Promoting early diagnosis of hemodynamic instability during simulated hemorrhage with the use of a real-time decision-assist algorithm

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BACKGROUND: This study aimed to test the hypothesis that the addition of a real-time decision-assist machine learning algorithm by emergency medical system personnel could shorten the time needed to identify an unstable patient during a hemorrhage profile as compared with vital sign information alone.

METHODS: Fifty emergency medical team-paramedics from a large, urban fire department participated as subjects. Subjects viewed a monitor screen on two occasions as follows: (1) display of standard vital signs alone and (2) with the addition of an index (Compensatory Reserve Index) associated with estimated central blood volume status. The subjects were asked to push a computer key at any point in the sequence they believed the patient had become unstable based on information provided by the monitor screen. The average difference in time to identify hemodynamic instability between experimental and control groups was assessed by paired, two-tailed *t* test and reported with 95% confidence intervals (95% CI).

RESULTS: The mean (SD) amount of time required to identify an unstable patient was 18.3 (4.1) minutes (95% CI, 17.2–19.4 minutes) without the algorithm and 10.7 (4.2) minutes (95% CI, 9.5–11.9 minutes) with the algorithm ($p < 0.001$).

CONCLUSION: In a simulated patient encounter involving uncontrolled hemorrhage, the use of a monitor that estimates central blood volume loss was associated with early identification of impending hemodynamic instability. Physiologic monitors capable of early identification and estimation of the physiologic capacity to compensate for blood loss during hemorrhage may enable optimal guidance for hypotensive resuscitation. They may also help identify casualties benefitting from forward administration of plasma, antifibrinolytics and procoagulants in a remote damage-control resuscitation model. (*J Trauma Acute Care Surg*. 2013;75: S184–S189. Copyright © 2013 by Lippincott Williams & Wilkins)

KEY WORDS: Medical monitoring; vital signs; hemorrhagic shock.

Current out-of-hospital clinical operating guidelines in civilian trauma systems and in military casualty care rely on standard vital signs (blood pressure, arterial oxygen saturation, heart rate [HR], respiration), for patient assessment and monitoring. These vital signs have proven to provide little forewarning in detecting the need to implement an intervention before hemodynamic decompensation or onset of hemorrhagic shock.[1] As such, greater than 20% of trauma patients with "normal vital signs" progress to require a lifesaving intervention.[2] This observation is most likely the result of complex compensatory physiologic mechanisms that are acting to maintain blood pressure and arterial oxygen saturation (i.e., standard vital signs are not changing) in the presence of reduced circulatory blood volume or tissue hypoperfusion.[1,3] However, once hemodynamic decompensation and circulatory shock occur, standard vital signs do become abnormal and are indicative of outcome rather than predictive of impending cardiovascular collapse. As such, current patient monitors used in emergency care cannot accurately assess the need for rapid intervention because they present measurements of outcome variables that change late and subsequently fail to provide early markers of progressive deterioration of the patient.[4]

The ability to construct an algorithm for accurate prediction of the magnitude and/or rate of progressive blood loss during the preshock phase of hemorrhage would require the accumulation of large volumes of data obtained from the study of severe hemorrhage in humans. Since such experiments are not ethically possible, we have developed a model for simulating ongoing hemorrhage in humans using lower-body negative-pressure (LBNP) that reduces central blood volume. We have conducted numerous experiments demonstrating that application of negative pressure to the lower body redistributes blood away from the cerebral and cardiac circulations, providing a unique method to progressively reduce central blood volume that results in similar hemodynamic, autonomic, and metabolic responses to those that occur during the early compensatory stage of hemorrhage.[5] LBNP is designed to

Submitted: October 15, 2012, Revised: November 27, 2012, Accepted: April 1, 2013.

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This study was conducted under a protocol reviewed and approved by the Institutional Review Board, Office of Research Protection, Medical Research and Materiel Command, and in accordance with the approved protocol.

The opinions or assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the Department of the Army or the Department of Defense.

