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Rapid response team review of hemodynamically unstable ward patients: The accuracy of cardiac index assessment

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ABSTRACT

Purpose: Intensive care doctors commonly attend rapid response team (RRT) reviews of hospital-ward patients with hemodynamic instability and estimate the patient's likely cardiac index (CI). We aimed to non-invasively measure the CI of such patients and assess the level of agreement between such measurements and clinically estimated CI categories (low <2L/min/m2, normal 2-2.99L/min/m2 or high ≥3L/min/m2).

Materials and methods: A prospective, observational study of non-invasive measurement and clinical estimation of CI categories in 50 adult hospital-ward patients who activated the RRT for 'hemodynamic instability' (tachycardia > 100BPM or hypotension < 90mmHg or both).

Results: The CI was measured in 47/50(94%) patients and the mean CI was 3.5(95% CI 3.2-3.7) L/min/m2. Overall, 30(64%) patients had a high CI, 13(28%) and 4(9%) had a normal and a low CI, respectively. The level of agreement between measured and clinically estimated CI categories was low(19.2%). Sensitivity and positive predictive values of clinical estimation were low(0% and 3.3% for high CI, and 0% and 50% for low CI, respectively).

Conclusions: Non-invasive CI measurement was possible in almost all hospital-ward patients triggering RRT review for hemodynamic instability. In such patients, the CI was high, and intensive care clinicians were unable to identify a low or a high CI state.

1. Introduction

Delay in assessment and management of deteriorating hospital-ward patients has been associated with increased morbidity and mortality [1-3]. In many countries, intensive care doctors have responded to these issues by implementing and staffing rapid response teams. Thus, rapid response teams (RRT) are now part of the work of many intensive care units worldwide and are an established approach to the recognition and treatment of such patients [4,5].

Approximately one third of RRT reviews are triggered by hypotension or tachycardia [6-8], hereafter termed 'hemodynamic instability' (HI). Currently, assessment of the hemodynamic state of such patients consists of clinical assessment based on examination and vital signs. Therefore, the diagnosis of either a low, a normal or a high cardiac index state is dependent on the skills and experience of the attending clinician.

Unfortunately, no studies to date have attempted to rapidly and objectively measure a patient's cardiac index during a RRT review for HI. This knowledge gap is due to the fact that currently available methods to measure cardiac output and index may be invasive, operator or reporter-dependent and intermittent (echocardiography), and require time and expertise to perform, monitor and evaluate. The ClearSight™ (Edwards, Irvine, CA, USA) is one of several novel non-invasive devices that can measure the CI and other hemodynamic parameters and is FDA approved for such use [9-12].

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Accordingly, the primary outcome was to non-invasively measure the CI of adult patients who trigger a RRT review for HI. The secondary outcomes were assessment of the level of agreement (LOA) between the CI obtained with such technology, and the CI estimated through clinical assessment by members of an intensive care-based RRT. Our hypothesis was that most patients would be in the low or normal CI category and that there would be a moderate level of agreement between clinical assessment and non-invasive measurement.

2. Material and methods

2.1. Selection and description of participants

This was a single-center, prospective, observational study conducted in a large metropolitan hospital where the RRT is intensive care led. Ethical approval (LNR/15/Austin/382) was obtained through the Institutional Review Board, which waived the need for informed consent. Adult patients age 18 or over who triggered a RRT review 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.

2.2. Technical information

The ClearSight™ uses volume-clamp, pulse-contour technology to estimate CI. This device has two cuffs, one placed at the distal phalanx of the index or middle finger and the other applied to the forearm. The finger cuff pressure is automatically adjusted to maintain a constant arterial volume that is examined by a photo-plethysmograph. This pulse contour information is analyzed using a physiological model of the circulation to calculate stroke volume and cardiac output [13]. Following calibration, the device records averaged data every 20 s. The validity, level of accuracy and precision appear comparable to that of alternative techniques of CI measurement, including pulmonary artery catheter (PAC) thermodilution [14,15], trans-pulmonary thermodilution [16], trans-thoracic echocardiography [17] and esophageal Doppler [18]. The device is FDA approved for the estimation of cardiac output and arterial blood pressure.

