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Original Article

An increase in heart rate variability can be an index for end point of resuscitation in trauma patients

Ali Foroutan [a], Shahram Paydar [b], Seyyed Taghi Heydari [c, *], Leila Mohammadi [c], Farnaz Rahbar [c]

[a] Burn and Wound Healing Research Center, Shiraz University of Medical Sciences, Shiraz, Iran
[b] Department of Surgery, Shiraz University of Medical Sciences, Shiraz, Iran
[c] Health Policy Research Center, Institute of Health, Shiraz University of Medical Sciences, Shiraz, Iran

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ABSTRACT

Purpose: The measurement of heart rate variability (HRV) is a non-invasive method to analyze the balance of the autonomic nervous system. The aim of this study was to compare the changes of HRV and base deficit (BD) during the treatment of trauma patients.

Methods: Forty-three trauma patients with a low injury severity scores (ISS < 24) and negative base excess on admission were included in this study. Based on the BD changes, patients were divided into three groups: 'end pointed' group ($n = 13$), patients' BDs instantly cleared after primary hydration; 'needs further resuscitation' group ($n = 21$), patients' BDs did not reach the end point and thus required further hydration or packed red blood cells transfusion; and 'hydration minimal change' group ($n = 9$), patients' BDs lower than 2.5 mmol/L at the onset of admission and thereafter had minimal change (near normal range). The changes in HRV during fluid resuscitation were detected and compared to BD changes in their arterial blood gases. All data were analysed using the SPSS software Version 15.0. Repeated measures ANOVA was used to determine the changes in HRV, heart rate, blood pressure, and BD among groups.

Results: A significant reverse correlation was found between the BD ratio and the HRV ratio ($r = -0.562$; $p = 0.01$). The HRV of patients with aggravated BDs after fluid resuscitation was decreased. There was an increase in HRV at the time of BD clearance. A decrease in HRV after primary crystalloid hydration bore a significant connection with the need for an ICU ($p = 0.021$) and transfusion of packed red blood cells ($p < 0.001$).

Conclusion: Increase in HRV may be a new non-invasive index for the end point of resuscitation in trauma patients.

Introduction

Cellular shock is defined as inadequate perfusion and oxygenation of the tissues. Resuscitation should be completed when adequate perfusion is restored.[1] The end point of resuscitation is when the tissues restore a normal aerobic metabolism.[2] Although readily available for measurement, traditional vital signs, such as blood pressure and heart rate (HR), cannot reliably indicate the adequacy of perfusion.[3] Finding an index to confirm the end point of resuscitation is still considered a challenge. Base deficit (BD) normalization is a standard index for the end point of resuscitation and an early clearance of BD decreases the incidence of infection and mortality in trauma patients.[4] But BD is obtained from the analysis of arterial blood gas, which therefore is laboratory-dependent, and cannot be used in battlefields or during the pre-hospital period.

Heart rate variability (HRV) measures the complexity of HR changes and is affected by cardiac activities controlled by the autonomic nervous system (ANS). A higher complexity of HRV is interpreted as a higher balance of sympathetic and para-sympathetic interaction.[5]

There are many mathematical methods for analyzing HRV including spectral analysis like fast Fourier transform. Using this mathematical technique, the wave of HRV can be broken into spectrums with different ranges of frequencies. Different regions in the power spectrum are related to specific physiologic phenomena.

* Corresponding author.
E-mail address: heydari.st@gmail.com (S.T. Heydari).
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High frequency power spectrum reflects vagal activity, whereas low frequency power spectrum reflects both sympathetic and vagal activities. The ratio of these two frequencies may reflect the sympathovagal balance.[6]

During haemorrhage, sympathetic overactivity occurs, which causes an imbalance in the ANS, and thereby brings about a lower HR complexity. It has been shown that a low HRV, even in the prehospital period, can predict mortality in the next several days.[7] It has also been reported that in patients with intra-abdominal bleeding, those required laparotomy had a lower HRV in comparison to those tolerated non-operative management.[5] Since the ANS imbalance is a predictor of the severity of haemorrhage, an increase in its balance may indicate the end point of resuscitation. For this purpose, we compared the changes in HRV and BD during the treatment of trauma patients.

Methods

This study has been approved by the Medical Ethics Committee of the Shiraz University of Medical Sciences.

