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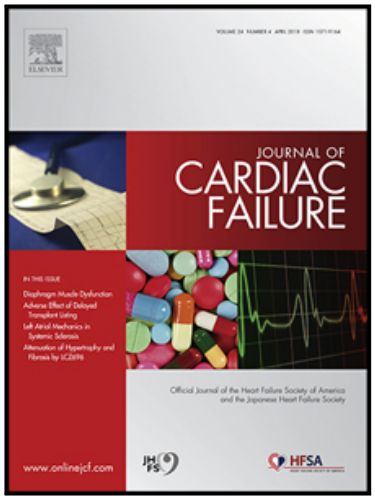

Non-Invasive Cardiac Output Monitoring in Cardiogenic Shock – The NICOM™ Study

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Title Page

Full Title

Non-Invasive Cardiac Output Monitoring in Cardiogenic Shock – The NICOM™ Study

Short Title

Non-Invasive Cardiac Output Monitoring in Cardiogenic Shock

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Abstract

Background

The bioreactance technique is a relatively new, totally non-invasive technique used to measure cardiac output that is easy to use. Non Invasive Cardiac Output Monitor (NICOM) is one such system (Cheetah Medical Inc). Although approved by FDA for measurement of stroke volume, there is a paucity of literature validating this technology in decompensated heart failure and cardiogenic shock (CS).

Methods and Results

Fifty patients admitted to our cardiac intensive care unit (CICU) for CS and Swan Ganz catheter guided therapy were prospectively enrolled in the study after informed consent. Simultaneous measurements of cardiac output (CO) were obtained using NICOM, indirect Fick (IF) and bolus thermodilution (TD). Intraclass correlation coefficient (ICC) was used to assess the precision of NICOM for CO using the three repeated measurements of CO over the pooled data. The agreement of the NICOM device in the defined clinical population compared to IF and TD, was evaluated by comparing the Pearson Correlation Coefficient, the Bland-Altman plot, and Lin's Concordance Correlation Coefficient.

ICC for cardiac output measured by NICOM showed excellent repeatability (ICC = 0.93, 95% CI = 0.92 – 0.94, n = 262) in the pooled data. Pearson Correlation Coefficient for cardiac output measured by NICOM was poor when compared to IF (n = 263, r = 0.132, p = 0.033) and TD (n = 258, r = 0.275, p < 0.001).

Conclusions

NICOM technology is not a reliable method of measuring CO in patients with decompensated heart failure and CS.

Introduction

Invasive nature of pulmonary artery catheter (PAC) is often cited as an added risk to the patients with unclear mortality benefit among critically ill patients. [1,2] Eisenberg *et al.* and Mimoz *et al.* demonstrated that physicians could predict cardiac output with only 50% accuracy in the absence of direct hemodynamic data [3, 4], indicating the need for hemodynamic monitoring in critically ill patients. Current guidelines support the use of invasive hemodynamic monitoring in selected patients in whom a clinical evaluation does not provide sufficient data to determine optimal medical therapy. [5] For these reasons, measurement of cardiac output (CO) using non-invasive or minimally invasive devices has gained popularity.

The bioreactance technique is a relatively new, non-invasive technique used to measure CO. Non Invasive Cardiac Output Monitor (NICOM) is one such system (Cheetah Medical Inc). This

device analyzes phase shifts of a delivered oscillating current that occurs as the current transverses through the thoracic cavity to calculate CO. [6,7] This technology has been validated in patients with septic shock, post-cardiotomy and in patients presenting with acute hypoxemic respiratory failure. [8-10] However, Fagnoul *et al.* evaluated the correlation between CO values obtained using NICOM with those measured using semi-continuous CO by thermodilution (TD) in 11 critically ill patients, finding poor correlation. [11] Furthermore, there is a paucity of literature on validation of this device in patients with decompensated heart failure and cardiogenic shock, despite stroke volume measurement being an FDA approved indication for use of the device.

The purpose of our study was to test the accuracy of CO measurements by NICOM with indirect Fick and TD techniques among patients in cardiogenic shock (CS).

