Injury, Int. J. Care Injured xxx (2018) xxx–xxx

Contents lists available at ScienceDirect

Injury

journal homepage: www.elsevier.com/locate/injury

Tachycardic and non-tachycardic responses in trauma patients with haemorrhagic injuries

Andrew T. Reisner[a], Shwetha Edla[b], Jianbo Liu[b], Jiankun Liu[b], Maxim Y. Khitrov[b], Jaques Reifman[b,*]

[a] Department of Emergency Medicine, Massachusetts General Hospital, Boston, MA, USA
[b] Department of Defense Biotechnology High Performance Computing Software Applications Institute, Telemedicine and Advanced Technology Research Center, U.S. Army Medical Research and Materiel Command, Fort Detrick, MD, USA

ARTICLE INFO

Article history:
Accepted 29 April 2018

Keywords:
ATLS
Blood loss
Heart rate
Tachycardia
Trauma
Vital signs

ABSTRACT

Background: Analyses of large databases have demonstrated that the association between heart rate (HR) and blood loss is weaker than what is taught by Advanced Trauma Life Support training. However, those studies had limited ability to generate a more descriptive paradigm, because they only examined a single HR value per patient.

Methods: In a comparative, retrospective analysis, we studied the temporal characteristics of HR through time in adult trauma patients with haemorrhage, based on documented injuries and transfusion of $\geq$3 units of red blood cells (RBCs). We analysed archived vital-sign data of up to 60 min during either pre-hospital or emergency department care.

Results: We identified 133 trauma patients who met the inclusion criteria for major haemorrhage and 1640 control patients without haemorrhage. There were 55 haemorrhage patients with a normal median HR and 78 with tachycardia. Median ΔHR was −0.8 and +0.7 bpm per 10 min, respectively. Median time to documented hypotension was 8 and 5 min, respectively. RBCs were not significantly different; median volumes were 6 (IQR: 4–13) and 10 units (IQR: 5–16), respectively. Time-to-hypotension and mortality were not significantly different. Tachycardic patients were significantly younger ($P < 0.05$). Only 10 patients with normal HR developed transient/temporary tachycardia, and only 11 tachycardic patients developed a transient/temporary normal HR.

Conclusions: The current analysis suggests that some trauma patients with haemorrhage are continuously tachycardic while others have a normal HR. For both cohorts, hypotension typically develops within 30 min, without any consistent temporal increases or trends in HR.

Published by Elsevier Ltd.

Introduction

Multiple reports have demonstrated that the current Advanced Trauma Life Support (ATLS) training course is inaccurate regarding vital-sign changes in trauma patients with haemorrhage [1–4]. Analyses of large datasets have demonstrated that the association between heart rate (HR) and blood loss is weaker than what is taught by ATLS [2,3]. Studying nearly 200,000 trauma patients in a trauma registry, Guly et al. [2] reported that "[w]ith increasing estimated blood loss there is a trend to increasing HR and a reduction in systolic blood pressure (SBP), but not to the degree suggested by the ATLS classification of shock." Studying over 35,000 trauma patients, Mutschler et al. [3] concluded that "[t]his study indicates that the ATLS classification of hypovolaemic shock does not seem to reflect clinical reality accurately."

If it has been established that ATLS is not accurate in describing HR changes during haemorrhage, an alternative paradigm describing HR patterns in trauma patients has not emerged. In part, this is because the aforementioned large registry studies only examined a single HR value per patient, whereas in reality, HR is continuously monitored during trauma patient management. By studying only single HR values per patient, it cannot be determined how often tachycardia develops as haemorrhage progresses. As well, it cannot be determined whether the weak association between HR and haemorrhage was *i*) because HR varied substantially in individual trauma patients (i.e. large intra-subject variability), and/or *ii*) because HR

* Corresponding author at: Department of Defense Biotechnology High Performance Computing Software Applications Institute, Telemedicine and Advanced Technology Research Center, U.S. Army Medical Research and Materiel Command, ATTN: MCMR–TT, 504 Scott Street, Fort Detrick, MD 21702, USA.
E-mail address: jaques.reifman.civ@mail.mil (J. Reifman).

https://doi.org/10.1016/j.injury.2018.04.032
0020-1383/Published by Elsevier Ltd.

responses varied substantially between patients (i.e. large inter-subject variability).

Having a better understanding of the temporal characteristics of HR through time in trauma patients with haemorrhage could contribute to a more accurate and useful alternative to ATLS. Accordingly, we analysed an archived dataset of continual vital signs in trauma patients, seeking to characterise the HR patterns recorded through time. We evaluated the extent to which trauma patients demonstrated tachycardia over time, and whether there were salient clinical differences between patients who demonstrated different types of HR responses.

Materials and methods

Study design, setting, population, and outcome

This was a comparative study carried out by a secondary analysis of three pooled datasets. We studied adult trauma patients with haemorrhagic injuries during initial care (either during pre-hospital transport or upon arrival in the emergency department). Dataset 1 was originally collected aboard air ambulances between February 2010 and December 2012 [5], Dataset 2 from an emergency department between June 2012 and December 2014 [6], and Dataset 3 during air transport between August 2001 and April 2004 [7,8]. All datasets were collected with the approval of local institutional review boards.

