International Journal of Environmental Sciences
ISSN: 2229-7359
Vol. 11 No. 21s, 2025
https://theaspd.com/index.php

Using Electrical Cardiometry For Noninvasive Hemodynamic Monitoring In Patients Managed With Extracorporeal Membrane Oxygenation.

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ABSTRACT
Background: *An early correction of shock state and tissue hypoperfusion at a proper time is important before the occurrence of irreversible shock.*
An extracorporeal membrane oxygenation (ECMO) patient requires strict hemodynamics follow up.
Objective: *This study was conducted to evaluate electrical cardiometry (ICON™) in stroke volume (SV), cardiac output (CO) and cardiac contractility measurement using transthoracic echocardiography in ECMO patients*
Patients and methods: The study is a prospective cross-sectional study on ten adult patients eligible to ECMO (both venoarterial V-A and venovenous V-V ECMO). ICON™ was utilized to assess hemodynamics. SV, CO and index of contractility (ICON parameter reflecting contractility) were estimated using electrical cardiometry and compared to transthoracic echocardiography.
- CO was estimated using electrical cardiometry (ICON OSYPKA medical, Germany) using bioimbedance technology through 4 electrodes connected to the left side of the body with good signal quality for accuracy of measurements {signal quality indicator (SQI) ranging from 70 to 100}
- Echocardiography measurements were taken using Pulsed Wave (PW) doppler over left ventricular outflow track (LVOT) (2-3 cm away from aortic valve in apical three or five chamber views) to calculated LVOT Velocity Time Integral (LVOT VTI).
- Stroke Volume (SV) = LVOT VTI × Cross sectional area (CSA) of LVOT (calculated from parasternal long axis 0.5 cm from aortic valve).
- CO = SV × Heart Rate (HR)
- EF was calculated by echocardiography using M-mode
- The two measurements were taken at the same time in 10 patients treated with ECMO (6 patients were connected on VV ECMO (675 paired values) and remaining 4 patients on VA ECMO (343 paired values)
- In VV ECMO patients, CO calculated by echocardiography and estimated by ICON equal native CO
- While CO estimated by ICON in VA ECMO patients equals native CO measured by echocardiography and ECMO flow.
Results: *There was statistically significance correlation between SV and CO estimated with ICON™ compared to echocardiography in patients connected to VV ECMO and CO estimated using ICON™ and total cardiac output in patients connected to VA ECMO.*
In both groups there was statistically significance correlation between cardiac contractility estimated by ICON™ and EF calculated by echocardiography.
Conclusion: *ICON™ can be used to monitor SV, CO and cardiac contractility in patients connected to ECMO.*
Keywords: *Extracorporeal Membrane Oxygenation, Stroke volume cardiac output, Electrical Cardiometry*
Abbreviations: *ECMO, SV, CO, LVOT VTI, VA ECMO, VV ECMO*

1. INTRODUCTION

Hemodynamic monitoring is essential for maintaining tissue perfusion and prevention of irreversible shock in critically ill patients. Intensive care practice is characterized by a very close relationship between monitoring, decision-making and treatment. Appropriate and early application of diagnostic information from hemodynamic monitoring has been shown to reduce mortality in critically ill patients[1].
ECM'O refers to a circuit that directly oxygenates and removes carbon dioxide from blood through an

extracorporeal gas exchange device, commonly referred to as a membrane oxygenator. According to ECMO configuration ECMO can support either the respiratory or cardiac functions[2].
When the drainage and reinfusion cannulas are both placed in central veins, the circuit is referred to as VV ECM'O, and the device achieves gas exchange support only (3) but when blood is drained from a vein and re-infused into an artery, it is referred to as VA ECM'O, and the device provides both gas exchange and Cardiac support (4).
ECM'O flows should be monitored for changes. Decrease in flow may be caused by decreased preload or excessive afterload. Decreases in preload may be secondary to hypovolemia or bleeding. The negative pressure generated by the pump in the hypovolemic state can cause hemolysis leading to rise in plasma free hemoglobin (significant if > 50mg/dL) and increase in lactate dehydrogenase [5].

PATIENTS AND METHODS:

The study is a prospective cross-sectional study on ten adult patients who were admitted to critical care department, Cairo University over a period of twenty months starting from June 2020 to February 2022and were eligible to ECMO (both VA and VV ECMO).

Inclusion criteria:

Adults more than 18 years
Genders eligible for study: both.

