**Title: Low Left Atrial Volume is an Independent Predictor of Persistent Hypotension After Carotid Artery Stenting**

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Figures and Tables: 2 Figures, 3 Tables

**Word count** (excluding title page, abstract, references, figures and tables): 2654/3500 words

**Running head:** Low LA volume and hypotension after CAS

**Abstract**

*Background:* Persistent hypotension (PH) after carotid artery stenting (CAS) is a relatively common complication; however, it is unclear which patients are more likely to experience this phenomenon. Recently, lower left atrial (LA) volume was associated with vasovagal syncope, which has a similar neurological mechanism to hypotension after CAS. This study aimed to investigate whether LA volume can predict PH after CAS.

*Methods:* This single-center retrospective analysis used data from 316 patients who had undergone CAS between March 2013 and February 2021. After the exclusion of urgent CAS, 212 procedures (202 patients) with transthoracic echocardiograms were included. The procedures were divided among two groups according to the presence or absence of PH for more than 1 hour after CAS.

*Results:* The mean age was 73.0±7.5 years. PH was observed during 52 (24.5%) procedures. The PH group exhibited a lower LA volume index (LAVI) than the no-PH group (29.7 ± 9.1 vs 37.7±12.5%, respectively; $p < .001$). The area under the receiver operating characteristic curve was 0.716. The optimal cut-off value was 33.5 mL/m$^2$ (sensitivity, 0.750 and specificity, 0.625). Multiple logistic regression analysis showed that LAVI < 33.5 mL/m$^2$ was an independent predictor for PH after CAS (odds ratio [OR], 4.950; 95% confidence interval

[CI], 2.190–11.200; $p < .001$). Preoperative hydration was negatively associated with PH (OR, 0.235; 95% CI, 0.070–0.794; p=.020).

*Conclusions:* A lower LA volume can predict PH after CAS, and preoperative hydration may prevent PH after CAS.

**What is already known on this topic**

Hemodynamic instability after CAS is relatively common, and it leads to prolonged hospital stay and increased mortality. Various factors, such as age, sex, coronary artery disease, degree of stenosis, plaque location, and calcification, have been implicated in the development of CAS-induced hemodynamic instability. However, its impact on cardiac function and morphology, which are the factors that actually control circulation, has received limited attention.

**What this study adds**

This study showed that low LA volume, represented by LAVI on a transthoracic echocardiogram, is an independent predictor of persistent hypotension after CAS. Patients with a lower LA volume reserve can experience a significant reduction of cardiac output due

to low LA reservoir function. This finding is supported by its similarity to the mechanisms of vasovagal syncope and hypotension after CAS.

**How this study might affect research, practice or policy**

Clinicians may focus more on transthoracic echocardiography before CAS to evaluate LA reservoir function and select patients at high risk for PH. Adequate hydration therapy in patients with low LAVI to increase fluid retention before and during CAS in preparation for preload reduction may prevent PH after CAS.

**Keywords:** Atherosclerosis, Blood pressure, Plaque, Stent, Catheter

## INTRODUCTION

Hemodynamic instability after carotid artery stenting (CAS) is relatively common and leads to prolonged intensive care unit (ICU) and hospital stay as well as increased mortality.[1,2] Although various risk factors for hemodynamic instability after CAS have been reported, little attention has been directed toward cardiac function and morphology, the factors which actually control circulation. The underlying mechanism of hemodynamic instability after CAS has been proposed as follows: stimulation of the baroreceptors by direct compression during CAS sends impulses to the nucleus of the solitary tract in the medulla oblongata. This causes the inhibition of sympathetic nerves and stimulation of parasympathetic nerves within the vagus nerve. Ultimately, this results in the inhibition of cardiac function and peripheral vasodilation.[3,4] Meanwhile, vasovagal syncope is also considered to cause loss of consciousness due to hypotension via the nucleus of the solitary tract, following the same mechanism described above for hemodynamic instability after CAS (Figure 1). Some studies have reported that low left atrial (LA) volumes, represented by the LA volume index (LAVI) on transthoracic echocardiography (TTE), are associated with the development of hypotension in vasovagal syncope. The intracardiac reserve volume estimated by the LA volume has been documented as an important factor in hemodynamic

stability during acute preload reduction.[5,6] However, no study has investigated the relationship between LAVI and hypotension after CAS. Thus, this study aimed to investigate the relationship between anatomical and functional properties of the cardiac chamber, including LAVI, and persistent hypotension (PH) after CAS.

