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Arterial Blood Pressure Management during Carotid Endarterectomy and Early Cognitive Dysfunction

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Abstract

Background—A common practice during cross-clamp of carotid endarterectomy (CEA) is to manage mean arterial pressure (MAP) above baseline to optimize collateral cerebral blood flow and reduce risk of ischemic stroke.

Objective—To determine whether MAP management 20% above baseline during cross-clamp is associated with lower risk of early cognitive dysfunction, a subtler form of neurologic injury than stroke.

Methods—One hundred eighty-three patients undergoing CEA were enrolled in this *ad hoc* study. All patients had radial arterial catheters placed prior to induction of general anesthesia. MAP was managed at the discretion of the anesthesiologist. All patients were evaluated with a battery of neuropsychometric tests pre-operatively and 24hrs post-operatively.

Results—Overall, 28.4% of CEA patients exhibited early cognitive dysfunction (eCD). Significantly fewer patients with MAP 20% above baseline during cross-clamp exhibited eCD than those managed <20% above (11.6% vs. 38.6%, $P<0.001$). In a multivariate logistic regression model, MAP 20% above baseline during the cross-clamp period was associated with significantly lower risk of eCD (OR: 0.18 [0.07–0.40], $P<0.001$), while diabetes mellitus (OR: 2.73 [1.14–6.61], $P=0.03$) and each additional year of education (OR: 1.19 [1.06–1.34], $P=0.003$) were associated with significantly higher risk of eCD.

Conclusion—The observations of this study suggest MAP management 20% above baseline during cross-clamp of the carotid artery may be associated with lower risk of eCD after CEA. More prospective work is necessary to determine whether MAP 20% above baseline during cross-clamp can improve the safety of this commonly performed procedure.

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Disclosure

The other authors have no personal financial or institutional interest in any of the drugs, materials, or devices described in this article.

Keywords

carotid endarterectomy; pressure management; cognitive dysfunction

Introduction

Carotid endarterectomy (CEA) is a surgical treatment for patients with high-grade carotid artery stenosis performed to reduce the risk of stroke¹⁻³. The neurologic risks associated with CEA include perioperative stroke and early cognitive dysfunction (eCD) exhibited 24hr post-operatively. Perioperative stroke has an incidence of approximately 5%⁴⁻⁶, and is due to either dislodged emboli or ischemia associated with inadequate collateral blood flow during cross-clamping of the carotid artery^{4, 7}. Approximately a quarter of CEA patients demonstrate eCD 24hrs after CEA^{8, 9}. It is a subtler form of neurologic injury than stroke and is similar to stroke in its pathophysiology; patients with eCD demonstrate significantly elevated markers of neuronal injury¹⁰ as well as asymmetric cerebral blood flow on magnetic resonance perfusion brain scans¹¹.

Although the exact etiology of eCD remains unclear, many studies have investigated a variety of factors that are associated with the incidence of eCD. Those associated with increased risk of eCD include age >75, diabetes mellitus, apolipoprotein-ε4 polymorphism, and a few complement polymorphisms¹²⁻¹⁵. Statin use is significantly associated with decreased risk of eCD in the asymptomatic CEA population¹⁶. However, there are no studies that investigate whether eCD is associated with intra-operative mean arterial pressure (MAP) management during the cross-clamp period.

A common practice during the cross-clamp period of CEA is to manage MAP above baseline MAP to optimize collateral cerebral blood flow to reduce the risk of ischemic stroke by adequately perfusing the hemispheres¹⁷⁻²⁰. As an unpublished rule of thumb, MAP management for CEA is often targeted to be approximately 20% above baseline MAP during the cross-clamp period, but this is not a standardized practice and is at the discretion of the anesthesiologist. During the cross-clamp period, electroencephalography (EEG) monitoring can be utilized to detect ischemic conditions that lead to stroke. The ischemic threshold for EEG is $\sim 18 \text{ mL} \cdot 100 \text{ g}^{-1} \cdot \text{min}^{-1}$, which is approximately a 60% reduction from normal baseline cerebral blood flow at $\sim 50 \text{ mL} \cdot 100 \text{ g}^{-1} \cdot \text{min}^{-1}$ ²¹. However, subtle neurologic injury may occur under mildly ischemic conditions that are undetected by EEG in the range between $18 \text{ mL} \cdot 100 \text{ g}^{-1} \cdot \text{min}^{-1}$ and $50 \text{ mL} \cdot 100 \text{ g}^{-1} \cdot \text{min}^{-1}$. CEA patients with simultaneous transcranial Doppler (TCD) and EEG monitoring demonstrate that a mild reduction in blood flow through the middle cerebral artery measured by TCD can remain undetected by EEG, but still strongly predict eCD as is shown in a previous study²². We have demonstrated that a 28% decrease in blood flow velocity through the middle cerebral artery predicts a higher incidence of eCD²³.

