Ultrasound imaging of congestion in heart failure – Examinations beyond the heart

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Abstract

Congestion, related to pressures and/or fluid overload, plays a central role in the pathophysiology, presentation and prognosis of heart failure and is an important therapeutic target. While symptoms and physical signs of fluid overload are required to make a clinical diagnosis of heart failure, they lack both sensitivity and specificity, which might lead to diagnostic delay and uncertainty. Over the last decades, new ultrasound methods for the detection of elevated intracardiac pressures and/or fluid overload have been developed that are more sensitive and specific, thereby enabling earlier and more accurate diagnosis and facilitating treatment strategies. Accordingly, we considered that a state-of-the-art review of ultrasound methods for the detection and quantification of congestion was timely, including imaging of the heart, lungs (B-lines), kidneys (intrarenal venous flow), and venous system (inferior vena cava and internal jugular vein diameter).

Key words: Ultrasound, heart failure, B-lines, inferior vena cava, intrarenal venous flow, jugular vein**.**

Background

Congestion, related to pressure and/or volume overload, is fundamental to the pathophysiology, presentation and prognosis of heart failure (HF) [1,2]. Early detection of elevated cardiac or venous pressures is important, as intensification of treatment before signs and symptoms worsen may reduce morbidity in patients with HF [3].

Despite their importance, the clinical identification and quantification of HF signs or symptoms remains challenging even for experienced physicians[4,5]. Clinical symptoms and signs are late manifestations of congestion and are neither sensitive nor specific for HF. Moreover, no agreement exists on how to grade signs of fluid overload[6]. The measurement of natriuretic peptides, a measure of myocardial wall stretch, is recommended as a diagnostic tool in the assessment of patients with suspected HF and provides important prognostic information[1]. However, natriuretic peptide levels are influenced by many factors, including age, body mass index and atrial fibrillation, and natriuretic peptide-guided treatment has not been convincingly shown to improve outcomes in patients with HF[7]. Other costly and invasive tools can monitor pulmonary artery pressure to help guide therapies. However, more evidence is needed on patients' selection and the cost-effectiveness of these devices [3,8]. Non-invasive technologies to assess fluid status such as weighing-scales, cardiac bio-impedance, and remote dielectric sensing (ReDS) are being investigated but, apart from weight, have not been widely adopted [9,10].

Ultrasound continues to play a key role in the non-invasive assessment of cardiac structure and function in patients with HF. The aim of this review is to describe ultrasound measurements that move beyond the heart and are associated with either a) elevated venous

pressures (inferior vena cava and internal jugular vein diameter and intrarenal venous flow) or b) extravascular fluid in the lungs (B-lines) that may be useful in the assessment and monitoring of patients with known or suspected HF. In the next paragraphs we will describe how to perform and interpret these techniques (central figure) and briefly summarise the current state of evidence supporting their clinical use.

Cardiac ultrasound (echocardiography)

Transthoracic echocardiography (TTE) plays a central role in the diagnosis and management of patients with HF. TTE is the most available method to measure left ventricular ejection fraction (LVEF), which is used to categorise patients as HF with reduced (HFrEF) or preserved LVEF (HFpEF), a distinction relevant for their management. TTE can also rapidly exclude, or identify, the presence of significant valvular disease, previously undetected congenital problems, and pleural or pericardial effusions. However, many people with breathlessness do not have reduced LVEF or valve disease to account for their symptoms, but left ventricular hypertrophy and impaired long-axis systolic dysfunction by global longitudinal strain are common findings[11]. The evaluation of mitral inflow, mitral annulus motion by tissue Doppler imaging and left atrial volumes and function provide additional estimates of left ventricular filling pressures [12], but no universal agreement exists on how to combine them to identify individuals at greater risk [1,13,14]. Pulmonary hypertension, right ventricular dysfunction and greater severity of tricuspid regurgitation all indicate a worse outcome and can be assessed on TTE, but their evaluation might be limited by poor acoustic window or inability to obtain a clear Doppler signal [15]. As the comprehensive evaluation of cardiac structure and function in HF goes beyond the scope of this review, the following sections focus on the extracardiac ultrasound methods for the assessment of raised venous pressures and extravascular lung fluid in HF [16].

Inferior vena cava ultrasound

The inferior vena cava (IVC) is a compliant vessel, in anatomical continuation with the right atrium. Any change in right atrial pressure is transmitted backward, and modifies IVC size: a substantial and sustained increase in right atrial pressure, as seen in heart failure, would eventually cause IVC distention. However, studies conducted in patients undergoing cardiac catheterisation have only found modest correlations between right atrial pressure and IVC diameter measured by echocardiography[17]; these relations are even weaker in those who are mechanically ventilated (table 1)[18].

