

Article

Effect of Controlled Expiratory Pressures on Cerebrovascular Changes During Valsalva Maneuver

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Abstract: This study aimed to investigate the effects of Valsalva maneuver (VM) with the controlled expiratory pressures on vascular stiffness of common carotid artery (CCA) and cerebral hemodynamic changes using diagnostic ultrasonography. Twenty-seven healthy participants (mean and standard deviation of age = 22.78 ± 1.89) performed 30 and 40 mmHg VM. The right CCA stiffness index and pulse wave velocity (PWV) were measured before (PRE) and after (POST) VM. The peak systolic velocity (PSV), resistance index (RI), and heart rate (HR) were measured before (PRE) and after (POST1 and POST2 during the first and the second 15 s, respectively) VM. Near-infrared spectroscopy (NIRS) was utilized to measure regional oxygen saturation (rSO₂) and oxyhemoglobin (HbO) on the left and right prefrontal cortex. Stiffness index decreased by 1.76 ($p < 0.001$) from PRE to POST only after 30 mmHg VM. PWV decreased by 0.69 m/s ($p < 0.001$, 30 mmHg) and 0.34 m/s ($p = 0.022$, 40 mmHg) in POST. Conversely, PSV increased by 5.36 cm/s ($p = 0.031$, 30 mmHg) and 4.77 cm/s ($p = 0.04$, 40 mmHg) in POST2. Increase in RI ($p = 0.017$) and decrease in HR ($p = 0.003$) occurred only after the 40 mmHg VM. Right HbO decreased after 30 mmHg VM ($p = 0.023$) from PRE to POST1, and right rSO₂ increased after 40 mmHg VM ($p = 0.036$) from VM (during) to POST1. Both 30 and 40 mmHg VM showed a significant improvement in PWV and an increase in PSV. However, at 30 mmHg VM, a significant decrease in HbO was observed after VM owing to increased cerebral oxygen exchange, and at 40 mmHg VM, an rSO₂ increase was observed after VM owing to high vascular pressure. Additionally, the increased pressure and rSO₂ at 40 mmHg may have been caused by increased RI. The results indicated that the 30 mmHg VM was more effective on CCA stiffness than the 40 mmHg VM.

Keywords: valsalva maneuver; common carotid artery; arterial stiffness; pulse wave velocity; ultrasonography; hemodynamic function

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1. Introduction

Valsalva maneuver (VM) is a common phenomenon that occurs during straining in daily life, such as lifting heavy objects, defecating, or coughing. In this phenomenon, increased intrathoracic pressure suddenly and rapidly increases the blood pressure, triggering changes in the cardiovascular and autonomic nervous systems. This same movement can also be achieved by performing a voluntary forced expiratory effort against a closed airway (e.g., closed mouth and nose). This technique is simple to perform, has a short performance time (generally 15 s), and is also non-invasive and highly reproducible;

therefore, it is currently used in various clinical fields. In particular, it can cause immediate changes in the cardiovascular and autonomic nervous systems; therefore, it has been used as a method to test heart disease (heart failure, heart murmurs, or atrial septal defects) and cardiac autonomic function or to evaluate cerebral autoregulation [1–6].

The VM can physiologically affect not only cardiac function but also vascular function. Vascular elasticity is its major function that provides a passive mechanism for smoothing the pulsatile blood flow from the heart to peripheral sites [7], and that is influenced by the constriction and relaxation of vascular smooth muscle cells. Therefore, dysfunction has been shown to contribute to arterial stiffness [8]. Accordingly, the balance of constriction and relaxation of arteries can improve vascular elasticity.

The VM directly provides pressure stimulation to the arteries and stimulates vascular smooth muscle cells, potentially changing vascular tone [9]. In particular, increased blood pressure and autonomic nerve activity during VM can change the vascular tone. Blood vessels undergo autoregulation of the myogenic response to prevent damage from increased blood pressure and blood vessel tension [9]. In addition, the parasympathetic nerve, which is activated to restore blood pressure in the final phase of the VM, can relax blood vessels [10]. Such changes in the constriction and relaxation of blood vessels can improve blood vessel function.

In addition, the VM also affects cerebral blood flow, and some studies have reported the risk of changes in cerebral blood flow. A previous study reported that when expiratory pressure increased to 40 mmHg, arterial pressure and cerebral blood flow increased, leading to the risk of aneurysm rupture and tissue damage [11]. In addition, low blood pressure caused by VM can reduce cerebral blood flow and cause syncope [12]. Therefore, to improve cerebrovascular function, it is necessary to perform the VM that can safely induce hemodynamic changes in the brain and improve vascular function.

Generally, 40 mmHg is the most representative standard for VM pressure. However, to date, VM research has been conducted at various intensities, generally of around 20–40 mmHg, to reduce potential side effects at 40 mmHg and allow easier application of the technique [11,13–15]. However, to date, the changes in cerebral hemodynamic changes in response to various VM strengths remain largely unknown. Therefore, it is necessary to determine which VM strength is more suitable for cerebrovascular response with low risk by comparing various pressure levels.

