

# Use of respiratory impedance in prehospital care of hypotensive patients associated with hemorrhage and trauma: A case series

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<b>BACKGROUND:</b>	The respiratory pump can be optimized to enhance circulation in patients with hypotension by having patients spontaneously breathe through a low level of inspiratory resistance. This can be achieved with an impedance threshold device (ITD) designed to provide 7 cm H <sub>2</sub> O resistance during spontaneous inspiration with minimal resistance during expiration. Little is known about the effects of harnessing this physiological concept to increase blood pressure (BP) in the prehospital setting of care for patients with hypotension caused by blood loss or trauma. In this case series, we report on the feasibility, effectiveness, and safety of rapidly deploying the ITD by first responders to treat hypotension secondary to blood loss and trauma in the urban setting by emergency medical services personnel.
<b>METHODS:</b>	Hemodynamic data from hypotensive patients (pretreatment systolic BP [SBP] <100 mm Hg) from 3 U.S. cities where the ITD is deployed were evaluated. The primary end point was maximum change in SBP and diastolic BP (DBP) from before to during ITD use in patients with hypotension secondary to documented blood loss or trauma. Secondary end points were device tolerance, whether the patient felt "better," change in heart rate, O <sub>2</sub> saturation, and adverse events.
<b>RESULTS:</b>	Of the 255 hypotensive patients treated, there were 26 categorized with blood loss and 13 with trauma. In this 39-patient subgroup, the SBP and DBP (mean $\pm$ SD) increased from 79 $\pm$ 14 mm Hg and 48 $\pm$ 12 mm Hg before ITD placement to 110 $\pm$ 17 mm Hg and 66 $\pm$ 14 mm Hg after ITD placement ( $p$ < 0.001). Breathing through the ITD resulted in no reported adverse events, was well tolerated, and resulted in feeling "better" in more than 85% of the patients.
<b>CONCLUSION:</b>	Use of an ITD by emergency medical services personnel on hypotensive spontaneously breathing patients secondary to blood loss and trauma increased SBP and DBP and was feasible, well tolerated, and not associated with adverse effects (e.g., increased bleeding). ( <i>J Trauma Acute Care Surg.</i> 2012;73: S54–S59. Copyright © 2012 by Lippincott Williams & Wilkins)
<b>LEVEL OF EVIDENCE:</b>	Therapeutic study, level III.
<b>KEY WORDS:</b>	Impedance threshold device; hypotension; lower body negative pressure.

Harnessing the basic physiological relationships between inspiration and the simultaneous resultant reductions in intrathoracic and intracranial pressure, along with augmentation of venous blood flow back to the heart, provides a new and dynamic opportunity to treat hypotensive emergencies. The impedance threshold device (ITD) is a noninvasive technology that has been developed to enhance these fundamental physiological interrelationships in an effort to benefit patients with hypotension and other states of decreased vital organ perfusion, especially in the prehospital setting, where invasive therapies may not be available or practical. Although originally developed for application during cardiopulmonary resuscitation,<sup>1</sup> the augmentation of negative intrathoracic pressure driven by inspira-

tory effort has been shown to ameliorate the hypotensive effects associated with acute reductions in central blood volume in animals and humans.<sup>2–9</sup> Using lower body negative pressure (LBNP) as a model for the study of hemorrhage in humans, we previously demonstrated that ITD use delayed presyncopal symptoms<sup>10</sup> and cardiovascular decompensation<sup>1,11</sup> by maintaining stroke volume, cardiac output, and arterial blood pressure (BP).<sup>12</sup> As such, a small resistance during inspiration produced by the ITD technology could be used as a circulatory enhancer during the initial treatment and transport of patients who manifest reduced central blood volume and the resulting hypotension. Such conditions might reasonably be expected in the settings of acute traumatic hemorrhage, sepsis, congestive heart failure, and in circumstances in which neurovascular tone is lost or intravascular volume otherwise decreases. Based on the results of these and other laboratory experiments,<sup>6,7,13</sup> we hypothesized that the ITD could be used in the prehospital setting on the battlefield and civilian patient transport as a way to "buy time" by providing a critical bridge to more definitive repair of the primary injury.<sup>14</sup>

Recently, this ITD technology has been used for treatment of hypotension in spontaneously breathing patients in several emergency medical services (EMS) systems across the United States. The new approach was first deployed with advanced life support (ALS) providers<sup>15</sup> and, more recently, by

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first responders who provide basic life support (BLS) and who are unable or unequipped to perform invasive hemodynamic interventions. We report here the results from the first case series of subjects experiencing hypotension secondary to both traumatic and nontraumatic hemorrhage. These patients represent two subgroups from a larger patient population with hypotension from multiple causes treated with this approach.

