Development and validation of the compensatory reserve measurement (CRM) in the emergency department

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DEVELOPMENT AND VALIDATION OF THE COMPENSATORY RESERVE MEASUREMENT (CRM) IN THE EMERGENCY DEPARTMENT

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14. ABSTRACT-

Background: The Compensatory Reserve Measurement (CRM) is a novel method used to provide early assessment of shock based on arterial waveform morphology changes. We hypothesized that 1) CRM would be significantly lower in those trauma patients who received life-saving interventions compared to those not receiving interventions, and 2) CRM in patients who received interventions would recover after the intervention was performed.

Study Design and Methods: We captured vital signs along with analog arterial waveform data from trauma patients meeting major activation criteria using a prospective study design. Study team members tracked interventions throughout the patients' emergency department stay.

Results: Ninety subjects met inclusion criteria, with 13 receiving a blood product and 10 receiving a major airway intervention. Most trauma was blunt (69%) with motor vehicle collisions making up the largest proportion (37%) of injury mechanism. Patients who received blood products had lower CRM values just prior to administration compared to those who did not (50% versus 58%), and had lower systolic (SBP; 95 versus 123 mmHg), diastolic (DBP; 62 versus 79 mmHg), and mean arterial pressures (MAP; 75 versus 95 mmHg), and a higher pulse rate (HR; 101 versus 89 bpm); all were $p<0.05$. Patients who received an airway intervention had lower CRM values just prior to administration compared to those who did not (48% versus 58%, $p=0.062$); however, SBP, DBP, MAP and HR were not statistically distinguishable ($p \geq 0.645$).

Discussion: Our results support our hypotheses, suggesting that CRM represents an advanced monitoring technology capable of distinguishing patients requiring blood and airway interventions and tracking their response.

15. SUBJECT TERMS- compensatory, reserve, emergency, trauma, resuscitation, blood

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1.0 EXECUTIVE SUMMARY

The Compensatory Reserve Measurement (CRM) is a novel method used to provide early assessment of shock based on arterial waveform morphology changes. We hypothesized that 1) CRM would be significantly lower in those trauma patients who received life-saving interventions compared to those not receiving interventions, and 2) CRM in patients who received interventions would recover after the intervention was performed.

<u>Methods:</u> We captured vital signs along with analog arterial waveform data from trauma patients meeting major activation criteria using a prospective study design. Study team members tracked interventions throughout the patients' emergency department (ED) stay.

<u>Results:</u> Ninety subjects met inclusion criteria, with 13 receiving a blood products and 10 receiving a major airway intervention. Most trauma was blunt (69%) with motor vehicle collisions making up the largest proportion (37%) of injury mechanism. Patients who received blood products had lower CRM values just prior to administration compared to those who did not (50% versus 58%), and had lower systolic (SBP; 95 versus 123 mmHg), diastolic (DBP; 62 versus 79 mmHg), and mean arterial pressures (MAP; 75 versus 95 mmHg), and a higher pulse rate (HR; 101 versus 89 bpm); all were $p<0.05$. Patients who received an airway intervention had lower CRM values just prior to administration compared to those who did not (48% versus 58%, $p=0.062$); however, SBP, DBP, MAP and HR were not statistically distinguishable ($p \geq 0.645$).

<u>Conclusions:</u> Our results support our hypotheses, suggesting that CRM represents an advanced monitoring technology capable of distinguishing patients requiring blood and airway interventions and tracking their response.

2.0 INTRODUCTION

Hemorrhagic shock is a leading cause of potentially preventable death in both civilian and military trauma.[1-3] Like any pathology, shock is easier to detect but harder to effectively treat as it progresses.[4] One of the primary challenges for effectively treating bleeding trauma patients is that the onset of hemorrhagic shock happens relatively quickly and is difficult to accurately detect in its early stages using traditional vital signs such as blood pressure, heart rate, and respiratory rate.[5-10] Traditional vital signs exhibit little change throughout the early stages of blood loss due to physiological compensatory responses that are sensitive to reductions in tissue oxygenation, but they change rather rapidly at the onset of hemodynamic decompensation when the maximal capacity for compensation is reached.