Exclusion criteria

Numerous factors may interfere with the accuracy of Electrical bioimpedance measurements as:
Inability to attach neck or chest leads (e.g., Surgical dressing)
Extensive chest wall edema
Dilatation of the aorta; severe mitral regurgitation; severe aortic regurgitation.
Electrical bioimpedance measurement may also be inaccurate if the patient is moving, agitated, restless, shivering, or hyperventilating.

Methods

Hemodynamic monitoring using Electrical cardiometry was done using ICON™ device from OSYPKA medical
ICON™ is connected to the patients though four electrodes on the left side of the body
A: Over the forehead.
B: Root of the neck over the neck veins.
C: Opposite to the level of the Xiphoid process.
D: over the thigh.
Every 48 hours measures were taken
Stroke volume and cardiac output
Index of contractility (ICON parameter) which reflects cardiac contractility
Signal quality indicator (SQI): which determined the quality of the signal received by the device and SQI ranged from 70 to 100 to ensure the accuracy of ICON™ data

Echocardiography

CO measurements were done using digital ultrasonic imaging system TOSHIBA Cardiac probe 2.5-5 MHZ

CO = SV X HR
SV = LVOT VTI X LVOT area

Measure the left ventricular outflow tract (LVOT) diameter (Parasternal long axis, 2D). Zoom in to be accurate. Measure up to 0.5cm back from the aortic valve leaflet insertion points.
LVOT is assumed to be roughly circular. Measuring the diameter, the area can be calculated
Using pulse wave Doppler (PW) at LVOT (2cm away from the aortic valve) in the apical views, either the apical 5 chamber or the apical 3 chamber. Then using device calculations to obtain LVOT VTI
Cardiac contractility was assessed by echocardiography (ejection fraction)

Patients connected to ECMO

VV ECMO through femoral to jugular veins

VA ECMO through femoral vein to femoral artery.
IN VA ECMO patients Total Cardiac output equals native Cardiac output and ECMO FLOW

Statistical methods:

Data were coded and entered using the statistical package for the Social Sciences (SPSS) version 28 (IBM Corp., Armonk, NY, USA). Data was summarized using mean and standard deviation for quantitative variables and frequencies (number of cases) and relative frequencies (percentages) for categorical variables. Comparisons between groups were done using unpaired t test. Comparison between paired values measured by the 2 methods was done using paired t test. Correlations between quantitative variables were done using Pearson correlation coefficient. Testing for inter-rater and intra-rater reliability was done using the Intra Class Coefficient (ICC) and Cronbach's alpha reliability coefficient with their 95% confidence interval (95%CI). P-values less than 0.05 were considered as statistically significant.

RESULTS:

Our study included 10 patients, who were supported by ECMO, six patients were connected to VV ECMO (675 paired values) and four patients were connected to VA ECMO (343 paired values)
In VV ECMO group patient was connected due to H1N1 viral pneumonia (16 %) and 5 (84%) patients due to COVID.19 viral pneumonia while in VA ECMO 3 (75%) patients were connected due to high-risk percutaneous coronary intervention (PCI) and one (25%) patient due to post COVID.19 cardiomyopathy

Descriptive data

The age of the studied patients in VA ECMO group ranged from 40 to 65 years with a mean of 51 years. While in VV ECMO group, the age of the studied patients ranged from 30 to 55 years with a mean of 39 years. Seven (70%) of the studied patients were males and three (30%) were females as in table 1.

Table (1): Descriptive data

	Mean	SD	Minimum	Maximum
Age of VV group	39.17	9.17	30.00	55.00
Age of VA group	51.00	10.98	40.00	65.00
SQI in VV group	89.52	11.86	70.00	100.00
SQI in VA group	90.39	14.15	70.00	100.00
HR in VV ECMO group	99.15	14.89	79.00	130.00
HR in VA ECMO group	109.64	24.50	68.00	138.00
SV by ICON™ in VV group	91.11	20.84	50.00	128.90
SV by ICON™ in VA group	53.14	20.48	26.91	90.00
CO by ICON™ in VV group	8.97	2.10	4.80	12.70
CO by ICON™ in VA group	5.35	1.13	3.61	8.46
ICON in VV ECMO group	50.36	17.95	34.00	96.00
ICON in VA ECMO group	26.89	10.14	13.30	44.10
LVOT VTI for VV ECMO group	18.88	2.86	11.80	28.40
LVOT VTI for VA ECMO group	7.59	5.88	1.60	19.20
SV by Echo in VV ECMO group	86.39	17.67	50.00	122.46
SV by Echo in VA ECMO group	31.11	23.75	6.60	73.00
CO by echo in VV ECMO group	8.42	1.84	4.60	12.40
Total CO in VA ECMO group	5.20	0.72	4.01	7.25
ECMO Flow VV group	4.54	0.50	3.00	5.30
ECMO Flow VA group	2.34	1.04	1.00	3.70

