Original article

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Continuous non-invasive measurement of stroke volume and cardiac index in infants and children: comparison of Impedance Cardiography NICaS® *vs* CardioQ® method

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Abstract

Background. Non-invasive measurement of cardiac output (CO) and cardiac index (CI) may become an important modality of monitoring in pediatrics. Among the several methods proposed, impedance cardiography (ICG) has gained attention among the scientists. There are 2 basic technologies of ICG: thoracic body bioimpedance (TEB) and whole body electrical bioimpedance (WBEB).

Purpose. The present study is aimed to test in infants and children the effectiveness of the Non-Invasive Cardiac System (NICaS®), a new ICG device working with a wrist-to-ankle configuration *vs* CardioQ® transesophageal doppler, a minimally invasive cardiac output monitor.

Methods. Whole-body bioimpedance measurements were obtained before and during the surgery with NICaS® and simultaneously with CardioQ®, demographic data were sampled, basement life monitoring were performed.

Results. Total of 42 patients aged from new born to 16 years old, were included in this study to evaluate heart rate (HR), stroke volume (SV), cardiac output (CO), cardiac index (CI), total peripheral resistance index (TPRI), total body water (TBW) and cardiac power index (CPI). 81 measurements were taken simultaneously by both devices from forty-two patients, with CardioQ® serving as the gold-standard for this evaluation and with NICaS®. The average values of CI in the study subjects for CardioQ® cardiac index (Q-CI) and NICaS® cardiac index (NI-CI) were 2.9±0.9 L/min/m^2 and 2.8±1.0 L/min/m^2 respectively (P<0.01). Overall, 2-tailed Pearson's correlation between NI-CI and Q-CI was r = 0.85. The Bland-Altman 1.96-standard deviation limit of agreement was -0.77 L/min and 0.87 L/min/m^2 with a small bias of 0.05 L/min/m^2.

Conclusion. Good correlation was observed in pediatric patients for CI measured with NICaS® in comparison with CardioQ® device. Continuous non-invasive monitoring of NI-CI can be particularly interesting for the pediatric population. ***Clin Ter 2018; 169(3):e110-113. doi: 10.7417/CT.2018.2064***

Key words: *Cardiac output, cardiac index, stroke volume, impedance cardiography, CardioQ®, non-invasive hemodynamic measurements, NICaS®, neonatal and pediatric*

Introduction

Impedance cardiography (ICG) has been proposed as a non-invasive method of hemodynamic monitoring of adult and pediatric patients (1,18). ICG when transmitting a small electrical current through the body, an impedance to its transmission (resistance, R) is being measured. According to Kirchov's law, electrical current passes faster through conduits of higher conductance (lowest resistance), for example through blood and plasma (2). The changes in the body resistance (R) over time (milliseconds) to electrical current passage are proportional to the dynamic changes during each cardiac cycle. Consequently, each systolic increase in the aortic blood volume is associated with a proportional increase in the measurable conductance of the whole body (3). Thus, for measuring the aortic SV by means of its impedance change, Frinerman and Tsoglin developed the following algorithm (4):

$$\mathbf{SV = Hctcorr/K\,(sex,age)\ x\ Kel\ x\ Kweight\ x\ IB\ x\ H2corr\ x\ \Delta R/R\ x\ (\alpha + \beta)/\alpha}$$

in which the ΔR/R is corrected for hematocrit (Hctcorr), electrolytes (Kel), body composition (K sex, age), weight (Kweight), time characteristics (α= systolic time, β= diastolic time), and index balance (IB), which measures the body water composition.

There are 2 basic technologies of ICG: thoracic body bioimpedance (TEB) and whole body electrical bioimpedance (WBEB). The idea of the WBEB was conceived and tested in the Soviet Union in 1941 (5), it remained dormant until recently. Meanwhile another bioimpedance approach, TEB, for measuring the CO was initially introduced by Kubicek et al (6), and further refined in 1974 (7). In WBEB, one electrode is applied to the wrist and the other to the ankle; in TEB, two electrodes are placed at the root of the neck on the bought side and another pair around the lower part of the chest cage. Both technologies allowed a reliable, simple and quick method to perform continuous monitoring of pa-

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tient's hemodynamic through calculation of cardiac index (CI), stroke volume (SV), total peripheral resistance index (TPRI) and other parameters.

