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Editorial

An Update of Armamentarium for Non Invasive Cardiac Haemodynamics and Congestion Evaluation for Acute Heart Failure Patients

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ABSTRACT

In the management of Acute Heart Failure (AHF) patients, current guidelines suggest making prompt clinical assessments that include patient's congestion and perfusion status evaluation, in order to start appropriate treatments. Unfortunately, so far, an accurate evaluation of the hemodynamic and fluid status of AHF patients is only possible using invasive methods; consequently, there is an unmet need for noninvasive technologies to easily detect different phenotypes of AHF subjects based on different cardiac hemodynamic profiles. Technological advances such as Biva, Nexfin, or NICas could allow for routine non-invasive continuous monitoring of Cardiac Hemodynamic and Fluid content in Acute Heart Failure patients. These non-invasive measurements may provide important information for improving diagnosis, developing individualized therapeutic management plans/disposition decisions, and predicting short term mortality

Introduction

Acute heart failure (AHF) is defined as rapid, new-onset, or worsening presentation of the symptoms and signs of heart failure (HF) resulting from any structural or functional impairment of the left ventricle.[1] It is a growing epidemic, with an estimated 670,000 new cases/year in the USA, and more than 15 million patients in Europe and represents also the leading cause of acute hospitalizations. Moreover, patients hospitalized with AHF suffer high rates of post-discharge re-hospitalizations (20–30%) and mortality (10–20%) within 3–6 months. Ultimately, AHF has a negative impact on both patient outcomes and health care systems costs.[1]

In AHF, systemic congestion is both a cause and result of worsening cardiovascular function Being the total body fluid overload the consequence of the activation of the neurohormonal system that then causes fluid redistribution and accumulation, increases systemic resistance, and reduces capacitance in large veins. Ultimately, these pathophysiological changes lead to clinical decompensation and are associated with elevations of b-type natriuretic peptides (NP's).[2]

Total body fluid overload is not only a benchmark for AHF diagnosis, but also for its prognosis.[3]

Different non-invasive methods for assessing clinical congestion are available (e.g., accurate physical examination, chest X-ray, thorax and inferior vena cava index, and chest ultrasound evaluation, however, they suffer from low sensitivity, insufficient specificity, and poor interrater reliability. Although chest ultrasound seems to be accurate in detecting lung congestion, it is very difficult to accurately assess total body water content and organ perfusion and it currently is estimated predominately on the basis of blood pressure.[4]

Current guidelines support treatments based on physician clinical assessments that include the immediate accurate evaluation of a patient's congestion and perfusion status, being this assessment necessary to start appropriately tailored treatments, mainly with diuretic and vasodilator drugs.[1,5]

Literature has shown that the prediction of the underlying hemodynamic profiles by cardiologists, intensivists, and emergency physicians using clinical evaluation alone is neither accurate nor reliable.[6-8] As consequence, while profiling of AHF patients based on clinical assessment of central congestion and peripheral perfusion (warm/dry, warm/wet [most patients], cold/dry or cold/wet) is proposed for rapid ED therapeutic decision making, there is only fair to poor interrater agreement for related categorical assignments.[9]

Bioimpedance Vector Analysis

All biological structures have a specific resistance, defined as the strength of opposition by tissue to the electric current flow. Bioimpedance vector analysis (BIVA) uses 4 electrodes to noninvasively measure impedance using a 300 µA, 50 kHz current, the results of

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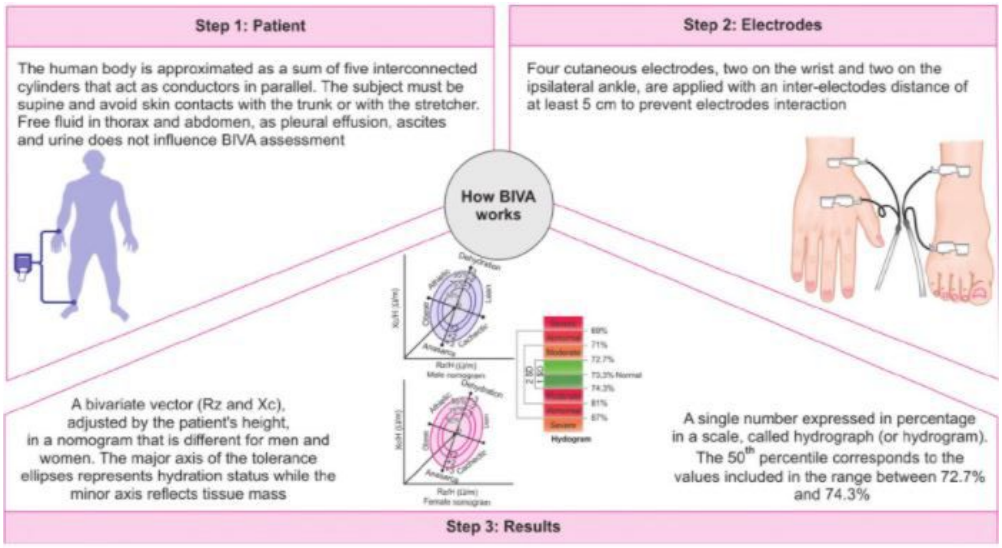

