Correlation between modified shock index and severity index in predicting outcome in patients with hemorrhagic shock

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Introduction
Trauma is the main cause of death in age group less than 45 years. A lot of clinical parameters including heart rate, pulse rate, blood pressure, shock index (SI), and modified shock index (MSI) are used to predict the severity of hemorrhage in trauma patients. In 2012 Choi and colleagues proposed for the first time a new index (NI) based on lactate concentration and peripheral perfusion index for assessment of shock in a rat model. In this trial, we propose for the first time a new severity predicting index (NI) based on lactate concentration/peripheral perfusion ratio as an indicator of hemorrhage-related mortality in humans.

Materials and methods
This prospective trial is a single-center study of 122 consecutive adult polytraumatized patients with hemorrhagic shock admitted to trauma center within 6 h of the trauma, and underwent resuscitation according to the advanced trauma life support protocol (2016). Protocol-related measurements were obtained immediately after admission and over 48 h postresuscitation for metabolic perfusion parameters, serum lactate, perfusion index, and other hemodynamic parameters. The period of the study corresponds to the outcome after 48 h of admission. Resuscitation measures were considered successful when lactate levels were less than or equal to 2 mmol/l in addition to stable macrohemodynamic parameters at the end of this period.

Results
Characteristically, the survivors had NI of 40 ± 2.7 on admission, compared with 87.1 ± 13 of nonsurvivors with highly significant difference. MSI showed a significant difference (nearly doubled) between survivors and nonsurvivors. SI showed nearly the same change, nearly doubled. NI showed lower prediction value for mortality than MSI and SI (P = 0.05) 0.884, 0.905, and 0.908, respectively.

Conclusion
This study confirms, for the first time in humans, the validity of severity index as independent parameter in prediction of mortality in comparison with MSI.

Keywords:
hemorrhagic shock, lactate and perfusion index, modified shock index, severity index, shock index

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Introduction

In 2010, there were 5.1 million deaths from injuries, greater than the number of deaths due to HIV, tuberculosis, and malaria combined (3.8 million) [1-4]. Worldwide the number of deaths from injuries increased by 24% between 1990 and 2010 [5]. In trauma, time is one of the most important factors affecting prognosis. Outcomes greatly improved when interventions are provided within the golden hour following injury. The management of polytrauma is based on the principle that the care provided to trauma patients in the first few hours can be absolutely critical in terms of predicting long-term recovery and that good trauma care involves getting the patient to right place in right time for the right treatment [1]. Deaths because of trauma occur rapidly, at a high rate, and in a consistent pattern. Early preventable deaths are mainly because of hemorrhagic shock [6]. Shock is a state of cellular hypoperfusion resulting from a mismatch of oxygen delivery and oxygen uptake required to maintain cellular aerobic metabolism. After injury and loss of blood, there is decreased tissue perfusion resulting in hemorrhagic shock; there may also be impaired cardiac and/or neurologic function, resulting in cardiovascular decompensation that will require supportive treatments to sustain survival [7]. Damaged and underperfused cells become distressed, and release

toxins. Anaerobic metabolism generates metabolic by-products (lactate and other acids) that cause more damage both locally and systemically. Other compounds are released by the ischemic cell, including interleukins, tumor necrosis factor, and complement proteins [8]. The presence of poor tissue perfusion in a shocked patient is usually associated with worse outcome. Persistently impaired perfusion despite adequate resuscitation is also associated with worse outcome [9].

Markers of local perfusion are temperature values, skin mottling, capillary refill time, perfusion index (PI), and sublingual microcirculation, whereas markers of global perfusion are lactic acid and mixed and central venous oxygen saturation. The shock index (SI) is obtained from the ratio between heart rate and systolic blood pressure (HR/SBP). It is a physiological score that can be used in the prehospital and initial emergency care to determine the severity of the trauma, and also to detect an early hemorrhagic shock [10]. SI is known as hemodynamic stability indicator. It is considered as a better marker for assessing the severity of shock than HR and BP alone. Thus, in clinical practice, SI has been used to assess the severity of emergency patients [3].

Clinically, mean BP can best represent tissue perfusion status. Diastolic blood pressure (DBP) of a critical patient usually decrease earlier than SBP, so mean BP is considered an accurate predictor for hemorrhage severity. If mean arterial pressure (MAP) replaces SBP in SI, modified shock index (MSI) can be obtained from the following equation: MSI = HR/MAP.

