Intrathoracic Pressure Regulator for Blood Loss

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LT COL KRISTINA CREECH       DR. RICHARD A. HERSACK
Chief, En Route Care Research Division       Chair, Aeromedical Research Department

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Hemorrhagic shock is a leading cause of death in combat, yet potentially survivable with early intervention. This is especially true in patients with head injury. Resuscitative measures, e.g., fluid therapy, can be lifesaving; however, delays in intravenous access and differential fluid responsiveness result in over- and under-resuscitation. Intrathoracic pressure regulation (ITPR) is an emerging technology used to treat hypovolemia and cardiac arrest. Preclinical trials demonstrate that ITPR increases venous return and thereby restores blood pressure and perfusion. We compared the effect of ITPR to placebo in restoring hemodynamics after hemorrhage under general anesthesia. A secondary aim was to determine if ITPR could reduce the fluid burden of hemorrhage. Based on group-to-group comparisons, ITPR had limited effect on improving mean arterial pressure and other hemodynamic responses. However, in some subjects, when ITPR is implemented, improvement in stroke volume, other indices of perfusion, and volume sparing occurs. While fluid resuscitation is the standard of care in hypovolemic hemorrhagic shock, delays in treatment can be potentially fatal. We have shown that there is an increase in the stroke volume and diastolic ventricular compliance using an ITPR in mild hypovolemic subjects. The mechanism of this process is unknown, but is likely due to the increased negative pressure generated throughout the thoracic cavity. In some patients, ITPR could bridge a delay in hemorrhage treatment. Further studies are needed to explore the precise mechanism and whether similar results are achieved.
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1.0 SUMMARY

Hemorrhagic shock is a leading cause of death in combat, yet potentially survivable with early intervention. This is especially true in patients with head injury. Resuscitative measures, e.g., fluid therapy, can be lifesaving; however, delays in intravenous access and differential fluid responsiveness result in over- and under-resuscitation. Intrathoracic pressure regulation (ITPR) is an emerging technology used to treat hypovolemia and cardiac arrest. Preclinical trials demonstrate that ITPR increases venous return and thereby restores blood pressure and perfusion. We compared the effect of ITPR to placebo in restoring hemodynamics after hemorrhage under general anesthesia. A secondary aim was to determine if ITPR could reduce the fluid burden of hemorrhage. Based on group-to-group comparisons, ITPR had limited effect on improving mean arterial pressure and other hemodynamic responses. However, in some subjects, when ITPR is implemented, improvement in stroke volume, other indices of perfusion, and volume sparing occurs. While fluid resuscitation is the standard of care in hypovolemic hemorrhagic shock, delays in treatment can be potentially fatal. We have shown that there is an increase in the stroke volume and diastolic ventricular compliance using an ITPR in mild hypovolemic subjects. The mechanism of this process is unknown, but is likely due to the increased negative pressure generated throughout the thoracic cavity. In some patients, ITPR could bridge a delay in hemorrhage treatment. Further studies are needed to explore the precise mechanism and whether similar results are achieved.

2.0 INTRODUCTION

Hemorrhagic shock and head injury are the leading causes of death due to combat. These injuries are also potentially survivable with early intervention. We have demonstrated a safe but reproducible drop in blood pressure (BP) in anesthetized healthy volunteers following mild hemorrhage. Blood pressure, in conscious subjects, does not decrease following mild hemorrhage, which may in part be due to preserved compensatory sympathetic responses. The study design for this research is modeled after the necessary tight control of BP in patients with sustained head injury, since low BP is a powerful predictor of outcome. Earlier restoration of BP and perfusion using intrathoracic pressure regulation (ITPR) could offer an immediate “first-line” treatment of hemorrhage or used to supplement other primary therapies. We will compare ITPR versus placebo (device without vacuum line) in subjects undergoing general anesthesia (GA) and hemorrhage. Our primary outcome measures will be the time to BP restoration – ITPR versus placebo. Secondary outcome measures include total fluid requirements and the distribution of fluid in the vascular and extravascular volume. Additionally, we will investigate if novel monitors (Massimo Rainbow 7) and interpretative indices can be used to detect and treat hemorrhage. Studies will be performed at the University of Texas Medical Branch’s (UTMB) Clinical Research Center (CRC).

