



Brief Reports

AN IMPEDANCE THRESHOLD DEVICE INCREASES BLOOD PRESSURE IN HYPOTENSIVE PATIENTS

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Abstract—Background: The impedance threshold device (ITD-7) augments the vacuum created in the thorax with each inspiration, thereby enhancing blood flow from the extrathoracic venous systems into the heart. **Objectives:** To the best of our knowledge, the ITD-7 has not previously been investigated in hypotensive patients in the emergency department (ED) or the prehospital setting. The objective of this study was to determine whether the ITD-7 would increase systolic arterial pressures in hypotensive spontaneously breathing patients. **Methods:** The ED study was a prospective, randomized, double-blind, sham control design. Patients with a systolic blood pressure ≤ 95 mm Hg were randomized to breathe for 10 min through an active or sham ITD. The primary endpoint was the change in systolic blood pressure measured non-invasively. The prehospital study was a prospective, non-blinded evaluation of the ITD-7 in hypotensive patients. **Results:** In the ED study, the mean \pm standard deviation rise in systolic blood pressure was 12.9 ± 8.5 mm Hg for patients ($n = 16$) treated with an active ITD-7 vs. 5.9 ± 5.9 mm Hg for patients ($n = 18$) treated with a sham ITD-7 ($p < 0.01$). In the prehospital study, the mean systolic blood pressure before the ITD-7 was 79.4 ± 10.2 mm Hg and 107.3 ± 17.6 mm Hg during ITD-7 use ($n = 47$ patients) ($p < 0.01$). **Conclusion:** During this clinical evaluation of the ITD-7 for the treatment of hypotensive

patients in the ED and in the prehospital setting, use of the device significantly increased systolic blood pressure and was safe and generally well tolerated. © 2011 Elsevier Inc.

Keywords—hypotension; impedance threshold device; sepsis; dehydration; hemorrhage

INTRODUCTION

The impedance threshold device (ITD-7) is a small, disposable, multi-valve device that causes a low level (-7 cm H₂O) of inspiratory resistance (Figure 1). During spontaneous breathing, this inspiratory resistance augments the vacuum created in the thorax with each inspiration, thereby enhancing blood flow from the extrathoracic venous systems into the heart. This results in an increase in cardiac output. Inspiration through the ITD-7 also lowers intracranial pressure, thereby enhancing cerebral perfusion pressure (1,2). Previous clinical studies of similar types of devices have been performed in patients in cardiac arrest, patients suffering from orthostatic hypotension, in subjects after blood donation, and in patients during renal dialysis who suffer from significant intradialytic hypotension (3–8). These clinical studies have demonstrated the potential of this non-invasive device to treat hypotensive states. The ITD-7 has also been extensively evaluated in hypotensive volunteers subjected

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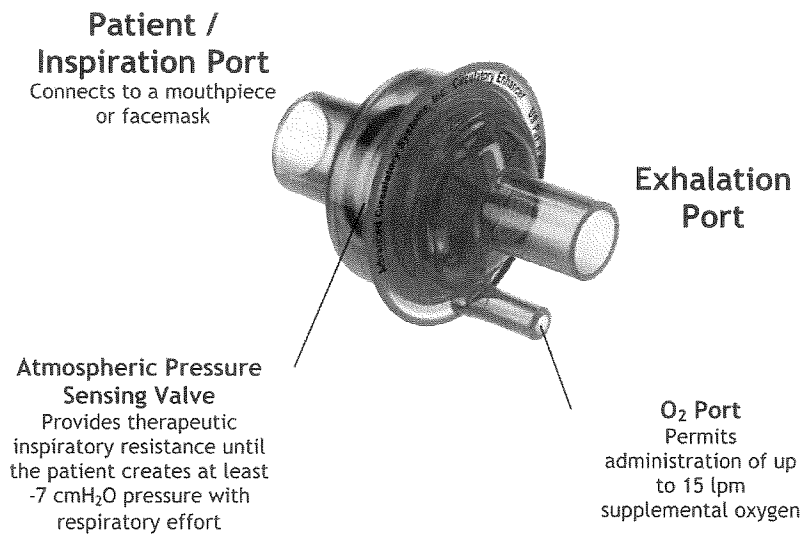


Figure 1. The Inspiratory Impedance Threshold Device (ITD-7). During the study the device was attached to a facemask or a mouthpiece.

to lower body negative pressure and in numerous animal models of hypotension (4,9–17). Building on those previous studies, this study tested the hypotheses that: 1) the ITD-7 would increase systolic blood pressure in hypotensive patients presenting to the emergency department (ED), without significant adverse events, and 2) the ITD-7 would be well tolerated, easy to apply, safe, and effective in the treatment of hypotensive patients in the prehospital setting.

