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Acute hemorrhagic shock decreases airway resistance in anesthetized rat

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Bayat S, Albu G, Layachi S, Portier F, Fathi M, Peták F, Habre W. Acute hemorrhagic shock decreases airway resistance in anesthetized rat. *J Appl Physiol* 111: 458–464, 2011. First published May 19, 2011; doi:10.1152/japplphysiol.00024.2011.—We studied the relation between changes in pulmonary and systemic hemodynamics to those in the airway resistance, respiratory tissue mechanics, and thoracic gas volume (TGV) following acute hemorrhage and blood reinfusion in rats. Forced oscillation technique was used to measure airway resistance (Raw), respiratory tissue damping, and elastance at baseline and after stepwise 1-ml blood withdrawals up to 5 ml total, followed by stepwise reinfusion up to full restoration. Mean systemic (Pam) and pulmonary arterial pressures and suprarenal aortic blood flow were measured at each step. In supplemental animals, plethysmographic TGV, Pam, and respiratory mechanics measurements were performed. Blood volume loss (BVL) led to proportional decreases in Raw (66.5 ± 8.8 vs. 44.8 ± 9.0 $cmH_2O \cdot s \cdot l^{-1}$ with 5 ml, $P < 0.001$), Pam, and aortic blood flow. In contrast, tissue damping increased significantly ($1{,}070 \pm 91$ vs. $1{,}235 \pm 105$ cmH_2O/l, $P = 0.009$ with 5 ml BVL), whereas tissue elastance did not change significantly. TGV significantly increased with acute BVL (3.7 ± 0.2 vs. 4.2 ± 0.2 ml, $P = 0.01$). Stepwise reinfusions produced opposite changes in the above parameters, with Raw reaching a higher value than baseline ($P = 0.001$) upon full volume restoration. Both adrenalin ($P = 0.015$) and noradrenalin levels were elevated ($P = 0.010$) after 5-ml blood withdrawal. Our data suggest that the decreases in Raw following BVL may be attributed to the following: *1*) an increased TGV enhancing airway parenchymal tethering forces; and *2*) an increase in circulating catecholamines. The apparent beneficial effect of a reduction in Raw in acute hemorrhagic shock is counteracted by an increase in dead space and the appearance of peripheral mechanical heterogeneities due to de-recruitment of the pulmonary vasculature.

pulmonary circulation; forced oscillations; circulatory shock; respiratory mechanics; airway resistance

ACUTE HEMORRHAGIC SHOCK IS a leading cause of traumatic death (33). Although a large proportion of patients with traumatic hemorrhage require tracheal intubation and mechanical ventilation (29), very few studies have characterized the pulmonary mechanical consequences of an acute hemorrhagic shock, with incomplete and often conflicting findings (6, 20, 35). Acute systemic hemorrhage was shown to have opposing effects on the total respiratory system resistance (Rrs), with studies demonstrating decreases (6, 20) and increases (35) under similar experimental conditions. Changes in the respiratory compliance following acute systemic hypovolemia are even more disperse, since respiratory compliance has been reported to decrease (35), to remain unchanged (14, 20), or to increase (6). Besides methodological and species differences, one of the major reasons for this controversy may result from the use of global parameters to characterize lung functional changes following acute blood loss. Changes in Rrs, for example, may be attributed to the altered respiratory tissue viscoelasticity or to a modulation in the airway tone. Since opposing alterations may occur in these compartments (10, 27), the net change in such a global parameter may be highly variable, as it may be biased by the individual contribution of each component.

Acute hemorrhage ultimately affects the pulmonary circulation and may cause substantial reductions in thoracic blood volume (5). Such changes can, in turn, increase the thoracic gas volume (TGV) (24), which may further affect the lung mechanics. However, measurements of pulmonary hemodynamics, lung volumes, and lung mechanics subsequent to acute hemorrhage have not been combined within a study. Moreover, the reversibility of the lung functional changes following restoration of the physiological blood volume has not been addressed systematically.

Therefore, the aims of the present study were to *1*) characterize the airway and respiratory tissue changes separately following acute hemorrhage; *2*) relate respiratory mechanical changes to those in the pulmonary hemodynamics and lung volume; and *3*) examine the reversibility of these changes after reinfusion of the withdrawn blood.