VV ECMO patients:

SV measured by ICON ranged from 50 to 128.9 ml with mean 91.1 ml ± 20.8 while SV measured by echocardiography ranged from 50 to 122.4 ml with mean 86.3 ml ± 17.6

There was statistically significance correlation between two group measurements (p value = <0.001)

Table (2): SV estimated by ICON™ VS measured by echocardiography in VV ECMO group

	Mean	SD	Minimum	Maximum	P value
SV estimated by ICON™	91.11	20.84	50.00	128.90	< 0.001
SV by Echocardiography	86.39	17.67	50.00	122.46	

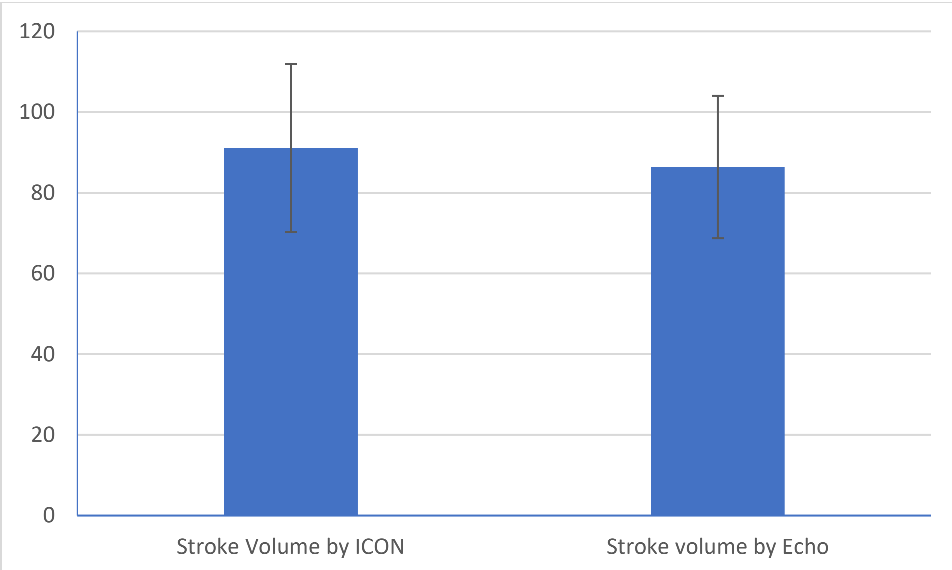

Figure (1): SV estimated by ICON™ VS measured by echocardiography in VV ECMO group.

And the agreement in SV measurements between the two group was statistically significant (p value <0.001) as in table (3 and 4)

Table (1): Correlation between SV measured by echocardiography and estimated by ICON™ in VV ECMO group.

		SV by Echocardiography
SV estimated by ICON™	r	0.883
	P value	< 0.001
	N	668

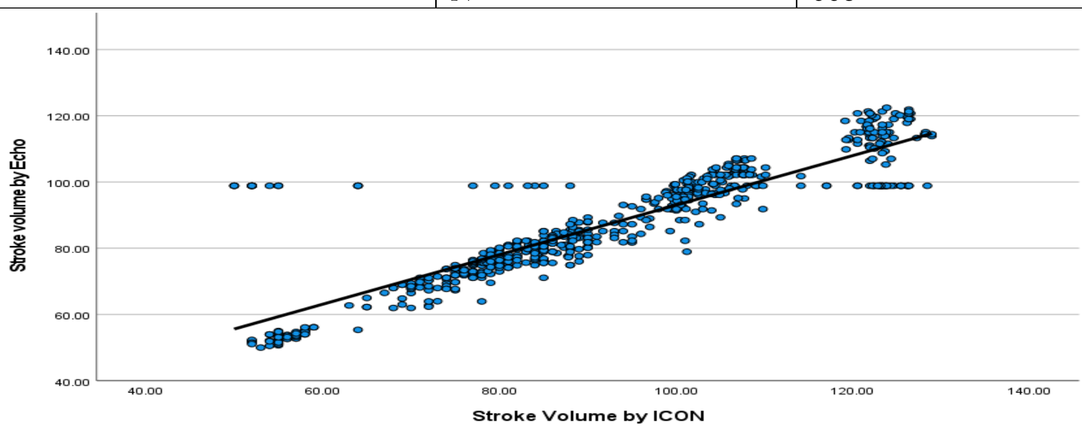

Figure (2): Agreement in SV measurements between Echocardiography and ICON™ in VV ECMO group.

