CONTINUOUS PULSE OXIMETRY PHOTOPLETYSMOGRAPH (PPG) WAVEFORMS PREDICT TRANSFUSION AFTER TRAUMA

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Abstract 390: Funded by USAF:FA8650-11-2-6D01(PI Colin Mackenzie MD, USAF PI Joseph Dubose MD) * Amechi Anazodo, Steven Barker, John Blenko, Patrick Boyle, Chein-I Chang, Hegang Chen, William Chiu, Theresa Dinardo, Joseph duBose, , Raymond Fang, Yvette Fouche, Sam Galvagno, Lisa Gettings, Linda Goetz, Tom Grissom, Victor Guistina, George Hagegeorge, Anthony Herrera, John Hess, Peter Hu, Cris Imle, Matthew Lissauer, Colin Mackenzie, Jay Menaker, Karen Murdock, Mayur Narayan, Tim Oates, Sarah Saccicchio, Thomas Scalea, Stacy Shackelford, Robert Sikorski, Lynn Smith, Lynn Stansbury, Deborah Stein, and Chris Stephens, Catriona Miller, and PhD candidates Shi-Ming Yang, Shih Yu Chen, Xian Shu Zhu, Yulei Wang, Yao Li

Disclosure Information

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Colin Mackenzie

I have no financial relationships to disclose.

