



Cardiovascular Reserve Index Versus Shock Index Prediction of Early Trauma Deaths: Trauma-Registry Based Study

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Abstract

Evaluation of trauma injuries is challenging as an apparently stable casualty may be eventually hemodynamically deteriorated but compensated. Shock index (SI) is bi-vital sign index proposed in 1967 for detecting severe hemodynamic deterioration. The cardio-vascular reserve index (CVRI) is a multi-vital sign index which previous studies revealed promising associations along the entire hemodynamic spectrum

Methods: A historical prospective study was conducted utilized the Israeli National Trauma Registry of 2015. Entry point was emergency department (ED) admission, and end point was either in-hospital death or survival to discharge. Both SI and CVRI were computed from the retrieved vital signs (on ED admission). Predictability of death was evaluated by Receiver Operating Characteristics area under the curve (AUC). The study aimed to evaluate SI and CVRI predictability of early trauma death as an add-on to the existing trauma death predictors such as Glasgow Coma Score (GCS) and Revised Trauma Score (RTS)

Results: Included were 27,910 trauma casualties, mean age 54.6 years, 56% male, 98.5% survived to discharge and 1.5% died (0.2% early trauma deaths). Both SI and CVRI were found to be a moderate predictors of early death (AUC=69%) in the entire trauma population, inferior to GCS (AUC=77%), and Revised Trauma Score (RTS) (AUC=85%). However, the vast majority of casualties were scored GCS \geq 14 including nearly half of the early deaths. In this subpopulation CVRI was a fair predictor of early death (AUC=0.74) preferable to SI (AUC=0.67). Similarly, the vast majority of casualties were scored RTS \geq 10 including nearly half of the early deaths. In this subpopulation CVRI was a fair predictor of early death (AUC=0.73) preferable to SI (AUC=0.64)

Conclusion: Both SI and CVRI were found to be moderate predictors of early trauma death, inferior to RTS and GCS. CVRI was a fair and preferable then SI in the subpopulations practically undetected either by GCS or RTS (each missed nearly half of early trauma deaths). Consideration of CVRI as a complementary measure to the existing scores may improve overall detectability of high risk casualties

Keywords: Cardiovascular Reserve Index (CVRI); Early trauma death; Glasgow Coma Scale (GCS); Hemodynamic deterioration; Revised Trauma Score (RTS); Shock Index (SI)

Abbreviations: AUC: Area Under The Curve; CVRI: Cardiovascular Reserve Index; DBP: Diastolic Blood Pressure; ED: Emergency Department; HR: Heart Rate; GCS: Glasgow Coma Score; INTR: Israeli National Trauma Registry; IRB: Institutional Review Board; ISS: Injury Severity Score; LOS: Length Of Stay; MABP: Mean Arterial Blood Pressure; OR: Operating Room; ROC: Receiver Operating Characteristics; RR: Respiratory Rate; RTS: Revised Trauma Score; SBP: Systolic Blood Pressure; VS: Vital Signs; WRTS: Weighted Revised Trauma Score

Introduction

Survival to discharge is the primary aim in hospitalized trauma casualties [1,2]. The trimodal trauma death defines immediate, early, and late trauma deaths [3,4]. Immediate deaths are defined as prehospital and ED deaths. Early trauma death is defined as in-hospital death that occurs within 24 hours of admission (excluding ED immediate deaths) [3,5-13]. The main causes of immediate and early trauma deaths are severe CNS injuries (predominantly head injury) and massive hemorrhage [8-10,14]. Late trauma deaths are defined as in-hospital deaths that occur after the first 24h associated with progressive consequences of the initial injury, exacerbated comorbidities, potential confounders and modifiers [15,16].

Severe head injury can carry poor prognosis, sometimes it is

untreatable hence some neurologic insult death are practically unpreventable while those who survive may carry severe sequels. An apparently stable casualty may be eventually hemodynamically deteriorated but compensated. Severe hemorrhage may be still treatable, hence many hemorrhagic deaths may be considered "preventable". The earlier the hemorrhage is detected the better the odds for successful outcome. Unfortunately, clinical findings may be misleading due to compensatory mechanisms that mask signs of hemodynamic deterioration. Detecting deterioration during the compensatory stage is a major challenge even to the experienced expert. Currently, vital signs and several severity scores such as Glasgow Coma Scale and revised trauma scale are used to categorize trauma severity.