Assessment of HRV

Trauma patients who were admitted to the Emergency Department were selected for this study. A Polar H7 HR sensor device, which was connected to smartphones, was used to capture the HR of included patients. Although a real time analysis was possible through the use of these applications, the raw data of HRs were saved as a time series for further analysis. Then, by using fast Fourier transform (spectral analysis), a high (0.15–0.40 Hz) and low (0.03–0.15 Hz) frequency spectrum was found; by employing this formula, HRV was calculated (which has to be a number between 0 and 100):

$$100 * (HF) / HF + LF$$

where HF means high frequencies and LF low frequencies. The MATLAB software (version 8.5) was used for this purpose. A higher HF indicates higher parasympathetic activity; hence, an increase in HRV indicates a higher balance of the ANS.

HRV was analysed first at the onset of admission, and then after primary hydration, by the use of 1 L lactated ringer. The BD was measured during the two occasions too. According to BD, if any further hydration or packed red blood cell (PRBC) transfusion was needed (based on the Advanced Trauma Life Support protocols), the HRV measurement was repeated when the surgeon in charge decided to terminate the fluid resuscitation (at the end point of resuscitation). Vital signs and demographic data were recorded simultaneously.

Inclusion and exclusion criteria

Fifty-two trauma patients with low injury severity scores (ISS < 24), who had a negative base excess at the onset of their admissions, were selected for the study. The reliability of the captured HR was checked by ECG monitoring devices. Five patients were excluded from this study due to agitation or different bedside surgical procedures, which prevented reliable capturing (during admission or follow-up capturing). Four other patients were excluded due to high respiratory rates that would make noise during the operations of the capturing or monitoring devices. The patients were studied until discharge or possible intra-hospital death.

Grouping

Based on BD changes, the patients were divided into three groups. Group 1 ($n = 13$) included patients whose BDs were instantly cleared after primary hydration. This group—by definition—reached the end point of resuscitation after crystalloid infusion; we, therefore, called this group 'end pointed'.

Group 2 (n = 21)included patients whose BDs did not reach the end point; hence, they required further hydration or PRBC transfusion (Group 2: 'needs further resuscitation'). The BDs of 19 patients deteriorated after primary hydration, and that in 2 patients improved. However, the BDs, in the latter, were still far from normality.

Group 3 ($n = 9$) consisted of patients who had BDs lower than 2.5 mmol/L at the onset of admission; after hydration, they witnessed minimal change in their BDs (near normal range). This group was called 'minimal change'. HRV changes less than 10 unit and BD changes less than 2 mmol/L were considered minimal changes.

Statistical analysis

All data were analysed using the SPSS software (SPSS Inc., Illinois, USA; Version 15.0). The results were reported as frequency (percentage) and mean ± standard deviation. Repeated measurement ANOVA was used to determine the changes in HRV, HR, blood pressure, and BD among the three aforementioned groups. $p < 0.05$ was considered statistically significant.

Results

The mean age of participants was (35.19 ± 14.57) years (range: 16–70 years) and 34 (79.1%) patients were male. The GCS was 13.14 ± 3.56 (range: 3–15). The three groups were matched for age, sex, and GCS.

The mean HRV in Group 1 (end pointed) increased from 57.85 on admission to 72.38 after primary resuscitation with lactated ringer. The mean HRV in Group 2 (requires further resuscitation) decreased from 65.95 to 43.19 after primary fluid resuscitation (Fig. 1). After further resuscitation (including possible PRBC transfusion) and reaching the end point (normalization of BD), HRV of these patients increased to 58.15 (Fig. 2). After resuscitation, HRV showed a minimal change in Group 3 (Fig. 1).

As illustrated in Table 1, Figs. 3 and 4, the mean arterial pressure (MAP) and HR changes were not varied among the three groups. In

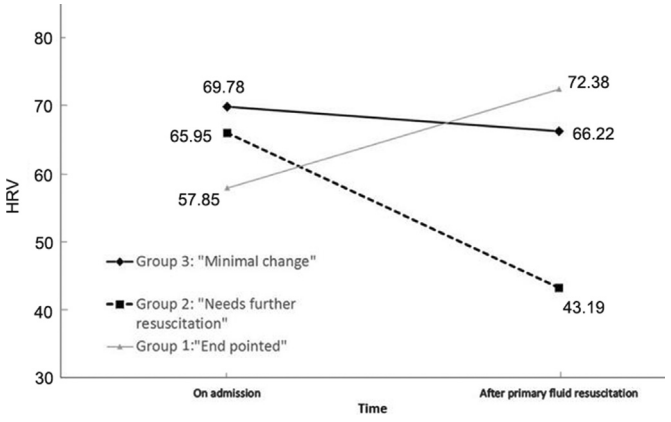

Fig. 1. Comparison of HRV changes among the three groups before and after primary crystalloid therapy (HRV: heart rate variability).

