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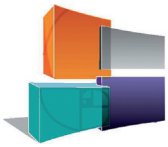

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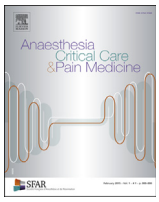

Short communication

Blood pressure variability in surgical and intensive care patients: Is there a potential for closed-loop vasopressor administration?

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ABSTRACT

Blood pressure management in the operating rooms (OR) and intensive care units (ICU) frequently involves manually titrated vasopressor therapy to an optimal range of mean arterial pressure (MAP). Ideally, changes in vasopressor infusion rates have to quickly follow variations in blood pressure measurements. However, such a tightly controlled feedback loop is difficult to achieve. Few studies have examined blood pressure control when vasopressor therapy is administered manually in OR and ICU patients. We extracted MAP data from 3623 patients (2530 from the ORs and 1093 from the ICU) on vasopressors from our electronic medical records. Coefficient of variation (= standard deviation/mean value) *100) was calculated and the values were additionally categorized into different MAP ranges (MAP < 60 mmHg, 60 < MAP < 80 and MAP > 80 mmHg). There was no statistically significant difference between both centres for MAP across all time points (80 ± 12 vs. 80 ± 16, P = 0.996, 95% CI −6 to 6). The coefficients of variation of MAP were 13.7 ± 5.4% and 18.4 ± 9.8% in the OR and in ICU respectively. Patients on vasopressors spent 48.8% treatment time with a MAP between 60 and 80 mmHg (11.2% time with MAP < 60 mmHg, and 40% with MAP > 80 mmHg). These results provide a reasonable baseline from which to establish whether 'reduced variability' may be achieved with a closed-loop vasopressor administration system.

1. Introduction

In the operating rooms (OR) and intensive care units (ICU), blood pressure management frequently involves vasopressor therapy manually titrated to a target range which may vary among different institutions and within institutions according to patients' pathophysiological conditions. In an ideal setting, changes in vasopressor infusion rate would quickly follow changes in blood pressure and vasopressor infusions would be maintained at the minimum level to maintain the target. However, due to a variety of factors including competing patient care tasks, workflow, and other distractions, compliance with protocol targets is often suboptimal [1–3]. The net result is that drips are often titrated to maintain a mean arterial pressure (MAP) higher than the target in order to provide a buffer above the minimum target. This may result in significant time where MAP remains well above the established minimum targets increasing the risk of side effects related to higher than necessary vasopressor doses [1].

Computer systems allowing to automatically titrating vasopressor infusions to predefined target ranges could help to improve patients' blood pressure management [4–7]. Our research group is currently developing such a closed-loop system [5]. In order to answer the questions of whether a "tighter" control of blood pressure on specific individualised patient targets using a closed-loop system can improve outcomes, data on current blood pressure control accuracy when vasopressor are administered manually are required.

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The aim of the present study was to report current blood pressure management in a large sample of OR and ICU patients receiving vasopressor therapy in order to assess the underlying MAP distribution and variability. Our hypothesis was that OR and ICU patients under vasopressor drips would show a large variability in their blood pressure distribution with a better correction of hypotension (under-treatment) than hypertension (over-treatment).

2. Materials and methods

The present retrospective study was conducted at the University of California Irvine (UCI) in Orange, USA for ICU patients and Erasme Hospital in Brussels, Belgium for OIR patients. IRB approvals (HS # 2017-3360 for UCI and P2017/181 for Erasme) were obtained prior to research activities. As the present study was retrospective and patient identity was kept anonymous, informed patient consent was waived.

2.1. Irvine ICU cohort

UCI is a 422-bed tertiary-care level-1 trauma centre. There are 68 intensive care unit beds across the medical, surgical, neurosurgical, and burn units. All ICU visits between January 1, 2015 and January 27, 2017 were included. This date range was chosen as it coincided with the implementation date of an electronic medical record system at Erasme and concluded with the date of the data pull, so identical time periods could be pulled from both institutions. Only adult patients were included in the study. MAP data of any de-identified patients under norepinephrine infusions were extracted from our electronic medical records at a rate of 1 sample per minute.

Standard clinical protocol at UCI for titration of vasopressor infusions in both the surgical and medical ICUs was to maintain MAP between 60 and 80 mmHg.

