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RESEARCH ARTICLE

Effects of Oral Leak Size on Valsalva Responses

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Abstract

Introduction: **We hypothesized that oral leak size, a hitherto unstudied technical variable, would influence hemodynamic responses and difficulty level in executing the Valsalva maneuver (VM).**

Methods: **Based on power analysis, 38 healthy participants were included. Oral leak size in random order was 0.35, 0.71, 1.01,1.40 mm. Level of difficulty was rated 1 to 10, with ≥7−10 being severe.VM was performed at 40 mmHg expiratory strain for 15 s. Three trials were averaged for each leak size. Data were analyzed by repeated measures ANOVA and pairwise comparisons with Tukey adjustment, a mixed effect model, and a generalized linear model.**

Results: **Of the 38 participants, 4 were excluded from analysis for protocol deviation. Phase II L mean BP (MBP) was significantly higher with the largest leak versus all others ($P < 0.001$). TL was significantly lower with the largest leak versus all others ($P = 0.0029$).Difficulty performing the VM increased significantly with every increase in leak size ($P < 0.001$), and a significantly higher percentage of participants reported severe difficulty with leak 4 compared with leak 1 ($P < 0.001$), 2 ($P = 0.0068$), and 3 ($P = 0.0068$). There was no significant effect of phase II E SBP decline on phase II L MBP increase ($P = 0.0752$). Difficulty increased significantly with one unit increase in phase II L MBP ($P = 0.0002$).**

Conclusions: **Oral leak size affected VM hemodynamic parameters and level of difficulty. Oral leak size exceeding 1.01 mm significantly affected phase II L MBP. Level of difficulty rose with increasing leak size and was significantly correlated with increase in phase II L MBP.**

Keywords: Valsalva maneuver, Technical variables, Oral leak size, Hemodynamic autonomic parameters

1. Introduction

The Valsalva maneuver (VM) is an established test for the measurement of cardiovagal, cardiovascular sympathetic, and baroreflex functions.[1] The test is simple, but several general and technical variables can alter the diagnostic accuracy, consistency, and reproducibility of hemodynamic responses. Besides general variables such as the subject's blood volume status and medications, several well-defined technical variables can confound the results of the VM, including posture, magnitude and duration of expiratory strain (ES), and the phase of respiration preceding ES.[2]

In addition to these substantial confounders of the VM, the size of oral leak may represent a potential source of variability in this important test. An oral leak in the apparatus ensures that the glottis is open during the maneuver. The VM is classically defined as forcible exhalation against a closed glottis to increase intrathoracic pressure.[3] Intrathoracic pressure is best approximated by measuring it from the pleural cavity or the esophagus, but that process is difficult and invasive. A linear correlation between intraoral and intrapleural pressure[4] allows the calculation of intrathoracic pressure based on intraoral pressure, provided that the VM is performed with an open glottis. Asking the subject to exhale with an open glottis against a known external pressure manometer allows for noninvasive measurement and quantitation of intraoral pressure.[3,5] However, an accurate measurement of intraoral/intrathoracic pressure can be defeated by the habit of performing spontaneous VM against a closed glottis in such typical activities as defecation and by the tendency of some individuals to bring together the tongue and soft palate to display a rise in intraoral pressure without increasing the intrathoracic pressure.[6] A leak in the system ensures an open glottis and an accurate measurement of intraoral pressure. However, published studies have

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not reported the exact size of oral leak[7–9] or the effect of leak size on VM hemodynamic responses. It seems reasonable to assume that oral leak size would have an effect on hemodynamic responses and also on the difficulty of maintaining the required level of forceful exhalation.

We studied VM hemodynamic parameters and difficulty level using four different oral leak sizes. We hypothesized that oral leak size would significantly influence hemodynamic responses and that the level of difficulty in executing the VM would increase significantly with larger leak size.