## MATERIALS AND METHODS

### Study population and design

We retrospectively analyzed data collected from patients who had undergone CAS between March 2013 and February 2021. A total of 316 consecutive CAS procedures had been performed at our institution to treat carotid artery stenosis during this period. The degree of stenosis was determined using the North American Symptomatic Carotid Endarterectomy Trial criteria.[7] The criteria for CAS were carotid artery stenosis of ≥50% for symptomatic cases and ≥70% for asymptomatic cases. The study exclusion criteria were emergency CAS for stroke in evolution or crescendo transient ischemic attack (n=66), scheduled CAS without TTE before the CAS procedure (n=31), CAS for restenosis after previous CAS (n=5), and CAS with general anesthesia after CAS due to hyperperfusion syndrome (n=2). Finally, a total of 212 procedures (202 patients) were included in this analysis. Procedures were divided into two groups: PH and no-PH after CAS. PH was defined as systolic blood pressure of less

than 90 mmHg lasting more than 1 hour; bradycardia was defined as a heartrate of less than 40 bpm.[8–10] All patients underwent preprocedural carotid ultrasound to evaluate plaque characteristics, and carotid artery calcification was defined by the presence of a bright echogenic sign with acoustic shadowing.[11]

**CAS procedures**

Aspirin (100 mg) and clopidogrel (75 mg) or cilostazol (200 mg) were administered for a minimum of 7 days before the procedure. Anti-hypertensive agents were discontinued on the day of treatment. Extracellular fluid (saline or lactate Ringer's solution) was administered before CAS at the surgeon's discretion. Preoperative hydration was defined as infusion of ≥500 mL of extracellular fluid before CAS. Compression stockings were worn during the perioperative period. CAS procedures were performed under local anesthesia via the percutaneous transfemoral route. A heparin bolus was administered immediately before the procedure to increase the activated clotting time to a minimum of 250 s. The primary embolic protection devices used in this study provided proximal and distal balloon protection using the Mo.Ma Ultra (Medtronic, Minneapolis, MN) and Carotid Guardwire (Medtronic, Dublin, Ireland) devices, respectively. Intravascular ultrasound was used to measure the diameters of

the proximal common carotid artery and distal internal carotid artery. Temporary pacing during CAS was implemented at the surgeon's discretion in cases with severe calcified plaque encountered before the procedure. Atropine (0.25 mg) was administered before balloon dilatation or stent deployment with the exception of one patient due to glaucoma. A fluid bolus of 500 mL extracellular fluid was administered immediately before balloon dilatation. If hypotension developed (systolic blood pressure of less than 90 mmHg), an additional fluid bolus of 500 mL of extracellular fluid was administered. After pre-dilatation of the balloon to 3.0–4.5 mm × 40 mm (inflation pressure, 6–10 atm), the following stents were deployed in the stenotic lesion: open cell stent (Precise [Cordis, Dublin, OH] and Protégé [Covidien, Irvine, CA]), closed cell stent (Wallstent [Boston Scientific, Watertown, MA]), or dual layered stent (CASPER stent [MicroVention Terumo, Aliso Viejo, CA]). After stent deployment, post-dilatation to the distal reference vessel diameter was performed with a balloon to achieve an optimal stenting result (4.0–4.5 mm × 20–30 mm; inflation pressure, 6–10 atm). Patients undergoing CAS were admitted to the ICU, where neurologic and hemodynamic status were continuously monitored after CAS. A total infusion of 2000 mL of extracellular fluid was administered after CAS until the following day of CAS. If hypotension developed (systolic pressure of less than 90 mmHg), an additional fluid bolus of

500 mL of extracellular fluid was administered. Regardless of hydration, patients who developed hypotension (systolic blood pressure of less than 80 mmHg) were treated with dopamine or norepinephrine. Patients with PH were kept in the supine position in the ICU. Patients were discharged from the ICU on the next day or later following CAS, if there were no major problems such as PH or neurological complications.