Unfortunately, recognition of the onset of shock and the timing of life saving interventions often occur too late in the process.[4] Trauma specific data have demonstrated that levels of hypotension that affect outcomes occur well before changes in physical exam or blood pressure measurements become clinically apparent.[11,12] Moreover, the signature mechanism of injury in recent conflicts – explosive trauma – often introduces concomitant traumatic brain injuries, which are hypersensitive to hemodynamic changes.[13] To further challenge interpretation of traditional vital signs in the setting of hemorrhagic and brain trauma, there are significant variances among individuals in their ability to both tolerate and compensate for hypovolemia.[4]

The US military is rapidly expanding the global battlespace into a footprint not seen during previous conflicts.[14,15] Advanced monitoring is listed as a top priority for both Tactical Combat Casualty Care and Prolonged Field Care research priorities.[16,17] Current methods do not provide adequate ability to assess hemodynamic changes, and perhaps more importantly, do not provide a method to assess the success of resuscitative interventions with sufficient sensitivity and specificity. Additionally, unlike the well-controlled setting of a hospital, the prehospital combat environment poses additional challenges of a potentially dynamic tactical situation necessitating mobile technology.

Since vital signs represent minimally changing outcomes dictated by mechanisms involved with compensation, it is reasonable to focus a clinical assessment of the status of exsanguinating patients on a measurement that reflects the integration of compensation. In this regard, the compensatory reserve has been recognized as a physiological phenomenon that represents the sum total of all mechanisms that contribute to compensation for blood loss and other conditions of compromised oxygen delivery or diffusion of oxygen (DO_2).[18] The measurement of compensatory reserve (CRM) is based on alterations in features of the arterial waveform during dynamic changes in hemodynamic status of bleeding patients.[4,18-21] The CRM has been measured with machine-learning technology that was developed from a robust database of analog arterial waveform data collected from validated laboratory-controlled hemorrhage models in volunteer human subjects.[22] The CRM has been shown in previous studies to have greater sensitivity and specificity when compared to standard vital signs measured in the ED in trauma patients with hemorrhage.[19,23] However, previous clinical investigations failed to assess the time relationship of CRM compared with standard vital signs when implementing life-saving interventions.

In this study, we captured continuous arterial waveform data in a trauma patient population to explore the feasibility of using CRM to distinguish trauma patients who received either whole blood transfusion, intubation, or pain management from those trauma patients who received no interventions during care in the emergency room setting. We hypothesized that 1) CRM would be significantly lower in those trauma patients who received life-saving interventions compared to those not receiving interventions, and 2) CRM in patients who received interventions would recover after the intervention.

3.0 METHODS, ASSUMPTIONS AND PROCEDURES

Subjects and Settings

The study setting was the Department of Emergency Medicine at Brooke Army Medical Center (BAMC). BAMC is the only level 1 trauma center in the Department of Defense and serves as a regional receiving hospital for the southwest region of Texas. We enrolled a convenience sample of patients transported from their injury scene and meeting institutional trauma activation criteria. The Regional Health Command – Central Institutional Review Board (IRB) reviewed and approved protocol C.2018.026 with a waiver of consent.

Data Collection

Trained study team members (MAE, CDL, DCR) placed a blood pressure cuff (Edwards Clearsight^{TM} EV1000, Irvine, California, USA) on an available digit of each trauma patient immediately upon arrival to the ED to allow non-invasive capture of continuous, beat-to-beat arterial waveform data for retrospective calculation of the CRM. In this manner, we blinded study team caregivers from any information provided in real-time by the collection of data for CRM estimations. As such, all clinical decisions for patient interventions reflected strictly routine clinical care at the direction of the attending physician. After device placement, the team member followed the patient throughout the course of the ED stay until the patient either was discharged, admitted to the hospital, transferred, taken to the operating room, or until the patient expired. Study team personnel captured in realtime documentation of demographic and prehospital intervention data as well as ED interventions including blood products and major airway interventions (e.g. intubation, cricothyrotomy, supraglottic airway), and outcome data previously described. Study team personnel further linked intervention and outcome data by time to the waveform data captured within the machine. All care was at the direction of the attending physician with data capture occurring in the background without altering the course of care. Standard vital sign information was available to the clinician, including systolic pressure, diastolic pressure, oxygen saturation, heart rate, and respiratory rate. Data from the Clearsight device was also available in real-time, including continuous systolic and diastolic pressure, heart rate, and calculated cardiac output.