How to perform IVC ultrasound

The diameter of the IVC should be measured with a phased array or curvilinear transducer with the patient in supine position in the subcostal view at 1.0 to 2.0 cm from the junction with the right atrium, using the long-axis view [19]. For accuracy, this measurement should be made perpendicular to the long axis of the IVC.

How to quantify and interpret IVC ultrasound

Measurement of the IVC diameter and its changes with respiration is possible in most adults. An IVC smaller than 21 mm that collapses >50% suggests normal right atrial pressures[19]. IVC diameter might detect increasing intravascular volume even prior to any change in symptoms or body weight in ambulatory HF patients [10], or monitor response to diuretics in hospitalised patients with heart failure [20]. Persistent IVC engorgement predicts a poor outcome[21-23]. Whether diuretic therapy guided by serial IVC assessments, compared with usual care, might decrease rehospitalisation in patients admitted for HF is currently under evaluation (NCT03140566; NCT02892227). In ambulatory patients with HF who are already on

treatment, guidelines do not recommend monitoring cardiac function or ventricular filling pressures routinely by echocardiography, unless there is substantial clinical deterioration. However, up to half of HF patients with minimal symptoms, and without clinical signs of congestion, have a dilated IVC and other abnormal ultrasonic markers of elevated intracardiac pressures or extravascular lung fluid, which are also associated with elevated NPs and an increase in mortality [24].

Internal jugular vein ultrasound

An elevated jugular venous pressure (JVP) is a marker of volume or pressure overload and right ventricular failure, and associated with an increase in mortality in patients with HF [25]. Clinical evaluation of the JVP is subjective, requires clinical expertise and can be challenging in obese patients. Therefore, identifying and quantifying JV distention is difficult and an elevated JVP may be missed clinically [26,27].

How to assess internal jugular vein by ultrasound

The internal jugular vein (IJV) is a superficial and distensible vessel, which lies close to the carotid artery, under the sternocleidomastoid muscle and can be easily visualised with ultrasound. Assessment of IJV should be performed with the patient reclining and head and neck elevated at 45° (semi-recumbent position). Care should be taken to avoid IJV compression during examination. When the patient is supine, the IJV is likely to be distended, but in a sitting position JVP drops and the IJV often collapses. When central venous pressure is low, it may be difficult to visualise the IJV; asking the patient to cough, or to perform a Valsalva manoeuvre, will lead to engorgement, allowing it to be identified on ultrasound.

The IJV can be imaged by placing a high frequency linear transducer (~10 MHz) just below the angle of the jaw, in the area of the sternocleidomastoid muscle, and then moving it inferiorly toward the angle of Louis (or manubriosternal junction). In most cases, the IJV is identified less than 5 cm below the angle of the jaw. Subsequently, the IJV diameter and its changes are measured continuously by M-mode, or in a 2-dimensional frame, at rest and during a Valsalva manoeuvre. The ratio between the maximal diameter during the Valsalva manoeuvre to that at rest (at the end of the expiratory phase) is called the JVD ratio (Figure 1). Measuring the JVD ratio can be done in almost all patients and inter-observer variability is low [28]. Other authors have proposed measuring the cross-sectional area of the IJV, and how it changes during the Valsalva manoeuvre, to identify patients with elevated right atrial pressure [29,30].

How to interpret images of the internal jugular vein

In people without HF, or in patients in whom congestion is adequately controlled, the diameter of the IJV is small at rest (~ 0.10-0.15 cm), but increases several-fold during a Valsalva manoeuvre (usually up to ~ 1 cm) [28,31.]. Because of limited vessel compliance, the maximal IJV diameter that can be achieved during a Valsalva maneuver is similar in people with or without HF. When intra-vascular congestion worsens, it increases the IJV diameter at rest, leading to a reduced JVD ratio. A JVD ratio below 4 is abnormal and, when congestion is severe, the ratio may decrease to <2 [24,28,31].

In ambulatory HF patients, a low JVD ratio is poorly related to measures of left ventricular size or systolic function, but strongly associated with severe symptoms, elevated NPs, right ventricular dysfunction and tricuspid regurgitation [28]. A low JVD ratio predicts a worse outcome in terms of HF hospitalisations or deaths, independently of NT-proBNP [24,27,31] .

When IJV cross-sectional area, rather than its diameter, is used, a large variation during a Valsalva manoeuvre identifies patients more likely to have normal right atrial pressure and better outcomes [29,30]. Obviously, a Valsalva maneuver depends on the patient's effort and ability to follow instructions. For those who are acutely unwell, or cannot perform a Valsalva maneuver, other techniques, such as passive leg raising, may increase central venous pressure (CVP) but their effects on IJV diameter have not been assessed yet.