**Transthoracic echocardiography**

All included patients underwent comprehensive TTE before CAS (median, 52 days; IQR, 21.5–97.5 days). Baseline echocardiographic recordings and measurements were obtained by cardiologists and echocardiographers. Echocardiography was performed using commercially available ultrasound machines (Epiq7 and iE33: Philips Healthcare, Amsterdam, The Netherlands; Artida: Canon Medical, Otawara, Japan). Measurements and recordings were obtained according to the American and European Society of Echocardiography recommendations.[12] Imaging included apical two- and four-chamber views. From these, the left ventricular (LV) and LA volumes were measured using the biplane method of disks using two-dimensional images. These volumes were used to calculate the LAVI and LV ejection fraction. E/e' was the mean value of septal and lateral E/e'. Using

continuous-wave Doppler, we determined the peak velocity of the tricuspid regurgitation velocity. Systolic pulmonary artery pressure was estimated as the sum of the trans-tricuspid systolic pressure gradient and right atrial (RA) pressure. The RA pressure was estimated based on the inferior vena cava diameter and collapsibility.

**Statistical analysis**

The baseline characteristics are summarized as the mean (standard deviation) or frequency count and proportion (%), as appropriate. Data were compared between procedures with and without PH after CAS as follows: categorical variables were compared using Fisher's exact tests and normally distributed continuous variables were compared using Student's *t*-tests. We evaluated the discrimination ability of LAVI for PH after CAS using the area under the receiver operating characteristic curve (AUROC). For internal validation, the optimism-corrected performance was estimated using 1,000 bootstrap samples.[13] The optimal cut-off value was chosen to maximize the sum of sensitivity and specificity. The odds ratios (ORs) for PH after CAS were calculated using multiple logistic regression models with several variables reported as risk factors in previous studies, including age, sex, plaque location, calcification, degree of stenosis, coronary artery diseases, hypertension, LAVI, and

preoperative hydration. Statistical analyses were performed using R, version 3.63 (R Development Core Team, Vienna, Austria). Differences were considered significant at $p < .05$.

## RESULTS

### Comparisons of baseline characteristics and peri-procedural parameters

Table 1 summarizes the main characteristics of the study population. The mean age was 73.0±7.5 years, and 89.1% of the patients were male. Of the procedures, 51.4% were performed in symptomatic patients. The mean degree of stenosis was 69.1±18.0%. Out of 212 procedures, PH was experienced in 52 (24.5%), with PH requiring vasopressor administration for more than 3 hours experienced in 36 (17.1%). Bradycardia was observed in four procedures (1.9%). Intraoperative bradycardia was transient and did not persist in any patient. Hypertension and the use of anti-hypertensive agent were significantly less frequent in the PH group than in the no-PH group (65.4% vs 85.0%; $p = .004$ and 63.5% vs 80.0%; $p = .024$, respectively). No significant between-group differences in other demographic features were identified. PH after CAS occurred significantly more frequently when a calcified lesion involving the carotid bulb was observed on carotid ultrasound (82.7% vs 62.5%, respectively;

$p$ =.006). The degrees of stenosis and plaque placement were not significantly different between the two groups. Preoperative hydration was less common in the PH group than in the no-PH group (9.6% vs 23.1%, respectively; $p$ =.044). Open cell stents were used in 188 procedures (88.7%) (Precise [n=184] and Protégé [n=4]), closed cell stents (Wallstent) in 2 (0.9%) procedures, and dual layered stent (CASPER) in 22 (10.4%) procedures, with no significant differences between the two groups. There were also no significant differences in other procedural characteristics including use of balloon dilatation or implementation of temporary pacing during CAS. While the length of hospital stay was not significantly different between the two groups, the duration of ICU stay was significantly longer in the PH group than in the no-PH group (1.5 ± 1.0 days vs 1.2 ± 0.9 days; $p$ =.017). The incidence of symptomatic ischemic stroke after CAS did not differ significantly between the two groups.

Table 1. Univariate analysis of demographic features and perioperative parameters related to postprocedural persistent hypotension

| | All (n=212) | PH group (n=52) | no-PH group (n=160) | *p*-value |
|---|---|---|---|---|
| Age, mean, years | 73.0 ± 7.5 | 73.2 ± 7.0 | 73.0 ± 7.7 | .91 |

