

Point-of-Care Ultrasonography for Acute Heart Failure

Letícia Braga Ferreira¹, Leonardo Carvalho da Paixão², Guilherme Ferraz Messina de Pádua Andrade³, Fernanda Cotrim Stefanelli⁴ and Milena Soriano Marcolino*⁴

¹Department of Cardiology, University Hospital of the Universidade Federal de Minas Gerais, Brazil

² Emergency Department, Hospital Municipal Odilon Behrens, Brazil

³Department of Cardiology, University Hospital of the Universidade Federal de Minas Gerais, Brazil

⁴Medical School, Universidade Federal de Minas Gerais, Brazil

***Corresponding author:** Milena Soriano Marcolino, Avenida Professor Alfredo Balena 190 room 246, Belo Horizonte, CEP 30130-100, Brazil, Tel: 55-3188130688; Email: milenamarc@gmail.com

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INTRODUCTION

Heart failure is a major public health problem worldwide. It is estimated that in Europe, there are currently 0.6 cases per 1000 for those aged below 65 years and 28 per 1000 in those aged above 65, which adds to around 20.8 million people affected by this condition [1]. In the USA, it is estimated a prevalence of over 5.8 million [2], and an additional 1.5 million new cases are diagnosed every year [3,4]. It is the only major cardiovascular disease whose prevalence and incidence are thought to be increasing, due to ageing of the population and improved survival rates following myocardial infarction [4]. Heart failure results in poor life expectancy, impaired quality of life, and consequently, it is a considerable economic burden to society [5]. Furthermore, it is associated with more extensive diagnostic workup and therapeutic efforts, increased healthcare costs, and higher rates of readmission and death [6]. Delay in diagnosis is associated with increased mortality; higher treatment costs and longer length of hospital stay [7]. It is currently the first cause of hospitalization in the elderly and the leading cause of health expenditure in the USA and in Europe [6].

Heart failure is usually a chronic condition, in which episodes of decompensation can occur, usually requiring hospitalization or more frequent outpatient visits. Alternatively, heart failure may present acutely with development of severe symptoms and signs within 24 hours [3]. Acute Heart Failure (**AHF**) refers to a quick start or an acute worsening of symptoms and signs of heart failure, along with elevated plasma levels of natriuretic peptides. It is a life-threatening condition that requires immediate medical attention and frequently leads to urgent hospitalization [8].

AHF may present as acute pulmonary edema secondary to cardiac dysfunction; cardiogenic shock, usually in the setting of an acute coronary syndrome; and acute decompensation of chronic heart failure, which corresponds to the majority of AHF cases [3]. The elevated left ventricular filling pressures, regardless of cardiac output, results in pulmonary congestion, responsible for the main symptoms of heart failure [9]. The majority of patients with AHF present with normal or high blood pressure and with symptoms or signs of congestion rather than low cardiac output [10].

Early diagnosis and prompt treatment are important to reduce morbidity and mortality. The Acute Decompensated Heart Failure Registry (**ADHERE**) is an electronic database in the United States, designed to assemble information on baseline characteristics, management strategies and outcomes of a broad sample of hospitalized patients with AHF. An analysis of the ADHERE Registry showed that patients admitted for AHF in emergency units had a shorter time to initiation of vasoactive drugs than those admitted to inpatient units (2.1 hours versus 35.9 hours). The group initially treated in the emergency department (ED) had shorter hospital stays (4.5 days versus 7 days) and lower hospital mortality (4.3% versus 10.9%) than the group initially treated in inpatient units [11].

Despite several critical steps forward in the management of heart failure, the diagnosis of AHF can still be challenging, as clinical, radiographic, and laboratory test parameters are insensitive and/or non-specific [12].

History and Physical Examination

A myriad of studies of heterogeneous quality agree on the poor accuracy of clinical examination findings for AHF diagnosis.