In the present study, we evaluated the accuracy of a novel method of CI measurement (whole-body electrical bioimpedance, WBEB) by NICaS® in different pediatric cardiac clinical settings (during pediatric cardiac, orthopedic, urologic or general pediatric surgery or for monitoring pediatric patients in ICU) in comparison with CardioQ®, approved non-invasive cardiac device for CI and CO measurements.

Materials and Methods

This single-center study was performed in the neonatal and Pediatric General Anesthesia and Pediatric Intensive Care, Pediatric Hospital "Giovanni XXIII", Bari, Italy. After the local ethics committee approval and the written informed consent, a total of 42 patients undergoing cardiac, urologic, orthopedic and general pediatric surgery, ages between new born and 16 years old, under general anesthesia were included in the study. Patient with one cardiac camera or other type of cardiac shunts were excluded. In the operation room or in PICU, HR (bpm), SV (ml) and CI (L/min/m^2), CO (L/min), TPRI (din*s/cm^5*m^2), TBW (%) were measured non-invasively by NICaS® (NICaS®, NI Medical, Petach Tikva, Israel) and SVI, CO, CI and flow corrected time (FTc) were measured by CardioQ® (CardioQ®, Deltex Medical,Terminus Rd, Chichester PO19 8TX, United Kingdom), acting CardioQ® as the gold standard. Mean arterial pressure (MAP) was measured by oschillometric method (Philips Medical Systems 3000; Minuteman Road Andover, MA, Nederland), arterial pulse oxygen saturation (SpO2) and five-lead ECG were applied as perioperative routine monitoring (Philips Intelli VueThe ICG™ Monitoring; Philips Medical Systems, Andover, MA, USA). To collect patient signals, the NICaS® electrodes were arranged in a wrist-to-ankle configuration, but in certain conditions was used a wrist-to-wrist configuration and the bioimpedance and its fluctuations over time was measured at T0 (before surgery) and from T1-T60 (from begun of anesthesia and during 60 minutes of surgery). The other variables required for SV and CI calculation (age, gender, weight, height, hematocrit, electrolytes) were introduced into the machine at the start of monitoring. Intravenous crystalloid (10 ml/kg) was administered during surgery. General anesthesia was performed following the protocols of department and all the patients were mechanically ventilated. Total of 81 measurements were taken simultaneously by both devices with NICaS® and with CardioQ® serving as the gold-standard for the evaluation. Stroke index (SI) and Cardiac index (CI) were then calculated by dividing these parameters by body surface area (BSA) which was calculated by the Du Boise formula (7). CI was chosen to be the leading parameter for the correlation between both devices.

Statistical Analysis

The normality of distribution of average CI of both devices were assessed by Shapiro-Wilkinson test. The average CO between both CardioQ® and NICaS® was not found to be normally distributed, but average CI was found to be normally distributed. As a result, CI was chosen to be the leading parameter for the comparison between both devices. To compare means, we used the Paired Student t test. Correlation between NICaS® and Cardio Q® was evaluated by calculating the Pearson correlation coefficient. Agreement between NICaS® and CardioQ® was evaluated by linear regression model. The differences between the paired values of the NICaS® and CardioQ® were plotted against the average values of both methods. This statistical method was recommended by Bland and Altman (8) for evaluating a new device (NICaS®) against an established method (Cardio Q®). Bias was defined as the mean difference between the NICaS® and CardioQ® values. Limits of agreement (precision) were calculated as bias ±1.96 X standard deviation (SD) of the differences between the NICaS® and CardioQ® values. Statistical analysis was performed by Statistical Package for the Social Sciences (SPSS Inc., Chicago, IL) v 15.0 for Windows.

Results

Total eighty-one (81) CI measurements were obtained from forty-two (42) patients who participated in the study. Patient's age from newborn to 16 years with median of 14.9 month and 83 % were boys. Complete demographic and base line data are shown in Table 1.

The average values of CI in the study subjects for CardioQ-CI and NICaS-CI were 2.9±0.9 L/min/m^2 and 2.8±1.0 L/min/m^2 respectively (P<0.01). The overall results of the Pearson correlation analysis were r = 0.85. The Bland-Altman 1.96-standard deviation limit of agreement was -0.77 L/min and 0.87 L/min/m^2 with a small bias of 0.05 L/min/m^2. No significant differences between the means of NI-CI and Q-CI, HR and SI between two devices were observed (Table 2).