MATERIALS AND METHODS

Study Design and Setting

The ED study was a prospective, double-blind, randomized clinical trial of an active vs. sham device and was performed in the ED of Hennepin County Medical Center in Minneapolis, MN, an inner-city Level I trauma center with 95,000 patient visits per year. The study was approved by the hospital's institutional review board (IRB) and the United States (US) Army Medical Research and Materiel Command Human Subjects Research Review Board, and informed consent was obtained for all patients before study enrollment.

The prehospital study was a prospective, non-blinded feasibility study designed to evaluate device tolerance, ease of use, and effectiveness when paired with standard intravenous fluid administration for hypotensive patients in an emergency medical services (EMS) setting. The prehospital study was performed in Lucas County, Toledo, OH, by Lucas County EMS providers, with approval by the Promedica IRB. There are eight advanced life support (ALS) ambulances in Lucas County, Toledo, OH, and the annual call volume is 57,000 runs.

Study Device

The ITD-7 (ResQGARD[®], Advanced Circulatory Systems, Inc.; Minneapolis, MN) is cleared for sale in the United States by the Food and Drug Administration (FDA) for the treatment of patients with low blood circulation. It is indicated for any patients with low blood circulation. It is contraindicated in patients with active congestive heart failure, dilatated cardiomyopathy, pulmonary hypertension, aortic stenosis, flail chest, chest pain, and shortness of breath. Some of the contraindications to the device (history of aortic stenosis, history of dilatated cardiomyopathy, and pulmonary hypertension) are not based upon clinical findings, but are due to a lack of data in these patient subgroups at the time the device was cleared for sale by the US FDA in 2003. The device used in the current investigation has an inspiratory resistance of -7 cm H₂O, dead space of 14 mL, weighs 34 grams, and can be used on either a facemask or mouthpiece. The ITD-7 also has a small port that allows caregivers to administer supplemental oxygen.

Population

For the ED study, inclusion criteria included patients with: 1) age 18 to 85 years, 2) conscious and able to pass an abbreviated mini-mental status examination before obtaining consent, 3) systolic blood pressure of ≤ 95 mm Hg, and 4) presumed cause of hypotension was hypovolemia or relative hypovolemia (e.g., blood loss, dehydration, or sepsis). Patients were excluded if they had: 1) occurrence of heart attack or stroke in the last 3 months, 2) history of dilatated cardiomyopathy,

3) unstable congestive heart failure, 4) pulmonary hypertension, 5) complaints of shortness of breath, 6) significant chest or face trauma, 7) aortic stenosis, 8) pneumothorax, 9) complaints of chest pain, 10) atrial fibrillation with an average ventricular response > 130 beats/min, and 11) known pregnancy.

For the prehospital study, the inclusion criteria for ITD-7 use included patient weight > 25 pounds, and systolic blood pressure < 100 mm Hg for adults and < 90 mm Hg for the pediatric population. Patients with hypotension secondary to dehydration, blood loss, sepsis, orthostatic hypotension, and those undergoing renal dialysis were treated. Exclusions to ITD-7 use were complaints of chest pain or shortness of breath, pulmonary hypertension, congestive heart failure, aortic stenosis, a history of dilated cardiomyopathy, or ongoing uncontrolled bleeding. Medics were told not to use the ITD-7 in patients with a primary complaint of difficulty breathing.

Emergency Department Study

The primary endpoint of the ED study was the maximum change in systolic blood pressure over the first 10 min of therapy. The secondary endpoints included the change in systolic blood pressure among those receiving no fluids, as well as change in heart rate, respiratory rate, quantity of fluid administration, change in transcutaneous oxygen saturation, device tolerance, and adverse events. Patients received the current standard of care for hypotension, including control of bleeding, reversal of other potential causes of hypotension such as administration of fluids or vasopressors, oxygen, blood products, and fever management as appropriate. Use of the ITD-7 did not interfere with standard therapy, and the treating physicians were not involved in the study.

