RESUSCITATION 143 (2019) 124–133

Available online at www.sciencedirect.com

Resuscitation

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

Rapid response systems

Non-invasive continuous haemodynamic monitoring and response to intervention in haemodynamically unstable patients during rapid response team review

Christopher T. Eyeington [a], Patryck Lloyd-Donald [a], Matthew J. Chan [a], Glenn M. Eastwood [a,b], Helen Young [a], Leah Peck [a], Nada Marhoon [d], Daryl A. Jones [a,b], Rinaldo Bellomo [a,b,c,d,*]

[a] Department of Intensive Care, Austin Hospital, Heidelberg, Victoria, Australia
[b] ANZIC Research Centre, School of Public Health and Preventative Medicine, Monash University, Melbourne, Victoria, Australia
[c] Centre for Integrated Critical Care, Melbourne University, Melbourne, Victoria, Australia
[d] Data Analytics Research and Evaluation Centre, The University of Melbourne and Austin Hospital, Melbourne, Australia

Abstract

Introduction: During rapid response team (RRT) management of haemodynamic instability (HI), continuous non-invasive haemodynamic monitoring may provide supplemental physiological information.

Objectives: To continuously and non-invasively obtain the cardiac index (CI) and mean arterial pressure (MAP) in patients with HI at baseline and during RRT management using the ClearSight™ device.

Methods: We performed a prospective observational study in adult patients managed by the RRT for tachycardia or hypotension or both. We assessed changes from baseline in heart rate (HR), MAP, CI, stroke volume index (SVI) and systemic vascular resistance index (SVRI) (i) at 5-minutely intervals up to 20 min, and (ii) over the entire 20-min period. We analysed patients by RRT trigger (tachycardia/hypotension) and intervention (fluid bolus therapy [FBT]/ no FBT).

Results: We successfully recorded the CI in 47 of 50 (94%) patients. RRT reviews triggered by hypotension rather than tachycardia had a lower baseline HR (−45.4 bpm, p = <0.0001), MAP (−16.1 mmHg, p = 0.0007) and CI (1.0 L/min/m^2, p = 0.0025). Compared to baseline, in the tachycardia group, there was a small increase in MAP overall and at the 15–20 min time-block from 83.2 mmHg to 87.1 mmHg (+3.9 mmHg, p = 0.0066) and 85.5 mmHg (+2.3 mmHg, p = 0.0061), respectively. In those who received FBT, there was a statistically significant increase in MAP overall and at the 15–20 min time-block compared to baseline, from 70.1 mmHg to 73.5 mmHg (+3.4 mmHg, p = 0.0036) and 74.3 mmHg (+4.2 mmHg, p = 0.0037), respectively. However, there were no statistically significant changes in mean HR, CI, SVI, or SVRI when comparing baseline to the entire 20-min period or 5-min time-blocks within any group.

Conclusions: Continuous non-invasive measurement of haemodynamics during RRT management for HI was possible for 20 min. Patients with hypotension rather than tachycardia had lower baseline HR, MAP and CI values. There was a statistically significant but small increase in MAP at the 15–20 min time-block and overall, for both the tachycardia and FBT groups.

Keywords: Intensive care, Critical care, Cardiac index, Cardiac output, Non-invasive, Haemodynamic monitoring, Medical emergency team, Rapid Response Team, Resuscitation, Tachycardia, Hypotension

Abbreviations: BMI, Body mass index; BSA, Body surface area; CI, Cardiac index; CO, Cardiac output; DO_2/I, Indexed delivery of oxygen; FBT, Fluid bolus therapy; Hb, Haemoglobin; HDR, Haemodynamic response; HI, Haemodynamic instability; ICU, Intensive care unit; IQR, Inter-quartile range; LOS, Length of stay; RRT, Rapid Response Team; PAC, Pulmonary artery catheter; SD, standard deviation; SpO_2, Peripheral oxygen saturation; SVI, Stroke volume index; SIRS, Systemic Inflammatory Response Syndrome; SVR, Systemic vascular resistance; SVRI, Systemic vascular resistance index.

* Corresponding author at: Intensive Care Department, Austin Hospital, Heidelberg, Melbourne, Victoria, Australia.
E-mail address: rinaldo.bellomo@austin.org.au (R. Bellomo).

https://doi.org/10.1016/j.resuscitation.2019.08.025
Received 27 January 2019; Received in revised form 7 July 2019; Accepted 2 August 2019

Introduction

During the course of their hospital stay, around 10% of hospital-ward patients deteriorate and require intensive care admission.[1] Several interventions have been proposed to improve the intensive care clinicians' ability to identify at-risk patients. Among these interventions, the Rapid Response Team [RRT] has become established in several countries.[2] Such RRT reviews may occur between 8.7 and 31 times per 1000 admissions.[3,4] One third of RRT activations are due to hypotension or tachycardia,[5–8] so-called 'haemodynamic instability' (HI).[9] At each RRT review, an assessment is made and a treatment strategy applied based upon bedside examination and the interpretation of the clinical situation: the patient's diagnosis, their past medical history and vital signs. The efficacy of such reviews is typically described using outcomes such as morbidity, mortality and patient disposition.[3,7,10,11] However, no study has assessed the physiological response to RRT intervention. In particular, no study has measured mean arterial pressure [MAP], heart rate [HR], cardiac index [CI], stroke volume index [SVI] and systemic vascular resistance index [SVRI]) and their changes in response to therapy during RRT management: the patient's so-called "haemodynamic response" [HDR]. This lack of monitoring and information is undesirable but is a consequence of the limitations of widely available methods, which may be invasive, operator or reporter-dependent, intermittent (echocardiography), and require time and expertise to perform and evaluate. More recently, however, non-invasive devices have been described to measure such parameters.[12–16] One of these, is the ClearSight™ (Edwards, Irvine, CA, USA) device, which is now approved for clinical use by FDA (see details in Methods section).

