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Are you bleeding? Validation of a machine-learning algorithm for determination of blood volume status: application to remote triage

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Rickards CA, Vyas N, Ryan KL, Ward KR, Andre D, Hurst GM, Barrera CR, Convertino VA. Are you bleeding? Validation of a machine-learning algorithm for determination of blood volume status: application to remote triage. *J Appl Physiol* 116: 486–494, 2014. First published January 9, 2014; doi:10.1152/japplphysiol.00012.2013.—Due to limited remote triage monitoring capabilities, combat medics cannot currently distinguish bleeding soldiers from those engaged in combat unless they have physical access to them. The purpose of this study was to test the hypothesis that low-level physiological signals can be used to develop a machine-learning algorithm for tracking changes in central blood volume that will subsequently distinguish central hypovolemia from physical activity. Twenty-four subjects underwent central hypovolemia via lower body negative pressure (LBNP), and a supine-cycle exercise protocol. Exercise workloads were determined by matching heart rate responses from each LBNP level. Heart rate and stroke volume (SV) were measured via Finometer. ECG, heat flux, skin temperature, galvanic skin response, and two-axis acceleration were obtained from an armband (SenseWear Pro2) and used to develop a machine-learning algorithm to predict changes in SV as an index of central blood volume under both conditions. The algorithm SV was retrospectively compared against Finometer SV. A model was developed to determine whether unknown data points could be correctly classified into these two conditions using leave-one-out cross-validation. Algorithm vs. Finometer SV values were strongly correlated for LBNP in individual subjects (mean $r = 0.92$; range 0.75–0.98), but only moderately correlated for exercise (mean $r = 0.50$; range −0.23–0.87). From the first level of LBNP/exercise, the machine-learning algorithm was able to distinguish between LBNP and exercise with high accuracy, sensitivity, and specificity (all ≥90%). In conclusion, a machine-learning algorithm developed from low-level physiological signals could reliably distinguish central hypovolemia from exercise, indicating that this device could provide battlefield remote triage capabilities.

triage algorithm; lower body negative pressure; exercise; central hypovolemia

RECENT DATA INDICATE THAT 80% of potentially survivable battlefield injuries were due to hemorrhage from major trauma (15), consistent with reports of previous studies in this population (14, 17, 20). These findings highlight the requirement to improve clinical training and monitoring technologies in the prehospital setting to ensure early and accurate detection and treatment of life-threatening hemorrhage. Extensive investigations have been conducted to determine the early physiological responses to hemorrhage to develop advanced monitoring technologies for prehospital battlefield use by the first responder combat medic (6, 8). One area of particular focus has been on the development of monitoring techniques for "remote triage" applications (10, 22, 24), where the medic does not have physical and/or visual access to the injured patient.

Since monitoring capabilities have not yet been developed for accurate clinical assessment of injuries in these remote battlefield settings, combat medics cannot currently distinguish a wounded and bleeding soldier from a soldier who is engaged in combat. Furthermore, current medical monitors do not provide adequate information for accurate determination of injury severity, even if the medic does have physical access to the patient (8). Our laboratory has previously shown that many vital signs, both standard [e.g., heart rate (HR), respiration rate] and derived (e.g., HR variability), lack the specificity required to distinguish a bleeding soldier from one who is physically active, as both conditions elicit similar physiological responses (e.g., increases in HR and decreases in HR variability) (22, 24). A measure of blood volume status, however, will be able to distinguish between these two conditions, as central blood volume increases with exercise and decreases during hemorrhage (22).

Our laboratory recently reviewed the current status of "remote triage" applications for monitoring hemorrhaging patients in the military setting (24). In this review, preliminary data were presented on a novel technology that incorporates a machine-learning algorithm for the assessment of central blood volume via pulse pressure [a noninvasive surrogate of stroke volume (SV)]. These data demonstrated the ability of the algorithm to track a physiological feature associated with alterations in central blood volume (i.e., pulse pressure) induced by progressive lower body negative pressure (LBNP) as a simulation of hemorrhage in healthy human subjects (24).

In the present "proof of concept" laboratory-based study, rather than assessing a surrogate of SV, we tested the hypothesis that a machine-learning algorithm could continuously track changes in actual SV (derived from the arterial pressure waveform), and subsequently distinguish central hypovolemia from exercise.

METHODS

Subjects

Sample size calculation. A correlation coefficient of 0.75 between actual and predicted SV values is considered practically relevant for this study; based on $r = 0.75$, a power of 0.8, and an α of 0.05, a