METHODS

Animal preparation. Animal care and procedures of the experiment were in accordance with the Guidelines for the Care and Use of Animals provided by the American Physiological Society and approved by the local institutional authorities. Studies were performed on two groups of Sprague-Dawley rats weighing 350–385 g. The rats were anesthetized with intraperitoneal injection of chloral hydrate (400 mg/kg). The trachea was intubated with a polyethylene cannula (14 gauge, Braun, Melsungen, Germany), and the rats were mechanically ventilated to achieve normocapnia with a tidal volume of 7 ml/kg body wt, a respiratory rate of 70–80 breaths/min, and an fraction of inspired O_2 of 40%, with a constant volume-cycled rodent ventilator (model 683, Harvard Apparatus, South Natick, MA). The end-expiratory pressure was set to zero. Anesthesia was maintained with hourly supplemental doses of intraperitoneal chloral hydrate (150 mg/kg). Body temperature was measured using a rectal thermistor probe and maintained at 37°C using a heating pad. The femoral artery was cannulated (22 G, Abbocath, Abbot Medical, Baar/Zug, Switzerland), connected to a pressure transducer (model 156 PCE 06-GW2, Honeywell, Zürich, Switzerland) for continuous blood pressure mon-

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itoring, and used to perform the blood withdrawals and sampling for blood-gas analysis (Abbot i-Stat Handheld, Baar/Zug, Switzerland) at baseline and after full reinfusion at the end of the protocol. In the group of animals in which the pulmonary hemodynamics were monitored, the abdomen was surgically opened, and an ultrasonic flow probe (Transonic Systems, Ithaca, NY) was installed around the abdominal descending aorta to measure blood flow ($\dot{Q}ao$). A polyethylene tube (0.58 mm inner diameter, 0.96 mm outer diameter, Portex, Hythe, UK) was then introduced via the right jugular vein and advanced under continuous hemodynamic monitoring to the main pulmonary artery for the recording of pulmonary arterial pressure (Ppa). The airway pressure, arterial pressures, $\dot{Q}ao$, and rectal temperature were continuously monitored by a data collection and acquisition system (Biopac, Santa Barbara, CA). End-tidal CO_2 was monitored continuously using a side-stream capnogram (Datex-Ohmeda Capnomac, Zürich, Switzerland).

Measurements of pulmonary hemodynamics. Ppa curves were analyzed to obtain systolic (Ppa_s), diastolic (Ppa_d), and mean pressures (Ppa_m). Stroke volume was calculated as $\dot{Q}ao$/heart rate (HR). Systemic vascular resistance (SVR) was estimated as mean systemic arterial pressure (Pam)/$\dot{Q}ao$. Total pulmonary vascular resistance (TPVR) was estimated as $Ppa_m/\dot{Q}ao$ (15).

Measurement of TGV. TGV measurements were performed with a body plethysmograph, as detailed previously (16), in the additional group of rats. Briefly, the trachea was occluded at end expiration until three to four spontaneous inspiratory efforts were generated by the animal in the closed plethysmograph. Changes in tracheal pressure and plethysmograph box pressure were recorded during these maneuvers. TGV was calculated by applying Boyle's law to the relationship between tracheal pressure and box pressure after correction for the box impedance (16). Due to technical difficulty, Ppa and $\dot{Q}ao$ could not be measured in the group of animals in whom TGV was measured; however, systemic blood pressure and respiratory mechanical parameters were measured in this group. Furthermore, TGV recordings were only performed at fewer phases of the protocol (0, 2.5, and 5 ml of blood withdrawal and restoration) to maintain similar time frames in this protocol than those followed in the main study group.

Measurement of airway and tissue mechanics. To characterize the airway and tissue mechanics separately, the input impedance of the respiratory system (Zrs) was measured by using the forced oscillatory technique, as described in detail previously (11, 28). Briefly, the tracheal cannula was switched from the respirator to a loudspeaker-in-box system at end expiration. The loudspeaker generated a small-amplitude pseudorandom signal with frequency components between 0.5 and 21 Hz through a polyethylene wave tube (length = 100 cm, inner diameter = 2 mm). Two identical pressure transducers (model 33NA002D, ICSensors, Milpitas, CA) were used for measurement of the lateral pressures at the loudspeaker and at the tracheal end of the wave tube. Zrs was calculated as the load impedance of the wave tube (37). To separate the airway and tissue parameters, a model was fitted to the Zrs spectra by minimizing the relative differences between the measured and modeled impedance values. The model contained a frequency-independent airway resistance (Raw) and inertance in series with a constant-phase tissue compartment, characterized by the coefficients of tissue damping (G) and elastance (H) (13). Tissue hysteresivity was calculated as $\eta = G/H$ (9). The impedance of the tracheal cannula and the connecting tubing was also determined, and Raw and airway inertance were corrected by subtracting the instrumental resistance and inertance values from them. Specific Raw (sRaw) and H (sH) were calculated using the corresponding TGV values.