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DOI: 10.1097/TA.0b013e31829b01db

Report Documentation Page

Form Approved
OMB No. 0704-0188

1. REPORT DATE	2. REPORT TYPE	3. DATES COVERED
01 AUG 2013	**N/A**	**-**

4. TITLE AND SUBTITLE	5a. CONTRACT NUMBER
Promoting early diagnosis of hemodynamic instability during simulated hemorrhage with the use of a real-time decision-assist algorithm.	5b. GRANT NUMBER
	5c. PROGRAM ELEMENT NUMBER
6. AUTHOR(S)	5d. PROJECT NUMBER
Muniz G. W., Wampler D. A., Manifold C. A., Grudic G. Z., Mulligan J., Moulton S. L., Gerhardt R. T., Convertino V. A.,	5e. TASK NUMBER
	5f. WORK UNIT NUMBER
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)	8. PERFORMING ORGANIZATION REPORT NUMBER
United States Army Institute of Surgical Research, JBSA Fort Sam Houston, TX	
9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)	10. SPONSOR/MONITOR'S ACRONYM(S)
	11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION/AVAILABILITY STATEMENT
Approved for public release, distribution unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

15. SUBJECT TERMS

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			
unclassified	**unclassified**	**unclassified**	**UU**	**6**	

extend and verify the utility of continuous recordings of both standard and novel vital signs that cannot be easily obtained from trauma patients because of the extreme difficulties associated with clinical assessments in austere environments. Profiles of changes in mean arterial pressure (MAP), cardiac output, and venous oxygen saturation during LBNP have been validated using a computer model that contained more than 4,000 parameters with detailed integration of physiologic responses in hemorrhaging patients.[6] Using this human model, we developed a database with multiple, continuous physiologic measurements in more than 200 subjects who have experienced progressive reductions in central blood volume leading to hemodynamic decompensation, that is, a precipitous decrease in systolic blood pressure (SBP) of less than 90 mm Hg concurrent with the onset of presyncopal symptoms such as bradycardia, gray-out (loss of color vision), tunnel vision, sweating, nausea, or dizziness. Using data sets from these subjects, a machine-learning algorithm has been developed that continuously integrates complex changes in the features of arterial wave forms into a single function that tracks the real-time reduction in central blood volume.[7] The Compensatory Reserve Index (CRI) algorithm analyzes and compares the entirety of each pulse wave form in a window of time to trend wave form features that are indicative of central volume loss caused by bleeding or dehydration, well before a subject experiences the symptoms of cardiovascular instability. Such pulse wave forms can be easily obtained in austere prehospital environments from a photoplethysmogram generated by a finger blood pressure cuff or a simple pulse oximeter.[8] This absolute reserve capacity or CRI differs significantly among individuals.[7] Thus, the objective of the present investigation was to test the hypothesis that use of a real-time decision-assist algorithm (CRI) by personnel of an emergency medical system (EMS) could shorten the time needed to identify an unstable patient during a simulated hemorrhage when compared with using only standard vital sign information.

PATIENTS AND METHODS

Subjects and Ethical Approval

Sixty-five individuals with training in prehospital care (e.g., paramedics, first responders) from the San Antonio Fire Department EMS Division were recruited to participate in this study. Subjects received a verbal briefing and written descriptions of all procedures and risks associated with the study and were made familiar with the protocol and procedures. Subjects were encouraged to ask questions of the investigators and then gave their written informed consent to participate in the study.