2.2. Erasme OR cohort

Erasme hospital is an 858-bed facility with 28 operating rooms. Members of the research team at Erasme retrospectively extracted a de-identified data set from the electronic medical records (Innovian®, Draeger, Inc, Telford, UK). This data set included surgical patients who received norepinephrine or phenylephrine infusions at any point during the procedure between January 1, 2015 and January 27, 2017. MAP data (at a rate of 1 sample per 20 seconds), vasopressor infusions, surgery type were included in the data set.

Standard clinical protocol for titration of vasopressor in the operating room at Erasme was to maintain MAP between 60 and 80 mmHg

2.3. Data preparation

After extraction, the data was merged and analysed. All MAP values were scanned and obvious artefacts and outliers were removed (MAP < 30, MAP > 140). Remaining cases with MAP < 30 or MAP > 140 were examined by the research team by hand for validation or removal as artefacts were present. Average, standard deviation, and coefficient of variation ("CoV", defined as (standard deviation/mean) *100) of MAP were calculated, and percent time of spent in each MAP range over each entire OR or ICU cases was tallied. As our both institutions used the same standard clinical protocol for the titration of norepinephrine (MAP between 60 and 80 mmHg), we decided to range the MAP values into three different categories: MAP < 60 mmHg (under-treatment); MAP between 60–80 mmHg (normal range) and MAP > 80 mmHg (over-treatment).

The data were analysed using Python (Python Software Foundation, python.org) and NumPy scientific computing package, and R statistics (www.r-project.org). Comparisons between groups were made with Student's *t*-test for scalar data and chi-square test for categorical data. Confidence intervals are reported at the 95% level. No correction for multiple comparisons was made preferring to risk type II error (false positives) in looking for any possible difference between groups.

3. Results

A total of 3623 cases of OR and ICU patients with vasopressor infusion were found in both centres (2530 from the Erasme ORs and 1093 from the UCI-ICU).

As main objective, patients on vasopressors had an overall CoV = 15.0 ± 7.3%. The CoV was 13.7 ± 5.4% in the OR and 18.4 ± 9.8% in ICU (Fig. 1).

For the secondary objectives, the times spent at different ranges of blood pressure are shown in Table 1. Blood pressure was maintained in normal range (60–80 mmHg) in 48.8% time. The MAP was < 60 and > 80 mmHg in 11.2% and 40% of treatment time, respectively ($P < 0.0001$, 95% CI 0.27 – 0.31). Only 0.3% of patients had no measurements outside of the range of MAP of 60-80. The average MAP throughout care across all cases in both institutions was 80 ± 13 mmHg.

There was no statistically significant difference between both centres for MAP across all time points (80 ± 12 vs. 80 ± 16, $P = 0.996$, 95% CI −6 to 6).

4. Discussion

In this bi-centre retrospective analysis, we showed that overall CoV was 15.0 ± 7.3% (The CoV was 18.4 ± 9.8% in ICU and 13.7 ± 5.4% in the OR) meaning that MAP was frequently out of the normal range (60–80 mmHg). Indeed, patients on vasopressors spend 11.2% of case time under target (MAP < 60 mmHg) and 40% of case time above target (MAP > 80 mmHg).

The present findings mirror the findings of Asfar et al. [1] comparing high versus low blood-pressure targets in septic shock. Interpretation of the results of that study was limited by the fact that although the low blood pressure group was supposed to target

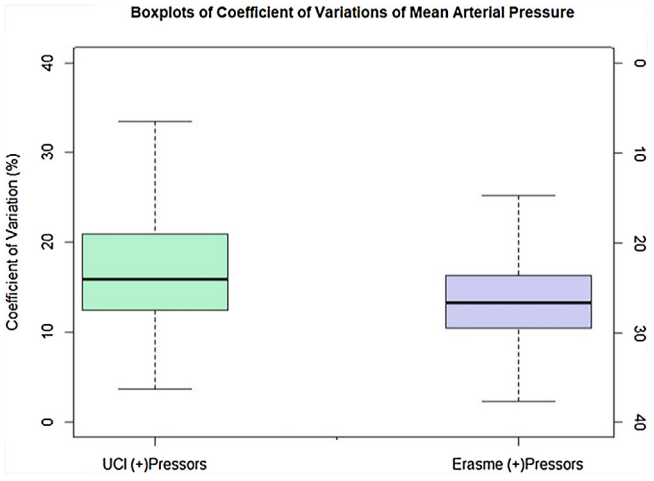

Fig. 1. Boxplots of Coefficient of Variation of Mean Arterial Pressure. Boxplots represent the summary of the distribution of each patient's individual coefficient of Variation in the cohort. UCI – University of California Irvine intensive care unit data; ERASME – Erasme Hospital operating room data.