Estimation of the Compensatory Reserve Measurement

Study personnel recorded and stored continuous analog arterial waveforms on the Clearsight blood pressure monitor and later downloaded these data to a PowerLab (Version 16/35, AD Instruments, Dunedin, New Zealand) data acquisition and integration system along with LabChart Pro (version 8.1.16, AD Instruments, Dunedin, New Zealand). We subsequently used these electronic arterial waveform recordings for retrospective calculation of the CRM using a machine-learning algorithm software based on 1-D convolutional neural networks and designed to interrogate subtle changes in waveform features.[24] We evaluated the CRM in 20-second intervals for each individual patient on a scale of 100% to 0%, where 100% reflects a maximal capacity to compensate for reduced circulating blood volume and 0% represents the onset of decompensated shock with thresholds of >60%, 30-60%, and <30%.[4,23,25] Thus, we used the CRM in the present investigation to assess the ability of the algorithm to distinguish trauma patients who received blood transfusion or airway management in the ED from those who received no interventions.

Data Analysis

We used the mean CRM for the first two minutes as a baseline value and calculated the mean CRM over 1 minute and up to 3 minutes before the intervention being assessed. Subject data were aggregated using Microsoft Excel (version 10, Redmond, Washington). All analyses were conducted using SAS version 9.4 (Cary, NC).

We summarized patient characteristics and interventions as percentages with 95% confidence intervals or medians with interquartile ranges. CRM and vital signs (SPB, DBP, MAP, HR) were reported as a mean with a 95% confidence interval. We categorized patients into groups based on whether they received or did not receive a particular intervention in the ED (e.g. blood products, airway intervention).

To determine if CRM differed between patients who did and did not receive life-saving interventions in the ED, we used independent one-tailed t-tests and compared the mean CRM and vital signs at baseline and up to 30 minutes for each intervention separately. We reported results as differences with 95% confidence intervals. The probability that any differences between measured parameters did not exist by greater than chance were expressed as exact 'p' values.

4.0 MAJOR EVENTS/MILESTONES/SUCCESS

In preparation for and during the execution of this project, we met the following major events and milestones:

- Kick Off Meeting – 30 June 2018
- IRB/IACUC Approval – 14 June 2018
- All experimental procedures completed – 30 August 2020
- Data Analysis – 01 November 2020
- Poster presentation \: Kissimmee, FL – August 2019, Virtual – May 2020
- Manuscript submitted to : Transfusion, December 2020; under review
- Dissemination of Results – December 2020

5.0 RISK ASSESSMENT

5.1 Risk Analysis:

The project was completed on time within cost targets. Risk assessment is low.

5.2 Technical Challenges

The major technical challenge was related to the use of the Edwards Lifesciences EV1000. The device was not as described and failed to capture algorithm data on a significant proportion of the subjects in the study despite being correctly applied.

We experienced challenges with collection of usable waveform data for obtaining CRM. The sensitivity to factors related to finger sensor placement and waveform acquisition (e.g., patient movement) limited the ability to collect usable data on approximately 45% of the patients who met inclusion criteria. However, this limitation does not negate the highly accurate and precise method of collecting arterial waveforms provided by a FIP volume-clamp technology on which the device is based.[22-25] We acknowledge that a potential limitation to the present investigation is the limited generalizability of data interpretation because of the relatively small number of life-saving interventions applied to patients in our blood and airway management groups. However, given the large variability inherent in clinical investigations that have multiple uncontrolled interfering factors, low ‘p’ values between CRM in ‘blood’ and ‘no blood’ groups and in airway and no airway groups represents differences that reflect statistically large and real effects (i.e., there was a high probability that differences in CRM between patients who received interventions and those who did not were greater than by chance alone).

6.0 TRANSITION PLAN

6.1 Military Relevance

Hemorrhagic shock is the leading cause of preventable death in the military sector and is easier to detect but difficult to treat as it progresses. Often times, it occurs quickly and the ability to detect with traditional vital signs (blood pressure, heart rate and respiratory rate) becomes difficult. These factors, along with the dynamic tactical situations encountered in the prehospital setting, further impose the need for advanced monitoring systems. The Compensatory Reserve Mechanism (CRM) is a physiological phenomenon that represents the sum total of all mechanism that contribute to compensation for blood loss and other conditions of compromised oxygen delivery. These include traditional vital signs such as blood pressure, heart rate and respiratory rate. The CRM was validated in the controlled laboratory setting using volunteer human subjects as hemorrhage models.