2.3. Data collection

Once a RRT review had been triggered, a member of the research team attended the call and assessed the patient for suitability. Data were obtained for a minimum of 15 consecutive readings over five minutes. The display was positioned such that the data was not available to the treating doctor.

After a minimum period of five minutes, the treating clinician was asked for their estimation of the CI: 1. low (< 2 L/min/m^2), 2. normal (2–2.99 L/min/m^2) or 3. high (≥ 3 L/min/m^2). Clinicians were also asked for their perception of the cause of HI from the following list: sepsis, bleeding, hypovolemia, heart failure, myocardial ischaemia, primary arrhythmia, pulmonary embolism, epidural related, medication side effect, exacerbation liver disease, pericardial tamponade, systemic inflammatory response syndrome (SIRS), other.

Additional data collected included basic demographic data, seniority and primary specialty of the treating clinician, organ system associated with admission, co-morbidities, resuscitation status and disposition of the patient after the RRT review, and upon hospital discharge.

2.4. Outcomes

The primary outcome was the proportion of RRT reviews for HI with a low, normal and high CI. Secondary outcomes were the LOA between clinical estimation (CE) and non-invasive measurement (NIM) of CI overall and depending on the proposed cause of HI or the trigger for RRT activation.

2.5. Statistical methods

Data were assessed for normality; 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 x height (cm)^0.725 x 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 x mean MAP / CO [CI]). The LOA of CI categories between NIM and CE was examined using un-weighted and weighted Cohen's kappa [20]. Assessment of kappa values for quality of agreement were based on Landis and Koch criteria [21]. Accuracy of the clinician's CI category estimate was assessed using specificity, sensitivity, positive predictive value (PPV) and negative predictive (NPV) values. This was based upon the assumption that the non-invasive device measured the correct CI.

The categories for the proposed cause of HI were compared using two groups, vasodilatation and hypovolemia. These groups were

Table 1
Demographics, baseline characteristics and outcomes.

Variables presented as n (%) or median (IQR)	
Age, years	66 (57–77)
Male	28 (60%)
Height, cm	165 (160–174)
Weight, kg	68 (55–79)
BSA[a], m^2	1.78 (1.59–1.89)
BMI[b], kg/m^2	24.2 (21.0–27.7)
Admitting team	
Cardiology	3 (6%)
Respiratory	3 (6%)
Renal	4 (9%)
Oncology	6 (13%)
General medicine	6 (13%)
Other medical	5 (11%)
General surgery	9 (19%)
Orthopaedics	9 (19%)
Other surgery	2 (4%)
Organ system affected	
Cardiovascular	4 (9%)
Respiratory	7 (15%)
Gastro-intestinal	12 (26%)
Renal	4 (9%)
Sepsis	2 (4%)
Other	18 (38%)
Elective hospital admission	16 (34%)
Medical admission	26 (57%)
No comorbidities	8 (17%)
One comorbidity	17 (36%)
Two comorbidities	13 (28%)
Three or more comorbidities	9 (19%)
Working Day[c]	39 (83%)
Typically reside at home	43 (92%)
No assistance of daily activities	30 (65%)
Multiple RRT calls	12 (26%)
No limitations on resuscitation	40 (85%)
RRT outcome	
Remain on ward	37 (79%)
Transferred to ICU	8 (17%)
Transferred to another ward	2 (4%)
RRT Treatment administered	
Fluid bolus therapy	29 (62%)
Vasopressor bolus	3 (6%)
Hospital LOS (days)	6 (3–11.5)
Discharge destination	
Own home	27 (57%)
Transferred	13 (28%)
Died	5 (11%)

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

Table 2
Rapid response team trigger, proposed cause and treating clinician's primary speciality and years in practice.