Figure 1. BIVA Measurement and Result[15]

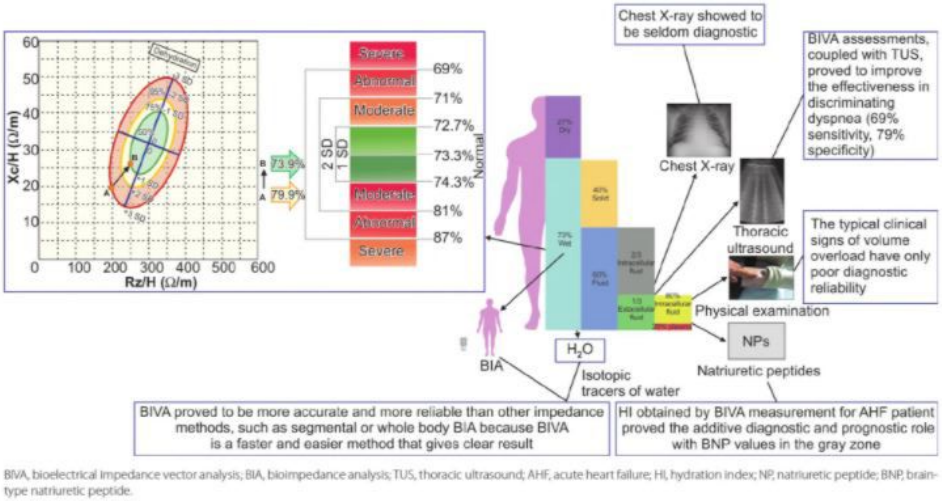

Figure 2. Additive Value of BIVA compared to other methods[15]

which correlate to body volume and composition. Bioelectrical impedance (Z) consists of two components, resistance (Rz) and reactance (Xc).) The mathematical solution to providing clinical data requires that the human body is approximated as the sum of five interconnected cylinders that act as conductors in parallel. While Rz is inversely related with the amount of total body water, Xc is considered proportional to body mass.[10,11]

To obtain BIVA measurement, two electrodes, 5 cm apart, are placed on the wrist and ipsilateral ankle in the supine subject. To prevent inaccurate results, the patient must avoid extremity contact with the trunk and with the stretcher. (Figure 1)

As fluids are good conductors, the length of the Z vector (representing the body's impedance), is inversely related to fluid volume. Several studies have agreed on the delineation of the 75% tolerance ellipse as the boundary of normal tissue hydration.[12] Consequently, vectors outside the upper pole of the 75% ellipse indicate dehydration, whereas vectors outside the lower pole of 75% confidence ellipse represent overhydration (Figure. 2), and shorter the vector, more severe is the condition of fluid overload.

In AHF patients, BIVA results are strongly related to b-type natriuretic peptide (BNP) values, New York Heart Association (NYHA) functional classes, and CVP. More importantly, it allows physicians to detect fluid overload even before the appearance of peripheral edema, thus potentially allowing treatment before the development of severe symptoms.[13]

Results from our group confirmed the additive diagnostic value of BIVA in easily and quickly detecting AHF.[14] As summarized in figure 3, patients' vectors were grouped as 95% confidence interval (CI) ellipses of point vectors (Figure 3). While the white ellipses of the no-AHF cohort demonstrated normal hydration status (inside the 50% ellipse) in both sexes, for congestive patients (grey ellipses) the 95% CI ellipse was displaced along the major axis, and between 75 and 95% ellipses both for females and males, indicating body fluid congestion (Figure 3). At ED admission, versus the no-AHF cohort, the mean hydration index (HI) was higher in the AHF group (81.2 ± 6.7% vs. 72.9 ± 3.6%, <0.001), while mean Xc/H and Rz/H values were significantly lower in congestive patients ($p < 0.001$).