The US Army Medical Capability Development Integration Directorate (MED CDID), the Committee on Tactical Combat Casualty Care (CoTCCC), and the Combat Casualty Care (C3) Capabilities-Based Assessment (CBA) sponsored by the Office of the Assistant Secretary of Defense for Health Affairs have all reaffirmed a requirement for development and fielding of monitoring technologies that enable prehospital combat medical personnel to better evaluate the need for whole blood resuscitation in combat casualties. We anticipate future military missions will comprise a complex multi-domain operations (MDO) battlefield with limited air superiority. The high potential for delays in early and rapid medical evacuation in addition to mass casualty scenarios will require individualized triage decisions to optimize medical resources and successfully execute prolonged field care. Integrating the CRM into prehospital medical monitoring on the battlefield could fill this capability gap by providing a medic with real-time clinical status of injured casualties that will lead to earlier recognition for the need to intervene.[31,32] Such continuous monitoring of

CRM could translate to optimizing combat casualty care of warfighters in austere, kinetic, and contested battlefield settings.

6.2 Transition Strategy

We will submit a technical report to the Defense Technical Information Center. Development of the algorithm has continued with the Mayo Clinic Special Processor Development Group through an existing CRADA with the USAISR. Our findings have been presented at relevant scientific and military venues. Our final findings will be published in a relevant peer-reviewed, PubMed-indexed journal.

7.0 RESULTS

Subjects. Of the 165 trauma patients initially enrolled in the study after meeting inclusion criteria, reliable waveform data acceptable for analysis were available for 90 subjects. Most subjects were male (79%), with a group median age of 42 (IQR 26-59), and a BMI of >30 (32%). Most trauma was blunt (69%) with motor vehicle collisions making up the largest proportion (37%) of injury mechanism (Table 1). Time of waveform data capture ranged from 2 to 1145 minutes with a mean of 224 minutes (standard deviation 240 minutes) and amedian 83 minutes (interquartile range 25-402 minutes). Of the 90 from whom we captured reliably ‘clean’ waveform data, 13 received a blood product and 10 had an airway intervention.

Patients receiving blood product. Patients who received blood products had lower CRM values just prior to administration compared to those who did not (50% versus 58%) and had lower systolic (95 versus 123 mmHg), lower diastolic pressure (62 versus 79 mmHg), and mean arterial pressures (75 versus 95 mmHg), and a higher pulse rate (101 versus 89 bpm, Table 2). The CRM continued to rise over a post-resuscitation period in those patients who received a blood transfusion until it exceeded the CRM of those patients who did not receive blood (Figure 1).

Patients receiving airway intervention. Patients undergoing an airway intubation had lower CRM values just prior to administration versus those who did not (48% versus 58%;p=0.031; Table 2). There were 13 endotracheal intubations, and zero cricothyrotomies or supraglottic airways placed. In contrast, those receiving an airway intervention had systolic pressures (105 versus 119), diastolic pressures (68 versus 77), mean arterial pressures (81 versus 93), and pulse rates (85 versus 91) that were statistically indistinguishable between those patients who were intubated compared to those who were not ($p \geq 0.405$). Similar to blood transfusion, the CRM continued to rise over a post-intervention period in those patients who were intubated until it reached the CRM level of those patients who were not intubated (Figure 2).

When patients who received blood were categorized into groups of patients with CRM of 30% to 60% (n = 9) and compared to patients with CRM >60% (n = 3), mean differences in heart rate, systolic pressure, diastolic pressure, or mean arterial pressure were statistically indistinguishable between groups (Table 3). We had one patient with a CRM <30% who received blood and was intubated. He had a mean CRM value of 18% for the 3 minutes prior to the blood and 17% the 3 minutes prior to the intubation. He was injured via motor vehicle collision (MVC) and presented with a ruptured bladder, hemoperitoneum, broken knee, pelvic fracture, and a positive focused assessment with sonography for trauma (FAST).