Once eligibility for enrollment was established and informed consent was obtained, subjects were randomized according to a computer-generated randomization list to either a sham (non-functional placebo) ITD-7 or an active (functional) ITD-7 by a research assistant, study coordinator, or principal investigator. Sham and active ITD-7s appeared identical. Both devices were packaged with a facemask. The devices were kept in an opaque package, preventing anyone involved with the study from knowing whether any given device was a sham or active ITD-7 based upon visual inspection. Furthermore, sham and active devices could be differentiated only with close inspection and intimate knowledge of their differences. All faculty attending physicians were aware of the study, but they were not involved with use of the device and were not told when their patient was enrolled; they would know of the use of the device on their patient only if they entered the room during its use.

Before definitive enrollment, systolic blood pressure was measured and then verified again 2 min later. If both readings were ≤ 95 mm Hg, the patient was enrolled and the second reading was recorded as systolic blood pressure at time zero. Blood pressure was measured with an automatic cuff. Baseline blood pressure, heart rate, respiratory rate, and oxygen saturation were recorded just before ITD-7 application. The ITD-7 was then placed immediately after baseline measurements were made. The mask and device combination was typically held in place by an elastic headband (ResQStrap™; Advanced Circulatory Systems, Inc.) and the patients were instructed to breathe normally. Hemodynamic parameters, including systolic and diastolic blood pressure, heart rate, respiratory rate, and pulse oximetry, were assessed every 2 min for 10 min, then for 6 min after removal of the device. Standard therapies, including intravenous fluids and oxygen, were administered as intravenous access was obtained and as deemed clinically necessary, regardless of the effect of the ITD-7.

The change in systolic blood pressure from the baseline value to the maximum value during the time the ITD was applied was the primary study endpoint. We calculated that, to find a difference of 8 mm Hg in systolic pressure with 80% power at a two-tailed significance level of 0.05, and assuming a standard deviation of 16, we would need 50 patients in each group. We did not do a power analysis for mean arterial pressure or diastolic pressure because these were not the primary outcome measures. 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. Significance was set at a value of $p < 0.05$. Results are reported as means \pm standard deviation (SD) unless otherwise noted.

Prehospital Study

The goal of the prehospital study was to determine if the ITD-7 was feasible to use by EMS personnel on hypotensive patients. The main endpoints of the prehospital study were ITD-7 tolerance, ease of use, change in heart rate and systolic and diastolic blood pressure, and adverse events. Once patients were identified by basic life support (BLS) or ALS providers as having hypotension and they met device use criteria, they were treated with the ITD-7 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, or patient positioning as appropriate. Use of the ITD-7 did not interfere with or change the delivery of standard therapy. Physiological parameters were assessed before,

