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Long-term outcomes of eversion and conventional carotid endarterectomy: A multicenter clinical trial

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Abstract

Aim: To compare the long-term results of eversion (ECEA) and conventional carotid endarterectomy (CCEA).
Methods: We designed a retrospective, multicenter study which included 25,106 patients who underwent ECEA (n = 18,362) or CCEA (n = 6744). The duration of follow-up was 124.7 ± 53.8 months.
Results: In the postoperative period, none of the interventions showed clear benefits reducing the frequency of complications: fatal outcome (ECEA: 0.19%, n = 36; CCEA: 0.17%, n = 12; OR = 1.1, 95% CI = 0.57–2.11, p = 0.89), myocardial infarction (ECEA: 0.15%, n = 28; CCEA: 0.13%, n = 9; p = 0.87; OR = 1.14; 95% CI = 0.53–2.42); acute cerebrovascular accident (CVA) (Group I: 0.33%, n = 62; Group II: 0.4%, n = 27; p = 0.53; OR = 0.84; 95% CI = 0, 53–1.32); bleeding with acute haematoma appearance in the area of intervention (Group I: 0.39%, n = 73; Group II: 0.41%, n = 28; p = 0.93; OR = 0.95; 95% CI = 0, 61–1.48); internal carotid artery (ICA) thrombosis (Group I: 0.05%, n = 11; Group II: 0.07%, n = 5; OR = 0.80, 95% CI = 0.28–2.32, p = 0.90). During the long-term follow-up, ECEA was associated with lower frequency of fatal outcome (ECEA: 2.7%, n = 492; CCEA: 9.1%, n = 616; OR = 0.27; 95% CI = 0.24–0.3, p < 0.0001), cerebrovascular death (ECEA: 1.0%, n = 180; CCEA: 5.5%, n = 371; OR = 0.17, 95% CI = 0.14–0.21, p < 0.0001), non-fatal ischaemic stroke (ECEA: 0.62%, n = 114; CCEA: 7.0%, n = 472; OR = 0.08; 95% CI = 0.06–0.1, p < 0.0001); repeated revascularization because of >60% restenosis (ECEA: 1.6%, n = 296; CCEA: 12.6%, n = 851; OR = 0.11, 95% CI = 0.09–0.12, p < 0.0001), and combined endpoint (ECEA: 2.2%, n = 397; CCEA: 13.2%, n = 888; OR = 0.14; 95% CI = 0.12–1.16, p < 0.0001).
Conclusion: ECEA is beneficial over CCEA in a long term.

Keywords

eversion carotid endarterectomy, conventional carotid endarterectomy, patch angioplasty, multicenter study, adverse outcomes, long-term follow-up

Introduction

For >50 years, both eversion (ECEA) and conventional carotid endarterectomy (CCEA) have been the 'gold standard' of cerebral revascularization, a surgical intervention aimed on treatment of internal carotid artery (ICA) stenosis [1–5]. ECEA is performed by cutting off the ICA from the bifurcation with the further endarterectomy after artery eversion[6,7]. In contrast, CCEA implies a longitudinal arteriotomy from the common carotid artery to the ICA[8,9]. In this surgical modality, plaque excision is followed by a patch angioplasty for closing the wound and preventing thrombosis[8–10]. These patches are fabricated from autologous saphenous veins, bovine or porcine pericardium, or poly (tetrafluoroethylene)[8,11–13] all having nearly equal efficiency[12–15]. Currently, the surgeon is fully responsible for the choice of the intervention and the patch, while needing to take into account both clinical scenario and healthcare setting[16–18].

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Short- and long-term efficiency of ECEA and CCEA remains a matter of debate[19–22]. While several studies showed equal efficiency of these interventions, others demonstrated the inferior outcomes upon CCEA as patch angioplasty is associated with higher incidence of ICA restenosis and subsequent stroke[20–24]. However, current national guidelines authorise both of the indicated techniques, largely due to the lack of relevant multicenter studies in Russian Federation[18]. This leads to an unacceptably large number of preventable adverse outcomes, as currently 144 specialised clinics in Russia perform ≈20,000 CEAs annually[25].

