

# Predictive Potential of Heart Rate Complexity Measurement: An Indication for Laparotomy Following Solid Organ Injury

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## Abstract

**Background:** Nonlinear analysis of heart rate variability (HRV) has been recently used as a predictor of prognosis in trauma patients.

**Objectives:** We applied nonlinear analysis of HRV in patients with blunt trauma and intraperitoneal bleeding to assess our ability to predict the outcome of conservative management.

**Patients and Methods:** An analysis of electrocardiography (ECG) from 120 patients with blunt trauma was conducted at the onset of admission to the emergency department. ECGs of 65 patients were excluded due to inadequacy of noise-free length. Of the remaining 55 patients, 47 survived (S group) and eight patients died in the hospital (Non-S group). Nineteen patients were found to have intra-abdominal bleeding, eight of which ultimately underwent laparotomy to control bleeding (Op group) and 11 underwent successful non-operative management (non-Op). Demographic data including vital signs, glasgow coma scale (GCS), arterial blood gas and injury severity scores (ISS) were recorded. Heart rate complexity (HRC) methods, including entropy, were used to analyze the ECG.

**Results:** There were no differences in age, gender, heart rate (HR) and blood pressure between the S and Non-S groups. However, approximate entropy, used as a method of HRC measurement, and GCS were significantly higher in S group, compared to the Non-S group. The base deficit and ISS were significantly higher in the Non-S group. Regarding age, sex, ISS, base deficit, vital signs and GCS, no difference was found between Op and Non-Op groups. Approximate entropy was significantly lower in the Op group, compared to the Non-Op group.

**Conclusions:** The loss of HRC at the onset of admission may predict mortality in patients with blunt trauma. Lower entropy, in recently admitted patients with intra-abdominal bleeding, may indicate laparotomy when the vital signs are stable.

**Keywords:** Heart, Blunt Injuries, Laparotomy, Entropy

## 1. Background

In the last two decades, non-operative management of solid organ (including liver and spleen) injury in hemodynamically stable patients without peritonitis has become a standard of care. This management includes intensive care unit (ICU) admission, close monitoring of vital signs, abdominal examination, volume resuscitation and transfusion of blood products. Failure of non-operative management, including hemodynamic instability indicates emergent laparotomy. Hilar injuries, pulverized splenic parenchyma or grade II or higher injury of the spleen in a coagulopathic patient are other indications for prompt laparotomy during conservative management (1, 2). It has been suggested that failure of non-operative management is often secondary to poor patient selection (1, 2). Vital signs, including heart rate (HR) and blood pressure, are not the ideal tools for this selection. Therefore, conservative management, along with monitoring vital signs, are started for most patients with

apparently stable hemodynamic status. Laparotomy is mandatory if the patient exhibits hemodynamic instability or does not respond to fluid resuscitation and blood transfusion, in the course of hospital stay. The optimum approach to early recognition of patients who ultimately need surgical intervention is yet to be determined. The heart rate variability (HRV), the variation in the length of the R-R interval (RRI) in a recorded electrocardiogram (ECG), is controlled by the autonomic nervous system. There are multiple mathematical methods for the analysis of HRV, including time domain, frequency domain and complexity analysis (3). One method of complexity analysis, generally called nonlinear analysis, is measuring the entropy. The reduction in the entropy of a system indicates that the complexity of the system has been reduced and the system is not as healthy as before. Several studies showed that measuring the heart rate complexity (HRC) can help predict mortality in a variety of medical

conditions. Most of these studies have confirmed that a decrease in HRC is associated with higher mortality in many patients (2-4). This can be explained by the reduced ability of the body's regulatory systems to control the heartbeat (5). The regulation depends on: baroreceptors within the heart and great vessels, respiratory changes, vasomotor regulation, thermoregulatory system, and alterations in endocrine function. In 2006, a survey conducted by Batchinsky and colleagues revealed that measuring the HRC in the prehospital period, in trauma patients, can predict mortality, a modality to be used in the future assessments (6). Therefore, HRC could be used for triage of patients in the battlefield. It would be worthwhile to measure HRC in trauma settings, because it may help decision making in regard to therapy. Hypovolemia can lower the HRC as it is associated with activation of the sympathetic system (7-9).

## 2. Objectives

The aim of this study was to evaluate the ability of nonlinear analysis of the RRI to differentiate trauma patients with internal bleeding, who cannot tolerate non-operative management. This may help us transfer patients with internal bleeding to the operating room, prior to instability. Also, it can help us make the appropriate decision in a setting with limited ICU availability or blood products.

