**Effect of Inferior Vena Cava Occlusion on Left Ventricular
End-Systolic Pressure-Volume Relations in Intact Canine Hearts**
— Modulation by the Autonomic Nervous System —

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The effect of inferior vena cava occlusion (IVCO) on end-systolic pressure-volume relations (ESPVR) of the left ventricle was studied in intact canine hearts. In 12 anesthetized open-chest dogs, left ventricular (LV) pressure and volume were measured simultaneously using a microtip catheter and a conductance catheter, respectively. ESPVR was constructed from LV pressure-volume loops during IVCO (10 sec) and subsequent IVCO release under 5 conditions: control, after right or left cardiac sympathetic nerve (CSN) stimulation, bilateral vagotomy (VAT), and both VAT and bilateral CSN resection. $E_{\max}$ in IVCO release was significantly greater than that in IVCO in the control state. Following right or left CSN stimulation, $E_{\max}$ was increased in both IVCO and IVCO release, with the same hysteretic change in $E_{\max}$. With VAT, however, no hysteretic change was observed because $E_{\max}$ was the same in IVCO and IVCO release. After VAT and CSN resection, $E_{\max}$ was decreased in both IVCO and IVCO release, and again no hysteretic change was observed. These data imply that a sudden decrease in venous return into the heart induces a decrease in afferent vagal nerve activity, and thus increases efferent CSN activity, resulting in enhanced myocardial contractility.

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E_{max}, the slope of end-systolic pressure-volume relations (ESPVR), is insensitive to loading conditions and has been used as an index of the ventricular contractile state^{1–5}. In 1971, Suga reported that instantaneous ventricular pressure was correlated with ventricular blood volume in a simple and direct manner. In addition, the time-dependent ratio of pressure to volume, $E(t)$, represented the elastance of the ventricle, and $E_{\max}$, the maximal value of

$E(t)$, was independent of preload and afterload and could be a reliable index of ventricular contractility. However, Kass et al⁶ recently found in an intact circulation model that $E_{\max}$ calculated during the release of inferior vena cava occlusion (IVCO) was greater than that in IVCO. These findings suggest that a sudden decrease in venous return in intact circulation may enhance baroreceptor reflexes and thus augment cardiac sympathetic nerve (CSN) activity in the heart.

To clarify the mechanism of the reflex which operates in IVCO, we studied changes in $E_{\max}$ under IVCO and subsequent IVCO

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release in 5 different conditions (control, after right or left CSN stimulation, bilateral vagotomy, and both bilateral CSN resection and bilateral vagotomy) in an intact circulation model in dogs.

MATERIALS AND METHODS

Surgical Preparation

Experiments were performed in 12 mongrel dogs with a mean body weight of 21.3 ± 3.7 (SD) kg. All of the experiments conformed to the guidelines for animal experimentations, Hirosaki University. Dogs were premedicated with a subcutaneous injection of xylazine (4 mg/kg) and atropine sulfate (0.05 mg/kg), and anesthetized with α -chloralose (100 mg/kg) and pancuronium bromide (0.7 mg/kg). Small supplemental doses of α -chloralose (10 mg/kg) were given to each dog when necessary throughout the experiments. Under anesthesia, dogs were intubated and ventilated by a fixed-volume positive-pressure respirator (Harvard, USA) with room air supplemented by oxygen. Arterial blood gases were measured, and $p\text{CO}_2$ and pH were corrected when necessary by adjusting tidal volume and administering sodium bicarbonate. Blood volume loss resulting from surgery was supplemented with 6% dextran in normal saline prior to initiating the experimental protocol.

With the animal in a supine position, bilateral femoral arteries and veins were isolated. Aortic pressure (AoP) was measured with a pressure transducer attached to a fluid-filled catheter (Cordis, USA) inserted through the right femoral artery. A balloon catheter (Medi-tech, USA) was placed just below the right atrium through the right femoral vein to briefly occlude the inferior vena cava. A midline cervical incision was used to expose the bilateral vagus nerves and carotid arteries, and a catheter-tip micro-manometer (Millar PC 780 N, 7F, USA) was inserted through the left carotid artery to the left ventricular chamber to measure left ventricular pressure (LVP). A conductance catheter (Leycom, Netherlands) was inserted into the left ventricular chamber through the right carotid artery to measure left ventricular volume (LVV). These catheters were positioned parallel to the long axis of the

left ventricle. A balloon-flotation catheter (Nihon Koden, Tokyo) was also inserted into the pulmonary artery through the right jugular vein.