Given this context, in the present study, we aimed to investigate changes in common carotid artery (CCA) blood velocity and vascular function, as well as hemodynamic changes in the brain during VM performed at pressure intensities of 30 mmHg and 40 mmHg, in order to ascertain the more suitable intensity for vascular stiffness. The hypotheses of this study were as follows: First, both 30 mmHg and 40 mmHg VM would cause changes in the hemodynamic response of the CCA and the prefrontal region. Second, graded (30 mmHg and 40 mmHg) VM would have different effects on vascular function.

2. Materials and Methods

2.1. Participants

The sample size was determined using G*Power ver.3.1.9.4, following assessment based on data from an internal pilot study. As hemodynamic changes due to VM are associated with increased blood pressure, the effect size for the appropriate number of participants was calculated from the change in systolic blood pressure (SBP) after VM. As a result, the average SBP values before and after the VM were found to be 111.645 and 113.161 mmHg, respectively, the partial eta squared was 0.084, and the effect size was calculated to be 0.303. By applying a power of 0.9 and an α error probability of 0.05, the requisite sample size was calculated as 26 participants. Considering a potential dropout rate of 10%, 29 participants were recruited. A total of 29 participants were prospectively recruited for this study after providing written informed consent. All participants were free from disease, were not taking any medication, and did not experience any problems

performing the 30 and 40 mmHg VM. Participants who had abnormal vital signs were excluded. The vital signs (SBP, diastolic blood pressure (DBP), and heart rate (HR)) were obtained using an electric blood pressure monitor (TMB-1112, Guangdong Transtek Medical Electronics, Guangdong, China), and participants who were not within the normal vitals range were excluded. The normal vitals range is as follows: SBP < 120 mmHg, DBP < 80 mmHg [16] (However, when the pulse pressure (PP) was normal, an SBP of up to 130 mmHg was allowed [17]), HR = 60~90 bpm [18].

Of the total cohort, two participants who could not maintain an expiratory pressure greater than 40 mmHg were excluded. All participants abstained from alcohol, smoking, and caffeine intake for at least 24 hours before the experimental trial due to their modulating effects on the cardiovascular system.

2.2. Institutional Review Board Statement

This study was approved by the Institutional Review Board of the Gachon University Bioethics Committee (IRB no. 1044396-202207-HR-146-01; approval date: 29 August 2022). The participants were recruited by flyers posted in public places in Incheon, Republic of Korea (Periods of recruitment: 12 June 2023 to 1 August 2023). No follow-up was performed, and all data were collected at Gachon University (Figure 1). Table 1 lists the personal characteristics and biosignals of 27 participants.

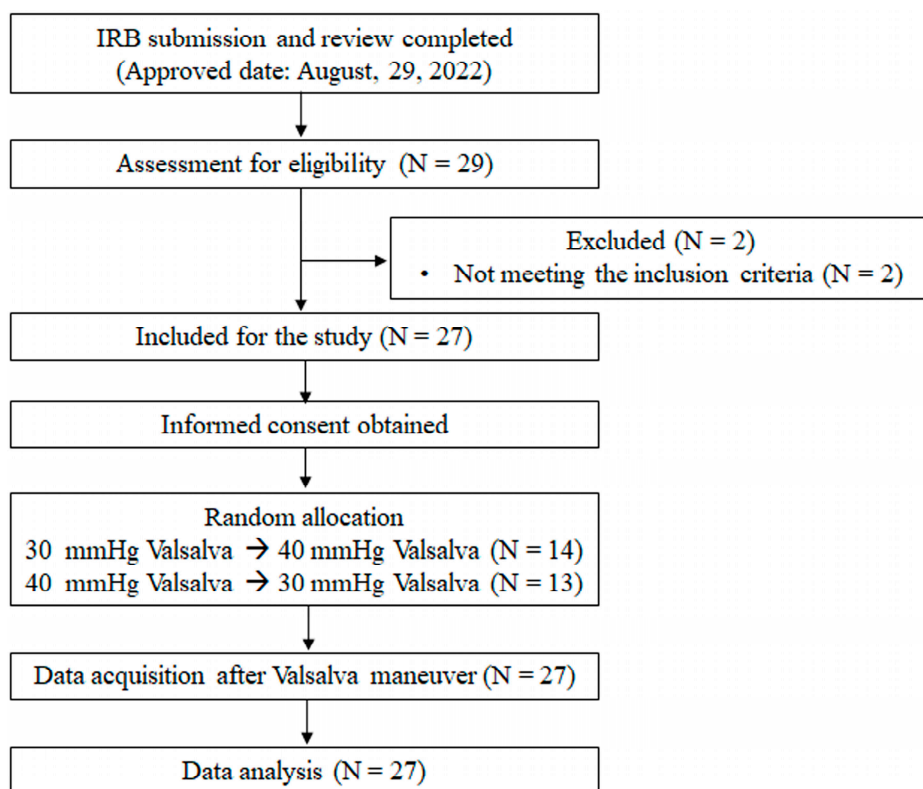


Figure 1. Flow chart of experimental protocol.

