



## Serial blood gas analysis during fluid resuscitation of hypovolemic dogs

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### ABSTRACT

It has been documented that hemodynamic disturbances occur in hypovolemic patients. Therefore, the early management of hypovolemia is essential to achieve optimal outcomes. Blood gas, which changes rapidly during hemodynamic instability, can be used as a diagnostic approach for monitoring emergency patients. The objective of the current study was to evaluate the results of resuscitation with hydroxyethyl starch (HES) or lactated Ringer's solution (LR) on venous and arterial blood gas. In addition, the difference between venous and arterial blood gas parameters is investigated to assess the possibility of using venous blood gas analysis as a successor for arterial blood gas analysis in the resuscitation of hypovolemic dogs. Venous and arterial pH, PO<sub>2</sub>, PCO<sub>2</sub>, HCO<sub>3</sub><sup>-</sup>, and base excess were analyzed at the end of each study stage as follow: 1) Establishment of anesthesia, 2) Blood collection to an arterial mean pressure of 40-50 mm Hg, 3) Maintaining dogs in a hypovolemic state, 4) Resuscitation with LR (group A) or HES (group B) in four steps, and 5) One hour after the final resuscitation step. Hypovolemia decreased the studied parameters, except venous PCO<sub>2</sub>, which showed a significant increase ( $p < 0.05$ ). Fluid resuscitation returned the studied parameters to the control values as venous PCO<sub>2</sub> in group A and HCO<sub>3</sub><sup>-</sup> in group B showed a significant change in comparison with the control values ( $p < 0.05$ ). We found that venous pH, HCO<sub>3</sub><sup>-</sup>, and PCO<sub>2</sub> can be used as less invasive and safer alternatives to similar arterial parameters to monitor the fluid resuscitation of hypovolemic dogs.

### Keywords

Arterial blood gas, Venous blood gas, Hydroxyethyl starch, Ringer's Lactate

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### Abbreviations

LR: Lactated ringer

HES: Hydroxyethyl starch

PO<sub>2</sub>: Partial pressures of oxygen

PCO<sub>2</sub>: Partial pressures of carbon dioxide

HCO<sub>3</sub><sup>-</sup>: Bicarbonate

BE: Base excess

## Introduction

About half of traumatic deaths are associated with hemorrhage. As a result, they are essential to be diagnosed early and well-resuscitated to prevent the noxious effects of hypovolemic shocks, such as cellular hypoperfusion, anaerobic metabolism, and metabolic acidosis [1]. Fluid resuscitation is the cornerstone of hypovolemic shock treatment because adequate fluid therapy is necessary to maintain cellular perfusion. However, there is no consensus on the best type of fluid resuscitation in terms of safety and effectiveness [2].

Monitoring hypovolemia is a daily challenge in the emergency department. Following acute and severe hemorrhage, robust compensatory physiological responses are activated, which have traditionally been used to diagnose hypovolemic shock and to guide fluid resuscitation. However, studies have demonstrated that monitoring these physiologic criteria, including heart rate, blood pressure, and respiratory rate may not be proportional to the hypovolemic states, and when the above-mentioned criteria are close to the reference range, occult hypoxemia is probable at the cellular level [1].

It is well-known in human medicine that blood gas changes rapidly during hypovolemic shock. Furthermore, the information provided by venous and arterial blood gas analysis can reflect the patient's true oxygenation and metabolic status at the cellular level. Sánchez-Díaz and colleagues have shown that blood gas parameters can be used as a tool to monitor shock severity and fluid resuscitation adequacy [3]. However, the effects of different types of fluids (e.g., crystalloid and colloidal solutions) on the blood gas parameters of veterinary patients are not well understood.

Although in the previous studies blood gas and acid-base status of healthy dogs were assessed [4, 5], according to our knowledge, changes in blood gas during resuscitation of hypovolemic dogs have not been investigated. Consequently, the primary objective of this study was to evaluate the effects of resuscitation with LR solution and HES on venous and arterial blood gas in dogs with experimental hypovolemic shock. The secondary objective of this study was to evaluate the difference between venous and arterial blood gas parameters and the possibility of using venous blood gas analysis as a less invasive and safer surrogate method for arterial blood gas analysis in the resuscitation of hypovolemic dogs.

## Result

The mean  $\pm$  SD of the collected blood volume was  $57.11 \pm 5.17$  and  $52.86 \pm 8.22$  ml/kg in the animals of groups A and B, respectively, which represent al-

most 61% of the blood volume (90 ml/kg) on average. There was no significant difference between the groups in this regard ( $p > 0.05$ ). In either group, the dogs were successfully resuscitated with fluid therapy without death. Animals in groups A and B in each of the resuscitation steps, received  $385.08 \pm 97.85$  ml LR and  $89.5 \pm 23.17$  ml HES, respectively. Moreover, mean arterial pressure did not have a significant difference in any of the study stages between the two groups ( $p > 0.05$ ).

In the hypovolemic stage, only venous  $PCO_2$  increased significantly ( $p < 0.05$ ), while other studied parameters decreased compared to the control stage. However, the decline in venous BE in both groups and venous bicarbonate in group A was not significant ( $p > 0.05$ , Tables 1 and 2). During the resuscitation stage, venous and arterial blood gas parameters in both groups almost returned to the control stage, so that in the eighth step of the study, no significant change was found among the control and post-resuscitation stages, except for venous  $PCO_2$  in group A and  $HCO_3^-$  in group B. The statistical analysis of the data did not show a significant difference between the two types of solutions used ( $p > 0.05$ ).

Statistical analysis revealed that in some stages of the research, there was a significant difference between the venous and arterial blood gas parameters (Figure 1). However, in all stages of the study, the venous and arterial partial pressures of oxygen were significantly different ( $p < 0.05$ ), while the venous and arterial bicarbonate concentration and pH did not have a significant difference ( $p > 0.05$ ).