I will not discuss off-label use and/or investigational use in my presentation

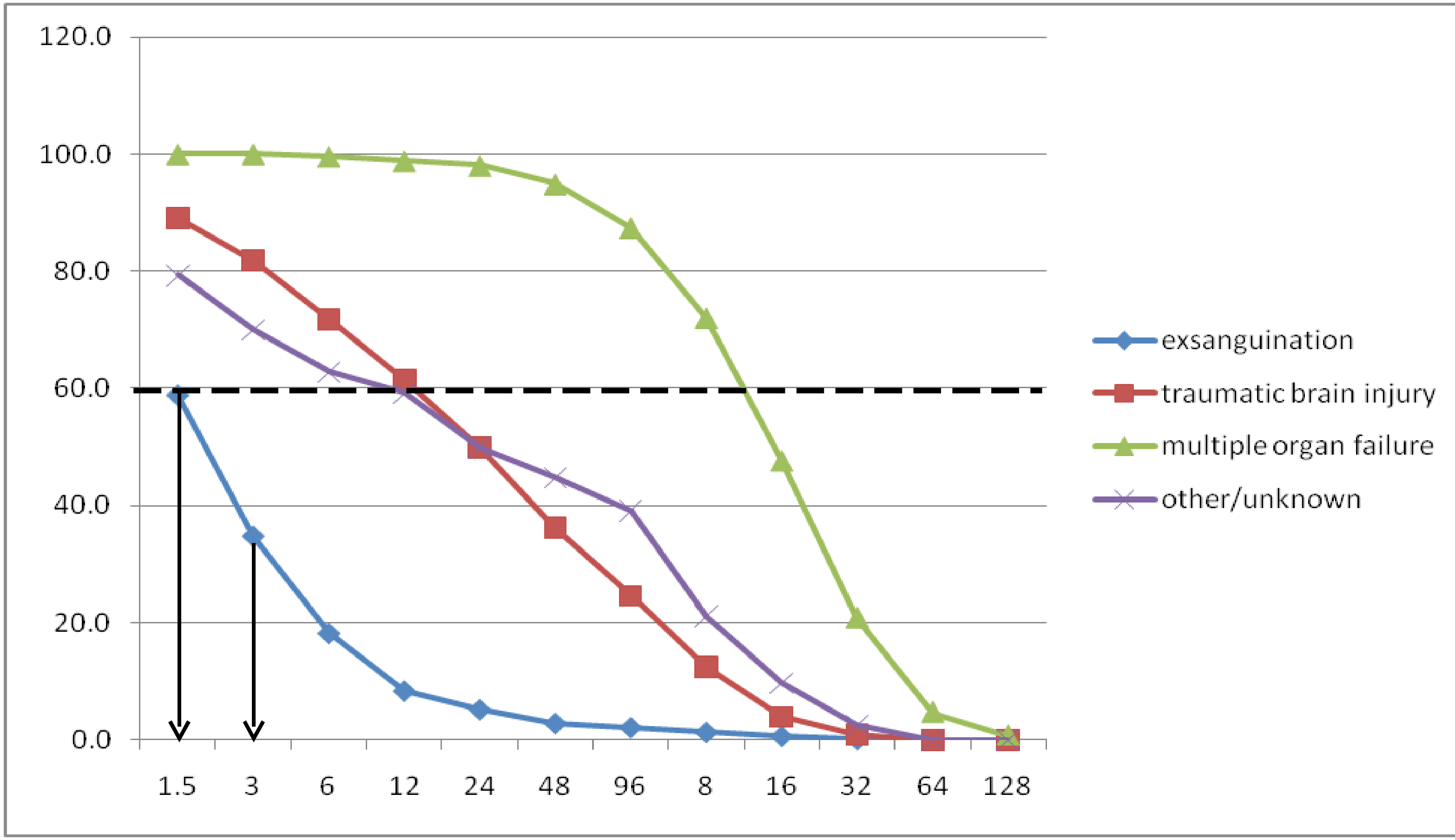
GAP ANALYSIS

- Advanced identification of bleeding casualties would assist triage.
- Notification of likely need for transfusion before aeromedical transport would speed blood bank preparations.
- Actionable Intervention: Casualties who are predicted to need massive transfusion (> 4 units pRBC in 4 h) should have hemorrhage control procedures initiated STAT

BACKGROUND

- Commonest causes of death in combat casualties are head injury followed by truncal exsanguinations.[1]
- Major hemorrhage is the most frequent avoidable cause of early mortality in combat casualties,[2] and the civilian setting,
- Among those who survive at least 15 minutes into advanced trauma care but go on to die of bleeding, half are dead within 2 hours.[3]
- Recognition of the acute coagulopathy of trauma and delivery of coagulation factors (as plasma) and platelets in near-equivalence with red cells must be done quickly.[4]
- Large numbers of units of Group O red cells (UnXRBC) can be provided immediately upon arrival
- Equivalent proportions of platelets and plasma require a 20 mins processing time. In the military setting, fresh whole blood may be from "walking blood donors," requires 30-60 minutes.
- *Refs: 1.   J Trauma. 2008; 64:295–9.;2.   Mil Med 1984;149:55–62 ; 3 J Trauma. 2010: 69:620-6. ;4.   . J Trauma. 2007; 63:805-13.78.*

Background



Percent survival over time (1.5 to 96 hours and 8-128 days) for the four major causes of death,R Adams Cowley Shock Trauma Center, FY 1997-2008

. Dutton RP, et al. Trauma mortality in mature trauma systems: Are we doing better? An analysis of trauma mortality patterns, 1997-2008. J Trauma. 2010: 69:620-6.

Historic Data on Shock Trauma Blood Use 2009-2010 (Lynn Stansbury MD MPH)

Group O Universal Donor blood on admission 2-3%

Mass. Transf. 1 (> 4 u pRBC

in 4 h)

Mass. Transf. 2 (>9 u pRBC in 6 h)

Mass. Transf. 3 (>9 u pRBC in 24 h)

Total Direct STC Trauma Admissions > 8,000 patients

(3-5% of patients get MT, 8% blood)

Hypothesis:

PPG features can predict transfusion better than the current routinely used pre hospital vital signs thresholds

[SBP < 90 mmHg, HR > 120/min Shock Index (HR/ SBP) >0.9]

ONPOINT ENROLLMENT
Prospective In-Hospital Data

- *Inclusion Criteria*
- Direct Trauma Admit
- Shock Index (SI) > 0.62
- Priority 1
- > 17 years
- Lived > 15 min
- VS and PPG waveforms

- *Exclusion Criteria*
- Non –Trauma
- SI <0.62
- <18 years

Timing and quantities of blood transfused were identified by observation, validated with blood bank data.