Table 1. General characteristics and resting vital signs of the participants.

Variables	Total (N = 27)	Men (N = 14)	Women (N = 13)
	Mean $\pm$ SD	Mean $\pm$ SD	Mean $\pm$ SD
Age (years)	22.78 $\pm$ 1.89	23.21 $\pm$ 2.19	22.31 $\pm$ 1.44
Height (cm)	168.59 $\pm$ 6.49	173.00 $\pm$ 4.32	163.85 $\pm$ 4.91
Weight (kg)	62.74 $\pm$ 9.32	68.71 $\pm$ 8.30	56.31 $\pm$ 5.20
SBP (mmHg)	116.82 $\pm$ 10.02	121.43 $\pm$ 9.19	111.85 $\pm$ 8.63
DBP (mmHg)	68.15 $\pm$ 6.36	67.43 $\pm$ 5.97	68.92 $\pm$ 6.91
HR (bpm)	82.23 $\pm$ 20.16	86.71 $\pm$ 14.00	77.39 $\pm$ 24.90

Abbreviations: DBP, diastolic blood pressure; HR, heart rate; SBP, systolic blood pressure.

2.3. Experimental Protocol and Task Design

This study used a crossover design to evaluate the effects of the VM. To ensure that two different intensities of the VM were performed clearly, we provided a detailed explanation of the VM experiment beforehand. After the explanation about how to perform VM, participants were tested to confirm whether they could maintain each VM pressure for 15 s. The test began with a 40 mmHg VM, and participants who could not maintain the 40 mmHg for 15 s were excluded after two attempts. Subsequently, participants practiced maintaining 30 mmHg VM for 15 s over two trials to ensure they could smoothly manage the pressure adjustments for both 30 mmHg and 40 mmHg. Afterward, we provided a sufficient recovery time of over five minutes. After that, we confirmed that vital signs such as BP and HR had returned to the resting range before proceeding with the experimental protocol. The VM was conducted in the supine position on a flat examination bed, and controlled expiratory pressure was detected through a digital pressure gauge (SBH, Sensys, Ansan, Republic of Korea) connected to a mouthpiece and tube. Participants maintained the predefined pressure by self-visual feedback with the display of a digital pressure gauge (Figure 2). The order of the 30 and 40 mmHg VM was randomly determined. During the 30 mmHg VM, participants were instructed to maintain their pressure 30 mmHg and not exceed 35 mmHg for 15 s. For the 40 mmHg VM, participants were instructed to maintain 40 mmHg and not below 40 mmHg. The VM procedure was as follows [19]: (1) participants inhaled deeply through the nose for 10 s, (2) exhaled forcefully through the mouthpiece at the onset of strain, (3) maintained pressure for 15 s, and (4) resumed normal breathing immediately upon the stop signal. Afterwards, they had a 10 min rest period before performing another VM procedure (Figure 3). Each task (30 or 40 mmHg) was performed as a single trial, and the experimenter gave the subjects a signal to start VM. All experiments were performed in an ultrasonography room at Gachon University. Transportation expenses were provided to increase participant compliance.

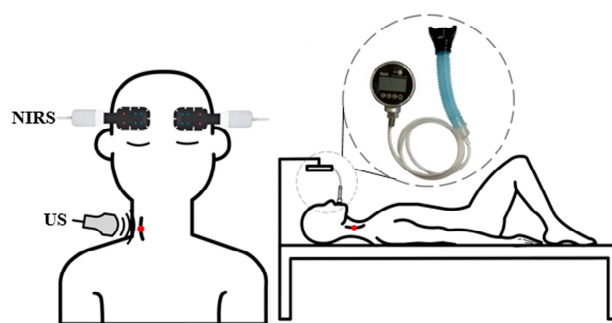


Figure 2. Ultrasound and near-infrared spectroscopy measurements and a schematic of the Valsalva maneuver system with a participant lying on the bed. Abbreviations: NIRS, near-infrared spectroscopy; US, ultrasound.