## Discussion

In this study, changes in venous and arterial blood gas parameters during endpoint resuscitation by LR solution and HES, as the most frequently used crystalloid and colloidal solutions, were analyzed in dogs with experimental hypovolemic shock.

Trauma-induced massive hemorrhage results in hypovolemia, hypotension, and reduced cardiac output. During a hypovolemic shock state, poor cellular oxygenation due to insufficient red cell mass and hemoglobin concentration causes anaerobic metabolism and subsequent metabolic acidosis [6, 7]. In the present study, pH,  $PO_2$ , and  $HCO_3^-$  declined during the hypovolemic stage, which confirms metabolic acidosis and hypoxia, and can be attributed to decreased oxygen delivery, increased lactate, and excess hydrogen ions. The BE represents the combined effects of  $HCO_3^-$  and hydrogen ion concentrations. Depletion of BE in the background of metabolic acidosis may indicate hypovolemia-induced pre-hepatic dysfunction in restoring the pH levels. In this situation, lactate removal is reduced as a result of sympathoadrenal

**Table 1.** Mean  $\pm$  SD of venous blood gas parameters during different steps of the study

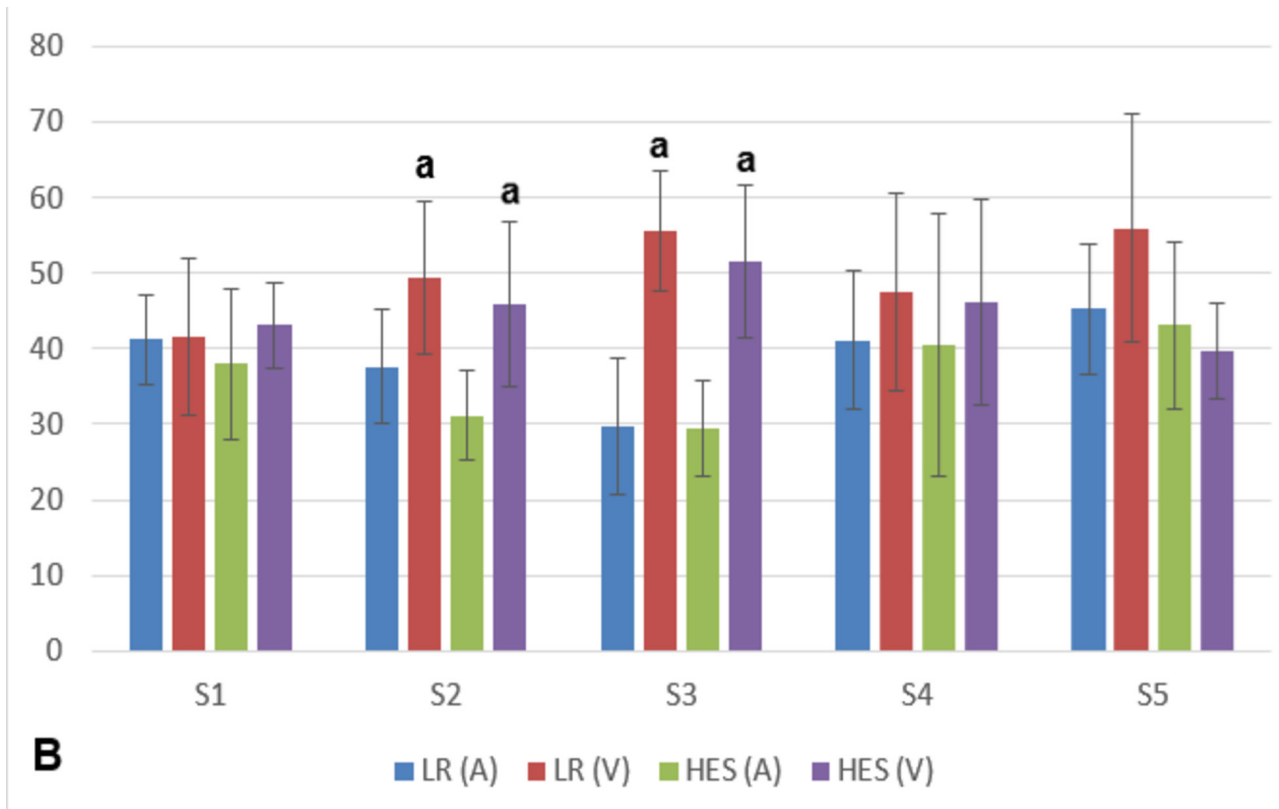
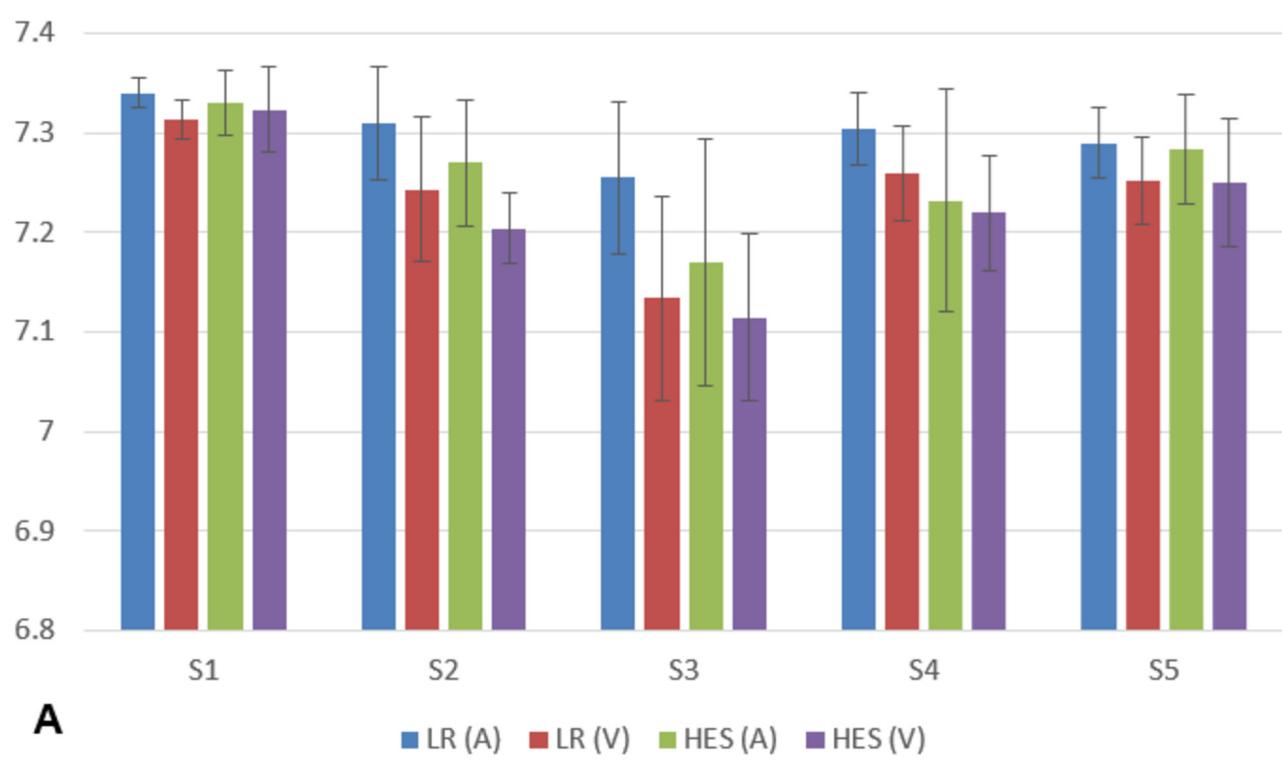
Factor	pH		PO <sub>2</sub> (mm Hg)		PCO <sub>2</sub> (mm Hg)		HCO <sub>3</sub> <sup>-</sup> (mmol/L)		BE (mmol/L)	
	LR	HES	LR	HES	LR	HES	LR	HES	LR	HES
A1	7.31 $\pm$ 0.01 <sup>a</sup>	7.32 $\pm$ 0.04 <sup>a</sup>	93.80 $\pm$ 37.47 <sup>a</sup>	108.20 $\pm$ 36.12 <sup>a</sup>	41.60 $\pm$ 10.31 <sup>c</sup>	43.10 $\pm$ 5.75 <sup>bc</sup>	20.72 $\pm$ 5.58 <sup>ab</sup>	21.90 $\pm$ 3.16 <sup>a</sup>	-5.52 $\pm$ 5.72 <sup>bc</sup>	-6.46 $\pm$ 3.21 <sup>b</sup>
A2	7.24 $\pm$ 0.07 <sup>b</sup>	7.20 $\pm$ 0.03 <sup>b</sup>	28.20 $\pm$ 12.47 <sup>c</sup>	31.60 $\pm$ 12.91 <sup>c</sup>	49.40 $\pm$ 0.11 <sup>b</sup>	45.98 $\pm$ 10.88 <sup>bc</sup>	21.10 $\pm$ 3.76 <sup>a</sup>	16.80 $\pm$ 1.93 <sup>b</sup>	-6.22 $\pm$ 4.17 <sup>bc</sup>	-11.58 $\pm$ 2.21 <sup>bc</sup>