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The shock index (SI) is a bi-vital sign index, first presented in 1967 as an indicator of pending shock [17] but had never become a standard of care in clinical practice.

The cardiovascular reserve index (CVRI) is a multi-vital sign index, derived from the control theory previously proposed by Gabbay & Bobrovsky as an estimate of their cardiovascular reserve hypothesis [18,19]. An initial CVRI verification study in diverse conditions of three existing databases (acute severe admissions-pending shock, heart failure and exercise capacity databases each was stratified to subgroups by severity), demonstrated promising association between CVRI and hemodynamic condition (along the hemodynamic spectrum) [19].

An evaluation of CVRI dynamics during exercise suited the assumed pattern of the cardiovascular reserve hypothesis; the highest individual patient's CVRI was at rest, it decreased with exercising, reaching similar CVRI minimum at peak exercise (regardless the exercise capacity) from which CVRI increased with recovery [20].

A swine exsanguination experiment evaluated Approximated CVRI (CVRI_A) had revealed near linear associated between CVRI_A with hemorrhage related hemodynamic deterioration pattern. Cardiac output on the other hand remained preserved even in considerable hemorrhage follow which it exhibited a sharp, stair-wise collapse [21]. These studies suggested CVRI may enable early detection of hemodynamic deterioration.

The aim of this study was to evaluate and compared SI and CVRI predictability of early trauma death as a complementary to the existing measures GCS and RTS.

Research Methodology

A historical prospective study was conducted, based on the INTR 2015 cohort. The data was retrieved and analyzed anonymously. The study was approved by Rabin Medical Center's institutional review board (IRB).

The Israeli National Trauma Registry (INTR) consolidates reports from nearly 20 countrywide Israeli trauma centers that treat and coordinate care of major injuries. INTR is reported after the casualty reaches endpoint (either in-hospital death or survive to discharge). The INTR is also reported on femur neck fractures (unlike most trauma registries where these pathological fractures are not considered as solely attributed to trauma).

Each INTR record includes demographics, clinical characteristics, vital signs at ED, diverse severity scores routinely used in trauma including Glasgow Coma Scale (GCS), Revised Trauma Score (RTS), Weighted Revised Trauma Score (WRTS) and Injury Severity Score (ISS). The latest is defined retrospectively hence, is not applicable as predictor of early death.

Inclusion criteria

INTR trauma cohort of 2015 –casualties admitted to ED trauma centers between 1 January 2015 and 31 December 2015.

Exclusion criteria

ED immediate death and records in which vital signs measurements (essential to compute either SI or CVRI) were practically missing. Each casualty was followed from the entry point on ED admissions to end point of either in-hospital death, or survived to discharge.

Calculated measures

SI was computed from the retrieved vital signs (measured on ED

admission) [17]:

$$SI = HR/SBP$$

where HR is heart rate and SBP is systolic blood pressure.

CVRI was computed from the retrieved vital signs (measured on ED admission) [19]:

$$CVRI = 18 \times MABP / (HR \times RR \times BSA)$$

where MABP is mean arterial blood pressure, HR is heart rate, RR is respiratory rate and BSA is body surface area.

As individual BSA was not available, gender specific BSA averages were posed (1.91m² for males and 1.71m² for females) [22].

Casualties with GCS \geq 14 were defined as subpopulation practically undetected as carrying risk by GCS.

Casualties with RTS \geq 10 were defined as subpopulation practically undetected as carrying risk by RTS.

SI and CVRI predictability of early trauma death were evaluated in the entire trauma population and in the subpopulations undetected by either GCS or RTS.

Data and statistical analysis

Comparison of means was evaluated by ANOVA. Associations between continuous measures were evaluated by Pearson correlation coefficients and parametric measures by Spearman correlation coefficients. Potential predictability was evaluated through Receiver Operating Characteristics (ROC) Area under the curve (AUC).