A low MSI indicates high systemic vascular resistance, and the patient is in a hyperdynamic state, which can also be a sign for sever conditions. MSI can be a valuable tool in predicting disease severity in patients with an MSI greater than 1.3, there is an increased probability of ICU admission and death, whereas high MSI denotes low systemic vascular resistance, a sign of hypodynamic circulation, so the patient may be compensating and the decompensation is rapid [11]. Therefore, both high and low MSI reflects the serious state of the emergency patients. MSI was considered as a better marker for mortality rate prediction [3]. Recent studies have focused on diagnosing shock severity according to evidence of tissue ischemia, including serum lactate concentration (LC) or peripheral perfusion (PP).

In 2012 Choi and colleagues proposed a new index (NI) based on LC/PP ratio as an indicator of hemorrhage-related mortality, demonstrating a sensitivity far exceeding shock assessment using conventional parameters. They reported that their newly devised hemorrhagic index based on LC/PP ratio is superior in predicting mortality resulting from acute hemorrhagic shock compared with other existing models [4].

Materials and methods

This clinical physiologic study was conducted in the Trauma Emergency Department and Trauma ICU of Assiut University Hospital, from November 2016 to November 2017. This prospective trial was a single-center observational cohort study of 122 consecutive adult polytraumatized patients with hemorrhagic shock because of blunt or penetrating trauma without head injury admitted to our trauma center within 6 h of the trauma, fulfilling the inclusion criteria and underwent resuscitation according to the advanced trauma life support protocol (2016) and surgical control of the source of hemorrhage (Fig. 1).

Inclusion criteria

Trauma patient with injury severity score (ISS) more than or equal to 15, age, 20–60 years with Glasgow coma scale: 14 or 15 and having SBP below 90 mmHg, mean BP below 60 mmHg or decrease of SBP 40 mmHg below normal value.

Exclusion criteria

Head trauma patients, patient with bilateral ischemic arm injury, and presence of preexisting conditions as severe cardiovascular disease.

Figure 1

Flow diagram of patients included in the study.

Study endpoints

The period of the study corresponds to the outcome after 48 h of admission to trauma unit or trauma ICU. Resuscitation measures were considered successful when lactate levels were less than or equal to 2 mmol/l in addition to stable macrohemodynamic parameters at the end of this period. All patients were managed according to ATLS algorithm (2016). Resuscitation aimed at normalization of perfusion parameters by immediate control of bleeding, intravenous fluids, and vasopressors when needed to maintain a MAP more than or equal to 65 mmHg.

On admission the following was done:

(1) Establishment of patent airway to ensure adequate ventilation and oxygenation.
(2) Establishment of central venous line and a blood sample was collected to detect hemoglobin and serum lactate level at T0.
(3) At the same time, patient was monitored to detect HR, BP, and PI at T0.
(4) Fluid resuscitation was started with 750 ml of warmed isotonic solutions, and then fluid was continued according to challenge test.
(5) Low molecular weight colloid (volven) solutions were also used to achieve intravascular volume expansion.

The goal of resuscitation was to restore organ perfusion. This was accomplished by the use of resuscitation fluids to replace lost intravascular volume and has been guided by restoring normal BP (systolic >90 mmHg or mean >60 mmHg). Patients, who did not respond to fluid resuscitation, were given cross-matched blood to achieve a target hematocrit more than or equal to 30%. This is guided with hemoglobin less than 8 mg/dl. Vasopressors as norepinephrine or epinephrine were used to achieve targeted perfusion pressures (systolic >90 mmHg or mean >60 mmHg). Failure to respond to crystalloid and blood administration in the emergency department indicates the need for immediate definitive intervention (e.g. surgical intervention). Protocol-related measurements were obtained at 0 h (immediately after admission), 8, 16, 24, 36, and 48 h postresuscitation for metabolic perfusion parameters, serum lactate, PI, and other hemodynamic parameters (HR, systolic, diastolic, mean BP, and central venous pressure), MSI (ratio of HR to MAP). MAP=[(DBP × 2)+SBP/3] and new severity predicting index (ratio of serum LC to PP index) were calculated. The outcome was recorded as survivor and nonsurvivor.