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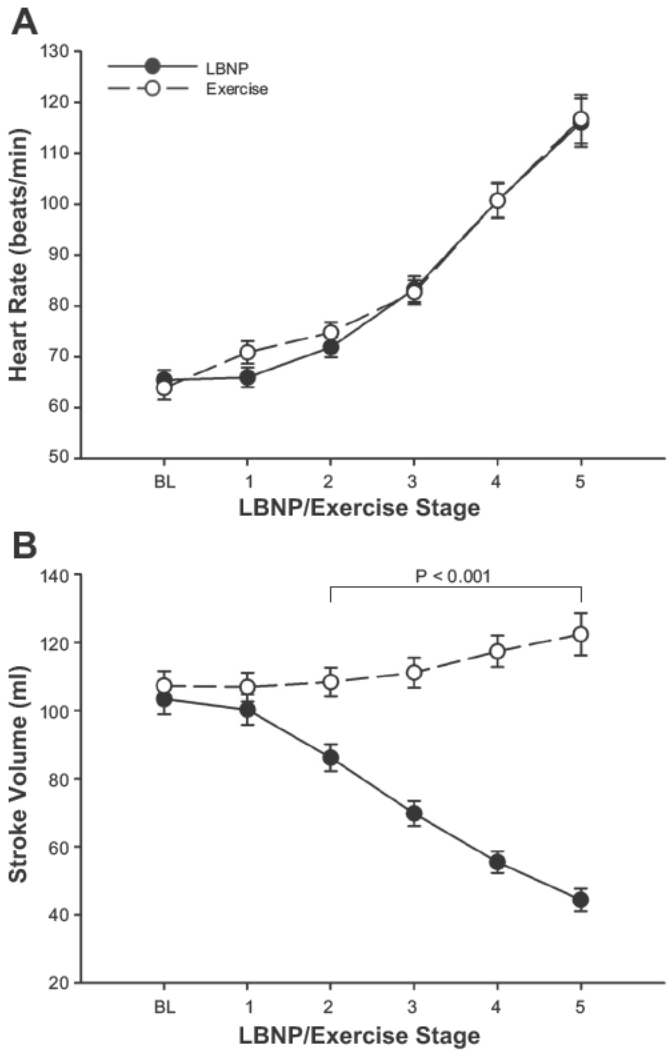

Fig. 1. Responses of heart rate (*A*) and stroke volume (*B*) during progressive lower body negative pressure (LBNP) and exercise. Values are means ± SE; $N = 24$ subjects. *P* value represents comparison between conditions at each level of LBNP/exercise.

minimum sample size of 12 subjects was required. Twenty-four healthy, normotensive, nonsmoking subjects (12 men, 12 women; age, 28 ± 7 yr; height, 171 ± 11 cm; weight, 70 ± 11 kg; means ± SD) volunteered to participate in this study. These subjects were specifically selected from a larger pool of 68 subjects (31 women, 37 men), according to two criteria: *1*) subject was wearing the SenseWear Pro2 Armband during exposure to a progressive LBNP protocol; and *2*) subject demonstrated linear increases in HR from baseline to presyncope. Inclusion only of subjects with linear increases in HR was required to elicit similar cardiovascular stress under both hypovolemia and exercise, hence removing this sensitive, but nonspecific metric as a distinguishing feature between conditions. Additionally, the LBNP-induced HR responses were subsequently used to set the exercise workloads (described in detail below). The studies were conducted at the US Army Institute of Surgical Research, Fort Sam Houston, TX, and all experimental protocols and procedures were reviewed and approved by the Institutional Review Board of the Brooke Army Medical Center, Fort Sam Houston, TX. A complete medical history and physical examination were conducted on each potential subject before participation, and all women were administered a urine pregnancy test before the LBNP portion of experimentation. Female subjects were excluded from involvement if pregnant. Because of potential effects on autonomic function, all subjects were instructed to maintain their normal sleep patterns in addition to abstaining from exercise, alcohol, caffeine, and other pharmacological stimulants 24 h before each protocol. After familiarization with the laboratory, subjects were briefed with a description of all procedures and risks associated with the experiments, and each gave written, informed consent to participate in the study.

Study Design

All subjects participated in two experimental protocols: *1*) progressive central hypovolemia via LBNP; and *2*) supine cycle exercise. Subjects completed the LBNP protocol first and returned to the laboratory at least 11 days later to perform the exercise protocol.

For each protocol, subjects were instrumented with a standard lead II ECG, infrared finger plethysmography to measure beat-to-beat arterial blood pressure (Finometer, TNO-TPD Biomedical Instrumentation, Amsterdam, The Netherlands), and an infrared end-tidal CO_2 sensor (Gambro, Entröm, Sweden) attached to a facemask. Subjects also wore a SenseWear Pro2 Armband on the upper left arm that measured heat flux (HF), HR, skin temperature, galvanic skin response, two-axis acceleration, and an ECG signal at a sampling rate of 128 Hz. Subjects wore shorts and t-shirts under both conditions.

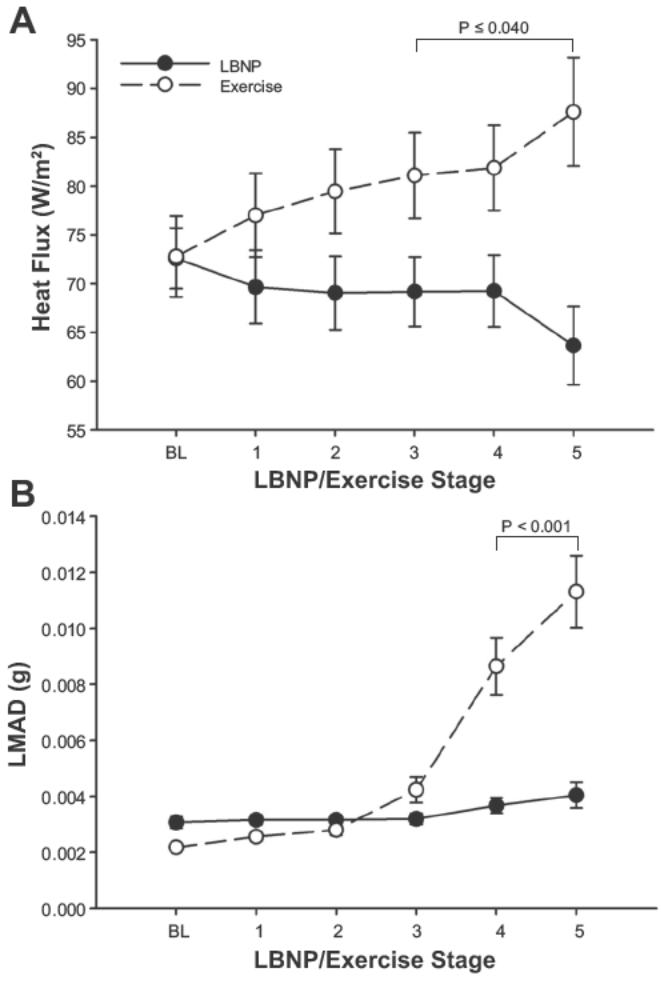

Fig. 2. Heat flux (*A*) and longitudinal mean absolute difference (LMAD; the 1-min averages of successive absolute differences for the longitudinal axis accelerometer values; *B*) responses to progressive LBNP and exercise. Values are means ± SE; $N = 21$ subjects. *P* value represents comparison between conditions at each level of LBNP/exercise.