No previous studies have evaluated MAP management 20% above baseline during the cross-clamp period and its association with neurologic injury in the context of eCD. We aim to determine if MAP management 20% above baseline during the cross-clamp period is associated with a lower risk of eCD.

Methods

Patients

Five hundred fifty-one patients were enrolled with written-informed consent in an IRB-approved observational study at Columbia University Medical Center from 1995 to 2012 (www.ClinicalTrials.gov NCT00597883). Eligible patients were scheduled for elective CEA, English-speaking, and had no axis-I psychiatric disorders. Exclusion criteria: 12 experienced a perioperative stroke, 12 were also enrolled in a confounding study, 24 had significant EEG changes during cross-clamp and subsequent shunt placement, 31 withdrew, 32 had post-operative pain exceeding subjective level 5 on a 0 to 10 scale, which has been shown to affect neuropsychometric performance²⁴, 47 did not complete the entire neuropsychometric battery, and 210 did not have cross-clamp times indicated on the anesthesia or EEG records. None of the 183 included patients in this study had significant EEG changes and therefore none had a shunt placed during the cross-clamp period.

Anesthesia

Standard monitors, which included a blood pressure cuff, pulse oximeter, 5-lead electrocardiogram, and esophageal temperature probe, were used for every case. The radial intra-arterial catheter used to measure intra-operative blood pressure was placed prior to induction of general anesthesia in every case. All patients received intravenous lines in the operating room. The intravenous fluid goal was 1 L total for each case. The anesthetic technique involved a pre-induction dose of midazolam (1–5 mg) and fentanyl (25–250 µg); induction by etomidate (0.15–0.3 mg/kg), propofol (1–2 mg/kg), or thiopental (3–5 mg/kg); and management with 70% nitrous oxide in oxygen and isoflurane (0.3%–0.7%).

MAP changes were achieved by a phenylephrine infusion using a Sigma Spectrum Infusion Pump (Baxter, Deerfield, IL), which is used to administer phenylephrine in µg/min, supplemented with boluses. Ephedrine boluses were administered at the discretion of the anesthesiologist if the patient exhibited significant bradycardia in conjunction with hypotension. The administration of drugs, including phenylephrine and ephedrine, were entered manually by the anesthesiologist.

A 16-channel EEG (Xltek, Natus Medical Incorporated, San Carlos, CA) was used for 91% of the CEA patients with either an EEG electrode cap (Electro-cap International Inc., Eaton, OH) or subdermal needle electrodes according to the 10–20 International electrode placement position in a bipolar “double-banana” montage. The remaining 9% of CEA patients had an 8-channel EEG (Neurotrac II; Moberg Medical, Inc, Ambler, PA) using a subset of the 10–20 International electrode placement in a referential montage referred to the ears. The EEGs were read by either a trained neurosurgical anesthesiologist or a board-certified neurologist. Significant EEG changes at cross-clamping of the carotid artery were defined as either a 50% decrease in amplitude in the alpha or beta frequencies and a similar increase in the delta or theta frequencies, or complete loss of all cerebral electrical activity.

Mean Arterial Pressure

Baseline MAP was recorded in the holding area prior to surgery via blood pressure cuff, and MAP during the procedure was recorded using an Anesthesia Information Management System (CompuRecord, Phillips North America, Andover, MA) via intra-arterial catheter. Cross-clamp time was defined as time during which there was no direct blood flow to the ipsilateral hemisphere; duration of cross-clamp was timed from the moment the clamp was applied to stop flow through the internal artery until the clamp was removed and flow restored to the ipsilateral hemisphere. The cross-clamp start and end times were identified via the anesthesia and EEG records. The “duration of cross-clamp” was the difference in the minutes between these two time points. Continuous MAP readings with an intra-arterial catheter were recorded at 15s intervals. The cross-clamp MAP value used in this analysis was determined using an Excel macro (Microsoft Corp., Redmond, WA). A previously developed algorithm identifies the stable MAP of the cross-clamp period²⁵.