Renal venous ultrasound

Worsening renal function in acute HF is common and has been linked to elevated CVP, leading to raised renal interstitial pressures, partial collapse of nephrons, ischemia and neurohormonal activation[32]. Recently, ultrasound techniques to assess renal blood flow in HF have been described [33-36]. Although renal arterial flow can be assessed with Doppler ultrasound and predicts HF progression [37], an elevated CVP primarily affects renal venous flow (RVF).

How to perform renal venous Doppler ultrasound

Doppler assessment of RVF is performed in the left lateral decubitus position, using a convex or sector transducer (2.5-5 MHz) aligned with the lowest intercostal space rendering a longitudinal view of the right kidney. Using color Doppler imaging with the flow scale adjusted to low-flow velocities (preferably not more than 20 cm/s), the interlobar veins are identified. The best aligned vein is then sampled with pulsed wave Doppler during an end-expiratory breath-hold. The scale should again be adjusted, maximizing the amplitude of the signal (usually around – 20 cm/s) and the ECG signal should be displayed to synchronize the RVF signal with the cardiac cycle.

How to interpret renal venous Doppler

In normal conditions, the interlobar RVF is continuous with a small varying amplitude during the cardiac cycle [38]. When CVP increases, the variation of amplitude increases with the minimal velocity gradually approaching zero and eventually leading to an early discontinuous flow or 'pulsatile' flow [39] (Figure 2). If CVP increases further, a biphasic pattern can be recognized with two separate flow phases during a cardiac cycle. In very severe cases, the RVF can become monophasic with a single flow phase in diastole. Analyzing the RVF pattern thus allows a semi-quantitative assessment of the effects of CVP on renal hemodynamics. Other more quantitative measures are the venous impedance index (VII) and the venous discontinuity index (VDI). The VII is the ratio of the difference between maximum and minimum velocity to the maximum velocity during a cardiac cycle with a number varying from 0 (no variation in velocity) to 1 (minimum velocity is zero) [38]. As CVP increases the variation in RVF amplitude, the VII also increases until flow becomes discontinuous and VII becomes 1. Higher VDI, expressed as the percentage of no-flow time during a cardiac cycle, is another measure of congestion. Of note, other conditions that increase CVP (i.e. obstruction), intra-abdominal pressure (i.e. ascites) or intraparenchymal renal pressure (i.e. obstructive uropathy) can also impair RVF [40].

Despite its potential, to date, only a few studies have evaluated the role of RVF assessment in HF management. For inpatients with HF (n=217), a monophasic pattern suggests very high right atrial pressures (RAP) and a poor prognosis [33]. Another study evaluated the effect of volume loading and diuretics on RVF in 50 patients with stable HFrEF or HFpEF [34]. After volume loading, the VII increased substantially and the number of patients with discontinuous RVF increased from 32% to 80% without any change in IVC estimated CVP, perhaps

suggesting that RVF is an earlier marker of the development of congestion. Interestingly, patients with a lower VII (indicating less renal congestion) had a better diuretic response.

Lung ultrasound

Lung ultrasound (LUS) can be used for the identification and quantification of extravascular lung fluid in patients with known or suspected HF, at rest or even with exercise[41,42]. So called 'B-lines' are vertical lines that arise from the pleural line and extend to the far-field of the ultrasound screen (Figure 3) [43]. B-lines are often observed in patients with HF, but can also occur in other conditions, such as non-cardiogenic pulmonary oedema and interstitial lung disease [44,45].

How to perform lung ultrasound

Several LUS image acquisition protocols have been described, ranging from 4 to 28 chest regions or "zones", but the simplified 8-zone protocol is increasingly used both in the clinical setting and for research. During LUS examination, patients are positioned either sitting upright, semi-recumbent or supine. Patients should preferably be imaged in the same position if serial examinations are being performed, as B-line number may be influenced by patient position, with higher B-line counts in supine position [46]. A phased array or curvilinear transducer is placed in an intercostal space in a chest zone either perpendicular (longitudinal, sagittal) or in parallel orientation (transverse) to the ribs at an imaging depth of ~15-18 cm. Once the gain settings are optimised for visualization of the pleural line and any B-lines, a 6 second clip is recorded with the patient breathing normally [47,48]. Large pleural effusions may interfere with B-lines identification and should be reported, if seen on ultrasound.