2. Methods

2.1. Participants

This prospective cohort study was approved by our institutional review board. Informed consent was obtained. Participants were recruited through hospital bulletin board notices and from the local community. A total of 38 healthy participants were included. Participants with history of cough-induced headache were excluded.

2.2. Equipment

The custom mouthpiece (W. R. Electronics Co. Stillwater, MN) consisted of a small chamber with three orifices, one end for the attachment of a disposable mouthpiece, the other end for the replaceable inserts of different size openings, and a side outlet for a tube that connected to a transducer for recording ES and to a mercury manometer for displaying expiratory pressure. Oral leak size was controlled by interchangeable inserts with openings 0.35, 0.71. 1.01, and 1.40 mm in diameter.

Blood pressure was recorded continuously and noninvasively by a photoplethysmographic device (Finapres 2300, Ohmeda, Englewood, CO). Heart rate was recorded from electro cardiograph, lead II, continuously by a Hewlett–Packard heart rate monitor. A transducer introduced in the circuit recorded the expiratory pressure. Systolic and diastolic blood pressure (SBP, DBP) mean blood pressure (MBP), heart rate (HR), and ES were displayed simultaneously during the VM. The data were transferred to a computer using Biopac Student Lab Pro and Microsoft Excel on a Windows platform for further analysis.

2.3. Procedure

All tests were performed between 9 am and 12 noon in a quiet laboratory at an ambient temperature of 22–23 °C. Participants were asked to avoid intake of nicotine, caffeine, or alcohol on the day of testing. They were familiarized with the equipment, technique, and purpose of the study to minimize apprehension. After instrumentation the participants practiced with the device to produce a consistent ES response. They were instructed to place the mouthpiece between the lips and teeth to create a good seal and to differentiate between normal versus deep breathing preceding forced exhalation. The procedure was performed with participants in supine position and the head propped up on a pillow. They initiated VM at the end of normal inspiration, raised expiratory pressure quickly to 40 mmHg, and were timed 15 s by an auditory cue from the investigator using a stopwatch. The target pressure was marked by a black line on the manometer, visible to the participants and the investigator. Expiratory pressure was monitored throughout the maneuver. The participants were asked to terminate the strain abruptly at 15 s and breathe normally. At least 3 min of recovery time was allowed after each VM.[2,8,10,11]

Four oral leaks were introduced in random order using a randomized number table, to control for possible order effect. We obtained three Valsalva recordings from each participant that showed all four phases of blood pressure for each leak size. Participants were asked to assess the level of difficulty in performing the VM for each leak size from a scale of 1–10, 10 being the most difficult.

2.4. Measurements

VM-induced changes in BP display a quadriphasic pattern as described by Hamilton.[2,12] The mechanical phase I, at the onset of ES, shows an abrupt rise in BP due to propulsion of blood from the thorax to the peripheral arteries. Phase II, during continued strain, is subdivided into early and late components. The early component shows a fall in BP due to elevated intrathoracic pressure impeding the cardiac venous return and reducing the cardiac output. This component triggers the phase II L reflex-mediated peripheral vasoconstriction, leading to a rise in BP. The mechanical phase III, at termination of strain, displays a brief and abrupt decline in BP. Phase IV exhibits a sustained increase (overshoot) in BP. HR changes follow almost inversely to BP changes with a "triphasic" pattern: 1 to 2 beats of bradycardia in phase I, tachycardia during phases II/III, and bradycardia during phase IV.[2] Indices for autonomic function assessment were devised almost in tandem with advances in technology. The introduction of electrocardiograph facilitated the

emergence of HR-based Valsalva ratio (VR) as a noninvasive test of cardiovagal function.[8] The advent of noninvasive continuous BP monitors promoted the quantification and analysis of BP based (II and IV phases) responses.[2] The ability to computerize and analyze the time-integral data facilitated the creation of more sensitive latency-based parameters between points on the ES graph and the resultant BP and HR response curves.[13] We selected one HR-based, three BP-based, and three latency-based VM circulatory measurements of autonomic function to investigate the confounding effect of oral leak size (Fig. 1).