Table (4): Agreement in SV measurements between Echocardiography and ICON™ in VV ECMO group

	Value	95% Confidence Interval		P value
		Lower Bound	Upper Bound	
Intraclass Correlation coefficient	0.871	0.852	0.888	< 0.001
Cronbach's Alpha	0.931	0.920	0.941	< 0.001

Comparing cardiac output (CO) measurements by echocardiography to ICON™ measurements:
VV ECCMO group

CO estimated by ICON™ ranged from 4.8 to 12.7 L/minute with mean 8.97 L/minute ± 2.1 while COP measured by echocardiography ranged from 4.6 to 12.4 L/minute with mean 8.42 L/minute ± 1.84

There was statistically significance correlation between two group measurements (p value = <0.001) as in table (5) and figure (3)

Table (5): CO estimated by ICON™ VS measured by echocardiography in VV ECMO group

	Mean	SD	Minimum	Maximum	P value
CO by ICON™	8.97	2.10	4.80	12.70	< 0.001
CO by echocardiography	8.42	1.84	4.60	12.40	

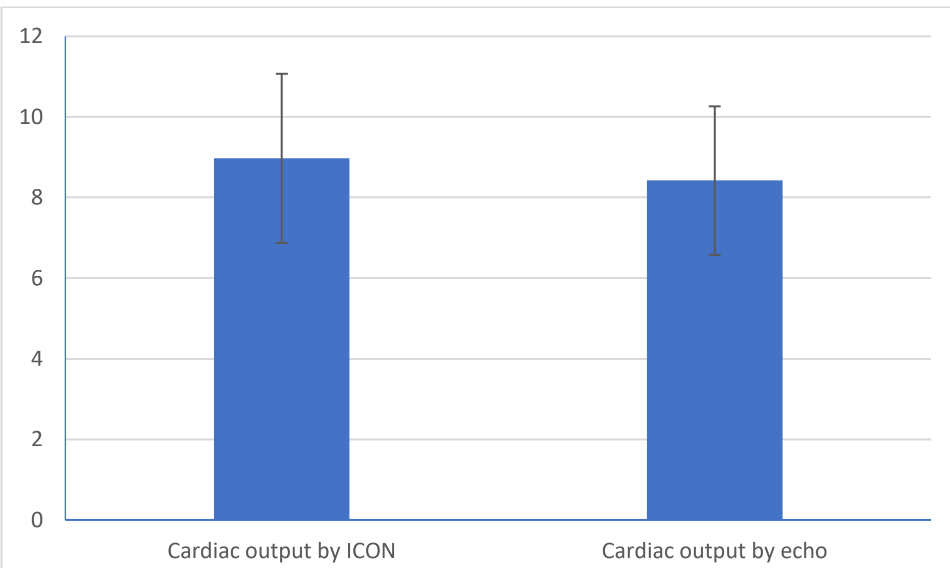

Figure (3): CO estimated by ICON™ VS measured by echocardiography in VV ECMO group

And the agreement between the two group SV measurements using Intraclass Correlation coefficient and Cronbach's Alpha was statistically significant (p value <0.001) as in table (6) and figure (4)

Table (6): Agreement in CO measurements between Echocardiography and ICON™ in VV ECMO group

	Value	95% Confidence Interval		P value
		Lower Bound	Upper Bound	
Intraclass Correlation coefficient	0.907	0.893	0.920	< 0.001
Cronbach's Alpha	0.951	0.943	0.958	< 0.001