Results

Overall analysis

Included were 27,925 trauma casualties retrieved from the INTR 2015 cohort; out of which 27,910 (99.9%) records were eligible for analysis. The mean age was 54.6 years with male predominance of 56.0%. Vital signs averages on ED admission were: BP 137/77, HR 82, RR=19.5 and MABP 97. Severity scores averages were: ISS 6.8, GCS 14.8, RTS 11.9; and WRTS 7.8. SI average was 0.62 and CVRI 0.63. 12357 (44.3%) casualties underwent surgery (most of which 94% on day one).

Orthopedics was the predominant admitting department with 15483 (55.5%) admissions, and in decreasing order: general surgery 4827 (17.3%), other surgical sub-specialties (not specifically mentioned here) 2868 (10.3%), non-surgical wards 2064 (7.4%), neurosurgery 1031 (3.7%), and cardiothoracic surgery 468 (1.7%). 1074 (3.8%) were treated in ICUs.

Most casualties 27491 (98.5%) survived to discharge, 419 (1.5%) died [51 early trauma death (0.2%) and 368 late trauma death (1.3%)].

The average length of stay (LOS) was 5.9 days; 5.8 days for survivors, one day for those who died early death, and 13.4 days for those who died late death. Of the 51 early deaths 32 (63%) had a documented cause of death in the INTR, out of which 32% were fatal brain injury, 32% were hemorrhage and 19% were multi system failure. The documented causes of late trauma deaths include multi system failure 24%, fatal brain injury 24%, sepsis 11%, respiratory failure 10%, myocardial infarction 6% but only 4% hemorrhage.

There were very high correlation coefficients in between the severity scores (RTS-GCS $r=0.891$, WRTS-GCS $r=0.935$, and RTS-

WRTS $r=0.986$), all of whom were statistically significant ($p < 0.001$).

There were some association between SI with RTS and WRTS but not with GCS (SI-GCS $r=-0.11$, $p < 0.001$; SI-RTS $r=-0.31$, $p = 0.007$; SI-WRTS $r=-0.28$, $p < 0.001$).

There was practically no association between CVRI with each severity scores (CVRI-GCS $r=0.023$, $p < 0.001$; CVRI-RTS $r=0.016$, $p < 0.007$; CVRI-WRTS $r=0.038$, $p < 0.001$).

There was some association between SI and CVRI $r=-0.37$ ($p < 0.0001$).

There were (as expected) high association between SI with SBP and HR but not with RR (SI-SBP $r=-0.53$, SI-DBP $r=-0.17$, SI-HR $r=0.48$, and SI-MABP $r=-0.39$, SI-RR $r=0.02$). There were (as expected) high association between CVRI with SBP, DBP, HR and RR (CVRI-SBP $r=0.39$, CVRI-DBP $r=0.29$, CVRI-HR $r=-0.53$, CVRI-RR $r=-0.38$ and CVRI-MABP $r=0.38$).

Survive to discharge vs. those who died early death and late death

Table 1 shows that age was younger in those survive to discharge compared to those who died early death, but those who died early death were significantly younger than those who died late death.

HR was significantly lower in survivors than in patients who died early death and slightly higher in those who died early death compared to those who died late death. SBP was higher in survivors than in those who died early death and lower in those who died early death compared to those who died late death. MABP was higher in survivors than in those who died early death and lower in those who died early death compared to those who died late death. All differences were significant.

ISS was lower (better) in survivors than in patients who died early death and higher (worse) in those who died early death than in those who died late death (all statistically significant). GCS was higher (better) in survivors than in those who died early death and lower (worse) in those who died early death than in those who died late death (all statistically significant). RTS was higher (better) in survivors than in those who died early death, and lower (worse) in those who died early death than those died late death (all statistically significant). WRTS was higher (better) in survivors than in those who died early death and lower (worse) in those who died early death than in those who died late death (all statistically significant).

SI was higher (better) in survivors than in patients who died early death and lower (worse) in those who died early death than in those who died late death (all statistically significant). CVRI was higher (better) in survivors than in patients who died early death and lower (worse) in those who died early death than in those who died late death (all statistically significant) (Table 1).

Overall trauma population

AUC for each potential predictor is presented in Table 2. Overall, predictability of early death was higher (in all predictors) than predictability of overall death. SI predictability of early death among the entire trauma casualties was fair (AUC=0.69) identical to CVRI predictability (AUC=0.69), but inferior in comparison with GCS, RTS and WRTS.