Measurement of plasma catecholamine levels. Plasma adrenalin and noradrenalin concentrations were determined in duplicate by high-pressure liquid chromatography, coupled with electrochemical detection. The lower limit of sensitivity for the assay was 0.3 and 0.1 nM/l for noradrenalin and adrenalin, respectively.

Measurement protocol. The main study group was used to assess the pulmonary and systemic hemodynamics and the concomitant respiratory mechanical changes, simultaneously ($n = 6$). In a second group of animals, lung volume changes, systemic hemodynamics, and respiratory mechanical parameters were measured ($n = 5$), since combined measurements of lung hemodynamics and lung volume were not feasible in the same animals. Since the measured changes in respiratory mechanics in response to blood loss were very similar in both groups, and to simplify data presentation, respiratory mechanical data of the main group are shown in the results, with the exception of sRaw and sH, which were measured in the second group. In the group of rats in which the pulmonary hemodynamic changes were measured at the same time as airway and tissue mechanics, 2 ml of blood were withdrawn and immediately replaced with normal saline: 1 ml was used for catecholamine measurement, and a 1-ml sample was spared in a heparinized syringe to replace later sampling for catecholamine measurements. In this group, an inspiratory maneuver was performed to an inspiratory pressure of 25 cmH_2O or total lung capacity, to standardize the volume history, and a set of Zrs recordings of three to four data epochs of 8 s were measured at 1-min intervals to establish the baseline respiratory mechanics. Baseline pulmonary and systemic hemodynamics were determined immediately before these impedance recordings from the Ppa, $\dot{Q}ao$, and systemic blood pressure recordings. One milliliter of blood was then gently withdrawn from the femoral artery in a heparinized syringe, a hyperinflation was again performed to reach the total lung capacity, and another set of Zrs and hemodynamic parameters was measured 5 min later. The same procedure was repeated after stepwise 1-ml withdrawals, up to a total 5 ml of arterial blood. At this point, a 1-ml sample was withdrawn for catecholamine measurement and replaced with the spare 1-ml blood sample taken at baseline. To assess the reversibility of the lung mechanical and hemodynamic changes, the withdrawn blood was readministered in five steps, including injections of 1 ml of blood taken previously, until the initial circulatory blood volume was reached.

In the second group of rats in which lung volume changes were related to those in Zrs, fewer steps in lung volume withdrawals were used in order to achieve the measurements within the same time frame as in the first group and thus to avoid time effects. An identical experimental procedure was performed in these rats, except recordings of Zrs and TGV were collected under the baseline condition and following withdrawal and readministration of 2.5 and 5 ml of arterial blood. In this group, total blood volume was estimated from the body weight according to Lee and Blaufox (17).

Statistical evaluation. Since the procedural data proved to be normally distributed, as analyzed by the Shapiro-Wilk test, data are reported as means ± SE. One-way repeated-measures ANOVA was used to test the significance of changes in the parameters after the blood withdrawals. For pairwise comparisons, 95% confidence intervals for the differences were computed by taking into account the significant interactions between the factors. The Student-Newman-Keuls test was used for post hoc comparisons. Pearson statistical test was used to assess the strength of correlations. The statistical tests were performed by using the SigmaStat 11.0 statistical program package (Systat Software, Chicago, IL). A $P < 0.05$ was considered significant.

RESULTS

Figure 1 demonstrates the changes in the airway and respiratory tissue parameters following stepwise withdrawal of systemic blood and after its reinfusions. Following stepwise blood withdrawals, statistically significant stepwise decreases were observed in Raw ($P < 0.001$), whereas G exhibited stepwise increases ($P < 0.001$). The lack of significant changes in H with the increases in G resulted in significant elevations in η ($P < 0.001$). Stepwise restoration of the blood resulted in