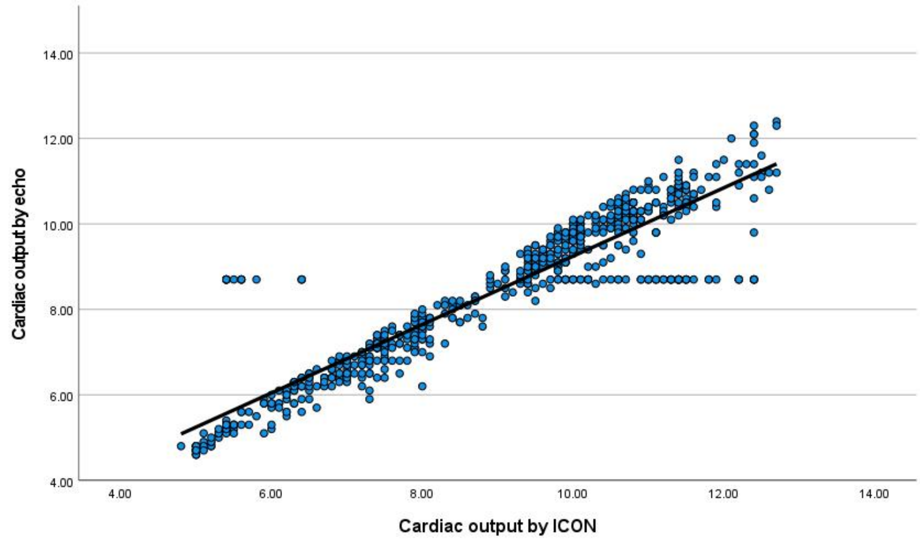

Figure (4): Agreement in CO measurements between Echocardiography and ICON™ in VV ECMO group

In VA ECMO group

CO estimated by ICON™ ranged from 4.3.61 to 8.46 L/minute with mean 8.535 L/minute ± 1.13 while total COP (native COP measured from echocardiography and ECMO flow) ranged from 4.01 to 7.25 L/minute with mean 5.2 L/minute ± 0.72. as in table (7) and figure (5)

Table (7): CO estimated by ICON™ VS total CO in VA ECMO group

	Mean	SD	Minimum	Maximum	P value
CO by ICON™	5.35	1.13	3.61	8.46	<0.001
Total cardiac output	5.20	0.72	4.01	7.25	

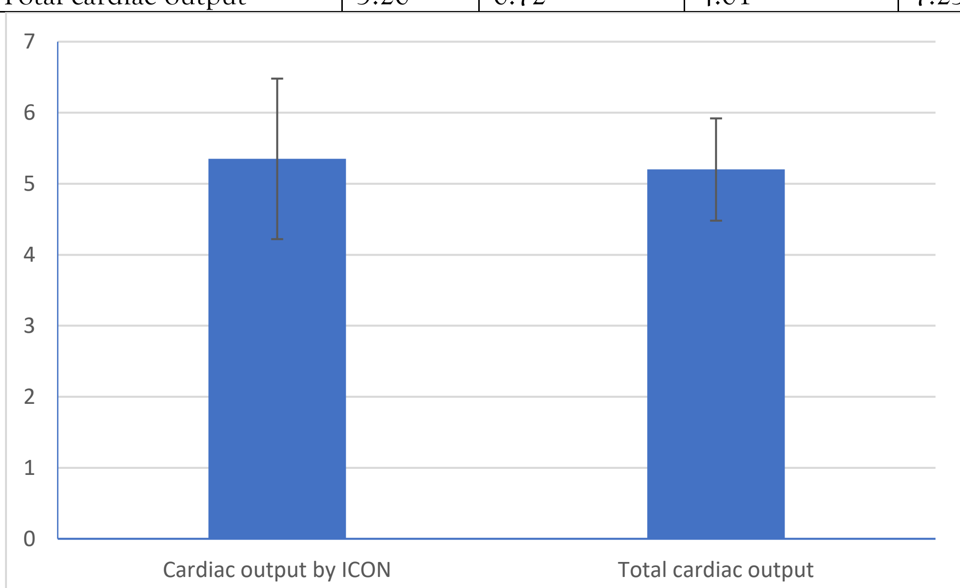

Figure (5): CO estimated by ICON™ VS total CO in VA ECMO group

There was statistically significant correlation between the Cardiac output estimated by ICON™ and total Cardiac output in VA ECMO patients (P value <0.001) as in table (8) and figure (6)

Table (8): Correlation between CO estimated by ICON™ and total CO in VA ECMO group