How to quantify and interpret B-lines

LUS is more sensitive for the diagnosis of interstitial pulmonary oedema and heart failure than the clinical examination or chest x-ray in patients with acute dyspnea (Figure 3) [49,50]. There are several different approaches to quantifying B-lines. Broadly, these can be grouped into two categories: score or count based methods. Score based methods consider a minimum number of B-lines in one intercostal space as a "positive" zone (typically at least 3 B-lines) and then adding up the number of positive zones [48,51]. B-lines can be counted either one by one in one chest zone[52,53] or, when confluent, their number can be estimated from the percentage of space they occupy on the screen below the pleural line, divided by 10 (i.e. if about 70% of the screen below the pleural line is occupied by B-lines, it would conventionally count as 7 B-lines, up to a maximum of 10 per zone)[54-57]. All these methods have demonstrated good intra- and inter-reader agreement [58,59]. In patients with dyspnea presenting to the emergency department, a cut off value of ≥3 B-lines in at least two zones per hemithorax (of 6-8 evaluated zones in total) identifies patients with acute HF with higher sensitivity (94-97%) and specificity (96-97%) than the physical examination and chest x-ray (and NT-proBNP) (sensitivity 85%, specificity 89-90%) compared to chart review by two physicians [49,51]. A high number of B-lines at the time of discharge from a hospitalisation for acute HF or in ambulatory patients with chronic HF identifies those at high risk of subsequent HF (re-) admissions or death in observational studies [24,53-56,60-64]. However, further information on the optimal cut-off values for risk stratification in a variety of clinical settings requires larger prospective studies. Other important methodological aspects of LUS image acquisition and B-line quantification are detailed in a recent consensus document [65]. A brief overview of a sample of the current evidence on LUS and other described techniques is provided in Table 1.

Future directions

Comprehensive, semi-quantitative, assessment of venous pressures (inferior vena cava and internal jugular vein diameter; intrarenal venous flow) and extravascular lung fluid (B-lines) with ultrasound has several advantages and potential applications in patients with HF. It requires relatively little training and can be rapidly done in about 15 minutes. It uses existing, largely available, technology (ranging from high-end ultrasound systems to pocket size devices), is non-invasive, does not involve radiation and allows for serial, quantifiable, examinations at the point-of-care in a variety of clinical settings. However, many echocardiographic laboratories currently lack the additional transducers needed for JVD ultrasound (linear) and renal ultrasound (curvilinear; Table 1), and sonographers are currently not trained in these new ultrasound techniques.

Currently, the European Society of Cardiology (ESC)-HF guidelines suggest that the IVC diameter can be used to assess volume status in patients with HF, whilst LUS can assist with the detection of extravascular lung fluid (class IIb, level of evidence: C, for both) [1]. In contrast, U.S. HF guidelines do not mention ultrasound as a tool for the evaluation of intra- or extravascular volume status [66]. While the current level of evidence of the described ultrasound methods varies, the inclusion of LUS for the detection of extravascular lung fluid in patients with undifferentiated dyspnea could be considered in future HF guidelines [49,51].

Further research is needed to gain a better understanding of the clinical utility of these novel ultrasound methods. For instance, more accurate assessment of congestion might optimize timing of discharge for patients hospitalized with HF or help tailor diuretic therapy for ambulatory patients. In addition to physicians, HF nurses and other health care providers can be trained to perform ultrasound examinations such as IVC ultrasound or LUS [67]. The role of non-physicians in performing point-of-care ultrasound examinations to guide HF management

warrants further investigation. Ultimately, randomized trials are required to demonstrate that treatment guided by sonographic assessment in HF is safe, improves symptoms and quality of life and long-term outcomes. Trials are currently ongoing for LUS in patients during an admission for acute HF (NCT03136198 and NCT03259165), after hospital discharge and in the outpatient clinic; preliminary results are encouraging[68-70].

Finally, with the advent of COVID-19 the sonographic assessment of patients with suspected HF who require hospitalization has become more complex. For instance, right ventricular and IVC dilation could be due to right ventricular failure in the setting of acute respiratory distress syndrome or pulmonary embolism associated with a COVID-19 infection [71]. As LUS findings in COVID-19 include B-lines, their presence is not specific to pulmonary congestion in undifferentiated patients [72]. However, other LUS findings, such as subpleural consolidations, are not usually seen in HF but can be found in COVID-19 or other pulmonary infections [73]. Importantly, the absence of B-lines on LUS might rule out substantial pulmonary congestion or involvement in patients in whom HF or COVID-19 are suspected. We will likely gain a better understanding of ultrasound findings in patients with COVID-19 with and without HF over the coming months as data emerge.