In order to understand the results of these studies, it is important to understand the concept of likelihood ratios (**LR**). The LR of a symptom or physical sign is the proportion of patients with disease who have a particular finding divided by the proportion of patients without the disease who also have the same finding [13]. The adjective positive or negative indicates whether the LR refers to the presence or to the absence of the symptom or sign. Therefore, negative LR is the proportion of patients with disease lacking a symptom or sign divided by the proportion of patients without disease also lacking the symptom or sign. “Positive LR” (**LR+**) describes how probability changes when the finding is present and “negative LR” (**LR-**) describes how probability changes when the finding is absent. Findings with LRs greater than 1 increase the probability of disease; and the greater the LR, the more compelling the argument for disease. Findings with LRs between zero

and 1 decrease the probability of disease; and the closer the LR is to zero, the more convincingly the finding argues against disease. Findings with LRs equal to 1 lack diagnostic value, as they do not change probability at all [13].

In a systematic review and meta-analysis [7] that included 22 studies and 5237 patients who presented to the ED with dyspnea, past history of heart failure was more useful to confirm (LR+ 5.8) than to exclude decompensation (LR- 0.45). The classical symptoms of paroxysmal nocturnal dyspnea (LR+ 2.6), orthopnea (LR+ 2.2), and dyspnea on exertion (LR+ 1.3) increased the likelihood of AHF less than desired. The absence of these symptoms performs even worse to exclude AHF diagnosis: LR- 0.48, LR- 0.65 and LR- 0.70, respectively.

The excellent LR+ of 11 of the third heart sound (**S3**) was antagonized by the combination of a poor interobserver reliability [14-16] and the inutility of its absence (LR- 0.88). The chaotic ED environment and the nature of the patient comorbid conditions help to understand the inaccurate performance of other physical examination findings, as shown in Table 1, and contribute to explain why the clinical judgment alone was just moderately accurate for the diagnosis of AHF (LR+ 4.4, LR- 0.45).

Table 1: Diagnostic accuracy of findings on history and physical examination for acute heart failure in emergency department patients.

	Sensitivity	Specificity	LR+	LR-
History				
Heart failure	0.60	0.90	5.8 (4.1-8.0)	0.45 (0.38-0.53)
Myocardial infarction	0.40	0.87	3.1 (2.0-4.9)	0.69 (0.58-0.82)
COPD	0.34	0.57	0.81 (0.60-1.1)	1.1 (0.95-1.4)
Symptoms				
Paroxysmal nocturnal dyspnea	0.41	0.84	2.6 (1.5-4.5)	0.70 (0.54-0.91)
Orthopnea	0.50	0.77	2.2 (1.2-3.9)	0.65 (0.45-0.92)
Edema	0.51	0.76	2.1 (0.92-5.0)	0.64 (0.39-1.1)
Dyspnea on exertion	0.84	0.34	1.3 (1.2-1.4)	0.48 (0.35-0.67)
Fatigue and weight gain	0.31	0.70	1.0 (0.74-1.4)	0.99 (0.85-1.1)
Cough	0.36	0.61	0.92 (0.70-1.2)	1.0 (0.87-1.3)
Physical examination				
Third heart sound	0.13	0.99	11 (4.9-25.0)	0.88 (0.83-0.94)
Jugular venous distension	0.39	0.92	5.1 (3.2-7.9)	0.66 (0.57-0.77)
Hepatojugular reflux	0.24	0.96	6.4 (0.81-51)	0.79 (0.62-1.0)
Rales	0.60	0.78	2.8 (1.9-4.1)	0.51 (0.37-0.70)
Any murmur	0.27	0.90	2.6 (1.7-4.1)	0.81 (0.73-0.90)
Lower extremity edema	0.50	0.78	2.3 (1.5-3.7)	0.64 (0.47-0.87)

LR: likelihood ratio; **COPD:** chronic obstructive pulmonary disease [7].

Chest X-Ray

Chest x-ray has classically been used to diagnose AHF in the ED, but it is also imperfect. Interstitial edema is the most specific radiologic finding, but it has low sensitivity (LR+ 12.0, LR- 0.68). Additionally, chest x-ray interpretation agreement between radiologist and emergency physician can be less than 50% [17]. This could result in many patients with AHF not receiving appropriate treatment.