		Total Cardiac output
Cardiac output by ICON™	r	0.808
	P value	< 0.001
	N	337

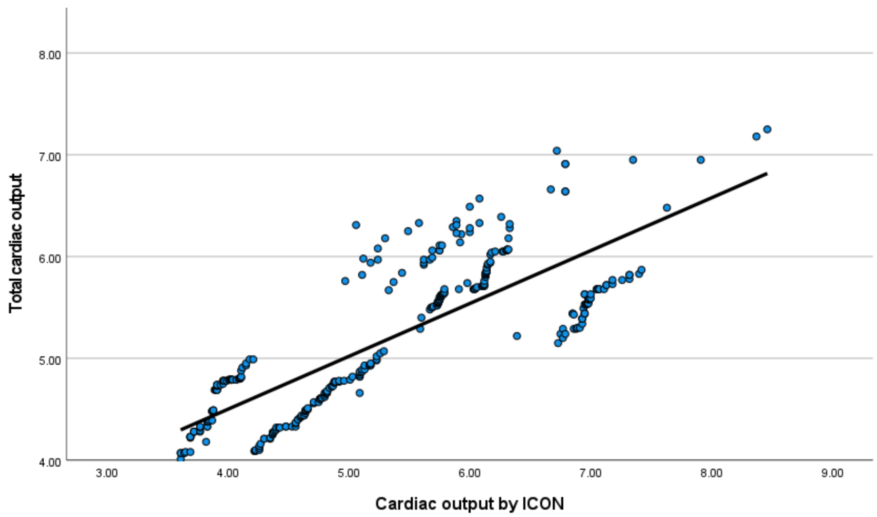

Figure (1): Agreement in CO estimated by ICON™ and total CO in VA ECMO group

The agreement between the two measurements using Intraclass Correlation coefficient and Cronbach's Alpha was statistically significant (P value = < 0.001) as in table (9).

Table (9): Agreement between CO estimated by ICON™ and total CO in VA ECMO group

	Value	95% Confidence Interval		P value
		Lower Bound	Upper Bound	
Intraclass Correlation coefficient	0.735	0.682	0.781	< 0.001
Cronbach's Alpha	0.847	0.811	0.877	< 0.001

Assess the accuracy of the ICON™ in prediction of Cardiac contractility (Index of contractility ICON)

VV ECMO group

ICON™ values of Cardiac contractility ranged from 34 to 96 and mean was 50.36 ± 17.95 while ejection fraction measured by echocardiography ranged from 60 to 65 % and mean was 62 % ± 0.2

All VV ECMO patients has normal EF and mean was 62 % ± 0.2 and ICON™ readings were within normal range so statistically there was no available correlation. as in table (10).

Table (10): ICON values of Cardiac contractility VS EF measured by echocardiography in VV ECMO group

	Mean	SD	Minimum	Maximum
ICON	50.36	17.95	34.0	96.0
EF by Echocardiography	62.0	0.2	60.0	65.00

VA ECMO group

ICON™ values of Cardiac contractility ranged from 13.3 to 44.1 and mean was 26.8 ± 10.1 while ejection fraction measured by echocardiography ranged from 15 to 32 % and mean was 22 % ± 6,

There was statistically significance correlation between the two measurements (P value <0.001) as in tables (11,12) and figures (7, 8)

Table (11): ICON values of cardiac contractility VS EF measured by echocardiography VA ECMO group

	Mean	SD	Minimum	Maximum	P value
ICON	26.89	10.14	13.30	44.10	<0.001
EF by Echocardiography	21.92	6.80	15.00	32.00	

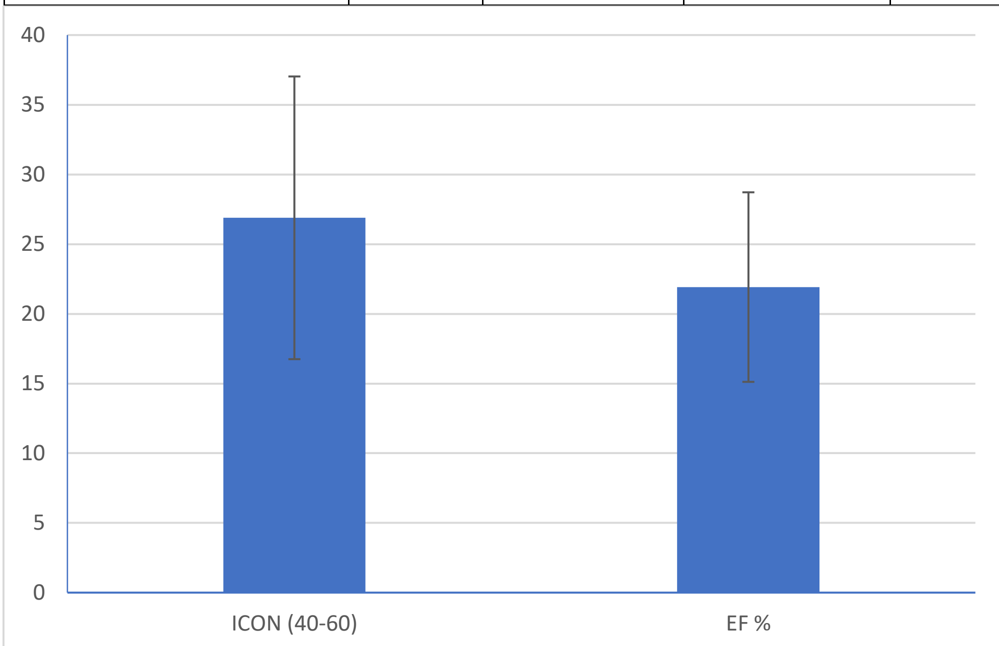

Figure (7): ICON values of Cardiac contractility VS EF measured by echocardiography