A3	7.13 $\pm$ 0.10 <sup>c</sup>	7.11 $\pm$ 0.08 <sup>c</sup>	32.61 $\pm$ 11.02 <sup>b</sup>	36.92 $\pm$ 13.68 <sup>b</sup>	55.63 $\pm$ 8.05 <sup>a</sup>	51.52 $\pm$ 10.02 <sup>a</sup>	20.14 $\pm$ 3.96 <sup>b</sup>	16.03 $\pm$ 1.67 <sup>c</sup>	-8.07 $\pm$ 3.62 <sup>c</sup>	-11.85 $\pm$ 2.13 <sup>bc</sup>
A4	7.22 $\pm$ 0.08 <sup>b</sup>	7.19 $\pm$ 0.06 <sup>b</sup>	57.80 $\pm$ 16.87 <sup>b</sup>	63.80 $\pm$ 19.61 <sup>b</sup>	50.50 $\pm$ 14.97 <sup>ab</sup>	48.22 $\pm$ 16.27 <sup>ab</sup>	20.26 $\pm$ 5.35 <sup>b</sup>	17.04 $\pm$ 1.21 <sup>b</sup>	-7.44 $\pm$ 5.97 <sup>bc</sup>	-11.00 $\pm$ 1.05 <sup>bc</sup>
A5	7.27 $\pm$ 0.04 <sup>ab</sup>	7.27 $\pm$ 0.05 <sup>a</sup>	132.20 $\pm$ 54.28 <sup>a</sup>	104.34 $\pm$ 50.66 <sup>a</sup>	47.43 $\pm$ 13.03 <sup>bc</sup>	46.05 $\pm$ 14.17 <sup>abc</sup>	21.44 $\pm$ 4.22 <sup>a</sup>	19.28 $\pm$ 1.41 <sup>a</sup>	-4.68 $\pm$ 4.45 <sup>ab</sup>	-0.86 $\pm$ 8.07 <sup>a</sup>
A6	7.28 $\pm$ 0.05 <sup>a</sup>	7.22 $\pm$ 0.07 <sup>b</sup>	213.80 $\pm$ 102.79 <sup>a</sup>	184.60 $\pm$ 142.10 <sup>a</sup>	46.74 $\pm$ 14.01 <sup>bc</sup>	46.48 $\pm$ 14.31 <sup>abc</sup>	21.52 $\pm$ 5.79 <sup>a</sup>	19.75 $\pm$ 3.88 <sup>a</sup>	-5.18 $\pm$ 5.84 <sup>abc</sup>	-7.26 $\pm$ 3.17 <sup>b</sup>
A7	7.31 $\pm$ 0.02 <sup>a</sup>	7.18 $\pm$ 0.06 <sup>bc</sup>	231.40 $\pm$ 145.46 <sup>a</sup>	189.20 $\pm$ 99.39 <sup>a</sup>	45.00 $\pm$ 11.50 <sup>bc</sup>	43.84 $\pm$ 11.22 <sup>bc</sup>	22.32 $\pm$ 4.13 <sup>a</sup>	16.60 $\pm$ 3.24 <sup>bc</sup>	-3.72 $\pm$ 3.71 <sup>a</sup>	-12.16 $\pm$ 2.55 <sup>c</sup>
A8	7.25 $\pm$ 0.04 <sup>ab</sup>	7.25 $\pm$ 0.06 <sup>a</sup>	155.40 $\pm$ 102.54 <sup>a</sup>	124.40 $\pm$ 105.91 <sup>a</sup>	55.98 $\pm$ 15.11 <sup>a</sup>	39.65 $\pm$ 6.31 <sup>c</sup>	23.90 $\pm$ 5.60 <sup>a</sup>	17.80 $\pm$ 3.24 <sup>b</sup>	-3.30 $\pm$ 5.42 <sup>a</sup>	-9.66 $\pm$ 2.30 <sup>bc</sup>