MAP values during the cross-clamp period were extracted and imported into the Excel macro. The average stable MAP during the cross-clamp period was calculated by generating a running MAP standard deviation (SD) curve. A curve is created by calculating the SD of 5 consecutive MAP recordings after the clamp was placed. Once the SD of the running average of MAP was below 5mmHg, the subsequent MAP values were averaged until the SD curve exceeded 10mmHg, or until the clamp was released. The stable MAP value during the cross-clamp period was then used in all analyses. Again, this technique has been used in prior studies²⁵.

The anesthesiologists managed MAP at their own discretion, as there were no protocols or randomizations in this study. All anesthesiologists were aware that the patient was participating in a research study, but were not aware that MAP values would be collected or studied. Seven (7) anesthesiologists administered the anesthetics for all patients.

An unpublished rule of thumb for MAP management during CEA is often approximately 20% above baseline during the cross-clamp period. For this reason, we utilized 20% as the threshold of interest. Change in MAP from baseline to cross-clamp was calculated by subtracting baseline MAP from stable cross-clamp MAP and then dividing by baseline MAP $[(MAP_{\text{cross-clamp}} - MAP_{\text{baseline}})/MAP_{\text{baseline}}]$.

Cognitive Measures

The outcome of eCD was evaluated using a battery of neuropsychometric tests pre-operatively and 24hr post-operatively. The outcome of eCD is binary (yes/no). The battery of neuropsychometric tests was developed by an experienced neuropsychologist. The tests utilized in this study have been well validated and widely used in the field of neuropsychological assessment²⁶⁻³². Furthermore, the same and/or similar tests have been used in other studies to determine cognitive dysfunction in CEA patients^{8, 33, 34}. The tests evaluate four cognitive domains – verbal memory (Hopkins Verbal Learning Test, Controlled Oral Word Association Test, Buschke), visuo-spatial organization (Rey-Osterrieth Complex Figure Copy and Recall), motor function (Grooved Pegboard and/or Finger Tapping Test), and executive action (Halstead-Reitan Trials A and B). The term

“domain” refers to cortical areas that are required to perform a cognitive task in conjunction with each other. For example, the language domain involves neurons in the frontal, parietal, and temporal lobes, specifically Broca’s area, the angular gyrus and Wernicke’s area. These areas have to be connected and function in an organized sequence for the cognitive task to be completed.

The criteria for eCD are based on difference scores calculated for each test by subtracting the pre-operative test performance from the post-operative test performance at 1 day. Similar to previous studies^{16, 35}, a Z-score was generated based on a surgical reference group’s performance to account for practice effect, general anesthesia, trauma of surgery, and the post-operative experience. The reference group was only used to generate normalized Z-scores; they were not included in any other analysis.

The surgical reference group was composed of 156 age- and education-matched patients undergoing lumbar level laminectomy or microdiscectomy 2 levels without fusion or blood loss necessitating transfusion. The reference group had a similar anesthetic to the CEA patients, which accounted for any pharmacologic influences on eCD in the post-operative period. The mean difference score of the reference group was subtracted from the difference score for the CEA patient and then divided by SD of the reference group ($[\text{Difference}_{\text{CEA}} - \text{Mean Difference}_{\text{Reference}}] / \text{SD}_{\text{Reference}}$). Therefore, each test was evaluated in units of SD of the reference group’s change in performance. CEA patient domains were evaluated to account for both focal and global/hemispheric deficits: (1) 2SD worse performance in 2 cognitive domains or (2) 1.5SD worse performance in all 4 cognitive domains.

Confounders

In effort to detect potential confounders, we evaluated whether the incidence of eCD was different among a number of variables. For example, we evaluated: the surgeons, closure techniques (with a patch or primary closure), durations of surgery, durations of carotid artery cross-clamp, and doses of midazolam ($\mu\text{g/kg}$) and/or fentanyl ($\mu\text{g/kg}$). Furthermore, to address whether the 7 anesthesiologists managed patients significantly differently, we evaluated the distribution of MAPs during cross-clamp in increments of 10% (i.e. below baseline, 10% above baseline, 20% above baseline, 30% above baseline, <40% above baseline, and 40%) above baseline MAP. Another consideration is whether the anesthesiologists altered their anesthetic goals as a function of the patient’s cardiac history of myocardial infarction (MI), coronary artery bypass-graft (CABG), or presence of peripheral vascular disease (PVD). We evaluated the incidence of eCD and MAP management for patients with MI, CABG, and PVD.