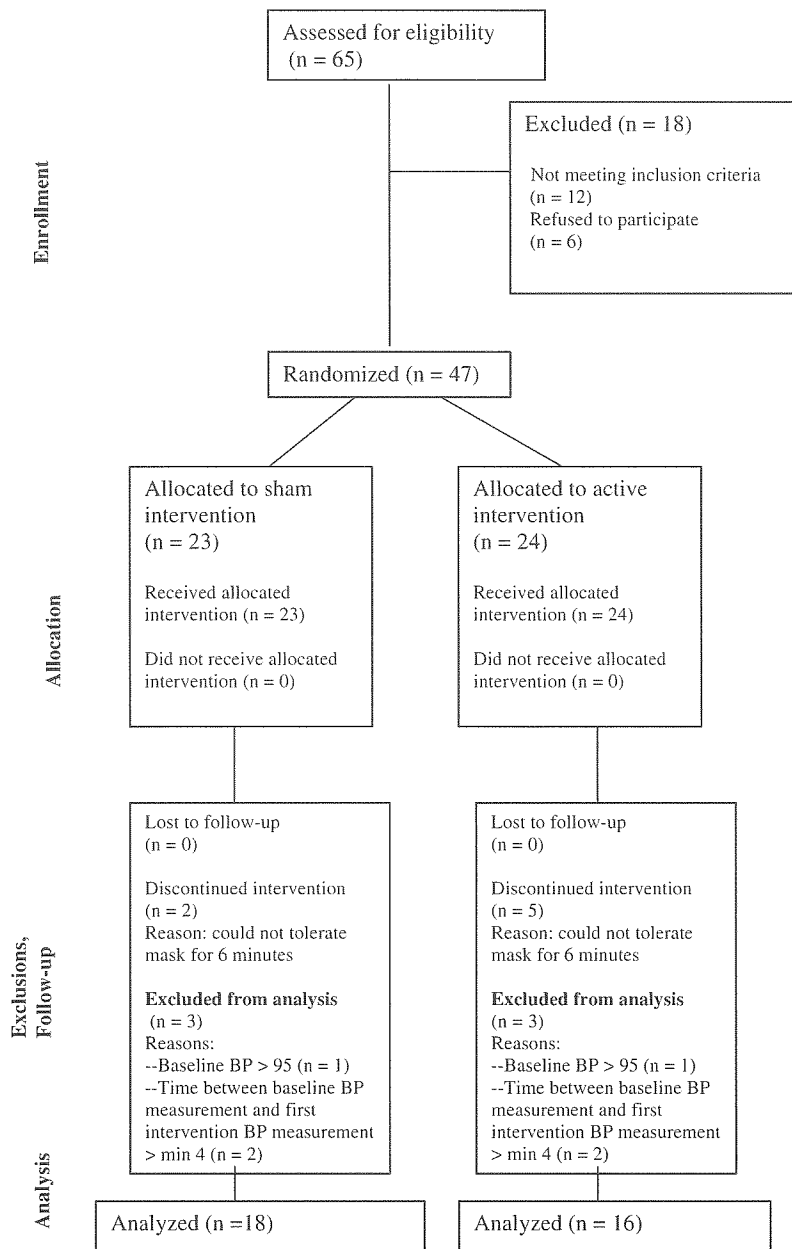


Figure 2. Subject enrollment flow chart.

during and after ITD-7 use as part of the standard clinical protocol. Similarly, administration of standard therapies such as intravenous fluid administration and oxygen were recorded and monitored.

To determine how well patients tolerated the ITD-7 and how comfortable it was for patients to wear, the paramedics completed a five-point Device Tolerance Index scale and five-point Device Comfort Index scale questionnaire after each use.

RESULTS

Emergency Department Study

A total of 47 patients were enrolled in the ED portion of the study. A flow diagram that details subject enrollment is shown in Figure 2. An interim analysis revealed that statistical significance was reached due to a lower standard deviation than originally hypothesized. An intention-to-treat

Table 1. Baseline Demographics for Each Treatment Group

	Sham (n = 18) Mean (SD)	Active (n = 16) Mean (SD)
Age (years)	50.4 (11.8)	49.9 (19.3)
% Male	39	38
Baseline SBP (mm Hg)	82.3 (8.4)	82.7 (9.1)
Baseline DBP (mm Hg)	44.9 (10.1)	43.1 (12.1)
Baseline MAP (mm Hg)	56.8 (8.6)	55.7 (10.1)
Baseline HR (beats/min)	78 (18)	79 (17)
Volume of fluids (mL) 30 min pre-device use	207 (288)	138 (261)
Volume of fluids (mL) During device use	175 (97)	92 (170)
Etiology of hypotension (n)	Sepsis: 3 Hemorrhage: 3 Dehydration: 11 Unspecified: 1	Sepsis: 7 Hemorrhage: 0 Dehydration: 6 Unspecified: 3

SD = standard deviation; SBP = systolic blood pressure; DBP = diastolic blood pressure; MAP = mean arterial pressure; HR = heart rate.

analysis was performed on 40 patients in whom sufficient data were collected for analysis. The mean (\pm SD) increase in systolic blood pressure from baseline to peak values was 13.0 ± 10.5 in the active group and 6.5 ± 6.4 in the sham group ($p = 0.02$). Differences in diastolic blood pressure and mean arterial pressure were not significant. Per protocol, 34 of these patients qualified for final inclusion in the study. A total of 13 patients were excluded due to device intolerance ($n = 7$) or because the device was not placed within 5 min of obtaining the study baseline, per protocol ($n = 6$). Therefore, a total of 16 patients were randomized to treatment with the active ITD-7 and 18 patients with the sham device. Table 1 summarizes the baseline demographics for each treatment group. The changes in systolic blood pressure based on the etiology of hypotension as well as the number of patients with each etiology are shown in Table 2.