## 3. Patients and Methods

The study was approved by the Ethics Committee of the Shiraz University of Medical Sciences, Shiraz, Iran. Patients with blunt trauma, who were brought into the emergency room at the onset of their admission were included in this study. Five minutes of electrocardiography (ECG) were captured using the PowerLab device (AD Instruments, Dunedin, New Zealand), with a sampling frequency of 200 Hz. The ECGs of 120 patients were recorded. Blood pressure, HR, glasgow coma scale (GCS), arterial blood gas, age, sex, associated injuries, result of the focused abdominal sonography for trauma (FAST) and injury severity score (ISS) were recorded upon admission. The blood pressure was recorded at the time of ECG capturing. The patients were then followed until discharge or death. The pediatric patients (younger than 12 years old) were not included in this study. ECGs of five pediatric patients with spleen and liver laceration were also separately recorded to compare with those of the adult group. Primarily non-operative management was started for all patients, except in one case, with internal bleeding, who needed urgent laparotomy due to unstable hemodynamics. This conservative management included ICU care, monitoring of vital signs, fluid resuscitation and packed red blood cells (PRBC) and other blood product transfusions. Laparotomy was performed if the patient was unresponsive to these measures. The captured ECG data were then transferred to the computer. A total of 65 pa-

tients were excluded from the study due to the lack noise and ectopic beats. Using standard software, the peak of R waves was detected and then confirmed manually. Lengths of R-R intervals were measured and recoded as single discrete data sets. For nonlinear analysis, 200 beats were selected from each data set. The following methods were used for data analysis.

- Approximate entropy: Entropy measures the probability of a repetitive pattern of changes in -R interval and therefore quantifies the amount of disorder in HRV. The MATLAB software (Natick, MA, USA) was used with a prepared code.

- Lyapunov exponent: The sensitive dependence upon initial conditions characteristic of complex systems was measured via chaos data analyzer (CDA) version 1.0 (Physics Academic Software, American Institute of Physics, North Carolina State University, Raleigh, NC, USA).

- Capacity dimension: The amount of disorder in the system was calculated by CDA. Statistical analysis was performed using statistical software SPSS version 15 (SPSS Inc., Chicago, IL, USA), using descriptive variables, such as mean and standard deviations. Chi Square was performed to compare categorical and independent sample, and paired T test was performed for continuous variables, between survivors and non-survivors. For operated and non-operated groups, the same tests were used. Also, the Mann-Whitney test was employed to confirm the accuracy. P value less than 0.05 was considered significant.

## 4. Results

The study comprised 55 patients, aged over 12 years, of which eight (14%) did not survive (non-S) and the remaining 47 were ultimately discharged from the hospital (S-group). Among the 55 patients, 19 (34%) were found to have intra-abdominal bleeding using FAST, namely injury to liver (11 cases) and spleen (eight cases). There were no signs of peritonitis in any of the patients with internal bleeding. Conservative management was started for all patients, except for one patient who required prompt laparotomy due to unstable hemodynamics. Ultimately, eight (42%) patients needed laparotomy (Op) due to transient or no response to non-operative management. These patients underwent operation within 30 minutes to 20 hours from their admission. Eleven patients tolerated non-operative management successfully (Non-Op).

### 4.1. Mortality

With regard to age and sex, no statistical differences were found between S and non-S groups. Mean arterial pressure (MAP) and HR at the onset of admission showed no difference between S and non-S groups. In the initial arterial blood gas test, the non-S group exhibited a significantly higher base deficit and ISS compared to the S-group. The GCS was significantly lower in the non-S compared to S-group (Table 1). Different methods of complexity measurement of HRV were applied to the ECG of

the patients, recorded at the onset of their admission. Lyapunov exponent, correlation and capacity dimension did not show any difference between the two groups. However, as shown in Table 2, approximate entropy (ApEn) was significantly lower in non-S compared to S-group (0.49 vs. 1.12,  $P = 0.008$ , Table 2).

#### 4.2. Operative vs. Non-Operative Management

Age, sex, hemodynamic data (HR and MAP) and GCS showed no statistical differences between the Op pa-

tients and non-Op. Although not statistically significant, the base deficit was relatively higher in the Op than in the non-Op group (7.25 vs. 3.69,  $P = 0.08$ , Table 3). The ApEn was significantly lower in the Op compared to non-Op group (0.47 vs. 0.86,  $P < 0.001$ ). There was no difference in the Lyapunov exponent, correlation and capacity dimension measurement between the two groups (Table 4). Also, there are significant differences between the heart rate diagrams of conservative vs. non-conservative management cases (Figures 1 and 2).