Accordingly, the primary outcome of this study was to assess the feasibility of continuously and non-invasively measuring the CI and associated haemodynamic parameters of adult hospital-ward patients who triggered a RRT review for HI. The secondary outcomes were the assessment of the baseline haemodynamics and the HDR according to RRT trigger and RRT intervention, and assessment of the response to such RRT intervention in the form of FBT. Further secondary outcomes included assessment of the indexed delivery of oxygen (DO_2/I) and whether this differed between RRT trigger and intervention groups. Our primary hypothesis was that it would be feasible to continuously record the CI in >75% of such patients over 20 min. Our secondary hypotheses were that there would be clinically significant baseline differences according to RRT trigger and RRT intervention, and that there would be a significant change in measured parameters following RRT intervention.

Methods

Study design

Ethics Committee approval (LNR/15/Austin/382) which included a waiver for consent, was obtained for this single-centre, prospective, observational study in a large university hospital.

Study participants

Adult patients aged 18 years or over who triggered a RRT response for tachycardia (>100 beats per minute (BPM)) or hypotension (<90 mmHg) were included. Patients with Raynaud's disease or severe peripheral vascular disease were excluded.

Technical information

The ClearSight™ is a non-invasive device that uses volume-clamp, pulse-contour technology to estimate CI. The device consists of two cuffs, one placed at the distal phalanx of a finger and the other applied to the forearm. The finger cuff pressure maintains a constant arterial volume that is assessed by a photo-plethysmograph to produce a pulse-contour. The stroke volume and cardiac output are derived from this information.[17] This data is presented and recorded at 20 s intervals. The validity, level of accuracy and precision of the ClearSight™ appears comparable to that of alternative CI measurement techniques (pulmonary artery catheter and trans-pulmonary thermodilution, oesophageal Doppler, trans-thoracic echocardiography and inert gas re-breathing) [18–23].

Data collection

A member of the research team attended RRT reviews and assessed the patient for inclusion. Data were obtained for at least 20 min and treating intensive care clinicians were blinded to this data. Additional data collected included demographics, seniority and primary specialty of the treating intensive care clinician, organ system associated with admission, co-morbidities, resuscitation status and disposition of the patient after the RRT response, and upon hospital discharge.

Outcomes

The primary outcome was to assess the feasibility of continuously and non-invasively measuring the CI and associated haemodynamic parameters for a period of at least 20 min, in adult hospital-ward patients who triggered a RRT review for HI. The secondary outcomes were assessment of the baseline haemodynamics and change in haemodynamics over time, according to RRT trigger (hypotension or tachycardia) and RRT intervention (fluid bolus therapy [FBT] or no FBT). Further secondary outcomes included assessment of the DO_2/I and whether this differed between RRT trigger and intervention groups.

Statistical analysis

Data cleaning consisted of systematic data inspection and range checks. Visual inspection of the frequency distributions of quantitative variables were performed to identify outliers and assess for normality. Categorical variables were assessed for consistency. Continuous variables were expressed as median and inter-quartile range (IQR) or mean and standard deviation (SD). Categorical values were expressed as number (n), percentage (%). Calculations were performed for body surface area (BSA) using the Dubois Formula (surface area (m^2) = 0.007184 × height (cm)^0.725 × weight(kg)^0.425)[19] and body mass index (BMI) (weight [kg]/height^2 [m]). SVR and SVRI were calculated assuming a right atrial pressure of 0 mmHg, (SVR[SVRI] = 80 × mean MAP / CO[CI]). DO_2/I was calculated as follows: CI × ((1.31 × haemoglobin [Hb] concentration [g/dL] × peripheral oxygen saturation [SpO_2] [fraction]) + (0.0225 × partial pressure of oxygen [PaO_2]) [24]. SpO_2 was taken as the level documented at the time of RRT trigger. PaO_2 was not recorded, therefore PaO_2 was fixed at 13.3 kPa. Dissolved oxygen content could therefore be calculated as follows: 0.0225 × 13.3 = 0.3 ml. This simplified to: DO_2/I = CI × ((1.31 × Hb × SpO_2) + (0.3)). With one exception, haemoglobin values were single values taken less than 12 h before or after RRT review. RRT trigger groups were divided into tachycardia or hypotension, and those with both were excluded from sub-group analysis. RRT treatment was separated into FBT or no FBT. DO_2/I was divided into low, normal or high categories.[25] Following sensitivity analysis, those treated with a vasopressor bolus (3, 6%) were excluded from analysis of the HDR. Continuous haemodynamic variables were presented in two ways: firstly, as averaged 5-min time-blocks: 0–5 (baseline), 5–10, 10–15 and 15–20 min and over the entire 20-min period and secondly, as correlated time-series. Assessment of the differences in the HDR between baseline and subsequent time-blocks, and between baseline and the entire 20-min period, was performed using paired students' T Test. The analysis of differences in the HDR between a priori defined groups (RRT trigger and RRT intervention) was performed in the same manner. Further assessment of change in continuous haemodynamic variables over time was performed using correlated time-series linear regression analysis. Graphical presentation of correlated time-series continuous haemodynamic variables was performed in the same manner. Associations between continuous haemodynamic variables and dichotomised variables were assessed using correlated time-series, univariate linear regression. Statistical analysis was undertaken with Stata 14®

Table 1 – Comparison of demographics, baseline characteristics and outcomes in tachycardia and hypotension groups.