The combined data demonstrated a significant difference in the rise in systolic blood pressure with active device use compared to sham device use; however, differences in diastolic blood pressure and mean arterial pressure were not significant. The mean rise in systolic blood pressure from baseline to peak values was 12.9 ± 8.5 mm Hg for patients treated with the active ITD-7

Table 2. Changes in Systolic Blood Pressure (SBP) (\pm SD) Dependent upon Etiology of Hypotension for Patients Treated in the Emergency Department

	Sham Rise in SBP \pm SD (mm Hg) (n)	Active Rise in SBP \pm SD (mm Hg) (n)	<i>p</i> -Value
Hemorrhage	7.7 ± 7.8 (3)	$n = 0$	NA
Dehydration	6.5 ± 6.3 (11)	12.7 ± 7.6 (6)	0.09
Sepsis	2.0 ± 2.6 (3)	10.7 ± 10.5 (7)	0.21
Undocumented	7.0 ± 0 (1)	18.7 ± 1.1 (3)	NS

SD = standard deviation.

vs. 5.9 ± 5.9 mm Hg for patients treated with the sham ITD-7 ($p = 0.009$). See Table 3 for ranges and means of initial, maximum, and delta systolic blood pressure values. The number of patients assigned to each etiology was insufficient to demonstrate a statistical significance between the active and sham devices based on etiology. The most common ED diagnosis was dehydration ($n = 17$), followed by sepsis ($n = 10$).

The mean time to achieve the maximum rise in systolic blood pressure was 6.1 min in the active group and 6.6 min in the sham group. Mean fluid volume given during device use was 93 ± 170 mL for the active ITD-7 and 175 ± 197 mL for the sham ITD-7 ($p = 0.20$). Results for several secondary endpoints including changes in diastolic blood pressure, heart rate, respiratory rate, oxygen saturation, and mean arterial pressure are summarized in Table 4.

In a sub-group of 18 patients who received no fluids during device use, the mean rise in systolic blood pressure was 12.3 ± 8.2 mm Hg for the active ITD ($n = 10$) vs. 5.1 ± 5.8 mm Hg for the sham ITD ($n = 8$, $p = 0.05$). The mean rise in mean arterial pressure was 7.9 ± 7.5 for the active ITD vs. 3.8 ± 3.8 for the sham ITD ($p = 0.18$). Five of 24 (21%) patients initiated in the active device group and 2 of 23 (9%) patients in the sham device group could not tolerate the device and it was immediately removed ($p = 0.42$). These patients complained of claustrophobia and difficulty breathing through the sham and active devices. There were no adverse events associated with ITD-7 use.

Prehospital Study

The ITD-7 was applied to 47 patients (21 males) with an average age of 62.8 ± 19.1 years. The ITD-7 was used on a mouthpiece six times and on a facemask 41 times. The mean duration of ITD-7 use was 17 ± 7 min, with a range from 6–31 min. In 46/47 patients, supplemental O₂ (range 1–15 L/min) was simultaneously administered through the ITD-7.

Figure 3 shows the results from the primary and secondary endpoints. The mean systolic pressure before and then during ITD-7 application in 47 patients was 79.4 ± 10.2 and 107.3 ± 17.6 , respectively ($p < 0.01$). Concomitant intravenous fluid administration was delivered to 40/47 patients.

Table 5 shows the results from the 7 patients in whom intravenous access was not established. The mean duration of ITD-7 use in these 7 patients was 19 ± 5.0 min. In these 7 patients without an intravenous line, systolic pressure before and then during ITD-7 use was 78.7 ± 12.2 and 98.8 ± 8.9 mm Hg, respectively ($p < 0.01$).

The vast majority of patients tolerated the device and found no significant discomfort. The mean Device Tolerance Index score was 0.7 ± 0.9 on a scale of 0 to 4, with 0 representing “not at all difficult to breathe through”

Table 3. Initial and Maximum Systolic Pressures, with Mean and Range of Systolic Blood Pressure (SBP) (mean \pm SD), for the Emergency Department Study

	Time 0		Maximum		Change	
	Range	Mean (\pm CI)	Range	Mean (\pm CI)	Range	Mean (\pm CI)
Sham	62–95	82.3 \pm 8.4	62–102	88.3 \pm 10.1	–4–16	5.9 \pm 5.9
Active	64–95	82.8 \pm 9.1	76–113	95.7 \pm 9.8	–4–26	12.9 \pm 8.5

SD = standard deviation; CI = confidence interval.

and 4 representing “unable to tolerate; device removed”. The mean Device Comfort Index as reported by the patient was 0.9 ± 0.9 on a scale of 0 to 4, with 0 representing “comfortable” and 4 representing “extremely uncomfortable.”