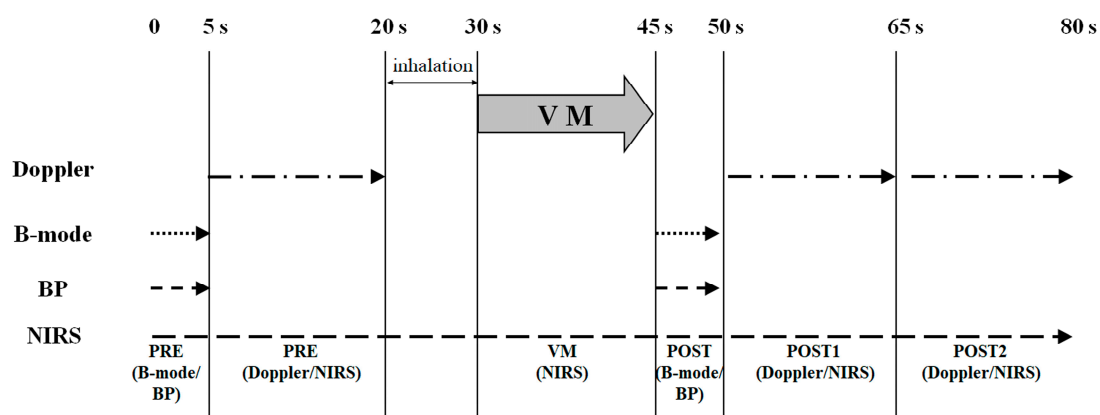


Figure 3. Protocol for biosignal acquisition before and after VM. Abbreviations: BP, blood pressure; NIRS, near-infrared spectroscopy; POST, after VM; PRE, before VM; VM, Valsalva maneuver.

2.4. Measurements

The experimental instruction and the biosignal measurement were assigned to different experimenters following single-blind procedures. Changes in blood velocity and function in the CCA were measured to investigate their effects on VM. Changes in CCA blood velocity during the VM were measured using diagnostic ultrasound with a 2–14 MHz linear transducer array (RS85, Samsung Medison, Seoul, Republic of Korea). The parameters, including peak systolic velocity (PSV), HR, and resistance index (RI), were obtained using Doppler-mode scanning. The RI is a widely used measure of resistance to arterial flow ($RI = (PSV - EDV) / PSV$; EDV, end-diastolic velocity). This reflects not only the resistance at the measurement site but also the resistance distal or downstream to the ultrasound probe. Functional changes in the CCA caused by the VM were evaluated using pulse wave velocity (PWV) and arterial stiffness index. To calculate the PWV and stiffness index, CCA diameters (including systolic and diastolic) were obtained using B-mode axial CCA images, and BP was obtained using a smartwatch (SM-R850, Samsung Electronics, Suwon, Republic of Korea) after being calibrated for each participant before the experiment. To calibrate the smartwatch's BP, an electric blood pressure monitor (TMB-1112 upper arm blood pressure monitor with cuff) was used. The location of the CCA for measurement was determined using an ultrasound image 2 cm below the CCA bifurcation. Hemodynamic changes in the brain were measured using near-infrared spectroscopy (NIRS) (NIRSIT ON, OBELAB, Seoul, Republic of Korea). Regional oxygen saturation (rSO₂) and oxyhemoglobin (HbO) were obtained in the left and right prefrontal cortices using NIRS. NIRS patches were attached above both eyebrows on the left and right prefrontal cortex [20].

Data collection was conducted according to the time flow (Figure 3). NIRS data were continuously collected in real-time for approximately 80 s, including both before and after the VM. Doppler ultrasound measurements were taken for 15 s before the VM and 30 s after the B-mode measurement for 5 s after the VM. BP and B-mode measurements started simultaneously.

Doppler measurements were collected 15 s before VM (PRE) and 30 s after VM (POST1 and POST2), in which the resulting data was divided into two sessions of 15 s each, POST1 and POST2, for further analyses. According to a previous study, the normalization time of BP after VM was confirmed to be less than 15 s [21]. CCA diameters and BP were measured before and after VM to calculate PWV and stiffness index. B-mode images were acquired immediately before Doppler mode measurement. Doppler and B-mode measurements during the VM were not performed because of neck muscle contraction and blood vessel movements. No follow-up was performed, and all data were collected at Gachon University.

2.5. Calculations of Stiffness Index and PWV

The stiffness index (β), which is a measure of blood vessel tension, was calculated by referencing previous studies [22,23]. PWV is a representative noninvasive indicator of arterial function [24], defined as the speed at which pressure waves generated in the cardiac systolic phase propagate along the arterial tree. This is an important clinical parameter for evaluating the risk of cardiovascular diseases and vascular conditions [25,26]. PWV can be calculated using the stiffness index and blood density (ρ) using the following formula [27,28]:

$$PWV = \sqrt{\beta \times \frac{DBP}{(2 \times \rho)}}$$

ρ = density of blood (1.05 g/cm³).