8.0 CONCLUSION/DISCUSSION

In the present prospective clinical investigation, we recorded continuous analog arterial waveform data that allowed for the measurement of compensatory reserve in trauma patients who were treated in the ED setting. Consistent with our first hypothesis, the CRM was distinguishably lower in those trauma patients who received either a blood transfusion or airway intubation. Such results suggest that the CRM would have been a useful monitoring tool for guiding triage decision support. Consistent with our second hypothesis, the CRM was lower prior to intervention and recovered back towards or above baseline after the intervention, suggesting that the CRM is capable of tracking responses to interventions.

We successfully enrolled 90 patients with reliable analog waveform data, making this the first clinical investigation to capture continuous data for the calculation of CRM compared with previous studies that relied on intermittent measurements.[26-29] Consistent with results reported in previous studies, most of our subjects were male and suffered from injuries secondary to blunt trauma, with MVCs making up the largest proportion.[3] Two significant observations manifested from our dataset. First, the CRM was lower for both patients who received an airway intervention or a blood product in the ED compared to their counterparts who did not receive intervention. This result foretells the potential for applying the CRM algorithm as a goal-directed guide in clinical conditions of compromised systemic DO_2 such as significant blood loss due to hemorrhage or an obstructed airway. Second, as clearly highlighted in Figures 1 and 2, the CRM accurately tracked both airway and blood product interventions as it trended toward the levels of the unaffected population after the invention. This result supports the potential use of the CRM for providing endpoints of resuscitation. However, we must note that our population varied from the combat population and future studies should target trauma that better matches combat trauma or start employing the devices in the deployed setting.[13]

As previously noted, our study is most comparable to the study by Benov et al.[27] In their study, they found that the algorithm predicted with better sensitivity and negative predictive value (83% and91%, respectively) than systolic blood pressure did (26%, 78%) for life-saving interventions specific to hemorrhage resuscitation. As expected in this study, the systolic, diastolic, and mean pressures were lower for patients who received a blood product intervention, as was the CRM value. This is expected as hypotension was the primary clinical determinant for the decision of administering blood products, and unlike the CRM, these values were available to the clinicians in real-time. However, unlike previous clinical investigations in which the CRM was measured in trauma patients,[26,28] we have significantly built on the science by measuring the CRM as a continuous variable with specific attention to both blood and airway interventions. Both interventions play a key role in returning the DO_2 back to a physiologically stable level. Lower CRM highlights the fact that a measurement reflecting the sum of all physiological mechanisms involved in the control of DO_2 provides greater specificity for airway management than standard vital signs. These results are not surprising given that the decision to intubate is primarily based on factors that are unrelated to the blood pressure measurements. As such, the recovery of CRM following intubation in the present study suggest that this monitoring technology may prove valuable in providing the clinician with a clinical tool for real-time assessment of enhancing DO_2 during airway intervention.

A previous clinical investigation conducted in trauma patients with hemorrhage revealed optimal threshold values for three zones of CRM to predict hemorrhage.[25] Statistical analysis demonstrated that CRM between 60% and 100% corresponded to an adequate reserve to compensate, while values between 30% and 59% reflected a clinically-compromised capacity to compensate for blood loss, and values lower than 30% indicated that the patient was at significant risk for experiencing the onset of decompensated shock. In an effort to assess the ability of CRM to distinguish patients who received either blood or airway management in the present study, we retrospectively categorized our patients into two groups according to the zones established by Convertino and co-workers.[25] Heart rate and blood pressures were similar between those patients with adequate reserve to compensate (i.e., CRM >60%) and those patients with compromised CRM (i.e., 30% to 60%;Table 3). These results provide clinically relevant insights and demonstrate the superiority in specificity of CRM over vital signs for assessing patient status for triage decision support. Despite the presence of hypotension in both groups, it is apparent that those patients with CRM >60% were minimally compromised, and unlikely needed blood, compared to those patients with a CRM of <60% who most likely would benefit by receiving a transfusion. Such decision support would not only save precious blood resources, but reduce the clinical risks associated with blood transfusion (e.g., infection, auto-immune responses).

One patient whose capacity to compensate was severely compromised with an average CRM of 18% received blood and intubation with significant polytrauma. This case highlights the clinical value of the CRM in assessment of a severely injured patient with primarily internal injuries that may not be readily apparent on physical exam in the prehospital setting (e.g., pelvic fracture, hemoperitoneum). In such a case in the field, this very low CRM would likely have prompted the medic to administer blood and perform the airway intervention at an earlier time of care.