## MATERIALS AND METHODS

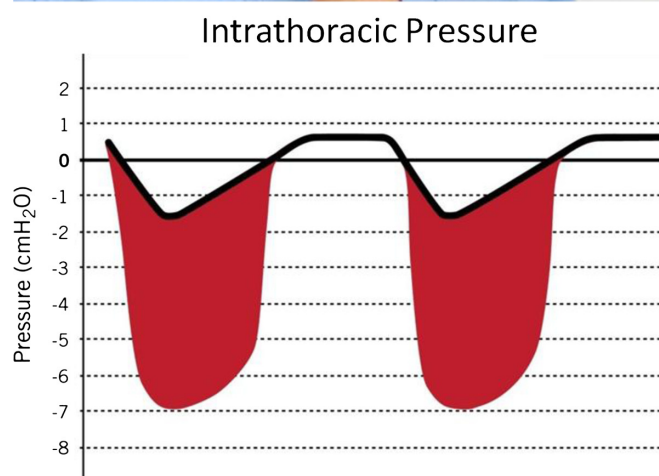
The case series described herein was part of an evaluation designed to assess device tolerance, ease of use, and effectiveness when paired with standard intravenous fluid administration for hypotensive patients in a prehospital EMS setting. The prehospital protocol was performed primarily in Lucas County, Ohio (population 450,000), by Lucas County EMS providers, with approval by the Promedica institutional review board. The execution of the protocol was supported by eight ALS ambulances in Lucas County with an annual call volume of 57,000 runs. Additional patients were included, who had trauma and/or blood loss from Cypress Creek, Texas, and Empress, New York, where the ITD was more recently introduced as a clinical tool to treat hypotension. To assure standardization of the prospective data collection method (i.e., vital signs, questions regarding tolerance, and mental status) between sites, all participating EMS personnel at all three study sites were trained by the same EM instructor. Information related to the etiology of the hypotension and all hemodynamic data were extracted from EMS run reports that included recordings of various physiological parameters before, during, and after ITD use.

### Study Device

The ITD-7 (ResQGARD, Advanced Circulatory Systems, Inc., St. Paul, MN) is cleared for sale in the United States by the Food and Drug Administration for the treatment of patients with low blood circulation (Fig. 1). A detailed description of the small lightweight device that can be used on either a facemask or a mouthpiece has been previously published.<sup>1</sup> Once applied, patients were instructed to breathe naturally through the device and report to the care providers if they experienced difficulty breathing. To quantify how well patients tolerated the ITD and how comfortable it was for patients to wear, the paramedics in Toledo, Ohio, completed a five-point Device Tolerance Index scale questionnaire following each use (0 = not difficult at all to breathe through; 1 = mildly difficult to breathe through; 2 = somewhat difficult to breathe through; 3 = very difficult to breathe through; 4 = unable to tolerate, device removed).

### Population

The inclusion criteria for prehospital use of the ITD included patient weight more than 25 pounds and systolic BP (SBP) less than 100 mm Hg. Patients with hypotension secondary to dehydration, blood loss, sepsis, trauma, orthostatic hypotension, and those undergoing renal dialysis were treated. Exclusions to ITD use were complaints of chest pain or shortness of breath, pulmonary hypertension, active congestive heart failure, known aortic stenosis, or a dilated cardiomyopathy. First responders (firefighters and EM technicians) and paramedics were taught not to use the ITD in patients with a primary complaint of difficulty breathing.



**Figure 1.** A subject breathing through the impedance threshold device (ResQGARD) with facemask (*right picture*). Right panel illustration depicts the reduction in intrathoracic pressure during normal inspiration (*open area under the zero line*) and breathing through a ResQGARD (*additional red area under the zero line*).

