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Eversion Carotid Endarterectomy is Associated with Decreased Baroreceptor Sensitivity Compared to the Conventional Technique

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WHAT THIS PAPER ADDS

- This study prospectively compares changes in baroreceptor sensitivity after eversion (E-CEA) and conventional CEA (C-CEA) with patch plasty. Due to sinus nerve dissection in eversion technique and sinus nerve preservation with conventional technique distinctive changes in baroreceptor sensitivity and thus haemodynamic response behaviour are apparent.
- We confirmed a reduction in baroreceptor sensitivity after E-CEA and an increase after C-CEA, with a countersteering shift of autonomic balance towards sympathetic dominance after eversion technique and the opposite effect after conventional CEA.

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ABSTRACT

Objective: Impairment of baroreceptor sensitivity (BRS) has been shown to be associated with blood pressure instability after carotid endarterectomy (CEA). The aim of this study was to determine whether there is a difference in postoperative BRS changes following eversion CEA (E-CEA) and conventional CEA (C-CEA).

Methods: Sixty-four patients undergoing E-CEA ($n = 37$) and C-CEA ($n = 27$) were prospectively studied. Non-invasive measurements of mean arterial pressure (MAP), cardiac output (CO) and total peripheral resistance (TPR) were perioperatively obtained over three 10-min periods. Baroreflex gain was calculated as the sequential cross-correlation between heart rate and beat-to-beat systolic blood pressure.

Results: Compared with changes observed after C-CEA, E-CEA was associated with an increase in systolic pressure (SP) ($P = 0.01$), diastolic pressure (DP) ($P = 0.008$), MAP ($P = 0.002$) and heart rate (HR) ($P = 0.03$) on postoperative day 1 (POD-1). BRS decreased after E-CEA from 6.33 to 4.71 ms mmHg^{-1} on POD-1 ($P = 0.001$) and to 5.26 ms mmHg^{-1} on POD-3 ($P = 0.0004$). By contrast, BRS increased after C-CEA from 4.59 to 6.13 ms mmHg^{-1} on POD-1 ($P = 0.002$) and to 6.27 ms mmHg^{-1} on POD-3 ($P < 0.0001$).

Conclusion: E-CEA and C-CEA have different effects on BRS. This is associated with an altered haemodynamic behaviour after E-CEA and C-CEA, respectively. These findings are likely the result of carotid sinus nerve interruption during E-CEA and preservation with C-CEA.

Carotid endarterectomy (CEA), first reported six decades ago,[1] quickly gained popularity as a safe and effective procedure for extracranial carotid occlusion.[2] So its value is well established in symptomatic and asymptomatic patients with carotid artery stenosis.[3–7] The procedure, however, is often accompanied by postoperative blood pressure alterations.[8–18] These haemodynamic perturbations may relate to an altered sensitivity of the carotid sinus baroreceptors residing at the origin of the internal carotid artery (ICA).[10,14] Baroreceptors responding to pressure are located at key places within the cardiovascular system and provide the brain with information regarding moment-to-moment changes in arterial blood pressure. This afferent input controls a variety of reflex responses encompassing autonomic and endocrine adjustments, each geared towards maintaining cardiovascular homeostasis.[19]

As such, the baroreflex participates in both short- and long-term blood pressure control.[20] Vascular distension from increased blood

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pressure triggers baroreceptor firing with a frequency that is directly proportional to the mean arterial pressure (MAP) and the rate of change in pressure.[21] Impulses are propagated through the glossopharyngeal and vagus nerves to the nucleus tractus solitarii of the medulla, with resultant activation of parasympathetic nuclei and inhibition of sympathetic nuclei.[22] As blood pressure increases, baroreceptor triggering leads to diminished sympathetic outflow to the heart, kidneys and peripheral vasculature, as well as heightened parasympathetic tone in the heart. The result is a fall in total peripheral (vascular) resistance (TPR), heart rate (HR), cardiac output (CO) and blood pressure. Baroreceptorsensitivity (BRS) is intensively studied in adults. Though its value is interindividually different (ranging between 2 and 30 ms $mmHg^{-1}$), its age-dependent decrease was proved.[23]

Conventional carotid endarterectomy (C-CEA) is performed through a longitudinal arteriotomy of the internal carotid artery and is the most frequently employed endarterectomy technique. Eversion carotid endarterectomy (E-CEA), initially described by DeBakey and later popularised by Etheredge amongst others,[24,25] is a commonly employed alternative to C-CEA. While E-CEA has the potential advantage that a patch angioplasty is not necessary, the technique requires transection of the longitudinal nerve fibres of the carotid sinus nerve (CSN) and the potential loss of the BRS.[26] This was supported by our previous results demonstrating the differential effect of E-CEA and C-CEA on postoperative blood pressure in the first 4 days after surgery.[27] The literature, however, is not consistent with respect to changes in BRS after C-CEA.[9,17,28–30] Likewise, to the best of our knowledge, no study has compared BRS activity after E-CEA versus the conventional technique.