We noted several challenges with the Edwards Clearsight EV1000 device for the recording of analog arterial waveform data. We initially enrolled 165 subjects that we collected clinical data on, yet only 90 had usable data for algorithm analysis and development. The missing and/or corrupt files affecting 75 patients without usable waveform data underscores the need for sensor technology development with optimized signal-to-noise capabilities.[30] Such improvements in monitoring technology would be beneficial in emergency care medical settings where the most critically injured patients are moved around the most, thus creating substantial background noise. We also acknowledge the relatively low numbers of life-saving interventions that limit the generalizability of our study results.

CONCLUSIONS

In this prospective study that included the capture of continuous waveform data, the CRM proved more specific in distinguishing patients who received blood transfusion and airway intubation compared to those who did not. Furthermore, continuous CRM was capable of tracking the post-intervention response, indicating its potential for assessment of intervention effectiveness in conditions of compromised DO_2.

9.0 DELIVERABLES

9.1 Publications:

Schauer SG, April MD, Arana AA, Maddry JK, Escandon MA, Linscomb CD, Rodriguez DC, Convertino VA, Efficacy of the Compensatory Reserve Measurement in an emergency department trauma population, Accepted 28FEB2021, Transfusion Journal.

9.2 Presentations:

Mireya Escandon, Development of the Compensatory Reserve Mechanism (CRM) in the Emergency Department: A Feasibility Phase Analysis, Special Operations Medicine Scientific Assembly, 2020

Dylan Rodriguez, Development of the Compensatory Reserve Mechanism (CRM) in the Emergency Department: A Feasibility Phase Analysis, SAMHS and Universities Research Forum (SURF), 2019

10.0 COST

The project was sponsored by the Defense Health Program J9. Costs were on target and within the allotted budget of $470k. All funds were expended.

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FIGURES AND TABLES:

Table 1. Patient characteristics

Variable	**% (95% CI) or median [IQR]**
Male gender	79 (70-87)
Age	42 [26-59]
Civilian	93 (88-99)
BMI	
<18.5	3 (0-7)
18.5-24.9	20 (12-28)
25-29.9	27 (17-36)
>30	32 (22-42)
Unknown	18 (10-26)
Major trauma activation	72 (63-82)
Type of injury	
Penetrating	31 (21-41)
Blunt	69 (59-79)
Mechanism of injury	
Fall	24 (15-33)
GSW	19 (11-27)
MVC	37 (27-47)
Stab	13 (6-20)
Other	7 (1-12)

Table 2 – Mean (±SD) values for compensatory reserve measurement (CRM), heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial blood pressure comparing patients who received intervention vs. those who did not

	No blood*	**Blood****	**p-value**	**Difference (95% CI)**
CRM	58 (14)	50 (16)	0.045	7 (-1 to 16)
HR	88 (17)	100 (10)	0.039	-11 (-24 to 1)
SBP	122 (27)	94 (36)	0.005	28 (6 to 49)
DBP	79 (18)	61 (22)	0.007	17 (3 to 31)
MAP	95 (20)	74 (28)	0.006	20 (4 to 36)
	No airway*	**Airway****	**p-value**	**Difference (95% CI)**
CRM	58 (14)	48 (18)	0.031	9 (-1 to 19)
HR	91 (17)	85 (25)	0.405	6 (-8 to 20)
SBP	119 (25)	105 (44)	0.431	14 (-27 to 55)
DBP	77 (17)	68 (28)	0.445	9 (-17 to 35)
MAP	93 (18)	81 (35)	0.439	11 (-21 to 43)

*for no blood, n=77 had CRM, n=67 had vitals

*for no airway, n=80 had CRM, n=67 had vitals

**for blood, n=13 had CRM, n=8 had vitals

**for airway, n=10 had CRM, n=7 had vitals

Table 3 – Mean (±SD) values for compensatory reserve measurement (CRM), heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial blood pressure **comparing patients who received blood based on CRM subgroups**

	CRM 30-60% (N = 9)	**CRM >60% (N = 3)**	**p-value**	**Difference (95% CI)**
HR	99 (12)	102 (5)	0.806	-2 (-24 to 20)
SBP	92 (41)	102 (24)	0.759	-10 (-88 to 67)
DBP	59 (24)	68 (14)	0.644	-9 (-56 to 37)
MAP	72 (32)	81 (17)	0.716	-9 (-71 to 52)

Figure 1. Comparison of the group average CRM response for patients who received blood (N = 13; red line) in the ED compared with those patients who did not (N = 77; black line). Colored bar area around lines represent 95% confidence intervals.