Experimental Protocol

Each EMS subject was provided a monitor to display continuous vital signs derived from an LBNP experimental subject to assist in determining the patient's management. The vital signs included electrocardiogram; SBP, diastolic blood pressure (DBP), and mean arterial blood pressures (MAPs), respiratory rate (RR), oxygen saturation (SpO_2), and end-tidal CO_2 measurements. Each subject received the following brief:

"You are functioning as an emergency care provider and are called upon to evaluate an individual who has just been injured in a motor vehicle crash at highway speed. Your patient was driving through an intersection across town when he was struck on the driver's side door of his vehicle by another driver, who had not noticed a red stoplight. The victim was appropriately restrained by his safety belt. There was no frontal airbag deployment; his vehicle was not equipped with a side airbag. A 20-inch driver's side door incursion was noted; however, there was no rollover, and extrication was accomplished within 10 minutes through the driver's side of the vehicle. There was no loss of consciousness. At the scene, the patient was alert and awake, mildly anxious, and complaining of moderate-to-severe left-sided lower chest wall pain. He was not diaphoretic, and capillary refill was brisk. His clinical examination results was as follows: no apparent head injury; respiration minimally labored secondary to left-sided chest pain; Best Motor Response of 5; airway patent, no hoarseness; breathing: trachea midline, contusion (bruise), left lower rib margin/left upper quadrant body wall, notable splinting on left, equal breath sounds bilaterally; tenderness over lower left chest/upper abdominal wall; circulation capillary refill of less than 2 seconds; radial and pedal pulse character strong/regular; pupils equal, round, reactive to light and accommodation. The patient is placed in a cervical spine collar and immobilized on a rigid spine board. No supplemental oxygen is administered, and he is monitored with 3-lead telemetry, blood pressure via automatic cuff, pulse oximetry, and capnography."

Each EMS subject was instructed to push the "play" computer key to initiate the monitoring process. After initiation of the patient profile, the EMS subjects watched the monitor to observe and evaluate the patient's status. The EMS subjects were instructed to respond to the decision-support information provided on the screen by pushing the "pause" computer key only if there was an indication from the monitor that led them to believe that the patient's condition was becoming unstable. Finally, the EMS subjects were instructed that they may be observing the vital signs of a patient who may remain stable through the demonstration (i.e., observing the control experimental condition). Most of the EMS subjects received a patient profile of a patient that was bleeding because of the vehicle accident (n = 50). A group of EMS subjects acted as a control group (n = 15) with a profile of a patient without blood loss.

As part of their decision support, the EMS subjects were provided the following guidelines as ranges of "normal" vital signs: HR (60–100 beats/min), RR (10–20 breaths/min), Spo_2 (>94%), $ETco_2$ (30–50%), SBP (100–150 mm Hg), and DBP (60–90 mm Hg).

Each EMS subject observed the vital sign data placed on the computer screen that was set up as a standard medical monitor (Fig. 1). The physiologic profile presented on the computer screen was that of an individual LBNP subject profile that represented a progressive reduction in central blood volume (experimental condition 1) or no change in central blood volume (control condition 1). The EMS subjects were then provided a monitor screen that displayed the same simulated hemorrhage profile with the addition of a decision-support algorithm.[8] The algorithm displayed a digital and color bar index (CRI) that was designed to estimate real-time tracking of

Figure 1. Monitor screen with display of continuous electrocardiogram; systolic (*SYS*), diastolic (*DIA*), and mean (*MAP*) arterial blood pressures; respiration (*RESP*); arterial oxygen saturation (Spo_2); and end-tidal CO_2 ($ETco_2$) used by EMS experimental subject to assist in determining the patient's management. Running clock time appears in the upper left corner of the screen.

central blood volume status of the patient (Fig. 2). The same LBNP subject profile was used for both tests with and without the CRI algorithm in an effort to eliminate interprofile variability. However, in an effort to minimize bias resulting from the observation of the same profile in two consecutive tests, each EMS subject (1) was told that each profile might be that of a different patient and (2) repeated the same profile test without the CRI algorithm a third time just after the test with the CRI algorithm. A member of the research team then read the following to describe the decision-support algorithm:

"Your monitor will now provide additional information about the status of your patient in the form of a color-changing "bar." This bar will function similar to a gas gauge in an automobile with the color and scale (1 to 0) of the bar changing as the tank empties. There will also be an arrow located at the top of the bar. This arrow will indicate the direction the bar is moving. A downward pointing direction in the arrow and movement of the bar represents bleeding or blood loss (emptying the "tank"). The bar displays 3 colors—green, yellow, and red—and will automatically change in color as the bar drops. Green, blood volume (the tank) is at a good level. Yellow, blood volume (the tank) is at a poor level. Red, blood volume (the tank) is at a critical level. This change to red can be thought of as similar to the indicator light on many gas gauges, indicating that the tank is almost empty. The bottom of the bar (scale = 0) represents the point at which the patient is predicted to become unstable; in other words, to clinically 'crash.' The patient will be in shock if the red bar reaches the bottom."

Each EMS subject was instructed by a member of the investigation team to initiate the start of the protocol by pressing a "play" button on the computer screen, and the vital sign data and/or decision-support algorithm was observed in real time on the monitor. Each EMS subject was instructed to press a specific key on the computer keyboard at the point in time that they observed a change in one or more vital signs that would indicate the need for initiating a medical intervention and to record the vital sign(s) that were used in their decision. A questionnaire was provided to each EMS subject to document the clinical criteria (i.e., vital signs, algorithm), the relative importance of the clinical criteria (on a scale of 1 [low] to 5[high]), and the threshold value (e.g., HR > 90) used to identify an unstable patient. As such, the time from the initiation of the protocol to the indication of an unstable patient was the primary outcome variable in the study, while clinical metrics were secondary outcome variables.

Statistical Analysis

A *t* test statistic for paired measures and 95% confidence intervals (95% CIs) were used to compare the total elapsed decision time between the no-algorithm condition and the total elapsed decision time of the algorithm condition for both experimental and control subject groups. All data are expressed as mean (SD) or 95% CI.

RESULTS

The years of emergency medical experience of the EMS subjects was 13.1 (8.3) years for the experimental group compared with 13.5 (8.1) years for the control group.

The total computer simulation run time for the control (no change in patient status) and experimental (point of hemodynamic decompensation with reduction in SBP from 130 to 69 in approximately 30 seconds) conditions was 22.3 minutes. The mean (SD) time required by the control group patient profile was 20.2 (3.6) minutes without and 21.3 (2.3) minutes with the decision-support algorithm ($p = 0.10$). The mean (SD) time required by the EMS subjects in the experimental group (i.e., observed a simulated hemorrhage profile) to identify an unstable patient was reduced ($p < 0.001$) by more than 40% from 18.3 (4.1) minutes (95% CI, 17.2–19.4) when vital signs alone were used, compared with 10.7 (4.2) minutes (95% CI, 9.5–11.9) when the algorithm was added to the vital sign information. The mean (SD) time to identify an unstable patient returned to 18.1 (2.9) minutes when the EMS subjects in the experimental group returned to the use of vital signs only after becoming familiar with the algorithm.

Table 1 provides the average values for each standard vital sign for the CRI and no-CRI experimental conditions at the average time that the EMS subjects identified their patient as being unstable. There were no statistical differences between the CRI and no-CRI experimental conditions for SBP, DBP, MAP, Spo_2, and $ETco_2$. At the time that the patient was identified as unstable, average HR was higher, and RR was lower in the no-CRI condition compared with the CRI condition. The average CRI value was 0.6 (yellow bar threshold) when the EMS subjects identified their patient as unstable in the presence of the color bar algorithm (Table 1, last line). With lower HR and higher RR, the CRI was the distinguishing factor associated with earlier identification of an unstable patient. The average relative importance of the clinical criteria (i.e., vital signs, CRI algorithm) and the threshold value (e.g., HR > 90) used to identify an unstable patient are presented in Table 2. Without availability of the CRI algorithm, RR, HR, and $ETco_2$