Variable	n (%)
Inclusion trigger	
Tachycardia (Heart rate > 100 bpm)	20 (43%)
Hypotension	22 (47%)
(Systolic blood pressure < 90 mmHg)	
Both	5 (11%)
Proposed cause of RRT review	
Sepsis	8 (17%)
Inflammatory response	2 (4%)
Hypovolemia	27 (57%)
Arrhythmia	3 (6%)
Other	7 (15%)
Clinician's Specialty	
Intensive care	22, (47%)
Anesthesia	9, (19%)
Internal medicine	7, (15%)
Emergency department	8, (17%)
Surgery	1, (2%)
Clinician's years in practice	
< 5	3, (6%)
5–10	31 (66%)
> 10	13 (28%)

selected because they were hypothesized to have contrasting clinical manifestations and subsequent management options for the observed HI: vasodilatation with low SVR and a high CI potentially treated with vasopressors and hypovolemia with high SVR with a low CI potentially treated with fluid bolus therapy. The vasodilatation group included the proposed causes of sepsis and systemic inflammation. Post-hoc subgroup analysis was performed on those who were Immediately Transferred (IT) to ICU and those who were immediately or Subsequently Transferred (ST) to ICU at any time during their hospital admission following RRT review for HI. A sample size of 50 was considered appropriate for this feasibility study. Statistical analysis was undertaken with Stata 14® (Stata Corporation, College Station, TX, USA). STROBE guidelines for observational studies were adhered to.

3. Results

3.1. Details of patient cohort

We non-invasively recorded the CI in almost all RRT reviews for HI (47 of 50, 94%). Three patients were excluded due to failure to obtain a reliable photoplethysmograph. In these 47 patients, we recorded over 4000 observations (median 115, IQR 73–137 observations per patient). Most were male (28, 60%), aged between 50 and 80 years (median 65, IQR: 57–77 years). Most patients had a least one comorbidity (39, 83%) and the median hospital length of stay was 6 days (IQR 3–11.5) (Table 1). Of the RRT review triggers, there was a near equal split between tachycardia (20, 43%) and hypotension (22, 47%) while 11% (5) triggered for both. The RRT was staffed by members of the intensive care unit or anesthesiology or internal medicine fellows undertaking their rotation in the ICU. For half of such attending clinicians, the primary specialty was intensive care (22; 47%) and nearly all had 5 or more years of clinical experience (44, 94%). The most commonly proposed causes for the RRT review were hypovolemia in just over half (57%) and sepsis in one in five (17%) (Table 2).

3.2. Hemodynamic variables and CI categories during initial assessment

The mean CI was high (3.5 L/min/m^2), and the mean systolic blood pressure (99.1 mmHg) and heart rate (104.2 bpm) were both around 100. The mean SVI was at the lower end of normal (35.2 mL/m^2) and the mean SVRI was low (1870.7 dyne s/cm^5 /m^2) (Table 3).

Table 3
Means of the averaged hemodynamic variables and cardiac index categories during the initial 5 min

Variable, $n = 47$	Mean (95% CI)
Systolic blood pressure (mmHg)	99.1 (91.9–106.3)
Diastolic blood pressure (mmHg)	59.7 (55.9–63.4)
Mean arterial pressure (mmHg)	73.7 (68.8–78.5)
Heart rate (beats per minute)	104.2 (95.7–112.6)
Cardiac output (L/min)	6.0 (5.5–6.5)
Cardiac index (L/min/m^2)	3.5 (3.2–3.8)
Stroke volume (mL)	60.9 (56.2–65.6)
Stroke volume index (mL/m^2)	35.2 (32.1–38.3)
SVR[a] (dyne s/cm^5)	1063.2 (974.5–1151.8)
SVRI[b] (dyne s/cm^5 /m^2)	1870.7 (1683.4–2058.1)
Measured Cardiac Index Category	n, (%)
Low (< 2 L/min/m^2)	4 (9%)
Normal (2 - 3 L/min/m^2)	13 (28%)
High (>3 L/min/m^2)	30 (64%)

[a] SVR = Systemic Vascular Resistance.
[b] SVRI = Systemic Vascular Resistance Index.

Overall, almost two-thirds of patients had a high CI (30, 64%). Most RRT reviews triggered for tachycardia recorded a high CI ($n = 16$, 80%). In RRT reviews triggered for hypotension, 10 (45%) measured a high CI, with 9 (41%) in the normal CI category. The measured CI was high in 8 (80%) of RRT reviews judged to be secondary to vasodilatation (Table 4).