Variable, n(%) / median(IQR)	Tachycardia (n = 20)	Hypotension (n = 22)
Age, years	67 (61–74)	69 (54–81)
Male	11 (55%)	12 (55%)
Height, cm	165 (161–170)	169 (160–175)
Weight, kg	65 (56–77)	73 (55–80)
BSA[a], m^2	1.7 (1.6–1.9)	1.8 (1.6–1.9)
BMI[b], kg/m^2	23.6 (21.1–27.5)	25.2 (21.3–28.3)
Organ system affected		
Cardiovascular	2 (10%)	2 (9%)
Respiratory	5 (25%)	1 (5%)
Gastro-intestinal	5 (25%)	7 (32%)
Renal	2 (10%)	2 (9%)
Sepsis	0 (0%)	2 (9%)
Other	6 (30%)	6 (30%)
Elective hospital admission	6 (30%)	10 (45%)
Medical admission	14 (70%)	10 (45%)
Comorbidities present	15 (75%)	19 (86%)
Working Day[c]	17 (85%)	18 (82%)
Typically reside at home	19 (95%)	19 (86%)
No assistance of daily activities	14 (70%)	13 (59%)
Multiple RRT reviews	6 (30%)	5 (23%)
No limitations on resuscitation	17 (85%)	20 (91%)
RRT Treatment administered		
Fluid bolus therapy	9 (45%)	19 (86%)
Vasopressor bolus	0 (0%)	2 (9%)
Immediate RRT outcome		
Remain on ward	15 (75%)	18 (82%)
Transfer other ward	3 (15%)	0 (0%)
Transfer ICU	2 (10%)	4 (18%)
Subsequent ICU transfer	1 (6%)	2 (11%)
Hospital outcome		
Hospital LOS[d] (days)	9.5 (4–15)	6 (3–7)
ICU LOS[d] (days)	5 (5–22)	3 (2–4)
Discharge destination		
Own home	14 (70%)	11 (55%)
Transferred	4 (20%)	7 (35%)
Died	2 (10%)	2 (10%)

[a] Dubois and Dubois.
[b] BMI = weight (kg) / height (m) squared.
[c] Monday to Friday, 08:00–18:00.
[d] Length of stay.

(Stata Corporation, College Station, TX, USA). Due to the large number of comparisons, statistical significance was set at a two-sided p-value of <0.01.

Results

We recorded continuous, non-invasive haemodynamic parameters for at least 20 min in 47 (94%) RRT reviews for HI. Information pertaining to the baseline characteristics and baseline haemodynamics have been previously published.[9]

Baseline haemodynamics and the HDR according to RRT trigger

As shown in Table 1, there was a near equal split between tachycardia and hypotension triggers, while 11% (5) triggered a RRT review for both. In the hypotension group, just under half were under the care of a medical team and had an elective hospital admission, compared with three-quarters and one third of the tachycardia group, respectively. Almost all hypotensive patients received FBT, while the majority of the tachycardia group did not. Further baseline demographics, characteristics and outcomes are presented in Table 1.

As shown in Table 2, those who triggered a RRT review for hypotension had a significantly lower HR (−45.4 bpm), MAP (−16.1 mmHg) and CI (−1.0 L/min/m^2) at baseline.

In the tachycardia group, there was an increase in MAP with the passage of time overall and at the 15–20-min time-block when compared to baseline, from 83.2 mmHg to 87.1 mmHg (+3.9 mmHg, $p = 0.0066$) and 85.5 mmHg (+2.3 mmHg, $p = 0.0061$), respectively. There were no other statistically significant changes in HR, MAP, CI, SVI and SVRI in any time-block or overall in either group (Fig. 1, Electronic Supplementary Material 1 and 2). When considering the HDR using correlated time-series data, there were significant changes in MAP (−17 mmHg, $p = <0.001$) HR (−43.2 bpm, $p = <0.001$) and CI (−0.91 L/min/m^2, $p = 0.004$) when comparing RRT triggers groups (Table 5).

Baseline haemodynamics and the HDR according to RRT intervention

As shown in Table 3, most patients received FBT while one third of patients did not receive FBT nor a vasopressor bolus. Similar proportions of each group (FBT vs no FBT) remained on the ward and had no limitations on resuscitation. Roughly twice as many patients treated with FBT had more than one RRT review and were admitted electively, while half as many were eventually discharged to their own home. As shown in Table 4, there were no statistically significant differences in any measured baseline haemodynamic parameter between FBT groups. In those who received FBT, there was a statistically significant increase in MAP overall and at the 15–20-min time-block compared to baseline (+3.4 mmHg, $p = 0.0036$) and (+4.2 mmHg, $p = 0.0037$), respectively. There were no other statistically significant changes in HR, MAP, CI, SVI and SVRI in any time-block or overall in either group (Fig. 2, Electronic Supplementary Material 3 and 4). When considering the HDR using correlated time-series data, there was a significant change in MAP over time when comparing RRT intervention groups (−12 mmHg, $p = 0.021$). There were no other statistically significant changes (Table 5).

Haemoglobin and indexed delivery of oxygen

The median haemoglobin concentration and DO_2/I were 112.5 g/L (IQR 89–134 g/L) and 524.4 ml/min/m^2 (IQR 346.1.7–610.3 ml/min/m^2), respectively. Mean Hb was lower in the hypotension (105.0 v 125.0 g/L, $p = 0.0179$) and FBT (103.7 v 133.3 g/L, $p = 0.0002$) groups (Table 2). Mean DO_2/I was lower in both hypotension and FBT groups also, 414.6 v 614.1 ml/min/m^2, $p = 0.0001$ and 454.1 v 611.7 ml/min/m^2, $p = 0.0026$, respectively (Table 4). The low DO_2/I group appeared to have a higher proportion of multiple RRT reviews, were more likely to have triggered RRT review due to hypotension, to have received RRT intervention, and to have required ICU transfer (Electronic Supplementary Material 5).

Table 2 – Comparison of baseline haemodynamics and proposed cause in tachycardia and hypotension groups.