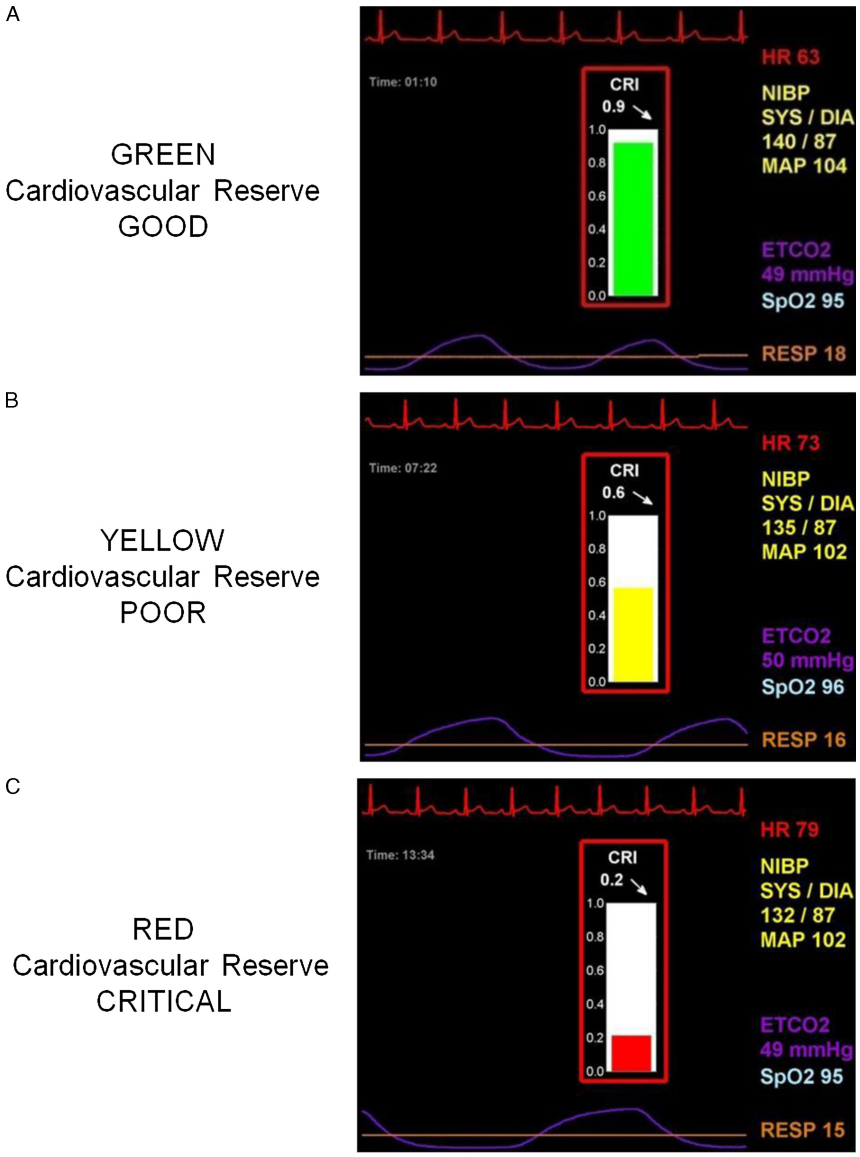

Figure 2. Monitor screens with display of the CRI algorithm in the form of a color-changing bar. The bar displays green when the reserve for compensation to reduced central blood volume is at a good level (*A*), yellow when the reserve is at a poor level (*B*), and red when the reserve is at a critical level (*C*). Note that all standard vital signs have remained virtually unchanged associated with the use of the physiologic reserve to compensate.

were identified by the EMS subjects as being the most prevalent vital signs used to assist them in determining the status of the patient. When the subjects were provided the CRI in addition to standard vital signs, the CRI became the most prevalent factor for all EMS subjects (100%) in their assessment of the stability of the patient, with the highest significance score for the CRI experimental condition.