Here, we designed and performed a retrospective multicenter study to compare in-hospital and long-term outcomes of ECEA and CCEA. We found that albeit short-term efficiency of these interventions is equal, ECEA is associated with a significant reduction in adverse outcomes, including cerebrovascular death and repeated revascularization, in a long term.

Materials and Methods

This retrospective multicenter study enrolled 25,106 patients who underwent ECEA (n = 18,362) or CCEA (n = 6,744) from 1 February 2006 to 1 September 2021. In CCEA, we used 3,187 (47.2%) xenopericardial patches, 2,354 (34.9%) poly (tetrafluoroethylene) patches and 1,203 (17.8%) patches fabricated from autologous veins. A 6/0 polypropylene suture was used to create anastomosis. To assess brain tolerance to ischaemia, we measured retrograde pressure and installed a temporary bypass if it was <60% from the systemic blood pressure.

Criteria of inclusion were indications for CEA according to the current Appendix I. Criteria of exclusion were:

- concomitant diseases limiting patient observation in the long term;
- contralateral neuropathy of glossopharyngeal and/or hypoglossal nerve;
- contralateral vocal cord paresis;
- severe neurological deficit;
- acute ischaemic stroke;
- acute coronary syndrome;
- bilateral severe ICA stenosis.

The severity of coronary atherosclerosis was calculated after the coronary angiography using the SYNTAX score. The duration of follow-up was 124.7 ± 53.8 months. Patient data have been regularly collected by a phone survey and during the follow-up examination at a specialised healthcare facility. Among the adverse outcomes were

- fatal outcome;
- all-cause death;
- cerebrovascular death;
- cerebrovascular accident;
- non-fatal ischaemic stroke;
- ICA thrombosis;
- ICA restenosis ≥60% requiring repeated revascularization;
- myocardial infarction;
- bleeding of type ≥ 3b (Bleeding Academic Research Consortium scale);
- combined endpoint (for the hospital observation: fatal outcome + myocardial infarction + cerebrovascular accident; for the long-term follow-up: cerebrovascular death + non-fatal ischaemic stroke + myocardial infarction.

A written informed consent was provided by all study participants after receiving a full explanation of the study. The investigation was carried out in accordance with the Good Clinical Practice and a latest revision of Declaration of Helsinki (2013).

Sample distribution was assessed using Kolmogorov–Smirnov test. For descriptive statistics, data were represented by the proportions or by the median, 25th and 75th percentiles, and range. Two independent groups were compared by Pearson's chi-squared test with Yates's correction for continuity or by Mann–Whitney U test. Calculation of odds ratio and respective 95% confidence intervals was conducted employing a respective MedCalc online calculator (MedCalc Software). Kaplan–Meier method was used to create survival curves during the long-term follow-up while log-rank test has been employed to compare survival distributions. p values ≤0.05 were regarded as statistically significant.

Results

The samples were comparable regarding all clinicopathological features (Table 1). Elderly and male patients were predominant (Table 1). Around 20% of patients suffered from stable angina or had a past medical history of cerebrovascular accident (Table 1). Other comorbid conditions included diabetes mellitus, chronic obstructive pulmonary disease, and chronic kidney disease (Table 1). Severity of ICA stenosis and coronary atherosclerosis, as well as frequency of temporary bypass placement and duration of ICA clamping, did not differ significantly between the groups (Table 2).

Postoperatively, none of the interventions showed clear benefits reducing the frequency of complications: fatal outcome (ECEA: 0.19%, n = 36; CCEA: 0.17%, n = 12;

Table 1. Clinicopathological features of patient groups.