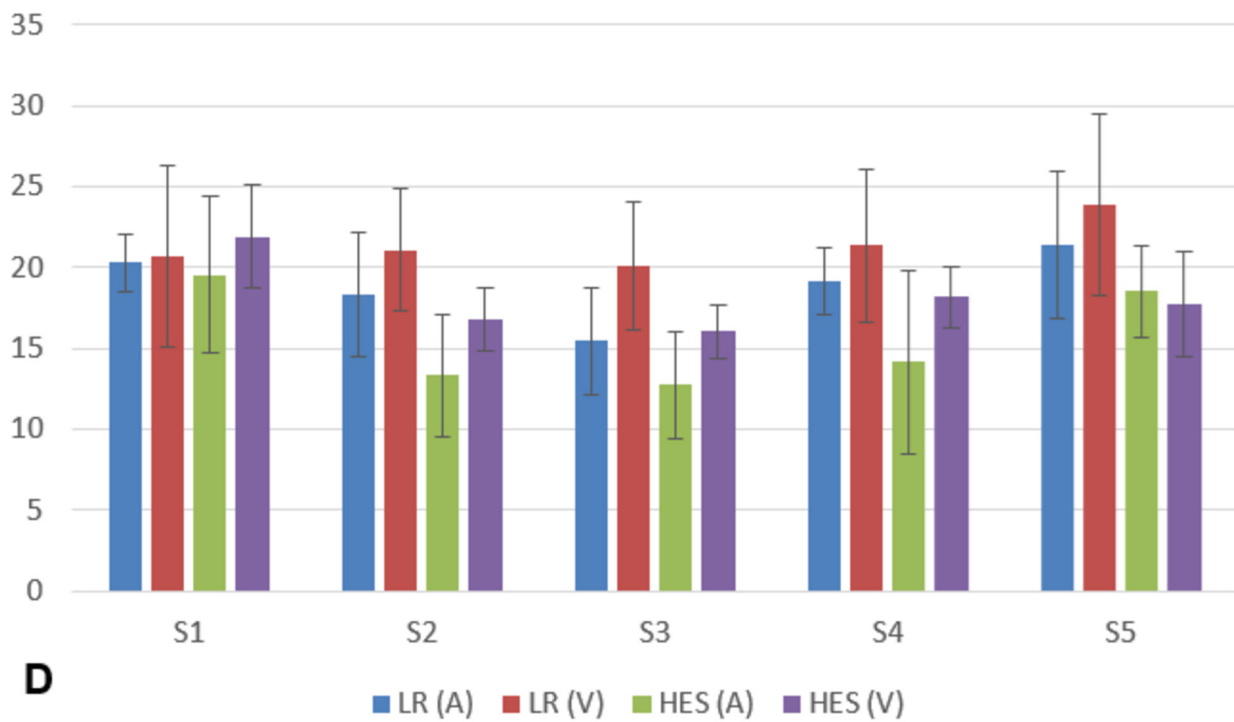
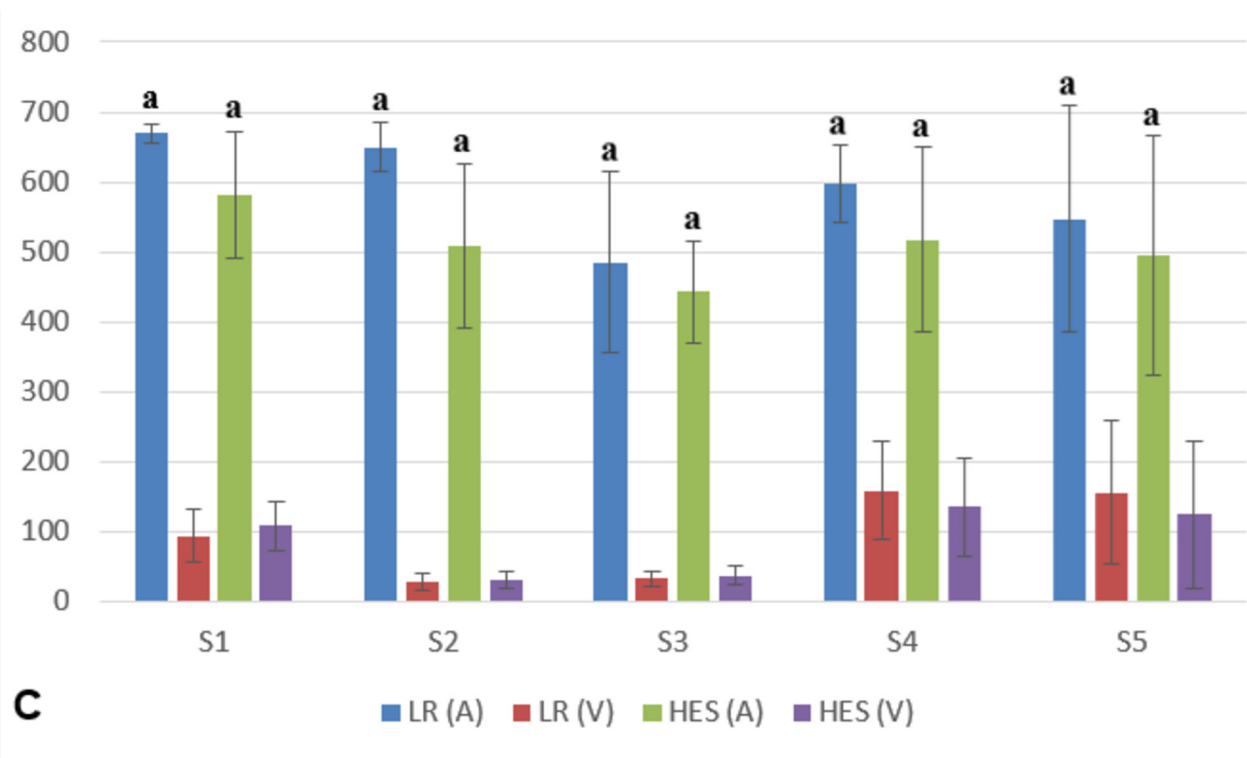
The different letters in each column represent significant differences ( $p < 0.05$ )