The aim of this study is to prospectively evaluate the BRS in eversion and conventional techniques. We hypothesise that related to the operative technique there might be substantial differences in BRS which might result in different haemodynamic behaviour in E-CEA and C-CEA.

Methods

From 1 May 2010 till 31 January 2011 consecutive patients admitted to our department with symptomatic and asymptomatic ICA stenosis were included in an open, prospective, comparative study approved by the Ethics Committee of Heidelberg. Patients who had experienced a severe stroke causing major disability (modified Rankin Scale of 3–5) as well as patients with prior carotid surgery were excluded from the study. After exclusion of 12 patients, from a total of 64 patients (E-CEA $n = 37$; C-CEA $n = 27$) informed consent was obtained.

Non-invasive estimates of BRS were calculated in the time-domain (BRS_{TD}) by the sequence (cross-correlation BRS) method, using the Finometer device (FMS; Finapres Medical Systems BV, Amsterdam, The Netherlands).

This device computes the cross-correlation in time-domain between beat-to-beat systolic blood pressure and R–R interval, resampled at 1 Hz, in a sliding 10-s window, with delays of 0–5 s for interval. The delay with the greatest positive correlation is selected and, when significant at $P = 0.01$, slope and delay are recorded as one xBRS value. Each 1 s of the recording is the start of a new computation. The potential advantages of this method over common sequential methods include a much larger number of estimates more regularly distributed over time, a halving of the estimation variance as validated in the EUROBAVAR database and the availability of the best delay as an extra BRS parameter. This technical improvement led to a lower within-patient variance of BRS values. Therefore, the xBRS method has been preferably considered for experimental and clinical use.[31]

Measurements were made on admission day and post-operatively on the first (POD-1) and third (POD-3) postoperative days. All patients were asked to lie down for at least 10 min before measurement. A cuff of appropriate size was attached to the middle finger of the non-dominant hand in the supine position and the hand was maintained at heart level. Blood pressure (mmHg) and heart rate (HR) (beats/min) were measured continuously. Stroke volume and TPR (mmHg $min\ l^{-1}$) were derived from the arterial pressure waveform using a pulse contour analysis method (Modelflow, Finapres, The Netherlands).[32] The Modelflow is a method and algorithm to compute an aortic flow curve from an arterial pressure pulsation by simulating a nonlinear, self-adaptive model of the aortic input impedance. The three-element model is well known from physiology for its ability to compute stroke volume. The aortic characteristic impedance and Windkessel compliance are nonlinearly depending on arterial pressure, the peripheral resistance adapts to changes in mean flow. Stroke volume is computed by taking the area under the flow pulse in systole. CO ($l\ min^{-1}$) is the product of stroke volume and HR. TPR equals the sum of the aortic characteristic impedance and the peripheral resistance. Hypertension was defined when the systolic pressure (SP) exceeded 140 mmHg or the diastolic pressure (DP) exceeded 90 mmHg. In patients receiving antihypertensive therapy with the potential to influence BRS, each measurement was standardised to be performed 1 h after administration of the antihypertensive agents. With regard to the possible influence of cervical plexus anaesthesia on BRS, the first postoperative measurement was performed 24 h after surgery.

Any modification in vasoactive medication due to postoperative hypertension, as well as the length of postoperative hospitalisation, was recorded. Postoperative hypertension was defined as the necessity for acute administration of vasodilators in SPs $\geq$180 mmHg or >40% rise above normal.

Operative technique

The preferable technique for asymptomatic patients was E-CEA with selective shunting based on neuromonitoring of the awake patient, unless the preoperative duplex ultrasonography showed high carotid bifurcation or an extensive arterial stenosis (long segment stenosis) of the ICA. Primary shunting was only used in symptomatic patients with visible signs of infarction on cranial computed tomography (CCT). This strategy is consistent with the experiences and suggestions of Aburahma AF et al.[33] Shunt placement is technically more arduous with the eversion technique, which explains the increased use of C-CEA in symptomatic patients. In symptomatic patients without signs of infarction in the CT scan selective shunting and therefore E-CEA was performed. The carotid sinus nerve was transected to provide complete mobilisation of the carotid bifurcation in E-CEA cases; the nerve was preserved in all C-CEA cases.

Statistics

The Shapiro–Wilk W test was used to test for normality. Medians with interquartile ranges (IQRs) and the nonparametric Wilcoxon signed-ranks test for paired samples were employed for all measures. The Fisher–Freeman–Halton exact test or the Mann–Whitney *U*-test was used to compare differences between proportions and the pre- and postoperative values of the two treatment groups. Differences were considered significant when the two-tailed *P*-value was less than 0.05. Statsdirect statistical software (version 2.7.3, Statsdirect Ltd., Cheshire, UK) was used for statistical analyses.

Table 1
Demographics and indication for surgery of patients undergoing C-CEA and E-CEA.