Electrocardiography

The electrocardiogram (ECG) is rarely normal in AHF patients, but it is non-diagnostic. It is more useful to assess arrhythmias as the cause for decompensation and to exclude ST segment elevation myocardial infarction [8].

Biomarkers

B-type natriuretic peptide (BNP) and N-Terminal proBNP (NT-proBNP) have emerged as promising markers for AHF diagnosis [18]. Both have good accuracy in predicting heart failure as the cause of dyspnea in patients admitted to the ED. Observational studies have shown that higher levels of BNP and NT-proBNP correlate with poorer left ventricle ejection fraction (LVEF), worse functional classes and higher mortality [19, 20].

A recent systematic review and meta-analysis on the accuracy of natriuretic peptides for the diagnosis of heart failure in the emergency setting, which included 37 studies and 15263 test results, found excellent sensitivity and modest and variable specificity (Table 2) [21]. These results confirm the important role of these biomarkers in ruling out heart failure as the cause of dyspnea in the ED [21]. As the specificity of the natriuretic peptides is modest and variable, confirmatory diagnostic testing by cardiac imaging is required in case of positive results.

Table 2: Diagnostic accuracy of B-type natriuretic peptide (BNP) and N-terminal proBNP (NT-proBNP) for heart failure in the acute care setting.

	Sensitivity (CI)	Specificity (CI)	LR+	LR-	AUC
BNP ≤ 100ng/l	0.95 (0.93-0.96)	0.63 (0.52-0.73)	2.57	0.08	0.79
NTproBNP ≤ 300ng/l	0.99 (0.97-1.00)	0.43 (0.23-0.62)	1.74	0.02	0.71

LR: likelihood ratio, AUC: area under the curve [21].

Furthermore, natriuretic peptide-guided treatment of chronic heart failure has been shown to reduce morbidity and mortality when compared to usual care [22,23]. A randomized controlled trial is in course to assess the impact of such a strategy on outcomes of patients with AHF [24].

POINT-OF-CARE ULTRASOUND FOR ACUTE HEART FAILURE

Point-of-care ultrasound examinations are performed in real-time at the bedside by clinicians to answer specific questions in order to improve patient care. These examinations are not intended to provide comprehensive surveys of anatomical areas. Instead, they provide imaging to rule in or rule out specific disease entities for which timely treatment is crucial. Point-of-care ultrasound has been widely referred to as “the new stethoscope”. It is easy to learn, fast, noninvasive and highly reproducible [25,26].

Thoracic ultrasound for assessment of interstitial edema and cardiac dysfunction and abdominal ultrasound for assessment of inferior vena cava (IVC) diameter, performed by emergency physicians during patient's initial evaluation, may represent an accurate and reproducible bedside tool for discriminating between cardiogenic and non-cardiogenic dyspnea [8,27]. In this chapter, we will briefly review the use of ultrasound in this context.

The Basics

The lungs have long been considered unsuitable for ultrasound imaging, since large changes in acoustic impedance (such as those occurring between air and anatomical tissues) result in ultrasound complete reflection [25]. However, the interposition of different media, such as fluids, between the aerated lung tissue and the ultrasound probe, generates artifacts that, when correctly interpreted, give physicians plenty information to diagnose respiratory disorders [26]. A better understanding of these artifacts was achieved through the last decades and led to the widespread use of this tool in acute healthcare settings. Artifacts resulting from high attenuation of sound waves by the aerated lung are currently being used to interpret lung pathophysiology, including in cases of interstitial edema. Volume status may be assessed by IVC diameter and its degree of change with respiratory cycle. Diagnostic transthoracic echocardiography plays a well-known role in the diagnosis and management of the patient presenting with cardiopulmonary symptoms. The combination of estimated volume status, left ventricular function and presence of interstitial edema by lung ultrasound are the mainstay of ultrasound evaluation in AHF [26].

The correct choice of the probes (Figure 1) may potentiate best images [26]:

- **Linear probe:** This high frequency probe (7-13 MHz) may help in pleural affections, but is a poor choice for the cardiac exam or volume status determination;
- **Curvilinear probe (2-5 MHz):** Ideal for abdominal images, it may bring challenges in cardiac exam;
- **Phased array probe:** Ideal for cardiac examination, it also gets good images of IVC and pleural effusions. Some examiners may find tricky to get interstitial lung images with this probe;
- **Micro convex probe:** The versatile probe.



