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Original Article

Thoracic Fluid Content: A Novel Parameter for Prediction of Successful Weaning of Neonates on Mechanical Ventilation. A Prospective Observational Study

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Abstract

Background: In an intensive care unit, weaning patients off of artificial breathing remains one of the most important decisions. **Aim of the work:** to assess thoracic fluid content (TFC) as an innovative measure for prediction of successful weaning of neonates on mechanical ventilation. **Patient and Methods:** Forty neonates who met the inclusion criteria for this prospective observational study were divided into 3 groups; first group: 25 patients who were successfully extubated from the first time, second group: 15 patients who failed extubation and were re-intubated and third group:15 who were successfully extubated after initial failure. Thoracic fluid content was assessed with the use of electrical cardiometry for each participant before and after extubation from mechanical ventilation and Echocardiography was also performed for each studied neonate before and after extubation. **Results:** Most baseline variables were similar among the groups under study; however, compared to the successful weaning groups, the failed weaning group's TFC was significantly higher. The optimal cut off point was determined by analyzing the region beneath the ROC, or receiver operating characteristic curve. Regarding the use of TFC prior to extubation in order to identify failure cases, the AUC was 0.997 at a cut-off point of >44, with 100% sensitivity and 96.0% specificity, a PPV of 93.7, and an NPV of 100.0. AUC was 100, PPV was 100, NPV was 100.0, and it had 100% sensitivity and 100% specificity at the cut-off point of >41. **Conclusion:** The thoracic fluid content (TFC) by Electric cardiometer prior to extubation is a good predictive marker of successful weaning, with high sensitivity and specificity. Patients with Thoracic fluid content >44 was expected to fail extubation and patients with TFC< 41 were expected to be extubated successfully.

Key words: Thoracic fluid content, Electric cardiometry, Mechanical ventilation

Introduction

At intensive care unit, weaning patients off of artificial breathing is still a crucial decision. Although it is advised that patients weaning from mechanical ventilation as soon as possible to prevent the consequences of continuing on it, doing so too soon carries the chance of unsuccessful extubation, which is associated with unfavorable results [1].

An innovative, potentially useful hemodynamic tool in intensive care units is electrocardiometry (EC). Owing to the nature of the apparatus, it is possible to continuously evaluate the patient's condition, enabling the provision of appropriate care. The primary benefits of Electrocardiometry (EC) comes from its non-intrusive process, which results in a low complication rate, and the measurements that are provided instantly and continuously [2, 3].

Thoracic fluid content (TFC) can be determined via electrical cardiometry by monitoring variations in the impedance of the thoracic tissue to the electric current. Since thoracic fluid content (TFC) encompasses all of the fluid in the thorax: intravascular, extravascular, and intrapleural, it was developed as a way to calculate the extravascular lung water.

These days, there is more focus on cardiac factors including lung congestion and hypervolemia that lead to weaning failure [4].

Aim of the study

To study the use of thoracic fluid content (TFC) assessed by electric cardiometry as a predictive marker for weaning from mechanical ventilation.

Patients and Methods

Forty newborns admitted to the neonatal intensive care unit (NICU) at Ain Shams University hospitals participated in this prospective observational study. The trial included all full-term newborns who were scheduled for extubation and were on invasive mechanical ventilation. The readiness for weaning was evaluated by: The principal reason of intubation must be resolved, and the conventional ventilation parameters are PIP<16 cm

H2O, PEEP <6 cm H2O, rate <20, and Fio2 <0.30 and appropriate arterial blood gases for the patients [5]. Neonates with heamodynamic compromise e.g: systemic hypotension, Pneumothorax, Pleural or pericardial effusion and Neonates on non-invasive ventilation were excluded from the study.

PASS 11.0 was used to compute the sample size according to a study carried out by Fathy et al. [6]. Using a two-sided z-test at a significant threshold of 0.05000, a sample of 40 neonates achieved 80% power to detect a difference of 0.1900 between the area under the ROC curve (AUC) under the alternative hypothesis of 0.7500 and an AUC under the null hypothesis of 0.5000. There were three groups of patients.