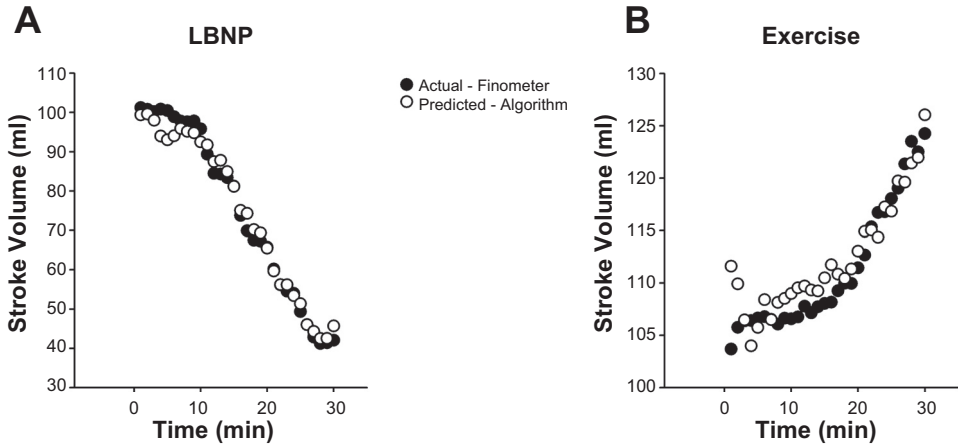

Fig. 3. Comparison of average stroke volume (SV) derived from the Finometer (actual) and the armband algorithm (predicted) up to −70 mmHg LBNP (*A*) and the fifth level of exercise (*B*).

The LBNP experiment consisted of a 5-min baseline period, followed by progressive 5-min stages of chamber decompression at −15, −30, −45, and −60 mmHg and the addition of −10-mmHg pressure every 5 min thereafter. LBNP was terminated with the onset of cardiovascular collapse, defined as one or a combination of symptoms, including sudden bradycardia, an abrupt fall in systolic arterial pressure (SAP) >15 mmHg, a progressive decrease in SAP reaching <80 mmHg, and/or voluntary subject termination due to the onset of presyncopal symptoms, such as gray-out, nausea, sweating, dizziness, or general discomfort. Following presyncope, subjects remained in the LBNP chamber for a 10-min recovery period.

For the subsequent graded exercise protocol, a supine cycle ergometer test was chosen to match the body positioning of the LBNP protocol. Following instrumentation, the exercise protocol commenced with a 5-min baseline period with subjects resting their legs flat beside the cycle ergometer (to ensure baseline measurements were not influenced by leg position), followed by an additional 5-min baseline period where subjects' feet were elevated and strapped into the cycle ergometer pedals in preparation for the commencement of exercise. The exercise protocol consisted of progressive increases in workload in 5-min increments, achieved through adjustments in cadence (i.e., revolutions per minute) and/or cycle resistance. Workloads were determined by matching the HR achieved during the last 3 min of the parallel LBNP level, as previously described (22). The number of exercise workloads matched the number of LBNP levels completed for each individual subject. The protocol concluded with a 10-min recovery.

Data Analysis

Waveform data. Using data acquisition software (WinDAQ, Dataq Instruments, Akron, OH), continuous end-tidal CO_2, ECG, and blood pressure waveforms were recorded at 500 Hz during both LBNP and exercise protocols. All waveform data were then exported to commercial analysis software (WinCPRS, Absolute Aliens, Turku, Finland). R waves generated from the ECG signal were detected and marked at their occurrence in time. Diastolic arterial pressure and SAP were marked from arterial blood pressure tracings. SV was estimated on a beat-to-beat basis by the Finometer using the established pulse contour method (19). All variables were calculated from the final 3 min for each level of LBNP and exercise. As most subjects (17 of 24) reached the −70-mmHg LBNP level (baseline plus 5 stages), we compared the hemodynamic responses over five stages of LBNP with the HR-matched five stages of exercise (the remaining 7 subjects reached the fourth stage of LBNP/exercise, and all data were included for these subjects). Two-way repeated-measures ANOVAs with Holm-Sidak post hoc tests were used to compare the responses of each variable between LBNP and exercise conditions (at each level). Unless otherwise stated, all data are presented as means ± SE, to indicate the uncertainty around the estimate of the mean measurement (1), and exact *P* values are presented for all comparisons.