1 VR. The ratio of maximum HR during VM phase II/III divided by the lowest HR of phase IV. It is a universally affordable noninvasive measure of cardiovagal function.[8]
2 Amplitude of early phase II (II E). This parameter measures the SBP decrease from the baseline to the trough of phase II. It results from the persistent reduction of venous return and provides stimulus for the reflex occurrence of vasoconstriction and tachycardia.[2,9]
3 Amplitude of late phase II (II L). The BP increase from the trough of early phase II to the beginning of phase III. We measured mean BP (MBP) response because the diastolic and MBP rise are more reliable than SBP as indicators of alpha-adrenergic sympathetic vasomotor function.[2,14,15]
4 Amplitude of SBP overshoot in phase IV. This factor measures SBP increase from baseline to the peak of phase IV. It is an index of sympathetically mediated cardioacceleration.[2]
5 Tachycardia latency (TL). This factor is measured from the point of lowest BP in phase III of the VM to the highest HR of the induced tachycardia.[13]
6 Bradycardia latency (BL). This factor is measured from the point of highest SBP in phase IV to the lowest HR of the subsequent bradycardia within 30 s of the VM.[13]
7 Overshoot latency (OVL). This factor was recorded from the point of the end of VM to the peak of systolic pressure overshoot, defined as BP reading exceeding the baseline within 30 s after the VM.[13]

Visualization of all four phases of cardiovascular response to VM was required to calculate parameters in our analysis. The data were collected from 30 s before the test until 30 s after the test. Baseline supine SBP, DBP, MBP, and HR averages were determined during a 30-s interval directly preceding the VM. All seven parameters were calculated for each VM. For each leak size, the results of the three trials were averaged.

2.5. Statistical analysis

To detect a moderate effect size of 0.50 in accordance with Cohen's criteria, 34 participants were needed for 80% power to detect a significant difference at the 0.05 probability level, assuming the data were analyzed with analysis of variance (ANOVA). A total of 38 participants were studied to account for an anticipated 10% dropout rate related to test problems. The level of difficulty data for each trial were tabulated and arbitrarily graded as mild (1–3), moderate (4–6), or severe (7–10).

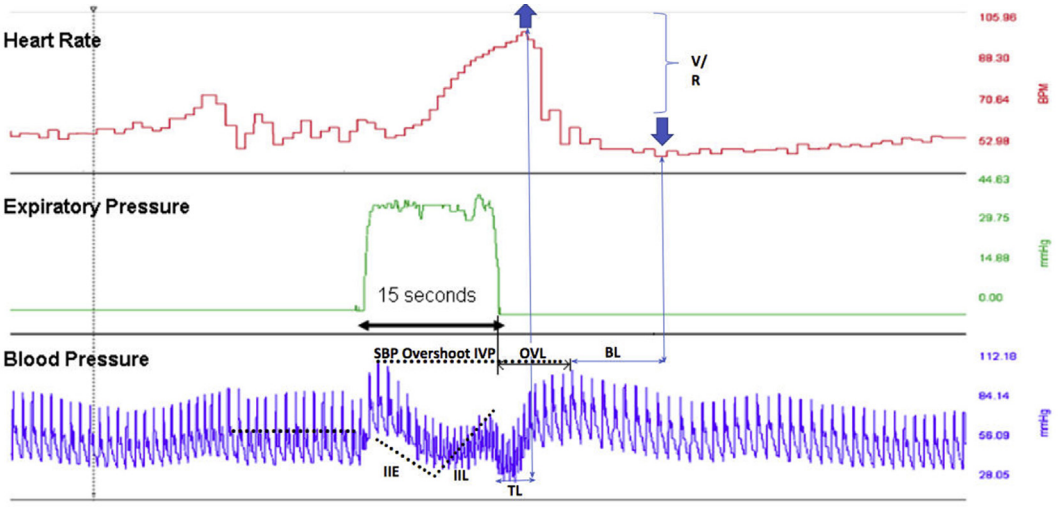

Fig. 1. Polygraphic recording of the Valsalva maneuver. Broken lines show BP phases II E, II L, and IV. Solid lines show the latencies TL, BL, and OVL. Solid arrows show tachycardia (↑) and bradycardia (↓) used to calculate the Valsalva ratio. BP, blood pressure; TL, tachycardia latency; BL, bradycardia latency; OVL, overshoot latency.