Methods

This cross-sectional prospective clinical study was conducted in the Cardiac Intensive Care Unit (CICU) at The University of Kansas Hospital in Kansas City, KS. After approval by the Institutional Review Board, we enrolled 50 consecutive eligible patients admitted for PAC-guided treatment of CS between December 2017 and September 2018. All patients received PAC based on the 2013 ACC/AHA guidelines. Patients were excluded if they had non-intact anatomy at the NICOM sensor placement site, contraindication to PAC placement (right ventricular mechanical support, right ventricular thrombus, pulmonary embolus in proximal PA or bleeding diathesis), or required mechanical circulatory support with continuous flow devices (i.e. Impella, LVAD, or VA-ECMO). Written consent was obtained from all patients during the index hospitalization.

Study Protocol

Simultaneous measurements of CO were obtained by trained critical care nurses using indirect Fick, TD and NICOM^{TM} techniques for the duration of the study. Frequency of simultaneous measurements was based on the patient's clinical management plan as deemed appropriate by the attending cardiologist. Measurements were obtained at least every 8 hours to allow for a minimum of 5 measurements per patient within a 48-hour period before the discontinuation of NICOM patches (per package insert recommendations). Patients were supine for at least 10 minutes prior to each measurement. At each time point and documented in the institutional electronic medical record, first measurement was obtained on NICOM, immediately followed by mixed venous saturation determination to be used for indirect Fick, a second NICOM measurement, TD measurement and then a third NICOM measurement.

All clinical decisions about patient's care were based on the measurements obtained by indirect Fick and TD and not NICOM measurements.

Statistical Analysis

All statistical analyses were performed using IBM SPSS 24, with the exception of Lin's Concordance Correlation Coefficient, which was performed using NCSS12. Continuous data

were summarized by their mean and standard deviation, and categorical data by their percentages. The precision of the NICOM device was evaluated using the intraclass correlation coefficient (ICC) of the three repeated measurements of CO over the pooled data. The ICC reflects both the degree of correlation and agreement between measurements and ranges from 0 to 1. ICC values between 0.75 and 0.9, and greater than 0.9 are indicative of good and excellent reliability, respectively. The intraclass correlation coefficient was based on a 2-way mixed effect model, absolute agreement, and single measurement.

The agreement of the NICOM device in the defined clinical population compared to Indirect Fick and TD, was evaluated by comparing the Pearson Correlation Coefficient, the Bland-Altman plot, and Lin's Concordance Correlation Coefficient. For this analysis the three repeated assessments using NICOM were averaged and this average then used in further analyses. For statistical analyses the measurements of CO over time were considered serial rather than repeated. Although the CO measurements were obtained in the same patient over multiple (average of 5) time points, most of the factors that would affect cardiac output (example: volume overload, inotropic support, hemodynamics, renal function, respiratory support, degree of hypoxemia, body temperature, etc.) were different at each point, even in the same patients. Given this significant time effect, CO measurements over time were analyzed as serial rather than repeated measurements. The Kolmogorov-Smirnov test was used to assess data normality. A p-value less than 0.05 was considered statistically significant.

Linear regression analysis was performed to evaluate the impact of baseline characteristics on the correlation between NICOM and indirect Fick and bolus thermodilution measurements.

Results

50 patients admitted to our CICU for treatment of CS (mean cardiac index by indirect Fick of 2.16±0.53 L/min/m^2, and mean cardiac index by bolus thermodilution of 2.08±0.65 L/min/m^2, with mean CVP of 10.9±6.2 mmHg and mean PASP of 48.5±11.9 mmHg) with PAC guided therapy were included in our study analysis. An average of 5 sets of measurements were obtained per patient. Baseline characteristics of our patients are summarized in Table 1.

Intraclass Correlation Coefficients (ICC) for CO measured by NICOM showed excellent repeatability (ICC = 0.93, 95% CI = 0.92 – 0.94, n = 262) in the pooled data. The excellent ICC among NICOM measurements of CO persisted when selected for patients with normalized cardiac index >2.2 L/m/m^2 by indirect Fick or TD (ICC = 0.94, 95% CI = 0.92 – 0.95, n = 173) and similarly for euvolemic patients with CVP <5 mmHg or PASP <25 mmHg (ICC = 0.94, 95% CI = 0.90 – 0.96, n = 52). (Figure 1)

Agreement between methods was demonstrated with Bland-Altman plots.[12] Figure 2A shows a scatter plot of the measurements of CO by NICOM and indirect Fick and their associated Pearson's correlation coefficient and Lin's concordance. Lin's concordance correlation (CCC) value of 0.101 reflects both the precision captured by Pearson's correlation coefficient

(r=0.132) and accuracy denoted by a measurement of how far the best fit line deviates from the 45^{o} line through the origin (bias concordance C_b=0.763)[CCC=rC_b]. Results from comparison of NICOM to TD are noted in figure 2B. Lin's concordance between NICOM and TD was 0.133 (with Pearson correlation coefficient of 0.275 and concordance bias correction of 0.4835). The precision of NICOM to TD and indirect FICK is low, with accuracy only slightly better. Overall, the concordance between methods is poor.