2.6. Statistical Analysis

Statistical analyses were performed using Jamovi ver. 2.2.5 (The Jamovi project (2021)). One-factorial repeated-measures (RM) ANOVA was used to analyze significant differences between before and after VM performance for every outcome. NIRS data measured in real-time were divided into four sections (PRE = before VM, VM = during VM, POST1 = the first after VM, and POST2 = the second after VM), and hemodynamic changes in the brain caused by VM were analyzed. To analyze the stable NIRS data, the PRE VM data used the average value of data acquired for 15 s, the VM data was the average of data for 15 s, which was the strain stage, and the POST1 section was 15 s after VM termination (the first 15 s of POST period). For POST2, the average value of the second 15 s after VM was used for analysis. Therefore, an RMANOVA with four within-factors was performed to analyze the NIRS data. The Doppler ultrasound data were divided into three sections (PRE, POST1, and POST2). The average data for 15 s in the pre-stage was used for PRE, and two 15 s averaged data measured for 30 s after VM were used for POST1 and POST2, respectively. Accordingly, RMANOVA with three within-factor analyses was performed. Where the assumption of sphericity could not be assumed, adjustments to the degrees of freedom were made ($\epsilon > 0.75$ = Huynh–Feldt; $\epsilon < 0.75$ = Greenhouse–Geisser). Post hoc pairwise comparisons were conducted using Scheffé's tests. Finally, a paired t-test was performed on PWV and stiffness index to compare changes before and after the VM. Both the PWV and stiffness index satisfied the assumption of normality by performing the Shapiro–Wilk test.

3. Results

3.1. Comparison of PWV and Stiffness Index

PWV significantly decreased after performing at both 30 and 40 mmHg VM, indicating that as the PWV decreases, the stiffness index of the blood vessels also decreases while the elasticity improves. In this study, PWV significantly decreased by 0.69 m/s ($T = 4.05$, $p < 0.001$) in POST compared to PRE at 30 mmHg VM, and by 0.34 m/s ($T = 2.43$, $p = 0.022$) at 40 mmHg. The stiffness index significantly decreased by 1.76 in POST compared to PRE in 30 mmHg VM ($T = 4.24$, $p < 0.001$). After 40 mmHg VM, it decreased by 0.79; however, the change did not reach significance ($T = 2.01$, $p = 0.056$) (Table 2).

Table 2. Changes in CCA function before and after VM.

Outcome Variable		Testing	Mean $\pm$ SD	Δ DIFF (Mean $\pm$ SE)	T	p
30 mmHg	Stiffness index	PRE	6.67 $\pm$ 2.23	1.76 $\pm$ 0.42	4.24	<0.001 *
		POST	4.91 $\pm$ 1.58			
	PWV (m/s)	PRE	5.19 $\pm$ 0.84	0.69 $\pm$ 0.17	4.05	<0.001 *
		POST	4.50 $\pm$ 0.69			
40 mmHg	Stiffness index	PRE	6.00 $\pm$ 2.79	0.79 $\pm$ 0.40	2.01	0.056
		POST	5.21 $\pm$ 3.21			
	PWV (m/s)	PRE	4.90 $\pm$ 0.99	0.34 $\pm$ 0.14	2.43	0.022 *
		POST	4.56 $\pm$ 1.14			

Abbreviations: CCA, common carotid artery; PWV, pulse wave velocity; SD, standard deviation; SE, standard error. * $p < 0.05$.

3.2. Comparison of Blood Velocity Changes

The PSV significantly increased after both 30 and 40 mmHg VM (Table 3). The change in PSV significantly increased in POST2 compared to PRE for both 30 and 40 mmHg VM, and no significant change was observed in POST1. For 30 mmHg, there was a significant increase of 5.36 cm/s ($T = -2.82$, $p = 0.031$) in POST2 compared to PRE, and for 40 mmHg, there was a significant increase of 4.77 cm/s ($T = -2.72$, $p = 0.04$) in POST2.

Table 3. CCA hemodynamic changes during 30 and 40 mmHg VM.

Repeated Measure Comparisons					Post Hoc Comparisons (Scheffé)				
Outcome Variable	Testing	Mean ± SD	F	p	Testing	T	p		
30 mmHg	PSV (cm/s)	PRE	96.69 ± 15.79	6.09	0.014 *	PRE	POST1	-2.23	0.102
		POST1	101.09 ± 16.81			POST2	-2.82	0.031 *	
		POST2	102.05 ± 16.50			POST1	POST2	-1.30	0.442
	RI	PRE	0.73 ± 0.06	3.09	0.069	PRE	POST1	-1.14	0.529
		POST1	0.74 ± 0.05			POST2	-2.30	0.090	
		POST2	0.74 ± 0.06			POST1	POST2	-1.68	0.263
	HR (bpm)	PRE	67.46 ± 8.09	2.28	0.129	PRE	POST1	1.66	0.270
		POST1	65.60 ± 8.84			POST2	1.53	0.324	
		POST2	66.18 ± 8.96			POST1	POST2	-0.89	0.678
40 mmHg	PSV (cm/s)	PRE	94.11 ± 13.42	5.83	0.012 *	PRE	POST1	-2.49	0.064
		POST1	98.83 ± 17.47			POST2	-2.72	0.040 *	
		POST2	98.88 ± 15.88			POST1	POST2	0.05	0.999
	RI	PRE	0.72 ± 0.05	4.92	0.016 *	PRE	POST1	-3.11	0.017 *
		POST1	0.74 ± 0.05			POST2	-1.85	0.201	
		POST2	0.73 ± 0.06			POST1	POST2	1.07	0.573
	HR (bpm)	PRE	66.78 ± 9.11	9.45	0.001 *	PRE	POST1	3.84	0.003 *
		POST1	62.78 ± 8.94			POST2	2.08	0.137	
		POST2	64.73 ± 9.96			POST1	POST2	-2.93	0.025 *

