Respiratory Pump Contributions to Hemodynamic Responses in Lower-Body Negative Pressure: Preliminary results

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Abstract

The goal of this work is to investigate the cardiovascular and respiratory responses to progressive hemorrhage simulated using lower body negative pressure (LBNP). Subjects were classified based on their tolerance to LBNP, participants who showed presyncope signs before reaching –60 mmHg were classified as non-finishers (12 participants) while the ones who completed the experiment without any presyncope symptoms were considered finishers (7 participants). Preliminary results showed that the non-finishers group has a lower mean arterial pressure at – 30mmHg, – 40mmHg, and – 50mmHg as compared to the finishers. The inhale time was lower in the non-finishers group at rest, and at – 50mmHg compared to the finishers group, while no difference in exhale time was observed between the two groups. In the non-finishers group, the inhale/exhale ratio was lower at – 30mmHg– 40mmHg and – 50mmHg compared to the finishers group. Our results suggest that the finishers group has the greatest compensation to the hypovolemic challenge, apparent in the increased inspiratory time resulting in a longer duration of intrathoracic pressure, and thus increasing mean arterial blood pressure via the respiratory pump mechanism. The findings of this study can help in distinguishing patients with a limited tolerance for hypovolemia who might necessitate life-saving interventions sooner than those with high tolerance.

1. Introduction

Hemorrhage is a physiological condition in which intravascular volume is reduced as a result of blood loss from circulation, leading to insufficient tissue perfusion[1]. Uncontrolled bleeding is life-threatening and one of the major causes of death in combat casualties, traumatic injuries, and postpartum hemorrhage [2]–[4]. Early assessment of hemorrhage progression is critical in preventing bleeding advancement through timely intervention [5]–[7]. Common vital signs such as arterial blood pressure, heart rate, pulse pressure, and arterial oxygen hemoglobin saturation are often late indicators of blood loss [8], [9]. These markers remain stable during hemorrhage until the onset of cardiovascular decompensation providing limited information on early alteration of blood volume [9]. Seismocardiogram (SCG) derived features such as left ventricular ejection time (LVET) and pre-ejection period (PEP)/LVET can early detect mild and moderate hemorrhage[10], however, SCG morphology is sensitive to sensors placement and varies between subjects making the annotation process of the signal challenging [10], [11]. Therefore, parameters for early, non-invasive and continuous monitoring of central hypovolemia are required to enable timely and effective intervention, particularly in severely injured patients. During hemorrhagic shock, and in the presence of reduced circulatory blood volume or tissue hypoperfusion, complex compensatory physiological mechanisms are recruited to maintain blood pressure and arterial oxygen saturation [12]. Loss of blood volume and associated decline in the arterial blood pressure is sensed by the stretch receptors located in the carotid sinus and the aortic arch resulting in baroreceptor discharge reduction to the nucleus of tractus solitarius center within the brain. A decrease in the firing of the baroreceptors triggers a rapid withdrawal of parasympathetic and activation of sympathetic neural activity leading to an increase in vascular resistance, myocardial contractility, and heart rate, all of which increase arterial blood pressure [7], [9]. During inspiration, intrathoracic pressure decreases as the thoracic cavity volume expands, this allows blood to easily flow into the right heart increasing cardiac filling, and venous return (so-called respiratory pump). The respiratory pump is considered as one of the body's natural responses mechanisms to low blood pressure resulting from reduced central blood volume [13], [14]. Thus, monitoring respiratory parameters could provide an indicator of hemorrhage progression.

Because of ethical concerns about withdrawing significant amounts of blood from healthy human volunteers, human

models for the controlled research of acute bleeding and hemorrhagic shock are restricted [8]. Lower Body Negative Pressure (LBNP) is a non-invasive technique to study hemodynamic effects associated with severe hemorrhage in humans [15]. LBNP exposes subjects to increasing levels of negative pressure applied to the lower body causing blood to be translocated to the lower extremities, resulting in central hypovolemia that induces hemodynamic responses similar to those seen during hemorrhage [15], [16]. In this paper, we studied the cardiovascular and respiratory responses to hemorrhage simulated using LBNP. Two groups were considered, the non-finishers who showed presyncope signs before the pressure in the chamber reached –60 mmHg and finishers who completed the experiment without any presyncope symptoms were considered finishers