Statistical Analysis

Statistical analysis was performed using JMP 10 software (SAS Institute Inc, Cary, NC). For univariate analyses, Student’s t-test, Wilcoxon rank sums test, Fisher’s exact test, Pearson’s χ^2 test, and simple logistic regression were used where appropriate. A multiple logistic regression model was constructed to identify independent predictors of eCD. All factors with $P < 0.20$ in simple univariate logistic regression with eCD were entered into the final

model. Of note, statin use was included, as previous work demonstrates that statins significantly reduce the incidence of eCD¹⁶. $P = 0.05$ was considered significant.

Results

Characteristics of the overall cohort are presented in Table 1. Sixty-nine (69) patients (37.7%) had a MAP managed $\geq 20\%$ above baseline. Patients managed $\geq 20\%$ above baseline MAP had significantly lower baseline MAP (109.6 ± 9.8 mmHg vs. 115.5 ± 14.1 mmHg, $P=0.002$) and higher cross-clamp MAP (141.1 ± 14.8 mmHg vs. 125.2 ± 15.1 mmHg, $P<0.001$) than patients managed $<20\%$.

Overall, 28.4% of CEA patients exhibited eCD. Baseline MAP was similar between patients with and without eCD (112.8 ± 10.1 mmHg vs. 113.5 ± 13.9 mmHg, $P=0.75$). MAP at cross-clamp was significantly lower in the patients with eCD (124.4 ± 13.4 mmHg vs. 133.9 ± 17.3 mmHg, $P<0.001$). The incidence of eCD was significantly lower in patients whose MAP was managed $\geq 20\%$ above baseline compared to those managed $<20\%$ above baseline (11.6% vs. 38.6%, $P<0.001$).

Seven (7) patients had a MAP below baseline during cross-clamp and exhibited a very high incidence of eCD (85.7%). With each 10% increase above baseline, the incidence of eCD consistently decreased until $\geq 40\%$ above baseline (Figure 1). Six patients had a MAP $\geq 40\%$ above baseline and exhibited a slightly higher incidence of eCD (16.7%); these 6 patients did not differ from the rest of the cohort in patient characteristics, medical histories, medication use, or operative experience.

Based on simple univariate regression, education, diabetes mellitus, statin use, and MAP $\geq 20\%$ above baseline during cross-clamp were the only variables included in the final multivariate regression. In the final model, MAP $\geq 20\%$ above baseline during cross-clamp was associated with significantly lower risk of eCD (OR: 0.18 [0.07–0.40], $P<0.001$) while diabetes mellitus (OR: 2.73 [1.14–6.61], $P=0.03$) and each additional year of education (OR: 1.19 [1.06–1.34], $P=0.003$) were associated with significantly higher risk (Table 2).

No significant differences in the incidence of eCD were found among these factors: surgeon ($P=0.19$), closure using a patch or primary closure ($P=0.74$), duration of surgery ($P=0.77$), duration of cross-clamp ($P=0.88$), dose of midazolam $\mu\text{g/kg}$ ($P=0.31$), dose of fentanyl $\mu\text{g/kg}$ ($P=0.77$). We found no evidence that patients with PVD or previous CABG may have been managed differently, though more patients with previous MI had MAP $<20\%$ above baseline during cross-clamp (48.3% vs. 64.9%, $P=0.09$). There is no significant evidence that the anesthesiologist altered anesthetic goals as a function of the presence of PVD. There were no differences in the incidence of eCD in patients who had previous CABG ($P=0.75$), PVD ($P=0.89$), or MI ($P=0.74$) compared to patients without these conditions. The distribution of MAPs during cross-clamp in increments of 10% was not significantly different among the 7 anesthesiologists ($P=0.99$, χ^2 test).