| | | | | |
|---|---|---|---|---|
| Sex (male) | 189 (89.1) | 46 (88.5) | 143 (89.4) | .80 |
| Diabetes mellitus | 80 (37.7) | 18 (34.6) | 62 (38.8) | .62 |
| Hypertension | 170 (80.2) | 34 (65.4) | 136 (85.0) | .004 |
| Anti-hypertensive agent | 161 (75.9) | 33 (63.5) | 128 (80.0) | .024 |
| Dyslipidemia | 149 (70.3) | 33 (63.5) | 116 (73.0) | .22 |
| Coronary artery disease | 37 (17.5) | 8 (15.4) | 29 (178.4) | .68 |
| Smoking | 106 (50.0) | 28 (53.8) | 78 (48.8) | .63 |
| Stenosis site: Left | 99 (46.7) | 24 (46.1) | 75 (46.9) | 1 |
| Symptomatic | 109 (51.4) | 25 (48.1) | 84 (52.5) | .36 |
| Degree of stenosis, % | 69.1 ± 18.0 | 69.0 ± 12.5 | 69.2 ± 19.4 | .96 |
| Carotid bulb involvement | 176 (83.0) | 44 (84.6) | 132 (82.5) | .83 |
| Calcification on carotid ultrasound | 143 (67.5) | 43 (82.7) | 100 (62.5) | .006 |
| Preoperative hydration | 42 (19.8) | 5 (9.6) | 37 (23.1) | .044 |
| Stent type | | | | .12 |
| Open cell | 188 (88.7) | 49 (94.2) | 139 (86.9) | |
| Closed cell | 2 (0.9) | 1 (2.0) | 1 (0.6) | |
| Dual layered | 22 (10.4) | 2 (3.8) | 20 (12.5) | |

| | | | | |
|---|---|---|---|---|
| Balloon dilatation | 210 (99.1) | 51 (98.1) | 159 (99.4) | .43 |
| Temporarily pacing during procedure | 78 (36.8) | 18 (36.7) | 60 (38.7) | .87 |
| Bradycardia | 4 (1.9) | 2 (3.8) | 2 (1.3) | .25 |
| Symptomatic periprocedural ischemic stroke | 2 (0.9) | 0 (0) | 2 (1.3) | 1 |
| Duration of intensive care unit stay, days | 1.2 ± 0.9 | 1.5 ± 1.0 | 1.2 ± 0.9 | .017 |
| Length of hospital stay, days | 9.7 ± 5.5 | 10.1 ± 4.2 | 9.6 ± 5.9 | .55 |

Binary data are presented as n (%) and continuous data are presented as mean ± SD.

PH, persistent hypotension; SD, standard deviation

**Comparisons of transthoracic echocardiography Indices**

The different echocardiographic indices in the two groups are summarized in Table 2. The PH group showed lower LA sizes than the no-PH group, as reflected by the lower LA maximum volumes (51.2 ± 17.9 vs 62.6 ± 21.0 mL, respectively; $p < .001$) and the lower LAVIs (29.7 ± 9.1 vs 37.7 ± 12.5 mL/m$^2$, respectively; $p < .001$). The LA ejection fraction was not significantly different between the two groups.

The PH group showed lower LV filling pressure than the no-PH group as reflected by the lower E/e' ratio (9.9 ± 2.6 vs 11.5 ± 5.0; $p$ = .034). LV sizes reflected by LV end-diastolic volume tended to be lower in the PH group than the no-PH group (68.4 ± 18.4 vs 74.3 ± 21.8, respectively; $p$ =.081), although this was not statistically significant. LV systolic function, as reflected by the LV ejection fraction was not significantly different between the two groups.

Table 2. Between-group comparison on transthoracic echocardiographic indices

| | All (n=212) | PH group (n=52) | no-PH group (n=160) | $p$-value |
|---|---|---|---|---|
| LV end-diastolic diameter, mm | 45.3 ± 5.2 | 44.4 ± 5.6 | 45.7 ± 5.0 | .12 |
| LV end-systolic diameter, mm | 30.4 ± 14.4 | 28.1 ± 4.7 | 31.1 ± 16.3 | .19 |
| LV ejection fraction, % | 62.0 ± 6.3 | 63.0 ± 4.8 | 61.7 ± 6.7 | .21 |
| LV end-diastolic volume, mL | 72.8 ± 21.1 | 68.4 ± 18.4 | 74.3 ± 21.8 | .081 |
| LV end-systolic volume, mL | 28.3 ± 13.6 | 25.4 ± 7.2 | 29.2 ± 15.0 | .10 |
| Interventricular septum, mm | 9.6 ± 1.4 | 9.5 ± 1.3 | 9.7 ± 1.4 | .27 |
| Posterior LV wall thickness, mm | 9.6 ± 1.3 | 9.3 ± 1.3 | 9.6 ± 1.3 | .16 |