Variable, n (%) or mean (95% CI)	Tachycardia (n = 20)	Hypotension (n = 22)	p-value
Systolic blood pressure (mmHg)	109.3 (96.9, 121.6)	92.4 (84.9, 99.9)	0.0169
Diastolic blood pressure (mmHg)	67.8 (62.0, 73.6)	53.8 (49.7, 58.0)	0.0002
Mean arterial pressure (mmHg)	83.2 (75.4, 91.0)	67.1 (62.0, 72.2)	0.0007
Heart rate (beats per minute)	127.4 (118.9, 135.8)	82 (73.2, 90.9)	<0.0001
Cardiac output (L/min)	6.8 (6.0, 7.6)	5.2 (4.7, 5.7)	0.0008
Cardiac index (L/min/m^2)	4.0 (3.5, 4.4)	3.0 (2.6, 3.4)	0.0025
Stroke volume (ml)	55.2 (49.3, 61.1)	66.0 (58.9, 73.2)	0.0212
Stroke volume index (ml/m^2)	32.2 (28.2, 36.2)	38.0 (32.8, 43.2)	0.07
SVR[a] (dyne s/cm^5)	1091.8 (933.0, 1250.7)	1082 (960.2, 1203.8)	0.92
SVRI[b] (dyne s/cm^5/m^2)	1871.6 (1571.9, 2171.2)	1954.0 (1659.0, 2249.0)	0.69
Haemoglobin (g/L)	125.0 (110.7, 139.2)	105.0 (95.7, 114.3)	0.0179
Delivery of Oxygen, Indexed (ml/min/m^2)	618.0 (531.8, 704.3)	404.6 (346.6, 462.6)	0.0001
Proposed cause of RRT response			
Sepsis	3 (15%)	4 (18%)	
Inflammatory response	2 (10%)	0 (0%)	
Hypovolaemia	6 (30%)	17 (77%)	
Arrhythmia	3 (15%)	0 (0%)	
Other	6 (30%)	1 (5%)	0.003

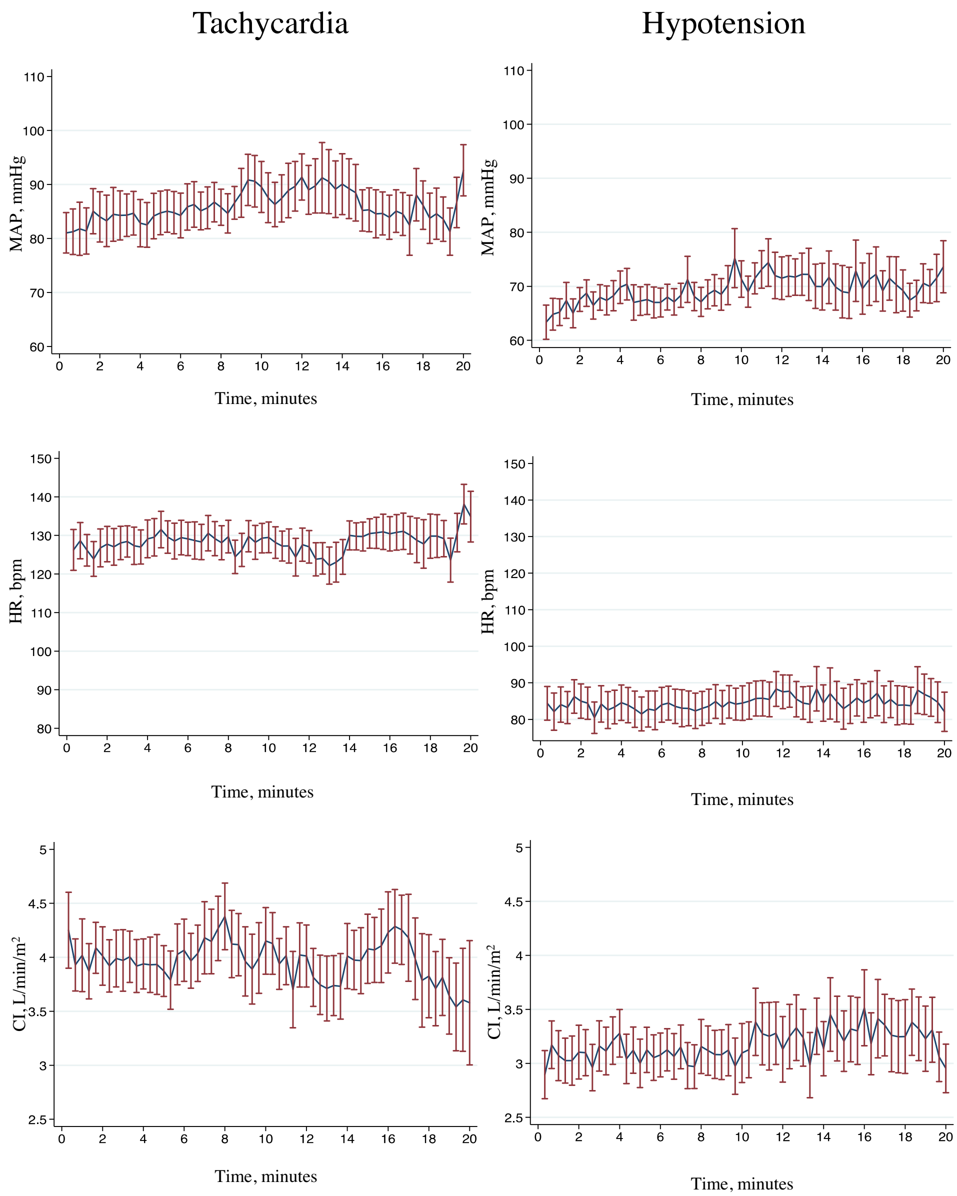

Fig. 1 – Changes in MAP, HR and CI over time by RRT trigger.

The hemodynamic response to vasopressor bolus

Despite the infrequency of their use (3 patients, 6%, who all received an intravenous metaraminol bolus), there was an observed visual change in MAP, SVI and SVRI of rapid onset and offset following administration (Electronic Supplementary Material 6). This was not assessed statistically due to the small numbers involved.