Patients	C-CEA ($n = 27$)	E-CEA ($n = 37$)	*P*-value
Male	24 (89%)	33 (89%)	
Female	3 (11%)	4 (11%)	>0.99
Age (y)	71	70	0.77
Symptomatic stenosis	12 (44%)	12 (32%)	0.43
Modified Rankin scale			
0	6	10	0.29
1	4	2	
2	2	0	
3	0	0	
4	0	0	
5	0	0	
HTN	27 (100%)	36 (97%)	>0.99
CAD	10(37%)	12 (32%)	0.71
DM	10 (37%)	12 (32%)	0.79
HLP	26 (96%)	34 (92%)	0.63
Symptomatic PAD	5 (19%)	16 (43%)	0.06
Arrythmia	9	11	0.49
Alcohol use	3 (11%)	4 (11%)	>0.99
Nicotine use	7 (26%)	16 (43%)	0.19
BMI (mean)	26.13	25.93	>0.99
ASA			
1	0	0	
2	9 (33%)	10 (27%)	0.59
3	18 (67%)	27 (73%)	
4	0	0	
Stenosis (%) – median	90%	90%	0.57
Contralateral stenosis ≥ 70%	7 (26%)	2 (5%)	0.02
Contralateral occlusion	1(4%)	0 (0%)	0.24
On antihypertensive medication	24 (89%)	34 (92%)	0.77

NS, not significant; HTN, hypertension; CAD, coronary artery disease; DM, diabetes mellitus; HLP, hyperlipoproteinemia; PAD, periphereal artery disease; BMI, body mass index; ASA, American Society of Anesthesiologists.

Results

Baseline demographics and clinical data were similar in the two treatment groups (Table 1); only the rate of contralateral stenosis achieved statistical significance between the groups, with a higher frequency in the C-CEA group (26% vs. 5%, $P = 0.02$). All 27 patients in the C-CEA group (100%) and 36 of 37 patients in the E-CEA group (97%) had a history of hypertension. Among patients with hypertension, 24 (89%) of the C-CEA group and 34 (94%) of the E-CEA group were receiving antihypertensive agents at the time of enrolment. Of those patients receiving antihypertensive therapy, 11 (46%) in the C-CEA group and 23 (68%) in the E-CEA group had normal blood pressure preoperatively. Hypertension despite antihypertensive therapy was present in 13 patients (54%) in the C-CEA group and 11 patients (32%) in the E-CEA group ($P = 0.04$). Preoperative BRS values were significantly different between both groups (median (IQR) C-CEA: 4.59 ms mmHg^{-1} (2.61–7.33) vs. E-CEA: 6.33 ms mmHg^{-1} (4.41–10.86), median difference: 2.35 ms mmHg^{-1}, 95% CI for difference between medians (0.44–4.37), $P = 0.02$). All preoperative haemodynamic parameters were without difference (median difference SP: 7.45 mmHg, $P = 0.26$; DP: 2.98 mmHg, $P = 0.37$; MAP: 5.72 mmHg, $P = 0.16$; HR: 4.33 beats/min, $P = 0.16$; CO: 0.2 l min^{-1}, $P = 0.69$; TPR: 9.63 mmHg min l^{-1}, $P = 0.90$). Changes in BRS and haemodynamic parameters are displayed in Tables 2A and 2B. On POD-1, there was a significant preoperative-to-postoperative BRS increase in the C-CEA group ($P = 0.002$), and a significant decrease in the E-CEA group ($P = 0.0001$) (Fig. 4). These differences persisted till POD-3 for both groups (C-CEA $P < 0.0001$; E-CEA $P = 0.0004$), even though there was a slight tendency towards restoration in the E-CEA group (Fig. 1). While patients undergoing E-CEA showed no significant differences between all pre- and postoperative haemodynamic parameters except HR, the postoperative SP, DP, MAP and TPR after C-CEA showed a marked decrease, particularly on POD-1 (Fig. 2). A significant preoperative-to-postoperative decrease in SP and a constant lower level of DP, MAP, HR, CO and TPR was persistent on POD-3 in the C-CEA group (Fig. 2). HR was significantly increased on POD-1 ($P = 0.0019$) and POD-3 ($P = 0.0005$) in the E-CEA group (Fig. 2).

Compared with patients undergoing E-CEA, C-CEA patients demonstrated an increased BRS on both POD-1 ($P < 0.001$) and POD-3 ($P < 0.001$). As the preoperative BRS showed a significant difference between both groups, a separate analysis after dividing the patient populations into two groups (BRS preop> and ≤median of the whole population (5.89 ms mmHg^{-1})) was done. Analysis of both operative techniques after splitting into these groups showed significant differences in BRS changes after 24 h. In case of a preop BRS >5.89 ms mmHg^{-1} the median difference was −4.94 ms mmHg^{-1} in the E-CEA group compared to

Table 2A
BRS and general haemodynamic parameters averaged over the 10-minute recording (preoperative versus postoperative 24 h).