DISCUSSION

The primary objective of the present investigation was to test the hypothesis that a machine-learning algorithm (the CRI) capable of continuously interpreting physiologic signals that reflect compensatory responses to hemorrhage would result in earlier identification of unstable patients. Our data support this hypothesis by demonstrating more than 40% reduction in the time to recognize an unstable patient, while a control group who observed a stable patient profile displayed no alteration in total assessment time with and without the CRI. These results provide the first compelling evidence that continuous, high-speed, computer-based interrogation of changes in arterial wave form features can reveal compensatory mechanisms that reflect ongoing hemorrhage in the absence of alterations in standard vital signs.

One limitation of our experimental design was the absence of a randomized, counterbalanced order of experimental conditions. We purposely chose to test EMS subjects by testing their triage decision in a set order with the non-CRI condition

TABLE 1. The Values for Standard Vital Signs at the Time of Identification of an Unstable Patient for the Two Experimental Conditions: (1) No CRI and (2) With CRI

	No CRI	CRI	Final Collapse Point
Stop time	**18:26 min**	**10:47 min**	**23:27 min**
HR, beats/min	90	70	101
SBP, mm Hg	130	138	69
DBP, mm Hg	89	88	45
MAP, mm Hg	102	104	53
Spo_2, %	96	95	95
RR, breaths/min	10	15	11
$ETco_2$, %	50	48	47
CRI	NA	0.6	NA

Far right column presents the standard vital signs at the time of hemodynamic decompensation (i.e., early decompensatory shock).

always preceding the CRI experimental condition because of our concern that if the CRI was seen first, this might bias the subsequent triage decision without the benefit of the machine-learning algorithm. We subsequently used three strategies to assess the probability that there was an "order" effect. First, all EMS subjects were instructed that each patient profile could be different, with one profile being that of a "stable" patient. Second, if there were an order effect, we might have expected the post-CRI condition to result in significantly less time for determination of an unstable patient. In contrast, the average time for determining an unstable patient was similar (18.3 minutes vs. 18.1 minutes), suggesting that observing the order of CRI presentation did not bias the time outcomes. Finally, our experimental design included a "true" control group of EMS subjects who were shown a stable patient profile in which vital signs and the CRI did not change to assess whether EMS subjects were not stopping the clinical profile based on a bias perception they anticipated having a sick patient. This premise was supported by the observation that 11 of the 15 control subjects allowed the clinical profile to complete its entire time course (22.33 minutes) without intervening both without and with use of the CRI. Interestingly, the remaining four control subjects indicated an unstable patient by intervening at an mean (SD) time of 14.5 (0.4) minutes when they did not have the CRI as part of their decision support compared with 18.4 (3.1) minutes when the CRI was used. These results suggest that for these four subjects, the CRI machine-learning algorithm contributed to a more accurate assessment of a stable patient, reducing the temptation to overtriage. Taken together, these results indicate that the significant reduction in time to identification of an unstable patient in this study was caused by the improved decision-assist capability provided by the CRI, rather than any bias resulting from order effects.

When the EMS subjects did not have use of the CRI, the identification of an unstable patient at approximately 18.5 minutes was associated with an elevated HR (90 beats/min) and a slowing of respiration (approximately 10 breaths/min) (Table 1). This observation is consistent with the evaluation made by the EMS subjects who on average scored HR and RR in addition to $ETco_2$ as the most "important" vital signs influencing their decision making for identifying when the patient became unstable (Table 2). Although changes in these vital signs were at a point in time in which blood pressures, Spo_2, and $ETco_2$ remained within normal clinical values, identification of an unstable patient came only 4 minutes before decompensation of the patient (Table 1). In contrast, use of the CRI as the most influencing decision-support tool dramatically decreased the time for identification of cardiovascular instability by more than 40%.

Although we provided the subjects with a description of the CRI before the profile testing, we purposely chose not to provide formal training that would include the instruction they stop the profile when the color bar changed from green to yellow (approximately 7.5 minutes). Although such instruction would have resulted in an additional 3 minutes for earlier patient intervention, the results of this investigation demonstrate the ease of training and implementation of advanced machine-learning algorithms into prehospital medicine for identification of patients who require early lifesaving intervention for treatment of undiagnosed hemorrhage.