Table 1

	Mean MAP (mmHg)	Mean percentage of case time in range (per-patient basis)		
		< 60 mmHg	60–80 mmHg	>80 mmHg
Both centres	80 ± 13	10.2	49.8	40
Erasme OR only	80 ± 12	10.8	52.2	37
Irvine ICU only	80 ± 16	9	43	48

MAP: mean arterial pressure.

a MAP of 65–70 mmHg, it ranges actually between 75 and 80 mmHg for most of the treatment period. The high blood pressure target of 85–90 also ran higher (between 90 and 95) in the actual management. The authors of the study hypothesised that infusions were not down adjusted appropriately. Our own data supports a similar conclusion, with 40% of MAP falling into the > 80 mmHg range and even 19% into the > 90 range.

All together, these results suggest room for improvement in the management of vasopressor infusions in both OR and ICU patients for a tighter blood pressure control. In the present study, patients on vasopressor infusions tended to run much higher than target with a high variability as well as in previously published trial [1]. The ability to conduct tightly controlled studies has been limited by the challenge of titrating infusions quickly in response to blood pressure changes. In the present study, the CoV of MAP under targeted vasopressor infusions was between 14–20% according to the studied population (OR or ICU). This finding gives us a benchmark for comparison by which to determine 'tighter management' in future closed-loop control trials.

Some limitations could be advanced. First, the data were retrospectively collected from electronic medical records and is subject to the common limitations of retrospective analysis. However, when data are checked as in the present study, retrospective studies are not submitted to the Osborn effect and could reflect the real life. Second, the reported data only reflect the MAP tendencies in two different centres in USA and Europa. However, no major difference was reported suggesting that the present findings could be extrapolated to numerous other centres, in ORs and ICUs. Thirdly, because we did not have access to post-operative complications (both institutions would have required a hand chart review to properly encode them) we could not assess the influence of the variation of MAP (low and/or high) on patient outcome. Finally, while we have well established practice standards in both cohorts, we are unable to link specific individual targets to the patients, preventing detailed conclusions about the exact accuracy of management.

In clinical practice, the present study shows that the overall CoV of MAP is 15.0 ± 7.3% and that the times spent with normal, low and high MAP (60–80, < 60 and > 80 mmHg, respectively), are 48.8, 11.2% and 40%, respectively. These findings may be due to insufficient or unnecessary vasopressor infusions combined with a significant lag time between blood pressure changes and vasopressor infusion rate adjustments. This suggests room for improvement in the blood pressure monitoring and management of patients receiving vasopressor therapy, especially to decrease over-treatment. These findings also provide a reasonable baseline from which to establish whether 'reduced variability' may be achieved with a closed-loop control system.

5. Conclusion

The present retrospective bi-centre study reported a CoV of MAP between 14 and 20%. Moreover, more than 50% of time is spent out of normal range of MAP, especially in too high level of MAP (over-treatment). This suggests that there room for improving the monitoring and the management of MAP in acute and instable patients.

Ethics approval and consent to participate

The study was conducted at the University of California, Irvine Medical Center (UCI) in Orange, CA, USA and Erasme University Hospital in Brussels, Belgium.

Ethics approval (HS # 2017-3360 for UCI and P2017/181 for Erasme hospital) was obtained prior to research activities.

Trial registration: NA.

Consent for publication

As it is a retrospective analysis, we did not need to obtain consent for publication from all the included patients.

Availability of data and material

The datasets used and analysed during the current study are available from the corresponding author on reasonable request.

Disclosure of interest

Joseph Rinehart – consultant for Edwards Lifesciences; ownership interest in Sironis Inc., patents on closed-loop fluid management.
Alexandre Joosten – consultant for Edwards Lifesciences, Irvine, California, USA.
The other authors declare that they have no competing interest.

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