The ITPR is a Food and Drug Administration approved non-invasive device that has been developed to increase circulation and blood pressure in non-spontaneously breathing patients. The ITPR is manufactured by Advanced Circulatory Systems, Inc., Eden Prairie, MN, and sold as CirQLator TM. The physiologic principle or mechanism for this effect is increasing venous return to the heart due to a lower intrathoracic pressure resulting in an increase in cardiac output (CO) and BP. Specifically, the device generates a subatmospheric intrathoracic pressure during the expiratory phase of ventilation (it is timed in-between mechanical positive pressure breaths).
Additionally, the lower intrathoracic pressure generated by the ITPR transmits across the entire body, which can further reduce intracranial and intra-abdominal pressure. Experimental animal studies have demonstrated marked improvement of overall hemodynamic status, vital organ perfusion, and survival in settings mimicking clinical conditions [1-4].

We will test the ITPR in healthy volunteers undergoing a fixed hemorrhage. Our hypothesis is that ITPR will augment the circulation by providing earlier restoration of BP and cerebral perfusion and reduce excess fluid requirements. The ITPR is an innovative non-invasive device that has been developed to increase circulation and BP in non-spontaneously breathing patients.

### 3.0 METHODS

#### 3.1 Prescreening

A complete history, physical examination, and a series of medical screening tests will be obtained to detect certain preexisting medical or physical conditions that may disqualify a volunteer from participating in this study. These screening tests include vital signs, blood tests (chemistries, auto-chemistry panel, lipids, iron, ferritin, complete blood count, coagulation profile, hepatitis B surface antigen, hepatitis A antibody, and human immunodeficiency virus antibody), urine tests (drug screen I-abuse, marijuana, and a pregnancy test), and a 12-lead electrocardiogram (ECG). Abnormal tests will be communicated to the subject and the subject will be excluded if the test is outside normal limits.

We will screen and enroll 15 subjects. We anticipate five of the subjects will not meet entry criteria or will not complete both arms of the study. Therefore, the first 10 healthy, non-obese volunteers (body mass index < 27.5), age 21 to 35 years, will undergo a randomized complete-block design study and will be used for this study. The 10 subjects will be their own controls and thus undergo two experiments each at least 4 weeks apart, for 20 experiments (n=10, per group) in the study. The two subject groups are Arm 1 (GA + hemorrhage + placebo) and Arm 2 (GA + hemorrhage + ITPR).

The subjects will report to UTMB’s CRC the morning of the study. Body weight will be recorded and the subjects will be given the opportunity to void, if necessary. Blood pressure and ECG will be continuously monitored throughout the entire protocol. Standard American Society of Anesthesiology monitors will be utilized for this study. An arterial catheter and a peripheral intravenous (IV) line will be placed using local anesthesia. The subjects will then be randomly assigned to one of the two arms of the study [T minus 60 (T-60)].

Each subject will undergo a 30-minute period of stabilization prior to GA. During this time, baseline plasma volume and blood volume will be determined using indocyanine green and a baseline hematocrit. Subjects will then undergo GA (T-30). After 30 minutes of GA, a fixed, gravity dependent, 10 mL/kg of blood will be removed (T0) via antecubital catheter. The hemorrhage will last 20 minutes (T20). At the end of hemorrhage, the ITPR or placebo device will be attached to the endotracheal tube (ETT). The device components for both arms are identical. For Arm 1 (placebo), no vacuum suction will be applied (vacuum line will be clamped). For Arm 2 (ITPR), -8 cmH2O of negative pressure (subatmospheric) will continuously be applied to the vacuum hose. The effects of ITPR or placebo on BP restoration, cerebral perfusion, blood volume expansion, hemodynamics, and supplemental fluid administration (fluid resuscitation – see conditions) will be followed for an additional 60 minutes (T80). At T80, the
blood collected during the hemorrhage from the subjects will be reinfused over 20 minutes (Figure 1). The subjects will be monitored during this time, but no data will be collected. A final body weight will be recorded and the subjects will be discharged when general CRC criteria are met. Hemodynamics, urinary output (UO) (by bladder ultrasound), echocardiography, and other non-invasive data will be collected throughout the protocol.

Figure 1. Experimental protocol.

3.2 Anesthesia

A faculty anesthesiologist (co-investigator on this protocol) will perform GA. The GA technique outlined is routine and performed for patients requiring surgery. The aspects of GA are discussed in detail – specifically from induction to emergence and how GA will be titrated. Anesthetics, like most drugs, affect people differently. People require different amounts of anesthesia to achieve the same depth. A bispectral index (BIS) monitor (Aspect Medical Systems, Inc., Norwood, MA) will be attached to the forehead and used to titrate the depth of anesthesia.