First successful weaning: patients who were successfully extubated from the first time with no need for re-intubation n=25. Failed weaning group: patients who failed extubation group and were re-intubated n=15. Second successful weaning group: patients who were successfully extubated after failure of etubation n=15 (The 15 patient who failed extubation and retested again at their second weaning).

Neonates were managed according to the protocol of NICU by attending clinicians, and were subjected and followed up for the following: Detailed antenatal, natal, postnatal history, Anthropometric measurements: body weight, length, OFC, Hemodynamic status: mean arterial blood pressure (MABP), heart rate, oxygen saturation, capillary refilling time, Mechanical ventilation: size of endotracheal tube inserted, mode of ventilation and Parameters (Pip, PEEP, FIO2, RR) initial and weaning settings. If re-intubated the time between re-intubation and extubation and the total duration of mechanical ventilation. Drug history: medications affecting cardiac functions e.g. inotropes, their types, doses, and duration during the study period and antibiotics, Recording Labs and serial arterial blood gases (initial, before and after) extubation., chest x ray: before and after mechacical ventilation according to Nicu protocol. Electric Cardiometry (EC) was performed for each participant before and after extubation from mechanical ventilation Device: Portable Noninvasive Cardiometer (ICON, Osypka Medical, GmbH, Berlin, Germany), Model: C3 SN: 2003207, Parameters: The lateral aspect of the left thigh, the left mid axillary line at the level of the xyphoid process, the forehead, and the left base of the neck are the four skin electrode sensors used by Thoracic Fluid Content (TFC) to measure fluid status [7].

Echocardiography:

Before and after the spontaneous breathing trial began, a transthoracic echocardiography was carried out. M mode measurements were made at the level of the mitral valve leaflets' tips in the parasternal long axis view of the left ventricle. Interventricular septum thickness (IVS), posterior wall thickness (PWT), left ventricular end diastolic diameter (LVED), left ventricular fractional shortening (FS), and ejection percent (EF) were among the metrics that were tracked. Time intervals and tissue Doppler imaging-derived cardiac performance index. After measuring the systolic and diastolic heart rates at the basal segments of the lateral LV wall and septal wall, the Tei index was computed using the formula ('b -'a)/b, where an is the time interval from a to e and b is the time interval from the beginning to the end of s.

The internal aortic and pulmonary artery diameters were measured, and the velocity time integral (VTI) through the outflow tract was calculated in order to evaluate the cardiac output. The flow via the superior vena cava (SVC) was monitored.

Ethical Considerations

The study was approved beforehand by the Research Ethics Committee of Ain Shams University Hospitals (FMASU MS 302022), and informed consent was provided by each participant's caregiver.

Data management and analysis

Before the data were imported into IBM SPSS, a statistical program for social science research, version 27, they were inputted, amended, coded, and updated. For quantitative data that was not parametric, the means, standard deviations, and ranges were given; for parametric data, these were the median and inter-quartile range (IQR). Quantitative data was also displayed using numbers and percentages. The independent t-test, the Chi-square test, or the Fisher exact test were used to evaluate the qualitative data between groups; the Mann-Whitney test was used for non-parametric distributions.

The Wilcoxon Rank test was used to compare the quantitative data from two paired groups with a non-parametric distribution, while the Paired t-test was used to analyze the parametric data from two groups. Within the same group, a relationship between two quantitative parameters was established using Spearman correlation coefficients. To determine the optimal cut off point, the investigated marker's area under the curve (AUC), sensitivity, specificity, positive predictive value, and negative predictive value were analyzed using the receiver operating characteristic curve (ROC). We examined the factors that contribute to an inadequate weaning process using both univariate and multivariate logistic regression analysis. A 95% confidence interval and a 5% allowable margin of error were established. As a result, a p-value of less than 0.05 was regarded as significant.