Discussion

Key findings

In this prospective study, we found that it was feasible to continuously and non-invasively measure haemodynamics during RRT management using the ClearSight™ device, for a period of 20 min. Moreover, RRT reviews triggered for hypotension rather than tachycardia had a lower baseline HR, MAP and CI. However, there no were differences in baseline HR, MAP, CI, SVI or SVRI between those who did or did not receive FBT. In addition, there were only minimal changes in MAP observed in both the tachycardia and FBT groups, over the observation period. Finally, there were no other statistically significant changes in any measured haemodynamic response parameter for any patient group.

Relationship to previous studies

To our knowledge, no previous studies have continuously and non-invasively assessed the haemodynamic response (HDR) of patients undergoing RRT review using parameters such as the CI or continuous MAP monitoring. Existing literature focuses on the ability of RRT teams to detect and respond to physiological deterioration "*the afferent limb*",[26,27] the efficacy of this response "*the efferent*

Table 3 – Comparison of demographics, baseline characteristics and outcomes in no fluid bolus therapy and fluid bolus therapy groups.

Variable, n(%) / median(IQR)	No fluid bolus therapy (n = 16)	Fluid bolus therapy (n = 31)
Age, years	63 (57–74)	69 (58–79)
Male	9 (56%)	19 (61%)
Height, cm	165 (161–171)	165 (160–175)
Weight, kg	67 (57–87)	70 (55–75)
BSA[a], m^2	1.8 (1.6–2.0)	1.8 (1.6–1.9)
BMI[b], kg/m^2	25.7 (21.3–30.1)	23.8 (20.5–27.5)
Organ system affected		
Cardiovascular	2 (13%)	2 (6%)
Respiratory	5 (31%)	0 (0%)
Gastro-intestinal	3 (19%)	9 (29%)
Renal	2 (13%)	2 (6%)
Sepsis	0 (0%)	2 (6%)
Other	4 (25%)	16 (52%)
Elective hospital admission	3 (19%)	13 (42%)
Medical admission	11 (69%)	15 (48%)
Comorbidities present	12 (81%)	26 (84%)
Working Day[c]	15 (94%)	24 (77%)
Typically reside at home	15 (94%)	28 (90%)
No assistance of daily activities	12 (75%)	18 (58%)
Multiple RRT reviews	3 (19%)	12 (39%)
No limitations on resuscitation	12 (75%)	28 (90%)
RRT Inclusion Trigger		
Tachycardia (Heart rate >100 bpm)	11(69%)	9 (29%)
Hypotension (systolic blood pressure <90 mmHg)	3 (19%)	19 (61%)
Both	2 (13%)	3 (10%)
RRT Treatment administered		
Vasopressor bolus	1 (6%)	2 (6%)
Immediate RRT outcome		
Remain on ward	13 (81%)	23 (74%)
Transfer other ward	1 (6%)	2 (6%)
Transfer ICU	2 (13%)	6 (19%)
Subsequent ICU transfer	1 (7%)	2 (8%)
Hospital outcome		
Hospital LOS[d] (days)	9 (3–15)	7 (4–13)
ICU LOS[d] (days)	5 (1–22)	3 (3–5)
Discharge destination		
Own home	13 (81%)	14 (48%)
Transferred	1 (6%)	12 (41%)
Died	2 (13%)	3 (10%)

[a] Dubois and Dubois.
[b] BMI = weight (kg) / height (m) squared.
[c] Monday to Friday, 08:00–18:00.
[d] Length of stay.

limb"[7,10,11,27–29] and the impact introducing the RRT service has on patient outcome.[3,4] However, in 2016, Silva and colleagues characterised RRT intervention actions in a retrospective study of 511 RRT responses at a tertiary centre.[30] Common interventions included FBT (41%) and the application of oxygen (37%), with 21% of patients transferred to ICU and 61% remaining on the ward. This is broadly in keeping with our findings on ICU transfers, while a lower proportion of our patients received FBT. However, Silva et al assessed patients with a RRT trigger of any kind and did not specifically focus on haemodynamic instability. Topple et al described the tasks completed by nursing staff at RRT response in a 2016 prospective observational study of 309 patients in a university hospital.[8] The authors found a

Table 4 – Comparison of baseline haemodynamics and proposed cause in no fluid bolus therapy and fluid bolus therapy groups.

Variable, n (%) or mean (95% CI)	No fluid bolus therapy (n = 16)	Fluid bolus therapy (n = 31)	p-value
Systolic blood pressure (mmHg)	109.4 (96.7, 122.1)	93.8 (85.2, 102.3)	0.0365
Diastolic blood pressure (mmHg)	65.8 (58.1, 73.5)	56.5 (52.6, 60.4)	0.0157
Mean arterial pressure (mmHg)	81.2 (71.7, 90.8)	69.7 (64.5, 75.0)	0.0209
Heart rate (beats per minute)	111.9 (100.3, 123.4)	100.2 (88.6, 111.7)	0.19
Cardiac output (L/min)	6.7 (5.8, 7.6)	5.6 (5.1, 6.1)	0.0254
Cardiac index (L/min/m^2)	3.8 (3.2, 4.4)	3.3 (3.0, 3.7)	0.10
Stroke volume (ml)	62.2 (56.5, 67.8)	60.3 (53.5, 67.1)	0.71
Stroke volume index (ml/m^2)	35.3 (31.0, 39.6)	35.2 (30.8, 39.5)	0.96
SVR[a] (dyne s/cm^5)	1083.6 (890.6, 1276.7)	1052.6 (952.9, 1152.3)	0.74
SVRI[b] (dyne s/cm^5/m^2)	1926.9 (1525.7, 2328.2)	1841.7 (1628.4, 2055.1)	0.67
Haemoglobin (g/L)	133.3 (118.2, 148.3)	103.7 (95.9, 111.4)	0.0002
Delivery of Oxygen, Indexed (ml/min/m^2)	619.9 (521.8, 718.0)	447.4 (388.0, 506.7)	0.0018
Proposed cause of RRT response			
Sepsis	4 (25%)	4 (13%)	
Inflammatory response	1 (6%)	1 (3%)	
Hypovolaemia	4 (25%)	23 (74%)	
Arrhythmia	2 (13%)	1 (3%)	
Other	5 (31%)	2 (6%)	0.007

[a] Systemic Vascular Resistance.
[b] Systemic Vascular Resistance Index.