Table (12): Correlation between ICON values of cardiac contractility VS EF measured by echocardiography

		EF % by Echocardiography
ICON	r	0.876
	P value	< 0.001
	N	337

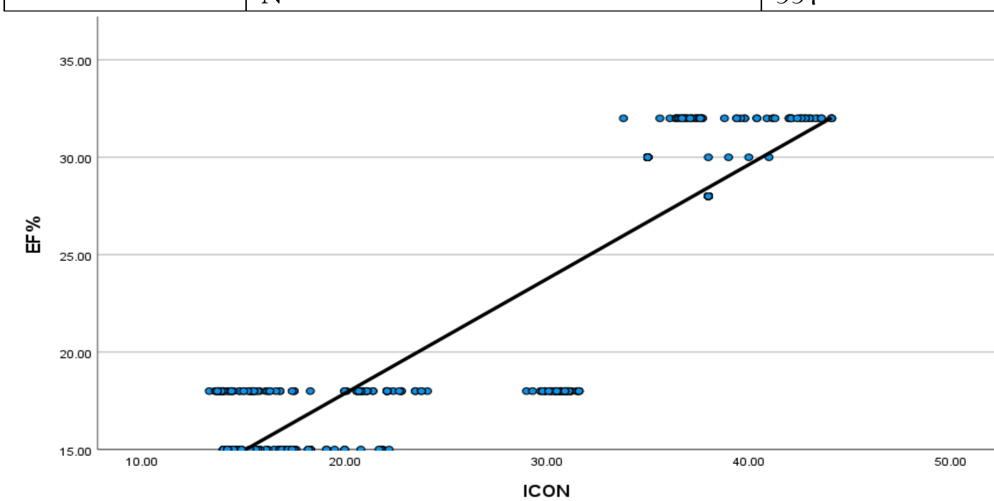

Figure (8): Agreement between Index of contractility (ICON) and EF calculated by Echocardiography
Also, the degree of agreement between Index of contractility (ICON) estimated by EC and EF was statistically significant (p value < 0.001) as in table (12).

Table (12): Agreement between Index of contractility (ICON) and EF calculated by Echocardiography

	Value	95% Confidence Interval		P value
		Lower Bound	Upper Bound	
Intraclass Correlation coefficient	0.810	0.770	0.844	< 0.001
Cronbach's Alpha	0.895	0.870	0.915	< 0.001

DISCUSSION:

Hemodynamic monitoring is essential for assessment of tissue perfusion. Timely and adequate correction of instability and tissue hypoperfusion is essential in critically ill patients especially patient on ECMO support.

ECMO provides support for patients with respiratory failure and cardiogenic shock

Previous methods for hemodynamic monitoring such as transpulmonary thermodilution (TPTD) e.g., pulmonary artery catheter which was the gold standard for hemodynamic assessment has a lot of limitations in patient with extracorporeal circuit due to heat loss leading to inaccurate measures, However there was a case report conducted by Tobias Lahmer et al reported that TPTD and pulse contour analysis can be used in patients connected to ECMO and/or renal replacement therapy (RRT) with lowest impact on TPTD when blood drained from femoral vein/distal vena cava , low blood flow and TPTD indicator injection using the jugular or subclavian CVC 6] Huber W et al conducted a recent study and proved the feasibility of TPTD during RRT[7]

Our study was aiming to assess electrical cardiometry as a noninvasive mode for hemodynamics monitoring in patients supported with ECMO using transthoracic echocardiography.

There was a significant correlation between stroke volume and cardiac output estimated by ICON™ and echocardiography in patients supported by VV ECMO (p < 0.001). Intraclass Correlation coefficient and Cronbach's Alpha analysis showed a good agreement between the two measurements (P value > 0.001).