It has been demonstrated that combining BIVA plus BNP may

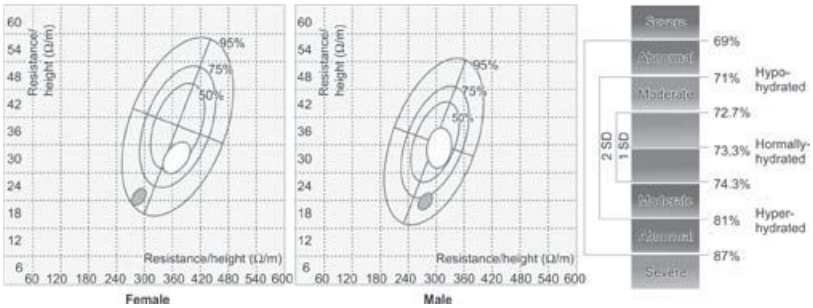

Figure 3. BIVA Result Interpretation

It has been demonstrated that combining BIVA plus BNP may improve the management of AHF patients in ED, compared to BNP alone. When considered separately, BNP is internationally recognized to be associate with increased left ventricle pressure and volume overload, while the HI, obtained using BIVA, is proportional to total body fluid congestion.[15] As BNP and BIVA data provide information on different aspects of cardiovascular function, their combined measurement may lead to earlier and more accurate AHF diagnosis. This may be especially relevant when the BNP result is in the "gray zone", between 100 and 400 pg/mL, where it has lower diagnostic accuracy.[16]

Other environments have recommended the adoption of BIVA. Patients with HF complicated by renal dysfunction termed "cardiorenal syndrome" represent a management challenge for whom the evaluation of total body fluid is fundamental.[17,18]

The prognostic value of BIVA in patients with AHF was also confirmed in a shorter follow-up period (30 days) and with a hydration assessment obtained at the moment of a patient's arrival at ED. An HI value greater than 74.3% was associated with worse 30-day outcomes.[16]

Whole Body (Regional) Impedance Cardiography (NICaS).

Millions of acutely ill patients are evaluated in theEmergency Department (ED) by clinicians who utilize vital signs and clinical evaluation to estimate underlying hemodynamic profiles. Based on these evaluations, a diagnostic and therapeutic plan is formulated for each patient.[5,8] However, blood flow (cardiac index) is not reliably inferred from vital signs.

Hemodynamic parameters, such as stroke volume (SV) and cardiac output (CO), are an essential component of fluid management

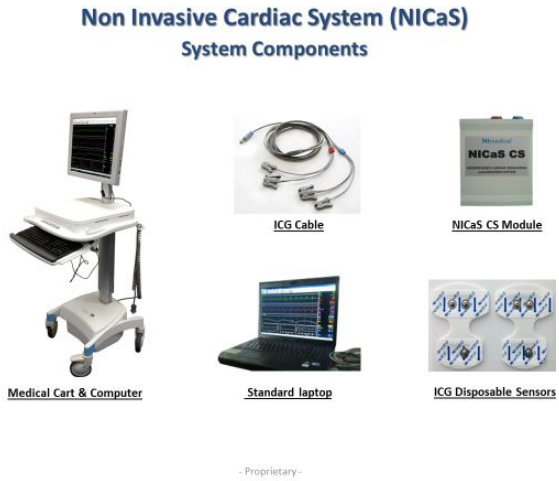

Figure 4. NICaS Component

in cardiac and intensive critical unit settings and also to evaluate AHF patients.[19]

The invasive Swan-Ganz pulmonary artery catheterization (PAC) thermodilution technique is considered the gold standard, despite controversies. For the past three decades, the measurement of hemodynamic profiles of patients has been limited to the critical care units because the measurement methods used were invasive in nature and/or complex to apply and time-consuming (pulmonary artery catheter).[20] Thus acutely ill or injured patients in the ED may have suboptimal physician clinical hemodynamic assessments made and with an unknown effect on patient outcomes in a variety of disease states. Consequently, a critical need exists for a non-invasive, inexpensive, reliable, and practical technique for measuring hemodynamic parameters in AHF patients.[21]

A regional bioimpedance cardiography device (NiCaS, NI Medical, Israel) has been validated in the cardiac care setting.[22,23] It has been shown to have better accuracy and precision compared with thoracic bioimpedance and modified-Fick techniques. This may represent a breakthrough technology capable of measuring hemodynamic parameters including cardiac output, cardiac power, total peripheral resistance, and total body water based on regional bioimpedance.