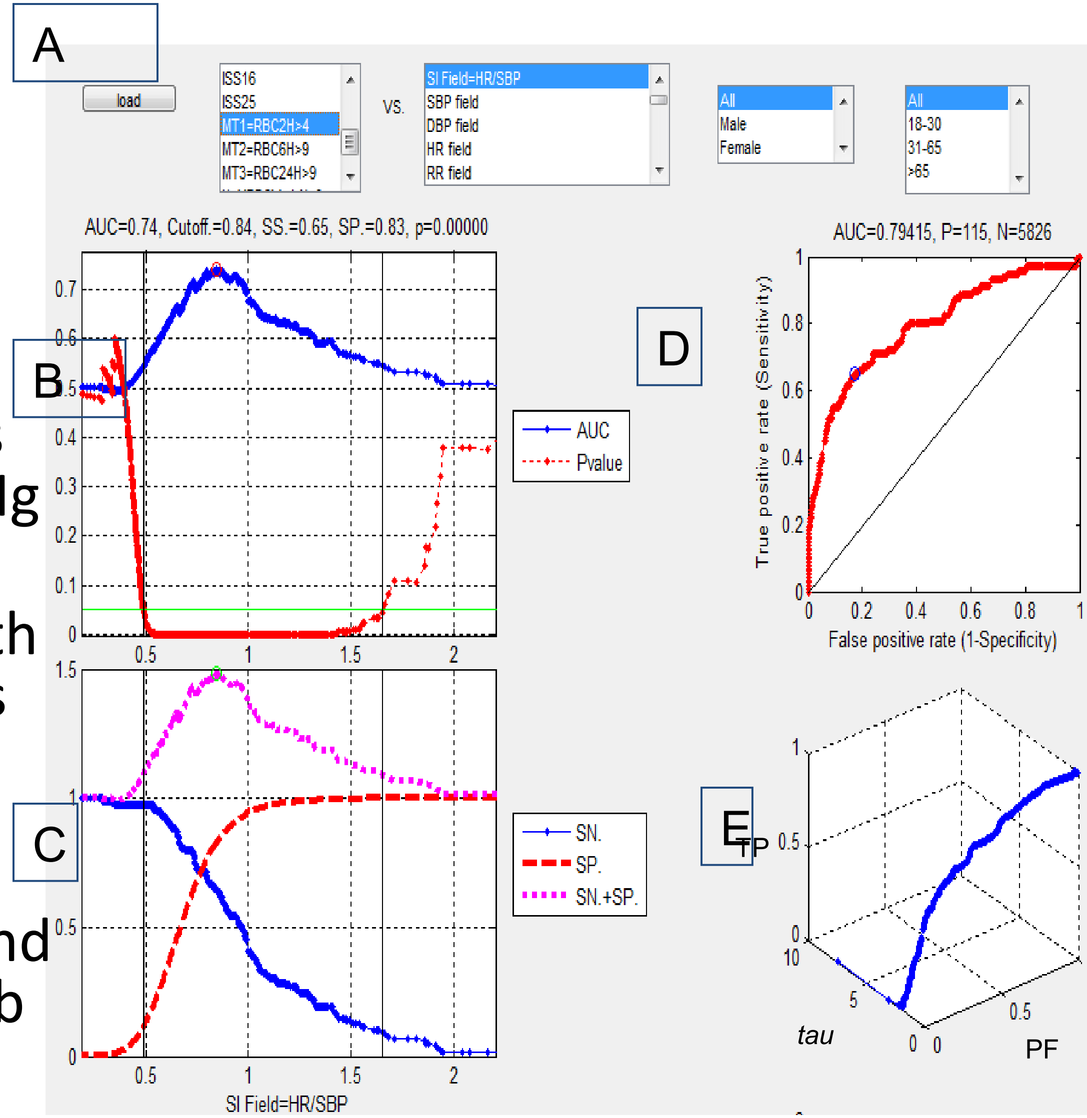
ONPOINT Study Patient Enrollement Sheet

Heart Rate (beats per min)

