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The approximated cardiovascular reserve index complies with haemorrhage related hemodynamic deterioration pattern: A swine exsanguination model

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HIGHLIGHTS

- Cardiovascular reserve index (CVRI) estimates the assumed cardiovascular reserve.
- CVRI is computed by routinely measured physiological parameters.
- Criteria for haemodynamic deterioration prediction were preset.
- CVRI met preset criteria (correlation, detecting threshold and indicative range).

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ABSTRACT

Background: To estimate the cardiovascular reserve we formulated the Cardiovascular Reserve Index (CVRI) based on physiological measurements. The aim of this study was to evaluate the pattern of CVRI in haemorrhage-related haemodynamic deterioration in an animal model simulating combat injury.

Methods: Data were collected retrospectively from a research database of swine exsanguination model in which serial physiological measurements were made under anesthesia in 12 swine of haemorrhagic injury and 5 controls. We calculated the approximated CVRI ($CVRI_A$). The course of haemodynamic deterioration was defined according to the cumulative blood loss until shock. The ability of heart rate (HR), mean arterial blood pressure (MABP), stroke volume (SV), cardiac output (CO) and systemic vascular resistance (SVR) and the $CVRI_A$ to predict haemodynamic deterioration was evaluated according to three criteria: strength of association with the course of haemodynamic deterioration ($r^2 > 0.5$); threshold for haemodynamic deterioration detection; and range at which the parameter remained consistently monotonous course of deterioration.

Results: Three parameters met the first criterion for prediction of haemodynamic deterioration: HR ($r^2 = 0.59$), SV ($r^2 = 0.57$) and $CVRI_A$ ($r^2 = 0.66$). Results were negative for MABP ($r^2 = 0.27$), CO ($r^2 = 0.33$) and SVR ($r^2 = 0.02$). The detection threshold of the $CVRI_A$ was 200–300 ml blood loss whereas HR, SV and CO showed a delay in detection, MABP and CVRI exhibited a wide indicative range toward shock.

Conclusions: The $CVRI_A$ met preset criteria of a potential predictor of haemorrhage-related haemodynamic deterioration. Prospective studies are required to evaluate use of the CVRI in combat medicine.

Level of evidence: Level III.

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1. Introduction

Haemorrhage is the leading underlying cause of preventable death in trauma, accounting for approximately 90% of all combat-associated preventable deaths [1–3]. Early control of haemorrhage, whether mechanical or surgical, coupled with haemodynamic stabilization by replacement of fluids and blood improves outcome dramatically [4,5]. However, the window of opportunity for successful intervention is very narrow, as deterioration to haemorrhagic shock and death may be very rapid [3,6,7]. Therefore, early and precise detection is crucial [8,9]. Occult haemorrhage in the field poses a particular challenge even to trained personnel, because it may be overlooked during the initial clinical assessment [6,10].

There are as yet no accurate and practical methods for detecting haemorrhage and predicting haemodynamic deterioration [11], either in the battlefield or in non-combat (e.g., postoperative) settings. Although blood pressure and heart rate (HR) are traditionally measured, their predictive value for the haemodynamic state is equivocal [12,13]. Oxygen saturation has become a crucial measure in emergency medicine, but its yield for the detection of haemorrhage is limited, at least in the early stages [14]. Several studies have suggested noninvasive tools for estimating cardiac output (CO), the classic measure of cardiovascular performance [15], but they have not yet become an accepted part of the initial evaluation [16]. Furthermore, CO may be preserved even in progressive haemorrhage due to compensatory mechanisms [17], especially in young and otherwise healthy individuals, such as military combatants. Pulmonary capillary wedge pressure, introduced by Swan and Ganz [18] as a reliable measure of heart failure, requires invasive means of measurement, and its significance in haemorrhage detection has not been established [19,20]. Central venous pressure (CVP) was traditionally considered a sensitive measure of hypovolemia, but questions regarding its predictive role have arisen in recent years [21]. Others have suggested using diagnostic algorithms such as the Shock Index [22] and the Compensatory Reserve Index [23], but these have not become a standard of care.

