;**69**:1962–74.
6 Maertens V, Maertens H, Kint M, Coucke C, Blomme Y. Complication rate after carotid endarterectomy comparing patch angioplasty and primary closure. *Ann Vasc Surg* 2016;**30**:248–52.
7 Dakour-Aridi H, Ou M, Locham S, AbuRahma A, Schneider JR, Malas M. Outcomes following eversion versus conventional endarterectomy in the Vascular Quality Initiative database. *Ann Vasc Surg* 2020;**65**:1–9.
8 Naylor R, Rantner B, Ancetti S, de Borst GJ, De Carlo M, Halliday A, et al. European Society for Vascular Surgery (ESVS) 2023 Clinical Practice Guidelines on the Management of Atherosclerotic Carotid and Vertebral Artery Disease. *Eur J Vasc Endovasc Surg* 2023;**65**:7–111.
9 Venermo M, Lees T. International Vascunet validation of the Swedvasc registry. *Eur J Vasc Endovasc Surg* 2015;**50**:802–8.
10 Söderholm A, Stegmayr B, Glader E-L, Asplund K, Riksstroke Collaboration. Validation of hospital performance measures of acute stroke care quality. Riksstroke, the Swedish Stroke Register. *Neuroepidemiology* 2016;**46**:229–34.
11 Bonati LH, Dobson J, Featherstone RL, Ederle J, van der Worp HB, de Borst GJ, et al. Long-term outcomes after stenting versus endarterectomy for treatment of symptomatic carotid stenosis: the International Carotid Stenting Study (ICSS) randomised trial. *Lancet* 2015;**385**:529–38.
12 Nana P, Spanos K, Piffaretti G, Koncar I, Kouvelos G, Zlatanovic P, et al. Long-term durability and safety of carotid endarterectomy closure techniques. *World J Surg* 2020;**44**:3545–54.
13 Cheng SF, Richards T, Gregson J, Brown MM, de Borst GJ, Bonati LH, et al. Long term restenosis rate after carotid endarterectomy: comparison of three surgical techniques and intraoperative shunt use. *Eur J Vasc Endovasc Surg* 2021;**62**:513–21.
14 Edenfield L, Blazick E, Healey C, Hawkins R, Bloch P, Eldrup-Jorgensen J, et al. Long-term impact of the Vascular Study Group of New England carotid patch quality initiative. *J Vasc Surg* 2019;**69**:1801–6.
15 Marien BJ, Raffetto JD, Seidman CS, LaMorte WW, Menzoian JO. Bovine pericardium vs Dacron for patch angioplasty after carotid endarterectomy: a prospective randomized study. *Arch Surg* 2002;**137**:785–8.
16 Edenfield L, Blazick E, Eldrup-Jorgensen J, Healey C, Bloch P, Hawkins R, et al. Outcomes of carotid endarterectomy in the Vascular Quality Initiative based on patch type. *J Vasc Surg* 2020;**71**:1260–7.
17 Paraskevas KI, Robertson V, Saratzis AN, Naylor AR. 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. *Eur J Vasc Endovasc Surg* 2018;**55**:465–73.