Machine-learning algorithm data. Data from 21 subjects were used for the machine-learning algorithm from the SenseWear Pro2 Armband due to technical difficulties in obtaining adequate data in three subjects (6 included subjects reached the fourth stage of LBNP/exercise; 15 subjects reached the fifth stage of LBNP/exercise). Utilizing leave-one-subject-out cross-validation (LOUCV), 1-min averages from the low-level signals obtained from the armband were used to develop an algorithm to track changes in SV during both the LBNP and exercise protocols. The LOUCV procedure involves removing the data of one subject at a time from the original sample (test data) and trains the algorithm on the remaining data (training data); this process is repeated for each subject. This approach ensures that potential subject-specific traits are removed from the training data set, and overfitting does not occur with time-dependent within-subject data. Features extracted from the QRS complex of the raw ECG signal generated from the armband included R-R and Q-Q intervals, Q-R and R-S width, Q-R and R-S height, and difference between Q-R and R-S height. These, as well as HR variability metrics (including those derived from discrete wavelet transformation) were used for model development. Lastly, changes in the galvanic skin response, and skin temperature were also used to increase the accuracy of regression models for SV determination. For the classification models (to distinguish between exercise and LBNP), additional data from the accelerometer and motion-based variables, such as peak counts, mean crossing counts, and derived toe strikes, were utilized. For feature selection, search methodologies, such as exhaustive search, forward variable search (hill climb), hill descent, simulated annealing, and selection at random (with multiple trials), were used; a total of eight features were used in the final algorithm (6 from the ECG signal, 1 based on energy expenditure, and HF). A model was then created to classify data as either the LBNP or exercise condition, and the

Table 1. *Relationships between actual and predicted stroke volume responses to central hypovolemia (via LBNP) and exercise utilizing the leave-one-out cross-validation approach*

	With Baseline		Without Baseline	
	r	MAPE	*r*	MAPE
LBNP	0.85	15.4	0.86	14.4
Exercise	0.71	11.7	0.71	11.4

$N = 21$ subjects. *r*, Correlation coefficient; MAPE, mean absolute percentage error; LBNP, lower body negative pressure. Calculations were made using all available data across all LBNP or exercise levels.

Table 2. *Mean and range of individual correlation coefficients between actual and predicted stroke volume across LBNP and exercise*

	With Baseline	Without Baseline
LBNP		
Mean	0.92	0.95
Range	0.75–0.98	0.90–0.98
Exercise		
Mean	0.50	0.49
Range	−0.23–0.87	−0.27–0.93

$N = 21$ subjects.

accuracy, sensitivity, specificity, and precision (see Table 3 for definitions) of the model were calculated at the first level and each successive level of LBNP/exercise.

To assess relationships between actual and predicted hemodynamic responses to both LBNP and exercise, correlation coefficients (r) and mean absolute percentage errors (MAPE) were calculated for each parameter, with and without baseline data included. MAPE is a measure of accuracy and is calculated by the following: *1*) subtracting the predicted value from the actual value, then dividing by the actual value for each data point; *2*) summing each of these values together for each data point and dividing by the total number of data points; and *3*) multiplying the final value by 100. Statistical agreement between the two methods for both the LBNP and exercise data was also assessed via Bland-Altman analysis (4) of the SV data, by plotting the average SV between methods vs. the difference in SV between methods for each 1-min average for all subjects. Bias was calculated as the mean difference between the two methods, while the upper and lower limits of agreement were estimated as the bias ± 2 SD (4).

RESULTS

Hemodynamic Responses

During LBNP, HR increased from 65 ± 2 beats/min at baseline to 116 ± 5 beats/min at the fifth stage. As demonstrated in Fig. 1*A*, HR was matched during each exercise level with the corresponding LBNP level. The highest HRs achieved at *stage 5* were 60 ± 3% (range, 42–77%) of estimated maximum HR (i.e., 220-age). The exercise workloads required to elicit these increases in HR were only mild-to-moderate, ranging from 16 ± 0.5 W at stage 1, to 68 ± 5 W at stage 5. Estimated SV decreased during LBNP and increased during exercise (Fig. 1*B*), distinguishing the two conditions from the second stage ($P < 0.001$).

Machine-Learning Algorithm

The machine-learning algorithm integrates responses from multiple sensors for assessment of changes in SV. Examples of responses from individual sensors are presented in Fig. 2 for HF and longitudinal mean absolute difference, the 1-min averages of successive absolute differences for the longitudinal axis accelerometer values.

The 1-min averages for predicted (algorithm) and actual (Finometer) SV for both LBNP and exercise conditions are presented in Fig. 3. Linear correlation coefficients (r values) and MAPEs presented in Table 1 were calculated using all available armband data from all subjects for the LBNP and exercise conditions. These results indicate that, on average, the algorithm was able to predict the reduction in SV with LBNP and the increase in SV with exercise, and performance of the algorithm improved slightly with exclusion of baseline data for both conditions.

For assessment of the utility of the algorithm in tracking SV in individual subjects, r values were calculated between actual and predicted SV during both LBNP and exercise conditions for each subject (Table 2). On an individual subject basis, and including baseline data, the algorithm was successfully able to track the reduction in SV during LBNP with a range of r values from 0.75 to 0.98; under the exercise condition the algorithm was less successful in tracking the mild increase in SV, with only 3 of the 21 subjects exhibiting r values > 0.75 (r values ranged from −0.23 to 0.87). These relationships improved slightly in the LBNP condition when baseline data was not included (Table 2).