Table 5 – Associations between haemodynamics and RRT triggers, and RRT treatments using correlated time-series univariate linear regression analysis.

Variable	β co-efficient	Standard error	95%[a] CI	p-value
RRT Trigger: Hypotension v Tachycardia				
MAP[b] (mmHg)	−17.0	4.6	−25.9, −8.0	<0.001
HR[c] (bpm)	−43.2	5.6	−54.2, −32.1	<0.001
CI[d] (L/min/m^2)	−0.91	0.32	−1.53, −0.29	0.004
SVI[e] (ml/m^2)	5.2	3.2	−1.0, 11.4	0.10
SVRI[f] (dyne s/cm^5/m^2)	58.3	218.8	−370.5, 487.2	0.79
RRT treatment: Fluid bolus therapy v No fluid bolus therapy				
MAP[b] (mmHg)	−12.0	5.2	−22.2, −1.8	0.021
HR[c] (bpm)	−9.5	8.8	−26.7, 7.7	0.28
CI[d] (L/min/m^2)	−0.42	0.33	−1.08, 0.23	0.21
SVI[e] (ml/m^2)	−0.6	3.3	−7.0, 5.7	0.85
SVRI[f] (dyne s/cm^5/m^2)	−105.7	218.4	−533.7, 322.2	0.63

[a] 95% Confidence interval.
[b] Mean arterial pressure.
[c] Heart rate.
[d] Cardiac index.
[e] Stroke volume index.
[f] Systemic vascular resistance index.

lower rate of ICU transfer (6% v 17%) and FBT administration (18% v 62%). However, this study included RRT triggers of all types and included those with limitations of medical therapy. A 2015 study by Sorenson et al assessed the performance of their RRT in a prospective observational study of 253 RRT responses in a university hospital.[11] The authors described a 32% and 53% ICU transfer and hospital-ward management rate, respectively. The rate of ICU transfer was higher (32% v 17%) and hospital-ward management was lower (53% v 79%). However, this included RRT calls for any trigger. A 2014 retrospective study of RRT response for hypotension in 410 patients in a tertiary teaching facility by Khalid et al,[31] assessed for differences in patients who were immediately transferred, transferred after initial RRT intervention or remained on the ward following initial RRT intervention. They described a higher proportion of ICU transfers (33% v 17%) and a lower proportion of hospital-ward management (67% v 79%). However, the study by Khalid et al differed in several aspects: only RRT responses for hypotension were included, the RRT team was led by an internal medical physician (junior staff or senior medical resident) rather than an ICU registrar and, dopamine at a dose of up to 5 mcg/kg/min was administered by

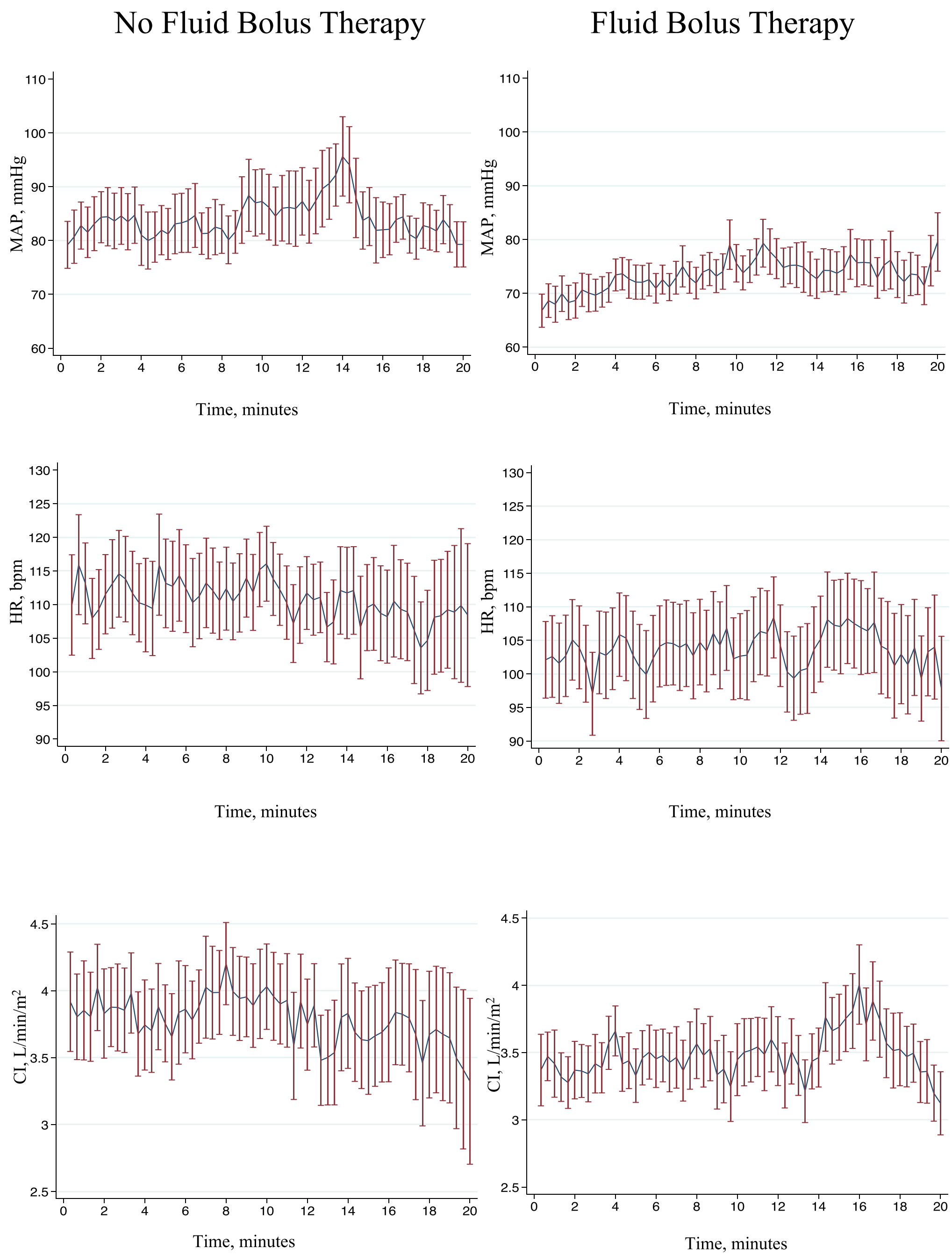

Fig. 2 – Changes in MAP, HR and CI over time by RRT intervention.