Abbreviations: CCA, common carotid artery; HR, heart rate; PSV, peak systolic velocity; RI, resistance index; SD, standard deviation. * $p < 0.05$.

In contrast, significant changes in RI occurred only in the 40 mmHg VM. The RI significantly increased by 0.015 in POST1 compared to PRE ($T = -3.11$, $p = 0.017$) and decreased by 0.004 in POST2 compared to POST1, but the difference was not significant ($T = 1.07$, $p = 0.573$). In contrast, at 30 mmHg VM, there was an average tendency to increase after the VM; however, the difference was not significant ($F = 3.09$, $p = 0.069$).

The HR decreased significantly only at 40 mmHg VM. HR showed a significant decrease of 4 bpm in POST1 compared to PRE ($T = 3.84$, $p = 0.003$), and it tended to significantly increase by approximately 2 bpm in POST2 compared to POST1 ($T = -2.93$, $p = 0.025$). Even at 30 mmHg VM, the HR tended to decrease after VM. It decreased by approximately 2 bpm in POST1 compared to PRE and tended to rise again by approximately 1 bpm in POST2 compared to POST1; however, the difference was not significant ($F = 2.28$, $p = 0.129$).

3.3. NIRS Measurements

The brain hemodynamic changes were different at 30 and 40 mmHg VM (Table 4). At 30 mmHg VM, the prefrontal HbO on the right side significantly decreased, while the left HbO showed a non-significant tendency to decrease. Furthermore, right HbO decreased on average during VM, POST1, and POST2 compared to PRE; in particular, POST1 showed a significant decrease compared to PRE ($T = 3.40$, $p = 0.023$). However, rSO2 showed no significant changes after the VM.

At 40 mmHg VM, the right rSO2 significantly increased after VM ($F = 3.86$, $p = 0.035$). The right rSO2 tended to increase on average during VM, POST1, and POST2 compared to PRE and showed a significant increase in POST1 compared to VM ($T = -3.17$, $p = 0.036$). However, there was no significant change in the HbO levels before and after VM.

Table 4. Cerebral hemodynamic changes in NIRS measurements during 30 and 40 mmHg VM.

Repeated Measure Comparisons					Post Hoc Comparisons (Scheffé)					
Outcome Variable		Testing	Mean ± SD	F	p	Testing	T	p		
30 mmHg	rSO2	Lt				VM	0.60	0.948		
			PRE	66.97 ± 11.13	0.21	0.792	PRE	POST1	0.13	0.999
			VM	66.64 ± 10.05			POST2	−0.05	1.000	
			POST1	66.89 ± 10.16			POST1	−0.67	0.930	
		POST2	67.01 ± 10.10	VM			POST2	−0.78	0.894	
		Rt			POST1	POST2	−0.48	0.972		
			PRE	63.89 ± 8.53	PRE	POST1	−0.55	0.958		
			VM	64.16 ± 7.78	POST2	−0.89	0.849			
	POST1		64.44 ± 7.56	POST2	−1.13	0.737				
	HbO	Lt			0.96	0.378	POST1	POST1	−1.19	0.705
			PRE	64.69 ± 7.42			POST2	−1.09	0.759	
			VM				POST2	−0.81	0.884	
			POST1				POST2			
		Rt			VM	1.92	0.323			
			PRE	−0.02 ± 0.09	PRE	POST1	2.83	0.072		
			VM	−0.03 ± 0.08	POST2	2.44	0.146			
POST1			−0.03 ± 0.08	POST1	−0.20	0.998				
40 mmHg	rSO2	Lt			3.97	0.037 *	POST2	0.05	1.000	
			PRE	−0.02 ± 0.08			POST1	0.67	0.929	
			VM	−0.03 ± 0.08			VM	2.70	0.093	
			POST1	−0.03 ± 0.08			POST2	3.40	0.023 *	
	HbO	Rt			5.37	0.009 *	POST2	2.55	0.120	
			PRE	−0.01 ± 0.04			POST1	−0.25	0.996	
			VM	−0.02 ± 0.03			POST2	0.12	1.000	
			POST1	−0.02 ± 0.03			POST1	0.53	0.963	
rSO2	Lt			1.85	0.181	POST2	0.12	1.000		
		PRE	65.22 ± 11.70			POST2	0.53	0.963		
		VM	65.67 ± 12.13			VM	−1.22	0.688		
		POST1	65.73 ± 12.73			PRE	POST1	−1.65	0.454	
HbO	Rt					POST2	−1.41	0.583		
		POST2	65.08 ± 12.73			VM	POST1	−1.30	0.644	