Bland-Altman analysis revealed that, on average, the predicted SV closely matched the actual SV for both LBNP and exercise conditions, evidenced by a bias close to zero, and the majority of data points falling within the upper and lower limits of agreement (Fig. 4). The plots presented in Fig. 4 also reveal, however, that SV was underestimated at values >115 ml for the LBNP condition [i.e., baseline and lowest level of LBNP (−15 mmHg); Fig. 4*A*], and at SVs of >155 ml for the exercise condition (i.e., higher levels of exercise; Fig. 4*B*). Additionally, the limits of agreement are broad for both LBNP (lower limit = −27.8 ml; upper limit = 27.1 ml) and exercise (lower limit =

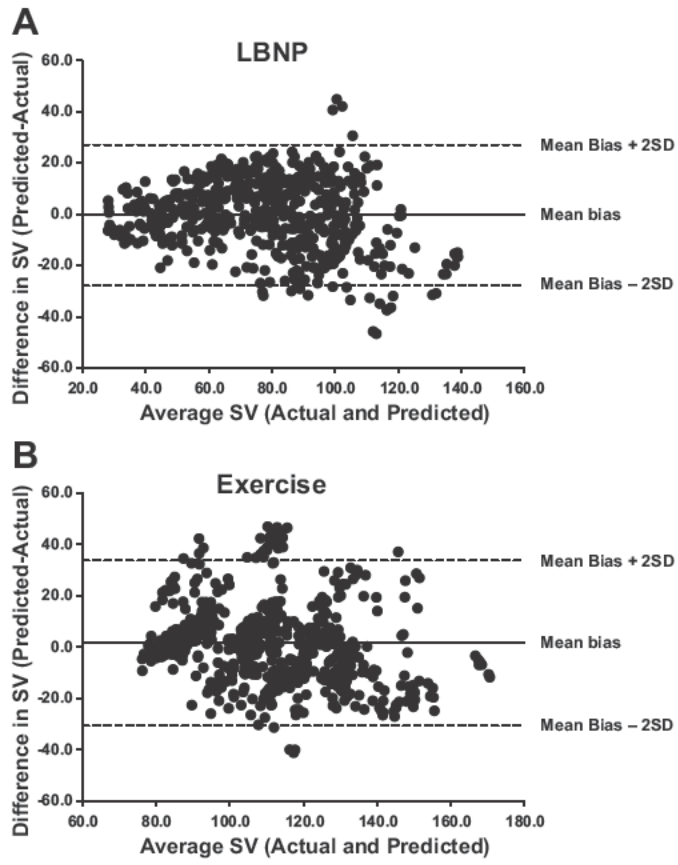

Fig. 4. Bland-Altman plots of SV values derived from the Finometer and armband algorithm methods up to −70 mmHg LBNP (*A*) and the fifth level of exercise (*B*). Solid horizontal line represents the mean bias between methods; dashed horizontal lines represent the limits of agreement (mean bias ± 2 SD).

Table 3. *Definitions of terms used for assessing capability of machine learning algorithm for detection of LBNP from exercise*

Term	Definition
True positive (TP)	No. of data points correctly classified as that of the LBNP protocol
True negative (TN)	No. of data points correctly classified as that of the exercise protocol
False positive (FP)	No. of data points incorrectly classified as that of LBNP protocol
False negative (FN)	No. of data points incorrectly classified as that of exercise protocol
Accuracy	(TP + TN)/(TP + TN + FP + FN): proportion of all data points correctly classified
Sensitivity	TP/(TP + FN): proportion of LBNP protocol data points that were correctly classified
Specificity	TN/(TN + FP): proportion of exercise protocol data points that were correctly classified
Precision	LBNP: TP/(TP + FP); Exercise: TN/(TN + FN): proportion of LBNP/exercise protocol data points that were truly LBNP/exercise data points

−30.6 ml; upper limit = 33.8 ml), indicating significant over- and underestimation of individual SV values based on this algorithm.

Table 3 provides definitions of the terms used to describe the efficacy of the machine-learning algorithm for distinguishing central hypovolemia from exercise; the values for these terms are presented in Tables 4 and 5. Values were initially calculated for each independent stage of exercise/LBNP (Table 4), and then additional data were added to the algorithm for each successive stage (Table 5). Under both conditions, the algorithm performed exceptionally well, with sensitivity, specificity, accuracy, and precision ≥90% from the first level.

DISCUSSION

In support of our hypothesis, the findings from this study demonstrate that a machine-learning algorithm utilizing low-level physiological signals collected from a wearable armband was able to reliably track changes in SV during central hypovolemia, when subjects were considered both as a group and as individuals. On an individual subject basis, the algorithm was less successful at tracking the mild increase in SV elicited by the exercise protocol. Despite this limitation, the armband algorithm was also able to successfully distinguish between reduced SV associated with central hypovolemia (i.e., simulated hemorrhage) and maintained or increased SV associated with physical exercise, even from the initial stages of each condition. These findings suggest that such a device could provide remote triage capabilities for future battlefield and civilian use.

Our initial investigations into development of a "remote triage" monitoring tool assessed the potential utility of ECG-derived HR variability metrics in distinguishing between central hypovolemia and exercise (22, 24). HR variability was targeted as a potential tool for this purpose as the ECG is a relatively basic, noninvasive, continuous signal routinely collected in the clinical setting, and HR variability had shown some initial promise in discriminating between prehospital trauma patients who lived and died (3, 12, 13). While we demonstrated that various measures of HR variability were not effective in distinguishing central hypovolemia from activity (22, 24) [predominantly due to the mathematical effect of reduced variability with elevated HR (25), independent of the stimulus], we reported that an indirect measure of central blood volume, such as pulse pressure, could be used for this purpose (22). In the present study, we evaluated SV as a noninvasive measure of central blood volume (5, 21) and found it to distinguish physiological conditions of central hypo- and hypervolemia with high sensitivity, specificity, accuracy, and precision. Importantly, the algorithm was also able to distinguish these two conditions without baseline measures, the most likely scenario when using point-of-care monitoring of trauma patients in any setting.