| | | | | |
|---|---|---|---|---|
| E-wave, cm/s | 67.9 ± 22.6 | 64.6 ± 15.9 | 69.0 ± 24.4 | .22 |
| A-wave, cm/s | 83.5 ± 19.3 | 79.1 ± 15.3 | 85.0 ± 20.3 | .056 |
| E/e' ratio | 11.1 ± 4.6 | 9.9 ± 2.6 | 11.5 ± 5.0 | .034 |
| E/A ratio | 0.82 ± 0.27 | 0.84 ± 0.24 | 0.81 ± 0.28 | .60 |
| LA maximum volume, mL | 59.7 ± 20.4 | 51.2 ± 17.9 | 62.6 ± 20.5 | <.001 |
| LA minimum volume, mL | 34.4 ± 16.6 | 29.6 ± 16.1 | 36.0 ± 16.5 | .055 |
| LA volume index, $mL/m^2$ | 35.7 ± 12.2 | 29.7 ± 9.1 | 37.7 ± 12.5 | <.001 |
| LA ejection fraction, % | 42.3 ± 12.6 | 42.3 ± 12.4 | 42.2 ± 12.7 | .96 |
| Systolic pulmonary artery pressure, mmHg | 26.5 ± 7.4 | 26.6 ± 7.3 | 26.5 ± 7.2 | .98 |

Continuous data are presented as mean ± SD.

LA, left atrium; LV, left ventricle; E, early transmitral flow velocity; A, late transmitral flow velocity; E', early diastolic mitral annular tissue velocity

**ROC curve analysis with AUROC**

Figure 2 shows the ROC curve for the prediction of PH after CAS using LAVI. The apparent and optimism-corrected AUROC were both 0.716, implying the estimated optimism

<.001. The optimal cut-off value was 33.5 mL/m$^2$ (sensitivity, 0.750 and specificity, 0.625).

**Multiple logistic regression analysis**

Multiple logistic regression analysis showed that the LAVI <33.5 mL/m$^2$ (OR, 4.950; 95% confidence interval [CI], 2.190–11.200; $p$< .001) and calcification on carotid ultrasound (OR, 4.160; 95% CI, 1.590–10.900; $p$= .004) were independent predictors of PH after CAS. Preoperative hydration was negatively associated with PH (OR, 0.235; 95% CI, 0.070–0.794; $p$= .020) (Table 3).

Table 3. Multiple logistic regression analysis for calculation of ORs for persistent hypotension after CAS

| | Crude OR (95% CI) | Adjusted OR (95% CI) | $p$-value |
|---|---|---|---|
| LA volume index <33.5 mL/m$^2$ | 4.430 | 4.950 (2.190–11.20) | <.001 |
| Preoperative hydration | 0.354 | 0.235 (0.070–0.794) | .020 |
| Age | 1.000 | 0.996 (0.946–1.050) | .87 |
| Sex (male) | 0.911 | 1.180 (0.311–4.480) | .81 |
| Hypertension | 0.333 | 0.411 (0.178–1.090) | .078 |

| | | | |
|---|---|---|---|
| Coronary artery diseases | 0.809 | 0.339 (0.095–1.210) | .095 |
| Degree of stenosis | 0.999 | 0.995 (0.973–1.020) | .63 |
| Calcification | 3.480 | 4.160 (1.590–10.900) | .004 |
| Carotid bulb involvement | 1.170 | 0.821 (0.252–2.680) | .74 |

CAS, carotid artery stenting; OR, odds ratio; CI, confidence interval; LV, left ventricle; LA, left atrium

## Discussion

The main finding of this study was that lower LAVI was an independent predictor of PH after CAS. In addition, preoperative hydration was negatively associated with PH. Similar to previous studies, calcification at the carotid bulb was associated with PH after CAS.

Hemodynamic instability after CAS has been reported to occur in 5–76% of cases.[10,14–16] In addition, the need for vasopressor infusion due to PH has been reported in 12–40% of cases.[14,17–19] In this cohort, 24.5% of patients undergoing CAS procedures experienced PH. Various factors, such as age, sex, coronary artery disease, degree of stenosis, plaque location, and calcification, have been implicated in the development of CAS-induced hemodynamic instability.[2,4,20,21] Although there were limited reports showing the relationship between cardiac function and morphology and hypotension after CAS,[15] this

was the first study to describe the relationship between the LAVI and PH after CAS.