The chest was opened via a midline sternotomy. The right and left cardiac sympathetic nerves running from the stellate ganglion and crossing the vagal trunk to the heart were carefully exposed. The cardiac sympathetic nerves were verified by increased heart rate and arterial blood pressure during electrical stimulation (6 Hz, 9 V) using a bipolar stimulator. For atrial pacing, a pair of pacing electrodes was attached to the right atrium (Fig 1 (a)).

Left Ventricular Volume Measurement

We used the conductance catheter method^{7,8} to measure LVV. Briefly, this method is based on measuring the time-dependent electrical conductance of blood in 5 segments of the left ventricle, and estimating LVV from blood conductivity. We used an eight-electrode conductance catheter (7F, Leycom, Netherlands) with an appropriate electrode distance, $L(7 \times L = 6\text{--}8\text{ cm})$, to match the LV long axis). When positioned in the left ventricle, the catheter lay parallel to the long axis with the most distal electrode placed at the apex and with the most proximal electrode cephalad to the aortic valve (Fig 1 (b)). An alternating current (0.07 mA root-mean-square at 20 kHz) passed through the distal and proximal electrodes. From the remaining six electrodes, the 5 time-dependent segmental conductances, $G_i(t)$, were measured and converted to total LV volume, $V(t)$, using the formula:

$$V(t) = 1/a(L^2/\sigma)[G(t) - G_p]$$

where σ represents blood conductivity, a is the slope constant, and $G(t)$ is the sum of the 5 segmental conductances, $\sum G_i(t)$. G_p , which represents the parallel conductance formed by tissue surrounding the LV cavity (myocardium, right ventricle contents, etc.), was determined in each experiment by injecting 1–2 ml of hypertonic saline (6 mol/L) through a balloon flotation catheter in the pulmonary artery. Current generation, conductance measurement, and analog computations to obtain the desired volume variable $G(t)$ were performed using a Sigma

Fig 1. Experimental preparation. Left ventricular volume and pressure were measured with a conductance catheter and a catheter-tip micromanometer, which were inserted into the left ventricular chamber.

LVV: left ventricular volume, LVP: left ventricular pressure, IVC: inferior vena cava, AoP: aortic pressure, RSN: right cardiac sympathetic nerve, LSN: left cardiac sympathetic nerve, Pacer: pacing electrodes, BO: balloon occluder, LA: left atrium, RV: right ventricle.

5 signal conditioner processor (Leycom, Netherlands).

Protocol and Data Recording

The experimental protocol consisted of ESPVR measurements under 5 conditions: control, after right or left CSN stimulation, bilateral vagotomy, and bilateral CSN resection with bilateral vagotomy. Before initiating the protocol, heart rate was set sufficiently high and constant by atrial pacing to prevent the undesirable effect of a changing heart rate on ESPVR; the pacing rate was fixed 10 beats higher than the basal, spontaneous heart rate 30 sec after right or left CSN electrical stimulation (6 Hz, 9 V, 40 sec). In measurements for ESPVR, the inferior vena cava was transiently (10 sec) occluded by inflating the balloon catheter with 10–15 ml of air. Measurements for LVP, LVV, AoP and ECG signals were obtained during a transient IVCO and subsequent IVCO release. After the control

study, the right CSN was electrically stimulated using a bipolar stimulator (6 Hz, 9 V, 40 sec) and the same measurements for LVP, LVV, AoP and ECG signals as in the control study were repeated 30 sec after electrical stimulation was terminated. The same measurements were repeated 30 sec after terminating left CSN stimulation, after bilateral vagotomy, and after bilateral CSN resection with bilateral vagotomy.

Throughout the experiments, LVP, LVV and ECG signals were fed into a personal computer (PC 9801 NX/C, NEC, Tokyo). LVP-LVV loops were displayed using a pressure-volume analysis program (Sigma 5, ver 4.1, Taishoika, Osaka). All pertinent signals (ECG, LVP, LVV, AoP) were also recorded on an 8 channel heat-stylus recorder (Nihon Koden, Tokyo) and stored on magnetic tape using an analog tape recorder (A-614, Sony, Tokyo) for future data processing.