Subjects will be pre-oxygenated with 100% oxygen for 3 minutes. An IV dose of propofol (2-3 mg/kg) will be administered to induce GA. The induction dose of propofol lasts approximately 5 minutes. During induction, a patent airway will be confirmed and the subject will be intubated and ventilated (see below).

After induction, GA will be maintained with a continuous infusion of propofol. The concentration of propofol delivered will be the quantity sufficient to ensure a state of GA. In young, healthy subjects, such as those recruited for this study, this corresponds to approximately 75-150 µg/kg/min of propofol. Our study design differs from a typical surgery, which has periods of stimulation and no-stimulation. The depth of anesthesia is rarely constant during surgery. Consequently, there are often periods of increased depth of anesthesia after induction followed by a shallow plane of anesthesia during surgery. The depth of anesthesia clearly influences BP, heart rate, and other cardiovascular variables, which are some of our endpoints.
To ensure that each subject has a similar depth of anesthesia, e.g., to prevent too little or too much anesthesia, propofol will be individually titrated to the BIS monitor. Specifically, the infusion of propofol will be targeted to achieve a numeric score of 50, which has been shown to ensure amnesia and an adequate plane of GA [2]. Once the BIS is equal to or asymptotically approaches 50, the propofol concentration will be noted and set at this concentration for the duration of the study. We appreciate that fine changes (±10 µg/kg/min) may be needed to maintain this depth of anesthesia. Since we are implementing GA without surgical stimulation, we will likely achieve a steady state of anesthesia within 15 minutes. To further substantiate a steady state of GA, we will not begin hemorrhage until 30 minutes after the onset of hemorrhage. The BIS and propofol infusion rate will be recorded every 15 minutes, as part of the anesthesiologist’s record, and the data will be transferred to our data file.

At the end of the study, the propofol infusion will be turned off. Propofol has a short half-life (3 minutes). Emergence is complete when the subject is awake enough to follow commands. This usually occurs within 10 minutes of turning off propofol.

A neuromuscular blocking agent (IV rocuronium 0.6 -1.0 mg/kg) will be administered to facilitate good intubating conditions. An ETT, using a laryngoscope, will be passed through the vocal cords. The subject will be mechanically ventilated using air/oxygen mixture. Minute ventilation will be adjusted to maintain an end-tidal carbon dioxide level between 35-40 mmHg. The neuromuscular blocking effects for a dose of rocuronium last between 30 and 60 minutes in healthy patients [1]. The depth of neuromuscular blockade will be measured using a standard train-of-four twitch monitor (4 out of 4 twitches represents recovery of neuromuscular blockade). During emergence, if the subject appears weak (unable to sustain a 5-second head-lift) and/or 4/4 twitches are not present, an agent to reverse the neuromuscular blockade will be administered. General endotracheal anesthesia using non-depolarizing neuromuscular blockers follows this standard approach. The anesthesiologist is highly tuned and trained to detect and treat persistent neuromuscular blockade.

3.3 Monitoring

We will monitor ECG, invasive BP, capnography, inspired oxygen analysis, pulse oximetry, continuous non-invasive hemoglobin, train-of-four twitch height, anesthetic agent analysis, and temperature. Body temperature will be maintained using a convection blanket. Anesthesia records will be routinely kept, as for all other anesthesia procedures. Our ongoing anesthetized human hemorrhage protocols have been safely performed despite reductions in BP after anesthesia and during hemorrhage with fluid resuscitation. Continuous vigilant monitoring is standard of care with the presence of a dedicated anesthesiologist. Note that another physician investigator is responsible for collecting data. The dedicated anesthesiologist’s sole responsibility is to perform continuous clinical monitoring for safety.

3.4 ITPR Device Background and Summary

The decrease in intrathoracic pressure creates a vacuum within the thorax relative to the rest of the body, thereby enhancing blood return to the heart and consequently increasing CO and BP [4-7]. Preliminary animal studies have demonstrated that when the intrathoracic pressure is lowered below -5 cmH₂O, venous return to the heart increases and intracranial pressure is reduced [3,8-13]. These beneficial effects in terms of increasing mean arterial pressure (MAP),
coronary perfusion pressure, and cerebral perfusion pressure have been observed in experimental shock. Ongoing testing in humans undergoing elective surgery is underway to determine if ITPR can better maintain hemodynamics during GA and surgery. The proposed protocol will further define ITPR and provide focused data on hemorrhage. Specifically, we will measure the volumetric, oximetric, and hemodynamic responses of ITPR after hemorrhage.