Linear regression analysis showed reliability of NICOM when compared to indirect Fick or TD is higher in women and among patients with lower BMI.

Discussion

This is the largest study to date evaluating the accuracy of NICOM technology among patients in CS. The key finding of our study was that NICOM correlates poorly with both indirect Fick and TD measurements of CO in patients with CS. This correlation does not improve with normalization of cardiac index (CI >2.2 L/min/m^2) or with achievement of euvolemic status (CVP <5 mmHg or PASP <25 mmHg).

There are several potential reasons why the NICOM measurements of CO would not correlate with indirect Fick or TD measurements in our study cohort. The bioreactance technology is reliant on diffusion of oscillating electrical current through the thoracic cavity and hence is likely to be affected by pulmonary and interstitial edema routinely seen with patients in CS. Similarly, elevated right and left sided preload in CS patients is also likely to affect intrathoracic impendence and hence alter current phase shifts used to estimate stroke volume and subsequently CO. Alterations in lymphatic flow in patients with long standing heart failure may also contribute to NICOM estimation measurements. Finally, the low flow state in CS may also contribute to the erroneous assessment of CO by bioreactance technique. Whatever may be the exact mechanism of error, our study results make a strong argument against the use of NICOM technology in estimating CO in patients with CS and using NICOM measurements to diagnose CS.

Based on our study findings, NICOM technology continues to remain an unreliable measure of CO in patients with advanced heart failure even after normalization of cardiac index and achievement of euvolemic status. This is an important clinical finding as it limits the transition to non-invasive hemodynamic monitoring after initial stabilization with invasive hemodynamics guided therapy in our study population.

Evaluating the temporal evolution of NICOM measurements of CO in response to medical therapy among our study population was beyond the scope of our initial study hypothesis. However, this remains an area of further investigation in addition to development of a mathematical model that could allow for better correlation between invasive and non-invasive hemodynamic measurements.

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Disclosures

All authors have no disclosures.

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Table 1: Baseline characteristics and comorbidities.

Characteristic	Summary Statistic
Gender (Men/Women)	36 (72.0%)/ 14(28%)
Age	59±14 (25 to 87)
BMI	28.7±5.70 (20.3 to 41.3)
Cardiac Output by FICK	4.40±1.32 (1.83 to 7.68)
Cardiac Index by FICK	2.16±0.53 (1.15 to 3.31)
Mix Venous Saturation by FICK	56.01±9.906 (39.4 to 80.6)
Cardiac Output by TD	4.09±1.094 (1.86 to 6.85)
Cardiac Index by TD	2.08±0.653 (0.95 to 5.04)
Pulmonary Artery Systolic Blood Pressure	48.5±11.9 (20 to 73)
Central Venous Pressure	10.9±6.2 (1 to 28)
Hypertension (No/Yes)	15 (30%)/ 35(70%)
Diabetes Mellitus (Type II) (No/Yes)	29 (58%)/ 21 (42%)
Dyslipidemia (No/Yes)	20 (40%)/ 30 (60%)
Chronic Kidney Disease (No/Yes)	23 (46%)/ 27 (54%)
Heart Failure with Ejection Fraction <40% (No/Yes)	1 (2.0%)/ 49 (98%)
Heart Failure with Diastolic Dysfunction (No/Yes)	26 (52%)/ 24(48%)
Atrial Fibrillation (No/Yes)	25 (50%)/ 25 (50%)
Obstructive Sleep Apnea (No/Yes)	33 (66%)/ 17 (34%)
Non-Invasive Ventilatory Support at some point during the Study Period (No/Yes)	42 (84%)/ 8 (16%)

Table 2: Correlation coefficient between cardiac output measured by NICOM and indirect Fick or bolus thermodilution across three patient subsets.