A total of 21 patients received intravenous 0.9% saline solution before ITD-7 application, 39 during ITD-7 application, and 31 after the device was removed. Volumes were difficult to calculate precisely but varied between 100 and 1000 mL. According to a questionnaire completed by the users, 94% of patients reported that the device made them feel better. A total of 28 of the medics reported that the device was easy to use; one medic reported difficulty in keeping the headstrap in place due to the subject’s long hair; one medic reported that the subject did not like the mask; and one medic reported difficulty in keeping a tight seal between the subject’s mouth and the facemask because the subject was talking.

DISCUSSION

This evaluation of the ITD-7 in patients in the ED and pre-hospital settings demonstrated that the device is safe and efficacious. The study showed that the therapy could be delivered rapidly in the ED and by BLS and ALS providers. Systolic blood pressure increased significantly with this non-invasive device, even in patients where intravenous access could not be achieved. The results demonstrate that hypotensive patients who are treated in the ED or by EMS personnel outside the hospital can inspire through a low level of resistance and harness the respiratory pump to significantly augment circulation, as measured indirectly by the change in systolic blood pressure.

Table 4. Comparisons of Secondary Endpoints from the Emergency Department Study for Active and Sham ITDs (mean \pm SD)

Endpoint	Active ITD Mean (SD)	Sham ITD Mean (SD)	<i>p</i> -Value
Increase in DBP (mm Hg)	6.2 \pm 9.8	4.0 \pm 3.8	0.39
Increase in HR (beats/min)	3.9 \pm 5.4	3.4 \pm 9.1	0.85
Respiratory rate (beats/min)	19.5 \pm 3.3	17.4 \pm 3.7	0.13
Oxygen saturation (%)	96.8 \pm 4.0	98.2 \pm 2.9	0.26
Increase in mean arterial pressure (mm Hg)	8.4 \pm 8.7	4.6 \pm 3.6	0.10

ITD = impedance threshold device; SD = standard deviation; DBP = diastolic blood pressure; HR = heart rate.

Combining both studies, 92% of patients (81/88) tolerated the device, which was also easy to implement and complementary to existing therapy. Whereas previous studies have demonstrated that the ITD-7 can be used in severely hypotensive animals and in relatively hypotensive or hypovolemic patients, this is the first application of the ITD-7 in patients presenting to the ED and prehospital setting in need of immediate therapy for hypotension (4,8,10–17).

The ED provided an excellent environment to evaluate whether the ITD-7 could be easily used to treat hypotensive patients, as it provided a well-controlled and monitored setting where it was possible to relatively rapidly obtain informed consent. The consent process did slow the application of the device and is a limitation of the results, as the potential benefit of the ITD-7 may have been greater if it could have been applied earlier. This study demonstrated that patients who received fluids as well as patients who could not receive intravenous fluids (as intravenous access was not yet available) had a significant rise in mean systolic blood pressure when the active ITD-7 was applied.

The large proportion of patients who did not receive intravenous fluids requires explanation. Patients who were clearly very ill were often treated so rapidly that the systolic blood pressure was restored to a safe level before study personnel could enroll many of these patients in the ED study. Patients who were hypotensive but did not appear to be too ill or who had more difficult intravenous access were less likely to receive rapid intravenous fluid administration. Thus, these patients were more likely to be identified for the study and have the time to be screened and enrolled in the study. The total number of potentially eligible patients during the time period is not known.

Building upon the results from the ED, the second part of this study demonstrated that use of the ITD-7 by EMS providers on hypotensive patients outside the hospital was practical and efficacious. The ITD-7 was used in a complementary manner with intravenous fluids and oxygen. In the 7 patients who did not receive intravenous access, ITD-7 use increased the systolic blood pressure by a mean of 20 mm Hg.

The ITD-7 was first studied in normal volunteers at the National Aeronautics and Space Administration (NASA) and the US Army Institute for Surgical Research in studies related to post-flight orthostatic hypotension (12,13).