3.5 Hemorrhage

Each subject will undergo a volume-controlled hemorrhage (10 mL/kg) or ≈15% blood volume (≈1.5 units of blood) via placement of a catheter in the antecubital vein on the same side as the intra-arterial catheter. The use of an antecubital vein for withdrawing blood is the traditional and perhaps safest approach. An intra-arterial catheter could also be used for withdrawing blood. The blood will be collected over 20 minutes and stored in a controlled sterile fashion, in accordance with and strict adherence to procedures by the UTMB blood bank. After the experiment, the blood will be reinfused back to the subject. The anesthesiologist has the discretion to stop the hemorrhage.

3.6 Fluid Administration

Intravenous fluid will be administered if systolic BP is lower than 85 mmHg. We anticipate that some fluid will be given to subjects. Fluid administration will be given in 250-mL increments of lactated Ringers solution by the anesthesiologist to increase systolic BP above 85 mmHg. The amount and timing of fluid administration will be recorded. All resuscitative fluids will be warmed to 41°C by Smiths Medical Ltd. fluid warmer (Level 1 Hotline, Kent, UK) at the end of hemorrhage (T20). The anesthesiologist in the study has ultimate control over fluid resuscitation. If the anesthesiologist feels that more fluid or less fluid is needed, it is his/her discretion.

Institutional Review Board consent was obtained. GA (propofol only) was induced at T-30 and maintained until T80 (study end). An ETT was secured and subjects were mechanically ventilated (fraction of inspired oxygen 0.4, tidal volume 6-8 mL/kg, respiratory rate of 10-12 was adjusted to achieve end-tidal carbon dioxide of 35 mmHg). At T0–T20, a 10-mL/kg hemorrhage was performed. From T20–T80, either ITPR (-10 mmHg of suction) or placebo (device but no suction) was placed between the ETT and ventilator. Fluid boluses (0.9% sodium chloride; 250 mL over 2.5 minutes) were administered if systolic BP < 85 mmHg. Blood pressure, other hemodynamics, UO, and total amount of fluid were recorded.

3.7 Data Analysis

Data for ITPR [n=6] and placebo [n=5] are presented as mean (M) ± standard error of the mean (SEM). General anesthesia reduced MAP by ≈11 ± 4 mmHg from T-30 to T0 (before hemorrhage) in both groups. Hemorrhage (T0-T20) further decreased MAP by 5-10 mmHg. Intrathoracic pressure regulation had little effect on MAP compared to placebo. Stroke volume (SV), determined by echocardiography, was similarly reduced by hemorrhage. In four of six ITPR subjects, SV improved (> 15 mL) by study end; SV increased in two of five subjects in the placebo group. Other hemodynamic variables were similar. A trend toward a reduction in amount of fluid administered (mL/kg) was observed in the ITPR (14.8 ± 3.2) vs. placebo.
(19.4 ± 5.9), with greater volume sparing in the subjects who had an improved SV. Urinary output (mL/kg) was similar between groups.

4.0 RESULTS

There were no significant differences between ITPR or control groups in any of the investigated variables at the start of the experiment (T-30 to T0). Heart rate and CO increased during the length of the study for both ITPR and control groups. However, there was no significant difference between the two groups. Mean arterial pressure showed a steady decrease from the beginning of the study until device placement, but showed no difference until the end of the study between ITPR and control groups. Systemic vascular resistance showed a stable decrease throughout the entirety of the study in both groups, but did not show any significant difference when compared (Table 1).