### End Points

The primary end point was the maximum change in BP from the period immediately before ITD application to destination arrival or discontinuance of ITD. Secondary end points were device tolerance (see criteria above), the answer to the question “Do you feel better?” (yes or no), change in heart rate (HR), respiratory rate (RR), arterial oxygen saturation (SpO<sub>2</sub>), and adverse events. Once patients were identified by BLS or ALS providers as having hypotension and they met device use criteria, they were treated with the ITD using either a facemask or a mouthpiece. They received concomitant standard therapy for hypotension, including reversal of other potential causes of

hypotension such as correcting hyperthermia and administration of fluids, oxygen, vasopressors, and/or patient positioning as appropriate. Use of the ITD did not interfere with standard therapy. Physiological parameters were assessed before, during, and after ITD use as part of the standard clinical protocol. Similarly, administration of standard therapies such as intravenous fluid administration and  $O_2$  were recorded and monitored.

### Statistical Analysis

Data were expressed as mean  $\pm$  SD and 95% confidence intervals (95% CIs). Comparisons were based on hemodynamic measurements made before and during ITD treatment. The change in SBP from the baseline value to the maximum value during the time of ITD application was the primary study end point. Mean values were analyzed with a two-tailed Student's *t* test after verifying that the data were normally distributed. Dichotomous variables were analyzed by two-tailed Fisher's exact test. The probability level,  $p = 0.05$ , was chosen as the statistical inference that reflected the chance of falsely concluding that the observed differences were attributable to factors other than random variability associated with the experimental methods or selection of the patients for the given sample size of this study.

### RESULTS

A total of 128 male and 127 female patients ranging in age from 19 to 89 years (mean,  $64 \pm 16$  years) met the criteria for inclusion into this case series. Of the total patient sample, there were 26 patients classified with nontraumatic blood loss and 13 additional patients who were classified with trauma defined as direct trauma or trauma after syncope with or without obvious blood loss.

For all 255 patients with hemodynamic data, mean ( $\pm$ SD; 95% CI) SBP and diastolic BP (DBP) increased ( $p < 0.001$ ) from  $78 \text{ mm Hg} \pm 13 \text{ mm Hg}$  (77–80 mm Hg) and  $47 \text{ mm Hg} \pm 11 \text{ mm Hg}$  (45–48 mm Hg) before ITD placement to  $111 \text{ mm Hg} \pm 20 \text{ mm Hg}$  (109–113 mm Hg) and  $65 \text{ mm Hg} \pm 15 \text{ mm Hg}$  (63–66 mm Hg) after ITD placement. These responses resulted in an increase ( $p < 0.001$ ) in pulse pressure (PP) from  $32 \text{ mm Hg} \pm 9 \text{ mm Hg}$  (31–33 mm Hg) before ITD placement to  $47 \text{ mm Hg} \pm 17 \text{ mm Hg}$  (45–49 mm Hg) after ITD placement. There was no statistical change in group averages for HR (81 vs. 80 beats/min), RR (17 vs. 17 breaths/min), and  $SpO_2$  (96 vs. 97%) from before to after ITD placement. Inquiry of patient symptoms resulted in 213 patients (84%) answering “yes” to the question “Do you feel better?” compared to before ITD placement whereas 31 patients answered “no” to the same inquiry (odds ratio, 5.25:1). Of the patients who failed to experience an improvement in symptoms, 16 either chose not to use the ITD because of intolerance or did not demonstrate an elevation in BP during ITD breathing.