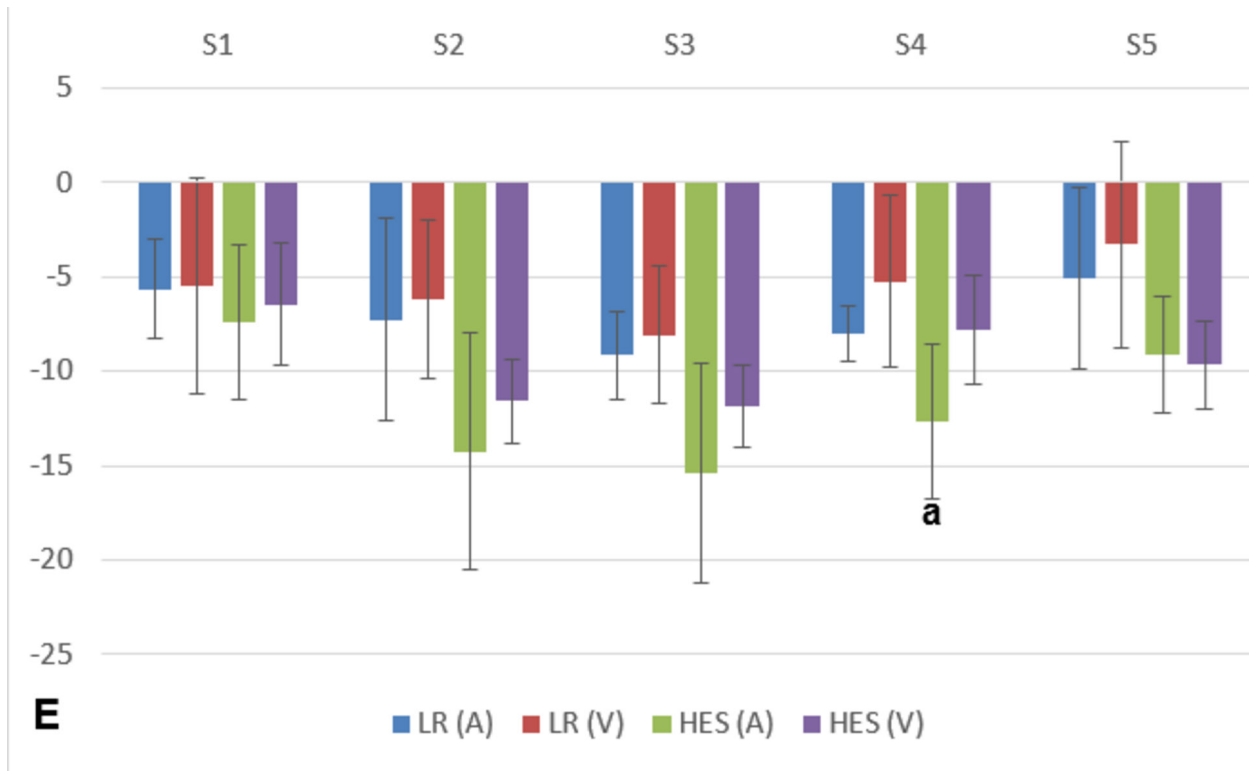
**Table 2.** Mean  $\pm$  SD of arterial blood gas parameters during different steps of the study