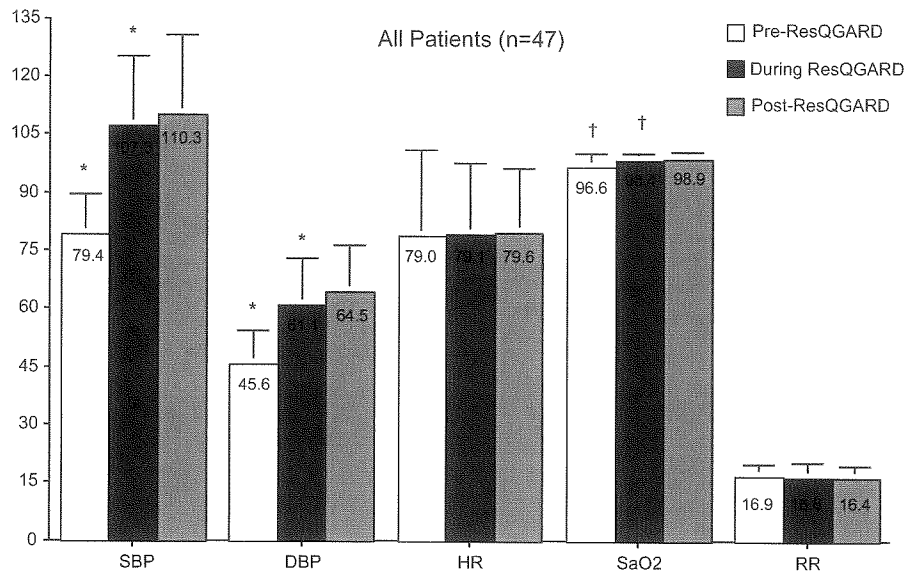


Figure 3. Primary and secondary endpoints from the prehospital portion of the study with data included from all 47 patients treated with the ITD-7. SBP = systolic blood pressure; DBP = diastolic; HR = heart rate; SaO₂ = oxygen saturation; RR = respiratory rate.

* $p < 0.001$.

† $p < 0.005$.

Inspiration through the ITD-7 increased cardiac output by approximately 1.5 L/min, was generally well tolerated, and decreased or prevented symptoms associated with transient hypotension. The ITD-7, compared to a placebo sham, has been shown to increase stroke volume and to maintain blood pressure in normal volunteers subjected to acute orthostatic stress, and also to enhance cerebral blood flow in patients with hypotension due to lower-body negative pressure (11,18). Use of the ITD-7 in animal and human studies results in an immediate increase in cardiac stroke volume, systolic blood pressure, diastolic pressure, and improved vital organ perfusion pressures (4,13,15–17). More recently, the ITD-7 has been shown to maintain perfusion pressures in the setting of severe hypotension associated with application of lower-body negative pressure in normal volunteers (14,19). The device can also prevent the decrease in blood pressure that can be associated with blood donations, and NASA has used the ITD-7 with oral fluids and fludrocortisone

to help maintain blood pressure in astronauts who develop low blood pressure upon exposure to gravity after prolonged space flight.

The current data demonstrate the relevance of the device to patients with hypotension and support the hypothesis that the hemodynamic benefits of the device demonstrated in normal volunteers can be translated to a hemodynamic benefit for hypotensive patients. From this perspective, the current data support the premise that the ITD-7 harnesses a natural extension of one of the most important normal physiological processes, the act of breathing. When a person inspires, the intrathoracic pressure decreases; this results in an increase in venous return (20). Additional negative intrathoracic pressure can be generated by breathing against a set level of resistance. The ITD-7 is a device that forces a person to breathe against a therapeutic level of resistance (equaling -7 cm H₂O when tested at a flow rate of 20 L/min); this augments the small vacuum created within the chest with

Table 5. Primary and Secondary Endpoints (mean \pm SD) from the Prehospital Study for the Seven Patients Treated with the ITD-7 for whom Intravenous Access Could Not Be or Was Not Obtained

	Pre-ResQGARD* Mean (\pm CI)	With ResQGARD Mean (\pm CI)	Post-ResQGARD Mean (\pm CI)
Systolic BP (mm Hg)	78.7 \pm 12.2	98.8 \pm 8.9	105.3 \pm 9.9
Diastolic BP (mm Hg)	47.8 \pm 10.8	65.0 \pm 7.5	65.3 \pm 9.6
Heart rate (beats/min)	88.5 \pm 15.5	85.6 \pm 13.6	84.7 \pm 12.4
Oxygen saturation (%)	88.0 \pm n/a	98.8 \pm 2.5	100.0 \pm 0.0
Respiratory rate (breaths/min)	16.8 \pm 1.1	18.0 \pm 4.2	13.7 \pm 3.2

ITD = impedance threshold device; CI = confidence interval; BP = blood pressure.