**Table 1.** Demographics, Vital Signs, Base Deficit, GCS and Injury Scores in Survivors (S) and Non Survivors (Non S) Group<sup>a,b</sup>

Variable, y	Non-S (n = 8)	S (n = 47)	P Value
Age, y	39.1 ± 20.9	32.8 ± 15.4	0.310
<b>Gender</b>			
Male	7	34	0.664
Female	1	13	
MAP	90.95 ± 34.2	91.12 ± 14.4	0.982
HR	114 ± 39.95	98 ± 19.94	0.07
Base deficit	11.3 ± 7.23	4.6 ± 3.74	< 0.001
ISS	25.5	12.4	< 0.001
GCS	8.25 ± 4.950	12.55 ± 3.425	0.03

<sup>a</sup> Abbreviations: GCS, glasgow coma scale; HR, Heart Rate; ISS, injury severity score; MAP, mean arterial pressure.

<sup>b</sup> Data are presented as mean ± SD.

**Table 2.** Complexity Measurements in Survivors (S) and Non Survivors (Non-S) Groups<sup>a</sup>

Variable	Non-S (n = 8)	S (n = 47)	P Value
Approximate entropy	0.49 ± 0.37	1.12 ± 0.63	0.008
Correlation dimension	1.86 ± 0.43	2.25 ± 1.14	0.37
Capacity dimension	1.17 ± 0.35	1.12 ± 0.25	0.61
Lyapunov exponent	0.81 ± 0.21	0.81 ± 0.16	0.93

<sup>a</sup> Data are presented as mean ± SD.

**Table 3.** Demographics, Vital Signs, Base Deficit and Injuries in Patients With Intra-Abdominal Bleeding<sup>a,b</sup>

Variable	Non-Op (n = 11)	Op (n = 8)	P Value
Age, y	24.45 ± 7.51	29.25 ± 10.27	0.255
<b>Gender</b>			
Male	9	7	0.99
Female	2	1	
MAP	92.29 ± 20.85	90.14 ± 7.22	0.776
HR	96.30 ± 15.67	111.75 ± 25.77	0.13
Base deficit	3.690 ± 3.68	7.250 ± 4.48	0.08
ISS	14.7	14.1	0.87
GCS	12.73 ± 3.90	13.13 ± 3.75	0.82

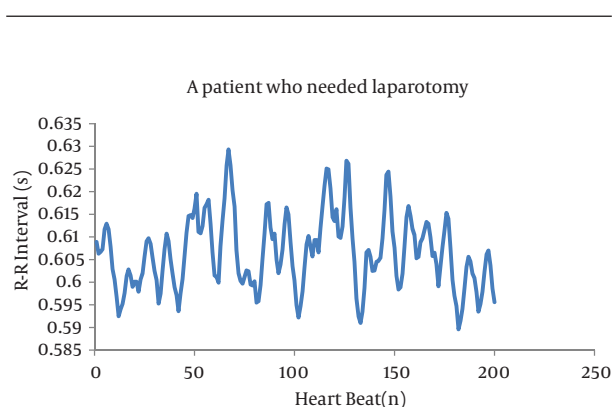
<sup>a</sup> Abbreviations: GCS, glasgow coma scale; HR, heart rate; ISS, injury Severity Score; MAP, mean arterial pressure.

<sup>b</sup> Data are presented as mean ± SD.

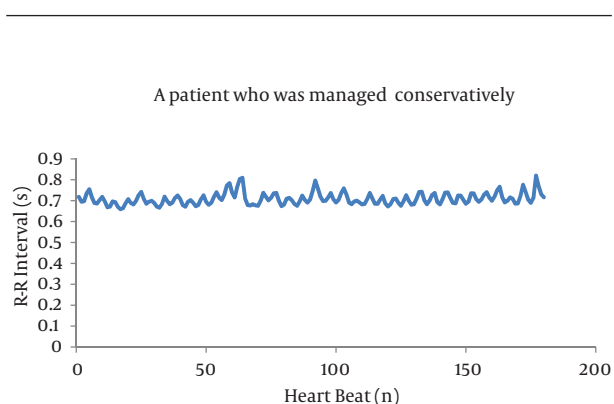
**Table 4.** Complexity Measurement in Patients With Intra-Abdominal Bleeding<sup>a</sup>

Variable	Non-Op (n = 11)	Op (n = 8)	P Value
Approximate entropy	0.86 ± 0.091	0.47 ± 0.08	< 0.001
Correlation dimension	2.25 ± 0.23	3.50 ± 3.05	0.18
Capacity dimension	1.10 ± 0.19	1.06 ± 0.09	0.66
Lyapunov exponent	0.75 ± 0.05	0.79 ± 0.12	0.43

<sup>a</sup> Data are presented as mean ± SD.