Features	Groups		p
	ECEA *n* = 18,362	CCEA *n* = 6,744	
Age, years (M ± m)	66.3 ± 6.1	65.1 ± 5.5	0.72
Male gender, *n* (%)	13646 (74.3)	4982 (73.9)	0.48
Cardiac fibrosis, *n* (%)	1953 (10.6)	720 (10.7)	0.94
Stable angina CCS class I-II	4067 (22.1)	1491 (22.1)	0.95
Diabetes mellitus, *n* (%)	1230 (6.7)	426 (6.3)	0.29
Chronic obstructive pulmonary disease, *n* (%)	512 (2.8)	193 (2.8)	0.78
Chronic kidney disease, *n* (%)	558 (3.0)	217 (3.2)	0.49
Peripheral atherosclerosis, *n* (%)	2461 (13.4)	854 (12.6)	0.13
Past medical history of myocardial revascularization, *n* (%)	2860 (15.6)	1059 (15.7)	0.82
Past medical history of stroke, *n* (%)	3752 (20.4)	1361 (20.2)	0.67

ECEA, eversion carotid endarterectomy; CCEA, conventional carotid endarterectomy.

Table 2. Angiographic and intraoperative features of patients.

Features	Groups		p
	ECEA *n* = 18,362	CCEA *n* = 6,744	
Angiographic features			
ICA stenosis, %	81.5 ± 5.3	83.3±6.0	0.7
SYNTAX score, M ± m	6.5 ± 2.1	5.9 ± 2.2	0.9
Intraoperative features			
Temporary bypass, *n* (%)	849 (4.6)	321 (4.7)	0.67
Duration of ICA clamping, minutes	24.5±3.8	25.6±4.5	0.2

ECEA, eversion carotid endarterectomy; CCEA, conventional carotid endarterectomy; ICA, internal carotid artery.

OR = 1.1, 95% CI = 0.57–2.11, p = 0.89), myocardial infarction (ECEA: 0.15%, n = 28; CCEA: 0.13%, n = 9; OR = 1.14, 95% CI = 0.53–2.42, p = 0.87); cerebrovascular accident (ECEA: 0.33%, n = 62; CCEA: 0.40%, n = 27; OR = 0.84, 95% CI = 0.53–1.32, p = 0.53); bleeding of type ≥ 3b (ECEA: 0.39%, n = 73; CCEA: 0.41%, n = 28; OR = 0.95, 95% CI = 0,61–1.48, p = 0.93); ICA thrombosis (ECEA: 0.05%, n = 11; CCEA: 0.07%, n = 5; OR = 0.80, 95% CI = 0.28–2.32, p = 0.90, Table 3).

ICA thrombosis (n = 15) was always accompanied by ischaemic stroke, being caused by (neo)intimal detachment behind the endarterectomy area (n = 10) or by arterial dissection upon temporary bypass placement (n = 5). These patients underwent urgent open thromboendarterectomy, ultimately leading to the neurological recovery in 11 out of 15 cases. Myocardial infarction (n = 37) was triggered by coronary artery thrombosis or in-stent restenosis and was successfully treated by percutaneous coronary intervention in all cases.

Among the cerebrovascular accidents (n = 89) were ischaemic stroke (n = 40), transient ischaemic attack (n = 29), haemorrhagic stroke (n = 12), and mixed stroke (n = 8). Fatal outcomes (n = 48) were caused by a cerebrovascular accident (n = 43) or myocardial infarction (n = 5). The prevalence of a combined endpoint was ≈1%.

During the long-term follow-up, ECEA was associated with a lower frequency of fatal outcome (ECEA: 2.7%, n = 492; CCEA: 9.1%, n = 616; OR = 0.27; 95% CI = 0.24–0.3, p < 0.0001), cerebrovascular death (ECEA: 1.0%, n = 180; CCEA: 5.5%, n = 371; OR = 0.17, 95% CI = 0.14–0.21, p < 0.0001), non-fatal ischaemic stroke (ECEA: 0.62%, n = 114; CCEA: 7.0%, n = 472; OR = 0.08; 95% CI = 0.06–0.1, p < 0.0001); repeated revascularization because of >60% restenosis (ECEA: 1.6%, n = 296; CCEA: 12.6%, n = 851; OR = 0.11, 95% CI = 0.09–0.12, p < 0.0001), and combined endpoint (ECEA: 2.2%, n = 397; CCEA: 13.2%, n = 888; OR = 0.14; 95% CI = 0.12–1.16, p < 0.0001, Table 3). Cerebrovascular death – (Figure 1), cerebrovascular accident – (Figure 2), restenosis (≥60%, Figure 3, and combined endpoint-free survival (Figure 4) was also higher upon ECEA as compared with CCEA. Notably, ≥ 50% of all adverse outcomes after CCEA were recorded within 1 year of follow-up and were provoked by neointimal hyperplasia, probably triggered by a patch implantation.

