Original Article

Association between chest congestion and mortality in ICU patients

Yasser Nassef[1*], Dung-Hung Chiang[2*], Ming-Chih Chou[1]

[1] *Nnstitute of Medicine, Chung Shan Medical University, Taichung City, Taiwan*
[2] *Department of Critical Care Medicine, Taipei Veterans General Hospital, Taipei City, Taiwan.*

Purpose: Recent years have seen significant progress in hemodynamic monitoring and management. There has been an evolution from invasive to less invasive technologies. This study evaluated the relationship between chest congestion via thoracic fluid content (TFC) and mortality among critically ill patients in the Intensive Care Unit (ICU).
Methods: This retrospective case-control study assessed 373 patients admitted to the ICU of Taipei Veterans General Hospital from December 2012 to June 2013. In total, 149 individuals (n = 149) were excluded due to incomplete or missing information. Patients who died during the study interval were selected as the case group while the surviving participants represented the control group. The (TFC) thoracic fluid content was collected by an ICON Electrical Cardiometry device in all patients. Mortality odds ratios (ORs) and 95% confidence intervals (CI) were estimated using multiple logistic regression models.
Results: A total of 224 patients (84 who died in the ICU and 140 who remained alive) were included in the final analysis. The aOR for mortality was significantly higher in patients with abnormal or high TFC ($\geq$50 kΩ^{-1}) than in those with TFC <50 kΩ^{-1} (aOR, 2.278; 95% CI 1.1216-4.268). Results from the sex stratified analysis model showed that the aOR for mortality was significantly higher among men (aOR, 2.209; 95% CI, 1.006-4.848; P = 0.0482) but not women (aOR, 2.085; 95% CI, 0.631-6.890; P = 0 .2284) with TFC $\geq$50 kΩ^{-1} compared to TFC <50 kΩ^{-1}.
Conclusions: In this study, high TFC was associated with a higher mortality rate in critically ill ICU patients. The mortality risk was more pronounced in male patients.

Keywords: thoracic fluid content; chest congestion; ICU mortality; electrical cardiometry; hemodynamic; critical care

1. Introduction

There has been significant improvement in hemodynamic monitoring (HDM) and management, with non-invasive technologies replacing highly invasive ones[1]. Hemodynamic monitoring is not intended to treat, but rather to provide clinical information that can be helpful in medical decision-making. [2] Critically ill patients require a hemodynamic assessment, which has both diagnostic and prognostic value. [3] Hemodynamics is defined as measuring the factors that influence the flow of blood, inotropy, resistance, and fluid in the body. Obtaining circulatory stability is a real challenge sometimes. Systemic blood flow cannot be accurately determined by indirect measures such as capillary refill time, heart rate, urine output, and blood pressure. [4]

Hemodynamic parameters can detect early

* Corresponding Author: Dung-Hung Chiang and Yasser Nassef
Address: No. 110, Sec. 1, Jianguo N. Rd., Taichung City, 40201, Taiwan
Tel: +886-4-24730022 ext. 11720
E-mail: dhchiang2@vghtpe.gov.tw (D.H,Chiang); yasser@nassef.org (Y,Nassef)

changes within the cardiovascular system in critical patients. Hemodynamic monitoring can enhance both diagnostic and therapeutic potential for all monitoring modalities by defining vasomotor tone, preload reserve, tissue perfusion, and cardiac performance[5]. According to recent findings,[6] several different technology platforms are available for non-invasive stroke volume monitors, all of which have performance characteristics that are distinct from one another. Moreover, these findings indicate that patients undergoing major surgery can benefit from these devices based on their clinical outcome data. Extravascular lung water measurements and respiratory variation are well validated for predicting respiratory outcomes. Effective use of these devices depends on understanding their scientific basis. [7]

A central component of effective management of the critically ill patient is hemodynamic monitoring, which aims to assess the functions of the cardiovascular system and determine the appropriate therapeutic intervention to optimize the delivery of oxygen to the organs [5, 7, 8].