Several studies had been made to validate ICON™ in assessment of cardiac output e.g. Jitin Narula et al conducted prospective observational study on 50 awake, spontaneously breathing patients undergoing cardiac catheterization for rheumatic heart disease (percutaneous trans-mitral commissurotomy) (PTMC) where CO, SV and systemic vascular resistance were estimated using electrical cardiometry compared to pulmonary artery catheter and they found EC is equivalent to PAC in these patients [8]

To our knowledge ICON™ was not used before to measure CO in patients supported with VV ECMO but other modalities as pulse contour analysis was studied by Ottavia Bond et al using (MostCareUp, France) and echocardiography in seventeen hemodynamically stable patients treated with VV ECMO and they found significant correlations between CO estimated by pulse contour method and echocardiography (r = 0.84, p < 0.001 and r = 0.87, p < 0.001, respectively). Bland–Altman analysis showed a good agreement (bias 0.5 L/min) and a low percentage of error (25%) for the CO values estimated by the two methods and they concluded that pulse contour method is a valuable alternative to echocardiography for the assessment of CO in patients treated with V-V ECMO[9].

In patients treated with VA ECMO, measurements of total cardiac output (which equals patient`s native CO and ECMO flow) were compared to CO estimated by ICON™ and showed statistically significant correlation (p value > 0.001), intraclass Correlation coefficient and Cronbach's Alpha analysis showed a good agreement between the two measurements (P value > 0.001).

To our knowledge ICON™ was not used before to measure cardiac output in patients supported with VV ECMO, even other modalities such as pulse counter analysis and TPTD methods still not validate in VA ECMO and echocardiography remains the gold standard modality to calculate native CO through measuring VTI of LVOT.

E. Woo1 et al conduced their study on two pigs (weights of 29 kg and 31 kg) were anesthetized and mechanically ventilated. Each pig was placed on ECMO (Rotaflow, Maquet, Germany) in both VV and

VA modes. A portable 16-channel electrical impedance tomography (EIT) device was used continuously to measure SV. The accuracy of SV measurements using the noninvasive EIT method was validated by simultaneously measuring stroke volume using the invasive TPTD method without ECMO and SV signals, and relative stroke volume changes (rSV) during ECMO at three different ECMO flows of 1, 2, and 3 L/min they found that an EIT device not only noninvasive, but also continuously method for assessment of SV in ECMO connection and recommended further studies for validation EIT for continuous SV and CO monitoring for ECMO patients [10]

S.M. Feng et al showed limited ICON™ accuracy compared to transthoracic echocardiography for cardiac output measurement during cesarean delivery [11] and they reported several factors could have contributed to the observed poor correlation between the ICON™ and TTE. First, there is a correlation of intrathoracic blood volume (VITBV) with the patient's body weight[12], the presence of a fetus may lead to overestimation of the patient's body weight that leads to CO overestimation by ICON™. Second, the significant increase in fat and fluid levels in the body during pregnancy might affect transthoracic electrical conduction and the measurement of SV and CO as reported by Teefy et al. [13]. Third, the cesarean operations may affect with the ICON™ measurement; specifically as abdominal surgeries have been reported to cause a shift of >1Lmin-1m-2 in the bioimpedance readings of the CO index with the shift direction being unpredictable [14] so Pregnant ECMO patients were excluded from the study.

Parrot et al., Hur E and Kaszuba et al compared ICG with echocardiography and showed a correlation between ICG parameters and (EF) so, they concluded that ICG determined changes in cardiac function both easily and cheaply[15; 16; 17].

Evaluation of cardiac function is essential during management of patients of VA ECMO to assess clinical progression and assess the possibility of weaning of ECMO and our study showed statistically significance correlation between ICON™ values of Cardiac contractility ranged from 13.3 to 44.1 and mean was 26.8 ± 10.1 while ejection fraction measured by echocardiography ranged from 15 to 32 % and mean was 22 % ± 6, (P value <0.001) in VA ECMO patients

To our knowledge ICON™ was not used before to assess cardiac contractility in patients supported with ECMO.

Meng-Chen Liu et al used EC for intensive hemodynamic monitoring during cheiloplasty in an infant, they focused on five parameters including index of contractility (ICON), TFC, SVV, and systemic vascular resistance (SVR) and they compared parameters with pulse contour analysis and they conceded that EC can detect hemodynamic changes more instantaneously and reliably than pulse contour analysis (FloTrac system) [18]

CONCLUSION:

EC (using ICON device) was accurate noninvasive cheap tool for assessment of SV, CO and cardiac function in both VV and VA ECMO patients compared to echocardiography

DECLARATION

Conflict of interest: Authors declare that no conflict of interest.

Ethical approval and consent to participate: The study was approved by the Medical Ethics Committee of Cairo faculty of Medicine and an informed written consent from the patients' next of kin or legal guardians before conducting the study regarding participation and publication of the study.

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