The continuous measurement of central blood volume also has important applications for medical care beyond remote triage. Current patient monitoring systems measure standard vital signs, including HR, arterial blood pressure (systolic and diastolic), and pulse oximetry. However, in a study of severely injured trauma patients in the prehospital setting, the measurement of pulse pressure (an indirect measure of volume status) could separate survivors from nonsurvivors when HR, SAP, and arterial oxygen saturation were indistinguishable, and within a range considered to be clinically unremarkable (12). These clinical findings are consistent with laboratory studies of simulated hemorrhage with LBNP, where SV and pulse pressure begin to fall from an early stage (5, 9), while SAP (5), arterial oxygen saturation (7), and pulse character (23) remain relatively stable until the onset of cardiovascular collapse. Taken together, these findings clearly indicate that current standard vital signs lack the sensitivity to be early indicators of physiological deterioration and change only when it may be too late for interventions to be effective. As indicated by the findings of the present investigation, a measure of volume status such as SV reflects a sensitive and specific early indi-

Table 4. *Detection of LBNP from exercise with the machine-learning algorithm using all available data at each level of LBNP or exercise, not including previous levels; baseline not included*

Level of LBNP/Exercise	TP	TN	FP	FN	Sensitivity	Specificity	Accuracy	Precision (LBNP)	Precision (Exercise)
1	100	97	8	5	0.952	0.924	0.938	0.926	0.951
2	104	100	5	1	0.991	0.952	0.971	0.954	0.990
3	105	99	6	0	1.00	0.943	0.971	0.946	1.00
4	89	94	11	9	0.908	0.895	0.902	0.890	0.913
5	52	79	1	6	0.897	0.988	0.949	0.981	0.929

$N = 21$ subjects.

Table 5. *Detection of LBNP from exercise with the machine-learning algorithm using all available data at each level of LBNP or exercise, including previous levels; baseline not included*

Level of LBNP/Exercise	TP	TN	FP	FN	Sensitivity	Specificity	Accuracy	Precision (LBNP)	Precision (Exercise)
1	100	97	8	5	0.952	0.924	0.938	0.926	0.951
2	204	197	13	6	0.971	0.938	0.955	0.940	0.970
3	309	296	19	6	0.981	0.940	0.960	0.942	0.980
4	398	390	30	15	0.964	0.929	0.946	0.930	0.963
5	450	469	31	21	0.955	0.938	0.946	0.936	0.957

$N = 21$ subjects.

cator of changes in central blood volume and would be a valuable decision support tool in addition to the standard vital signs measured in the prehospital, emergency department, operating room, and intensive care settings.

Current methods of measuring SV in humans, however, are either invasive (e.g., thermodilution), require expensive and cumbersome equipment (e.g., carbon monoxide rebreathing, thoracic electrical bioimpedance, Doppler ultrasound), and/or restrict movement and dexterity (e.g., finger photoplethysmography). While some of these techniques provide continuous beat-to-beat measurements of SV, none are easily portable or could be worn on a continuous basis (e.g., ≥24 h). In contrast, advantages of the technology utilized in this study include the ability to continuously collect low-level physiological signals without limiting movement or causing any discomfort to the wearer and no requirement for wires or moving mechanical parts such as an inflatable cuff. Since this technology is wireless and requires no tethering to mounted monitors, it could be valuable in mass-casualty situations where fast and accurate triage is required, and also as an early warning system for patients admitted to general medical wards.

The results of the present study show that, while the algorithm was limited in predicting actual SV under either condition, it was able to reliably track the reduction in SV with LBNP in individual subjects and was also able to successfully differentiate LBNP from exercise from an early stage. The requirement to know the absolute value of SV at any point in time, however, is not as meaningful to the assessment of patient status as tracking the trajectory of SV over time as an indicator of hemorrhage progression. The difficulty in tracking the change in SV with exercise was likely due to the supine exercise posture and the mild intensities of exercise used to elicit the required increase in HR. These two factors resulted in elevated baseline SV due to posture-induced increases in left ventricular filling pressure (2, 26), followed by small increases in SV across the increasing levels of exercise (i.e., 16.3 ± 2.6% increase from baseline to stage 5), consistent with other supine exercise studies (26, 27). The resultant relative homogeneity of SV over the exercise protocol leads to generally poor correlations between the actual and predicted values (18) (see Fig. 5*B* for example; Table 2 for intersubject range). By comparison, SV decreased by 57.5 ± 1.9% from baseline to *stage 5* during LBNP, resulting in greater spread of the data (heterogeneity) and very good correlations between actual and predicted values on an individual subject basis (see Fig. 5*A* for example; Table 2 for intersubject range). Future studies should be designed to assess the ability of the algorithm to track greater increases in SV with more intense levels of exercise in the upright posture to better simulate the proposed monitoring environments (e.g., soldier in combat, emergency first responder).

The machine-learning algorithm developed for this study modeled the known physiological responses to LBNP and exercise (i.e., SV) with the low-level physiological signals of HF, galvanic skin response, skin temperature, two-axis accelerometry, and a 128-Hz ECG. The HF response is an example