Statistical analysis

Variables and measurements

This study calculated the new severity index, SI, MSI, serum lactate and PI. Data were expressed as mean, SD, number, and percentage. Data were collected and analyzed by computer program SPSS, version 23 (SPSS Inc., Chicago, Illinois, USA). *t* test (and Mann–Whitney if necessary) was used to determine significance for numeric variables. χ^2 and Fisher's exact test were used to determine significance for categorical variables. Receiver operating characteristic (ROC) curve was used to determine sensitivity and specificity and area under the curve (AUC) to predict mortality among the patients included. Pearson's correlation to determine correlation between NI and other numeric variables associated with survival. Multiple regression analysis using survival a 'dependent variable' excluding other dependent variables included in calculation such as HR, BP, PI, and lactate. Only SI, MSI, and NI were chosen for prediction of mortality.

P value less than 0.05 is considered significant.

Correlation coefficient of all parameters with mortality using Cox analysis showed a strong correlation with MSI followed by SI then NI, which correlate with the data of ROC AUC (Fig. 1).

Results

Patients included were young and had traffic accidents, and all were admitted to trauma department with SBP less than 90 mmHg and ISS more than 15, divided into two group according to mortality in the first 48 h (end point of the study), into survivors and nonsurvivors.

Characteristically, the survivors had NI of 40 ± 2.7 on admission, compared with 87.1 ± 13 of nonsurvivors with highly significant difference (Table 1).

This study analyzed each component of NI, and showed that on admission, PI in survivors were 0.29 ± 0.02, versus 0.11 ± 0.008 in nonsurvivors (Table 2).

LC as well, showed a significant difference between survivors and nonsurvivors (Table 3).

Table 1 New index in survival and death groups

Items	Survival (*n*=100)	Death (*n*=22)	*P*
NI.0	40.45±2.79	87.14±13.25	*P*<0.000***
NI.6	23.42±2.14	56.93±6.58	*P*<0.000***
NI.12	15.75±7.19	46.06±7.40	*P*<0.000***
NI.18	7.91±0.96	33.79±4.66	*P*<0.000***
NI.24	4.83±0.63	32.08±4.67	*P*<0.000***
NI.30	3.40±0.56	34.91±5.11	*P*<0.000***
NI.36	1.86±0.26	31.57±13.98	*P*<0.000***
NI.42	0.86±0.28	56.84±50.44	*P*<0.000***
NI.48	0.66±0.17	104.19±34.72	*P*<0.000***

Data are presented as mean±SD. With highly significance difference between survival and death groups with lower in mean value in survival group than death group. NI, new index. ***Highly significance difference.

MSI showed a significant difference (nearly doubled) between survivors and nonsurvivors (Table 4).

SI showed the same nearly the same change, nearly doubled (Tables 5–8).

The second part of the study, compared the AUROC of each index for prediction of mortality.

NI showed higher predictive power than lactate and PI alone.

AUC was 0.884 versus 0.719 and 0.781, respectively (Fig. 2).

Table 2 Perfusion index in survival and death groups

Items	Survival (*n*=100)	Death (*n*=22)	*P*
PI.0	0.29±0.02	0.11±0.008	*P*<0.000***
PI.6	0.42±0.02	0.21±0.03	*P*<0.000***
PI.12	0.69±0.04	0.28±0.04	*P*<0.000***
PI.18	0.99±0.06	0.32±0.03	*P*<0.000***
PI.24	1.16±0.76	0.34±0.03	*P*<0.000***
PI.30	1.33±0.83	0.37±0.15	*P*<0.000***
PI.36	1.55±0.08	0.36±0.02	*P*<0.000***
PI.42	1.69±0.92	0.39±0.18	*P*<0.000***
PI.48	1.86±0.99	0.39±0.05	*P*<0.000***

Data are presented as mean±SD. With highly significance difference between survival and death groups with higher in mean value in survival group than death group. PI, perfusion index. ***Highly significance difference.

Table 3 Lactate in survival and death groups

Items	Survival (*n*=100)	Death (*n*=22)	*P*
Lactate. 0	7.57±1.56	9.68±2.81	*P*<0.000***
Lactate. 6	5.94±1.36	9.21±3.19	*P*<0.000***
Lactate. 12	5.19±1.96	9.10±3.71	*P*<0.000***
Lactate. 18	4.12±1.78	9.02±4.15	*P*<0.000***
Lactate. 24	3.11±1.38	8.90±4.25	*P*<0.000***
Lactate. 30	2.40±1.01	9.52±4.12	*P*<0.000***
Lactate. 36	1.93±0.76	9.85±4.18	*P*<0.000***
Lactate. 42	1.88±0.50	13.35±1.34	*P*<0.000***
Lactate. 48	1.59±0.27	13.41±1.39	*P*<0.000***