Discussion

Neurologic risks of CEA include perioperative stroke and eCD exhibited 24hr post-operatively. MAP managed above baseline during the cross-clamp period optimizes collateral blood flow to adequately perfuse the hemispheres and reduces the risk of ischemia^{17–20, 36}. Although a rule of thumb often utilized in CEA procedures is to maintain MAP approximately 20% above baseline, no studies have investigated MAP 20% in the context of neurologic outcomes following surgery. This study measured eCD as a function of MAP management. The observations of this study suggest MAP managed 20% above baseline during the cross-clamp period is associated with less risk of eCD and may improve the neurologic safety of this commonly performed procedure.

The etiology of eCD is likely associated with mild ischemia, which produces subclinical events during cross-clamp that remain undetected by EEG^{22, 37}. Previous work demonstrates eCD is not associated with cerebral ischemia severe enough to be measured by magnetic resonance imaging (MRI) with diffusion weighted imaging (DWI)^{37, 38}. Additionally, scalp EEG electrodes sum large areas of cortical electrical activity that may be up to 45 cm²³⁹. Therefore, significant subclinical cortical functional changes likely occur even when not reflected by scalp EEG changes or by MRI with DWI. However, eCD is reflective of cerebral parenchymal injury as documented by elevations in serum S100B concentrations. S100B is a glial protein associated with the volume of ischemic cerebral tissue⁴⁰.

We are uncertain whether the mechanism behind the greater incidence of eCD in patients maintained <20% above baseline MAP during cross-clamp is associated with lack of adequate perfusion of collaterals; patients may have impaired autoregulation and when systemic blood pressure is reduced below the patient's lower limit of autoregulation, cerebral perfusion can be pressure dependent. Furthermore, patients with carotid stenosis are likely to have systemic atherosclerosis, and as such may have chronic hemispheric ischemia. For example, the stenotic area distal to the carotid occlusion may already be maximally dilated and autoregulation may not be fully intact. This idea is supported by Schoof et al. in a study of impaired cerebral autoregulation in cardiac surgery as related to carotid stenosis⁴¹. They similarly reported that increased pressure may be necessary to compensate for "exhausted cerebrovascular reserve", but remark that increasing pressure can be controversial in terms of stroke risk⁴¹. In summary, there is definite evidence to support reasoning that autoregulation is impaired in CEA patients, making cerebral blood flow pressure dependent. We did not directly evaluate autoregulation as a part of this study but found several studies that utilize transcranial Doppler to confirm this^{42–45}. Regardless of the etiology in CEA, this study demonstrates that maintaining MAP 20% of baseline is significantly associated with lower incidence of eCD.

Limitations

We acknowledge the limitations of this study. While there were a number of potential confounders in this study, we found no evidence that any of the factors were associated with the incidence of eCD or MAP management. This is a single center observational study, therefore it does not have strong external validity. The hemodynamic management was

neither standardized nor randomized. The hemodynamic intentions of the anesthesiologist were not recorded. More patients with previous MI had MAP <20% above baseline during cross-clamp and while not significantly so, this raises a potential confounding variable; patients with previous myocardial infarction may not only be treated differently hemodynamically, but they may have different cerebrovascular systems. We are uncertain of the influence this has on our findings. While history of MI was implicated in maintenance of MAP during cross-clamp, it is important to note that eCD is not associated with previous MI when compared to patients who had no history of MI ($P=0.73$). Years of education were significantly associated with increased risk of eCD; this finding was unexpected, and currently, we do not have a plausible suggestion as to why or how this association exists. We can, however, speculate that because patients with increased years of education perform better (on the battery of neuropsychometric tests) at baseline, they subsequently appear to decline more than less educated patients.

It is unclear why 6 patients were managed 40% above baseline during cross-clamp and how this influenced their incidence of eCD. We acknowledge that this small subset of patients is not comparable to the greater population; we cannot assert that MAP maintained 40% above baseline is always deleterious, but we do believe it is an interesting observation that should be evaluated in future research. We speculate that increasing MAP too high (ie. 40% above baseline) could potentially dislodge emboli, hyperperfuse the affected hemisphere, or otherwise result in poor outcomes⁴⁶.