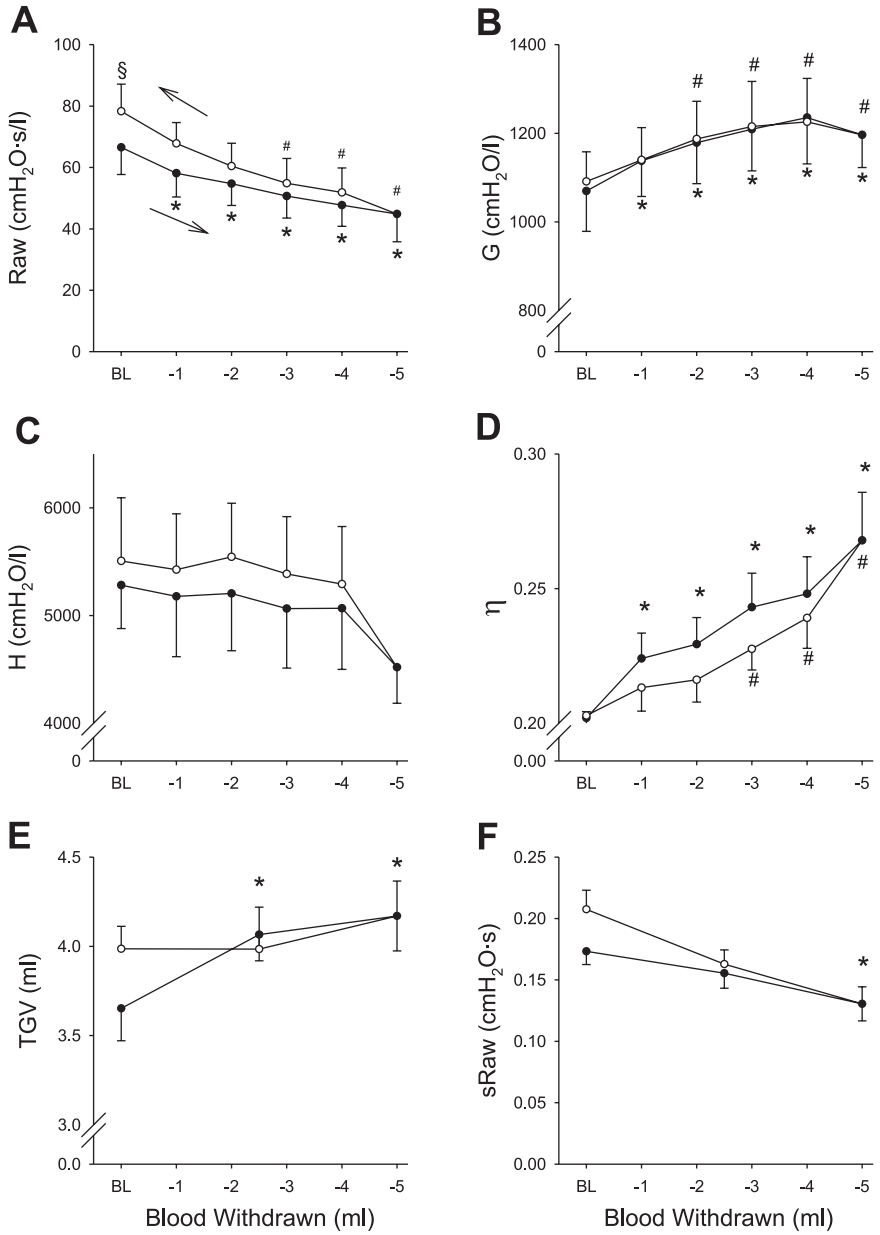

Fig. 1. Changes in the airway and respiratory tissue parameters following stepwise blood withdrawal (solid symbols) and after reinfusion (open symbols). *A*: airway resistance (Raw). *B*: tissue damping (G). *C*: tissue elastance (H). *D*: tissue hysteresivity (η). *E*: thoracic gas volume (TGV). *F*: specific airway resistance (sRaw). Values are means ± SE; $n = 6$ (*A–D*) and $n = 5$ (*E* and *F*). *$P < 0.05$ vs. the initial baseline (BL) level (solid symbols). #$P < 0.05$ vs. the complete recovery of blood volume (open symbols). §$P < 0.05$ within a blood volume level.

proportional returns in the respiratory mechanical parameters to their corresponding levels measured during the blood withdrawals. A slight but significant elevation in Raw was observed at the end of the protocol, upon full blood volume restoration ($P = 0.001$). TGV exhibited significant increases following acute hypovolemia (3.7 ± 0.6 vs. 4.1 ± 0.4 ml, $P = 0.01$), whereas sRaw decreased ($P = 0.017$). sH significantly decreased with a blood withdrawal of 5 ml ($P = 0.039$). The withdrawal of 5 ml represented an 18.8 ± 0.7% drop in total blood volume, as estimated based on body weight. The increase in TGV was inversely correlated to the estimated total blood volume ($R = -0.55$, $P = 0.011$). With blood volume restoration, TGV returned to a higher value than baseline; however, this difference was not statistically significant.