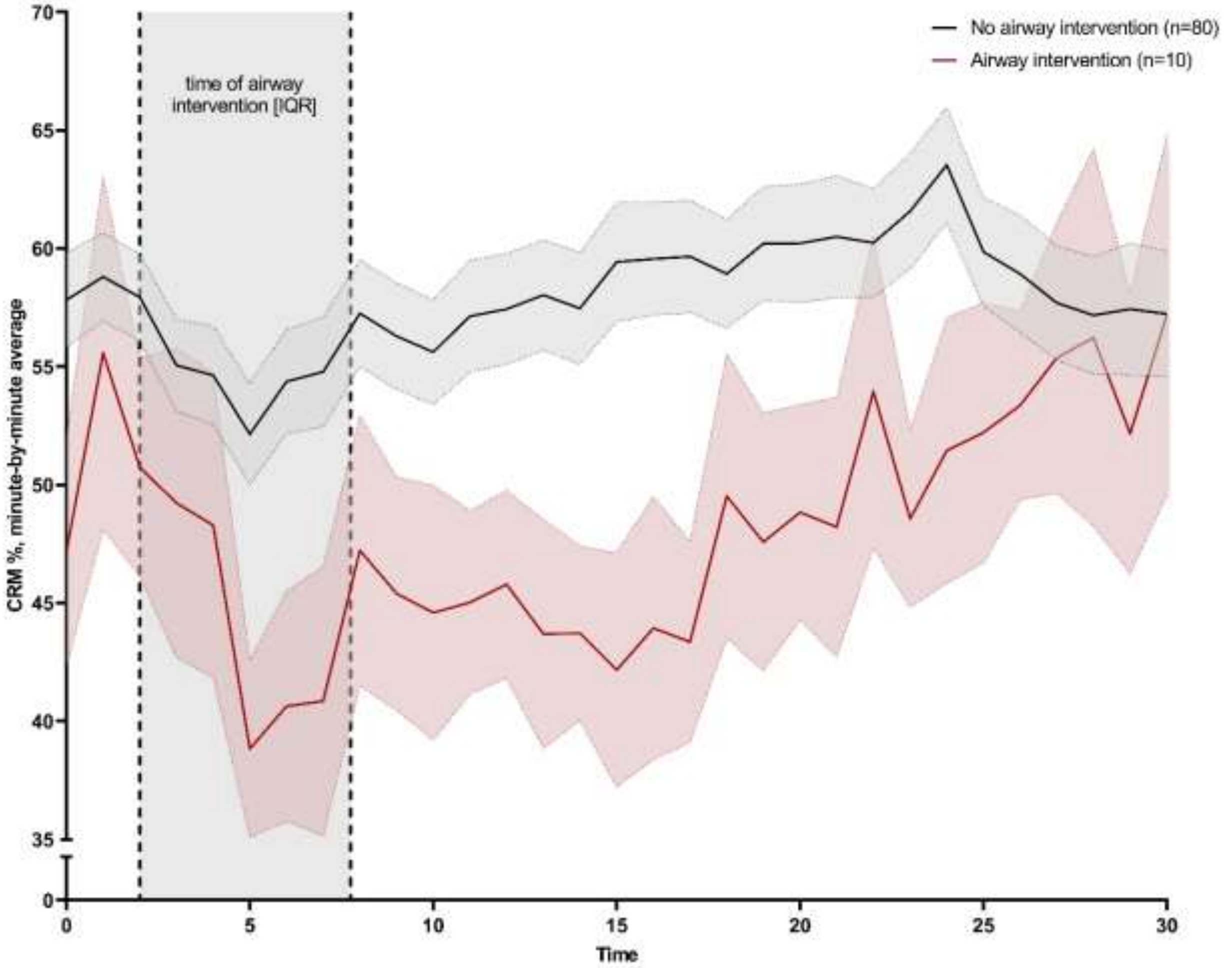
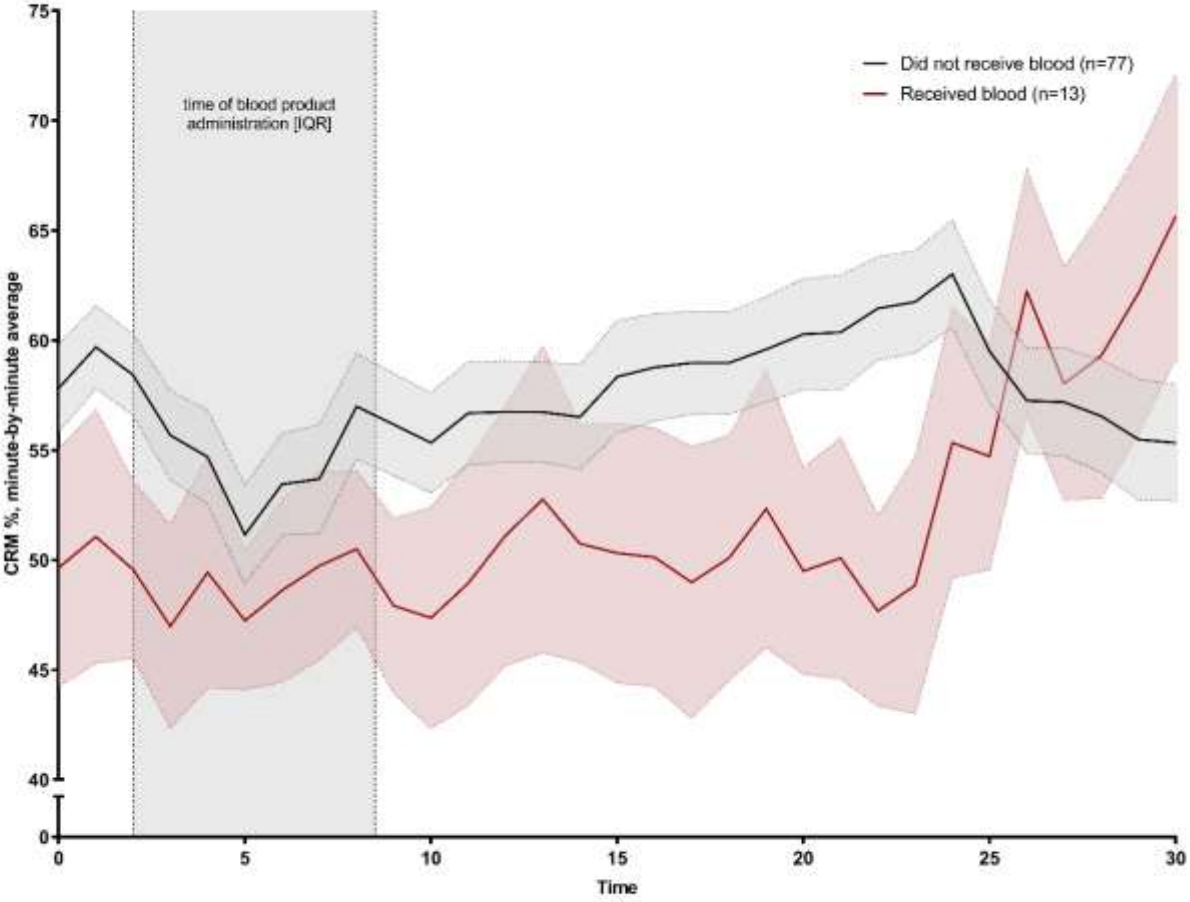


Figure 2 Figure 2. Comparison of the group average CRM response for patients who received airway intervention (N = 10; red line) in the ED compared with those patients who did not (N = 80; black line). Colored bar area around lines represent 95% confidence intervals.



12.0 LIST OF SYMBOLS, ABBREVIATIONS AND ACRONYMS

BAMC = Brooke Army Medical Center

BMI = Body mass index

CDID = Capabilities Development and Integration Directorate

CRADA = Cooperative Research and Development Agreement

CRM = Compensatory reserve measurement

DO2 = Diffusion of oxygen

ED = Emergency department

FAST = Focused assessment of sonography for trauma

MDO = Multi-domain operations

MVC = Motor vehicle collision

TCCC = Tactical Combat Casualty Care