	C-CEA ($n = 27$)			E-CEA ($n = 37$)			[b]Significances of differences between C-CEA and E-CEA effect
	Preop [median (IQR)]	Postop 24 h [median (IQR)]	[a]Significances pre-post	Preop [median (IQR)]	Postop 24 h [median (IQR)]	[a]Significances pre-post	
BRS_{TD} (ms/mmHg)	4.59 (2.61–7.33)	6.13 (3.81–13.2)	0.002	6.33 (4.81–10.86	4.71 (3.03–6.09)	0.0001	<0.0001
Arterial blood pressure (mm Hg)							
SP	140.15 (118.68–164.76)	110.85 (97.32–123.12)	<0.0001	130.15 (115.94–145.14)	126.96 (155.02–141.24)	0.18	0.01
DP	70.36 (58.23–76.59)	54.69 (49.42–64.56)	0.0003	65.23 (56.65–72.72)	63.6 (56.46–73.51)	0.56	0.008
MAP	95.43 (80.52–104.38)	74.65 (68.63–83.46)	<0.0001	87.03 (79.71–97.16)	85.96 (77.16–96.25)	0.33	0.002
HR (beats/min)	68.11 (61.03–76.09)	66.67 (60.58–79.07)	0.77	63.26 (57.93–72.78)	68.95 (61.85–75.53)	0.002	0.03
CO (l/min)	6.29 (5.17–7.34)	5.75 (4.43–7.95)	0.20	5.99 (5.03–7.38)	6.15 (5.07–7.6)	0.59	0.20
TPR (mmHg min/l)	1274.38 (937.95–1477.43)	1085.74 (753.2–1372.16)	0.04	1149.66 (939.6–1626.47)	1137.82 (947.85–1465.2)	0.37	0.39

C-CEA, conventional carotid endarterectomy; E-CEA, eversion carotid endarterectomy; BRS_{TD}, baroreceptor sensitivity in the time-domain; SP, systolic pressure; DP, diastolic pressure; MAP, mean arterial pressure; HR, heart rate; CO, cardiac output; TPR, total peripheral resistance.

[a] Comparison of non-normally distributed values with Wilcoxon's signed-ranks test.

[b] For statistical comparison of the surgical influence on BRS and haemodynamic parameters differences between preoperative and postoperative values were calculated and analyzed with Mann–Whitney *U*-test.

Table 2B
BRS and general haemodynamic parameters averaged over the 10-minute recording (preoperative versus postoperative 72 h).

	C-CEA ($n = 24$)			E-CEA ($n = 36$)			[b]Significances of differences between C-CEA and E-CEA effect
	Preop [median (IQR)]	Postop 72 h [median (IQR)]	[a]Significances pre-post	Preop [median (IQR)]	Postop 72 h [median (IQR)]	[a]Significances pre-post	
BRS_{TD} (ms/mmHg)	4,59 (2.61–7.33)	6,27 (3.62–13.68)	<0.0001	6.33 (4.81–10.86)	5.26 (3.14–7.62)	0.0004	<0.0001
Arterial blood pressure (mm Hg)							
SP	140.15 (118.68–164.76)	129.83 (112.07–137.73)	0.04	130.15 (115.94–145.14)	136.91 (112.73–156)	0.87	0.26
DP	70.36 (58.23–76.59)	61.48 (53.93–73.08)	0.26	65.23 (56.65–72.72)	68.12 (56.12–75.19)	0.49	0.22
MAP	95.43 (80.52–104.38)	85.71 (72.35–93.01)	0.05	87.03 (79.71–97.16)	91.78 (78.13–101.70)	0.83	0.07
HR (beats/min)	68.11 (61.03–76.09)	70.94 (60.91–79.27)	0.81	63.26 (57.93–72.78)	69.07 (65.9–77.04)	0.0005	0.92
CO (l/min)	6.29 (5.17–7.34)	6.55 (4.63–11.8)	0.83	5.99 (5.03–7.38)	6.39 (4.92–7.99)	0.40	0.90
TPR (mmHg min/l)	1274.38 (937.95–1477.43)	1070.59 (857.96–1574.01)	0.67	1149.66 (939.6–1626.47)	1132.95 (926.07–1489.84)	0.96	>0.99

C-CEA, conventional carotid endarterectomy; E-CEA, eversion carotid endarterectomy; BRS_{TD}, baroreceptor sensitivity in the time-domain; SP, systolic pressure; DP, siastolic pressure; MAP, sean arterial pressure; HR, heart rate; CO, cardiac output; TPR, total peripheral resistance.
[a] Comparison of non-normally distributed values with Wilcoxon's signed rank test.
[b] For statistical comparison of the surgical influence on BRS and haemodynamic parameters differences between preoperative and postoperative values were calculated and analyzed with Mann–Whitney *U*-test.

6.66 ms $mmHg^{-1}$ in the C-CEA group; $P = 0.0004$. In case of a preop BRS $\leq$5.89 ms $mmHg^{-1}$ the median difference was −0.21 ms $mmHg^{-1}$ in the E-CEA group compared to 2.1 ms $mmHg^{-1}$ in the C-CEA group; $P = 0.009$.

Effects on SP, DP, MAP and HR were also in opposite directions in the two groups; decreasing in the C-CEA group compared with the E-CEA patients on POD-1 (Table 2A and Fig. 3) – an effect that lost significance on POD-3 (Table 2B). The Shapiro–Wilk W test detected non-normality for the variables BRS ($P < 0.0001$), HR ($P = 0.02$) and TPR ($P < 0.0001$) as well as for the between groups paired (preoperative-to-postoperative) data.