Table 3. In-hospital and long-term outcomes.

Features	Groups ECEA *n* = 18,362	Groups CCEA *n* = 6,744	p	OR	95% CI
In-hospital outcomes					
Fatal outcome, *n* (%)	36 (0.19)	12 (0.17)	0.89	1.1	0.57–2.11
Myocardial infarction, *n* (%)	28 (0.15)	9 (0.13)	0.87	1.14	0.53–2.42
Cerebrovascular accident, *n* (%)	62 (0.33)	27 (0.4)	0.53	0.84	0.53–1.32
Bleeding of type ≥ 3b (BARC scale), *n* (%)	73 (0.39)	28 (0.41)	0.93	0.95	0.61–1.48
ICA thrombosis, *n* (%)	11 (0.05)	5 (0.07)	0.9	0.8	0.28–2.32
Combined endpoint, *n* (%)	126 (0.68)	48 (0.71)	0.89	0.96	0.69–1.34
Long-term outcomes					
All-cause death, *n* (%)	492 (2.7)	616 (9.1)	<0.0001	0.27	0.24–0.3
Cerebrovascular death, *n* (%)	180 (1.0)	371 (5.5)	<0.0001	0.17	0.14–0.21
Myocardial infarction, *n* (%)	103 (0.56)	45 (0.66)	0.37	0.84	0.59–1.19
Non-fatal ischaemic stroke, *n* (%)	114 (0.62)	472 (7.0)	<0.0001	0.08	0.06–0.1
Repeated revascularization because of ≥60% internal carotid artery restenosis, *n* (%)	296 (1.6)	851 (12.6)	<0.0001	0.11	0.09–0.12
Combined endpoint, *n* (%)	397 (2.2)	888 (13.2)	<0.0001	0.14	0.12–0.16

ECEA, eversion carotid endarterectomy; CCEA, conventional carotid endarterectomy; ICA, internal carotid artery; BARC, Bleeding Academic Research Consortium; OR, odds ratio; CI, confidence interval.

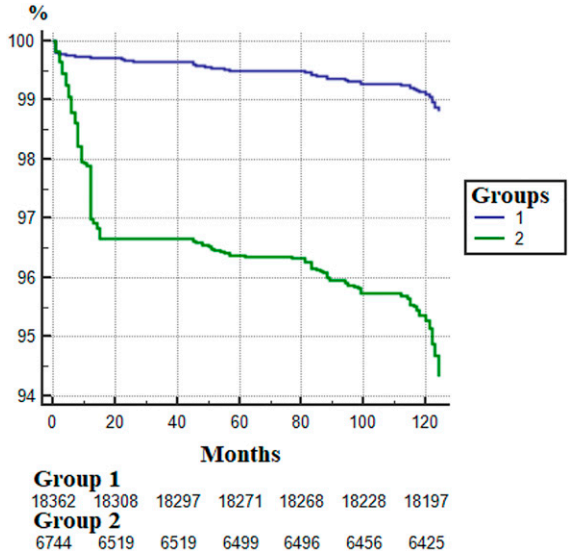

Figure 1. Cerebrovascular death-free survival.