Results

The basic demographic data were comparable among the three groups except for statistically high significant difference at length between failed and first successful weaning groups, and also statistically high significant difference at third line antibiotic use between failed weaning and second successful weaning group than the first successful weaning group (table 1).

Comparison between first successful weaning, failed weaning and second successful weaning groups regarding Electric cardiometry parameters before extubation and after extubation with statistically higher significant difference in TFC before and after extubation and SVV in failed weaning group and significant difference in CI and ICON (table 2).

Figures (1 and 2) & tables (3 and 4) showed ROC curve to assess TFC before extubation to detect failure cases at cut off >44 and at cut off >41

Table (1): Demographic data and characteristics of the studied neonates

Item		First Success No. = 25	Failed No. = 15	Second Success No. = 15	Test value	P-value	Sig.
Gender	Female	12 (48.0%)	1066.7%)	–	1.320*	1.320	NS
	Male	13 (52.0%)	533.3%)	–			
Age (days)	Median (IQR)	6 (2 – 8)	5 (5 – 8)	–	-0.465≠	0.642	NS
	Range	1 – 19	3 – 15	–			
Weight (kg)	Mean ± SD	3.02 ± 0.26	3.03 ± 0.23	–	-0.037•	0.971	NS
	Range	2.5 – 3.5	2.7 – 3.5	–			
Length (cm)	Mean ± SD	47.92 ± 1.47	49.87 ± 0.83	–	-4.682•	0.000	HS
	Range	45 – 50	48 – 52	–			
Chest X-ray initial	Normal	6 (24.0%)	2 (13.3%)	1 (8.3%)	13.333*	0.038	S
	RDS	6 (24.0%)	0 (0.0%)	0 (0.0%)			
	Pneumonia	10 (40.0%)	11 (73.3%)	11 (91.7%)			
	Meconium Aspiratio syndrome	3 (12.0%)	2 (13.3%)	0 (0.0%)			
Inotropes	Not used	22 (88.0%)	10 (66.7%)	11 (73.3%)	9.281*	0.158	NS
	Dopamine (5 mic)	2 (8.0%)	0 (0.0%)	0 (0.0%)			
	Dobutrex	1 (4.0%)	1 (6.7%)	1 (6.7%)			
	Dopamine, dobutrex	0 (0.0%)	4 (26.7%)	3 (20.0%)			
Feeding	Ryle feeding	22 (88.0%)	15 (100.0%)	15 (100.0%)	3.808*	0.433	NS
	full enteral feeding	1 (4.0%)	0 (0.0%)	0 (0.0%)			
	Breast Milk by ryle	2 (8.0%)	0 (0.0%)	0 (0.0%)			
Antibiotics							
1st line	No	15 (60.0%)	3 (20.0%)	8 (53.3%)	6.322*	0.042	S
	Yes	10 (40.0%)	12 (80.0%)	7 (46.7%)			
2nd line	No	10 (40.0%)	10 (66.7%)	7 (46.7%)	2.716*	0.257	NS
	Yes	15 (60.0%)	5 (33.3%)	8 (53.3%)			
3rd line	No	18 (72.0%)	3 (20.0%)	3 (20.0%)	14.992*	0.001	HS
	Yes	7 (28.0%)	12 (80.0%)	12 (80.0%)			

1st line antibiotics: ampicillin and amikin, 2nd line antibiotics:vancomycin and meropenem, 3rd line antibiotics:tazocinand ciprofloxacin.

P-values greater than 0.05 indicate non-significance, 0.05 indicate significance, and 0.01 indicate highly significance.