the RRT team to 91% of patients who remained on the ward for a mean time of 3.9 h. None of the above studies reported on the details of the haemodynamic response to RRT intervention nor delivery of oxygen.

Study implications

Our findings imply that non-invasive, continuous monitoring of those patients who trigger a RRT review for HI is feasible using the ClearSight^{TM} device for a period of at least 20 min. They also imply that there is a clear CI difference between patients who trigger a RRT review for tachycardia rather than for hypotension, and as such, there may be alternative treatment strategies for each group that warrant further investigation. However, as there were no clinically important short-term changes in the HDR in such patients, our findings suggests that current therapy does not deliver a clinically important short-term change in CI and associated haemodynamic parameters. There was a suggestion that those with lower DO_2/I may present with worsened haemodynamic variables, be more likely to receive RRT intervention and intensive care transfer. Therefore, this cohort may represent an identifiable at-risk population that might benefit from early detection and intervention. There were no statistically significant differences in baseline HR, MAP, CI, SVI or SVRI between those who did or did not receive FBT, this implies that the current process for selection of a patient for FBT does not discriminate well between those with altered CI and associated physiological parameters at baseline. Moreover, given the lack of a clinically significant change in any measured physiological parameter during the HDR in such patients, our findings imply that current therapy does not achieve a clinically relevant short-term physiological response. Therefore, if the primary aim of the RRT team is the clinically apparent short-term resolution of abnormal physiology, our observations imply that current RRT interventions require re-evaluation.

Study strengths and limitations

To our knowledge, our study is the first to use cardiac index and associated haemodynamic parameters, including delivery of oxygen, to continuously assess the short-term HDR following RRT review. Data were collected prospectively, continuously, non-invasively, with clinician blinding, and in an institution representative of teaching hospitals with a developed RRT system. Such methodology attempted to minimise potential bias, and maximise internal and external validity. Furthermore, data collected included haemodynamic parameters not typically available without invasive monitoring or critical care admission, thus providing novel, previously inaccessible physiological information. Moreover, the device was easy to apply, data was obtained in >90% of patients and there were no adverse events recorded.

This study also has several limitations. It was a single centre, observational study with the limitations of such studies. However, this was performed in large, university hospital with a mature RRT system which provides some external validity. Invasive devices are not suitable for use in response to a RRT trigger for hospital-ward patients. To facilitate data collection, we accepted the limitations of the devices that were capable of such data capture. The potential for introducing bias with the device utilised has been the subject of debate[32] as it provides an estimate of haemodynamics that rely upon assumptions. However, this device has been validated for both accuracy and precision against several comparable alternatives[18–23] and is FDA approved. Our observations are short term and it is possible that significant changes would occur at a later time following intervention. However, the nature and duration of haemodynamic interventions during RRT review are typically short-term. Due to the clinician-blinded, observational nature of the study, the haemodynamic data did not influence clinical practice. Therefore, we cannot draw conclusions regarding the effect of such monitoring on clinical practice and patient outcomes. This would need to be addressed in a subsequent study.

Conclusions

For a period of at least 20 min, using the ClearSight™ device, it was feasible to continuously and non-invasively record the cardiac index and associated parameters in almost all hospital-ward patients following RRT review for HI. RRT reviews triggered by hypotension appeared clearly physiologically distinct to those triggered for tachycardia, with a lower baseline HR, MAP and CI. However, there were only small and probably clinically unimportant changes over time in the HDR of such patients. There was a suggestion that those with a lower DO_2/I may represent a physiologically discrete cohort with comparatively inferior haemodynamic variables. There were no statistically significant differences in baseline HR, MAP, CI, SVI or SVRI between those who did or did not receive FBT only small changes in the HDR of such patients after FBT. As such, our findings imply that, in the first 20 min of intervention, RRT review and treatment does not achieve clinically relevant changes in patient cardiovascular physiology.

Sources of funding

This study was supported by a $10,000 (AUD) unrestricted educational grant from Edwards Lifesciences, who also supplied some of the single-use finger probes. Edwards Lifesciences were not involved in any other capacity (study concept and design; data collection, analysis, and interpretation; writing and editing of the manuscript; decision to submit for publication). This work was supported by an unrestricted educational grant from the Austin Hospital Anaesthesia and Intensive Care Trust Fund.

Conflict of interest

None.

Acknowledgements

Preliminary data was presented in at the 2017 Australian and New Zealand Intensive Care Society Rapid Response Team Safety and Quality Annual Meeting in Sydney, 7th august 2017 and in poster form at the 2017 Australian and New Zealand Intensive Care Society Annual Scientific Meeting in the Gold Coast, 12th October 2017.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.resuscitation.2019.08.025.