	NICOM to FICK			NICOM to TD		
	R (p value)	CCC 95% CI	C_b (bias)	R (p value)	CCC 95% CI	C_b (bias)
All Observations	0.132 (p=0.033) n=263	0.101 (0.008, 0.191)	0.763	0.275 (p<0.001) n=258	0.133 (0.073,0.192)	0.484
Where CI>2.2 by FICK or TD	0.169 (p=0.026) n=173	0.159 (0.019,0.293)	0.941	0.351 (p<0.001) n=169	0.212 (0.122, 0.299)	0.604
Where PASP<25 or CVP<5	0.080 (p=0.574) n=52	0.070 (-0.172, 0.305)	0.875	0.257 (p=0.068) n=51	0.135 (-0.012,0.276)	0

Figure 1: Intraclass correlation coefficients for NICOM measurements of cardiac output across three patient subsets.

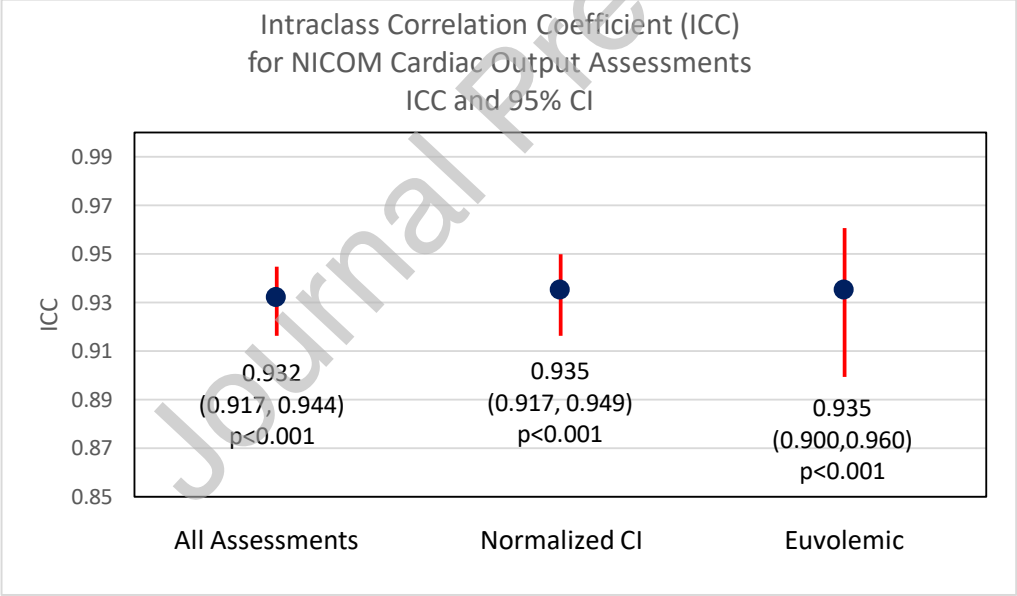
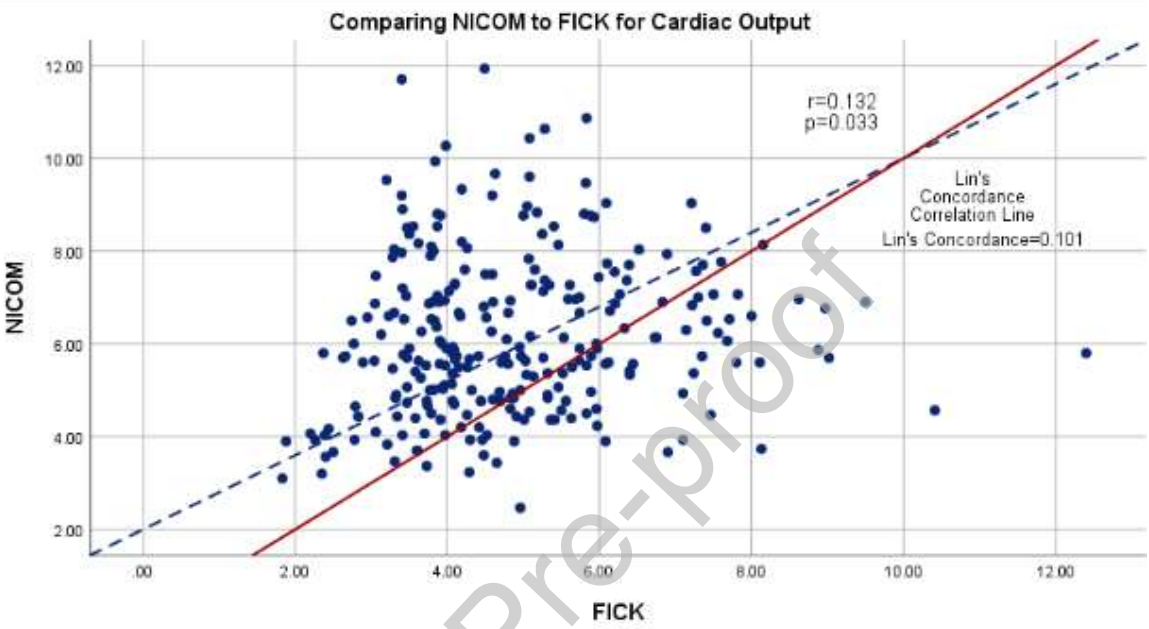