Subpopulation undetected as carrying risk by GCS

The vast majority (27324) of casualties and nearly half of all early deaths were practically undetected as carrying risk by GCS.

Measure type	Measure	Survive	Early death	Late death	p-value ANOVA
Age	Years	54	64	75	<0.001
Vital signs	HR	82	93	87	<0.001
	RR	19.5	18.7	19.3	<0.001
	SBP	137	117	138	<0.001
	DBP	77	64	74	<0.001
	MABP	97	82	95	<0.001
Severity scores	ISS	6.6	29.8	19.3	<0.001
	GCS	14.9	9.2	12.1	<0.001
	RTS	11.9	9.4	10.9	<0.001
	RTS2	7.8	5.7	6.9	<0.001
Multi vital sign index	SI	0.62	0.96	0.70	<0.001
	CVRI	0.63	0.51	0.62	<0.001

Table 1: Comparison of measurements averages between patients, who survived, died early death or late death.

Measure type	Potential predictor	Predicting death AUC	Predicting early death AUC
Vital signs	SBP	0.51	0.65
	MABP	0.54	0.66
	HR	0.56	0.63
	RR	0.53	0.54
Severity scores	ISS	0.82	0.91
	GCS	0.66	0.77
	RTS	0.67	0.85
Multi vital sign index	SI	0.55	0.69
	CVRI	0.56	0.69

Table 2: ROC Area under the curve in overall death prediction and early death prediction by potential predictors.

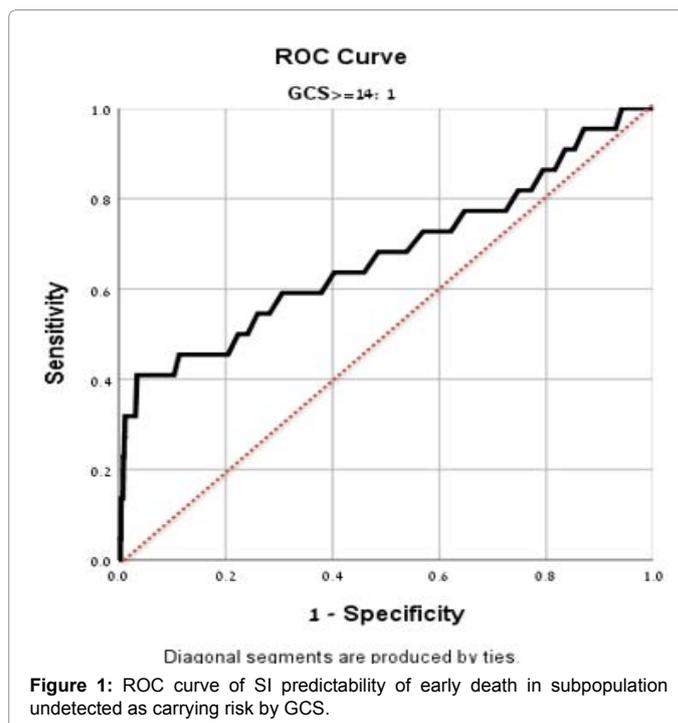


Figure 1: ROC curve of SI predictability of early death in subpopulation undetected as carrying risk by GCS.

Figure 1 presents ROC curve of SI fair predictability of early trauma death (AUC=0.67) in the subpopulation undetected as carrying risk by GCS (GCS \geq 14).

Figure 2 presents ROC curve of CVRI fair predictability of early trauma death (AUC=0.73) in the subpopulation undetected as carrying risk by GCS (GCS \geq 14).

Sub-population undetected as carrying risk by RTS

Figure 3 presents ROC curve of SI fair predictability of early death (AUC=0.64) in the subpopulation undetected as carrying risk by RTS (RTS \geq 10).

Figure 4 presents ROC curve of CVRI fair predictability of early death (AUC=0.73) in the subpopulation undetected as carrying risk by RTS (RTS \geq 10).

Discussion

The overall mortality was relatively low (1.5%), most of which late deaths after nearly two weeks hospital stay on average, that were older than patients who died early trauma death. Elderly are assumed to carry more co-morbidities, modifiers, confounders and complications that contribute to late trauma deaths.