Conclusions

Sonographic assessment of the inferior vena cava, internal jugular vein diameter and intrarenal venous flow can facilitate detection of elevated venous pressures, while LUS enables detection and quantification of extravascular lung fluid in patients with HF. These non-invasive techniques could complement clinical skills, traditional diagnostic and monitoring tools and potentially allow for improved diagnosis and management of patients with known or suspected HF.

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Central illustration: Ultrasound framework for the comprehensive evaluation of cardiac and venous pressure, and extravascular lung fluid

Figure 1. Jugular Vein Diameter (JVD) Ultrasound. With the patient reclining and head and neck elevated at 45°, the internal jugular vein is identified and its diameter (JVD) is measured at rest (at the end of expiratory phase, figure on the left) and during a Valsalva manoeuvre (figure on right). The ratio between the maximum diameter during Valsalva to that at rest is the JVD ratio. In the panel on the right, different examples of JVD patterns at rest and during Valsalva are shown, in patients without congestion (normal JVD ratio: >4; on the top) and in those with increasing congestion (mid and bottom).

Figure 2. Renal Venous Doppler. Once one of the interlobar veins has been identified, its venous flow can be assessed with pulsed Doppler. Four distinct venous flow patterns can be recognised (normal continuous, discontinuous pulsatile, discontinuous biphasic and discontinuous monophasic), according to increasing renal congestion (top to bottom). The bottom panel illustrates two proposed methods for renal flow quantification (venous impedance index and venous discontinuity index).

Figure 3. Lung Ultrasound. In the top left panel, the 8 (left) and 28 (right) chest zones methods are shown**. Count method:** B-lines are counted in each zone and summed to obtain their total count. B-lines can be counted individually as seen (bottom left panel, figure on the left). Alternatively, when confluent, their number can be estimated from the percentage of space they occupy on the screen below the pleural line, divided by 10 (bottom left panel, figure on the right, in which confluent B-lines occupy about 60% of the screen below the pleural line: conventionally, this equates to 6 B-lines). **Score method:** ≥3 B-lines in one

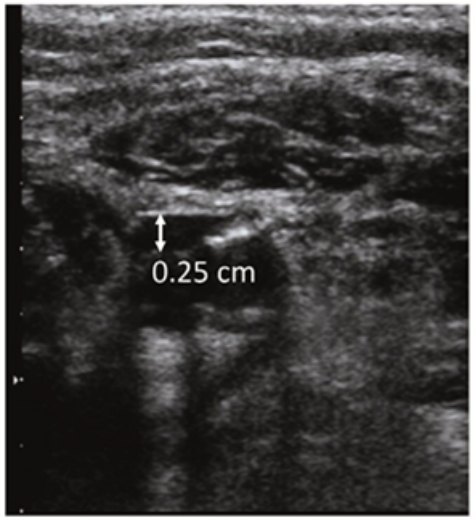
intercostal space per zone is considered a “positive” zone (bottom left panel, figure on the right). Different B-lines patterns are shown in the panel on the right: a normal lung should appear “dark” on lung ultrasound below the pleural line (top), but as pulmonary congestion develops and increases, more B-lines are seen.

	Inferior vena cava	JVD ratio	Venous Renal Doppler	Lung ultrasound (B-lines)
Ultrasound transducer	Phased array or curvilinear	Linear	Curvilinear	Phased array or curvilinear
Correlation with invasive cardiac hemodynamics	Moderate [17,18, 74-76]	No data	Moderate [33]	Moderate [77,78]
Correlation with natriuretic peptides	Low to moderate [23,24]	Low to moderate [24,28,31]	Moderate [33]	Moderate to good [24, 54,78]
Diagnostic value*	Little evidence [79]	Not enough evidence	Not enough evidence	Yes [49,51,79,80]
Monitoring	Yes [10,20-22]	No data	Yes [34]	Yes [56,81]
Prognostic value	Yes [20-24, 82-85].	Yes [24,27,31]	Yes [33,35]	Yes [24, 53-56, 60-64]
Intra-reader agreement [mean difference, 95% limits of agreement]	--	0.42 (-1.26, 2.11) [28]	Reproducibility [34] Venous impedance index: 4±13%	Count method: 0.05 B-lines/8 zones (-1.3, 1.4) [45]
Inter-reader agreement [mean difference, 95% limits of agreement]	-0.04 mm (-2.48, 2.40)[23]	-0.22 (-1.24, 0.80) [28]	Reproducibility [34] Venous impedance index: 5±12%	Count method: -0.3 B-lines/8 zones (-1.9,1.3)[53] Count-percentage method: 0.03 B-lines/zone (−1.52,1.45) [59] Score method: Cohen's Kappa 0.70-0.81/zone[48]
Limitations	Body habitus/obesity, Mechanical ventilation, Inability to perform a deep inspiration.	Inability to perform Valsalva, It varies with patient's position	Obesity, Severe breathlessness	Some diseases may increase B-lines (e.g. interstitial lung disease, acute respiratory distress syndrome), or limit their visualization (pneumothorax, large pleural effusion, morbid obesity).