The mean admission hemoglobin was available for 23 of 39 of the patients categorized with traumatic or nontraumatic blood loss and was  $10.0 \text{ g/dL} \pm 2.8 \text{ g/dL}$ . Regardless of age, these patients with nontraumatic blood loss and with all-cause trauma displayed similar responses, with elevations in SBP from  $79 \text{ mm Hg} \pm 14 \text{ mm Hg}$  (72–86 mm Hg) to  $110 \text{ mm Hg} \pm 17 \text{ mm Hg}$  (102–118 mm Hg), DBP from  $48 \text{ mm Hg} \pm 12 \text{ mm Hg}$

(42–55 mm Hg) to  $66 \text{ mm Hg} \pm 14 \text{ mm Hg}$  (60–73 mm Hg), and PP from  $33 \text{ mm Hg} \pm 11 \text{ mm Hg}$  (27–37 mm Hg) to  $44 \text{ mm Hg} \pm 12 \text{ mm Hg}$  (39–51 mm Hg). There were no statistical changes in group averages for HR (88 vs. 85 beats/min), RR (17 vs. 17 breaths/min), and  $SpO_2$  (97 vs. 98%). Changes in SBP, DBP, and PP for all subgroups are shown in Figure 2. The ITD was effective in both male and female patients with hypotension caused by traumatic or nontraumatic blood loss: 17 of 39 of all blood loss patients were female and their SBP increased from

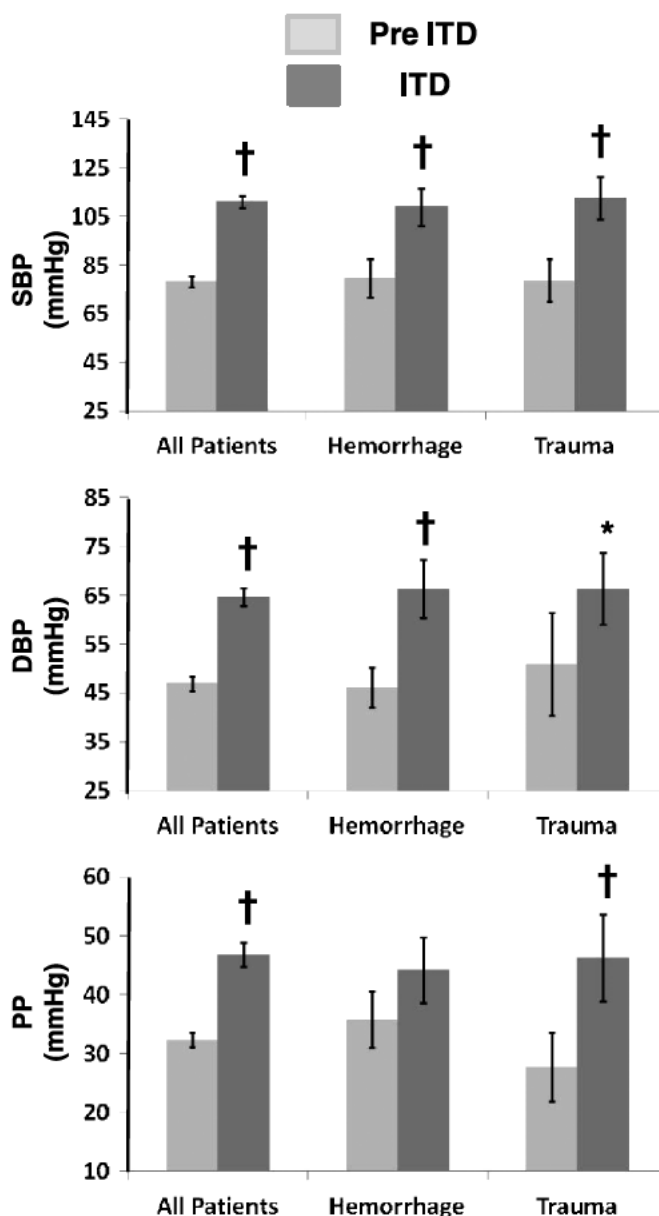


Figure 2. Average (bars) and 95% CI (lines) values for SBP, DBP, and PP in all patients (N = 255), patients with hemorrhage (n = 26), and trauma patients (n = 13) before ITD placement (light gray) and during ITD breathing (dark gray). †  $p < 0.001$  and \*  $p < 0.01$  indicate statistical differences between the pre-ITD and ITD conditions.