It is essential to monitor the hemodynamic status of patients on a regular basis and also to measure the systemic vascular resistance (SVR), cardiac output (CO), and other hemodynamic parameters using non-invasive methods such as trans-thoracic/ trans-esophageal Dopplers, echocardiography, and electrical cardiometry for in order to personalize and adapt the treatment over time[9]. This may serve as a framework for managing fluid therapy, inotropes, as well as vasoactive drugs.[8, 9]

There are numerous noninvasive methods for monitoring hemodynamics and fluids in critically ill patients. Currently, techniques such as Electrical Cardiometry (EC) and Impedance Cardiography (ICG) have been developed to measure cardiac output (CO), stroke volume variation (SVV) and TFC, systemic vascular resistance (SVR), stroke volume (SV), and other hemodynamic parameters[10]. Cardiac output is determined by measuring the thoracic electrical bioimpedance during ICG and EC. The continuous CO derived from the pulmonary arterial catheter (PAC) and EC-CO electrical cardiometry are clinically acceptable techniques that can be used interchangeably. [11] The new index, TFC indicates total fluid volume (both intravascular and extravascular) the chest cavity. An inverse relationship exists between it and the patient's transthoracic electrical bioimpedance. The TFC was proposed as a way to estimate extravascular lung water. [12] Without an evaluation of fluid volume status, especially in the lungs, it can be difficult and incomplete to determine cardiac status.[13] Consequently, TFC has been found to be a reliable indicator of chest fluid volume and changes. [14]

Cardiovascular conditions such as lung congestion and hypervolemia are increasingly being studied today, various measures have been previously reported to evaluate volume status. In the past, most measures required frequent blood sampling or experienced operators.

The TFC was first introduced in 1998 by CardioDynamics International Corporation (CIDIC) and can be measured noninvasively by bioimpedance cardiac output. Hypothetically, impedance cardiography could identify TFC or changes in hemodynamic variables that are relevant to clinical practice more effectively and earlier than conventional clinical evaluations. According to previous reports, the amount of aspirated pleural effusion varies with changes in thoracic fluid contents (measured using Bioimpedance).[14-16]

According to Hammad et al.[17], if pulmonary edema is identified in time, fluid management can be improved and severe cases can be detected early enough. They also suggested that lung ultrasound scores and thoracic fluid content are excellent diagnostic indicators of pulmonary edema. Electrical Cardiometry offers a high predictive value for TFC, thus making it an important screening tool for pulmonary edema. Furthermore, previous studies have indicated that electrical cardiometry might be a suitable alternative to ultrasound in assessing extravascular lung water. [14-16]

A reliable measurement of CO is vital in modern healthcare, especially with patients undergoing surgery or in critical conditions. Kobe et al [18] found that CO monitoring, in combination with intravenous therapy and inotropic support can enhance perioperative outcomes among high-risk surgical patients. He and his colleagues also stated that CO devises might provide anesthesia and intensive care providers with numerical trend information to assist them in selecting the best method of managing their patients. However, the devices do not entirely prevent,

but limit the use of pulmonary artery catheter. [5, 8, 19]

Pulmonary artery catheterization is a technique that involves inserting an intravascular catheter into the right side of the heart through the central vein. Using this procedure, one can estimate CO and VR as well as right-sided filling pressures. Due to the availability of non-invasive tools, the use of PAC for evaluating and managing critically ill patients has decreased.[20]

Changes in TFC determined using a noninvasive CO monitoring device are positively correlated with chest fluid [21]. In infants undergoing cardiac surgery, TFC might serve as a useful indicator of intraoperative fluid management. [21-23] Thoracic fluid content value ≥34 $k\Omega^{-1}$ measured by ICG correlated with higher lethal outcomes in heart failure patients [21-23]. Since TFC could increase in patients with impaired hemodynamics or respiratory distress, an increase in this value may indicate a higher mortality risk, although this has never been investigated. [16, 24, 25]

The current study was designed to evaluate the association between high chest congestion derived by electrical cardiometry and mortality among critically ill patients. Furthermore, sex-related differences in the association of TFC with mortality were also investigated.