For our outcome, haemorrhagic injury, we used the following criteria: documented haemorrhagic injuries, and transfusion of three or more units of red blood cells within 24 h (24-h RBCs). Explicitly documented haemorrhagic injuries were identified by chart review, and defined as solid organ injuries, thoracic or abdominal haematomas noted in imaging or operative reports, vascular injuries that required a procedure for haemostasis, or limb amputations.

For Dataset 1, eligible patients were identified by querying the air ambulance administrative database for adult trauma transports. Next, we queried the receiving hospital's electronic medical records to identify the subset who received at least three units of 24-h RBCs. This review was conducted by either a physician or nurse practitioner with clinical experience in trauma care, and who was blinded to subjects' physiological data. These data were collected and managed using REDCap electronic data capture tools [9]. Abstractors were first trained using training cases from Dataset 3. Next, the abstractors' adjudications about whether or not the subject had a haemorrhagic injury were confirmed by running an automated text-search through the trauma registry database, to independently corroborate that the subject had at least one of a list of haemorrhagic injuries. Cohen's K between the data abstractor adjudication and automated text search results was 0.67. All discrepancies were subsequently resolved by two-investigator adjudication.

For Dataset 2, eligible patients were first identified by electronically querying the source hospital's trauma registry for adult trauma patients. The remainder of the subject selection methodology, in terms of 24-h RBC volume and presence of haemorrhagic injury, was the same as that used for Dataset 1.

Data collection for Dataset 3 was conducted under a protocol that yielded an inventory of injuries and 24-h RBCs in a convenience sample of high-acuity trauma patients [7]. The methodology for determining presence of haemorrhagic injury was the same as that used for Dataset 1.

Study measurements

To collect HR and blood pressure (BP) data during real-time care, data streaming from patients' vital-sign monitors were electronically recorded via software solutions [8,10,11]. The electronic recording system used for Dataset 1 was an *ad hoc* software system described by Reisner et al. [10]. The recording system used for Dataset 2 was the BedMasterEx system (Excel Medical, Jupiter FL). The recording system used for Dataset 3 was another *ad hoc* system described by Cooke et al. [7].

From these recordings, we analysed vital-sign data of up to 60 min in duration, beginning with the first recorded non-zero vital sign. We studied HR from intervals with high-quality electrocardiograms (ECGs), as determined by the consensus of an automated algorithm (which has been shown to be more conservative than human expert evaluation [12]) and a human adjudicator. When there was disagreement, a second human adjudicator evaluated the reliability of the data segment.

For Datasets 1 and 2, study staff performed retrospective chart review to extract additional clinical data, including demographics, injury descriptions, clinical interventions, and mortality, using the methodology detailed above. All of these data were compared with an electronic report from the hospital's independent trauma registry, and discrepancies were resolved by two-investigator adjudication. Clinical data abstraction for Dataset 3 was conducted in accord with a previous study [7].

Data analysis

By convention, tachycardia is defined as a HR of 100 bpm or greater. We examined whether 100 bpm was a clinically valid cut-off to discriminate between patients with and without haemorrhage, and calculated the diagnostic testing characteristics of tachycardia and the associated receiver operating characteristic (ROC) curve [13]. To investigate whether patients with haemorrhage demonstrated tachycardia at variable time intervals, we calculated how often those with a normal HR developed transient/temporary tachycardia (at least 5 min of tachycardia within any 10-min time window), and how often those with tachycardia developed a transient/temporary normal HR (at least 5 min of normal HR within any 10-min time window). We also performed a sensitivity analysis to investigate whether our findings were sensitive to the definition of clinical haemorrhage, by computing ROC curves for predicting a set of secondary outcomes: 24-h RBCs $\geq$1, $\geq$3, $\geq$5, $\geq$7, and $\geq$10 units, regardless of documented injuries. In addition to the aforementioned analyses using median HR, we developed a logistic regression model using median HR for estimating the probability of haemorrhage, and tested its goodness-of-fit using the Hosmer-Lemeshow test.

We compared the haemodynamic and clinical characteristics of haemorrhage patients with a normal HR to those of haemorrhage patients with tachycardia. Variability in HR was quantified by the root mean square (RMS) around the mean of each patient's HR time series, while slope of HR as a function of time was computed using linear regression. We computed the BP characteristics of both cohorts, including the incidence of measured hypotension and the time elapsed until hypotension was first measured. Hypotension was defined as an SBP of less than 90 mmHg or a mean arterial pressure (MAP) of less than 70 mmHg. We also computed the pulse pressure (SBP – diastolic BP) and the Shock Index (SI = HR/SBP) for both cohorts. We compared clinical characteristics, including demographics, injury descriptions, clinical interventions, and mortality. We performed analyses in MATLAB version 9.0 (The MathWorks, Inc., Natick, MA). Data distributions were compared using the Wilcoxon rank-sum test for continuous variables and categorical variables using Fisher's exact test. We used a threshold for statistical significance of $P < 0.05$.

Finally, we studied the change in HR in the subset of haemorrhage patients who developed new onset hypotension. New onset hypotension was defined as follows: *i*) at least one non-hypotensive