Data were analyzed by repeated measures ANOVA and by pairwise comparisons with Tukey adjustment when the ANOVA result was significant ($P < 0.05$). A mixed effect model was used to determine whether a correlation existed between phase II E and II L, and a generalized linear model was used to compare leak sizes in terms of percentage of subjects who reported severe difficulty in performing the test.

3. Results

Of the 38 participants, 4 were excluded from analysis because of inability to maintain the target strain pressure or because they looked at the hole size before reporting the level of difficulty. Of the 34 remaining participants, 20 were males and 14 females with mean age of 24 years (range, 22–31 years). The subjects were non-smokers and were free of drug use (both prescription and non-prescription). None had history of cardiovascular, respiratory, or neurologic disease.

There was no significant difference in expiratory strain (ES) magnitude or duration (Table 1). Phase II E SBP showed significant unadjusted variation with no differences after adjustment. Phase II L MBP was significantly higher with leak 4 versus all other leak sizes ($P < 0.001$). TL was significantly lower with leak 4 than with all other leak sizes ($P = 0.0029$). BL was significantly higher with leak 4 versus leak 2 ($P = 0.0193$). No significant difference was observed among leak sizes in phase IV SBP overshoot, OVL, and VR.

All participants reported some level of difficulty when performing the VM. The number of participants reporting the highest level (10) of difficulty increased from one at leak size 1 to six with leak size 4. Difficulty performing the VM increased significantly with every increase in leak size ($P < 0.001$), and significantly higher odds of severe difficulty with the maneuver were found with the largest leak size (leak 4) compared with all other leak sizes (Table 2).

There was no linear correlation between phase II E SBP decline and phase II L MBP increase ($P = 0.0752$) (Fig. 2). The difficulty level increase displayed significant linear correlation with a one-unit increase in phase II L MBP ($P = 0.0002$) (Fig. 3).

4. Discussion

These data demonstrate that the oral leak size, a hitherto unstudied technical variable, significantly affected VM hemodynamic parameters. Enlarging oral leak size produced a statistically significant effect on the phase II L MBP response, an important clinical autonomic parameter. Further, every increase in leak size significantly increased the difficulty of the maneuver, and difficulty was significantly correlated with increase in phase II L MBP. These findings indicate that oral leak size influences both the rise in phase II L MBP and the level of difficulty of the test.

In this study, posture, ES magnitude, and ES duration were controlled as well as possible in a clinical setting.[3–7] The variation of oral leak size selectively affected the hemodynamic VM parameters of phase II L amplitude, tachycardia latency, and bradycardia latency. Late phase II is an established and extremely useful index of adrenergic

Table 1. Oral leak size and values (mean ± SD) of hemodynamic parameters (N = 34).