2. Materials and methods

2.1. Ethical Declaration

The study adhered to the Declaration of Helsinki in 1964 and its late amendment. The Institutional Review Board of Taipei Veterans General Hospital approved the study (2021-11-007CC). Each participant signed an informed consent form.

2.2. Data source and patient selection

The current study used data from the Taipei Veterans General Hospital, which included 373 ICU patients admitted between December 2012 and June 2013. We excluded those with incomplete information (n = 149). Informed consent was available from each patient or the legal representative. Data were collected from the hospital's medical database and included age, sex, height, weight, use of a vasopressor agent including epinephrine, norepinephrine, and dopamine, use of a ventilator, fluid administration, and history of prominent diseases including hypertension, diabetes mellitus (DM), and coronary arterial disease (CAD). Patients who met one of the following criteria were excluded from the current study: (1) the admission time was less than one month (2) the measurement of hemodynamic parameters was less than three times or more than 10 times during the admission period (3) the basic characters mentioned above were not recorded clearly in the medical database. Patients who died during the study interval were considered as the study group, while those who survived were considered the control group.

2.3. Main outcome measurement

Electrical cardiometry (ICON®, Osypka Medical, Berlin, Germany) was used to measure the hemodynamic parameters such as TFC, SVV, cardiac output, systemic vascular resistance, and cardiac contractility. Each participant was measured once per week (Monday morning).

The TFC data were presented as numeric variables. A mean value for each hemodynamic parameter was calculated. Where the value of any parameter in a single measurement differed from the nearest value by 50 percent or more, that episode of measurement was excluded after confirming the low signal quality index. The normal TFC for an adult is 25:35 (1/kΩ). Values above 35:49 are considered high and indicate mild to moderate chest congestion. A value over 50 indicates severe chest congestion.

2.4. Statistical analysis

Statistics were run using SAS 9.4 software (SAS Institute, Cary, NC). Numbers and percentages, as well as mean and standard deviation (SD) were used to present data. Comparisons of baseline parameters were conducted with the T-test (continuous variables) and Chi-square test (categorical variables). Multiple logistic regression analysis models were used to study the association between TFC and other hemodynamic parameters and mortality. In the current study, TFC values for deceased patients changed over time - they were always above 35 $k\Omega^{-1}$ at admission, always exceeding 50 $k\Omega^{-1}$, and sometimes reached 100 $k\Omega^{-1}$. In those who survived, TFC values were always below 50 at admission

and remained so when discharged or transferred to normal wards. In the analysis models, a TFC greater than 50 $k\Omega^{-1}$ was regarded abnormal. Sex stratified analysis was also performed and the overall and sex-specific ORs for ICU mortality and their 95% CI were estimated. Statistical significance was defined as a p-value less than 0.05.

3. Results

After exclusions, 224 critically ill patients were recruited. Among those selected, 84 patients who died during the study period constituted the study group while the rest (n = 140) were enrolled into the control group (Table 1). The mean age (±SD) was 66.821 (19.303) years for the study group and 66.814 (17.421) years for the control group. The male to female ratio was 28 to 56 in the study group and 56 to 84 in the control group. The TFC, SVV, weight, DM, and hypertension were significantly different between the two groups while other indexes remained similar

In a multiple logistic regression model (Table 2), patients with TFC ≥50 $k\Omega^{-1}$ had higher mortality than those with TFC <50 $k\Omega^{-1}$ (aOR, 2.278; 95% CI