Changes in the systemic and pulmonary hemodynamic parameters are shown in Fig. 2 following acute hemorrhage and restoration of the withdrawn blood. No change occurred in Ppa_s ($P = 0.28$), whereas Ppa_d increased markedly following acute hypovolemia ($P = 0.007$), resulting in significant elevations in Ppa_m ($P = 0.04$). As concerns the systemic blood pressure, systolic arterial pressure, diastolic arterial pressure, and Pam decreased substantially following acute induction of hypovolemia ($P < 0.001$ for all). $\dot{Q}ao$ and stroke volume also exhibited considerable decreases subsequent to acute hemorrhage ($P < 0.001$ for both). Stepwise marked increases were observed in TPVR following blood withdrawals ($P < 0.001$), whereas SVR was elevated only after a loss of 5 ml of blood ($P = 0.03$). The HR decreased proportionately and significantly (from 350 ± 21 to 302 ± 19 beats/min, $P = 0.03$) during volume withdrawal. No significant differences were detectable between the initial levels of the hemodynamic parameters and those reestablished after blood reinfusions, indicating a complete recovery of the systemic and pulmonary hemodynamics.

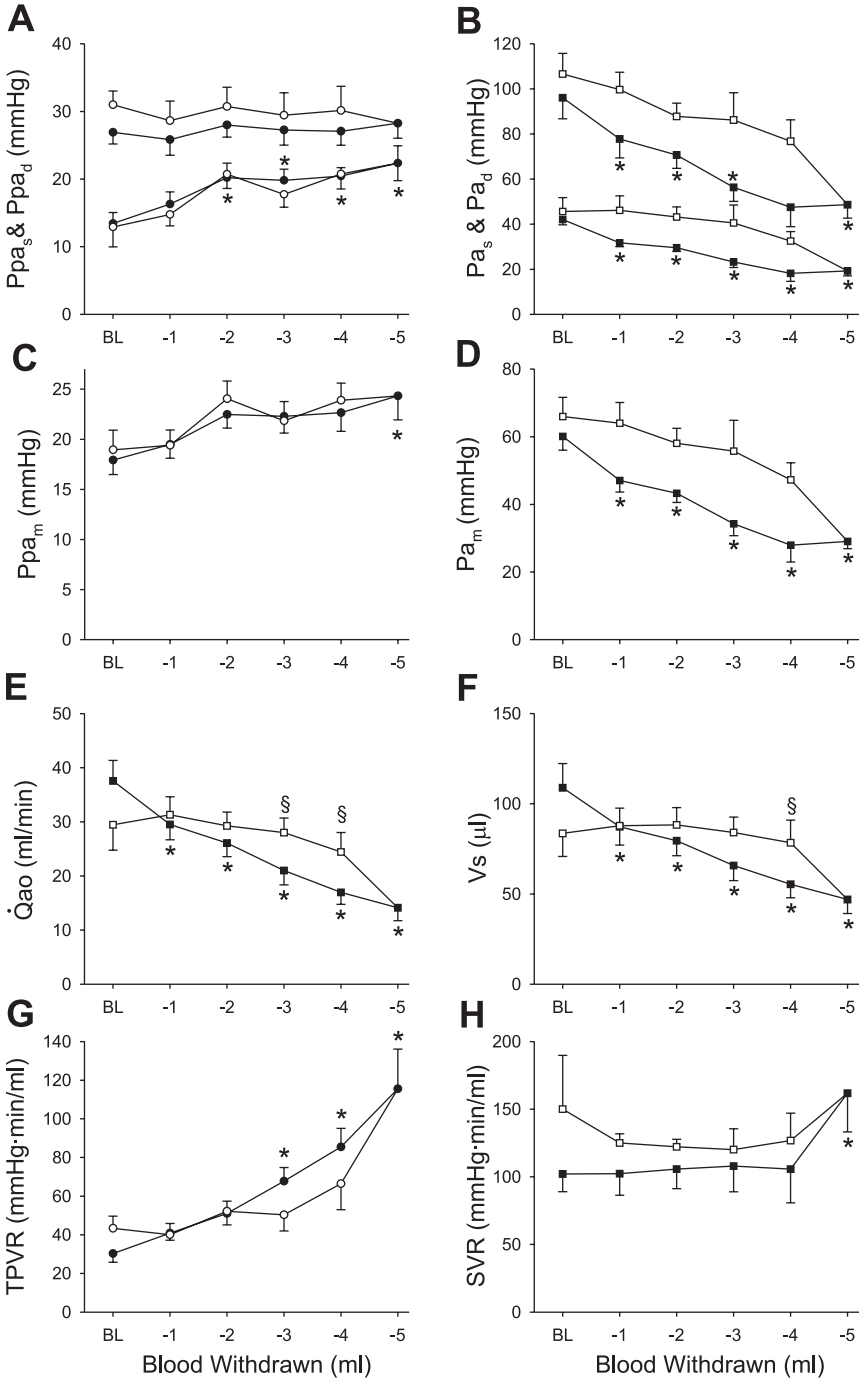

Fig. 2. Changes in the systemic (squares) and pulmonary hemodynamic parameters (circles) following stepwise induction of acute hemorrhage (solid symbols) and after reinfusion of the withdrawn blood (open symbols). *A* and *C*: systolic (Ppa_s) and diastolic (Ppa_d) and mean pulmonary arterial pressures (Ppa_m), respectively. *B* and *D*: systolic (Pas) and diastolic (Pad) and mean systemic arterial pressures (Pam), respectively. *E*: aortic blood flow ($\dot{Q}ao$). *F*: stroke volume (Vs). *G*: pulmonary vascular resistance (TPVR). *H*: systemic vascular resistance (SVR). Values are means ± SE, $n = 6$. *$P < 0.05$ vs. the initial BL level (solid symbol). §$P < 0.05$ within a blood volume level.