3.3. Level of agreement (LOA) of CI categories between NIM and CE

Overall, the LOA between NIM and CE was approximately one in five (19.2%, $\kappa = -0.09$). This LOA occurred in one of ten (10%, $\kappa = -0.14$) and one quarter (27.3%, $\kappa = -0.07$) for RRT responses triggered by tachycardia and hypotension, respectively. The LOA was zero (0%, $\kappa = -0.16$) and three in ten (29.6%, $\kappa = -0.006$) in RRT reviews judged to be caused by vasodilatation and hypovolemia, respectively. All LOAs were close to 50% (45 to 59.3%, $\kappa = -0.18$ to 0.00) when weighted (Table 4).

3.4. Accuracy of the clinician's CI category estimate

In patients with a low (<2 L/min/m^2) or a high CI (≥3 L/min/m^2), both the sensitivity (0% and 3.3%) and PPV of CE were low (0% and 50%). Specificity and NPV were 14.7% and 50%, respectively, in patients with a normal CI. In patients where the cause was judged to be vasodilatation, the sensitivity and PPV were 0% for each of the three CI categories (Table 5).

3.5. Treatment and outcomes

Around one in five patients required immediate transfer to ICU (IT group, $n = 8$, 17%) and a further three required subsequent transfer to ICU (ST group, $n = 11$, 23%). Most patients (29, 62%) received fluid bolus therapy (FBT) and a small proportion were administered a vasopressor bolus of metaraminol (3, 6%). All patients who received a vasopressor were in the IT group. The median hospital length of stay was just under one week (6 days, IQR 3 days–11.5 days), which appeared longer for those in the IT (14 days, 6–29.5 days) and ST (12 days, 7–26 days) groups. Overall, one in ten patients (5, 11%) died in hospital, which included one of the three ST patients (Electronic Supplementary Material 1).

3.6. Hemodynamic variables and CI category estimation in IT and ST groups

The median cardiac index appeared lower in both IT and ST groups, at 3.0 L/min/m^2 (2.5–3.5 L/min/m^2) and 3.1 L/min/m^2 (2.5–3.8 L/min/m^2), respectively. The level of agreement between cardiac index measurement and estimation remained poor in the both groups, 12.5% and 9.1%, respectively (Electronic Supplementary Material 2).

Table 4
Measured cardiac index categories and the level of agreement between measured and estimated cardiac index categories.

Cardiac Index, L/min/m^2	< 2	2–2.99	> 3	Agreement (%)	Agreement (%) (weighted[a])
Whole cohort, n = 47					
ClearSight	4, (9%)	13, (28%)	30, (64%)		
Clinician	8, (17%)	37, (79%)	2, (4%)	19.2	55.3
Trigger					
Tachycardia, n = 20					
ClearSight	1, (5%)	3, (15%)	16, (80%)		
Clinician	1, (5%)	17, (85%)	2, (10%)	10	55.0
Hypotension, n = 22					
ClearSight	3, (14%)	9, (41%)	10, (45%)		
Clinician	7, (32%)	15, (68%)	0, (0%)	27.3	54.6
Proposed cause					
Vasodilatation, n = 10					
ClearSight	0, (0%)	2, (20%)	8, (80%)		
Clinician	3, (30%)	7, (70%)	0, (0%)	0	45.0
Hypovolemia, n = 27					
ClearSight	3, (11%)	9, (44%)	15, (56%)		
Clinician	5, (19%)	21, (78%)	1, (4%)	29.6	59.3

[a] Weighted Kappa: if the category estimates are not the same but one above or below, 0.33 is attributed to the estimate rather than 0. 1 (i.e 100% agreement) is attributed to category estimates that are identical and 0 is attributed to those that are greater than one category away from the category estimates.

4. Discussion

We non-invasively recorded the CI in hospital-ward patients triggering RRT review for HI. Two thirds of such patients had a high CI and a low CI was uncommon. Almost all patients with tachycardia or suspected vasodilatation had a high CI. However, there was poor agreement between the non-invasively measured and clinically estimated CI categories. Moreover, no clinicians correctly identified the CI category if the suspected cause for RRT activation was vasodilatation. Finally, clinicians were unable to correctly identify a low CI or a high CI.