No significant postoperative neurological, surgical or cardiac complications developed in any patient in either group. The requirement for at least one vasodilator for postoperative hypertension tended to be lower in the C-CEA group than in the E-CEA group (10/27, 37% vs. 23/37, 62%), although this difference did not attain statistical significance ($P = 0.14$). There was no difference in the length of hospitalisation of patients in either group (5 days in each).

In the C-CEA group there was no difference in intensity of preoperative-to-postoperative BRS increase between patients with ($n = 8$) and without ($n = 19$) greater than 70% contralateral stenosis or occlusion ($P = 0.77$). To address the limitation related to the different baseline BRS values between both groups multiple linear regression analysis was performed. Apart from 'operative technique' the independent variables 'history of hypertension', 'on antihypertensive medication' and 'uncontrolled preoperative hypertension (RR >140 mmHg)' were not associated with an altered BRS response after 24 h (Table 3).

Discussion

In the current study, the two commonly employed techniques for CEA were associated with a differential effect on BRS, with decrease after E-CEA and increase after C-CEA, which is a plausible explanation for the different haemodynamics of the respective operative technique.

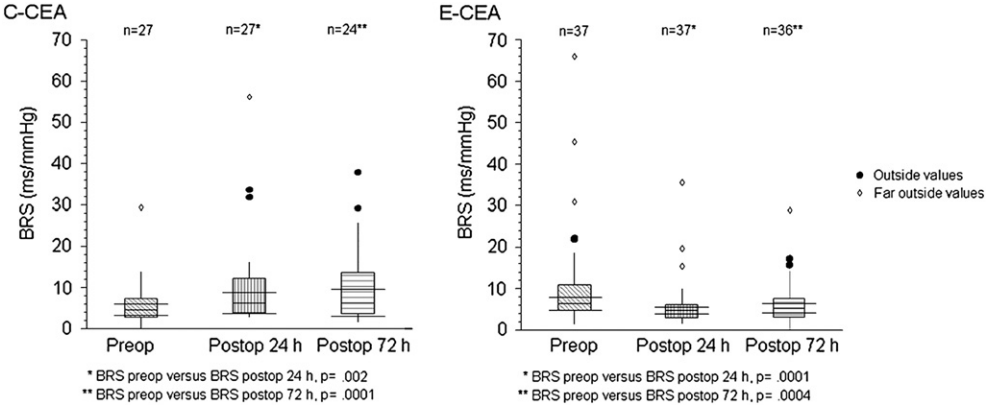

Figure 1. Extended box-and-whisker plots displaying postoperative change of baroreceptor sensitivity (BRS) after C-CEA and E-CEA. Points beyond the whiskers are displayed using ● and ◇. The length of each box represents the interquartile range, defined as the distance between the 25th and the 75th percentiles. The three horizontal lines running through the box represent the median (middle line) and the upper and lower bounds of the 95% confidence interval around the median (median ± 1.58 × the quartile range.) The length of the whiskers above each box depicts 1.5 times the interquartile distance and the length of the whiskers below each box represent the interquartile distance times 1.5 as measured down from the top of the box. Outside values are defined as those data points that are 1.5–3.0 times the interquartile distance, while far outside values are defined as those that exceed 3 times the interquartile distance.