	50	55	60	65	70	75	80	85	90	95	100	105	110	115	120	125	130	135	140
60	0.83	0.92	1.00	1.08	1.17	1.25	1.33	1.42	1.50	1.58	1.67	1.75	1.83	1.92	2.00	2.08	2.17	2.25	2.33
65	0.77	0.85	0.92	1.00	1.08	1.15	1.23	1.31	1.38	1.46	1.54	1.62	1.69	1.77	1.85	1.92	2.00	2.08	2.15
70	0.71	0.79	0.86	0.93	1.00	1.07	1.14	1.21	1.29	1.36	1.43	1.50	1.57	1.64	1.71	1.79	1.86	1.93	2.00
75	0.67	0.73	0.80	0.87	0.93	1.00	1.07	1.13	1.20	1.27	1.33	1.40	1.47	1.53	1.60	1.67	1.73	1.80	1.87
80	0.63	0.69	0.75	0.81	0.88	0.94	1.00	1.06	1.13	1.19	1.25	1.31	1.38	1.44	1.50	1.56	1.63	1.69	1.75
85	0.59	0.65	0.71	0.76	0.82	0.88	0.94	1.00	1.06	1.12	1.18	1.24	1.29	1.35	1.41	1.47	1.53	1.59	1.65
90	0.56	0.61	0.67	0.72	0.78	0.83	0.89	0.94	1.00	1.06	1.11	1.17	1.22	1.28	1.33	1.39	1.44	1.50	1.56
95	0.53	0.58	0.63	0.68	0.74	0.79	0.84	0.89	0.95	1.00	1.05	1.11	1.16	1.21	1.26	1.32	1.37	1.42	1.47
100	0.50	0.55	0.60	0.65	0.70	0.75	0.80	0.85	0.90	0.95	1.00	1.05	1.10	1.15	1.20	1.25	1.30	1.35	1.40
105	0.48	0.52	0.57	0.62	0.67	0.71	0.76	0.81	0.86	0.90	0.95	1.00	1.05	1.10	1.14	1.19	1.24	1.29	1.33
110	0.45	0.50	0.55	0.59	0.64	0.68	0.73	0.77	0.82	0.86	0.91	0.95	1.00	1.05	1.09	1.14	1.18	1.23	1.27
115	0.43	0.48	0.52	0.57	0.61	0.65	0.70	0.74	0.78	0.83	0.87	0.91	0.96	1.00	1.04	1.09	1.13	1.17	1.22
120	0.42	0.46	0.50	0.54	0.58	0.63	0.67	0.71	0.75	0.79	0.83	0.88	0.92	0.96	1.00	1.04	1.08	1.13	1.17
125	0.40	0.44	0.48	0.52	0.56	0.60	0.64	0.68	0.72	0.76	0.80	0.84	0.88	0.92	0.96	1.00	1.04	1.08	1.12
130	0.38	0.42	0.46	0.50	0.54	0.58	0.62	0.65	0.69	0.73	0.77	0.81	0.85	0.88	0.92	0.96	1.00	1.04	1.08
135	0.37	0.41	0.44	0.48	0.52	0.56	0.59	0.63	0.67	0.70	0.74	0.78	0.81	0.85	0.89	0.93	0.96	1.00	1.04
140	0.36	0.39	0.43	0.46	0.50	0.54	0.57	0.61	0.64	0.68	0.71	0.75	0.79	0.82	0.86	0.89	0.93	0.96	1.00
145	0.34	0.38	0.41	0.45	0.48	0.52	0.55	0.59	0.62	0.66	0.69	0.72	0.76	0.79	0.83	0.86	0.90	0.93	0.97
150	0.33	0.37	0.40	0.43	0.47	0.50	0.53	0.57	0.60	0.63	0.67	0.70	0.73	0.77	0.80	0.83	0.87	0.90	0.93
155	0.32	0.35	0.39	0.42	0.45	0.48	0.52	0.55	0.58	0.61	0.65	0.68	0.71	0.74	0.77	0.81	0.84	0.87	0.90
160	0.31	0.34	0.38	0.41	0.44	0.47	0.50	0.53	0.56	0.59	0.63	0.66	0.69	0.72	0.75	0.78	0.81	0.84	0.88
165	0.30	0.33	0.36	0.39	0.42	0.45	0.48	0.52	0.55	0.58	0.61	0.64	0.67	0.70	0.73	0.76	0.79	0.82	0.85
170	0.29	0.32	0.35	0.38	0.41	0.44	0.47	0.50	0.53	0.56	0.59	0.62	0.65	0.68	0.71	0.74	0.76	0.79	0.82
175	0.29	0.31	0.34	0.37	0.40	0.43	0.46	0.49	0.51	0.54	0.57	0.60	0.63	0.66	0.69	0.71	0.74	0.77	0.80
180	0.28	0.31	0.33	0.36	0.39	0.42	0.44	0.47	0.50	0.53	0.56	0.58	0.61	0.64	0.67	0.69	0.72	0.75	0.78