To our knowledge, no previous studies have measured the CI during a RRT review. The presented mean CI is within references ranges [22–26] and in keeping with a study of CI in 33 Emergency Department patients [27], which found a similar LOA of the clinical estimation of CI by attending clinicians as well as poor performance in estimating CI categories [27]. However, these ED patients were mechanically ventilated, the study investigators utilized an alternative CI category range and more patients had a low CI.

Table 5
Assessment of the accuracy of clinically estimated cardiac index categories.

Cardiac index category, L/min/m^2	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
Whole cohort, n = 47				
Low, < 2	0	81.4	0	89.7
Normal, 2–2.99	61.5	14.7	21.6	50
High, > 3	3.3	94.1	50	35.6
Trigger				
Tachycardia, n = 20				
Low, 2	0	94.7	0	94.7
Normal, 2–2.99	33.3	5.9	5.9	33.3
High, > 3	6.3	75	50	16.7
Hypotension, n = 22				
Low, < 2	0	63.2	0	80
Normal, 2–2.99	66.7	30.8	40	57.1
High, > 3	0	100	0	54.5
Proposed cause				
Vasodilatation, n = 10				
Low, < 2	0	70	0	100
Normal, 2–2.99	0	12.5	0	33.3
High, > 3	0	100	0	20
Hypovolemia, n = 27				
Low, < 2	0	79.2	0	86.4
Normal, 2–2.99	77.8	22.2	33.3	66.7
High, > 3	6.7	100	100	38.5

In contrast, others found higher unweighted LOA of 50% [28], 51% [29] and 51% [30], respectively. However, these studies differed in patient selection, methodological approach and hemodynamic assessment. For example, a questionnaire study performed in ICU patients with hypotension or hypoxemia used a different CI range of low ≤3 L/min/m^2, normal = 3-5 L/min/m^2 and high ≥5 L/min/m^2 [28]. Another assessed surgical ICU patients, compared clinical assessment with PAC data and used cardiac output, rather than CI [29]. Finally, the third study was performed on patients in whom it was deemed appropriate to place a PAC and utilized cardiac output rather than CI [30]. Forrester et al. described a higher rate of clinical accuracy of 83% in a 1977 study of 200 patients [31]. However, this study used broad descriptors and fixed clinical signs to direct CI category selection, rather than independent clinical judgement, and was performed in post myocardial infarction patients using a PAC.

A 2012 single-center study of 45 critically ill ICU patients by Monnet et al. utilized the ClearSight™ to compare absolute CI and changes in CI with trans-pulmonary derived CO using the PiCCO2 (Pulsion Medical Systems, Munich, Germany) device [32]. An arterial waveform was obtained in a similar proportion of patients (84%). However, the population being studied differed from ours in several aspects: they were ICU patients, the mean MAP was much lower (43 v 74 mmHg), and almost half had ARDS, were receiving a noradrenaline infusion or were mechanically ventilated, respectively.

Hospital-ward patients who trigger a RRT review are at an increased risk of unexpected death and unplanned ICU admission [33-35], which was reflected in our data with one in five patients having an unplanned ICU admission and one in ten dying in hospital. This was supported by a study of 200 RRT reviews, which described a similar in-hospital mortality (12%) [7].

Our findings imply that hemodynamically unstable patients typically have a high CI, especially in the presence of tachycardia or suspected vasodilatation. They also imply that a low CI is uncommon, but that, when present, it cannot be identified by clinicians. As such, our findings finally imply that, clinical assessment-based therapy may often fail to deliver logical physiological management of hemodynamic instability (e.g. fluid bolus therapy for hypovolemia, vasopressors for vasodilatation, inotropes for a low CI state or tolerance of mildly abnormal parameters with an appropriate CI for the patient's disease-state and preserved markers of end-organ perfusion).