Factor	pH		PO <sub>2</sub> (mm Hg)		PCO <sub>2</sub> (mm Hg)		HCO <sub>3</sub> <sup>-</sup> (mmol/L)		BE (mmol/L)	
	LR	HES	LR	HES	LR	HES	LR	HES	LR	HES
A1	7.34 $\pm$ 0.01 <sup>a</sup>	7.33 $\pm$ 0.03 <sup>a</sup>	669.00 $\pm$ 13.76 <sup>a</sup>	581.40 $\pm$ 90.77 <sup>a</sup>	41.24 $\pm$ 5.89 <sup>a</sup>	37.94 $\pm$ 9.90 <sup>a</sup>	20.28 $\pm$ 1.81 <sup>a</sup>	19.56 $\pm$ 4.86 <sup>a</sup>	-5.65 $\pm$ 2.60 <sup>a</sup>	-7.40 $\pm$ 4.07 <sup>a</sup>
A2	7.31 $\pm$ 0.05 <sup>a</sup>	7.27 $\pm$ 0.06 <sup>ab</sup>	650.00 $\pm$ 34.87 <sup>ab</sup>	509.20 $\pm$ 117.25 <sup>a</sup>	37.64 $\pm$ 7.63 <sup>a</sup>	31.16 $\pm$ 6.03 <sup>b</sup>	18.32 $\pm$ 3.84 <sup>ab</sup>	13.34 $\pm$ 3.77 <sup>ab</sup>	-7.26 $\pm$ 5.34 <sup>ab</sup>	-14.28 $\pm$ 6.27 <sup>b</sup>
A3	7.25 $\pm$ 0.07 <sup>b</sup>	7.17 $\pm$ 0.12 <sup>b</sup>	485.20 $\pm$ 128.77 <sup>c</sup>	442.80 $\pm$ 73.81 <sup>c</sup>	29.63 $\pm$ 9.02 <sup>b</sup>	29.52 $\pm$ 6.34 <sup>c</sup>	15.45 $\pm$ 3.30 <sup>c</sup>	12.73 $\pm$ 3.31 <sup>bc</sup>	-9.17 $\pm$ 2.32 <sup>c</sup>	-15.41 $\pm$ 5.84 <sup>b</sup>
A4	7.33 $\pm$ 0.04 <sup>a</sup>	7.21 $\pm$ 0.1 <sup>b</sup>	606.80 $\pm$ 138.29 <sup>ab</sup>	417.20 $\pm$ 161.93 <sup>c</sup>	36.74 $\pm$ 9.87 <sup>a</sup>	39.26 $\pm$ 11.34 <sup>a</sup>	20.14 $\pm$ 2.16 <sup>a</sup>	10.52 $\pm$ 6.27 <sup>c</sup>	-6.64 $\pm$ 4.03 <sup>a</sup>	-15.68 $\pm$ 5.37 <sup>b</sup>
A5	7.29 $\pm$ 0.0 <sup>ab</sup>	7.21 $\pm$ 0.1 <sup>b</sup>	612.60 $\pm$ 80.88 <sup>ab</sup>	463.20 $\pm$ 190.61 <sup>bc</sup>	40.40 $\pm$ 6.74 <sup>a</sup>	36.30 $\pm$ 21.33 <sup>ab</sup>	17.90 $\pm$ 4.70 <sup>bc</sup>	12.86 $\pm$ 8.94 <sup>ab</sup>	-8.10 $\pm$ 2.78 <sup>bc</sup>	-13.98 $\pm$ 7.66 <sup>b</sup>
A6	7.27 $\pm$ 0.0 <sup>ab</sup>	7.23 $\pm$ 0.12 <sup>ab</sup>	509.80 $\pm$ 159.42 <sup>bc</sup>	583.00 $\pm$ 172.64 <sup>a</sup>	42.28 $\pm$ 17.03 <sup>a</sup>	43.71 $\pm$ 21.87 <sup>a</sup>	16.98 $\pm$ 7.03 <sup>bc</sup>	15.88 $\pm$ 4.76 <sup>ab</sup>	-11.78 $\pm$ 10.39 <sup>c</sup>	-11.46 $\pm$ 4.28 <sup>ab</sup>
A7	7.32 $\pm$ 0.05 <sup>a</sup>	7.26 $\pm$ 0.10 <sup>ab</sup>	661.40 $\pm$ 23.33 <sup>ab</sup>	617.20 $\pm$ 137.76 <sup>a</sup>	45.18 $\pm$ 11.92 <sup>a</sup>	43.94 $\pm$ 19.28 <sup>a</sup>	21.48 $\pm$ 2.70 <sup>a</sup>	17.90 $\pm$ 5.18 <sup>a</sup>	-5.54 $\pm$ 1.98 <sup>a</sup>	-9.38 $\pm$ 5.12 <sup>a</sup>
A8	7.29 $\pm$ 0.0 <sup>ab</sup>	7.28 $\pm$ 0.05 <sup>a</sup>	547.20 $\pm$ 162.66 <sup>ab</sup>	495.20 $\pm$ 170.97 <sup>ab</sup>	45.26 $\pm$ 8.60 <sup>a</sup>	43.12 $\pm$ 11.04 <sup>a</sup>	21.44 $\pm$ 4.53 <sup>a</sup>	18.54 $\pm$ 2.84 <sup>a</sup>	-5.08 $\pm$ 4.81 <sup>a</sup>	-9.14 $\pm$ 3.09 <sup>a</sup>

The different letters in each column represent significant differences ( $p < 0.05$ )







**Figure 1.** Mean  $\pm$  SD of venous (V) and arterial (A) blood gas parameters in the studied stages. A) pH, B) PCO<sub>2</sub>, C) PO<sub>2</sub>, D) HCO<sub>3</sub><sup>-</sup>, E) BE. S1: Control stage, S2: Hemorrhagic stage, S3: Hypovolemic stage, S4: Resuscitation stage, S5: Post-resuscitation stage. <sup>a</sup>*p* < 0.05

vasoconstriction and decreased blood flow to the liver as the primary consumer of lactate. It is worth noting that excess hydrogen ions can reduce the sensitivity of cardiomyocytes to calcium and consequently reduce cardiac contractility. Poor cardiac contractility leads to decreased cardiac output and worsening cellular oxygenation [6, 8-10]. Following diminished cardiac output, venous CO<sub>2</sub> delivery and elimination in the pulmonary alveoli are reduced and venous hypercarbia is exacerbated [7]. This probably explains the rise in venous PCO<sub>2</sub> in the hypovolemic dogs investigated in the present research. These findings are confirmed by other studies as similar changes in the blood gas parameters of different species with hemorrhagic shock (e.g., cats, rabbits, and pigs) [7, 9, 11].