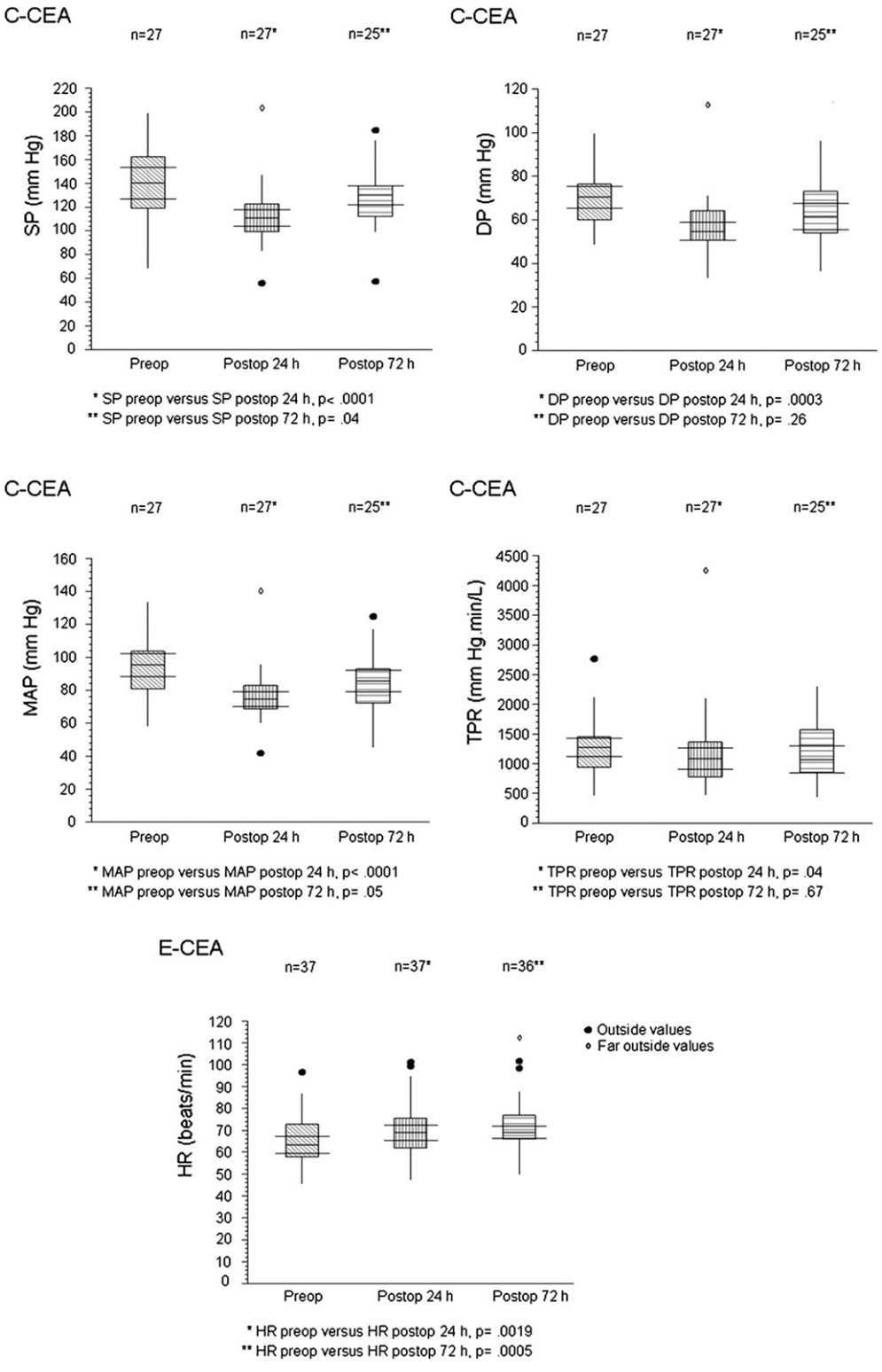

Figure 2. Extended box-and-whisker plots displaying postoperative change of systolic pressure (SP), diastolic pressure (DP), mean arterial pressure (MAP), and total peripheral resistance (TPR) after C-CEA, and heart rate (HR) after E-CEA. Points beyond the whiskers are displayed using ● and ◇.

Consequently, C-CEA and E-CEA appear to have distinct and opposite effects on blood pressure and HR, with increases after E-CEA and decreases following C-CEA persisting to at least the third postoperative day. This observation can most likely be attributed to the baroreceptor apparatus, and the almost certain necessity of carotid sinus nerve transection with eversion technique. Consistent with our findings, a randomised study of local anaesthetic injection of the CSN documented an unacceptably high rate of perioperative hypertension.[34] The failure to detect significant changes in blood pressure values such as SP, DP, MAP, CO as well as TPR after E-CEA suggests that medical interventions successfully controlled blood pressure despite impaired BRS. On the contrary, increases in carotid