TABLE I CHARACTERISTICS OF THE EXPERIMENTAL DOGS

No	BW (Kg)	LV Weight (g)	HR (bpm)	meanAoP (mmHg)
1	19.5	94.2	92	72.4
2	17.5	90.6	100	61.2
3	24.0	120.6	94	83.0
4	20.5	96.0	85	51.2
5	22.6	88.0	103	68.7
6	28.0	137.6	90	74.0
7	20.0	85.2	120	55.7
8	25.3	102.5	98	61.4
9	19.0	97.3	103	76.0
10	16.0	71.4	117	81.0
11	18.0	62.3	102	58.7
12	25.0	103.0	90	65.0
Mean $\pm$ SD	21.3 $\pm$ 3.7	95.7 $\pm$ 20.0	99.5 $\pm$ 10.6	67.4 $\pm$ 10.1

BW: body weight, LV Weight: left ventricular weight, HR: spontaneous heart rate under anesthesia, mean AoP: mean aortic pressure under anesthesia

TABLE II HEMODYNAMIC CHANGES DURING IVCO AND IVCO RELEASE

		mean AoP (mmHg)	LVESP (mmHg)	LVESV (ml)
Control	Preocclusion	62.2 $\pm$ 12.5	82.3 $\pm$ 12.8	32.4 $\pm$ 8.77
	Occlusion (10)	51.2 $\pm$ 15.7 *	61.2 $\pm$ 21.5 *	18.7 $\pm$ 7.28 *
	Release (10)	72.0 $\pm$ 13.0 *	101.1 $\pm$ 17.0 *	31.8 $\pm$ 4.28
RSNS	Preocclusion	78.2 $\pm$ 25.4 **	108.8 $\pm$ 31.6 **	30.9 $\pm$ 5.89
	Occlusion (10)	62.1 $\pm$ 36.5 *	85.2 $\pm$ 38.0 *	18.8 $\pm$ 10.9 *
	Release (10)	89.8 $\pm$ 27.8 *	126.7 $\pm$ 31.8 *	29.7 $\pm$ 8.13
LSNS	Preocclusion	84.0 $\pm$ 12.1 **	111.6 $\pm$ 15.3 **	29.8 $\pm$ 9.40
	Occlusion (10)	70.3 $\pm$ 27.7 *	91.3 $\pm$ 28.1 *	15.6 $\pm$ 9.45 *
	Release (10)	100.6 $\pm$ 17.1 *	139.6 $\pm$ 13.5 *	29.1 $\pm$ 9.36
VAT	Preocclusion	64.6 $\pm$ 7.7	86.8 $\pm$ 10.7	31.1 $\pm$ 6.25
	Occlusion (10)	52.9 $\pm$ 12.6 *	68.9 $\pm$ 15.1 *	20.5 $\pm$ 7.31 *
	Release (10)	63.0 $\pm$ 9.1	84.2 $\pm$ 9.7	31.3 $\pm$ 2.84
CSNR	Preocclusion	56.4 $\pm$ 13.2	72.0 $\pm$ 14.2	33.7 $\pm$ 2.75
	Occlusion (10)	43.6 $\pm$ 13.8 *	51.3 $\pm$ 13.8 *	25.1 $\pm$ 4.63 *
	Release (10)	56.9 $\pm$ 13.1	72.5 $\pm$ 14.3	33.5 $\pm$ 4.17

mean $\pm$ SD

mean AoP: mean aortic pressure, LVESP: left ventricular end-systolic pressure, LVESV: left ventricular end-systolic volume, RSNS: right cardiac sympathetic nerve stimulation, LSNS: left cardiac sympathetic nerve stimulation, VAT: bilateral vagotomy, CSNR: bilateral cardiac sympathetic nerve resection with VAT, Occlusion (10): 10 beats after IVCO, Release (10): 10 beats after IVCO release

* $p < 0.05$ compared to preocclusion value, ** $p < 0.05$ compared to control preocclusion value

Data Analyses

For analyses of hemodynamics and ESPVR, data signals (ECG, AoP, LVP, LVV) were played back and recorded on paper at speeds of 25 mm/sec and 100 mm/sec. These signals were digitized per 10 msec with a digitizer (KD-4600, Graphtec, Tokyo) and reconstructed on a personal computer (PC 9801 NX/C, NEC, Tokyo).

ESPVR was generated by linear regression using 10 points at end-systole that were obtained during IVCO and subsequent IVCO release. $E_{\max}$ and V_0 were calculated as the slope and the volume intercept of ESPVR, respectively. In this study, end-systole was considered to be 20 msec before the minimum dP/dt .

Numerical data were expressed as

Fig 2. An example of the pressure-volume loop during IVCO and IVCO release in each state.

A: control, B: right cardiac sympathetic nerve stimulation, C: left cardiac sympathetic nerve stimulation, D: bilateral vagotomy, E: bilateral cardiac sympathetic nerve resection with bilateral vagotomy.