* ResQGARD[®]; Advanced Circulatory Systems, Inc., Minneapolis, MN.

each inspiration, thereby enhancing blood flow from the extrathoracic venous system into the heart with each breath (15,17,21,22). As such, the ITD-7 transforms the normal respiratory muscle function from a primary gas exchange function to the dual functions of gas exchange and augmentation of venous return as well as enhancement of cardiac stroke volume.

In order for the ITD-7 to be clinically useful, the effort required to breathe through the device needs to be acceptable. In a study of 19 healthy, normotensive volunteers, Idris et al. previously determined that although the effort or power required to breathe through the ITD-7 was significantly higher than breathing through a sham device, all subjects were able to tolerate the respiratory work load (23). This was confirmed in the current ED and prehospital study, as most hypotensive patients tolerated the ITD-7 well. Those who did not primarily complained about feeling claustrophobic, which may have been at least partly the result of the presence of the facemask, rather than the resistance of the active ITD-7. When both the ED portion of this study and the prehospital data were combined, a total of 83 hypotensive patients (92%) tolerated the active ITD-7.

Limitations

The study has several limitations. First, the etiology of hypotension was heterogeneous, so it is unknown if patients with hypotension from one cause, for example, early sepsis, may benefit more or less from the device than other patients with hypotension from a different cause. Second, unlike many hypotensive patients, the study population in the ED portion of this study was required to be relatively alert, pass a mini-mental status examination, and give consent. That process took approximately 10 min and, as such, the sickest patients were excluded from this study. On the other hand, the patients treated by the EMS providers in the field were treated with the ITD-7 as part of their standard protocol, and many of these patients were quite sick and hypotensive. Some of these patients used the ITD-7 for up to 30 min, per the standard protocol, without difficulties. Third, the ITD-7 was not applied sequentially to all patients presenting to the ED who met study entry criteria; research personnel had to be available. However, because the study was randomized and blinded, this limitation is unlikely to affect the study outcomes. For the prehospital study, the ITD-7 was applied sequentially but in some cases was not used, as intravenous fluid therapy by itself resulted in a rapid resolution of symptoms and measurable hypotension. We did not power the study to show a difference in mean arterial or diastolic pressures. Finally, although there was no statistical difference in patient tolerance of the ITD-7 in the ED portion of the study

between active (21% intolerant) and sham (9% intolerant) groups, there was not enough power to detect a difference. The vast majority of patients in the ED and prehospital setting tolerated the ITD-7; there were no adverse events, and patients could easily and quickly remove the device. Despite these limitations, the study demonstrated that ITD use in the ED and prehospital settings increases systolic blood pressure and is safe and well tolerated by most patients. As such, the device was found to safely provide complementary therapy to rapidly increase circulation and blood pressure until more definitive therapy, if needed, is available. It is important to emphasize that there are certain contraindications for the ITD-7; most importantly, that it should not be used in patients who are having difficulty breathing.

CONCLUSIONS

During this clinical trial of the ITD-7 in hypotensive patients in the ED and prehospital settings, use of the device significantly increased systolic and mean arterial blood pressures in hypotensive patients, was safe and efficacious, and generally well tolerated.

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ARTICLE SUMMARY

1. Why is this topic important?

The clinical studies are the first to evaluate the impedance threshold device in the emergency department (ED) and prehospital setting to evaluate the clinical benefit of this non-invasive device.

2. What does this study attempt to show?

These studies attempt to show that the impedance threshold device can be used to safely and effectively increase systolic blood pressures in hypotensive patients presenting to the ED or in the prehospital setting.

3. What are the key findings?

These studies show that the device can be used to treat hypotension and is effective in increasing blood pressures with and without concurrent use of fluids.

4. How is patient care impacted?

When intravenous access is difficult or not immediately available, patients can be given the impedance threshold device to breathe through to increase blood pressures as required. The device is non-invasive, easy to use, and tolerated by most patients.