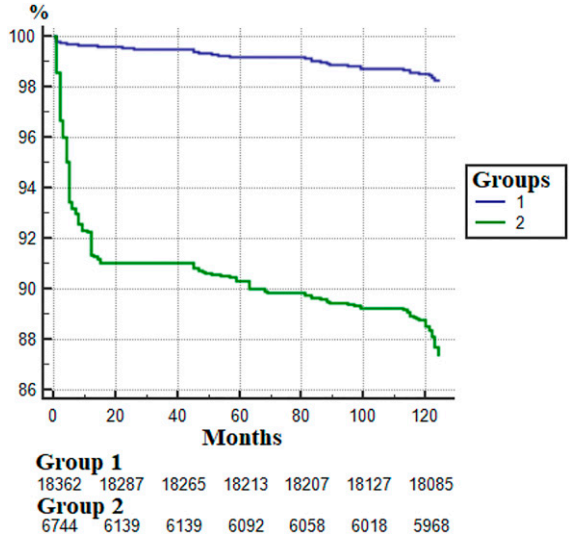

Figure 2. Cerebrovascular accident-free survival.

Discussion

The reasons behind ICA restenosis upon CEA performance can be of local (e.g. patch-associated neointimal hyperplasia), systemic (e.g. arterial hypertension, severe dyslipidaemia, diabetes mellitus and smoking), and iatrogenic (e.g. technical errors) origin.

Excessive expansion of carotid bifurcation often results in the alterations of the flow pattern which becomes turbulent, entailing thrombosis and neointimal hyperplasia [26–30]. This, the inferiority of CCEA revealed in our trial concurs with those obtained in other studies[5,20,31]. A personalised computer simulation approach to patch selection to match arterial geometry remains the only option

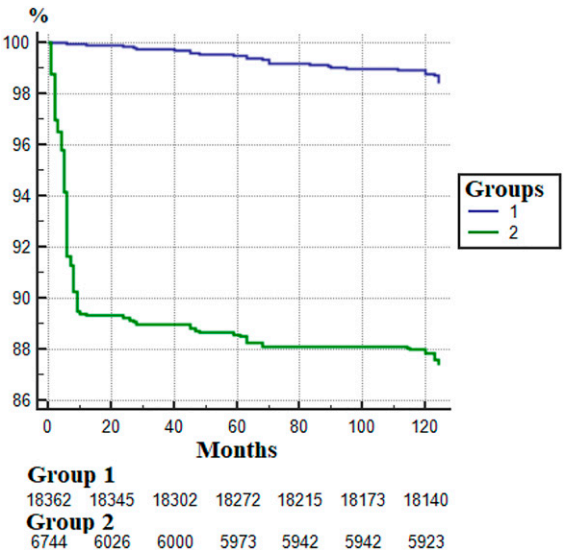

Figure 3. Restenosis (≥60%)-free survival.

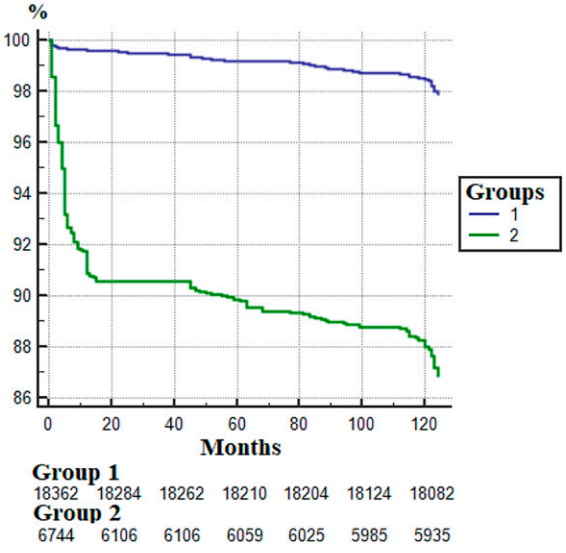

Figure 4. Combined endpoint-free survival.

for the prevention of CCEA-associated complications which, however, remains rarely available[26–30]. Successful performance of virtual CCEA involving the implantation of a tailored patch provides a technical rationale for this treatment modality[26–30]. Albeit current guidelines do not specify the benefits of either ECEA or virtually assisted CCEA[18], we suggest that cerebral revascularization should become increasingly personalised.

Systemic risk factors for the development of restenosis affect CEA outcomes regardless of intervention type[32–36]. Most of them are modifiable, yet it has been shown that genetic background also affects the long-term outcomes[37–41]. Additional supervision of high-risk patients might permit early detection of ICA restenosis and timely repeated revascularization, preventing cerebrovascular accidents and death[37–41].