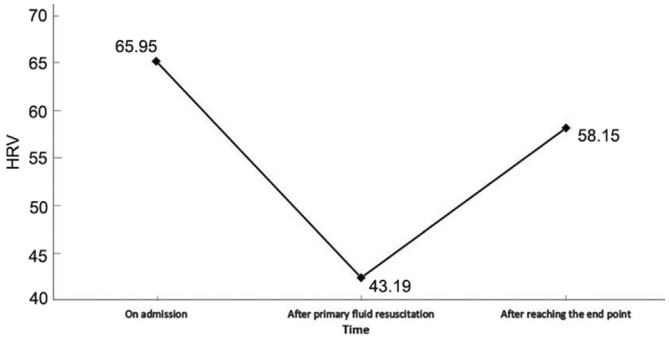

Fig. 2. HRV changes in Group 2 (needs further resuscitation) during the treatment till the end point was reached.

Group 1, The mean MAP (mmHg) changed from 94.64 to 96.00 after primary resuscitation and HR (beats/min) from 93.31 on admission to 86.92 after hydration. Detailed data of other groups are shown in Figs 3 and 4.

HRV ratio, calculated as (HRV1 − HRV2)/HRV1, was used to show the changes in HRV (Table 1). HRV1 is the HRV on admission and HRV2 is the HRV after resuscitation. There was a significant difference in the changes of HRV among the three groups ($p < 0.001$). The mean ratio of (BD1 − BD2)/BD1 was also calculated as the BD ratio for all the patients. BD1 and BD2 are the BDs before and after resuscitation. A significant reverse correlation was found between the BD ratio and the HRV ratio ($r = -0.562$; $p = 0.01$).

Seventeen patients were admitted to the ICU and there was a significant correlation between the HRV ratio and need for an ICU ($p = 0.021$). Fifteen patients required transfusion to reach the end point of resuscitation. In addition, there was a significant correlation between the HRV ratio and the need for transfusion ($p < 0.001$).

Discussion

Adequate tissue perfusion and oxygenation are the goals of any treatment catering to cellular shock after haemorrhage in trauma patients.[8] It has been shown that normalization of the HR and blood pressure can be obtained in about 80% of trauma patients, despite inadequate resuscitation.[1]

Other indices have been investigated as surrogates for the end point, rather than traditional vital signs.[9] These include cellular indices and systemic indices. Most of these end points are invasive for measurement and are not widely available.[10–12]

BD and lactate are the most widely available indices.[13] It has been shown that an early clearance of these indices will decrease the infectious rate and the mortality rate in trauma patients.[2] There is no definitive normal range for lactate for all individuals. The BD measurement needs arterial blood gas, which would be invasive in the case of repeated measurement. In addition, both BD and lactate are laboratory-dependent values, which are not available on battlefields or any other prehospital conditions.

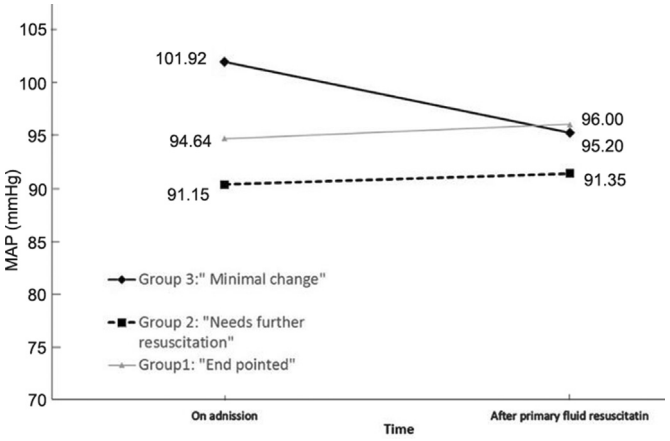

Fig. 3. Comparison of the mean arterial pressure changes in the three groups before and after primary crystalloid therapy (MAP: mean arterial pressure).