77.5 mm Hg  $\pm$  16.5 mm Hg to 108.9 mm Hg  $\pm$  17.9 mm Hg ( $p = 0.0001$ ), whereas 22 of 39 were male and their SBP increased from 80.8 mm Hg  $\pm$  10.2 mm Hg to 111.0 mm Hg  $\pm$  17.5 mm Hg ( $p < 0.0001$ ). A total of 31 of 36 patients with nontraumatic blood loss and with all-cause trauma were queried on their experience breathing through the ITD; 27 of the patients expressed that they felt “better” while breathing through the ITD. Of the 4 patients who failed to experience an improvement in symptoms, three remained hypotensive (SBP,  $\leq 80$  mm Hg; DBP,  $\leq 50$  mm Hg).

The ITD was used, together with standard treatment protocols, for hypotensive patients that included intravenous fluids and use of the Trendelenberg position based on the patient’s clinical status. In this case series, intravenous access was not obtained before or during ITD use in 53 patients. Of these, nine were in the subgroup of patients with nontraumatic blood loss and all-cause trauma. The SBP and DBP in these patients for whom intravenous access could not be obtained before, during, and after ITD use are shown in Figure 3.

Data related to patient tolerance was available from 244 patients. For those, the average tolerance index for using the ITD was  $0.7 \pm 1.1$ . The median tolerance index for using the ITD was 0.0 with first (Q1) and third (Q3) quartile scores of (Q1 = 0; Q3 = 1). The median tolerance index score was 0.5 (Q1 = 0; Q3 = 1) in those patients with nontraumatic hemorrhage and 0.0 (Q1 = 0, Q3 = 1) with all-cause trauma. The duration of time patients used the ITD without removing it because of discomfort ( $n = 237$ ) during treatment at the scene and transport to the emergency department ranged from 3 to 50 minutes (mean  $\pm$  SD,  $22.5 \pm 9.8$  minutes). Fourteen patients reported that they could not tolerate the ITD, and of these, 10 used it long enough to collect hemodynamic data. A total of 2 of the 10 patients who reported that they found it difficult to breathe through the ITD had hypotension secondary to trauma. The changes in SBP from before to during ITD use for these 10 patients was 73 mm Hg  $\pm$  17 mm Hg to 87 mm Hg  $\pm$  19 mm Hg ( $p = 0.004$ ).

## DISCUSSION

The primary objective of this case series was to report the results of using intentional resistance during inspiration as a therapy to treat spontaneously breathing patients with hypotension secondary to either traumatic or nontraumatic blood loss. The focus was on a patient population that developed hypotension secondary to either blood loss or trauma and thus is similar to combat casualties who, under current Tactical Combat Casualty Care (TCCC) guidelines, would receive intravascular access but not intravascular fluid administration. It is this hypotensive population that we hypothesized might benefit significantly from a noninvasive and resource non-intensive “hemodynamic bridge” between initial tactical field care and arrival at a surgical facility. The primary finding of the study was that application of an ITD by BLS and ALS personnel in the prehospital setting resulted in a more than 37% elevation of BP from 79/48 mm Hg to 110/66 mm Hg concomitant with subjective reports expressing a sensation of improved well-being. The changes in BP and HR were similar between those patients with hypotension secondary to blood