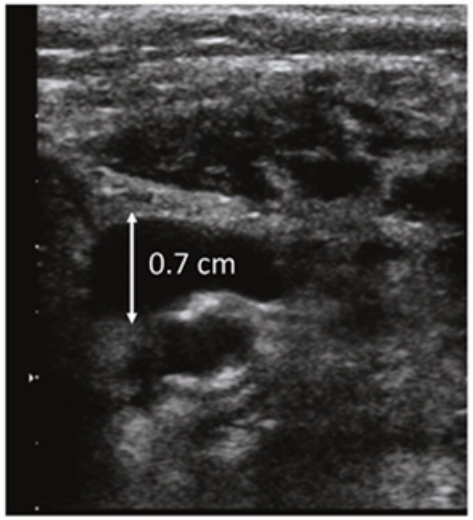
Table 1. Novel sonographic methods that quantify congestion in patients with heart failure: evidences and limitations. *For acute heart failure

JVD ULTRASOUND

JVD AT REST

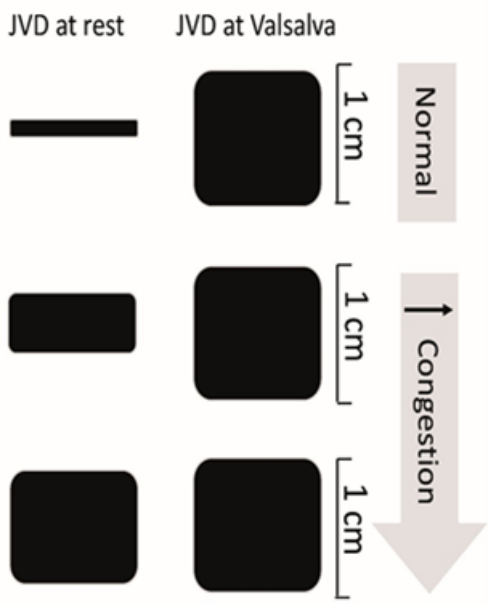


JVD AT VALSALVA

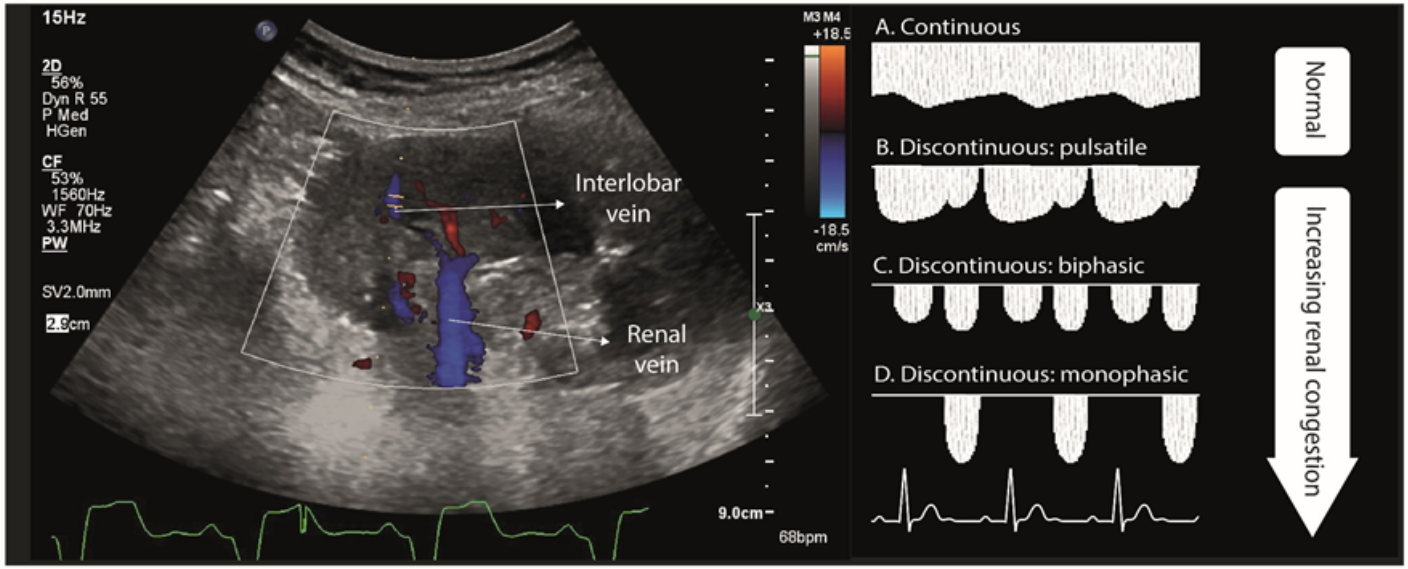


THE JVD RATIO (VALSALVA/REST) IS 2.8

INTERNAL JUGULAR VEIN PATTERNS



RENAL VENOUS DOPPLER