To our knowledge, this is the first study to non-invasively and continuously measure CI in hospital-ward patients activating a RRT review for HI. There were no adverse events recorded and we successfully recorded the CI in almost all patients. Our observations are similar to those of other studies in ED patients, which provides a degree of face validity, concurrent validity, construct validity, and content validity. This study was performed in a large metropolitan hospital with a well-established RRT review system, which confers external validity. However, our study has several limitations. First, it was a single center study; however, it was performed in a hospital with an established RRT system and similar characteristics of university hospitals in other developed countries. This was a non-randomized, observational study, though the treating clinicians were blinded to hemodynamic variables. Limitations encountered in observational studies such as the Hawthorn effect were present. However, this study would not have been feasible without bedside data collection. The accuracy of CE was based on the assumption that the measurement device recorded the true CI. This monitoring tool, like any other, will never be perfect. However, this device has the benefits of being non-invasive, objective, reproducible, non-user and non-reporter dependent. Additionally, this device has been validated against several comparable alternatives [14-18,36] and is FDA approved for such purposes. The delineation of low, normal and high CI categories included part of the CI range typically seen in healthy adults. However, the anticipated CI in health is different to that expected of a hospital-ward patient. Furthermore, there is no available data pertaining to the expected CI of hospital-ward patients who have a RRT review for HI. Therefore, the CI categories used were based upon values observed in critically ill emergency department patients [27]. CE was not standardized, which may be considered a limitation. However, the aim of the study was to compare current real-world practice with a non-invasive device. The sub-group analyses of the proposed causes for RRT review of vasodilatation and hypovolemia are unlikely to be mutually exclusive. However, this subdivision was deemed relevant because the clinical management strategies of these two proposed causes may differ greatly. For example, those with HI due to vasodilation may be treated with vasopressor therapy and ICU transfer, while those with HI due to hypovolemia may be appropriate for administration of fluid bolus therapy with a period of observation on the hospital-ward. Sub-group analysis of patients immediately transferred to ICU and subsequently admitted to ICU was affected by small study numbers. This limits the generalizability of information related to those patients who required an ICU admission. This was a feasibility study and had a small sample size. However, the data collected was measured at 20 s intervals, which provided a robust assessment of averaged hemodynamic variables. The sample did not include alternative RRT reviews that may indicate HI, such as altered conscious state, elevated respiratory rate or oliguria. However, the inclusion of RRT reviews for altered conscious state may have introduced confounders and respiratory rate and urine output have been reported to be inaccurately or incompletely measured or monitored [37,38]. The clinical interpretation of what an appropriate CI is in a patient with a RRT review for HI is dependent on the patient's pre-morbid state (co-morbidities, cardiorespiratory function), concurrent disease-state and physiological markers of the adequacy of oxygen delivery and utilization. However, the assessment and interpretation of such information is influenced by expected baseline hemodynamic data for such patients. Therefore, this study provides valuable, previously unknown reference information for patients who trigger a RRT review for HI and may assist in RRT training of intensive care doctors (35).

5. Conclusions

We applied a novel non-operator dependent device to non-invasively measure CI in hospital-ward patients triggering review by an intensive care-based RRT for HI. We found that a high mean CI and a high CI category were common, while a low CI category was uncommon. Moreover, we found that ICU-based clinicians were unable to accurately estimate the CI category. Finally, such ICU-based clinicians were unable to identify the presence of a low CI or a high CI. These findings imply that, in selected patients, objective measurement of CI is possible and provides additional information that cannot be obtained by clinical assessment.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jcrc.2018.09.002.

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All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. STROBE guidelines for observational studies were adhered to.

Non-regular abbreviations

BMI	Body Mass Index
BSA	Body Surface Area
CE	Clinical Estimation
CI	Cardiac Index
CO	Cardiac Output
HI	Hemodynamic Instability
LOA	Level of Agreement
RRT	Rapid Response Team
NPV	Negative Predictive Value
NIM	Non-Invasive Measurement
PPV	Positive Predictive Value
PAC	Pulmonary Artery Catheter
SVI	Stroke Volume Index
SIRS	Systemic Inflammatory Response Syndrome
SVR	Systemic Vascular resistance
SVRI	Systemic Vascular Resistance Index

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