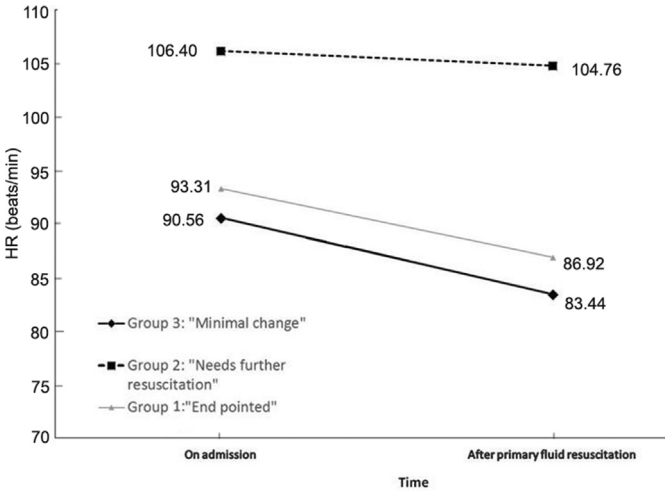

Fig. 4. Comparison of HR changes in the three groups before and after primary crystalloid therapy (HR: heart rate).

On the other hand, HRV is a non-invasive method that is comparable to BD measurement.[14] HRV only needs a portable device and a smart phone to be connected to approve applications. This study shows that the Polar H7 was a reliable HR-capturing device. However, its reliability may be in question while capturing HRs in agitated or severely tachypnic patients.

Bachinsky et al.[7] found that trauma patients with low HRV in the prehospital period had higher mortality. This low HRV is interpreted as imbalance in the ANS. It has also been shown that a low HRV predicts the need for lifesaving interventions, even in patients with normal vital signs.[15,16]

A different study showed that in trauma patients with internal bleedings, who were selected for conservative therapy, a low

Table 1
Comparison of the three groups considering the HR, mean arterial blood pressure and HRV changes.

Groups	HRV ratio[a]	Mean arterial pressure changes (mmHg)	HR changes during treatment (beats/min)
End pointed ($n = 13$)	−0.3758 ± 0.4770	1.36 ± 8.30	7.11 ± 9.56
Needs further resuscitation ($n = 21$)	0.3486 ± 0.19317	0.20 ± 12.72	1.38 ± 24.82
Minimal changes ($n = 9$)	0.0424 ± 0.13374	−6.70 ± 9.92	6.38 ± 11.30
p value	<0.001	0.208	0.661

[a] HRV ratio = HRV1-HRV2/HRV1.

complexity of HRV at the onset of admission can predict the failure of conservative management, and, therefore, brings about the need for laparotomy.[5] Some authors suggest that HRV can be considered a new vital sign.[15]

Changes in HRV during admission have been previously investigated in trauma patients. The decrease in HRV during ICU admission was associated with a higher ICU complications, sepsis, and mortality. The decrease in HRV is called cardiac uncoupling, which implies a loss of autonomic cardiac control.[17–19]

During a haemorrhage, there is overactivity of the sympathetic system in order to maintain the blood pressure within the normal range. An unopposed sympathetic overactivity is considered an imbalance, according to the ANS; after fluid resuscitation or PRBC transfusion, there should be a return to a higher balance. Detection of an imbalance (sympathetic overactivity that is reflected by a reduced HRV) can be interpreted as not reaching the end point. This means that there is a need for further resuscitation (including fluid and blood products transfusion or a procedure to stop bleeding).

The HRV will increase after adequate resuscitation, which can be interpreted as restoring the previously disturbed ANS balance (an increase in vagal activity). This can be called 'cardiac recoupling'.

The abovementioned delicate changes that can be detected in HRV are not apparent in the traditional vital signs, such as HR and blood pressure.[17] As found in our study, the changes in the traditional vital signs are not significantly different between the patients who reached the end point (Group 1) and the patients who did not (Group 2). It has been mentioned in different studies that the amount of parasympathetic activity opposing the sympathetic overactivity in bleeding patients can be surrogate data for anti-inflammatory activities.[20] Anti-inflammatory dominance might be considered an index for the end point of resuscitation in future.

It is difficult to define a normal range for HRV in different individuals, but evaluating the changes in each patient can be very useful for the monitoring of cardiac uncoupling and recoupling.

As a decrease in HRV could also predict the need for an ICU and transfusion, this may be useful for resource allocation in war situations and disasters through the use of widely available devices.

Further studies are required to confirm the applicability of HRV increase (cardiac recoupling) as the end point of resuscitation because we did not include severely injured patients with very high BDs (higher than 10 mmol/L),[1] who may require multiple steps of treatment (including massive transfusions) to reach the end point. BD may not be reliable in some situations such as hypothermia and alcohol poisoning. The reliability of HRV should be further tested by other standard indices for the end point of resuscitation. Other methods of complexity measurement should be tested for the omission of the potential wave noises that may disturb the analysis.

Funding

Nil.

Ethical statement

This study has been approved by the Medical Ethics Committee of the Shiraz University of Medical Sciences.

Conflicts of interest

The authors declare no conflicts of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.cjtee.2019.01.011.

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