Table 1. Comparison of Control to ITPR Groups

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group</th>
<th>Baseline (T-30) M±SEM</th>
<th>Before Hemorrhage (T0) M±SEM</th>
<th>Start Device (T20) M±SEM</th>
<th>Study End (T80) M±SEM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac output (L/min) ITPR</td>
<td>6.7±0.7</td>
<td>6.6±0.6</td>
<td>7.2±0.9</td>
<td>6.9±0.8</td>
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<tr>
<td>Placebo</td>
<td>6.0±0.6</td>
<td>5.8±0.6</td>
<td>7.2±0.7</td>
<td>7.3±0.7</td>
<td></td>
</tr>
<tr>
<td>Heart rate (bpm) ITPR</td>
<td>70±2</td>
<td>80±5</td>
<td>88±7</td>
<td>84±6</td>
<td></td>
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<tr>
<td>Placebo</td>
<td>69±4</td>
<td>78±4</td>
<td>87±5</td>
<td>89±4</td>
<td></td>
</tr>
<tr>
<td>Mean arterial pressure (mmHg) ITPR</td>
<td>92±3</td>
<td>82±5</td>
<td>67±3</td>
<td>70±2</td>
<td></td>
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<tr>
<td>Placebo</td>
<td>89±3</td>
<td>74±2</td>
<td>69±3</td>
<td>70±5</td>
<td></td>
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<tr>
<td>Systemic vascular resistance (dynes*s/cm5) ITPR</td>
<td>1338±50</td>
<td>1218±130</td>
<td>977±145</td>
<td>910±117</td>
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<tr>
<td>Placebo</td>
<td>1324±70</td>
<td>1151±49</td>
<td>1059±173</td>
<td>798±97</td>
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Stroke volume, in both groups, increased from the end of hemorrhage and ITPR device or placebo attachment (T20) until the end of the study (T80). However, there was a significant increase only in the ITPR group during this time interval when compared to the control group [ΔSV] (ITPR: 22 ± 4.6 mL vs. placebo: 6 ± 4.5 mL; p = 0.03). Similarly, ejection fraction (EF) increased in the ITPR group during the same timeframe (T20 to T80), while the placebo group remained unchanged (T20 vs. T80 EF ITPR: 60.2 ± 1.3 vs. 64.3 ± 1.5; EF placebo: 58.0 ± 3.3 vs. 58.1 ± 2.0; p = 0.02). End diastolic volume (EDV) decreased in both groups during hemorrhage (T0 to T20), but increased after that point until the end of the study. The ITPR group had a more substantial increase during this interval compared to the placebo group (T20 vs. T80 EDV ITPR: 100.4 ± 4.0 mL vs. 127.6 ±9.0 mL; EDV placebo: 110.0 ± 4.1 mL vs. 118.9 ± 4.6 mL). End systolic volume had a similar increase in both groups (Table 2). Diastolic compliance was assessed by using the ratio of mitral peak velocity of early filling (E) to early diastolic mitral annular velocity (E'). There was a significant difference between the two groups during the entire length of the study T-60 to T80 [ΔE/E'] (ITPR -0.43 ± 1.2 vs. placebo 0.81 ± 1.6; p = 0.03), which shows an increase cardiac compliance in the ITPR group (Figure 2).
Table 2. Stroke Volume

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group</th>
<th>Baseline (T-30) M±SEM</th>
<th>Before Hemorrhage (T0) M±SEM</th>
<th>Start Device (T20) M±SEM</th>
<th>Study End (T80) M±SEM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ejection fraction (%)</td>
<td>ITPR</td>
<td>59.0±2.6</td>
<td>58.1±2.4</td>
<td>60.2±1.3</td>
<td>64.3±1.5</td>
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<tr>
<td></td>
<td>Placebo</td>
<td>54.8±3.1</td>
<td>59.9±3.6</td>
<td>58.0±3.3</td>
<td>58.1±2.0</td>
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<tr>
<td>Stroke volume (mL)</td>
<td>ITPR</td>
<td>75.6±5.3</td>
<td>70.1±2.9</td>
<td>60.4±2.6</td>
<td>82.1±6.2</td>
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<tr>
<td></td>
<td>Placebo</td>
<td>62.1±10.8</td>
<td>71.7±4.3</td>
<td>64.1±5.4</td>
<td>68.9±3.1</td>
</tr>
<tr>
<td>End diastolic volume (mL)</td>
<td>ITPR</td>
<td>128.7±8.2</td>
<td>121.7±6.2</td>
<td>100.4±4.0</td>
<td>127.6±9.0</td>
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<tr>
<td></td>
<td>Placebo</td>
<td>133.0±4.3</td>
<td>120.4±4.4</td>
<td>110.0±5.1</td>
<td>118.9±4.6</td>
</tr>
<tr>
<td>End systolic volume (mL)</td>
<td>ITPR</td>
<td>53.1±5.1</td>
<td>51.6±5.4</td>
<td>40.0±2.2</td>
<td>45.4±3.5</td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td>60.5±5.6</td>
<td>48.7±5.6</td>
<td>45.9±3.2</td>
<td>50.0±3.5</td>
</tr>
</tbody>
</table>

Figure 2. Diastolic compliance.