**Figure 1.** Heart Rate Variability Diagram of a Patient who Required Laparotomy After Blunt Abdominal Trauma



**Figure 2.** Heart Rate Variability Diagram of a Patient who was Managed Conservatively

## 5. Discussion

In this study, we showed the ability of complexity measurement of HRV to predict the mortality and the

need for laparotomy in trauma patients with intra-abdominal bleeding upon admission. We also found that ApEn was reliable for the complexity measurement in trauma patients. Batchinsky and colleagues discovered that ApEn measurement of HRV in the prehospital period can be an independent factor for prediction of in-hospital mortality (6). Among the data collected from the patients, we found that GCS, base deficit and ISS were also significantly different between S and non-S patients. These findings were supported by previous studies (6, 10, 11). This is the first report that suggests the use of complexity measurement for determination of therapy. In the past 2 decades, conservative management of trauma patients with solid organ injury and intra-abdominal bleeding has become the standard of care (1, 2). Hemodynamic instability is the most common reason for laparotomy (12). Other indications include the need for PRBC transfusion in the first several hours, in cases of peritonitis and other associated intra-abdominal injuries. The established strategy (12), in patients with solid organ injury and apparently stable hemodynamic status, in the absence of other indications for laparotomy, is to manage the patient non-operatively, along with careful monitoring. Laparotomy for control of bleeding is indicated when the hemodynamic measures cannot be corrected after fluid resuscitation, PRBC and other blood product transfusions. In our study, except for one patient who needed an urgent operation, primarily conservative management was started for patients with internal bleeding. With regard to predicting the lack of response to non-operative management, McIntyre and colleagues conducted a survey on a large population. They concluded that age older than 55 years and an ISS higher than 25 can be a predictor of failure for non-operative management in patients with spleen lacerations (1). This study also supports the idea that conventional vital signs at admission play no role in this prediction. In our study, we did not find any significant difference in the age and ISS, between non-Op and Op patients. This could be due to our small sample size. The age of the patients in our study did not exceed 50 years. We showed that the Op group had a lower ApEn than the



non-Op group. This reflects a lower complexity in the Op group. Several studies support the conclusion that, in a variety of medical conditions, low complexity in HRV is associated with morbidity and predicts a higher mortality (13, 14). HRV is controlled by the autonomic nervous system and this regulation is under the control of multiple other systems, including baroreceptors, endocrine, thermoregulatory, respiratory, vasomotor and inflammatory systems. As the complexity of this system is decreased in an injured patient, the system can tolerate a smaller range of changes and is thus more prone to failure. Lack of tolerance of conservative management (which was the case in the Op group), may be due to a higher rate of bleeding from the solid organ injury, or as a result of summation of different sites of bleeding that could not be compensated with fluid and or blood product resuscitation. It is also possible that hypothermia, coagulopathy and higher inflammatory response in an individual, resulted in the failure of non-operative management. All these pathologies can lower the HRC. Other methods that we applied for measuring complexity could not elucidate the difference in complexity. It seems that ApEn could be more reliable for evaluation of cardiac complexity, as suggested by other studies (3, 6). The grading of injuries of solid organs was not recorded in our study, a condition that could affect decision making regarding laparotomy. However, regardless of the type of injury, ApEn can be helpful in predicting laparotomy. With regard to solid organ injury, we also measured the ApEn in five pediatric patients aged 5 to 10 years. All of these patients tolerated non-operative management, although they showed very low entropy ranging from 0.1 to 0.52. Even though, due to small sample size, no statistics can be offered, our findings suggests that autonomic regulation in children differs from that in adults. This may be due to immaturity of the autonomic nervous system. Considering our sample size, further investigations, including a larger population, are needed to confirm our findings. If decision to perform laparotomy is made on admission, the patients able to tolerate non-operative management may need less intensive care, especially in limited ICU facilities. Furthermore, the patients with lower complexity may be transferred to the operating room more expediently while in a more stable condition. This is particularly beneficial with regard to blood product limitations, like battlefield conditions. One of the limitations of the HRC measurement is sensitivity to noise and ectopic beat. Capturing a noise free ECG is difficult in the emergency setting. This can be circumvented by using smaller data sets for analysis. In this context, Batchinsky et al. (15) found that a data set as short as 100 beats can be used for this purpose in trauma patients. To the best of our knowledge, this is the first report that predicts the potential of HRC measurement for the treatment of patients with solid organ injuries. It can aid in faster decision making for lapa-

rotomy, mainly in settings with limitations in ICU bed availability and shortage of blood products.

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## Footnotes

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