The hemodynamic changes with blood withdrawal were accompanied by a significant decrease in pH (7.51 ± 0.06 and 7.42 ± 0.06 before and after 5-ml blood withdrawal, respectively; $P = 0.005$), and bicarbonate (19.9 ± 1.9 and 13.7 ± 4.0 mmol/l before and after 5-ml blood withdrawal, respectively; $P = 0.036$), suggesting metabolic acidosis. No significant changes in arterial P_{O_2} and P_{CO_2} were observed.

The assessments of the plasma levels of catecholamines revealed that acute hemorrhage led to consistent elevations in both adrenalin (0.32 ± 0.11 and 1.0 ± 0.25 nM/l before and after 5-ml blood withdrawal, respectively; $P = 0.015$) and noradrenalin (1.0 ± 0.22 and 2.8 ± 0.42 nM/l before and after 5-ml blood withdrawal, respectively; $P = 0.010$) levels. These elevations were not statistically detectable after the reestablishment of the original circulatory blood volume (0.38 ± 0.15 and 1.58 ± 0.35 nM/ml for adrenalin and noradrenalin, respectively), however, only four valid measurements could be obtained after full blood volume recovery.

The drop in Raw showed a significant correlation with Pam ($R = 0.95$), $\dot{Q}ao$ ($R = 0.95$), and TPVR ($R = -0.87$). The relationship between the changes in Ppa_d and G following the stepwise blood withdrawals and reinfusions is demonstrated in Fig. 3. The reason for choosing this pair of variables was based on the consideration that changes in Ppa_d may alter ventilation

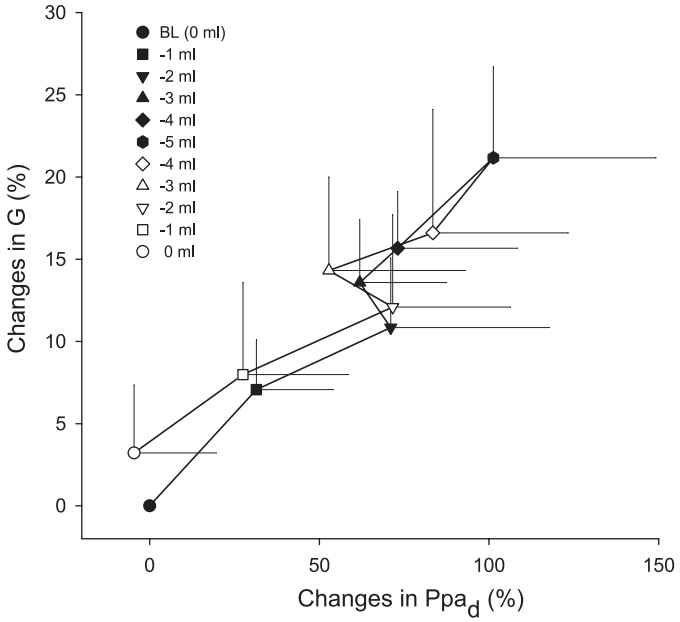

Fig. 3. The relationship between the changes vs. BL value, in Ppa_d and those in the G parameter following stepwise blood withdrawals (solid symbols) and reinfusions (open symbols). Values are means ± SE; $n = 6$.

heterogeneities, best reflected by the changes in G. Statistically significant correlations were observed between the changes in G, Ppa_d ($R = 0.35$, $P = 0.008$), and TPVR ($R = 0.48$, $P < 0.001$).