Although most of our EMS subjects used some combination of the vital signs available to them on the monitor screen (Fig. 1), our analysis of the relative importance of each vital sign (Table 2) revealed that prehospital emergency care professionals are trained to pay close attention to changes in

TABLE 2. The Clinical Criteria (i.e., Vital Signs, Algorithm), Their Relative Importance Based on a Scale of 1 (Low) to 5 (High), and the Percentage of EMS Subjects Who Used Specific Clinical Criteria to Identify an Unstable Patient During the Three Experimental Conditions

	Decision-Support Monitoring Before Use of CRI			Decision-Support Monitoring With Use of CRI			After Decision-Support Monitoring Without Use of CRI		
Vital Signs	**Mean**	**SD**	**Percentage**	**Mean**	**SD**	**Percentage**	**Mean**	**SD**	**Percentage**
ECG	4.25	0.96	9.1	1.00	0.00	2.3	0.00	0.00	0.0
HR	3.93	0.83	61.4	4.11	1.20	43.2	4.18	0.98	73.3
SBP	4.29	0.77	38.6	4.57	0.53	15.9	4.00	0.89	40.0
DBP	4.29	0.77	38.6	4.57	0.53	15.9	4.20	0.84	33.3
Spo_2	4.11	0.78	20.5	4.00	1.00	6.8	4.00	0.00	13.3
RR	4.74	0.58	70.5	4.13	1.13	18.2	4.93	0.26	100.0
$ETco_2$	4.15	1.08	59.1	3.67	0.78	27.3	4.43	0.53	46.7
CRI	—	—	—	4.75	0.53	100.0	—	—	—

Values are mean (SD).

respiration patterns during their clinical assessment of their patients. The finding that the average time for identification of an unstable patient in the present study with an emphasis on the use of respiratory patterns was relatively late in the progression toward hemodynamic decompensation is consistent with experimental data from humans undergoing simulated hemorrhage, which reveal that significant alterations in respiration do not occur until more than 40% reduction in central blood volume.[9]

CONCLUSION

We tested the hypothesis that a machine-learning algorithm designed to continuously interrogate changes in the features of pulse wave forms can provide EMS paramedics a user-friendly advanced decision-assist tool for early identification of an unstable patient. Our results support this hypothesis by demonstrating that the time required to identify a patient with hemodynamic instability was reduced by more than 40% when the monitor screen included a continuous display of an index (i.e., CRI) that reflected the hemorrhagic status of the patient, even in the absence of alterations in standard vital signs. Early accurate diagnosis and application of effective lifesaving interventions are associated with lower morbidity and mortality[10,11] specifically in combat casualties.[12–16] Although it is unclear if a 40% reduction in time will translate to clinical significance, our results provide inferential evidence that the use of an algorithm similar to the CRI medical monitor as an adjunctive decision-support tool to standard vital signs could lead to improved outcomes, particularly in prehospital emergency care settings that involve patients with hemorrhage. Physiologic monitors capable of early identification and estimation of the physiologic capacity to compensate for blood loss during hemorrhage may also enable optimal guidance for hypotensive resuscitation[8] as well as identify casualties benefitting from forward administration of plasma, antifibrinolytics and procoagulants in a remote damage-control resuscitation model.

AUTHORSHIP

G.W.M and V.A.C collected and analyzed the data, and all authors assisted in the design, interpretation, and writing of this article.

ACKNOWLEDGMENT

We thank the men and women of the San Antonio Fire Department paramedics for their cheerful participation and input, as well as the University of Texas Health Sciences Center for allowing us the use of their classroom facilities.

DISCLOSURE

This research was supported in part by funding from the US Army Medical Research and Materiel Command Combat Casualty Research Program and the Small Business Innovative Research program. Drs. Grudic and Mulligan are developers of the CRI model used in this study. Dr. Moulton is a cofounder and medical consultant to Flashback Technologies Inc. The other authors have disclosed no conflicts of interest.

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