2. Methodology

Simultaneous blood pressure (BP), electrocardiogram (ECG), and respiration were recorded from 19 young, healthy participants (age: 28 ± 6 years; height: 170 ± 7 cm; weight: 68 ± 10 kg) who underwent graded LBNP. Blood pressure was recorded using a Portapres device (Finapres Medical Systems, Amsterdam, the Netherlands), ECG signal was acquired in a lead II configuration using LifePak8 (Medtronic Inc., MN, USA) and the respiration signal was acquired using an oronasal cannula which was connected to a pressure transducer (Braebon Medical Corporation, Ontario, Canada). The lower body of each participant was placed in the LBNP chamber and sealed at the level of the iliac crest. The participant laid supine inside the chamber for 5 minutes before the pressure was progressively lowered to – 20 mmHg. From there, the pressure was gradually reduced in 10 mmHg steps to –60 mmHg. Participants who showed presyncope signs before the pressure in the chamber reached –60 mmHg were classified as non-finishers (12 participants) while the ones who completed the experiment without any presyncope symptoms were considered finishers (7 participants). The data acquisition was performed using an NI 9205 analog input module (National Instruments Inc., TX, USA) at a sampling frequency of 1000 Hz. Heart rate (HR) and mean arterial pressure (MAP) were derived from ECG and BP waveforms, respectively. The respiratory signal was annotated manually to avoid any errors that might affect the output of this study. All data were recorded at the Aerospace Physiology Laboratory in the Department of Biomedical Physiology and Kinesiology, Simon Fraser University (SFU), Canada. The study was conducted under ethics approval from Simon Fraser University and all participants signed informed consent forms prior to the experiment. Since not all participants made it to –60mmHg and some of the response variables were not normally distributed, we used a nonparametric approach suggested by [17] to study the differences between the groups over LBNP stages. For multiple comparisons, Kruskal–Wallis test was employed and post hoc analysis was conducted using Dunn's test. All analyses were made using R [18] at the significance level of 0.05.

3. Results

The cardiovascular parameters (HR, MAP), as well as the respiratory responses (inhale and exhale times, inhale/exhale ratio) during rest and at – 50mmHg for the two groups, are summarized in Table 1. The non-finishers group exhibited a lower mean arterial pressure at – 30mmHg ($p = 0.02$), – 40mmHg ($p = 0.01$), and at – 50mmHg ($p = 0.01$) as shown in Table 1 and Figure 1.

Table 1. Comparison of cardiovascular and respiratory parameters between the finishers and non-finishers at rest and – 50mmHg. Table lists mean ± SD. * represent a significant difference between the groups.

Parameter	Finishers	Non-finishers	p-value
Rest			
MAP	93.37 ± 16.51	80.32 ± 12.42	0.12
HR	65.60 ± 10.74	68.73 ± 7.79	0.43
Inhale time	0.97 ± 0.17	0.73 ± 0.16	0.007*
Exhale time	3.04 ± 0.90	2.63 ± 0.35	0.65
Inhale/Exhale	0.35 ± 0.06	0.29 ± 0.06	0.06
–50 mmHg			
MAP	104.69 ± 22.15	75.31 ± 15.83	0.01*
HR	90.24 ± 9.78	98.31 ± 10.84	0.96
Inhale time	0.82 ± 0.09	0.60 ± 0.13	0.01*
Exhale time	2.46 ± 0.44	2.66 ± 0.6	0.1
Inhale/Exhale	0.36 ± 0.07	0.25 ± 0.06	0.001*

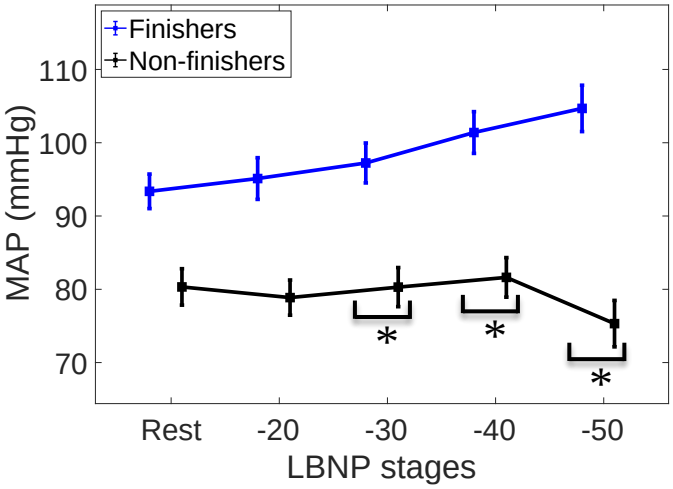

Figure 1. Changes of MAP in the finishers and non-finishers groups as a response to LBNP. Figure shows mean ± SE. * represent a significant difference between the

groups.

Inhale time was lower in the non-finishers group at rest ($p = 0.007$), and at – 50mmHg ($p = 0.01$) compared to the finishers group (Table 1, Figure 2), while no difference ($p = 0.57$) in exhale time was observed between the two groups.