Parameter	Leak size, no. (mm)				P value[a]	Pairwise comparison, adjusted P value
	1 (0.35)	2 (0.71)	3 (1.01)	4 (1.40)		
VR	1.93 ± 0.49	2.00 ± 0.45	2.00 ± 0.52	1.97 ± 0.42	0.3492	–
ES magnitude	43.21 ± 3.22	43.50 ± 4.30	42.85 ± 3.42	42.80 ± 3.09	0.6869	–
ES duration	15.42 ± 0.34	15.46 ± 0.35	15.40 ± 0.39	15.39 ± 0.40	0.6759	–
Phase II E amplitude (SBP, mmHg)	−17.37 ± 15.08	−17.35 ± 19.65	−11.08 ± 17.26	−16.54 ± 16.73	0.0349	No pairs significantly different after adjustment
Phase II L amplitude (MBP, mmHg)	11.62 ± 7.04	12.40 ± 7.79	14.25 ± 6.62	22.02 ± 8.81	<0.001	1 versus 4 2 versus 4 3 versus 4 All <0.001
SBP overshoot phase IV (mm Hg	15.21 ± 12.76	15.76 ± 12.83	16.87 ± 11.85	15.09 ± 11.20	0.59	–
TL (sec)	2.40 ± 1.25	2.11 ± 0.68	2.03 ± 0.89	1.63 ± 0.76	0.0029	1 versus 4 (P = 0.0131) 2 versus 4 (P = 0.0083) 3 versus 4 (P = 0.0050)
BL (sec)	6.76 ± 4.01	5.39 ± 3.65	6.55 ± 4.53	7.66 ± 4.29	0.0193	2 versus 4 (P = 0.0099)
OVL (sec)	8.80 ± 3.57	8.10 ± 3.35	8.66 ± 4.11	7.49 ± 4.59	0.3671	–

VR, Valsalva ratio; ES, expiratory strain; MBP, mean blood pressure; SBP, systolic blood pressure; TL, tachycardia latency; BL, bradycardia latency; OVL, overshoot latency.

[a] Repeated measures ANOVA with pairwise comparisons adjusted for multiple comparisons with Tukey adjustment.

Table 2. Level of difficulty with change in oral leak size (N = 34).

Factor	Leak size no. (mm)				P Value	Adjusted value
	1 (0.35)	2 (0.71)	3 (1.01)	4 (1.40)		
Difficulty level, mean±SD[a]	6.09 ± 1.80	6.82 ± 1.78	7.09 ± 1.68	8.06 ± 1.61	<0.001	Pairwise comparison 1 versus 2 (P = 0.0214) 1 versus 3 (P = 0.0047) 1 versus 4 (P < 0.001) 2 versus 4 (P < 0.001) 3 versus 4 (P < 0.001)
Subjects with severe difficulty (level 7–10), n (%)[b]	14 (41.2%)	20 (58.8%)	20 (58.8%)	29 (85.3%)	–	OR (95% CI) 4 versus 1, OR 8.29 (95% CI 3.18, 21.58) 4 versus 2, OR 4.06 (95% CI 1.73, 9.51) 4 versus 3, OR 4.06 (95% CI 1.73, 9.51)

OR, odds ratio; CI, confidence interval.
[a] Using repeated measures ANOVA.
[b] Using a generalized linear model for repeated measures.

vasomotor function. It is abolished by α-adrenergic blockade with phentolamine and correlates well with graded orthostatic hypotension during the head-up tilt test.[14,15] The current study shows a significant effect on phase II Lwith increasing oral leak size, especially with leak size exceeding 1.01 mm. The effect of leak size on tachycardia latency, bradycardia latency, and overshoot latency is relatively unimportant because they are infrequently employed in clinical autonomic assessment. Moreover, TL and BL alterations did not impact VR, the primary outcome variable for cardiac response. VR, a parameter of cardiovagal function, correlates well with responses to vagolytic (atropinization) and vagotonic (cold face test) stimuli.[16] VR is less likely to be influenced by technical variables, as shown in the current study. Thus, VR is a cost-effective, noninvasive, quantitative, and universally affordable autonomic parameter for comparison between different autonomic laboratories.