DISCUSSION

In the present study, airway and respiratory tissue mechanical measurements were combined with those of the TGV and systemic and pulmonary hemodynamics to characterize the changes in lung function and circulation following an acute hypovolemia induced by systemic hemorrhage and their reversibility after restoration of the physiological blood volume. Acute stepwise blood volume loss led to a proportional dilation of the airways, which was associated with an increase in TGV and stepwise increases in the respiratory tissue viscous pressure losses. Stepwise blood reinfusion produced opposite changes in respiratory mechanical and hemodynamic parameters than those observed with blood loss. On full blood volume restoration, Raw returned to significantly higher values than baseline.

In agreement with previous studies applying similar blood withdrawals (6, 20, 24, 35), the adopted experimental model in the present study led to hypovolemic shock, with hallmark features of marked decreases in systemic blood pressure and subsequent elevations in the levels of plasma adrenalin and noradrenalin (12, 36). This model is, therefore, appropriate to investigate the effects of acute hemorrhage on lung function and pulmonary hemodynamics. As far as we are aware, this is the first study in which separate measures for the changes in the airway and tissue mechanics were applied to describe the pulmonary mechanical consequences of acute hemorrhage. The importance of such investigation stems from the great deal of controversy that appears in the literature concerning the effects of acute hypovolemic shock on the lung mechanics. To shed light on the underlying pathophysiological mechanism in an attempt to resolve this controversy, the detailed respiratory mechanical changes were completed with measurements of absolute lung volumes in the same time frame and were also related to concomitant alterations in the systemic and pulmonary hemodynamics.

In this study, TPVR was estimated using the $Ppa_m/\dot{Q}ao$ relationship, which neglects the left atrial pressure (Pla). Pulmonary arterial wedge pressure could have been used to estimate Pla; however, reliable measurements of Pulmonary arterial wedge pressure were technically difficult to obtain in our rat model during hemorrhage. Similarly, since the pulmonary arterial catheter was inserted through the jugular vein, the right atrial pressure could not be measured at the same time as the Ppa. Consequently, SVR and TPVR were estimated without taking central venous pressure and Pla, respectively, into account. These approximations may have caused slight misestimations of PVR and SVR. However, considering that acute hemorrhage decreases both central venous pressure and Pla in proportion to blood volume loss (23), we do not expect that our estimations have affected the trends observed in the reported TPVR and SVR values in relation to blood loss, which are in line with previous data in the literature (1).

One of the main findings in the present study is the stepwise development of bronchodilation following acute hemorrhage (Fig. 1). Since earlier studies used global resistive parameters (such as Rrs) incorporating resistive components from the airflow and the from the respiratory tissue viscoelasticity, the detection of the increased airway caliber may have been masked by the concomitant increase in the tissue-resistive component after hypovolemia. Various mechanisms may contribute to the development of bronchodilation following acute hemorrhage, including passive processes involving airway-parenchymal tethering forces due to the increase in TGV or active decrease in the airway smooth muscle tone subsequent to either a release of bronchoactive relaxing mediators (12, 20) or modulation of the autonomous nervous system (22).

The TGV values measured in the present study are in agreement with previous measurements reported in the literature (7). The rise of TGV with blood withdrawal was a consistent feature in all of the studied animals. At the end of the measurement protocol, a repeat 5-ml withdrawal in all animals again produced an increase in TGV from 3.9 ± 0.4 to 4.2 ± 0.8 ml ($P = 0.008$), demonstrating the reproducibility of this phenomenon. Different mechanisms may explain the observed increases in TGV with blood loss. The thoracic blood volume can considerably decrease as a result of acute hemorrhage (30). This decrease can contribute to the increase in TGV by the replacement of blood by gas in the thoracic cavity. This mechanism is further suggested by the significant correlation between TGV and the volume of withdrawn blood. Nagy et al. (24) found that, in dog, the increase in TGV and the bled volume correlated up to a certain point beyond which TGV remained elevated, even after reinfusion. The increase in respiratory drive and inspiratory muscle tone as a result of tissue hypoxia and metabolic acidosis is another potential mechanism involved in the increase in TGV. The increase in TGV can contribute to the drop in Raw by increasing parenchymal tethering forces, thereby increasing intrapulmonary airway diameters. It should be kept in mind, however, that such tethering forces may have been affected by mechanical ventilation vs. spontaneous breathing during the respective forced

oscillatory measurements of respiratory mechanical parameters and that of TGV.