REFERENCES

1. Garland A, Olafson K, Ramsey CD, Yogendran M, Fransoo R. Epidemiology of critically ill patients in intensive care units: a population-based observational study. Crit Care 2013;17:R212.
2. Jones DA, DeVita MA, Bellomo R. Rapid-response teams. N Engl J Med 2011;365:139–46.
3. Hillman K, Chen J, Cretikos M, et al. Introduction of the medical emergency team (MET) system: a cluster-randomised controlled trial. Lancet (London, England) 2005;365:2091–7.
4. Aneman A, Frost SA, Parr MJ, Hillman KM. Characteristics and outcomes of patients admitted to ICU following activation of the medical emergency team: impact of introducing a two-tier response system. Crit Care Med 2015;43:765–73.
5. Jones D, Duke G, Green J, et al. Medical emergency team syndromes and an approach to their management. Crit Care 2006;10:R30.
6. Sprogis SK, Currey J, Considine J, Baldwin I, Jones D. Physiological antecedents and ward clinician responses before medical emergency team activation. Crit Care Resusc 2017;19:50–6.
7. Downey AW, Quach JL, Haase M, Haase-Fielitz A, Jones D, Bellomo R. Characteristics and outcomes of patients receiving a medical emergency team review for acute change in conscious state or arrhythmias. Crit Care Med 2008;36:477–81.
8. Topple M, Ryan B, Baldwin I, et al. Tasks completed by nursing members of a teaching hospital Medical Emergency Team. Intensive Crit Care Nurs 2016;32:12–9.

9. Eyeington CT, Lloyd-Donald P, Chan MJ, et al. Rapid response team review of hemodynamically unstable ward patients: The accuracy of cardiac index assessment. J Crit Care 2019;49:187–92.
10. Quach JL, Downey AW, Haase M, Haase-Fielitz A, Jones D, Bellomo R. Characteristics and outcomes of patients receiving a medical emergency team review for respiratory distress or hypotension. J Crit Care 2008;23:325–31.
11. Sorensen EM, Petersen JA. Performance of the efferent limb of a rapid response system: an observational study of medical emergency team calls. Scand J Trauma Resusc Emerg Med 2015;23:69.
12. Chaney JC, Derdak S. Minimally invasive hemodynamic monitoring for the intensivist: current and emerging technology. Crit Care Med 2002;30:2338–45.
13. Cholley BP, Payen D. Noninvasive techniques for measurements of cardiac output. Curr Opin Crit Care 2005;11:424–9.
14. Parmley CL, Pousman RM. Noninvasive cardiac output monitoring. Curr Opin Anaesthesiol 2002;15:675–80.
15. Peyton PJ, Chong SW. Minimally invasive measurement of cardiac output during surgery and critical care: a meta-analysis of accuracy and precision. Anesthesiology 2010;113:1220–35.
16. Eyeington CT, Ancona P, Cioccari L, et al. Non-invasive estimation of cardiac index in healthy volunteers. Anaesth Intensive Care 2018;46:290–6.
17. Edwards Life Sciences L. ClearSight System - Technology Overview. In: Edwards Life Sciences L, editor. 1-4.
18. Bogert LW, Wesseling KH, Schraa O, et al. Pulse contour cardiac output derived from non-invasive arterial pressure in cardiovascular disease. Anaesthesia 2010;65:1119–25.
19. Broch O, Renner J, Gruenewald M, et al. A comparison of the Nexfin(R) and transcardiopulmonary thermodilution to estimate cardiac output during coronary artery surgery. Anaesthesia 2012;67:377–83.
20. Chen G, Meng L, Alexander B, Tran NP, Kain ZN, Cannesson M. Comparison of noninvasive cardiac output measurements using the Nexfin monitoring device and the esophageal Doppler. J Clin Anesth 2012;24:275–83.
21. Fischer MO, Avram R, Carjaliu I, et al. Non-invasive continuous arterial pressure and cardiac index monitoring with Nexfin after cardiac surgery. Br J Anaesth 2012;109:514–21.
22. van der Spoel AG, Voogel AJ, Folkers A, Boer C, Bouwman RA. Comparison of noninvasive continuous arterial waveform analysis (Nexfin) with transthoracic Doppler echocardiography for monitoring of cardiac output. J Clin Anesth 2012;24:304–9.
23. Bartels SA, Stok WJ, Bezemer R, et al. Noninvasive cardiac output monitoring during exercise testing: Nexfin pulse contour analysis compared to an inert gas rebreathing method and respired gas analysis. J Clin Monit Comput 2011;25:315–21.
24. Dunn J-O, Mythen M, Grocott M. Physiology of oxygen transport. BJA Educ 2016;16:341–8.
25. Bersten AD, Handy J. Oh's intensive care manual e-book: expert consult: online and print. seventh ed Elsevier Health Sciences; 2013.
26. Bell MB, Konrad D, Granath F, Ekbom A, Martling CR. Prevalence and sensitivity of MET-criteria in a Scandinavian University Hospital. Resuscitation 2006;70:66–73.
27. Parr MJ, Hadfield JH, Flabouris A, Bishop G, Hillman K. The medical emergency team: 12 month analysis of reasons for activation, immediate outcome and not-for-resuscitation orders. Resuscitation 2001;50:39–44.
28. Calzavacca P, Licari E, Tee A, et al. A prospective study of factors influencing the outcome of patients after a medical emergency team review. Intensive Care Med 2008;34:2112–6.
29. Schneider AG, Warrillow S, Robbins R, Jones DA, Bellomo R. An assessment of the triage performance of the efferent arm of the rapid response system. Resuscitation 2013;84:477–82.
30. Silva R, Saraiva M, Cardoso T, Aragao IC. Medical emergency team: how do we play when we stay? characterization of MET actions at the scene. Scand J Trauma Resusc Emerg Med 2016;24:33.
31. Khalid I, Qabajah MR, Hamad WJ, Khalid TJ, Digiovine B. Outcome of hypotensive ward patients who re-deteriorate after initial stabilization by the medical emergency team. J Crit Care 2014;29:54–9.
32. Ameloot K, Palmers PJ, Malbrain ML. The accuracy of noninvasive cardiac output and pressure measurements with finger cuff: a concise review. Curr Opin Crit Care 2015;21:232–9.