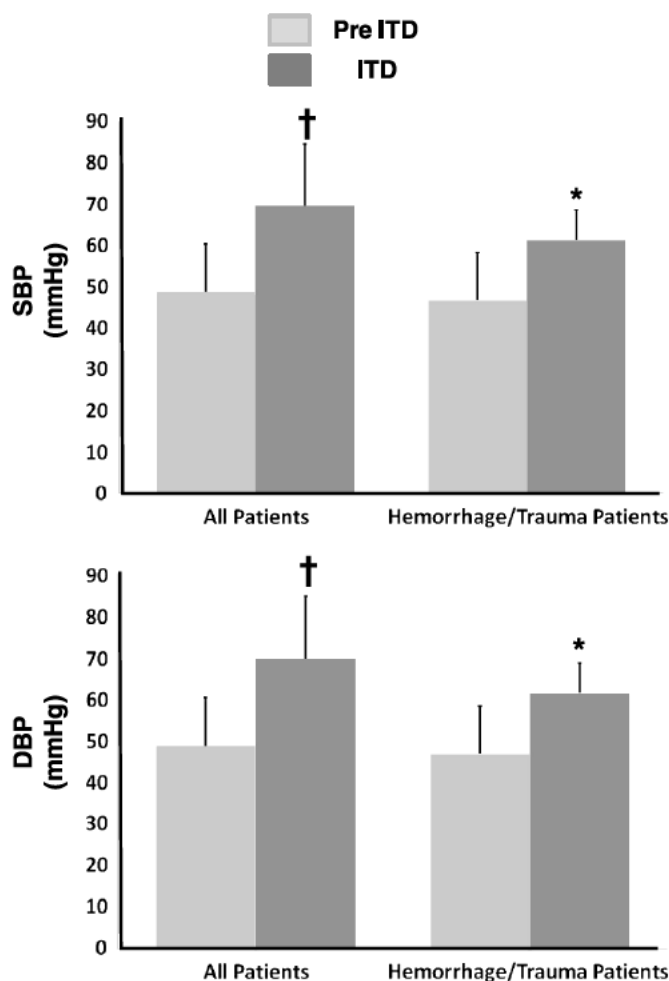


Figure 3. Average (bars) and 1 SD (lines) values for SBP and DBP before ITD placement (light gray) and during ITD breathing (dark gray) in all patients not receiving fluids ( $n = 53$ ) and patients with hemorrhage and trauma ( $n = 9$ ) not receiving fluids. †  $p < 0.001$  and \*  $p < 0.01$  indicate statistical differences between the pre-ITD and ITD conditions.

loss and trauma and those patients with hypotension from a variety of other causes.

Application of an ITD in this prospective case series resulted in BP elevations that approached the current definitions of “normal” without overcompensating. This notion is supported by the absence of clinical evidence of resumed bleeding reported during application of the ITD in the patients in the present study, and the ability to maintain BPs. Although the patients in the present investigation served as their own controls, the outcomes are similar to those generated from studies where historical controls (for more than a decade) using sham and active ITDs in animals and humans subjected to a variety of hypovolemic challenges resulting in hypotension also demonstrated that ITD use was not associated with restoration of BP to above-normal values.<sup>6–9,11</sup> Our results support the hypothesis that application of the ITD technology represents a “fluidless” hypotensive resuscitation that results in improved central circulating blood volume capable of

enhancing tissue perfusion without the clinical and logistical disadvantages associated with intravascular crystalloid infusion. This application may provide an optimal solution for trauma patients known to have ongoing hemorrhage, but who are not yet clinically in a shock state. A prime example of such a “bridging application” within the TCCC paradigm may be in cases where the casualty has been identified with noncompressible hemorrhage but remains alert and possesses a palpable peripheral pulse. Under these conditions, the casualty would receive intravascular access (intravenous saline lock or intraosseous access); however, fluids would be withheld. In such a situation, the casualty could be issued a self-administered ITD, instructed to begin use if they become lightheaded or otherwise worse while summoning the medic or other proximate caregiver.

The elevation in BP caused by the application of the ITD was nearly the same in all patient subgroups independent of whether they received intravenous fluids or were victims of trauma. First, this observation suggests that the ITD may represent a replacement for the need for immediate fluid resuscitation during short-duration prehospital transports and be equally effective in enhancing circulation. Second, the observation that the elevation of arterial pressure was similar in patients who had lost blood independent of the presence of traumatic injury suggests that the systemic circulatory physiology of a hypotensive trauma patient is similar to that of other patients who are hypotensive as a result of reduced central blood volume. Third, the observation that the elevation of arterial pressure was similar in patients who had lost blood independent of the presence of traumatic injury suggests that the circulatory physiology of a hypotensive trauma patient is similar to that of other patients who are hypotensive as a result of reduced central blood volume.