ONPOINT DATA COLLECTION

- Ten amplitude related features of PPG waveforms were compared to the pre hospital VS based predictors (HR>120 /min, SBP<90 mmHg and SI>0.9).
- Prediction of transfusion with 15 minutes of PPG data was by receiver operator characteristics(ROC) area under curve(AUC) and their associated sensitivity (SN) and specificity (SP)using MathLab and MedCalc



(A), data table sources: outcomes, specific vital signs (VS) features, age and gender subgroupings; (B) threshold vs. receiver operator characteristic (ROC) and probability (P); (C): threshold vs. sensitivity and specificity; (D): two-dimensional ROC and the ROC-area-under-curve (AUC) values; (E): spatial graph of the three-dimensional ROC (3DROC) curve

RESULTS
Continuous PPG amplitude features

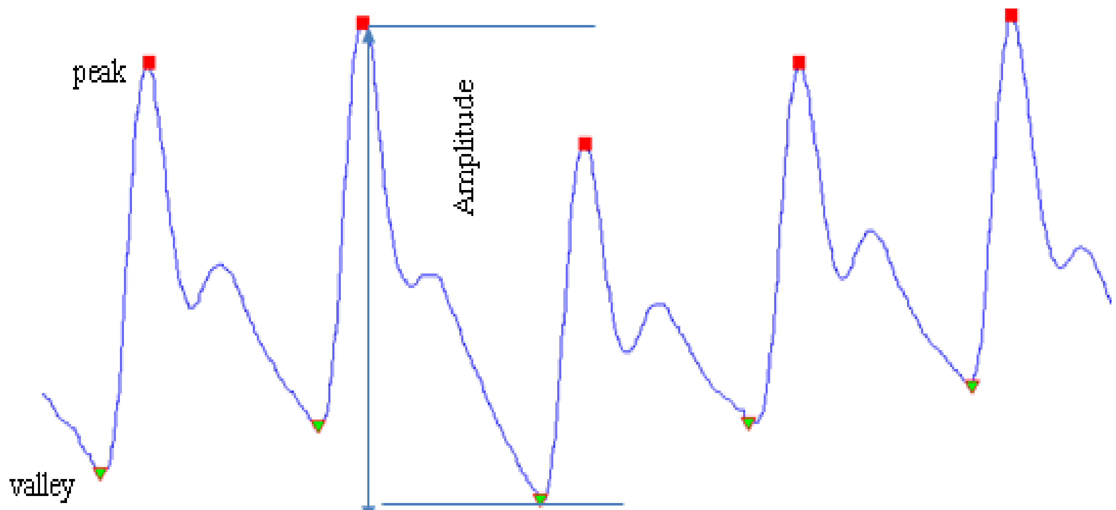
- PPG and other VS data were collected in 374 patients with SI>0.62
- 13 patients received blood within 3hours(h), 11 within 6 h, and 23 patients within

  24 h.

- 10 Features extracted from continuous PPG waveforms

  P1~P9 represent 9 percentile amplitude (10%~90%) of the continuous PPG waveform

  IQ1 & IQ2represent interquartile range of 25% & 75% amplitude



RESULTS TABLE

	pRBC 1-3h			pRBC 3-6H			pRBC 12-24h		
Vital Sign	**AUC**	**Sn%**	**Sp%**	**AUC**	**Sn%**	**Sp%**	**AUC**	**Sn%**	**Sp%**
PPG Features*	0.79	69.0	86.0	0.7	55.0	85.0	0.84	89	79.0
SBP<90	0.6	23.1	91.1	0.52	9.1	95.5	0.52	100	4.7
HR>120	0.55	23.1	86.4	0.52	90.9	14.0	0.57	100	14.2
SI>0.9	0.7	61.5	79.4	0.62	45.4	78.6	0.62	44.4	78.5

N = 374 patients

*** p<0.001 all other predictions for pRBC use**

Predicting on-going hemorrhage and transfusion requirement after severe trauma: a validation of six scoring systems and algorithms on the TraumaRegister DGU® Brockamp et al. *Critical Care* 2012, 16:R129

Table 3 Performance of compared scores.