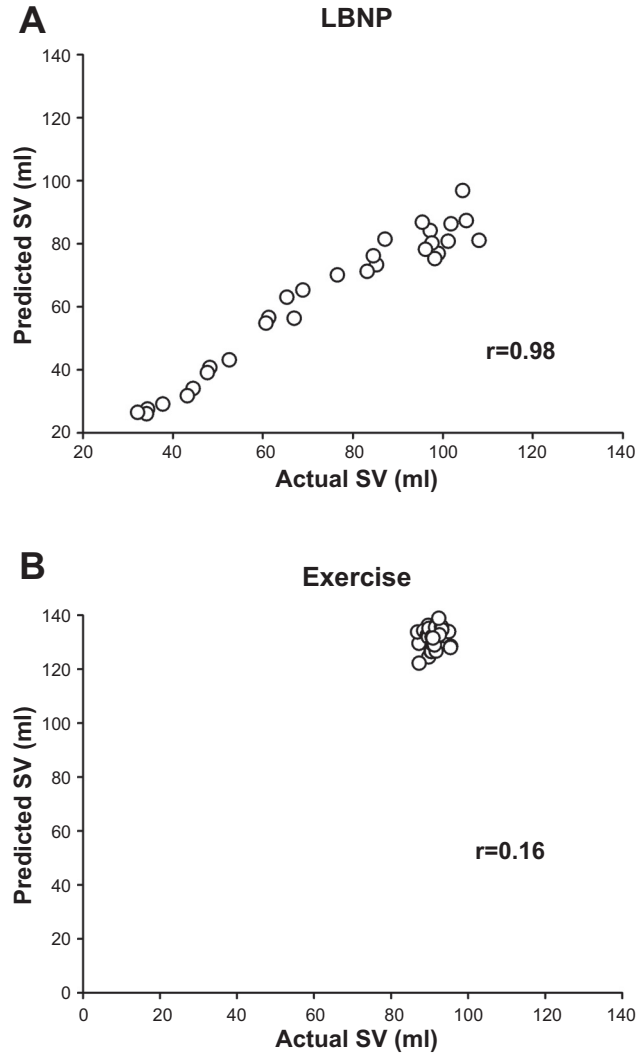

Fig. 5. Representative examples of the relationships between actual and predicted SV with heterogeneous data during LBNP, resulting in a strong correlation (*A*), and homogeneous data during exercise, resulting in a poor correlation (*B*). Data were obtained from the same subject under both conditions.

of how these signals were used for distinguishing central hypovolemia from exercise (see Fig. 2). Heat generated during physical exercise is detected by the increase in HF at the level of the sensor, while the passive nature of central hypovolemia in this study generally results in a reduction in HF below baseline levels. Theoretically, any known physiological parameter could be modeled using these sophisticated machine-learning techniques (e.g., tissue pH, intracranial pressure, blood glucose), highlighting the potential for advanced signal analysis for medical monitoring capabilities on the battlefield and in the civilian medical community. In fact, the physiological signals utilized in this study have been used for the development of algorithms for measurement of energy expenditure (16). To our knowledge, the present investigation represents a novel application of this analytic approach in which machine-learning technologies can be used to integrate and interpret low-level physiological signals for continuous, real-time assessment of the clinical status of individual patients with life-threatening injuries.

Potential implementation of this volume-sensing algorithm is outlined in the flowchart presented in Fig. 6. Using this framework, the algorithm could be used to initially distinguish a bleeding from active individual, and then track the progression of blood loss over time, including whether effective control of hemorrhage had occurred. It is anticipated that simplified, easy-to-interpret output from this algorithm (e.g., one of the six outcomes at the bottom of the flowchart) would be displayed for the medic to effectively treat the injured patient. One significant limitation of this decision-assist flowchart in its present form is the inability to differentiate a bleeding and decompensating patient from a resting soldier recovering from physical activity. Under both circumstances, SV and HR are decreasing, due to either continued bleeding and inappropriate bradycardia during the decompensatory phase of hemorrhage, or reduced metabolic demand during recovery from exercise. To distinguish these two conditions, additional information from the current signals obtained from the armband (e.g., ECG-derived respiratory patterns), or adjunct physiological signals (e.g., characteristics of blood pressure or pulse oximetry waveforms) will be required for training of an algorithm. In the current study, while 21 of the 24 subjects exhibited bradycardia before LBNP termination, the time of onset ranged from only 0.6 s to 117.7 s, with a median time of only 12.5 s. These time intervals may not be of sufficient length for accurate assessment of waveform characteristics between LBNP-induced bradycardia and bradycardia resulting from recovery from exercise; further investigations in this area are required to accurately differentiate these two conditions.