Table (2): Comparison between first successful weaning, failed weaning and second successful weaning groups regarding electric cardiometry parameters before extubation and after extubation

Item		First Success No. = 25	Failed No. = 15	Second Success No. = 15	Test value	P-value	Sig.
TFC before extubation	Mean ± SD	34.04 ± 6.30	52.47 ± 5.05	36.80 ± 3.67	58.468•	0.000	HS
	Range	21 – 45	45 – 62	29 – 41			
TFC after extubation	Mean ± SD	33.80 ± 6.68	51.27 ± 6.02	35.27 ± 4.08	45.088•	0.000	HS
	Range	23 – 53	42 – 64	31 – 46			
CI (BSA) before extubation	Mean ± SD	3.17 ± 0.29	3.38 ± 0.48	3.21 ± 0.22	1.909•	0.159	NS
	Range	2.5 – 3.6	2.7 – 4.5	2.9 – 3.6			
CI (BSA) after extubation	Mean ± SD	3.28 ± 0.41	3.69 ± 0.65	3.31 ± 0.28	4.079•	0.023	S
	Range	2.5 – 3.8	3 – 5.3	2.9 – 3.9			
FTC (ms) before extubation	Mean ± SD	244.92 ± 34.14	261.80 ± 31.32	247.53 ± 28.46	1.383•	0.260	NS
	Range	172 – 341	195 – 307	172 – 290			
FTC (ms) after extubation	Mean ± SD	257.88 ± 35.62	240.07 ± 32.83	250.53 ± 21.50	1.490•	0.235	NS
	Range	170 – 343	179 – 283	208 – 290			
ICON before extubation	Mean ± SD	88.26 ± 34.22	123.81 ± 63.40	94.03 ± 36.82	3.136•	0.052	NS
	Range	0.21 – 151.1	78.8 – 278	1.87 – 168.8			
ICON after extubation	Mean ± SD	83.06 ± 23.78	110.08 ± 37.09	92.86 ± 31.64	3.801•	0.029	S
	Range	0.21 – 112.6	45.2 – 173.7	2.6 – 161.2			
SVV (%) before extubation	Mean ± SD	21.09 ± 9.31	21.00 ± 7.33	20.86 ± 6.74	0.004•	0.996	NS
	Range	8 – 45	13 – 39	13 – 42			
SVV (%) after extubation	Mean ± SD	16.50 ± 9.90	25.57 ± 6.95	19.26 ± 4.78	5.880•	0.005	HS
	Range	8 – 58	16 – 37	13 – 28			

Post Hoc analysis	Success Vs failed	Success Vs second success	Failed Vs second success
TFC before extubation	0.000	0.122	0.000
TFC after extubation	0.000	0.450	0.000
CI (BSA) after extubation	0.009	0.858	0.028
ICON after extubation	0.008	0.322	0.122
SVV (%) after extubation	0.001	0.315	0.038

•*: Independent t-test; ≠: Mann-Whitney test P-values greater than 0.05 indicate non-significance, 0.05 indicate significance, and 0.01 indicate highly significance.*
TFC: Thoracic fluid content; CI: Cardiac index; FTC:
ICON: Inde of contractility; SVV: Stroke volume variation.

Table (3): ROC curve to assess TFC before extubation to detect failure cases at cut off >44

Cut off point	AUC	Sensitivity	Specificity	+PV	-PV
>44	0.997	100.00	96.00	93.7	100.0

Table (4): ROC curve to assess TFC before extubation to detect failure cases at cut off >41

Cut off point	AUC	Sensitivity	Specificity	+PV	-PV
>41	1.000	100.00	100.00	100.0	100.0

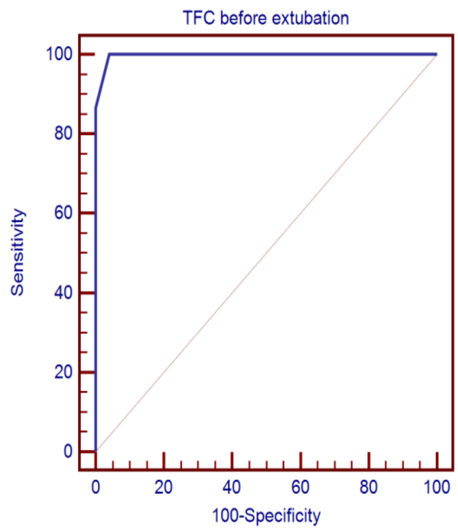

Figure (1): ROC curve to assess TFC before extubation to detect failure cases at cut off >44