Figure 1: Linear (A), curvilinear (B) and phased array (C) probes.

Volume Status

The absolute diameter and respiratory variation (or collapsibility) of IVC are useful ultrasonographic parameters for the diagnosis of AHF. The primary role of IVC bedside evaluation is to help in the assessment of the intravascular volume status, as the vessel diameter and its collapsibility with respiration may give an estimate of central venous pressure (CVP) and correlate with invasive measurements [25,26].

In the classical approach, ideally with a phased array or microconvex probe (low-frequency probe), in sub costal sagittal view (or subxiphoid), IVC is usually measured about 3-4 cm distal to its junction with the atrium or 2-cm distal to the entry of the hepatic veins (Figure 2) [25].

During physiologic inspiration, negative intrathoracic pressure increases venous return to the right atrium, leading to a reduction in IVC diameter. Hypervolemia and ventricular dysfunction cause IVC distension and attenuate its collapsibility during inspiration. Collapsibility index is the ratio of IVC variation and IVC maximal diameter, calculated as [25,26]:

IVC collapsibility index = (IVC maximal diameter - IVC minimum diameter) / IVC maximal diameter

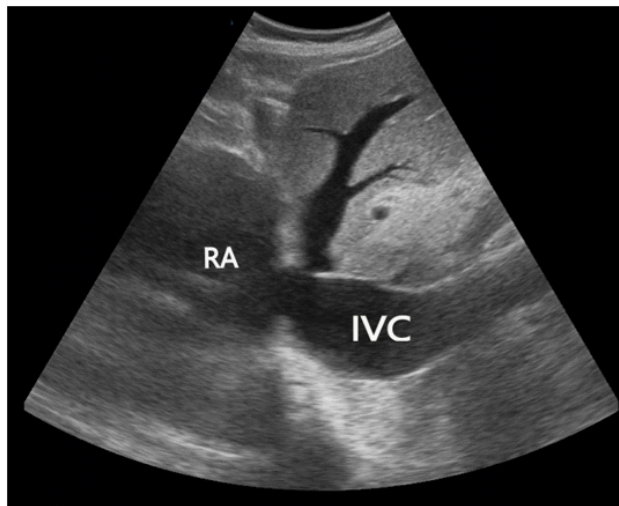


Figure 2: Inferior vena cava, subxiphoid view. IVC diameter is measured 3-4 cm distal to its junction with the atrium or 2-cm distal to the entry of the hepatic veins. **HV:** hepatic vein, **IVC:** inferior vena cava, **RA:** right atrium.

Classically, the following absolute measures and their variations could be used as guidance [26]:

- IVC < 1.5cm and total collapse: CVP probably < 5cm H₂O
- IVC > 2.5cm and no collapse: CVP probably < 20cm H₂O
- IVC 1.5-2.5 cm and with collapsibility index > 50%: CVP probably 5-15cm H₂O
- IVC 1.5-2.5 cm and with collapsibility index < 50%: CVP probably 10-20cm H₂O

M-mode assessment of the IVC makes it easier to measure the diameter throughout the respiratory cycle, as shown in (Figure 3).



Figure 3: Inferior vena cava (IVC), M Mode. Placing the sampling line through the point in the IVC designated for measurement allows for assessment of respiratory cycle variations. In this example, it is possible to observe lack of inspiratory collapse due to fluid overload.

Cardiac Ultrasound

The primary role of emergency cardiac ultrasound, or Focused Cardiac Ultrasound (**FOCUS**), is the timely assessment of life-threatening conditions that may affect the heart, directly or indirectly (Table 3). In AHF and other settings, this is achieved by visual assessment (“eyeballing”) of the heart chambers sizes, global function, and specifically, left ventricle (**LV**) systolic function, pericardial effusions and marked segmental wall-motion abnormalities. It is useful as a diagnostic tool and also to guide emergent invasive procedures, but should not preclude referral for comprehensive echocardiography, when indicated [28].