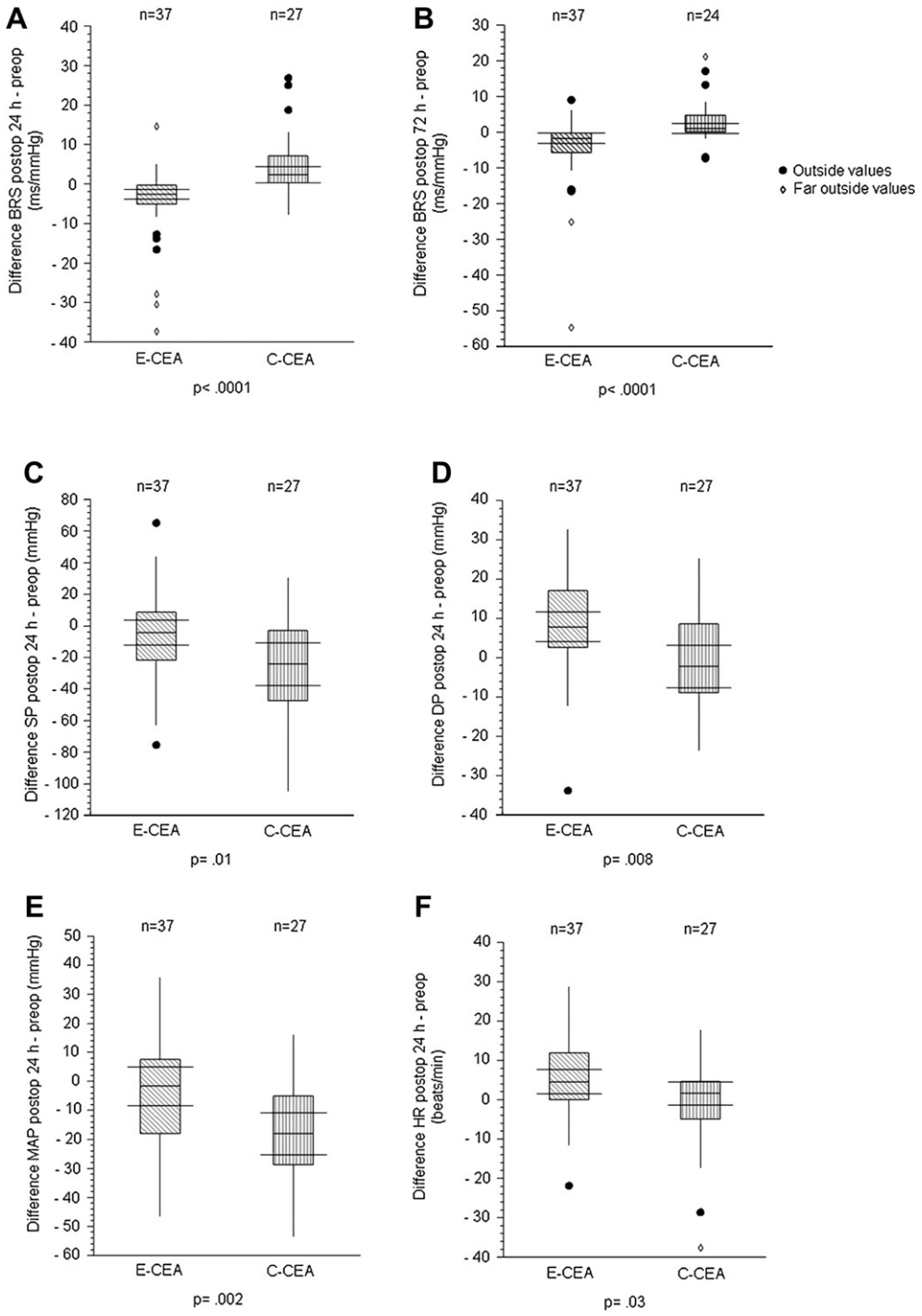

Figure 3. Extended box-and-whisker plots comparing the differences of both operative techniques between pre- and postoperative values of (A/B) baroreceptor sensitivity (BRS), (C) systolic pressure (SP), (D) diastolic pressure (DP), (E) mean arterial pressure (MAP), and (F) total peripheral resistance (TPR). Points beyond the whiskers are displayed using ● and ◇.

bulb diameter from patch angioplasty after C-CEA may result in increased wall tension at the same intraluminal arterial pressure. Under preservation of the CSN, an increased BRS after plaque removal results in an increase of the CSN activity, followed by lowered HR, and decreased blood pressure.

In 1974, at a time when most procedures were performed with the C-CEA technique, Angell-James and colleagues assessed carotid sinus baroreceptor function in nine patients with C-CEA.[9] Using neck suction, reflex bradycardia and a fall in blood pressure were induced pre- and postoperatively, an effect greatest when the carotid sinus nerve had carefully been preserved at the time of operation. The authors speculated that the removal of the rigid atheroma with preservation of the carotid sinus nerve might improve baroreflex sensitivity due to increased vessel compliance. A decade ago, Mehta et al. theorised that in E-CEA postoperative HTN after E-CEA may be attributable to the destruction of the baroreceptor apparatus.[26] In a prior retrospective study we demonstrated that hypertension for the first 4 postoperative days was more frequent after E-CEA than after the conventional technique.[27] Not all studies have demonstrated an increase in BRS after

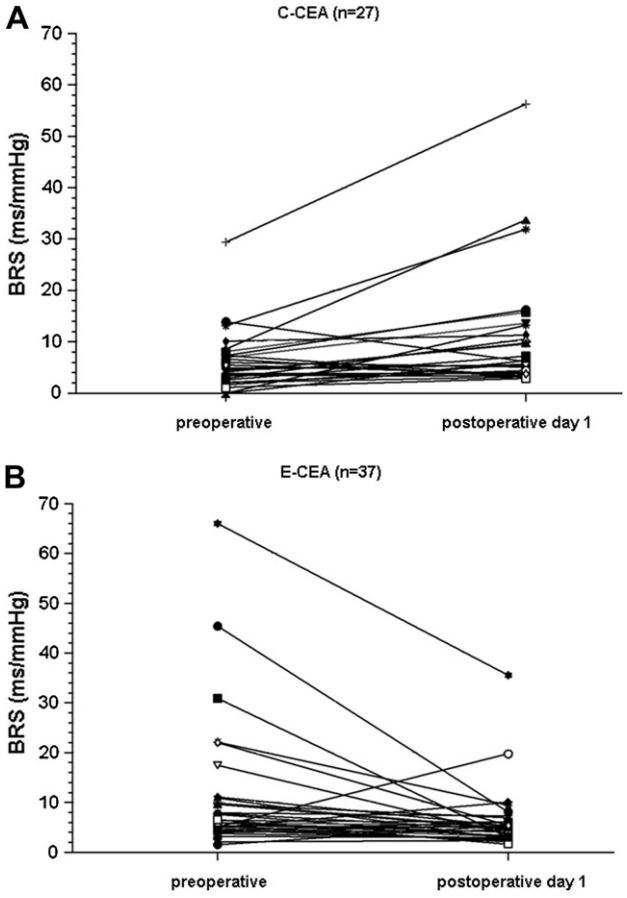

Figure 4. Intra-individual baroreceptor sensitivity (BRS) change from baseline at 24 h following (A) C-CEA and (B) E-CEA.