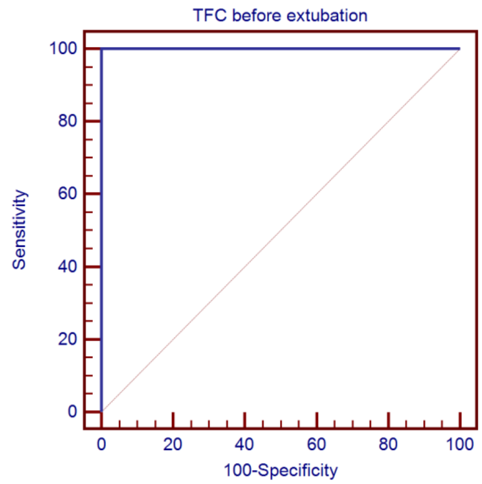

Figure (2): ROC curve to assess TFC before extubation to detect failure cases at cut off >41

Discussion

The respiratory care continuum includes neonatal mechanical ventilation (MV), which is essential for the survival of both preterm and critically ill newborns [8].

Thoracic fluid content was thought to offer an estimate of the extravascular lung water in the absence of a large pleural or pericardial effusion because thoracic fluid content comprises the entire intravascular, extravascular, and intrapleural fluid component in the thorax [9].

Lung congestion is a major factor in failure of weaning, particularly in cardiac patients. Because of increased left ventricular afterload, increased venous return, and consequently elevated cardiac preload, the spontaneous breathing trial (SBT) may potentially cause lung congestion. Both extra- and intravascular thoracic fluid are measured by the TFC index; however, when estimating extravascular lung water, the TFC exhibited a strong connection with ultrasound. A high TFC value may indicate hypervolemia or lung congestion, which are risk factors for failure of weaning [10].

So, this study aimed to assess TFC as a novel parameter for prediction of successful weaning of neonates on mechanical ventilation.

Forty neonates on MV were included in this prospective observational study. They were divided into three groups: a first successful weaning group (n = 25), a second successful weaning group (n = 15), and a failure weaning group (n = 15). The studied neonates were comparable as regards the age, gender and weight, except for the length which was significantly lower among first success group (47.92 ± 1.47 cm) compared to failed group (49.87 ± 0.83 cm).

There was insignificant difference between the three groups as regards inotrope use and feeding.

Comparison between first successful weaning, failed weaning and second successful weaning groups regarding Electric cardiometry parameters before extubation and after extubation revealed statistically higher significant difference in TFC before and after extubation and SVV in failed weaning group and significant difference in Cardiac index (CI) and ICON.

This agrees with Fathy et al. [6] study in which neonates in the unsuccessful weaning group had a notably greater TFC than the successful weaning group. On comparing thoracic fluid content (TFC) between first successful weaning and second successful weaning groups before and after extubationit shows no significant difference, indicating that TFC in failed extubation patients is a reverse for lung congestion hindering extubation and after improvement of lung congestion patients were successfully extubated as indicated by the measured thoracic fluid content.

As regards TFC before extubation was to detect failure cases; at cut-off point of >44, AUC was 0.997 it had 100% sensitivity and 96.0% specificity, with

PPV of 93.7 and NPV of 100.0.thus patients with TFC > 44 are suspected to fail extubation and weaning should be postponed According to Fathy et al. study found that among neonates on MV TFC at cut-off > 50 AUC was 0.69, with 65.2% sensitivity and 75.6% specificity. It showed 60% PPV and 79.5% NPV [6].

Univariate analysis in this study showed that Hco3 before <= 21 was a significant predictor of failure of weaning. While, multivariate logistic regression analysis showed that Hco3 before <= 21 was insignificant predictor.

Fathy et al. [6] study agreed with this study that serum HCO3 failed to predict weaning failure among neonates on MV.

On comparing between first successful weaning and failed weaning and second successful weaning neonates regarding vital data and ABG before extubation (HR, CRT, Temperature, SBP, DBP, O2 sat (%), UoP, PH, Pco_2, Hco_3 and BE), insignificant difference was found.