Table 3: What and how: goals of the Focused Cardiac Ultrasound (**FOCUS**) in acute settings.

WHAT	HOW
Global cardiac function (specially LV systolic function and size)	Based on eyeballing technique; should differentiate “normal” from “depressed” global function and identify dilated chambers.
Pericardial effusion	Use multiple views to confirm the presence of, and quantify pericardial effusion. Must match clinical findings in order to diagnose cardiac tamponade: hypotension, tachycardia, pulsus paradoxus; RA and RV diastolic collapse are early signs of hemodynamic repercussion and may be perceived on FOCUS
Prominent right ventricular enlargement	Helpful if positive in the suspicion of massive pulmonary embolus (RV dilatation and decreased systolic function); negative findings are insufficient to exclude PE

LV: left ventricle; PE: pulmonary embolism; RA: right atrium; RV: right ventricle.

The phased array probe is the first choice for cardiac imaging, but a microconvex probe is also a suitable option. The four standard views are subcostal (or subxiphoid) view, apical four-chamber view (Figure 4) and parasternal long axis (Figure 5) and short axis (Figure 6) views.

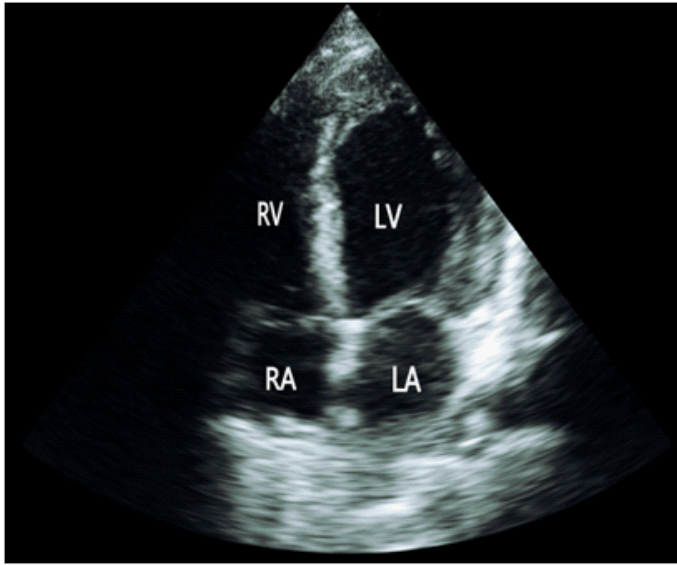


Figure 4: Apical four-chamber view. This view is good for visual assessment (“eyeballing”) of the heart chambers sizes, global function, and specifically, left ventricle systolic function, wall thickness, and segmental wall function. **LA:** left atrium, **LV:** Left ventricle, **RA:** right atrium, **RV:** right ventricle.

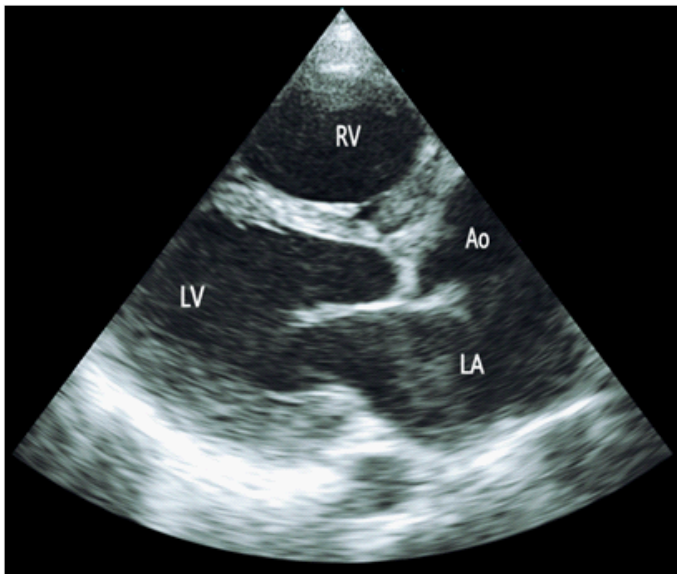


Figure 5: Parasternal long axis view. In this view, the right ventricular outflow tract is in the upper portion of the image, as it is the closest to the probe. This view is useful for assessment of left ventricle chamber size and contractility, segmental wall function, wall thickness, and the interventricular septum.