HbO	Rt					POST1	POST2	−0.98	0.809
						POST1	POST2	−0.26	0.995
						VM		−1.15	0.725
		PRE	61.89 ± 11.00			PRE	POST1	−2.47	0.138
		VM	62.22 ± 10.70	3.86	0.035 *		POST2	−1.87	0.344
		POST1	62.81 ± 10.43			VM	POST1	−3.17	0.036 *
	Lt	POST2	62.71 ± 10.41				POST2	−1.71	0.424
						POST1	POST2	0.49	0.971
						VM		1.50	0.535
		PRE	−0.02 ± 0.04			PRE	POST1	1.88	0.340
		VM	−0.03 ± 0.06	2.82	0.103		POST2	1.86	0.350
		POST1	−0.03 ± 0.05			VM	POST1	0.09	1.000
HbO	Rt	POST2	−0.03 ± 0.05				POST2	0.52	0.965
						POST1	POST2	0.77	0.898
						VM		1.80	0.377
		PRE	−0.012 ± 0.03			PRE	POST1	1.66	0.447
		VM	−0.02 ± 0.03	3.12	0.078		POST2	2.06	0.265
		POST1	−0.02 ± 0.03			VM	POST1	0.31	0.992
	Lt	POST2	−0.02 ± 0.03−0.02 ± 0.03				POST2	1.04	0.784
						POST1	POST2	1.16	0.719

Abbreviations: HbO, oxygenated hemoglobin; Lt, left; rSO₂, regional oxygen saturation; Rt, right; SD, standard deviation; VM, Valsalva maneuver. * $p < 0.05$.

4. Discussion

Overall, this study demonstrated that two expiratory pressures, 30 and 40 mmHg VM, resulted in significant changes in CCA blood velocity, PWV, and brain hemodynamics. In particular, HR and RI changed significantly only at a 40 mmHg VM. Therefore, it can be concluded that there were differences between the biosignals according to the intensity of expiratory pressure.

Both the 30 and 40 mmHg VM achieved an improvement in PWV and an increase in PSV. After VM at the two pressures, the PSV significantly increased in POST2, corresponding to VM phase IV. Phase IV of VM involves a blood pressure overshoot above baseline levels [4,29], leading to an increase in the blood velocity. In fact, according to previous research, the change in cerebral blood velocity following VM showed the greatest increase in phase IV [30].

Temporary changes in PWV can occur because the VM can stimulate the vascular tone. Vascular tone increases as blood pressure increases to protect blood vessels. In phase III, decreased blood pressure and increased venous return can cause vasodilation and decreased vascular tone [9,15]. Similarly, changes in vasoconstriction and dilation have been reported during resistance exercises accompanied by VM [19,31,32]. Even at 30 mmHg VM, in this study, both the PWV and stiffness index were significantly reduced, indicating an immediate effect of alleviating vascular stiffness. A significant decrease in PWV was also observed at 40 mmHg VM, but only a slight decrease in stiffness index was observed, which was not statistically significant. Furthermore, the PRE and POST differences in PWV and stiffness index at 40 mmHg VM were relatively smaller than those at 30 mmHg VM. Thus, the temporary effect of the VM on vascular stiffness may be greater at 30 mmHg than at 40 mmHg. This seems to be because the relatively high hypertensive stimuli induced excessive baroreflex activation at 40 mmHg VM, which increased sympathetic nerve activity and suppressed vasodilation. Previous studies have reported that as the intensity of the VM increased to 10 mmHg, 40 mmHg, and 60 mmHg, the rate of increase in heart rate during Phase IIa correspondingly increased [33]. This suggests that higher pressure intensities lead to enhanced sympathetic activity through the baroreflex. As with

the results of previous studies, a significant increase in HR and RI appeared only in 40 mmHg VM.

In contrast, a previous study reported an increase in vascular stiffness following the VM, which differs from the finding of this study [34]. This discrepancy may be due to the fact that the referenced study involved repeated VMs and measured vascular stiffness 20 min afterward. Repeated VM stimulation, particularly with a high-pressure VM of 40 mmHg, can increase the RI. Since RI tends to increase as vascular stiffness increases, repeated VMs could lead to an increase in PWV.