Using LBNP as a model for hemorrhage, we previously reported that human subjects exposed to progressive reductions in central blood volume experienced hemodynamic decompensation, defined by the TCCC paradigm as alteration in mental status (lightheadedness, decreased level of consciousness, or confusion) with concurrent loss of palpable radial pulse. At an average SBP of 79 mm Hg and DBP of 57 mm Hg,<sup>11</sup> these LBNP subjects displayed BPs similar to those observed in the prehospital patients studied in the present investigation. When an ITD was applied to the LBNP subjects, BP was elevated in a similar manner (SBP = 102 mm Hg; DBP = 77 mm Hg) to that observed in the patients of the present study. The mechanisms associated with the use of an ITD during LBNP-induced central hypovolemia included increased stroke volume and cardiac output,<sup>12</sup> improved dynamics of cerebral blood flow,<sup>16</sup> and a delay in the onset of symptoms (i.e., extended time for feeling of well-being).<sup>10</sup> The data obtained from the patients of the present study (where the average blood loss in the group of patients could be estimated at about 25% to 30% of the total blood volume based on an average hemoglobin value of 10 g/dL) are consistent with mechanisms of increased stroke volume and cerebral perfusion, as suggested by significant elevations in PP and improved feelings of well-being.

The current results show that the ITD was well tolerated by most patients, and that the technology can be applied safely and

effectively in hypotensive patients during emergent prehospital care and transport, with or without concurrent use of intravascular fluid resuscitation. These findings provide compelling evidence that the approach of applying a small resistance during inspiration introduces rapid noninvasive hemodynamic support in patients with hypotension and consequently could delay the onset of overt circulatory shock while the patient undergoes evacuation to hemostatic surgical care. However, it is important to recognize that not all patients tolerated the ITD or received the benefit of feeling “better” from its application. In the current evaluation, 14 (5.4%) of 259 patients reported significant discomfort breathing through the ITD and 4 of 14 did not tolerate it long enough to assess BPs. Furthermore, most of the patients who reported no subjective benefit continued to experience hypotension. We speculate that the failure of some patients to feel better may reflect an inability to optimize the patient-powered thoracic pump mechanism that requires the generation of some negative intrathoracic pressure with each inspiratory effort. Another potential reason is that the rate of hemorrhage exceeded the capacity of the ITD to compensate adequately during the aforementioned “bridge” period.

Currently, the U.S. Army Medical Department issues an ITD as part of the medical equipment set for use by licensed practitioners at battalion aid stations and forward support medical companies. Given the numerous obstacles related to clinical data collection in the prehospital phases of combat casualty care, the current data provide support for use of the ITD in hypotensive patients. Further data are still needed on the feasibility of its issue and employment further forward toward point of injury, where its impact might be more valuable in decreasing the rate of potentially survivable combat mortality.

With the exception of several patients with either a gunshot or a stabbing wound or sudden gastrointestinal bleeding, the bleeding was controlled in most of the patients treated in this case series. During this evaluation, several patients did not receive intravenous fluid resuscitation. Nonetheless, the ITD provided a similar boost in BP with or without intravenous fluids. Regardless of the cause of the hypotension, data from this blood loss/trauma subgroup, and the overall patient population treated, strongly support the benefits associated with harnessing the changes associated with normal inspiration to safely augment central blood volume and buy time until more definitive therapies are available. It is important to emphasize that the patients studied, including those with a known average hemoglobin value of 10 g/dL, did not have evidence of ongoing blood loss. Further study of the potential for harnessing the intrathoracic pump to enhance circulation is needed in this patient population.

In conclusion, the findings provide, for the first time, evidence from hypotensive patients secondary to blood loss or trauma that use of the ITD during BLS and ALS prehospital care was successful in improving perfusion (arterial) pressures and/or symptoms without adverse clinical outcomes. The ITD significantly enhanced BP and without obvious clinical exacerbation of bleeding. No cases of hemodynamic overcompensation or other adverse effects of the ITD were observed or reported by the paramedics who transported these patients. Self-administration of the ITD may be a valuable addition to the prehospital trauma care armamentarium and may represent the next addition to the TCCC paradigm if issued for more

extensive use. Further investigation to confirm efficacy on the battlefield, define optimal applications, and evaluation of logistical issues associated with this application of ITD is warranted.

#### AUTHORSHIP

All authors contributed to the preparation of this manuscript. V.C., B.P., K.L., and D.L. designed the study. A.M., M.S., V.C., and K.L. analyzed the data and prepared the manuscript. B.P., J.Z., K.T., D.B., M.B., and L.V. executed the study. R.G. critically reviewed the manuscript and revised its contents.

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#### DISCLOSURE

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