NiCaS transmits an imperceptible electrical signal through the blood in the arterial system through two sensors arranged in a wrist-to-ankle configuration (figure 4). With each heartbeat, the volume of blood in the arterial system changes and results in a change in the body electrical resistance. Because the volume of moving fluid is associated with resistance changes, NiCaS can calculate cardiac output by integrating the area under the time-resistance curve multiplied by the heart rate well. From these parameters, other hemodynamic and respiratory outputs can be calculated. NiCaS measurements are non-invasive, low cost, and easy to perform (about 3 minutes, no need to undress (figure 5,6).

NEXFIN

A novel monitoring device (Nexfin; BMEYE, Edwards Lifesciences, Irvine, California) to noninvasively and continuously measure beat-to-beat hemodynamic measurements in ED adult patients with clinically suspected AHF has been recently available.[24-26] Cardiac output and other hemodynamic variables are determined from a reconstructed brachial artery waveform using the Nexfin COTrel pulse contour method [and systemic vascular resistance (SVR) is calculated. These are displayed beat-to-beat, time-averaged, trended, and indexed by height and weight. The Nexfin device has been shown to have acceptable measurements [limits of agreement of up to ±30%] for cardiac output when compared to invasive pulmonary artery catheter measurements (figure 7)

The Premium Registry using Nexfin in ED AHF subjects showed that AHF patients with similar clinical parameters available in

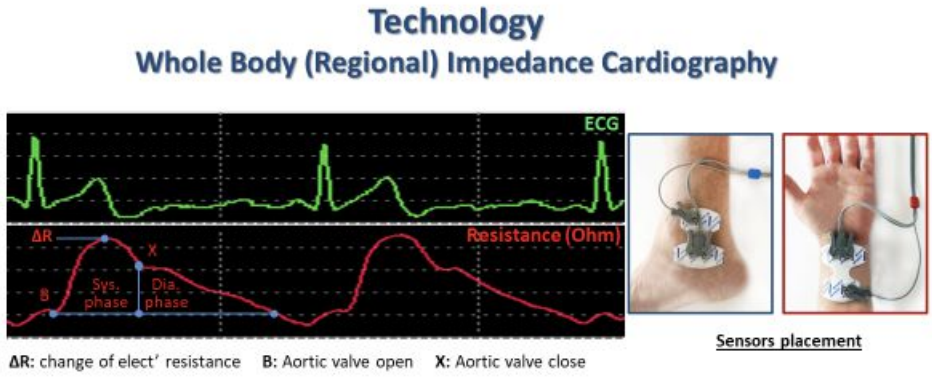

Figure 5. Whole Body (Regional) Impedance Cardiography

NICaS Parameters

Parameter		Definition	Normal Range	Derivation/Formula
Heart Rate	HR	Number of heart beats each minute	60 - 90 bpm (beats per minute)	Measurement of the R-R interval on the ECG
Stroke Volume	SV	Amount of blood pumped by the left ventricle each heartbeat	60 - 130 ml	SV ~ ΔR / R
Stroke Index	SI	Stroke volume normalized for body surface area	35 - 65 ml/m^2	SI = SV/ BSA
Cardiac Output	CO	Amount of blood pumped by the left ventricle each minute	4.0 – 8.0 l/min	CO = HR x SV / 1000
Cardiac Index	CI	Cardiac Output normalized for body surface area	2.5 - 4.0 l/min/m^2	CI = CO / BSA
Cardiac Power Index	CPI	An indicator of myocardial contractility	0.45 – 0.85 w/m^2	CPI = CI x MAP x 0.0022
Granov Goor Index	GGI	An indicator of Left Ventricular Function, which is strongly related to Ejection Fraction	> 10.0 (equals an Ejection Fraction > 55%)	GGI = ΔR/R x α x HR
Total Peripheral Resistance	TPR	The resistance to the flow of blood in the arterial system ("Afterload")	770 - 1500 dynes x sec /cm5	TPR = MAP / CO x 80
Total Peripheral Resistance Index	TPRI	The resistance to the flow of blood in the arterial system normalized for body surface area	1600 - 3000 dynes x sec /cm5 x m^2	TPRI = MAP / CI x 80
Total Body Water	TBW	The amount of extracellular fluid in % of body weight	Individually calculated as per gender and BMI	TBW ~ Ht^2 / R
Respiration Rate	RR	Number of breaths each minute	8 – 24 breaths / minute	