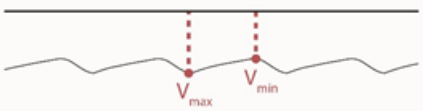


RENAL VENOUS FLOW PATTERNS

QUANTIFICATION

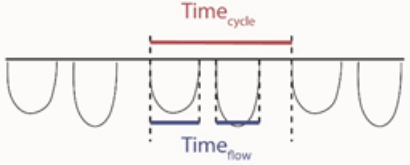
CONTINUOUS FLOW

$$\text{Venous impedance index (VII)} = \frac{V_{max} - V_{min}}{V_{max}}$$

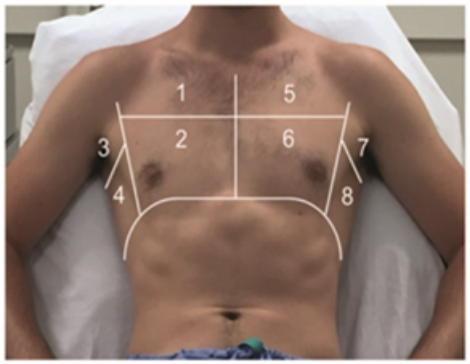


DISCONTINUOUS FLOW

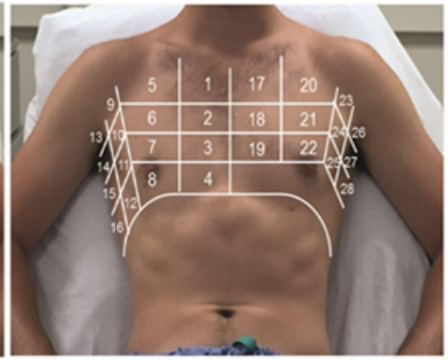
$$\text{Venous discontinuity index (VDI)} = \frac{Time_{cycle} - Time_{flow}}{Time_{cycle}}$$