Shehab et al. [11] reported in concordance with the recent study that pre-extubation HCO_3 showed insignificant different in neonates with extubation failre comapred to those with successful extubation.

Likewise, Chawla et al. [12] reported that neoantes with successful extubation had insignificantly different $PaCO_2$ and FiO_2 compared to those with failed extubation.

This comes disagreeing with Hermeto et al. [13] where neonates with successful extubation showed significant difference compared to noenates with extubation failure as regards the preextubation PH and $PaCO_2$.

The same outcome was found in the study conducted by He and colleagues to investigate if higher FiO2 and higher PCO2 before to extubation were associated with failure extubation. Stepwise multivariate regression was employed in this analysis.

Additionally, Chawla et al. [14] noted that preextubation FiO2, pH, and pCO2 significantly differed between extubation failed newborns and extubation successfully neonates.

In their investigation on preterm newborns, Spaggiari et al. found that while greater pre-extubation FiO2 values were linked to failure, the sensitivity and specificity of a single FiO2 cut-off value were poor [15]. Thus, this could account for study heterogeneity. In the present study on comparing between first successful weaning, failed weaning and second successful weaning groups regarding echocardiographic parameters prior to and following extubation, no statistically significant difference was noted.

Zhang et al. [16] study independently discovered relations between the heart function indicated by hemodynamic measures and the status of mechanical breathing.

There was a statistically non-significant difference between the echo-cardoigraphic parameters in failed weaning cases before and after extubation. Before extubation compared to after extubation, LVED was considerably higher among patients with a second successful weaning. TVI was considerably lower in the neonates in the second successful weaning group prior to extubation than it was following extubation. Other than that, there was no discernible change in the ECHO parameters between the neonates in the second successful weaning group before and after extubation.

Among first successful weaning group it was revealed that LVED before extubation was significantly negatively correlated with Cardiac index (CI). SW/PW ratio before extubation was significantly correlated with SVV%. Left ventricular FS% before extubation, Ejection fraction % before extubation and heart rate showed significant correlation with ICON.

As far as we know, this was the first study to this was the first study to assess the correlation of echocardiographic parameters and electric cardiometry parameters with MV weaning.

Although no studies conducted to correlate electric cardiometry parameters with echocardiographic parameters in MV weaning neonates, previous study detected that there was a modest, positive relation between LVEF and cardiac contractility index in newly diagnosed with chronic heart failure [17].

In the present study myocardial performance index (MPI) showed significant negative correlation with Cardiac index (CI).

As previously reported cardiac index = cardiac output/BSA [18]. The myocardial performance index (MPI) or Tei indexhas been suggested as a helpful marker of cardiac involvement in newborns experiencing respiratory distress and prenatal hypoxia. This is because it may be used to assess the left ventricle's combined systolic and diastolic function. The Tei index and the ejection fraction have an inverse association [19].

LV MPI among adolescent cardiac transplant patients showed a negative connection with CI (r - 0.41), according to Savage et al. [20] despite the fact that they evaluated a different study population. These findings corroborated the findings of the current investigation.

Conclusions

The thoracic fluid content (TFC) by Electric cardiometer prior to extubation is a good predictive tool for assessment of successful weaning, with high sensitivity and specificity.TFC before <41 is a predictor of successful weaning and TFC >44 is a predictor weaning failure and weaning should be postponed till improvement and decrease of TFC

Data Availability

The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

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Author's contributions

AA helped in the study design, acquisition of data, and drafting the manuscript. MI was responsible for conception of the idea, study design, analysis of the data, and drafting of the first manuscript. Mi was responsible for analysis and interpretation of the data, writing the manuscript, and responding to the reviewer comments. NS,MIand AA helped in the acquisition of data, management of the patients, and revising the manuscript. RA is the senior author who was responsible for supervision of the whole research and revising the final manuscript. All authors approved the manuscript and agreed to be accountable for all aspects of the work.

Conflict of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper

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