Given that metabolic acidosis in hypovolemic patients is usually due to tissue hypoperfusion, the best approach to correcting acidosis is fluid resuscitation [8]. We used the endpoint resuscitation method to serially evaluate the blood gas parameters during the fluid therapy of hypovolemic dogs. Crystalloid and colloid solutions can affect the acid-base status differently. Compared to LR, HES has more chloride (109 vs. 154 mmol/l) and a lower pH (6.5 vs. 5.4) [2]. This difference caused a decline in pH during the resusci-

tation stage in group B compared to A. However, this difference was not statistically significant.

Although most of the blood gas parameters in both groups returned to baseline values by the end of the fluid resuscitation steps, venous PCO<sub>2</sub> and HCO<sub>3</sub><sup>-</sup> showed a significant difference between the last and first stages of the study in the LR and HES resuscitated groups, respectively. The main reason for this significant difference might be discrepancies in the mechanism of action and durability of the solutions used. About 80% of an isotonic crystalloid solution, such as LR, is transferred to the interstitial space within 1 h after infusion [12]. Accordingly, continued fluid therapy or a change in the resuscitation protocol in group A could be necessary because despite fluid therapy with about a quarter of the full shock dose (80-90 ml/kg) in four 15-minute intervals, venous PCO<sub>2</sub>, as a reliable indicator of tissue perfusion [7], was slightly beyond the baseline value in the post-resuscitation stage.

A significant decrease in HCO<sub>3</sub><sup>-</sup> concentration in the post-resuscitation stage compared to the control stage in group B could be related to the lower pH of HES and renal dysfunction in producing bicarbonate [9]. As a result, in human medicine, serious concerns

about the occurrence of acute kidney injury because of HES administration, especially in critically ill patients, have increased. Bae et al. reported that following the administration of HES to a Golden retriever, acute kidney injury remarkably developed, which is probably due to the nephrotoxicity of HES [13].

Serial arterial blood gas analyses, known as the gold standard method to evaluate the acid-base status and blood oxygenation in critically ill patients is a helpful method in monitoring resuscitation efforts [7]. However, arterial puncture can have serious complications, including arterial injury, hemorrhage, hematoma formation, thrombosis, pseudoaneurysm, and limb ischemia [14]. Venous blood gas analysis is usually less painful and easier. In addition, most critically ill patients require venipuncture as a part of clinical evaluations. Hence, many researchers have recently focused on evaluating the accuracy and reliability of venous blood gas as an alternative to arterial blood gas.

In human medicine, Kelly showed in a review article that in patients who are not in a shock state, venous and arterial pH, BE, and bicarbonate had a good agreement to be an alternative for arterial parameters. However, venous and arterial PCO<sub>2</sub> agreement was poor and unpredictable to be useful in emergency medical care [15]. Rudkin et al. demonstrated that in hypovolemic patients, due to peripheral vasoconstriction and blood shunting to vital organs, peripheral venous pH, HCO<sub>3</sub><sup>-</sup>, and PCO<sub>2</sub> do not agree sufficiently to surrogate their arterial equivalents [16].

In veterinary medicine, Tamura and colleagues documented good agreement between BE in arterial and venous samples. However, there were considerable differences in the pH, PCO<sub>2</sub>, PO<sub>2</sub>, and HCO<sub>3</sub><sup>-</sup> between central venous and arterial blood gas in conscious dogs. These authors suggested that the analysis of both venous and arterial blood gas is indispensable for hemodynamic evaluation in dogs [5]. Another study on rabbits with hemorrhagic shock showed a significant difference for arteriovenous PCO<sub>2</sub>, while the statistical difference for pH was not significant [7].

Blood gas is principally analyzed to assess acid-base status (typically pH and bicarbonate) and respiratory function (typically PCO<sub>2</sub> and to some extent pH) in the emergency department [15]. Our results demonstrated no difference between arterial and venous pH, HCO<sub>3</sub><sup>-</sup>, and PCO<sub>2</sub> during fluid resuscitation of hypovolemic dogs. Therefore, these parameters can be used interchangeably. The partial pressure of oxygen is an indicator of efficient oxygenation of the lungs and BE is considered the best marker of changes in blood volume. A decrease in BE indicates an increased oxygen debt [4, 6]. According to the results of this study, due to statistical differences, venous PO<sub>2</sub>

and BE are not valid alternatives to similar arterial parameters in the fluid resuscitation of hypovolemic dogs.

The differences in our results with prior studies and the published reference ranges may be due to discrepancies in the methodology of experience. Blood gas parameters can change in a few seconds with wide ranges. Therefore, there may be some degrees of discrepancy between the parameters obtained from the two standard blood gas analyzers [11]. The composition of the blood gas largely depends on the site of blood collection, so that in a hypovolemic state, the occurrence of compensatory peripheral vasoconstriction uncouples the central and peripheral vascular compartments [16]. Several venous samples (e.g., central vein, jugular vein, and mixed venous blood) can reliably present the acid-base status. Previous human medicine studies have shown central venous blood gas authenticity as a successor to arterial blood gas. In the current study, jugular blood samples were used to evaluate venous blood gas because it was found that the values of jugular vein samples are similar to the central vein [5]. Furthermore, to minimize the errors during the analysis of blood samples, we used the evacuated syringe technique and expelled the air in the syringes immediately. The analysis was completed in 5 min after blood collection.