The current study showed that a lower LA volume was associated with PH after CAS. The LA plays an important role in LV filling and overall cardiac performance: as a "reservoir," receiving blood from pulmonary venous return and storing energy in the form of pressure; as a "conduit" for the transfer of blood into the LV after mitral valve opening via a pressure gradient; and for the "contractile" function of the LA that normally serves to augment the LV stroke volume.[22] Therefore, our results suggested that patients with a lower LA volume can experience a significant reduction in cardiac output due to low reservoir function of the LA, resulting in hypotension after CAS. This relationship between lower LA volume and hypotension after CAS is supported by the fact that hypotension after CAS follows a similar mechanism to vasovagal syncope (Figure 1). In vasovagal syncope, the decrease in venous return due to blood stasis in the lower body during prolonged standing causes sympathetic tone and parasympathetic inhibition to maintain systemic circulation by increasing the heart rate, cardiac contractility, and vascular resistance. However, paradoxically, mechanoreceptors in the LV respond to enhanced LV contraction with augmented firing that is relayed to the nucleus of the solitary tract. This results in a decrease in systemic blood pressure due to reduced venous return as in CAS.[23] Consistent

with our findings, previous studies have shown that lower LA volume was associated with the development of hypotension in patients with vasovagal syncope.[5,6] Patients with LAVI ≥36 mL/$m^2$ did not experience fainting during a head-up tilt test.[6] Therefore, the cut-off value of 33.5 mL/$m^2$ for LAVI in the present study is considered reasonable. More aggressive hydration management has been reported to be preferable for these patients in vasovagal syncope.[5] In addition, preoperative hydration was more common in the no-PH group than in the PH group in our study, and thus this intervention may be useful for preventing PH after CAS.

Our results also showed that duration of ICU stay was significantly longer in the PH group than in no-PH group, consistent with previous studies.[2,24] Intravenous administration of vasopressors requires monitoring and titration in an ICU environment, and as this results in a significant increase in healthcare costs, prevention of PH after CAS is important.[24]

The current investigation has the following limitations. First, this is a retrospective single-center investigation. Second, the evaluation of right cardiac chamber function was inadequate in this study. A previous study showed that the function of the right cardiac chamber was also associated with the occurrence of vasovagal syncope.[5] Third, carotid

calcification was evaluated only using carotid ultrasound in the present study because CT and magnetic resonance angiography were only performed in 62.2% (n=132) and 90.5% (n=192) of the procedures, respectively. Fourth, only four patients (1.9%) had bradycardia during the intraoperative period. This may have been due to the prophylactic administration of atropine before balloon dilatation in almost all cases, consistent with a previous study in which prophylactic atropine decreased the incidence of intraoperative bradycardia. [23] Fifth, although previous studies have shown the use of open cell stents to be strongly associated with hypotension after CAS due to greater radial force compared to the other stent types, no significant difference was found in stent type in the current study. [25,26] This may have been because most patients in this study received open cell stents and the sample sizes for the other stent types were too small to draw definitive conclusions. Sixth, as we determined the optimal cut-off value of the LAVI for the predicting PH after CAS in this study, this requires further validation in an external population in the future.

We concluded that patients with PH after CAS exhibit lower LA volume. These patients are susceptible to preload reduction caused by inhibition of the sympathetic innervation of the nucleus of the solitary tract. Thus, clinicians may focus more on TTE before CAS to evaluate LA reservoir function and select patients at high risk for PH.

Moreover, adequate hydration therapy in patients with low LA volume to increase fluid retention before and during CAS in preparation for preload reduction might prevent PH after CAS.

**Contributorship Statement**

KM substantially contributed to the study conceptualization, acquisition of the data, analysis and interpretation of data, and drafting manuscript. NO substantially contributed to the study conceptualization, analysis and interpretation of data, and drafting manuscript. JT substantially contributed to analysis and interpretation of data, and drafting manuscript. TO and CM contributed to the analysis and interpretation of data and drafting manuscript. HI significantly contributed to acquisition of data. NS and others contributed to revising the manuscript critically for important intellectual content. All authors approved the final version of the manuscript to be published.

**Acknowledgements**

The authors would like to thank Editage (www.editage.jp) for their English language editing services.