Data are presented as mean±SD. With highly significance difference between survival and death groups with lower in mean value in survival group than death group. ***Highly significance difference

Table 4 Modified shock index in survival and death groups

Items	Survival (*n*=100)	Death (*n*=22)	*P*
MSI.0	2.78±0.82	4.57±1.07	*P*<0.000***
MSI.6	2.18±0.51	2.97±0.40	*P*<0.000***
MSI.12	1.99±0.47	2.87±0.65	*P*<0.000***
MSI.18	1.88±0.42	2.81±0.72	*P*<0.000***
MSI.24	1.75±0.42	2.79±0.87	*P*<0.000***
MSI.30	1.67±0.38	2.70±0.96	*P*<0.000***
MSI.36	1.38±0.25	2.75±1.13	*P*<0.000***
MSI.42	1.33±0.28	2.68±1.12	*P*<0.000***
MSI.48	1.20±0.22	3.85±0.93	*P*<0.000***

Data are presented as mean±SD. With highly significance difference between survival and death groups with lower in mean value in survival group than death group. MSI, modified shock index. ***Highly significance difference.

NI showed lower prediction value for mortality than MSI and SI (P = 0.05) 0.884, 0.905, and 0.908, respectively.

There was no difference between MSI and SI in this group of patients as regard this point.

Discussion

The early assessment of hypovolemic shock and the prediction of transfusion requirement and mortality in multiinjured patients are still among the most challenging tasks in the initial management of trauma patients [12].

Early and accurately classifying hemorrhagic shock could improve the outcome of patients suffering from hemorrhagic shock and reduce delays during management.

In 2012 Choi and colleagues proposed for the first time a NI based on LC/PP ratio as an indicator of

Table 5 Shock index in survival and death groups

Items	Survival (*n*=100)	Death (*n*=22)	*P*
SI.0	1.85±0.45	2.98±0.58	*P*<0.000***
SI.6	1.40±0.34	1.88±0.31	*P*<0.000***
SI.12	1.31±0.32	1.72±0.24	*P*<0.000***
SI.18	1.30±0.27	1.67±0.20	*P*<0.000***
SI.24	1.18±0.28	1.67±0.26	*P*<0.000***
SI.30	1.15±0.26	1.64±0.26	*P*<0.000***
SI.36	1.05±0.27	1.64±0.31	*P*<0.000***
SI.42	1.01±0.26	1.63±0.36	*P*<0.000***
SI.48	0.98±0.26	1.61±0.41	*P*<0.000***

Data are presented as mean±SD. With highly significance difference between survival and death groups with lower in mean value in survival group than death group. SI, shock index. ***Highly significance difference

Table 6 Cut-off, sensitivity, and specificity in study group

Items	Cut-off	Sensitivity (%)	Specificity (%)	AUC
PI.0	0.103	67.0	73	0.781
SI.0	1.87	100	56	0.908
Lactate. 0	7.45	72.0	56	0.719
MSI.0	2.76	100	62	0.905
NI.0	43.96	100	51	0.884

AUC, area under the curve; MSI, modified shock index; NI, new index; PI, perfusion index; SI, shock index.

Table 7 Multiple regression analysis in study group

	Coefficients				
Model	Unstandardized coefficients		Standardized coefficients	*t*	Significance
	B	SE	Beta		
Constant	−0.114	1.334		−0.085	0.932
SI.0	−0.250	0.886	−0.272	−0.283	0.778
MSI.0	0.652	0.373	1.286	1.751	0.085
NI.0	0.007	0.002	0.653	4.210	0.000

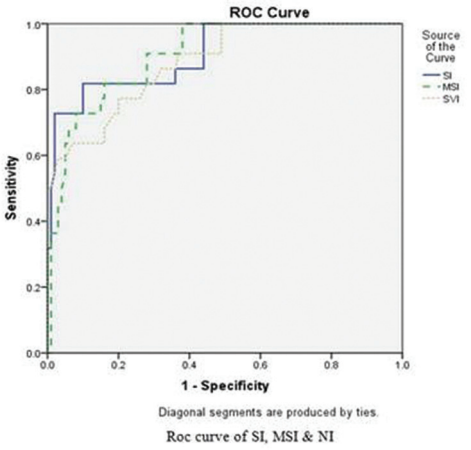
NI at admission highly significance (*P*<0.000). Dependent variable: survival. MSI, modified shock index; NI, new index; SI, shock index.