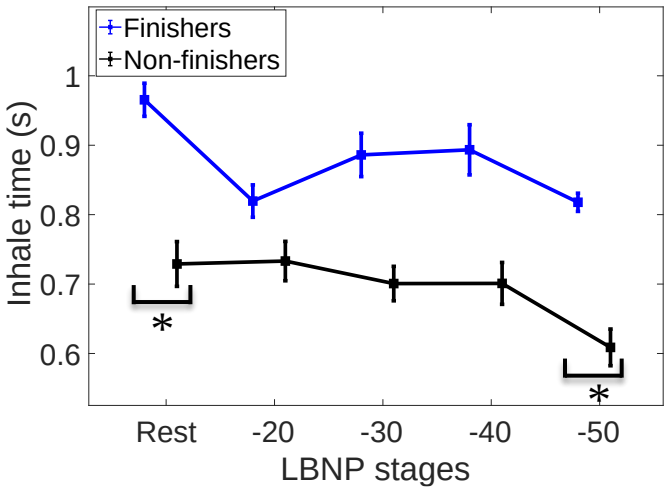

Figure 2. Inhale time changes in the finishers and non-finishers as a response to graded lower-body negative pressure. Figure shows mean ± SE. * represent a significant difference between the groups.

In the non-finishers group, the inhale/exhale ratio was lower at – 30mmHg ($p = 0.01$), – 40mmHg ($p = 0.02$), and – 50mmHg ($p = 0.001$) compared to the finishers group (Table 1, Figure 3).

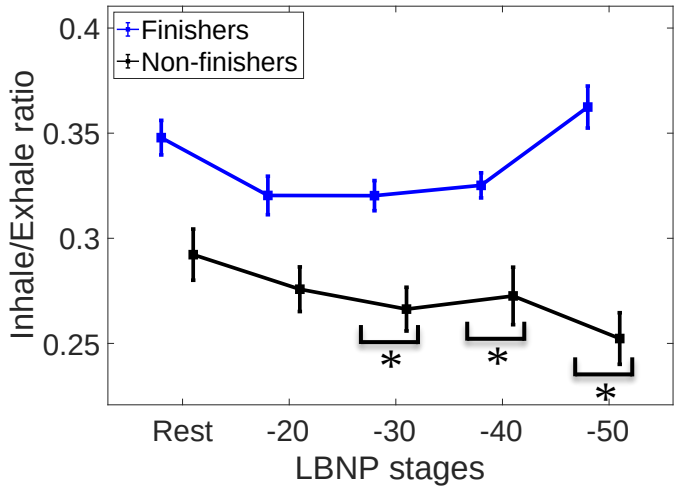

Figure 3. Inhale/exhale ratio changes in the finishers and non-finishers as a response to graded lower-body negative pressure. Figure shows mean ± SE. * represent a significant difference between the groups.

4. Discussion

Hemorrhage is the loss of blood from the circulatory system and the leading cause of battlefield and postpartum-related deaths. Early detection of hemorrhage remains the most effective strategy to reduce the mortality rate caused by traumatic injuries. During hemorrhagic shock, patients with a limited tolerance for hypovolemia would reach cardiovascular collapse in a shorter period for equal blood loss, and thus might necessitate life-saving interventions sooner than those with high tolerance [19]. Identifying physiological markers and understanding the mechanisms that influence hypovolemia tolerance may help to recognize subjects with low tolerance to central hypovolemia before the onset of symptoms. In this study, we investigated the cardiovascular and respiratory responses in two groups (finishers and non-finishers) at rest and under different hemorrhage conditions simulated through LBNP. Mean arterial pressure was higher in the finishers group at –20mmHg, – 30mmHg, and –50mmHg compared to the non-finishers group. This suggests that the finishers group has the greatest compensation to the hypovolemic challenge and thus doesn't display any presyncope symptoms. We argue, that the increased inhale time in the finishers group could lead to a greater duration of intrathoracic pressure generating vacuum effect within the thorax resulting in increased venous return, cardiac output, mean arterial blood pressure, and improved tolerance to hemorrhage. In addition, the diminished inhale time in the non-finishers group at – 50mmHg might be due to a reduced resting inspiratory time and thus can distinguish between the finishers and non-finishers subjects before the onset of LBNP. The finishers also exhibited a higher inhale/exhale ratio at – 30mmHg, – 40mmHg, and – 50mmHg, when compared to the non-finishers group. An increase in the inhale/exhale ratio is associated with longer episodes of intrathoracic pressure and thus increasing mean arterial blood pressure via the respiratory pump mechanism [20].

5. Conclusions

In this study, we investigated the cardiovascular and respiratory responses to progressive hemorrhage simulated using lower body negative pressure (LBNP). Subjects who developed presyncope symptoms before reaching –60 mmHg were categorized as non-finishers, whereas those who finished the experiment without any presyncope symptoms were designated as finishers. Our results showed that the finishers group elicited a respiratory pump response to maintain mean arterial pressure and fight against central hypovolemia induced by LBNP. This is supported by the reduced inspiratory and inhale/exhale ratio in the finishers group, both of which are associated with longer episodes of intrathoracic pressure resulting in

increased venous return, cardiac output, mean arterial blood pressure, and improved tolerance to central hypovolemia. These findings provide insights on the value of monitoring respiration during central hypovolemia and can be utilized as an early marker of individuals who have a low tolerance for hypovolemia and may require life-saving interventions sooner than those who have a high tolerance. Future work will focus on studying the interaction between the cardiovascular and respiratory systems towards maintaining blood pressure during hypovolemia.

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