There was no difference between the ITPR and placebo group for UO (ITPR 4.1 ± 0.6 mL/kg vs. placebo 4.7 ± 0.8 mL/kg) (Figure 3) and fluid infused (ITPR 17.4 ± 3.8 mL/kg vs. placebo 18.6 ± 5.0 mL/kg) (Figure 4) during the length of the study. Carbon dioxide production also showed no significant difference between both groups (Figure 5).
Figure 3. Urinary output.

Figure 4. Fluid in.
5.0 DISCUSSION

The results of the study show a significant increase in SV and diastolic compliance in the ITPR group while MAP and CO remained similar. While the studies of Yannopolous et al. [1-3,5] had shown improved hemodynamics in porcine models, the data collected on human subjects did not replicate their conclusion concerning an increase of MAP. Huffmyer et al. [4] revealed a significant increase of CO but no differences in systemic BP, SV, or EF. This study differed from the present study due to the fact ITPR was used on hypovolemic, not normovolemic, subjects.

Ventricular diastolic compliance refers to the stretching ability of the left ventricle. With a more compliant heart, the left ventricle can accommodate more blood volume without a significant increase in left-sided pressures. As seen in the study, the increase in diastolic volume correlates to an increase in SV when blood is pumped out of the heart and into circulation [14].

The negative pressure on the thorax induced by the ITPR could have actively stretched the cardiac muscle, therefore allowing more blood into the ventricles. This concept can be similarly compared to the physiologic mechanism of lung inflation due to negative pressure generated by the diaphragm.

Mean arterial pressure did not show a significant change with ITPR in this study. However, changing pressures have been shown to occur with propofol-induced anesthesia. The amount of propofol given by the anesthesiologist can vary depending on the anesthetic plane of the subject. The potential ability of the ITPR mechanism to irritate patients through the ETT can also affect BP. However, the total amount of propofol (placebo 1113 mg vs. ITPR 1111 mg) used as well as the anesthetic plane (placebo 34.5 vs. ITPR 34.3] was not significant when comparing both placebo and ITPR groups.
5.1 Limitations

The primary limitation in this study was that these observations were made with healthy volunteers. Changes in SV and ventricular compliance could be very different with pre-morbid conditions such as hypertension, congestive heart failure, and even diabetes. Hypertrophic and dilated cardiomyopathy impairs the heart’s ability to adequately pump blood throughout the body. The observations made from this study cannot adequately predict outcomes in these patient types.

5.2 Conclusion

While fluid resuscitation is the standard of care in hypovolemic hemorrhagic shock, delays in treatment can be potentially fatal. We have shown that there is an increase in the stroke volume and diastolic ventricular compliance using an intrathoracic pressure regulator in mild hypovolemic subjects. The mechanism of this process is unknown, but is likely due to the increased negative pressure generated throughout the thoracic cavity. Further studies are needed to explore the precise mechanism and whether similar results are achieved.

6.0 REFERENCES


## LIST OF ABBREVIATIONS AND ACRONYMS

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>BIS</td>
<td>bispectral index</td>
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<tr>
<td>BP</td>
<td>blood pressure</td>
</tr>
<tr>
<td>CO</td>
<td>cardiac output</td>
</tr>
<tr>
<td>CRC</td>
<td>Clinical Research Center</td>
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<tr>
<td>ECG</td>
<td>electrocardiogram</td>
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<tr>
<td>EDV</td>
<td>end diastolic volume</td>
</tr>
<tr>
<td>EF</td>
<td>ejection fraction</td>
</tr>
<tr>
<td>ETT</td>
<td>endotracheal tube</td>
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<tr>
<td>GA</td>
<td>general anesthesia</td>
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<tr>
<td>ITPR</td>
<td>intrathoracic pressure regulation</td>
</tr>
<tr>
<td>IV</td>
<td>intravenous</td>
</tr>
<tr>
<td>M</td>
<td>mean</td>
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<tr>
<td>MAP</td>
<td>mean arterial pressure</td>
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<tr>
<td>SEM</td>
<td>standard error of the mean</td>
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<td>SV</td>
<td>stroke volume</td>
</tr>
<tr>
<td>UO</td>
<td>urinary output</td>
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<tr>
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<td>University of Texas Medical Branch</td>
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