Generalizability

While this is an *ad hoc* study, we consider it unethical to have performed a prospective study, since lowering MAP during cross-clamp would be considered a significant deviation from “standard of care”. Further prospective work is necessary to determine if increasing MAP to 20% above baseline is an appropriate and safe threshold for the cross-clamp period of CEA. Future studies also need to consider each patient’s co-morbidities and determine their influences on safe MAP management. The key observation of this study is that MAP managed 20% above baseline may be associated with less risk of eCD and improved neurologic safety of CEA. We speculate this observation is due to optimized collateral blood flow and reduced risk of mildly ischemic conditions. Future studies exploring and confirming these observations can improve the safety of CEA.

Conclusion

This study suggests MAP management 20% above baseline during cross-clamp of the carotid artery may be associated with a significantly lower risk of eCD after CEA. More work is necessary to determine whether MAP 20% above baseline during cross-clamp can improve the safety of this commonly performed procedure.

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Figure 1.

Bar graph of the incidence of eCD by MAP management during cross-clamp; y-axis is the percentage of patients with eCD and x-axis is the MAP percentage range during cross-clamp relative to baseline. Values above each bar is the respective number of patients with eCD in the management group/total number of patients managed in that management group, and the percentage of eCD. Error bars represent 95% confidence intervals.

Table 1

Patient Characteristics *.

	All Patients N=183	≥20% Above N=69	<20% Above N=114	P
Age >75	33.3%	31.2%	34.2%	0.75
Sex, male	59.0%	66.7%	54.4%	0.10
BMI [†] , kg/m ²	26.9±4.5	27.4±4.5	26.9±4.4	0.43
Education, years	14.6±3.3	14.7±3.3	14.7±3.3	0.95
Symptomatic [†]	41.5%	42.0%	41.2%	0.92
Diabetes Mellitus	18.0%	17.4%	18.4%	0.86
Hypertension	57.9%	60.9%	56.1%	0.53
Smoking History	68.3%	75.4%	64.0%	0.11
History of MI [†]	15.9%	12.3%	21.7%	0.09
History of CABG [†]	16.8%	15.2%	17.7%	0.66
Statin	80.3%	76.8%	82.5%	0.36
Operative Side, Right	52.6%	54.7%	51.2%	0.64
Cross-Clamp, mins	44.2±17.4	43.2±18.4	42.1±12.9	0.35
Primary Closure (vs. Patch)	72.4%	70.7%	73.5%	0.66
Baseline MAP, mmHg	113.3±12.9	109.6±9.8	115.5±14.1	0.002
MAP during Cross-Clamp, mmHg	131.2±16.8	141.1±14.8	125.2±15.1	<0.001
Change in MAP	16.1%	28.7%	8.5%	<0.001
Incidence of eCD	28.4%	11.6%	38.6%	<0.001

* Mean ± standard deviation or percentage.

[†] BMI – body mass index; symptomatic – history of stroke or transient ischemic attack; MI – myocardial infarction, CABG – coronary artery bypass graft.

Table 2

Logistic Regression Model.

	Univariate Odds Ratio	P	Multivariate Odds Ratio	P
Age >75	1.22 (0.62–2.38)	0.56		
Sex, male	1.21 (0.63–2.31)	0.57		
BMI [†] , per kg/m ²	1.02 (0.95–1.10)	0.63		
Education, per year	1.16 (1.05–1.31)	0.11	1.19 (1.06–1.34)	0.003
Symptomatic [†]	1.09 (0.74–1.61)	0.65		
Diabetes Mellitus	2.55 (1.16–5.56)	0.02	2.73 (1.14–6.61)	0.03
Hypertension	1.02 (0.70–1.50)	0.91		
Smoking History	1.09 (0.72–1.64)	0.70		
History of MI [†]	1.02 (0.70–1.69)	0.73		
History of CABG [†]	1.00 (0.52–1.89)	0.99		
Statin Use	0.64 (0.30–1.41)	0.26	0.52 (0.21–1.28)	0.16
Right Operative Side	1.04 (0.71–1.52)	0.85		
Cross-Clamp, per min	1.00 (0.98–1.02)	0.88		
Primary Closure (ref=Patch)	0.93 (0.62–1.41)	0.74		
Baseline MAP, per mmHg	1.00 (0.98–1.03)	0.74		
20% Above Baseline MAP	0.21 (0.09–0.46)	<0.001	0.18 (0.07–0.40)	<0.001

* Mean ± standard deviation or percentage.

[†] BMI – body mass index; symptomatic – history of stroke or transient ischemic attack; MI – myocardial infarction, CABG – coronary artery bypass graft