RI and HR showed significant differences between PRE and POST VM only at 40 mmHg VM, likely due to the baroreceptor reflex response. In POST1, HR decreased in response to an overshoot in BP. The increase in peripheral vascular resistance due to sympathetic activation in phase II could increase RI until phase IV. In other words, the response to hypertensive stimuli appeared more clearly at 40 mmHg than at 30 mmHg VM. In particular, an increase in RI indicates a limitation of the end-diastolic velocity, which suggests a circulation problem in small vessels [35]. Thus, 40 mmHg VM may be useful for testing sympathetic responses, but it seems less suitable as a stimulus to relieve vascular stiffness.

Brain hemodynamic function showed different changes following VM at the two pressures. A decrease in the right HbO after VM was observed only at 30 mmHg VM, while no significant change was observed at 40 mmHg VM. A decrease in HbO level implies an increase in cerebral oxygen consumption during the VM [36]. Previous studies have shown that VM causes changes in autonomic regulation mechanisms and cardiovascular function and contributes to increased brain activity in the brainstem and cerebellum [37].

At 40 mmHg VM, the right rSO₂ significantly increased after VM ($p = 0.035$). In particular, an increase occurred during the VM, while a significant increase was observed in POST1. This shows that VM influences an increase in rSO₂. According to the cerebral autoregulation system, intracranial pressure (ICP) and cerebral perfusion pressure (CPP) affect cerebral blood flow. Generally, when BP increases at VM onset, ICP also rises, which does not significantly alter CPP, leading to only a slight increase in cerebral blood velocity (Phase I). Moreover, in Phase IIa, there is a significant decrease in CPP due to suppressed venous return, reduced BP, and increased ICP, which has been reported to lead to a substantial reduction in cerebral flow. However, in phase IV, increased BP and cerebral blood velocity were observed [11]. This phenomenon may explain the notable increase in rSO₂ during POST1 compared to the VM phase in this study.

Indeed, one previous study reported that as blood pressure increases, cerebral saturation also increases [38], and it was also reported that there is a positive correlation with HbO [39]. In other words, the blood flow rate and blood pressure increased by the VM have a strong relationship with increased rSO₂, and increased arterial oxygen saturation can act as a stimulus for vasoconstriction, which appears to be the mechanism for increasing RI [40].

Based on the results, the 30 mmHg VM can improve vascular function with fewer changes in hemodynamics compared to the 40 mmHg VM. This suggests that the VM can be used not only as a conventional method for assessing autonomic nervous system function but also for stimulating vascular elasticity.

Limitations

In this study, we observed no increase in the RI at 30 mmHg VM; however, because the RI was measured in the large-diameter CCA, the RI in the peripheral blood vessels of the brain was unknown. Considering the small diameter of the peripheral blood vessels in the brain, vascular resistance may be higher; therefore, it will be necessary to observe hemodynamic changes at pressures lower than 30 mmHg. In addition, considering the research results showing that the increased blood velocity in POST2 can increase cerebrovascular risk, it is necessary to confirm the expiratory pressure that can stimulate only vascular stiffness while minimizing the increase in PSV and RI. In this study, cerebral

blood velocity, including in the MCA, was not directly measured. Future studies should further investigate changes in cerebral blood velocity.

The cerebral hemodynamics (rSO₂ and HbO) and vascular system were depended on strain intensity, body position, and VM phases. Thus, future studies should include time-specific dynamic responses corresponding to the phases of VM and the factors influencing hemodynamics and vascular system. Finally, because this study was conducted in healthy young adults, the results cannot be extrapolated to patients with vascular diseases or the elderly. Furthermore, in this study, vascular stiffness was measured only once immediately after the VM, so only temporary changes in vascular stiffness were confirmed. To achieve clinical implications, a future study investigating the changes in PWV after VM to determine the duration of its effect is necessary. In addition, customized VM pressures that take into account individual characteristics, including age, disease, and vascular health status, should be considered. Therefore, additional research for VM is needed on appropriate and/or personalized pressures in patients with vascular diseases.

5. Conclusions

In this study, we demonstrated changes in CCA blood velocity, arterial stiffness, and brain hemodynamics at two different VM pressures. The 30 and 40 mmHg VM achieved similar improvements in PWV and increases in PSV, but HR and RI changed significantly only after 40 mmHg VM, showing differences depending on the intensity of pressure. This is because excessive baroreflex activation at 40 mmHg VM inhibits vascular relaxation and influences the increase in RI, suggesting that the effect on improving vascular elasticity may be lower than that at 30 mmHg VM. Brain hemodynamics also showed a decrease in HbO due to increased brain activity at 30 mmHg VM, but an increase in rSO₂ was observed at 40 mmHg VM. Increased rSO₂ could be a stimulating factor for vasoconstriction, suggesting that vascular dilatability was relatively suppressed compared to the 30 mmHg VM. Therefore, the 30 mmHg VM is more effective in safely improving vascular function than the 40 mmHg VM. This study will provide a foundation for the broader application of VM in improving arterial stiffness.

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Data Availability Statement: The raw data supporting the conclusions of this article will be made available by the authors without undue reservation.

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