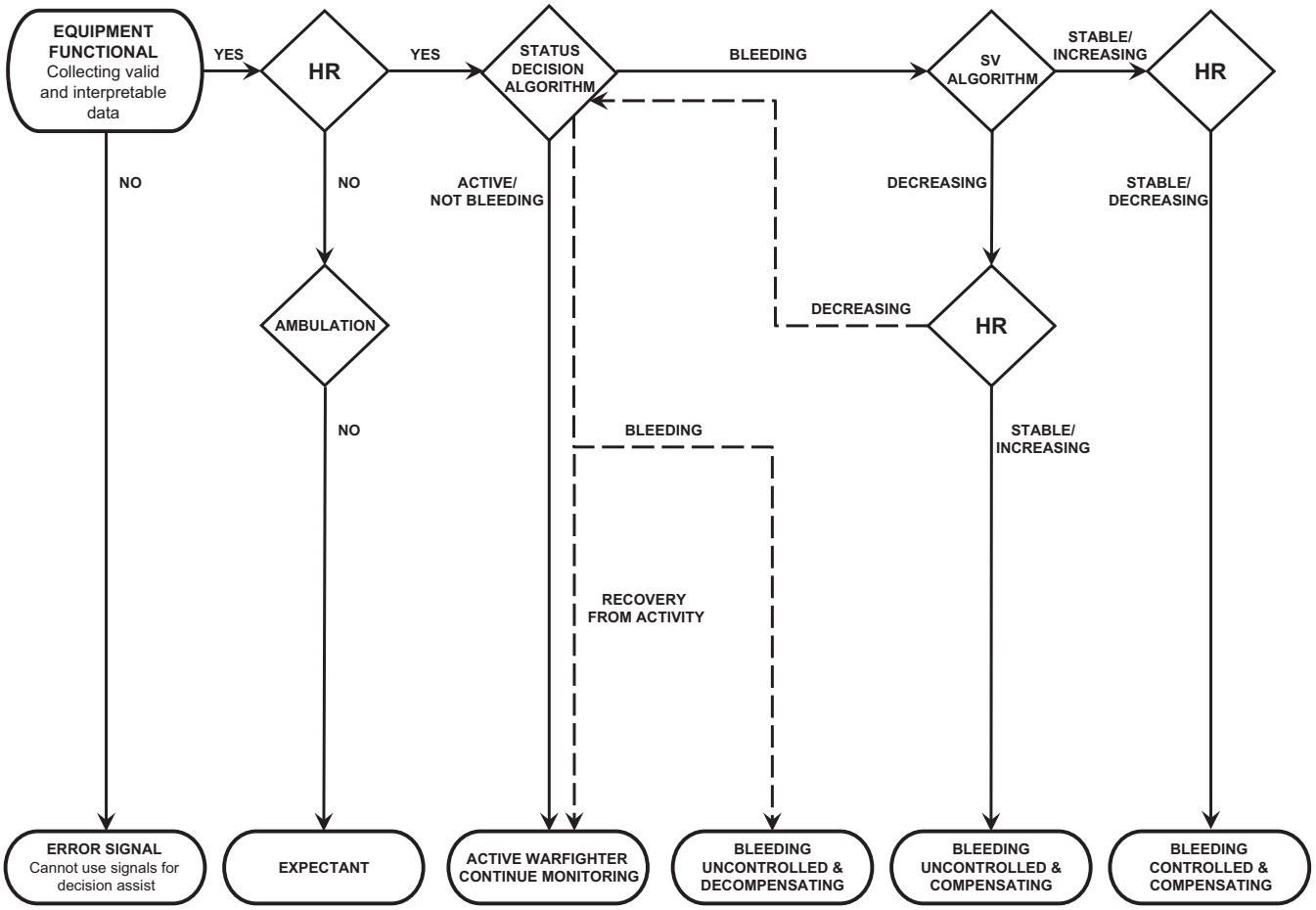

Fig. 6. Schematic representation of decision-assist flowchart for volume-sensing algorithm in the detection of hemorrhage from physical activity. Dashed lines represent a current capability gap for the volume-sensing algorithm in distinguishing a bleeding and decompensating patient from an active soldier recovering from activity.

Other Methodological Considerations

These findings are presently limited to the conditions tested in this experimental design. While the level of central hypovolemia simulates actual hemorrhage of >20% total blood volume (11), the HR-matched exercise levels were relatively low and are probably not representative of the more intense levels of physical activity often experienced in the combat setting. Despite this, assessing the algorithm under conditions of more realistic exercise intensities is likely to yield improved results in the distinction of central hypovolemia from physical activity, as previously discussed. Additional environmental and physiological factors, such as variable HR responses, temperature extremes (environmental and body), dehydration, heavy full-length clothing (e.g., military uniform), pain, and anxiety should also be incorporated into future training, testing, and refinement of these machine-learning algorithms. Furthermore, for advanced development of these algorithms for application to the clinical and field settings, data should be collected on actual hemorrhaging trauma patients and on soldiers and first responders in the field. The latter condition will be necessary to ascertain wearability and general acceptance of these devices for physiological status monitoring, which will eventually dictate user compliance of the final form factor.

CONCLUSIONS

Medical monitoring technologies can be designed for application at various echelons of care, including at the point of injury, during transport from the field to the hospital, and/or within the hospital environment. The monitoring device (and associated machine-learning algorithms) described in this study is designed to be worn continuously as a "physiological status monitor," with the potential to record and store baseline data from the individual wearer, then transforming into a "remote triage monitor" if the individual is injured. It is envisioned that this remote triage capability will provide essential decision support to the medic who may not have visual or physical contact with the soldier due to a variety of combat scenarios (e.g., terrain, hostile fire, limited visibility, multiple casualties). The present study provides evidence that this technology could eventually meet these requirements, as it can distinguish between central hypovolemia and physical activity from an early stage and can reliability track the reduction in central blood volume in individual subjects.

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DISCLAIMER

The views expressed herein are the private views of the authors and are not to be construed as representing those of the Department of Defense or the Department of the Army.

DISCLOSURES

N. Vyas has a total final interest worth more than US $10,000 (from consultancy, honoraria, expert testimony, corporate grants/patents pending, royalties, other) and has patents pending on the technology through BodyMedia, Inc. K. R. Ward has intellectual property and patents pending on the technology described in this manuscript through Virginia Commonwealth University and BodyMedia, Inc. D. Andre is a part-time research consultant to BodyMedia and a shareholder in the company (<5%), worked for BodyMedia from 2002–2008, and is an inventor of many of BodyMedia's patents.

AUTHOR CONTRIBUTIONS

Author contributions: C.A.R., K.L.R., K.R.W., and V.A.C. conception and design of research; C.A.R., K.L.R., G.M.H., and C.R.B. performed experiments; C.A.R., N.V., K.L.R., D.A., G.M.H., and C.R.B. analyzed data; C.A.R., N.V., K.L.R., K.R.W., D.A., G.M.H., and V.A.C. interpreted results of experiments; C.A.R., N.V., and C.R.B. prepared figures; C.A.R. and C.R.B. drafted manuscript; C.A.R., N.V., K.L.R., K.R.W., and V.A.C. edited and revised manuscript; C.A.R., N.V., K.L.R., K.R.W., D.A., G.M.H., C.R.B., and V.A.C. approved final version of manuscript.

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