**Funding disclosure**

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

**Conflicts of Interest**

H.I received speakers' bureau/honoraria from Medtronic Japan Co., Daiichi Sankyo Co., Johnson & Johnson Co., Stryker Japan Co. S., Terumo Co, and Asahi Intecc Co. NS reports a research grant from Biomedical Solutions Co., Medtronic Co. and Terumo Co.; lecturer's fees from Asahi-Intec Co., Biomedical Solutions Co., Medtronic Co., and Terumo Co.; membership on the advisory boards for Johnson & Johnson Co., Medtronic Co. and Terumo Co. outside the submitted work. The other authors declare that they have no conflicts of interest to disclose.

**Ethics Approval**

This study has been approved by the institutional review board of Kobe City Medical Center General Hospital (permission number: zn220104). The study protocol

conformed to the ethical guidelines of the 1975 Declaration of Helsinki. The requirement for written informed consent was waived because of the retrospective study design.

## References


1 Wong JH, Findlay JM, Suarez-Almazor ME. Hemodynamic instability after carotid endarterectomy: risk factors and associations with operative complications. *Neurosurgery* 1997;**41**:35–41; discussion 41–3. doi:10.1097/00006123-199707000-00009

2 Dangas G, Laird JR, Satler LF, *et al.* Postprocedural hypotension after carotid artery stent placement: predictors and short- and long-term clinical outcomes. *Radiology* 2000;**215**:677–83. doi:10.1148/radiology.215.3.r00jn04677

3 Nanto M, Goto Y, Yamamoto H, *et al.* Complications and predictors of hypotension requiring vasopressor after carotid artery stenting. *Neurol Med Chir (Tokyo)* 2017;**57**:115–21. doi:10.2176/nmc.oa.2016-0155

4 Lian X, Lin M, Liu M, *et al.* Complications and predictors associated with persistent hemodynamic depression after carotid artery stenting. *Clin Neurol Neurosurg* 2014;**124**:81–4. doi:10.1016/j.clineuro.2014.06.008

5 Sotiriadou M, Papadopoulos CE, Antoniadis AP, *et al.* The impact of atrial mechanical function on age-dependent presentation of neurocardiogenic syncope. *Clin Cardiol*

2021;**44**:1440–7. doi:10.1002/clc.23704

6 Moon J, Shim J, Park JH, *et al.* Small left atrial volume is an independent predictor for fainting during head-up tilt test: the impact of intracardiac volume reserve in vasovagal syncope. *Int J Cardiol* 2013;**166**:44–9. doi:10.1016/j.ijcard.2011.09.076

7 Ferguson GG, Eliasziw M, Barr HWK, *et al.* The North American Symptomatic Carotid Endarterectomy Trial: surgical results in 1415 patients. *Stroke* 1999;**30**:1751–8. doi:10.1161/01.STR.30.9.1751

8 Cayne NS, Faries PL, Trocciola SM, *et al.* Carotid angioplasty and stent-induced bradycardia and hypotension: impact of prophylactic atropine administration and prior carotid endarterectomy. *J Vasc Surg* 2005;**41**:956–61. doi:10.1016/j.jvs.2005.02.038

9 Huibers A, Calvet D, Kennedy F, *et al.* Mechanism of procedural stroke following carotid endarterectomy or carotid artery stenting within the International Carotid Stenting Study (ICSS) randomised trial. *Eur J Vasc Endovasc Surg* 2015;**50**:281–8. doi:10.1016/j.ejvs.2015.05.017

10 Nano G, Dalainas I, Bianchi P, *et al.* Ballooning-induced bradycardia during carotid stenting in primary stenosis and restenosis. *Neuroradiology* 2006;**48**:533–6.

doi:10.1007/s00234-006-0096-x

11 Ehara S, Kobayashi Y, Yoshiyama M, *et al.* Spotty calcification typifies the culprit plaque in patients with acute myocardial infarction: an intravascular ultrasound study. *Circulation* 2004;**110**:3424–9. doi:10.1161/01.CIR.0000148131.41425.E9

12 Nagueh SF, Smiseth OA, Appleton CP, *et al.* Recommendations for the evaluation of left ventricular diastolic function by echocardiography: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *J Am Soc Echocardiogr* 2016;**29**:277–314. doi:10.1016/j.echo.2016.01.011

13 Steyerberg EW, Harrell FE, Borsboom GJJM, *et al.* Internal validation of predictive models: efficiency of some procedures for logistic regression analysis. *J Clin Epidemiol* 2001;**54**:774–81. doi:10.1016/S0895-4356(01)00341-9