Iatrogenic complications include narrowing of the arterial lumen as a result of the imposition of secondary sutures to prevent bleeding, crude patch-patient mismatch [42,43], or residual stenosis because of incomplete plaque excision or intimal detachment after the blood flow restoration[44,45]. Unfortunately, approaches to predict a behaviour of (neo) intima behind the endarterectomy area upon restarting the blood flow are still lacking[42–45].

To summarise, better long-term results of ECEA and its lower costs in comparison with CCEA prompt to recommend it as an only appropriate surgical option. Although ICA restenosis is a multifactorial condition and immense efforts are required to minimise the adverse outcomes, replacement of CCEA with ECEA would probably be a significant step on this route.

Conclusion

ECEA is beneficial over CCEA in a long term.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Appendix I

Criteria for CEA of current Russian national guidelines for the management of patients with diseases brachiocephal arteries (download link angiolsurgery. org/recommendations/2013/recommendations_brachiocephalic.pdf).

Recommendations for treatment tactics depending on the neurological symptoms and the degree of stenosis of the carotid arteries:

1. Surgical treatment of stenosis of the carotid arteries is absolutely indicated in symptomatic patients with stenosis of more than 60% (NASCET) [A], if the anticipated rate of periprocedural stroke or mortality is less than 3% for patients with TIA and less than 5% for patients with stroke. The overall mortality rate should not exceed 2%. Carotid endarterectomy is contraindicated in symptomatic patients with stenosis less than 50% [A].

2. It is possible to perform carotid endarterectomy in symptomatic patients with ICA stenosis from 50 to 60%, taking into account the morphological instability of the atherosclerotic plaque (ulceration, haemorrhage into the plaque, intimal flotation and parietal thrombus).
3. It is advisable to perform carotid endarterectomy within 2 weeks from the onset of the last episode of stroke with TIA or minor strokes (mRs < 3), 6–8 weeks after major strokes. Carotid endarterectomy can be performed within days after TIA [B].
4. Carotid endarterectomy can be recommended for asymptomatic patients with stenosis from 70 to 99% if the operational risk is less than 3% [A].

Recommendations for choosing a method of treatment depending on an associated pathology:

1. CEA can be performed in high-risk patients with rates of stroke, death and heart complications within acceptable standards [B].
2. For asymptomatic patients with 'exceptionally' high risk (multiple comorbidities at the same time), the best drug therapy may be the optimal choice over invasive procedures [C].
3. CAS is associated with a high risk of embolization in elderly patients of old age. CEA can be performed in elderly patients without increasing the risk of embolization and with an acceptable incidence of neurological and cardiac complications [C].
4. CAS should not be offered to asymptomatic high-risk patients if the likelihood of perioperative stroke and mortality is greater than 3% [C].

On the choice of the method of treatment depending on the features of the vascular and local anatomy and the structure of the atherosclerotic plaque:

1. CAS is indicated in the following cases:
   - restenosis after a previously performed CEA,
   - contralateral paresis of the cranial nerves, previous surgical intervention on the organs of the neck,
   - radiation therapy of the neck organs, the spread of atherosclerotic lesions to the intracranial parts of the ICA.
2. CAS can be recommended in case of high the location of the CCA bifurcation.
3. CAS should be performed with extreme caution with ICA stenosis more than 90% and morphologically unstable atherosclerotic ICA plaque. In these situations, the use of a proximal protection is advisable.
4. CAS is not recommended:
   - in patients with calcified atherosclerotic plaques,
   - with a combination of stenosis with pathological tortuosity of the ICA,
   - with widespread atherosclerotic lesions of the aortic arch and its branches (this is possible only in centres with high surgical activity and a documented low perioperative risk of stroke and death).

Appendix A

Abbreviations and acronyms

ECEA – eversion carotid endarterectomy
CCEA – conventional carotid endarterectomy
ICA – internal carotid artery
BARC – Bleeding Academic Research Consortium