Figure 6. NICaS Parameters

the ED have different underlying hemodynamic profiles.[9] These may be clustered into three separate phenotypes. Importantly, ED phenotype clusters could not be reliably recognized through the use of current clinical ED assessments and laboratory testing. Although the Premium observational registry was not powered for outcomes there were trendsto more and relatively high rates of in-hospital (10%) and 30 days (20%) deaths in cluster 3 vs. other groups. This may be explained as a result of diuretic therapy in patients with low cardiac output in the face of markedly increased systemic vascular resistance.

In this attempt, The Nexfin device has been shown to have acceptable measurements [limits of agreement of up to ±30%] for cardiac output when compared to invasive pulmonary artery catheter measurements. Unfortunately, in patients with very low cardiac output (e.g., shock) finger perfusion may be too low to properly detect the device signal and thus in this situation, it may not be considered as an ideal monitor. Conversely, NIcas technology has been shown to be a very good tool in monitoring therapeutic efficacy. Ultimately, NIcas could provide a very good estimation of total body fluid content and could be considered the more appropriate tool for non-invasively evaluating Cardiac hemodynamics and congestion in AHF patients.[27-30]

Discussion

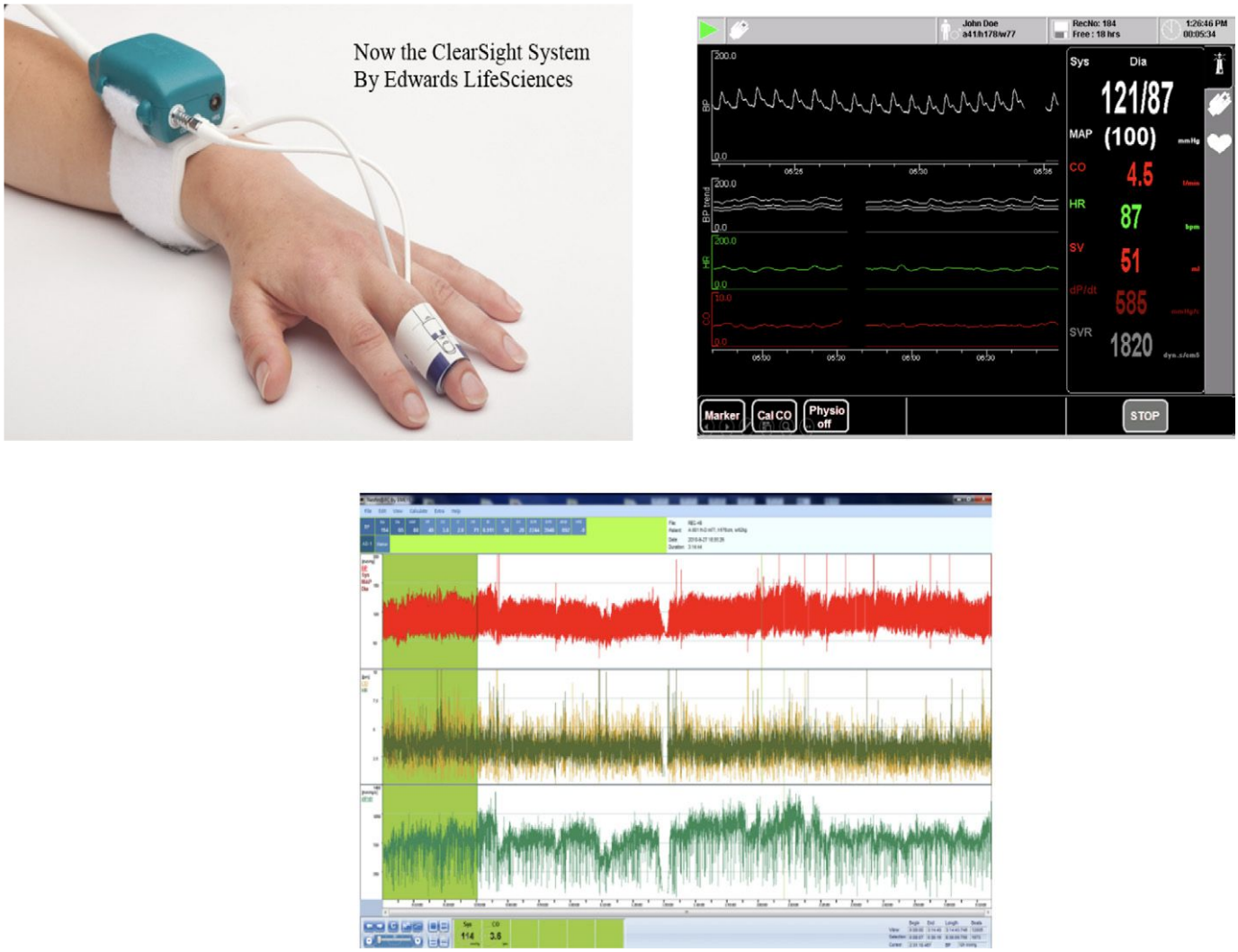

Figure 7. NEXFIN System

In AHF patients a delay in ED treatment has been associated with an increase in acute mortality and hospital length of stay. Consequently, fast and accurate evaluation of organ perfusion and total body congestion, consistent with the current ESC guidelines, are needed to start a tailored treatment using diuretic, vasodilators, or inotropic drugs. Clinical evaluation for the presence of peripheral edema, jugular vein distention, hepato-jugular reflux), lung rales, or the S3, are of great utility for therapeutical decision making.[8]

One of the most common diagnostic tools for detecting clinical congestion is the chest X-ray, which is commonly recommended and routinely performed. Nevertheless, in 86,376 patients from the ADHF Registry (ADHERE), the frequency of patient admission with negative chest radiography exceeded that of patients with positive chest radiography such that it is not possible to exclude the presence of congestion with a normal Chest Xray.[31] In an expert consensus document of the Group of the Acute Cardiovascular Care Association and the Committee of Acute Heart Failure from the Heart Failure Association of the European Society of Cardiology, the role of Echocardiography and lung ultrasonography for the proper assessment of congestion and cardiac hemodynamics has been clearly demonstrated.