In contrast to the decrease in Raw, acute hypovolemia induced increases in the parameters related to the respiratory tissue mechanics: G and η. Regarding the mechanisms responsible for such a pattern of change, the increases in G and η in the absence of significant changes in H have been shown to be the hallmark feature for development of ventilation heterogeneities in the lung periphery (19). Changes in the pulmonary hemodynamics have a major impact on the lung mechanical parameters related to the lung periphery. In this study, we found a significant correlation between the increases in G and in those in Ppa_d (Fig. 3) and TPVR. A similar increase in TPVR in response to acute blood loss has previously been observed in both dog and primate (1). These correlations suggest that the loss of blood in the pulmonary capillaries resulting in pulmonary vascular de-recruitment manifested in stepwise increases in TPVR were associated with the development of peripheral ventilation inhomogeneities. This vascular de-recruitment can result in the loss of tethering forces exerted by the filled pulmonary capillary network on the alveolar walls (2, 26), which can promote both a decrease in sH and mechanical heterogeneity in the lung periphery. This primary role of the mechanical interdependence between the pulmonary vasculature and lung mechanics is further confirmed by the complete recoveries in G and η with blood restoration.

Since our results demonstrate significant decreases, even in the lung-volume-corrected sRaw, active processes are likely to be involved in the reduction in Raw, in addition to the increases in TGV (24). Similar to previous findings (12, 36), in the present study, we observed marked increases in plasma adrenalin and noradrenalin levels following acute hemorrhage. Considering the potent bronchodilator role of endogenous catecholamines (3, 20), the involvement of active airway smooth muscle relaxation following hypovolemic shock is further substantiated. Moreover, the elevations in endogenous catecholamine levels can contribute to the increase in TPVR, since the pulmonary vasoconstrictive effect of these agents have been demonstrated both in rat (31) and in other species (4).

The direct role of sympathetic autonomic activation in the decrease in Raw is more questionable however. This is due to the fact that HR consistently decreased in proportion to blood withdrawal and gradually returned to baseline values with volume restoration, which is in agreement with previous studies in the literature (34, 38). The bradycardia observed in the decompensated stage of hemorrhagic shock has been attributed to a reduction in sympathetic tone in most organs except the adrenal medulla (25), which may explain why endogenous catecholamines were elevated, despite apparent cardiac sympathoinhibition. In humans, parasympathetic activation has been shown to be involved in the bradycardia associated with lower body negative pressure-induced hypovolemia (32). Previous studies in the literature suggest that reflex vagal activation is involved in the bradycardia associated with hypovolemia in the rat model of hemorrhagic shock (18, 21). Parasympathetic activation is a possible mechanism for the overshoot observed in Raw on blood volume restoration. It is unlikely that the latter observation was related to inflammatory changes, since G, H, and η were not significantly different after blood volume restoration. Further study is needed to elucidate the precise mechanisms involved in the increase in Raw with full blood volume restoration.

In conclusion, separation of airway and respiratory tissue mechanical changes following acute hemorrhage revealed opposite changes in these compartments during hemorrhagic shock. Our data show that the mechanism responsible for the bronchodilation developed after blood withdrawal is complex and likely involves both an increase in the TGV and elevated plasma levels of endogenous catecholamines. Stepwise reinfusion of the bled volume produced opposite changes in respiratory mechanical and hemodynamic parameters than those observed with blood loss and proportionally increased Raw, which reached significantly higher values compared with baseline on full blood volume restoration. Although the bronchodilation observed after blood withdrawal can be viewed as beneficial by reducing the work of breathing, this effect is counteracted by at least two concurrent negative effects on the respiratory system mechanics. One is that the increase in TGV can increase dead space and reduce the inspiratory reserve capacity, thereby reducing the maximum effort developed by the inspiratory muscles (8, 24). The second is that de-recruitment of the pulmonary vasculature leads to increased peripheral ventilation heterogeneities via mechanical interdependence between the pulmonary microvascular network and the lung periphery. These phenomena are detrimental to the maintenance of an adequate level of alveolar ventilation in hemorrhagic shock. Further study is underway to confirm the role of endogenous catecholamines and to characterize the role of the autonomic nervous system in the observed changes in respiratory mechanics during hemorrhagic shock and volume resuscitation.

GRANTS

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

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