The cardiovascular reserve hypothesis suggests that haemodynamic deterioration is associated with decreased (momentary) cardiovascular reserve. The cardiovascular reserve may be described as the momentary haemodynamic capability to comply with an increasing metabolic demand by increasing CO. During exercise, CO rises, and the cardiovascular reserve decreases accordingly, until it reaches an assumed threshold at which dyspnea and exhaustion limit further effort. In healthy well-trained individuals, the threshold is reached following intensive exercise. However in individuals with an acute morbidity or injury that causes haemodynamic deterioration (e.g. myocardial infarction, haemorrhage, sepsis, etc.), the cardiovascular reserve may drop below the exhaustion threshold to an assumed sustainability limit which leads to shock [24]. In military combatants, reduced cardiovascular reserve may be associated with heat, physical exhaustion, dehydration, and haemorrhage.

In 2015, Gabbay and Bobrovsky [25] formulated the Cardio-Vascular Reserve Index (CVRI) for estimation of the assumed cardiovascular reserve. The CVRI index is based on principles of control theory in general and open loop gain (OLG) in particular. OLG which defines the robustness of the control loop, is proportional to the product of each of the individual gains in the system. The control loop of the cardiovascular system, also termed the cardiovascular feedback mechanism, is composed of three main elements. These include the heart, in which gain is represented by stroke volume (SV), the vasculature, in which gain is represented by systemic vascular resistance (SVR), and baro-receptor sensitivity (BRS), yielding the formula for the OLG of the cardiovascular system OLGcv: OLGcv ~ SVxSVRxBRS.

Several studies have indicated that BRS is reciprocally associated with respiratory rate (RR). Accordingly, the CVRI was proposed as a product of SV by SVR by 1/RR, divided by body surface area (BSA) for standardization of body size and by 4 in order to normalize the CVRI of healthy individuals to about 1 [25–27]. The basic CVRI formula is thus represented as:

$$CVRI = SVxSVR/(RRxBSAx4) \quad (1)$$

where SV = stroke volume, SVR = systemic vascular resistance, RR = respiratory rate, and BSA = body surface area.

Thus, a low CVRI may indicate a lesser adaptation capability due, for example, to acute volume loss and consequent haemodynamic deterioration.

As neither SV nor SVR can be reliably measured noninvasively, the CVRI formula shown above was converted to an equivalent clinical formula using conventional haemodynamic equations, namely, SV=CO/HR and SVR = 80*x*[(MABP−CVP)/CO]. Accordingly, CVRI=(CO/HR) *x*(80*x*(MABP−CVP)/CO)/(RR*x*BSA) *x*4, yielding the formula:

$$CVRI = 20(MABP-CVP)/(HRxRRxBSA), \quad (2)$$

where MABP = mean arterial blood pressure, CVP = central venous pressure, HR = heart rate, RR = respiratory rate and BSA = body surface area.

Previous studies have demonstrated an association of the CVRI with diverse morbidities and exercise capacity levels. A high CVRI of around 1 was associated with normal exercise capacity, a lower CVRI with a decreased exercise capacity, and an even lower CVRI, with morbidity. The lowest CVRI of around 0.2 was associated with shock of any type [26]. Others found that the CVRI decreased with increasing exercise, reaching a minimum of about 0.35 at peak exercise, regardless of the exercise capacity [27].

The aim of the present study was to determine if the pattern of the approximated CVRI ($CVRI_A$) complies with the course of haemorrhage-related haemodynamic deterioration in an experimental model simulating combat injury.

2. Methods

The original study was conducted at the Center for Innovative Surgery of the Hadassah Medical Center, Jerusalem with the Institute for Research in Military Medicine and the Trauma and Combat Medicine Branch of the Medical Corps of the Israel Defense Forces to study haemorrhage-related haemodynamic deterioration in the combat setting using a swine model. Swine were selected owing to their size and physiological similarity to humans [28,29]. The original study included 17 white domestic female pigs (Laboratory Animals Farm, Lahav, Israel) aged 12.4 months and weighing 41–50 kg. Twelve swine were randomly selected to undergo controlled haemorrhage and 5 served as controls. Animals in both groups were anesthetized and monitored according to an identical protocol. Serial measurements of a range of physiologic parameters were made during the course of haemodynamic deterioration, and each was documented with a time stamp. The cumulative blood loss was also monitored continuously, and each measurement was documented with a respective time stamp. In the experimental arm, controlled bleeding was stopped when MABP dropped to 30 mmHg, indicating shock. The findings were stored on a computerized spreadsheet in the Trauma Branch of the Surgeon General's Headquarters of the Israel Defense Forces.

Data of all 17 swine were used in the present study. Because both the physiologic parameters and the cumulative blood loss of