	TASH	Rainer	Vandromme	Larson	Schreiber	ABC
AUC	0.889	0.860	0.840	0.823	0.800	0.763
95% CI	0.871, 0.907	0.839, 0.881	0.817, 0.863	0.800, 0.847	0.773, 0.828	0.732, 0.794
Cut-off point	≥ 8.5	≥ 2.5	≥ 1.5	≥ 1.5	≥ 0.5	≥ 0.5
Sensitivity, %	84.4	80.6	78.9	70.9	85.8	76.1
Specificity, %	78.4	77.7	76.2	80.4	61.7	70.3
PPV, %	18.9	17.7	16.5	17.4	11.8	13.2
NPV, %	98.8	98.5	98.4	97.9	98.7	98.0

AUC: area under the curve; CI: confidence interval; PPV: positive predictive value; NPV: negative predictive value; TASH: trauma-associated severe hemorrhage score; ABC: assessment of blood consumption.

Approaches to MT prediction

TASH score: 7 variables:SBP; Sex; Hb;FAST;HR;BE; ext or pelvic Fx.

(= probability of MT > 50%).

PWH Score: 7 variables:SBP <90; HR >120; GCS<8; displ pelvic Fx CT or FAST +, BD>5,Hb<7, Hb 7-10 g /dl

(Predicts >10 units pRBC in 24 hrs)

Larson Score(1,124 Combat victims:420 MT) *Independent predictors Hb; HR,SBP, BD.*

Vandromme Score: Lactate > 5; HR > 105; INR > 1.5; Hb < 11 g/dl; SBP < 110

ABC score: SBP< 90; HR > 120, FAST +; penetrating mech

Predicts >10 units pRBC in 24 hrs

Schreiber Score(558 combat victims: 44% MT): Independent predictors Hb; INR; penetrating mechanism

We used one vital sign waveform feature analyses & numeric values and obtained AUC 0.84 Sn 89% Sp 79%

CONCLUSION

- PPG feature analysis is significantly better than routinely used VS thresholds in prediction of blood transfusion need.
- A single VS device providing continuous automatic transfusion decision assistance by PPG waveform analysis is advantageous compared to the need for both HR(Pulse Ox or ECG) and SBP (NIBP) devices and other tests.

CONCLUSION

- Near real-time PPG Feature Analysis could be added to existing pulse oximeters as a software upgrade, with no “cost” in footprint size or weight.
- Fully automated (no user input) predictions of transfusion need communicated to the blood bank before/during transport allows advanced preparation of the full range of blood products to minimize coagulopathy and potentially decrease hemorrhagic deaths.
- Funded by USAF:FA8650-11-2-6D01(PI Colin Mackenzie MD, USAF PI Joseph Dubose MD)

Thank You

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Approaches to MT prediction

__TASH score__: 7 variables:SBP; Sex; Hb;FAST;HR;BE; ext or pelvic Fx.

(p = 1/(1 + exp(5.4 − 0.3∗TASH))) score ≥ 16 points= probability of MT > 50%.

__PWH Score__: 7 variables:SBP <90; HR >120; GCS<8; displ pelvic Fx CT or FAST +, BD>5,Hb<7, Hb 7-10 g /dl

Predicts >10 units pRBC in 24 hrs

__Vandromme Score__: Lactate > 5; HR > 105; INR > 1.5; Hb < 11 g/dl; SBP < 110

__ABC score__: SBP< 90; HR > 120, FAST +; penetrating mech *Predicts >10 units pRBC in 24 hrs*

__Schreiber Score__(558 combat victims: 44% MT): Independent predictors Hb; INR; penetrating mechanism

__Larson Score__(1,124 Combat victims:420 MT) *Independent predictors Hb; HR,SBP, BD.*

__ROPE index__: PR / pulse pressure method of predicting early hemorrhage

__Shock Index__ (SI): HR/ SBP

We will use vital signs waveform feature analyses & numeric values.

__Waveform feature__ analyses includes “dose” , AUC, ML (SVM,Kernel, Entropy)

__Numeric__ Value: Concentrate on HR, SpO2, Hb trend (from Pulse Ox).

ADD Clinical data