Values of $E_{\max}$, V_0 , r during IVCO (IVCO release) were as follows. A: 2.62 (3.42) mmHg/ml, 0.7 (2.8) ml, 0.95 (0.94), B: 3.42 (4.22) mmHg/ml, 6.8 (9.8) ml, 0.99 (0.98), C: 3.48 (4.30) mmHg/ml, 5.4 (7.9) ml, 0.90 (0.91), D: 2.75 (2.60) mmHg/ml, 3.6 (1.6) ml, 0.88 (0.89), E: 1.88 (1.90) mmHg/ml, 0.1 (-3.2) ml, 0.91 (0.92).

mean $\pm$ SD. Statistical analyses were performed using a two-way analysis of variance and the Student-Newman-Keuls method for multiple comparisons. Values were considered statistically significant when $p < 0.05$.

RESULTS

Table I shows body weight, LV weight, mean AoP and spontaneous heart rate of the dogs used for this study. Table II shows mean AoP, LV end systolic pressure (LVESP), and LV end-systolic volume (LVESV) during IVCO and IVCO release in these dogs. Fig 2 shows typical pressure-volume loops during IVCO and subsequent IVCO release under each of the 5 conditions. $E_{\max}$ and V_0 in each state are compared in Fig 3 and 4, respectively.

1) Changes in Hemodynamics and ESPVR Under the Control State

Pre-occlusion LVESP was 82.3 ± 12.8 mmHg, which decreased to 61.2 ± 21.5 mmHg 10 beats after IVCO. $E_{\max}$ and V_0

on IVCO were 2.62 ± 0.38 mmHg/ml and 1.6 ± 1.2 ml, respectively ($r = 0.96 \pm 0.06$). LVESP at the start of IVCO release was 59.6 ± 15.6 mmHg, which increased to 101.1 ± 17.0 mmHg 10 beats after IVCO release. $E_{\max}$ and V_0 on IVCO release were 3.21 ± 0.50 mmHg/ml and 3.1 ± 1.3 ml ($r = 0.94 \pm 0.05$), respectively. These values were both significantly greater than those under IVCO.

2) Changes in Hemodynamics and ESPVR After Right CSN Stimulation

Right CSN stimulation increased LVESP by 32.2% ($p < 0.05$). Pre-occlusion LVESP was 108.8 ± 31.6 mmHg, which decreased to 85.2 ± 38.0 mmHg 10 beats after IVCO. $E_{\max}$ and V_0 on IVCO were 3.42 ± 0.93 mmHg/ml and 6.9 ± 1.9 ml, respectively ($r = 0.98 \pm 0.09$). These values were significantly greater than those in the control state. LVESP at the start of IVCO release was 84.4 ± 23.4 mmHg, which increased to 126.7 ± 31.8 mmHg 10 beats after IVCO release. $E_{\max}$ and V_0 on IVCO release were

Fig 3. E_{max} during IVCO and IVCO release in each state. Data are expressed as the mean $\pm$ SD. *: $P < 0.05$ vs occlusion value, #: $P < 0.05$ vs control occlusion value, ns: not significant, RSNS: right cardiac sympathetic nerve stimulation, LSNS: left cardiac sympathetic nerve stimulation, VAT: bilateral vagotomy, CSNR: bilateral cardiac sympathetic nerve resection with bilateral vagotomy.

Fig 4. V_o during IVCO and IVCO release in each state. Data are expressed as the mean $\pm$ SD. *: $P < 0.05$ vs occlusion value, #: $P < 0.05$ vs control occlusion value, RSNS: right cardiac sympathetic nerve stimulation, LSNS: left cardiac sympathetic nerve stimulation, VAT: bilateral vagotomy, CSNR: bilateral cardiac sympathetic nerve resection with bilateral vagotomy.

4.22 ± 1.15 mmHg/ml and 10.1 ± 2.8 ml ($r = 0.97 \pm 0.06$), respectively. These values were significantly greater than those on under IVCO.

3) Changes in Hemodynamics and ESPVR After Left CSN Stimulation

Left CSN stimulation increased LVESP by 35.6% ($p < 0.05$). Pre-occlusion LVESP was

111.6 ± 15.3 mmHg, which decreased to 91.3 ± 28.1 mmHg 10 beats after IVCO. E_{max} and V_o on IVCO were 3.48 ± 0.52 mmHg/ml and 6.3 ± 1.9 ml, respectively ($r = 0.97 \pm 0.07$). These values were significantly greater than those in the control state. LVESP at the start of IVCO release was 89.6 ± 22.6 mmHg, which increased to

139.6±13.5 mmHg 10 beats after IVCO release. $E_{\max}$ and V_o on IVCO release were 4.30±0.42 mmHg/ml and 10.2±3.4 ml ($r=0.98\pm0.06$), respectively. These values were significantly greater than those under IVCO.