LUNG ULTRASOUND

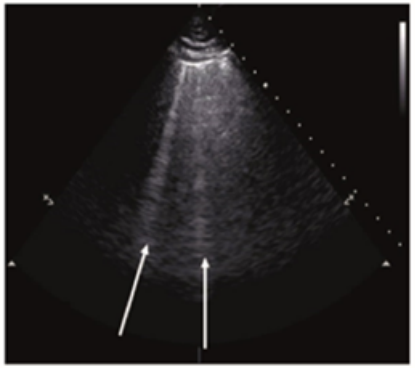


8 chest zones

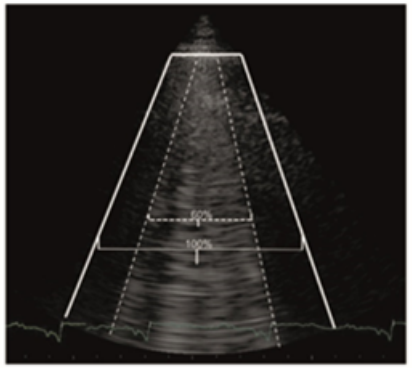


28 chest zones

Quantification

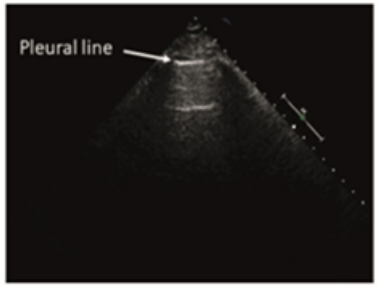


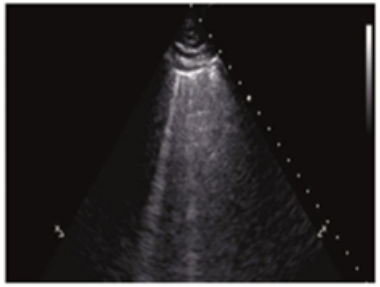
Individual Count

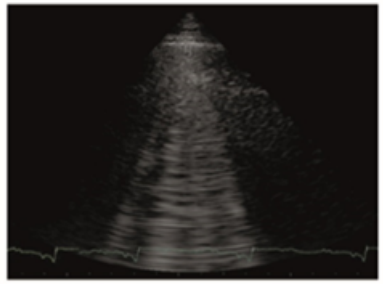


Percentage

B-LINES PATTERNS

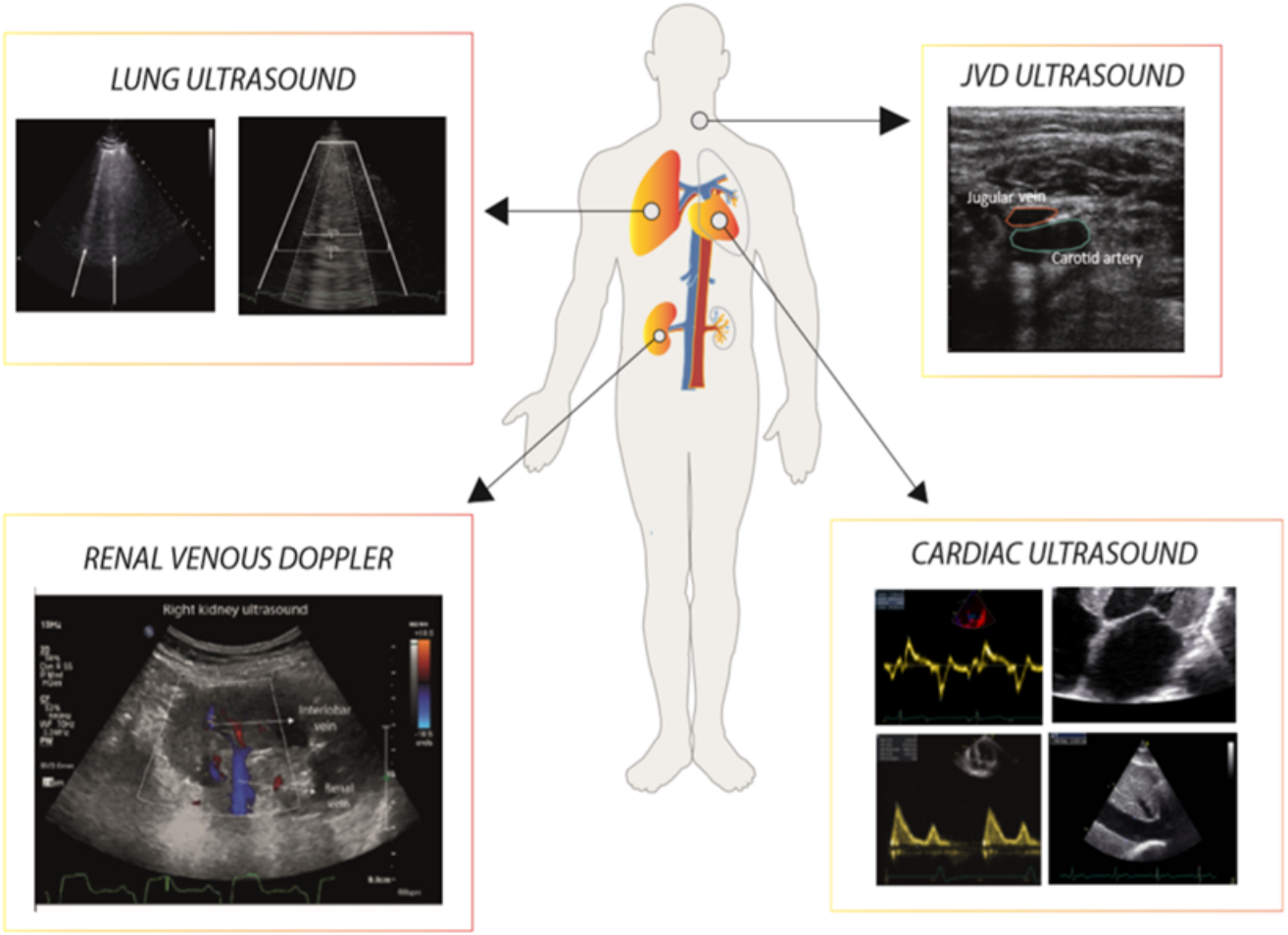






Normal

Congestion


LUNG ULTRASOUND
JVD ULTRASOUND
Jugular vein
Carotid artery
RENAL VENOUS DOPPLER
Right kidney ultrasound
Interlobar vein
Renal vein
CARDIAC ULTRASOUND