Vital signs averages among those who died early were different than among survivors, but were not alarming. GCS, RTS and WRTS were worse in those who died early death. SI average was considerably and statistically significantly higher (worse) in those who died early death. CVRI average was considerably and statistically significantly lower (worse) in those who died early death.

The very high associations in between the diverse severity scores may suggest common mechanism and overlapping predictability. The low associations between SI with each of the severity scores and the

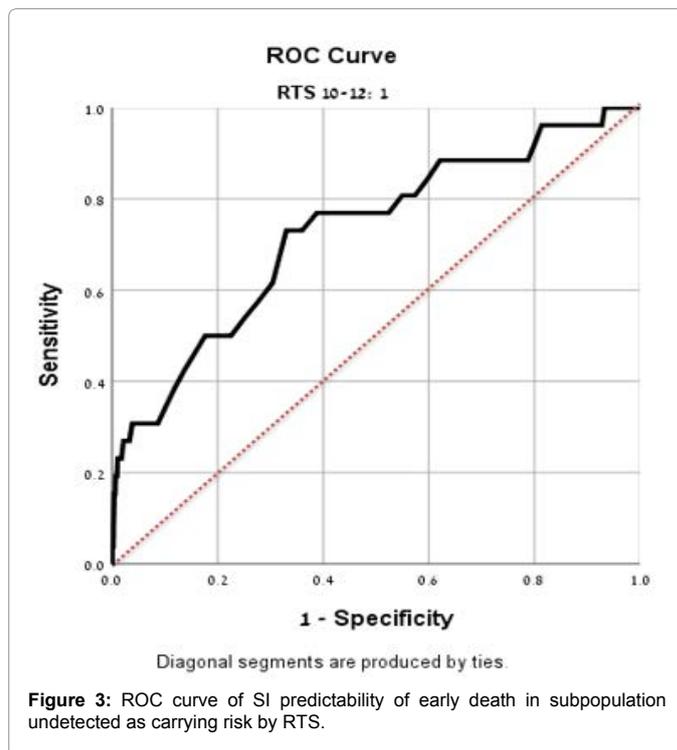


Figure 3: ROC curve of SI predictability of early death in subpopulation undetected as carrying risk by RTS.

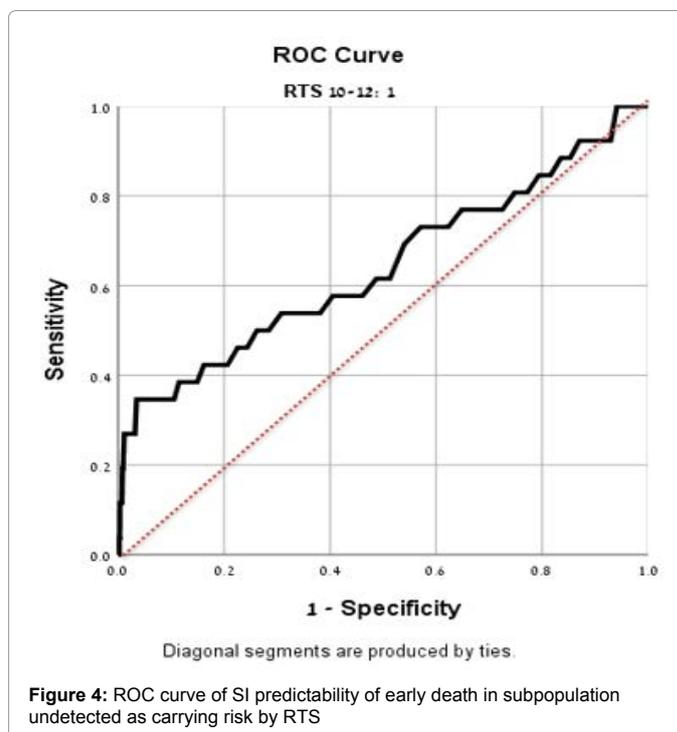


Figure 4: ROC curve of SI predictability of early death in subpopulation undetected as carrying risk by RTS