Our study had two main limitations that need to be highlighted. First, this research was not conducted on conscious dogs. Therefore, the possible compensatory response of the respiratory system in a hypovolemic state was not investigated. However, performing this experiment without the induction of anesthesia was certainly stressful for the animals. Second, the post-resuscitation monitoring period was short. It has been documented that acidosis can reduce myocardial contractility and affect the inflammatory response [17]. Interestingly, higher BE and PCO<sub>2</sub> have been shown to be related to improved survival in patients with hemorrhagic shock [6]. Nonetheless, in this canine model of hypovolemic shock, no casualties were observed following the one-week animal monitoring period.

In conclusion, we analyzed all the commonly used venous and arterial blood gas parameters during resuscitation with LR and HES in hypovolemic dogs. We found that dogs with hypovolemic shock experienced acidosis. Moreover, following fluid resuscitation, most of the parameters, except for venous PCO<sub>2</sub> and HCO<sub>3</sub><sup>-</sup> in the groups resuscitated with LR and HES, respectively, returned to the control stage values. In addition, our results showed that arterial and venous pH, HCO<sub>3</sub><sup>-</sup>, and PCO<sub>2</sub> could be used interchangeably to serially monitor the hypovolemic dogs during fluid resuscitation. Arterial and venous PO<sub>2</sub>

and BE had significant differences in the resuscitation stage. However, a clinically acceptable difference between venous and arterial parameters is not known and should be investigated in the future. Given that blood gas parameters should be interpreted according to the individual patient's clinical status, it is recommended that blood gas analysis, as a reliable method to identify and manage critically ill patients, be performed on the other types of shock in small animals.

## Materials and Methods

### Animals

The present survey was authorized by the Research Ethical Committee of the Shahid Chamran University of Ahvaz with code EE/97.24.3.49872/Scu.ac.ir. Ten male Iranian native dogs with an approximate age of 1.5-3.5 years and body weight of  $18.57 \pm 4.82$  kg were evaluated. The dogs included in the study were healthy based on clinical, electrocardiographic, and echocardiographic parameters, and were excluded in the case of cardiopulmonary disease. The dogs had free access to water, but the food was withheld for 12 h before the experiment. In this study, splenectomy was not performed.

### Instrumentation

Initially, the right cephalic vein (for medication administration and fluid resuscitation) and the left external jugular vein (for collecting venous blood samples) were cannulated with an 18-gauge catheter. Next, the induction of anesthesia was performed with an intravenous dosage of 6 mg/kg propofol (Lipuro 1%, Melsungen, Germany) and 5 µg/kg fentanyl (Caspian, Rasht, Iran). Following the intubation of dogs with an 8-8.5 mm cuffed endotracheal tube and immobilization in right recumbency, the maintenance of anesthesia was performed using 1.8% isoflurane in 100% oxygen. The medial surface of the right hind limb of dogs was dissected and the exposed femoral artery was catheterized with a 14-gauge angiocath connected to a three-way stopcock for bleeding, direct blood pressure measurement, and collecting arterial blood samples [18]. Using a multi-parameter monitor system (PM-9000Vet, Burtons, Kent, UK), vital parameters, such as respiratory rate, blood pressure, and heart rate were assessed during the experiment. Furthermore, body temperature was monitored by a rectal probe and was preserved at 37°C-38°C using a heating mattress.

### Experimental Protocol

In the present study, the eight-step (A1-A8) analysis of venous and arterial blood gas was performed in five divided stages as below [18]:

Control stage (A1): Base-line blood gas analysis was performed after instrumentation and establishment of anesthesia.

Hemorrhagic stage (A2): Blood was collected from each dog up to an arterial mean pressure of 40-50 mm Hg. This step lasted 30 min and the collected blood was stored in blood packets.

Hypovolemic stage (A3): Dogs were maintained in a hypovolemia state for 30 min during which no fluid was administered. In the case of compensatory physiological responses and an increase in mean arterial pressure, more blood was collected to return the mean arterial pressure to the range of 40-50 mm Hg.

Resuscitation stage (A4-A7): Dogs were accidentally divided into two identical groups and fluid resuscitation was performed in four consecutive 15-min steps. The animals in groups A and B were resuscitated with 20 ml/kg of LR (Shahid Ghazi Pharmaceu-

tical, Tabriz, Iran) and 5 ml/kg of HES (Voluven 6%, Homburg, Germany), respectively.

Post-resuscitation stage (A8): The last step of blood gas analysis was accomplished 60 min after the end of fluid therapy. Afterward, the dogs recovered from the anesthesia.

### Blood gas analysis

In each of the mentioned steps, 1 ml of venous and arterial blood samples was taken with pre-heparinized (5000 unit/ml of sodium heparin, Alborz Darou Pharmaceutical, Tehran, Iran) insulin syringes. Next, blood samples were analyzed as soon as possible for pH, PCO<sub>2</sub>, PO<sub>2</sub>, HCO<sub>3</sub><sup>-</sup>, and BE using a portable blood gas analyzer (EDAN, i15 Blood Gas and Chemistry Analyzer, Shenzhen, China).

### Data analysis

The SPSS software version 24 (IBM Corporation, New York, USA) was utilized for statistical analysis. All data are shown as mean ± standard deviation (SD). The Kolmogorov-Smirnov test was applied to evaluate the normal distribution of data. Changes in the studied parameters during the experimental steps were tested by repeated measures analysis of variance. Moreover, in order to evaluate the difference between venous and arterial blood gas parameters, paired sample t-test was used. A p-value of 0.05 or less means that a finding is statistically significant.

### Authors' Contributions

S.Y, S.A., E.Ç., B.E.K. and N.S. conceived and planned the experiments. All authors took part in the operations. S.Y. took part in the writing of the play.

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### Conflict of Interest

The authors declare that there is no conflict of interest.

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