[4] However, issues on total body fluid content, cardiac output, and total peripheral resistance evaluations are still unsolved. Ultrasound technology has confirmed that, on the basis of vector length by BIVA measurement, it is possible to distinguish between dyspneic patients with and without AHF.

Natriuretic peptides (NPs) are widely used and recommended in AHF.[1] Their diagnostic role is a function of the relationship with intravascular pressure and volume overload, where they are used as a surrogate for cardiac hemodynamics of fluid overload.

One promising strategy is the combination of BIVA and BNP. This is because BIVA provides a more accurate estimation of peripheral congestion than BNP, while BNP provides superior prognostic characteristics. Therefore, BIVA in combination with BNP may be a fundamental tool, in consideration with the physical examination, in order to better stratify HF patients and detect the onset of peripheral congestion earlier.[13-16]

Conclusion

In summary, technological advances such as Biva, Nexfin, or NICas could allow for routine non-invasive continuous monitoring of Cardiac Hemodynamic and Fluid content in Acute Heart Failure patients. These initial non-invasive measurements may provide

important information for improving diagnosis, developing individualized therapeutic management plans/disposition decisions, and predicting

Take Home Message

1. An integrated approach to assess congestion by means of Biomarkers plus simple, non-invasive, highly reproducible methods (Natriuretic Peptides, +BIVA, Echocardiogram, LUS, and IVC US) would be more useful;

2. Invasive hemodynamic monitoring (Swan Ganz) is still considered of utility, but should not be used as a routine procedure (high cost, invasive).

3. Compared to currently used tools, New Biomarkers of Congestion such as Bio Adrenomedullin[32] together with Non- invasive cardiac hemodynamic and total fluid status monitoring by NICaS could provide Better Diagnostic and prognostic value (in-hospital mortality and readmission) also allowing monitoring of decongestion efficacy and organ perfusion of used treatment.

4. Further clinical studies are needed to confirm the real utility of all the actual used devices of non-invasive cardiac hemodynamics measurements in AHF patients in a wider numeric sample and multicentric study and to determine how to best use them.

Conflict of interest

There is no conflict of interest.

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