Linear regression between the predictor CardioQ CI and estimator (dependent variable) NICaS CI where CI. Black circles represent observations (N=81). The line represents the regression line (NICaS CI = CardioQ CI x 1.06) (Fig. 1).

Table 1. Patients' Demographics.

Parameter	*Min, Median. Max*
No. of patients	*42*
No. of correlations	*81*
Male	*35 (83%)*
Age [y]	*Newborn, 14.9m, 16y*
Weight [kg]	*2.4, 10.0, 59.0*
Height [cm]	*47, 77, 170*

Data are expressed as minimum, Median, maximum or number

Table 2. Statistical analysis of CI measured by NICaS® Vs CardioQ®

Parameter	Cardio Q	NICaS
HR	130±28	130±28
SI	23.2±9.2	23.1±10.4
CI	2.9±0.9	2.8±1.0
Pearson 2 tailed correlation, r	0.85	
P value	< 0.01	
Bias	0.05 L/min/m^2	
SD	0.42 L/min/m^2	
Lower level of agreement	-0.77 L/min/m^2	
Upper level of agrrement	0.87 L/min/m^2	

HR = heart rate (bpm), SI = Stroke volume index (ml/m2), CI = cardiac index (L/min/m2), SD = standard deviation
Data are expressed as mean ± standard deviation or number

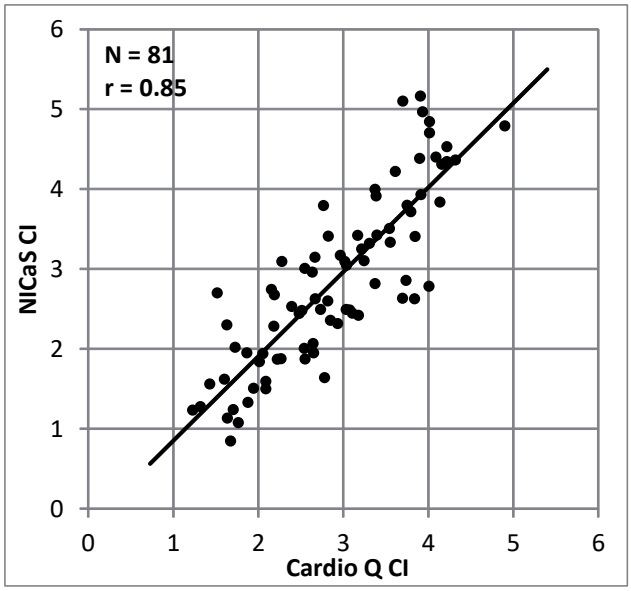

Fig. 1. Linear regression between the predictor CardioQ CI and estimator (dependent variable) NICaS CI where CI=Cardiac index. Black circles represent observations (N=81). The line represents the regression line (NICaS CI = CardioQ CI x 1.06).

We made Bland-Altman scatter plot of difference against average of CI results measured by NICaS® and CardioQ methods, because we measure the same parametar with two different device, the new measurment technique NICaS® vs gold standard method CardioQ®. Solid line represents the mean difference between CardioQ CI and NICaS CI (Bias) which was 0.05 L/min/m^2. The dotted lines represent the limit of agreement which was -0.77 and 0.87 L/min/m^2 and were derived from 1.96 X SD. The differences were not clinically important between two device (Fig. 2).

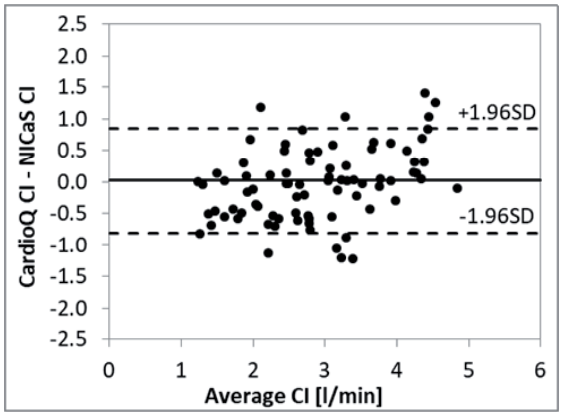

Fig. 2 Bland-Altman scatter plot of difference against average of CI results measured by NICaS® and CardioQ methods. Solid line represents the mean difference between CardioQ CI and NICaS CI (Bias) which was 0.05 L/min/m^2. The dotted lines represent the limit of agreement which was -0.77 and 0.87 L/min/m^2 and were derived from 1.96 X SD.