C-CEA, however. Sigaudo-Roussel et al. observed a significant reduction in BRS 2 days after endarterectomy, falling from 5.1 ± 0.5 to 3.7 ± 0.4,[30] but this finding may have been related to a partial disruption of the carotid sinus nerve during the operations.

In a prospective study by Hirschl and colleagues, baroreflex sensitivity was identified as a factor of long-term prognostic relevance after C-CEA with patch closure.[29] Improvement in receptor sensitivity was associated with a 5-year reduction in the absolute

Table 3
Multiple linear regression analysis showing the influence of different independent variables on BRS change 24 h after surgery.

	Partial regression coefficient	Regression coefficient	*t*-value	*P*-value
Intercept	7.78		0.82	0.41
Syst>140	0.68	0.04	0.28	0.78
On medication	6.13	0.18	1.43	0.16
Operative technique	−10.13	−0.48	−4.25	<0.0001
Hypertension	−8.73	−0.11	−0.86	0.39
Multiple linear regression – Best sub-set				
Intercept	4.86		2.78	0.007
Operative technique	−9.85	−0.48	−4.28	< 0.0001

Multiple linear regression analysis with dependent variable "preoperative-to-postoperative (24 h) BRS change" and independent variables "preoperative systolic blood pressure >140 mmHg, being on antihypertensive medication, operative technique and known hypertension" shows a highly significant model for operative technique. The analysis of the best sub-set confirms that the operative technique is the only significant predictor concerning the BRS difference 24 h after surgery. Even the intercept is significant in this regression model.

level and lability of blood pressure. Besides, patients with at least partially restored postoperative BRS had significant benefit in postoperative left ventricular thickness 5 years following endarterectomy. Furthermore, patients without a postoperative increase of BRS had a significantly higher risk of major vascular events, presumably due to chronic impairment of the BRS. The link between BRS and long-term morbidity was supported by several other studies, noting an increased risk of heart failure, myocardial infarction and stroke.[35–38] Decreased BRS (<3 ms $mmHg^{-1}$) is associated with an increased mortality in patients with a history of myocardial infarction or heart failure.[37–39]

Preoperative neurologic deficits have been reported to be an independent predictor of hypertension after CEA.[16,18] This phenomenon could be attributed to impairment of the central component of the baroreflex.[36] Patients with prior contralateral or ipsilateral carotid surgery might have altered baroreflex function from damage to the carotid sinus nerve and the carotid sinus baroreceptors.[26] Therefore, patients who had experienced a severe stroke causing major disability (modified Rankin Scale of 3–5) as well as patients with prior carotid surgery were excluded from the study.

Our results support the hypothesis that unilateral carotid sinus nerve denervation is sufficient to generate significant physiological changes, in parallel with the clinical findings of a previous study that demonstrated a rise in systolic blood pressure until the fourth day following E-CEA.[27] Our current results show that with eversion technique the BRS dropped significantly on postoperative day 1 and remained markedly reduced on postoperative day 3, but showing a trend towards BRS recovery. Speculatively, the explanation for the transience of this phenomenon may relate to recovery of BRS through the baroreflex apparatus located on the contralateral side and the aortic arch – compensatory mechanisms that may require several days to adapt. Scher et al. demonstrated a rise in mean blood pressure lasting for 1 week in a large animal model of bilateral carotid sinus nerve denervation.[40] However, to our knowledge, no experimental data exist on unilateral carotid sinus nerve denervation.

There are at least two shortcomings in the design of the current study. First, the small sample size may have precluded the identification of true differences in outcome. Second, by virtue of its non-randomised design, differences in baseline variables had the potential to confound the observations. Foremost in this regard was the higher rate of significant contralateral carotid bifurcation disease and a significant lower baseline BRS value in the C-CEA group. This limitation was evaluated with a comparison of subgroups with and without severe contralateral disease, and, while not definitive, this analysis found no relationship between BRS and the degree of contralateral stenosis. Furthermore, we showed that the kind of operative procedure significantly influenced the BRS postoperatively, irrespective of different baseline BRS values.

To sum up, the current study demonstrates that, as compared to the conventional technique, E-CEA is associated with increased sympathetic activity during the early perioperative period, an observation most likely attributable to the transection of the CSN. C-CEA improves BRS resulting in decreased sympathetic activity. Clinically, this implies that patients operated with the eversion technique are postoperatively more prone to blood pressure derailment than those operated with the conventional technique and might be in need for a more thorough blood pressure monitoring. However, longer-term comparative studies are needed to determine if this difference persists beyond the early postoperative period and whether it is associated with protection against hypertension-related cardiovascular and neurologic morbidity.

Conflict of Interest

None.

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