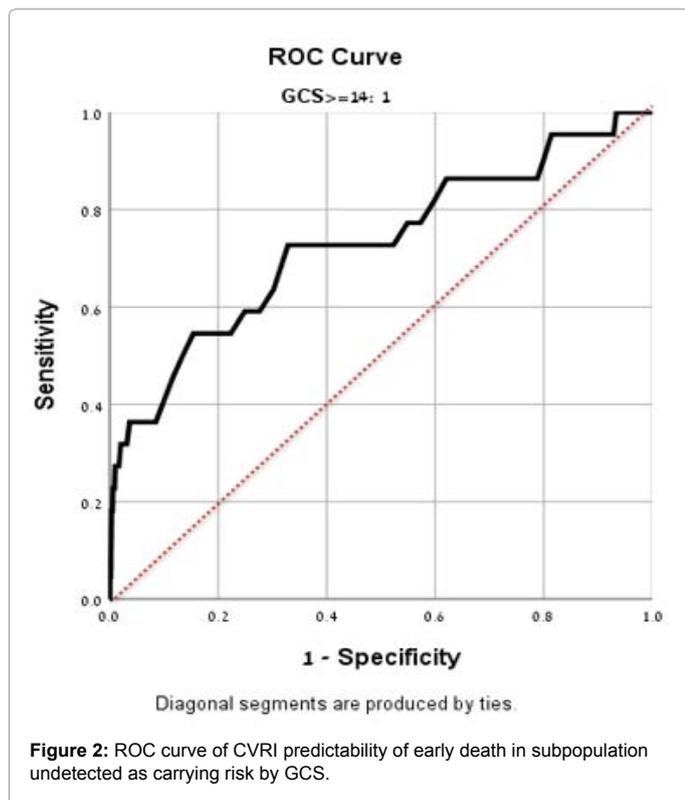


Figure 2: ROC curve of CVRI predictability of early death in subpopulation undetected as carrying risk by GCS.

lack of associations between CVRI with each of the severity scores may suggest that SI and CVRI are related to different mechanism. GCS, RTS and WRTS were found to be good to excellent predictors of early death.

Both SI and CVRI predictability of early deaths in the entire trauma population were fair (AUC=0.69), though considerably inferior to RTS/WRTS (AUC=0.85) and GCS (AUC=0.77).

CVRI predictability of early death in the subpopulation practically undetected as carrying risk by GCS was fair (AUC=0.73) and preferable on SI predictability (AUC=0.67). Similarly, CVRI predictability of early death in the subpopulation practically undetected as carrying risk by RTS was fair (AUC=0.73) and preferable on SI predictability (AUC=0.64).

Glasgow Coma Scale (GCS) was initially proposed to assess head injury, but found applicable to other acute and severe medical conditions and trauma. GCS is also a considerable component in both RTS and WRTS.

The true challenge is detecting deterioration rather than predicting death. Catastrophic head injuries are considered many times untreatable and deaths are less preventable. Major hemorrhage is theoretically treatable and accordingly hemorrhage related deaths may be preventable. Hence, death prediction may underestimate hemorrhagic deterioration detectability.

CVRI fair predictability of early death in the populations undetected as carrying risk by either GCS or RTS (each missed nearly half of all early deaths) and the low association between CVRI with all other scores strongly suggest that CVRI may be influenced by different underlying mechanism namely hemodynamic deterioration (as the main causes of early death are either fatal brain injury and hemodynamic-hemorrhage).

The limitations of this study are that the data is on ED admission rather than on site. It is registry based, which is limited to the available data, incomplete data (for example the lack of individual BSAs) and imprecise documentation.

Conclusion

Trauma registry is a legitimate source for research but carries several limitations that should be considered. Both SI and CVRI were similar moderate predictors of early death in the entire trauma population though inferior to GCS, RTS and WRTS hence cannot be considered competing predictors of death. CVRI was found a fair predictor of early death preferable to SI in the subpopulations undetected as carrying risk by either GCS and RTS each of which missed nearly half of the entire early trauma deaths.

Recommendations

We recommend measuring CVRI in parallel to GCS, RTS and WRTS, as a complementary predictor which may improve the overall deterioration detection. Further prospective trauma studies are recommended to reveal more accurate evaluation of CVRI detectability in detection of the hemodynamic response.

Disclosure

In accordance with my ethical obligation as a researcher, I am reporting that I (Uri Gabbay) am an inventor of a Patent regarding the cardiovascular reserve index. All other authors have no conflict of interest.

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