Discussion

The main result of our study was the existence for excellent correlation between two confronted devices and the two methods may be used interchangeably. In addition, biompedance is simple, continuous, non-invasive method applicable in each situation, as in the pediatrics also in the adult patients (19).

In recent years it has been suggested that CO and SV measurement and the calculation of CP and TPRI might be instrumental in the diagnosis, treatment and risk stratification of pediatric cardiac patients, but only a few methods are available.

In this study we measured CO and CI for neonatal and pediatrics of large rang of ages (from new born to 16 years). As CO significantly varies with age, we selected to use CI (normalized CO by body surface area) as the leading parameter for the comparison; we used the Shapiro-Wilkinson test to confirm normality distribution of the average CI of both devices.

In many studies CO has been measured only during invasive right heart catheterization, which requires intensive care admission and may be associated with complications (10-12). Hence, CO was measured only rarely, and in the sickest pediatric patients. Therefore, a simple, reliable, noninvasive, and continuous method for CO measurement has become necessary in order to enable its application to pediatric cardiac patients with different degrees of medical severity and in diverse settings. We chose CI to be the leading parameter for the comparison between both devices, because CI was more suitable during physical development and it represents better cardiac function during the body growth of pediatric populations.

Currently there are only few accepted methods for noninvasive CO measurement such as Doppler echocardiogram and CO2 rebreathing techniques, but these methods are limited by the requirement for expensive equipment and specialized personnel. Thoracic bioimpedance has been used in the last decade for continuous CO measurement. TEB can be useful for monitoring the hemodynamic state in various clinical conditions such as trauma, massive surgery, sepsis, but when it comes to monitoring and managing pathologic cardiac conditions TEB requires further improvement (13-15).

Kedrov, (5) who was the first, compared the average CI measured by the WBEB in 57 subjects with normal hearts in published results of the Fick method, revealing 3.3 ± 28% vs 3.31 L/min/m^2 (range, 2.4 to 4.2 L/min/m^2), respectively. Tischenko (16) compared the CI results measured by WBEB in three groups of subjects with normal hearts vs three standard methods. There were 31 cases vs acetylene (r = 0.84), 28 cases vs thermodilution (r = 0.95), and 28 cases vs Fick (r = 0.99). Using a modified Tischenko algorithm vs thermodilution, Koobi et al (17) obtained simultaneous measurements in 74 patients with coronary disease, reaching a bias between the two methods of 0.25 ± 0.8 L/min (SD), where the limits of agreement (2 SD) were – 1.37 L/min and 1.897 L/min, respectively. Using the NICaS® apparatus, Cohen et al (4) study 274 subjects, compared its performance against thermodilution by measuring the CO in patients undergoing CABG operations, with a correlation of r = 0.91. Moreover, in none of these publications the authors have expressed reservations on the functioning of the WBEB. Oh, et al (18) in his recent study of pediatric patients, hypothesized that the percent change in resistance (%ΔR) from bioimpedance analysis (BIA) measurements during hemodialysis (HD) can provide information on pediatric HD patients' hydration status, the percent change in body water (%ΔBW) and showed that %ΔR was strongly correlated with %ΔBW.

In the present study, the agreement between NICaS CI and CardioQ CI was tested by comparisons of the means were highly significant. Following the recommendations of Bland and Altman (9), the differences between the two measurements were plotted against their means. This plot demonstrates that the range of differences were similar along the different values of the average.

It is important to underline that the obtained results could have the limits connected to the context of the study. This study is limited by relative small cohort size and our data represented a single center trial. Despite these limitations, this is first pediatric study to show strong correlation between NICaS® non-invasive method and CardioQ® approved minimally invasive method.

Although the main purpose of this work was to compare the performance of the NICaS® vs CardioQ® in pediatric population, although CardioQ® tends to underestimate CI for 30 %. The results of this analysis have shown that the CardioQ CI measurements were slightly lower than the NICaS CI, but no significant differences between the means of NICaS CI and CardioQ CI were observed. Furthermore, large clinical trials are needed to confirm our findings.

In conclusion, the NICaS® device offers a simple, noninvasive, reliable, and continuous measurement of CI in cardiac and non-cardiac pediatric patients. This measurement combined with MAP measurement and the calculation of TPRI and SVRI is destined to become a safe, simple, rapid, noninvasive method for evaluating and treating cardiac and non-cardiac pediatric patients.

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