Table 1. Baseline characteristics of the case and control groups

Parameters (mean ± SD)	Patients	Controls	P-value
	N=84	N=140	
TFC (1/kΩ)			0.0011*
Normal (<50)	34±40.48	88±62.86	
Abnormal (≥50)	50±59.52	52±37.14	
SVV (%)			0.0193*
Normal (<14)	16±19.05	47±33.57	
Abnormal (≥14)	68±80.95	93±66.43	
Sex (male/female)	28/57	56/83	0.2704
Age (year)	66.821±19.303	66.814±17.421	0.9977
Height (cm)	161.700±7.433	160.600±9.347	0.3411
Weight (kg)	55.995±13.577	61.527±17.397	0.0087*
Disease history			
DM	20±23.81	51±36.43	0.0494*
Hypertension	18±21.43	68±48.57	<0.0001*
CAD	6±7.14	14±10.00	0.4678
Vasopressor agent			0.0527
No	32±38.10	72±51.43	
Yes	52±61.90	68±48.57	
Air breather			0.6402
No	21±25.00	39±27.86	
Yes	63±75.00	101±72.14	

SD: standard deviation, TFC: thoracic fluid content, SVV: stroke volume variation, DM: diabetes mellitus, CAD: coronary artery disease
* denotes significant difference

Table 2. Multiple logistic regression analysis showing the association between ICU mortality and potential risk factors

Risk factors	aOR	p-value	95% CI
TFC (ref: <50)			
≥50	2.278	0.0101*	1.216-4.268
Sex (ref: Female)			
Male	1.459	0.3450	0.666-3.196
Age	1.007	0.4274	0.989-1.025
Height	1.026	0.3285	0.975-1.079
Weight	0.975	0.0470	0.951-1.000
DM (ref: No)			
Yes	1.129	0.7655	0.509-2.504
CAD (ref: No)			
Yes	0.681	0.5049	0.220-2.107
Vasopressor agent (ref: No)			
Yes	1.428	0.2589	0.769-2.653

Abbreviation: aOR: adjusted odds ratio, CI: confidential interval, TFC: thoracic fluid content, SVV: stroke volume variation, DM: diabetes mellitus, CAD: coronary artery disease
Adjusted for SVV, hypertension, and air breather
* denotes significant difference

Table 3. Mean values of hemodynamic parameters in male and female patients

Hemodynamic parameters (mean ± SD)	overall (N=224)	Female (N=85)	Male (N=139)
TFC (1/kΩ)			
Normal (<50)	35.893±8.946	34.957±9.236	36.480±8.771
Abnormal (≥50)	69.176±15.151	71.947±17.064	67.531±13.770
SVV (%)			
Normal (<14)	10.333±2.300	10.348±2.757	10.325±2.030
Abnormal (≥14)	22.826±8.176	22.258±7.250	23.182±9.539

Abbreviation: SD: standard deviation, TFC: thoracic fluid content; SVV: variation in stroke volume variation.

1.1216-4.268). The aORs for mortality associated with age, height, weight, diabetes mellitus, and CAD were not significant (p>0.05). The general and sex-specific hemodynamic estimates are shown in Table 3. For abnormal TFC, the mean value was 71.947 $k\Omega^{-1}$ in women, 67.531 $k\Omega^{-1}$ in men, and 69.176 $k\Omega^{-1}$ in the overall patients. In the sex stratified analysis, the aORs for mortality was significantly higher among men (aOR, 2.209; 95% CI, 1.006-4.848; p=0.0482) but not women (aOR, 2.085; 95% CI, 0.631-6.890; p=0.2284) with TFC ≥50 $k\Omega^{-1}$ compared to TFC <50 $k\Omega^{-1}$ (Table 4).

4. Discussion

The current study demonstrates a significantly

Table 4. Adjusted odds ratios for the association between ICU mortality and potential risk factors stratified by sex

Risk factors	Female			Male		
	aOR	*p*-value	95% CI	aOR	*p*-value	95% CI
TFC (ref: <50)						
≥50	2.085	0.2284	0.631-6.890	2.209	0.0482*	1.006-4.848
Age	1.019	0.3190	0.982-1.059	1.003	0.7684	0.982-1.026
Height	1.157	0.0126*	1.032-1.297	0.992	0.7944	0.931-1.056
Weight	0.934	0.0584	0.870-1.002	0.985	0.2812	0.957-1.103
Diabetes (ref: No)						
Yes	0.291	0.1437	0.056-1.523	1.777	0.2671	0.644-4.905
CAD (ref: No)						
Yes	0.485	0.5699	0.040-5.884	0.605	0.4865	0.147-2.491
Vasopressor agent (ref: No)						
Yes	2.516	0.1450	0.728-8.700	1.304	0.4947	0.609-2.791