Figure 2 (A-B): Assessment of agreement between cardiac output (liters/minute) measured by NICOM and indirect Fick methods. On the Bland-Altman Plot difference is NICOM minus indirect Fick.



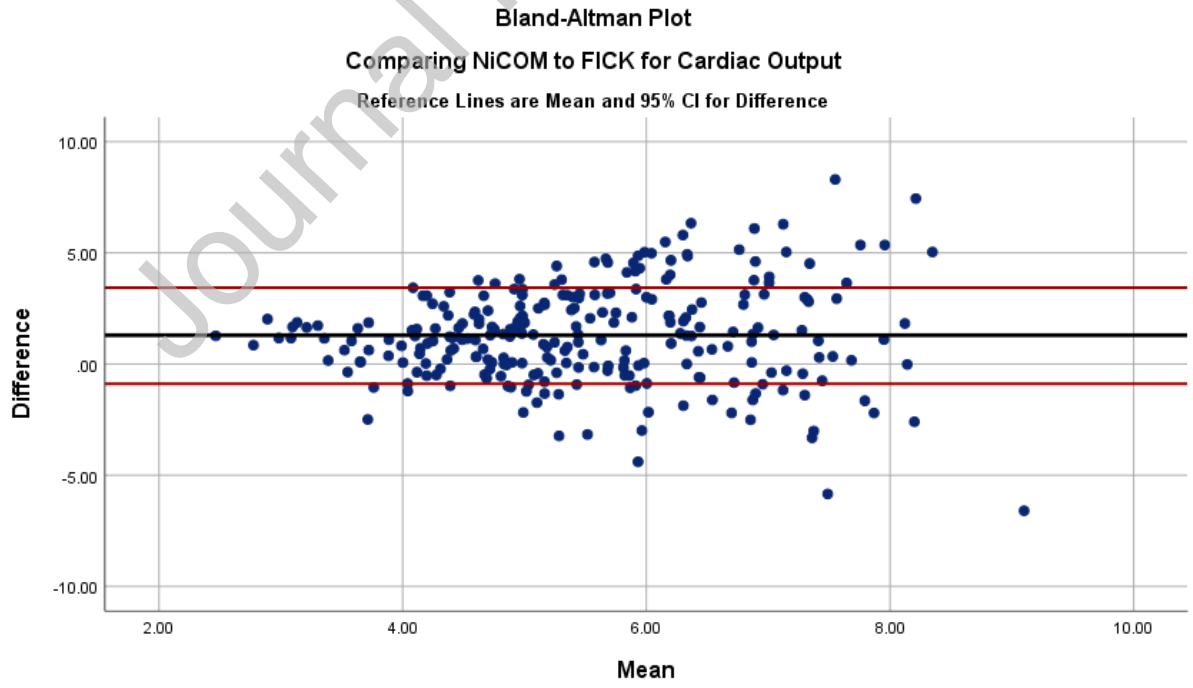


Figure 2 (C-D): Assessment of agreement between cardiac output (liters/minute) measured by NICOM and bolus thermodilution methods. On the Bland-Altman Plot difference is NICOM minus bolus thermodilution.