Table 8 Correlation between modified shock index, new index, and other variables on admission

Correlations					
	MSI.0	NI.0	SI.0	Lactate. 0	PI.0
MSI0					
r	1	0.654**	0.952**	0.014	−0.551**
P		0.000	0.000	0.879	0.000
NI.0					
r	0.654**	1	0.681**	0.423**	−0.767**
P	0.000		0.000	0.000	0.000
SI.0					
r	0.952**	0.681**	1	0.016	−0.581**
P	0.000	0.000		0.858	0.000
Lactate. 0					
r	0.014	0.423**	0.016	1	−0.070
P	0.879	0.000	0.858		0.446
PI.0					
r	−0.551**	−0.767**	−0.581**	−0.070	1
P	0.000	0.000	0.000	0.446	

MSI, modified shock index; NI, new index; PI, perfusion index; SI, shock index. **Correlation is significant at the 0.01 level (two-tailed).

Figure 2



ROC curve of SI, MSI, and NI. MSI, modified shock index; NI, new index; ROC, receiver operating characteristic; SI, shock index.

hemorrhage-related mortality in rats, demonstrating a sensitivity far exceeding shock assessment using conventional parameters. The newly proposed index in that study showed better performance in regard to AUC, correlation with mortality, and multivariable logistic regression analysis in comparison with vital signs, including the SI, in acute lethal hemorrhagic shock in rats [4].

In 2015 Choi and colleagues performed another study, to overcome the limitations of using vital signs for ATLS. They included PI and LC in addition to the primary vital signs to determine the associations between several indices and blood loss for precise ATLS classification. By systematically applying the ATLS guidelines to animal model of hemorrhagic shock, they found associations between blood loss and some variables, including the PI and LC, as well as primary vital signs [10].

In this trial, we propose for the first time a new severity predicting index (NI) based on LC/PP ratio as an indicator of hemorrhage-related mortality in humans.

In this study, to overcome the limitations of using vital signs for early triage of trauma patients, we included PI and LC in addition to the primary vital signs to determine the associations between several indices and patient outcome. This prospective observational cohort study included 122 patients with traumatic hemorrhagic shock presented to our tertiary center trauma unit and ICU with ISS more than or equal to 15, who received mean crystalloid volume (6700 ± 1110.23 ml), mean colloid volume (1190 ± 655.22), mean packed red blood cells (6.34 ± 1.95 U), and mean fresh frozen plasma (5.08 ± 2.94 U), with study end point 48 h.

There is a highly significant difference in PI between survival and death groups with higher in mean value in survival group than death group, with cut-off value of 0.103. On the other hand, there is a highly significant difference in LC between survival and death groups with lower in mean value in survival group than death group, with cut-off value of 7.45.

Considering SI, there is a highly significant difference in SI between survival and death groups with lower in mean value in survival group than death group, with cut-off value of 1.87.

Correlation coefficient of all parameters with mortality using Cox analysis showed a strong correlation with MSI followed by SI then NI, which correlate with the data of ROC AUC.

Multiple regression analysis in study group shows NI at admission is highly significant ($P < 0.000$). However, there was moderate significance difference ($P < 0.002$) at PI at admission.

This prospective observational study showed that there was a statistically highly significant difference in PI, LC, SI, MSI, and NI between survival group and death group on admission and postresuscitation of adult polytraumatized patients having hemorrhagic shock without head injury.

This study was designed primarily to test the sensitivity and specificity and cutoff point of the newly reported severity index, tested with high superiority over SI and vital signs in rats.

The main results of this study using AUC ROC curve of the NI was lower than that of SI and MSI.

However, NI has better AUC than lactate and PI alone. This raises the importance of this index than these two important variables. Utility of this index in prediction of mortality seems to be better than using PI or serum lactate alone.

Conclusion

This study confirms, for the first time in humans, the validity of severity index as independent parameter in prediction of mortality in comparison with MSI. The NI seems to be valid index with less sensitivity and specificity than MSI and SI, and could be added as dependent variable in classifying patients with hemorrhagic shock. Also this NI seems to be superior in prognostic value than PI and serum lactate. This study demonstrates the validity of both MSI and SI with no difference.

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Conflicts of interest

There are no conflicts of interest.

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