Abbreviations aOR: adjusted odds ratio, CI: confidential interval, TFC: thoracic fluid content, SVV: stroke volume variation, DM: diabetes mellitus, CAD: coronary artery disease
Adjusted for SVV, hypertension, and air breather
* denotes significant difference

high risk of mortality in ICU critical patients with high TFC (≥50 $k\Omega^{-1}$) relative to those with low TFC (<50 $k\Omega^{-1}$). When data were stratified by sex, significant association was found only in men.

The TFC and other hemodynamic parameters have been widely investigated in recent years. With the help of electrical cardiometry, it is now possible to predict patients' prognosis in case of community-acquired pneumonia. An increase in the thoracic fluid content is associated with adverse patient outcomes, including in-hospital mortality. Electrical cardiometry makes it possible to measure thoracic fluid content without restraint or the need for invasive catheters.[26]

In the current study, TFC ≥50 $k\Omega^{-}$ was related to higher ICU mortality in critical patients after controlling multiple potential risk factors. To our knowledge, this is a preliminary finding to illustrate that increased TFC could be a risk factor for mortality in critically ill patients. The TFC data used in the current study were obtained weeks to months before the mortality event developed. Consequently, further investigation is required to determine whether a high TFC may also serve as an early sign of mortality in critical patients.

Women and men treated with diuretics had a lower TFC than those treated with other antihypertensive drugs and the healthy controls [27]. ICG parameter TFC is linked to diuretics and can be used to optimize and tailor antihypertensive treatment.[28]

The relatively few CAD events in the current study may have led to statistical bias. In the aspect of medical management for the study population, neither the use of vasopressors nor the application of mechanical ventilation were significantly related to a higher risk of mortality. The possible explanation is that both data were collected in the early phase thus could not provide information on the disease severity just before the mortality event.

Critically ill patients require hemodynamic monitoring regularly to determine a treatment plan. It allows precise fluid administration as well as accurate adjustment of inotropes and vasoactive drugs when necessary, non-invasive monitoring presents

the advantage of having no complications while providing a better outcome. [7, 29] In a previous study comparing CO obtained using EC and PAC [30], cardiac indices measured using EC reliably represented absolute values obtained by PAC. The study also reported that EC technology provides noninvasive beat-to-beat tracking of CO and other parameters without requiring invasive monitoring procedures. We collected hemodynamic data involving TFC in the current study using a non-invasive CO monitor without encountering any adverse effects in any of the participants, indicating that this technique and equipment could be applied more widely to provide proper hemodynamic parameters.

A number of limitations apply to this study. First, the retrospective nature may limit the standardization of health status in each participant and lead to some bias. Second, we only considered critical patients who received medical treatment in the ICU as a whole group, but there were several indications for admission to the ICU in our study population, and subgroup analyses were not performed on hemodynamic parameters and different initial diseases. Furthermore, the number of hemodynamic measurements was different between patients, which may be attributed to retrospective designs. However, since the number of hemodynamic measurements ranged from three to 10 in the study population, bias arising from the different frequency measurements might have been minimized.

5. Conclusions

Based on the results of the current study, a high TFC was associated with a higher mortality in critically ill ICU patients. Furthermore, this association was more obvious in male than in female patients. Even so, these associations need to be clarified by larger-scale scientific studies.

Ethics approval and consent to participate

The Institutional Review Board of Taipei Veterans General Hospital approved the study (2021-11-007CC). Informed written consent was obtained from all participants.

Availability of data and materials

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

Conflicts of interest:

Yasser Nassef is a member of the advisory board of Osypka Medical. No financial or commercial support had been taken for this study.

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