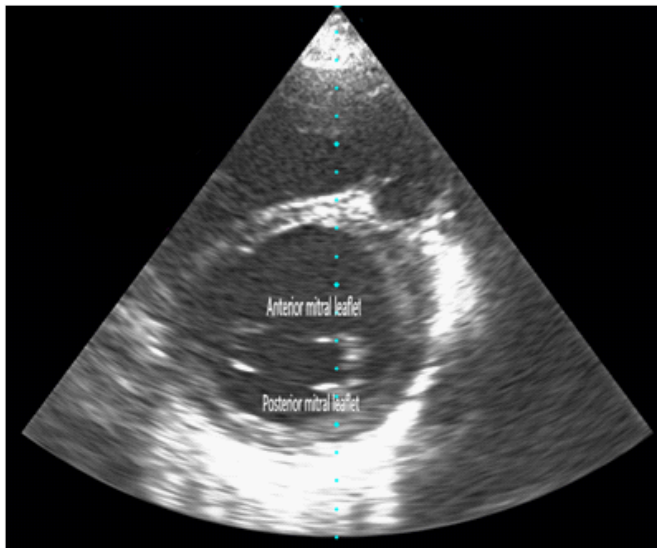


Figure 6: Parasternal short-axis view at the level of mitral valve leaflets. This view allows assessment of segmental endocardial motion, wall thickening, and septal kinetics.

To a full integration of ultrasound evaluation in the acute ill patient, we suggest:

- Integrate the ultrasound examination in the ABCDE paradigm;
- Do not delay already established necessary interventions (oxygen, patient position optimization, analgesics) and try not to unsettle multidisciplinary proceedings (cardiopulmonary resuscitation, intubation, non-invasive ventilation);
- Previous knowledge of the ultrasound equipment.

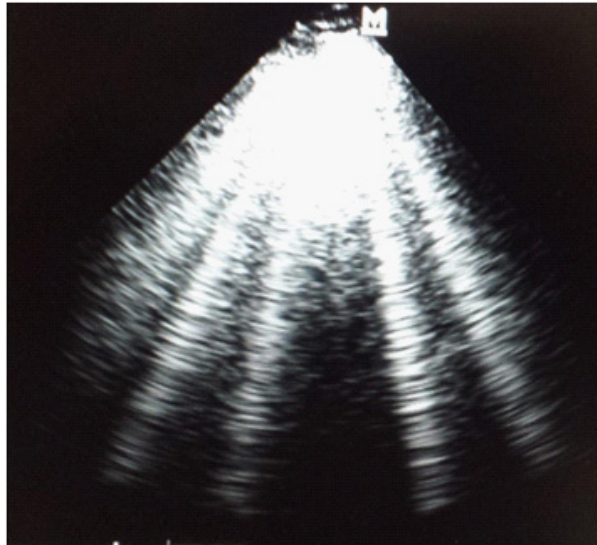
Lung Ultrasound (LUS)

In the absence of an acoustic mismatch, the ultrasound beam dissipates quickly in the air. The normal, aerated lung, do not produce visible image on ultrasound except for the pleura. The reverberation artifacts of repetition between the pleura and the skin surface produce horizontal, motionless, regularly spaced hyperechogenic lines, parallel to the pleural line, which are called A-lines [27,29].

When this content of air decreases, usually substituted either by liquid or by fibrosis, new images, sound artifacts, appear. The interpretations of the information provided by these artifacts are responsible for the innovation in the bedside ultrasound. B-lines (also called comet tail artifacts) are hyperechoic reverberation artifacts that originate at the pleural line and extend radially outwards to the edge of the screen, perpendicular to the pleural line [27,29]. They move across the screen with pleural sliding and do not fade as they extend. B-lines are artifacts indicative of interstitial thickening, and are the cornerstone of LUS. When interstitia and alveoli become edematous with fluid, as in AHF, B-lines become more prominent, numerous, and diffuse (Figure 6), and obliterate the A-lines. Single B-lines can be a normal finding. Multiple B-lines have also been described in pneumonia, acute respiratory distress syndrome, and pulmonary fibrosis [27,29]. Therefore, the

analyses of the features and the numbers of these B-lines will help to differentiate single B-lines to those that are due to interstitial fluid and to assess the severity of the edema (Figure 7).