4) Changes in Hemodynamics and ESPVR After Bilateral Vagotomy

LVESP was not significantly changed by bilateral vagotomy. Pre-occlusion LVESP was 86.8±10.7 mmHg, which decreased to 68.9±15.1 mmHg 10 beats after IVCO. $E_{\max}$ and V_o on IVCO were 2.75±0.31 mmHg/ml and 2.7±1.3 ml, respectively ($r=0.95\pm0.08$). These values were not significantly different from those in the control state. LVESP at the start of IVCO release was 67.5±15.2 mmHg, which increased to 84.2±9.7 mmHg 10 beats after IVCO release. $E_{\max}$ and V_o on IVCO release were 2.60±0.28 mmHg/ml and 2.1±1.4 ml ($r=0.94\pm0.06$), respectively. These values were not significantly different from those under IVCO.

5) Changes in Hemodynamics and ESPVR After Bilateral CSN Resection With Bilateral Vagotomy

LVESP was not significantly changed by bilateral CSN resection with bilateral vagotomy. Pre-occlusion LVESP was 72.0±14.2 mmHg, which decreased to 51.3±13.8 mmHg 10 beats after IVCO. $E_{\max}$ and V_o on IVCO were 1.88±0.45 mmHg/ml and 1.3±1.2 ml, respectively ($r=0.92\pm0.10$). These values were significantly less than those in the control state. LVESP at the start of IVCO release was 49.5±11.6 mmHg, which increased to 72.5±14.3 mmHg 10 beats after IVCO release. $E_{\max}$ and V_o on IVCO release were 1.90±0.45 mmHg/ml and -0.4±2.1 ml ($r=0.90\pm0.09$), respectively. These values were not significantly different from those under IVCO.

6) The Range of End-systolic Points for ESPVR Measurements

ESPVR was measured using 10 end-systolic points. The minimum LVESP at these points under IVCO was not different from that under IVCO release in each state. The maximum LVESP at these points under IVCO release was significantly greater than that under IVCO in each state.

DISCUSSION

In the present study, we investigated the effect of IVCO on ESPVR. In the control state (reflex intact), $E_{\max}$ and V_o on IVCO release were significantly greater than those on IVCO, respectively. However, autonomic blockade eliminated the hysteric change in $E_{\max}$ in the control state. This finding strongly suggests that $E_{\max}$ is modulated by activation of the autonomic nervous system. Kass et al⁶ also reported a hysteric change in $E_{\max}$. In their investigation, they found that the hysteric change was eliminated by bilateral vagotomy and pharmacologic sympathectomy (hexamethonium). They concluded that the hysteric change originated in the baroreceptor reflex. However, the details of the reflex arc which modulates $E_{\max}$ remain unclear. Thus, we examined the reflex arc by electrical stimulation and resection of autonomic nerves.

The Effect of Cardiac Sympathetic Nerve Stimulation on ESPVR

Stimulation of the right and left CSN significantly increased $E_{\max}$ on IVCO by 30.6% and 33.1%, respectively. There was no significant change in the increase in $E_{\max}$ between these 2 conditions. Therefore, it seems that both CSN stimulations increased cardiac contractility by increasing the release of norepinephrine!¹⁰ However, an increase in arterial pressure was observed about 5 sec after CSN stimulation in this study. Therefore, CSN excitation may affect $E_{\max}$ with a time delay of a few seconds. On the other hand, bilateral CSN resection reduced $E_{\max}$ on IVCO by 28.2%. This may be the basal activity of the CSN in the control state.

The Effect of Vagus Nerve on ESPVR

Bilateral vagotomy increased $E_{\max}$ by 5.1%. This may be the basal activity of the vagus nerve in the control state. It is interesting that bilateral vagotomy eliminated the hysteric change of in $E_{\max}$ in the control state. Our results suggest that the vagus nerve may be involved in the hysteric change in $E_{\max}$.