The magnitude of the phase II E SBP decline, a presumed stimulus for the baroreflex-mediated phase II L, was expected to be greater with increasing leak size. This would have explained

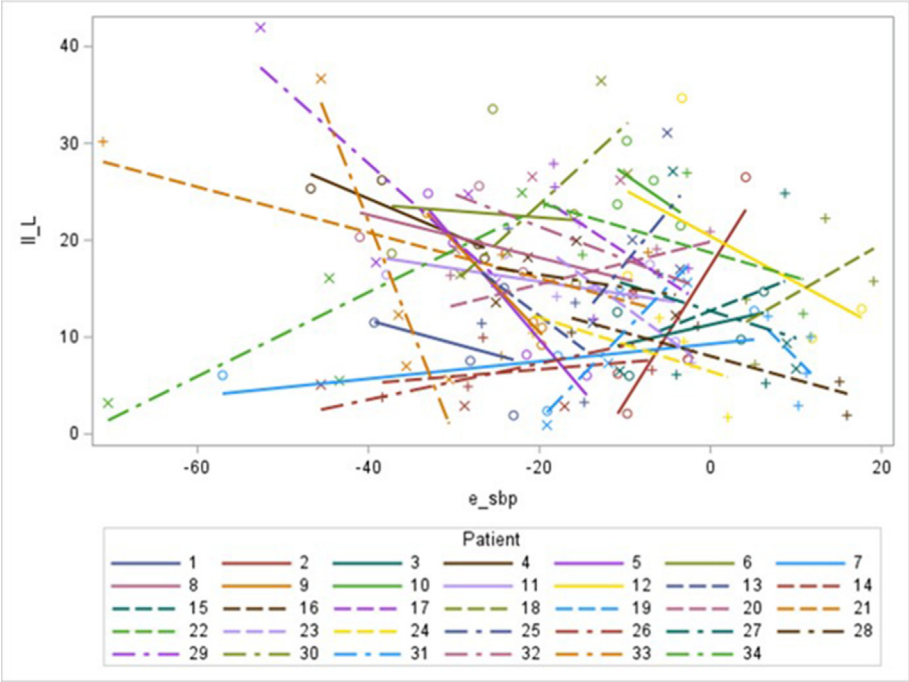

Fig. 2. Linear correlation between phase II E SBP (e_sbp) and phase II L MBP (II_L) for each subject. Line going up indicates positive correlation, line going down indicates negative correlation, and flat line indicates phase zero correlation. There was no consistent trend among subjects.

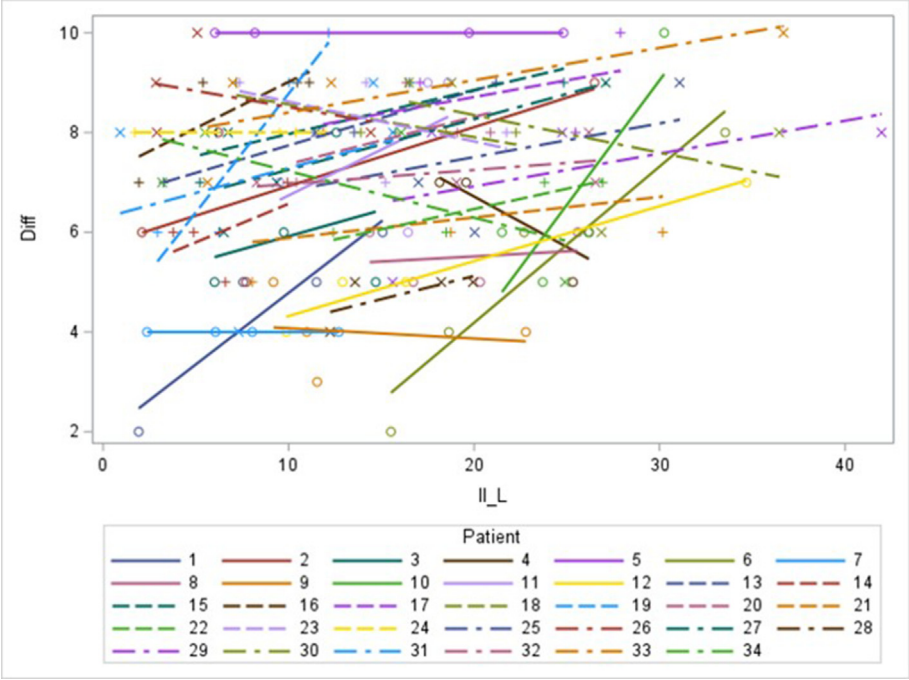

Fig. 3. Linear correlation between difficulty performing VM (Diff) and phase II L MBP (II_L). Line going up indicates positive correlation, line going down indicates negative correlation, and flat line indicates phase zero correlation. A significant correlation was found, with difficulty increasing by 0.059 for each unit increase in phase II L MBP (P = 0.0002).