Figure 7: Pulmonary B-lines.



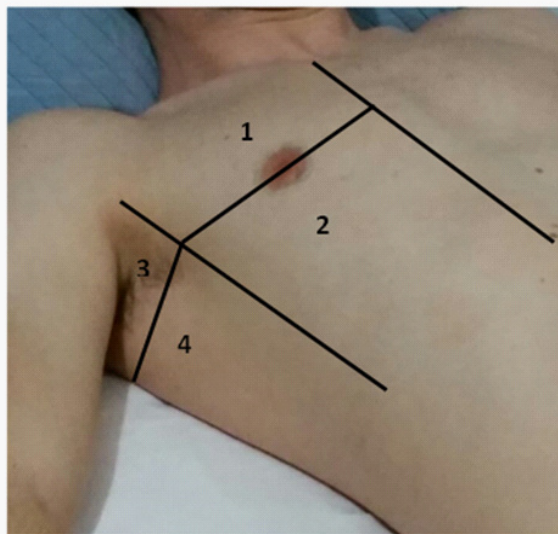
BEDSIDE ULTRASONOGRAPHY ACCURACY IN DIAGNOSING ACUTE HEART FAILURE

Several studies have evaluated the accuracy of bedside ultrasound in diagnosing AHF and other conditions. Most of them have been prospective cohorts and have chosen as the standard criterion the final diagnosis established by complete chart review including clinical exam, laboratory and image methods and response to therapy.

A meta-analysis published in 2014 [30] included 7 studies of average to high quality, comprising 1075 patients with dyspnea, and assessed the accuracy of B-lines detected by different lung US protocols to predict AHF. They found a pooled sensitivity of 94.1% (95% confidence interval [CI] = 81.3% to 98.3%), and a pooled specificity of 92.4% (95% CI = 84.2% to 96.4%).

A more recent paper [31] divided B-lines profiles in lung ultrasound in 5 different categories, showing that the number and distribution of B-lines affect the accuracy of the findings. The thorax was divided in 8 zones (Figure 8) and a lung zone was considered positive if three or more B-lines were identified in an intercostal space, ranging from “anything positive” (one or more lung zones having ≥ 3 B-lines) to “all positive” (all 8 lung zones exhibiting ≥ 3 B-lines). While the category “anything positive” had the highest sensitivity with low specificity [sensitivity 85% (95%CI 78–90%), specificity 58% (95% CI 52–64%), LR+2.1 (95% CI 1.7–2.4) and LR- 0.3 (95% CI 0.2–0.4)], the category “all positive” had the highest specificity and the lowest sensitivity [sensitivity: 12% (95% CI 7–18%), specificity: 99% (95% CI 96–100%), LR+ 9.2 (95% CI 2.7–31.3), LR- 0.9 (95% CI 0.8–1.0)].

Figure 8: The right chest divided into four lung zones according to the Volpicelli method



[32]. Zones 1 and 2 correspond to the anterior superior and inferior lung zones, respectively. Zones 3 and 4 correspond to the axillary superior and inferior zones. On the left chest, zones 5 and 6 correspond to zones 1 and 2, and zones 7 and 8 correspond to zones 3 and 4, respectively. The margins delineating the anterior chest are the parasternal and anterior axillary lines, while the lateral chest margins are defined by the anterior and posterior axillary lines. The horizontal border is the nipple line or fourth intercostal space.

Yamanoglu et al [33] evaluated different methods and cutoffs of IVC diameters and collapsibility in a cohort of 74 patients with dyspnea, and found that IVC minimum diameter (measured at end-inspiration on bidimensional mode) had the larger area under the ROC curve (0.876) to predict AHF at a cutoff of 9 millimeters (sensitivity 84.4%; specificity 92.7% LR+ 11.8 LR- 0.16). IVC collapsibility index measured on bidimensional mode also had a good performance, with sensitivity of 84.4% and specificity of 90.5% at a cutoff of 50.5% (LR+ 8.8 and LR- 0.17).