14 Gupta R, Abou-Chebl A, Bajzer CT, *et al.* Rate, predictors, and consequences of hemodynamic depression after carotid artery stenting. *J Am Coll Cardiol* 2006;**47**:1538–43. doi:10.1016/j.jacc.2005.08.079

15 Lin PH, Zhou W, Kougias P, *et al.* Factors associated with hypotension and bradycardia after carotid angioplasty and stenting. *J Vasc Surg* 2007;**46**:846–53; discussion 853–4.

doi:10.1016/j.jvs.2007.07.020

16 Pappadà G, Beghi E, Marina R, *et al.* Hemodynamic instability after extracranial carotid stenting. *Acta Neurochir (Wien)* 2006;**148**:639–45. doi:10.1007/s00701-006-0752-2

17 Mylonas SN, Moulakakis KG, Antonopoulos CN, *et al.* Carotid artery stenting-induced hemodynamic instability. *J Endovasc Ther* 2013;**20**:48–60. doi:10.1583/12-4015.1

18 Rubio G, Karwowski JK, DeAmorim H, *et al.* Predicting factors associated with postoperative hypotension following carotid artery stenting. *Ann Vasc Surg* 2019;**54**:193–9. doi:10.1016/j.avsg.2018.06.005

19 Wu TY, Ham SW, Katz SG. Predictors and consequences of hemodynamic instability after carotid artery stenting. *Ann Vasc Surg* 2015;**29**:1281–5. doi:10.1016/j.avsg.2015.03.035

20 Cieri E, de Rango P, Maccaroni MR, *et al.* Is haemodynamic depression during carotid stenting a predictor of peri-procedural complications? *Eur J Vasc Endovasc Surg* 2008;**35**:399–404. doi:10.1016/j.ejvs.2007.10.020

21 Qureshi AI, Luft AR, Sharma M, *et al.* Frequency and determinants of postprocedural

hemodynamic instability after carotid angioplasty and stenting. *Stroke* 1999;**30**:2086–93. doi:10.1161/01.str.30.10.2086

22 Abhayaratna WP, Seward JB, Appleton CP, *et al.* Left atrial size: physiologic determinants and clinical applications. *J Am Coll Cardiol* 2006;**47**:2357–63. doi:10.1016/j.jacc.2006.02.048

23 Rea RF, Thames MD. Neural control mechanisms and vasovagal syncope. *J Cardiovasc Electrophysiol* 1993;**4**:587–95. doi:10.1111/j.1540-8167.1993.tb01246.x

24 Sharma S, Lardizabal JA, Bhambi B. Oral midodrine is effective for the treatment of hypotension associated with carotid artery stenting. *J Cardiovasc Pharmacol Ther* 2008;**13**:94–7. doi:10.1177/1074248408317709

25 Nonaka T, Oka S, Miyata K, *et al.* Prediction of prolonged postprocedural hypotension after carotid artery stenting. *Neurosurgery* 2005;**57**:472–7; discussion 472. doi:10.1227/01.NEU.0000170541.23101.81

26 Oshin O, Varcoe R, Wong J, *et al.* Multivariable analysis of patients with severe persistent postprocedural hypotension after carotid artery stenting. *J Endovasc Ther* 2019;**26**:759–67. doi:10.1177/1526602819869929

**Figure legends**

Figure 1. Similarities in the mechanisms of hemodynamic instability between carotid artery stenting (CAS) and vasovagal syncope (VVS)

During CAS, stimulation of the baroreceptors by direct compression sends impulses to the nucleus of the solitary tract in the medulla oblongata. This causes the inhibition of sympathetic nerves and stimulation of parasympathetic nerves within the vagus nerve. In vasovagal syncope, the decrease in venous return due to blood stasis in the lower body during prolonged standing causes sympathetic tone and parasympathetic inhibition to maintain systemic circulation by increasing heart rate, cardiac contractility, and vascular resistance. However, paradoxically, mechanoreceptors in the LV respond to enhanced LV contraction with augmented firing that is relayed to the nucleus of the solitary tract. Both result in a decrease in systemic blood pressure due to reduced venous return.

Figure 2. Receiver operating characteristic curve analysis for the prediction of persistent hypotension after carotid artery stenting using the left atrial volume index

This article has been accepted for publication in [*Journal of NeuroInterventional Surgery, 2023]* following peer review, and the Version of Record can be accessed online at [*http://dx.doi.org/10.1136/neurintsurg-2022-019094*].