The Assessment of V_o

V_o on IVCO release was significantly greater than that on IVCO in both the

control state and under right or left CSN stimulation. In contrast, the difference in V_o between IVCO and IVCO release was insignificant under bilateral vagotomy and CSN resection. These findings are partly in agreement with those of Kass et al⁶ who suggested that the hysteretic change originated in the baroreceptor reflex. However, the results of the present investigation can not explain why V_o values on IVCO and IVCO release in CSN stimulation were greater than those in the control state. It is not uncommon to observe seemingly negative values for V_o , which could be explained by the nonlinearity of ESPVR in situ^{5,11}. In fact, V_o on IVCO release under CSN resection was calculated to have a negative value in this study. Accordingly, V_o calculated by linear approximation is likely to be underestimated because ESPVRs are convex to the pressure axis. This underestimation might have caused the discrepancy in V_o in this study.

The Effect of Hemodynamic Changes During IVCO on ESPVR

In the present study, IVCO reduced mean AoP by 17.7% (62.2 ± 12.5 mmHg $\rightarrow$ 51.2 ± 15.7 mmHg) in the control state. The decrease in coronary perfusion pressure may have affected cardiac contractility. In an isolated heart study, Sunagawa et al¹² demonstrated that if coronary perfusion pressure was permitted to decrease simultaneously with left ventricular pressure during the measurement of ESPVR, then ESPVR was nonlinear below a critical pressure of 60 mmHg. They showed that the slope of ESPVR in this low range was seemingly greater than that in the control. In this study, coronary perfusion pressure was reduced below 60 mmHg during IVCO; thus the increase in $E_{\max}$ on IVCO release may have reflected an apparent increase due to some degree of global ischemia. However, in several animals, an increase in $E_{\max}$ on IVCO release under CSN stimulation was observed at a pressure well above 70 mmHg. Most importantly, the lack of a similar increase in $E_{\max}$ on IVCO release after autonomic blockade makes it highly unlikely that reduced coronary perfusion pressure played a major role in the hysteretic change in $E_{\max}$.

On the other hand, the reduction in arteri-

al pressure by IVCO may have stimulated baroreceptor reflexes. The carotid sinus baroreflex system, the aortic baroreflex system, and the cardiopulmonary baroreflex system are generally considered to control arterial pressure. Their complicated interactions have been previously reported¹³⁻¹⁶. In this study, bilateral carotid arteries were ligated when a conductance catheter and a catheter-tip micromanometer were inserted. Accordingly, the effect of the carotid sinus baroreflex system would be negligible. The vagus nerve of the dog conducts signals from the aortic baroreceptors and the cardiopulmonary receptors to the central nervous system. Linden and Kappagoda¹⁷ reported that the atria contained receptors discharging into myelinated vagal afferent nerve fibers, receptors discharging into non-myelinated vagal afferent nerve fibers, and receptors discharging into sympathetic afferent nerve fibers. Kappagoda et al¹⁸ reported that stimulation of these atrial receptors with myelinated vagal afferent nerves caused a reflex increase in efferent cardiac sympathetic nerve activity. In addition, other investigators have reported that the vagus nerve acts as an afferent reflex pathway¹⁹⁻²². Thus, it seems reasonable that the afferent vagal nerve mediates a sudden decrease in venous flow return and the reduction in arterial pressure with IVCO.

In conclusion, our results suggest the following mechanism for the hysteretic change in $E_{\max}$. The reductions in venous flow return and arterial pressure during IVCO are mediated by atrial receptors and aortic baroreceptors via the afferent vagal nerve to the reflex center, respectively. This causes a reflex increase in efferent cardiac sympathetic nerve activity that increases $E_{\max}$ on IVCO release with a time delay (Fig 5). In an experimental study in which nerve activity was directly recorded, Honda et al²³ noticed an increase in efferent cardiac sympathetic nerve activity during IVCO. Thus, the mechanism mentioned above seems reasonable to account for the hysteretic change in $E_{\max}$ during IVCO. Recently, the conductance catheter method has made it possible to measure ESPVR in humans. A brief IVCO for $E_{\max}$ measurement has been believed to minimize reflex alterations in heart rate and contractility that influence ESPVR²⁴.

Fig 5. Mechanism of the hysteretic change in $E_{\max}$. The decrease in venous return and arterial pressure during IVCO mediated by the afferent vagal nerve to the reflex center causes a reflex increase in efferent cardiac sympathetic nerve activity that increases $E_{\max}$ on IVCO release.

However, the results presented here indicate that IVCO for 10 sec may cause a baroreflex increase in myocardial contractility. We should consider modulation by the autonomic nervous system in ESPVR measurements using IVCO.

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