In another cohort, by Kajimoto et al [34], which included 90 patients admitted to the emergency room with acute dyspnea who underwent ultrasound examination within 30 minutes of admission, IVC collapsibility index <50% had sensitivity of 83.0% and specificity of 81.1% for AHF.

Finally, estimation of heart dimensions and function on bedside ultrasound help diagnosing AHF. Depressed left ventricular ejection fraction had sensitivity of 77% and specificity of 74% at a cutoff of 45%, resulting in an accuracy of 82.2% [35]. Left ventricular end-diastolic diameter, at a cutoff of 28.6 millimeters, had a similar performance with an area under the ROC curve of 0.76 (sensitivity: 80.4% and specificity: 68.4%) [36]. A more detailed cardiac ultrasound, with visual estimation of LVEF and pulsed and tissue doppler of mitral valve for estimation of left ventricular filling pressures had a higher accuracy (85%), with sensitivity of 80% and specificity of 93% [37].

Combining two or more findings significantly increases accuracy of bedside ultrasound. The

combination of estimated left ejection fraction of less than 45%, 10 or more B-lines on lung ultrasound and IVC collapsibility index of less than 20% achieved a virtually perfect specificity (100%) at the expense of a low sensitivity (36%) [35]. The most accurate combination was positive lung ultrasound (2 or more zones with B-lines bilaterally), left ventricular dysfunction (LVEF<40%) and IVC collapsibility index <50% (sensitivity: 94.3%, specificity: 91.9%, LR+ 11.64, LR- 0.06 and AUC 93.3) [34].

Reproducibility and Interobserver Variability

When evaluating the usefulness of a diagnostic test, our attention is generally focused on items such as sensitivity, specificity and likelihood ratios. However, if the physicians who actually interpret the test cannot agree on the interpretation, the test results will be of little use. Therefore, as important as the validity of the test is the reproducibility and interobserver variability [38].

Kappa statistic (κ) is a measurement of interobserver agreement for categorical items. It is more robust than simple percent agreement calculation, once it takes into account the agreement occurring by chance. Kappa is standardized to lie on a -1 to 1 scale, where 1 is perfect agreement, 0 is exactly what would be expected by chance, and negative values indicate agreement less than expected by chance. Kappa values of 0.81-1.0 are considered to be almost perfect agreement [38].

In addition to having good sensitivity and specificity for the diagnosis and management of patients with AHF, point-of-care ultrasonography also has excellent reproducibility, making it a more reliable tool than classical physical examination and chest radiography assessment.

In a study that used a lung and cardiac ultrasound protocol performed by 3 experienced emergency physician sonographers in evaluation of 99 patients presenting to the ED with undifferentiated dyspnea, the interobserver agreement was 93% ($\kappa = 0.82$) for the diagnosis of AHF [39].

Even when performed by inexperienced sonographers, bedside ultrasound shows good reproducibility. In an Italian study that used ultrasound for the diagnosis of 56 non-consecutive patients who presented in the ED with a chief complaint of dyspnea, agreement between experienced and inexperienced examiners was 92.2% for the diagnosis of acute interstitial syndrome and 95% for the diagnosis of pleural effusion [40].

In a cohort of 66 emergency medicine resident physicians who had received a brief 30-minute lecture on technique and recognition of sonographic B-lines, performance was similar to expert sonographers for diagnosis of AHF in 380 patients presenting to the ED with a chief complaint of dyspnea (AUCs for novice and expert sonographer were 0.77 and 0.76, respectively) [31].

CONCLUSION

In conclusion, point-of-care ultrasonography is fast, inexpensive, easy to learn and provides immediate information to the clinician. It has good accuracy, superior to standard diagnostic tests alone for establishing a correct diagnosis of AHF. Therefore, it is very useful for diagnosis and management of patients admitted to the ED with dyspnea.

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