increasing phase II L MBP rise with increasing leak size. Contrary to expectations, there was no linear correlation between phase II E SBP decrease and phase II L MBP increase. Phase II L MBP rise, however, correlated linearly with level of difficulty. These findings raise the possibility that the neuromuscular effort involved in initiating and maintaining ES may influence hemodynamic responses. Although the complex interaction between intrathoracic pressure, arterial baroreceptors, chemoreceptors, cardiopulmonary receptors, and cardiovascular end organs have been extensively studied, the role of neuromuscular effort and its contribution to the complex VM cardiovascular responses has received scant attention. The current data suggest that neuromuscular effort contributes to the rise in phase II L MBP.

Compared with the passive event of exhalation during regular breathing, VM is forced exhalation, an active event dependent upon contraction of expiratory muscles.[3] Increased oral leak size is likely to increase the force of expiratory effort necessary not only to maintain intrathoracic pressure, but also to supply extra air for the leak. The production of expiratory strain for VM is a complex motor act requiring coordination across jaw muscles (such as masseter and temporalis) to hold the bugle in position; facial muscles (orbicularis oris) to close lips tightly around the mouthpiece; orofacial, lingual, and velopharyngeal muscles (such as buccinator and levator veli palatini) to integrate airflow with lip movements; and respiratory muscles to maintain constant expiratory airflow during varying lung volume.[17–19] A study using a fixed leak to allow airway pressure to decrease from 40 mm Hg to 20 mm Hg during ES recorded forceful contraction of the abdominal muscles and a marked rise in intragastric pressure.[20] VM, a task-specific neuromuscular activity, generates afferent input from multiple musculoskeletal structures that activate central, sensorimotor, and autonomic networks to alter somatosympathetic response. Supportive evidence is also provided by teeth clenching causing cardiovagal inhibition and sympathoexcitation, and expiratory muscular effort augmenting sympathetic vasomotor outflow.[21,22] Although input from the arterial baroreflexes plays the main role, somatosympathetic response from the muscular effort may modulate the hemodynamic response and increasing difficulty level with enlarging leak size may enhance the degree of somatosympathetic modulation. Grading the degree of somatosympathetic modulation may improve the diagnostic accuracy of the test.

In this study, VM difficulty level was rated as severe by almost half of the normal participants at the smallest leak size and by most participants at the largest leak size. It is likely that patients with autonomic dysfunction may experience even greater difficulty sustaining ES at a larger leak size. The

current difficulty findings suggest that the smallest leak size created the least difficulty for participants. It is possible that even smaller leak size may further reduce difficulty without sacrificing diagnostic accuracy.

This study has several limitations. The four oral leak sizes were arbitrarily selected. The analyses were extensive, involving 2856 measurements from 408 VM maneuvers in 34 individuals, and therefore we chose to focus on representative parameters. However, several other established and newer parameters for studying autonomic dysfunction[23,24] may be selectively influenced by oral leak size with alteration of diagnostic accuracy and possibly reproducibility.

5. Conclusions

These data demonstrate that the largest oral leak size tested significantly affected VM hemodynamic parameters. Further, every increase in leak size significantly increased the difficulty of the maneuver, and difficulty was significantly correlated with increase in phase II L MBP. These findings suggest that the use of smaller oral leak size in the VM can minimize the level of difficulty while maintaining diagnostic accuracy.

Declaration of competing interest

Both authors declare no potential conflicts of interest in connection with this study.

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