Review Article

Assessment of Fluid responsiveness in the Acute Medical Patient and the Role of Echocardiography

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Abstract

Both hyper and hypovolaemia have been associated with poor outcomes. Assessment of fluid responsiveness is challenging in the acute medical patient, due to time constraints, limited evidence and quite often the lack of accurate assessment tools on the Acute Medicine Unit (AMU). This article explains how focused echo assessment is quick and easy to use for this purpose on the acute medical take and highlights key principles to bear in mind when assessing for hypovolaemia and whether to administer fluid therapy. The increasing familiarity with focused echo such as Focused Intensive Care Echocardiography (FICE) and Point Of Care Ultrasound (POCUS) makes extension of these skill sets to assess for fluid responsiveness a relatively straightforward next step for acute physicians.

Key Learning Points

- Bedside echo is a key assessment tool for the management of the shocked patient.
- Echo is ideal for this as it measures pressure, volume and flow on both sides of the heart.
- Every patient has their own Starling curve and so measuring markers of preload to assess for fluid responsiveness will not be accurate.
- Passive leg raise with focused echo is a quick way to assess for fluid responsiveness in the acute medical patient.

Introduction

Assessment of fluid status and fluid responsiveness can be very challenging in acute medical patients. Firstly, most studies for fluid responsiveness have been performed in the Intensive Care Unit (ICU) setting. Secondly, sophisticated assessment tools found on the ICU, such as invasive blood pressure and cardiac output monitoring, are not present on the Acute Medical Unit (AMU). Thirdly, the high patient volume makes a full detailed assessment of fluid responsiveness impractical.

Conventional evaluation of fluid status derives from thorough clinical assessment with review of haemodynamic parameters. However, studies have shown that clinicians can accurately predict haemodynamic status using clinical findings and examination in only 50% of cases.[1] Hence the need for a simple, cheap, non-invasive bedside tool to identify stroke volume/cardiac output (and therefore define shock syndromes and fluid responsiveness) to aid the acute physician. Echo offers these properties. There are many protocols and courses that teach clinicians to perform a limited echo focussing on the haemodynamic parameters in cardiac arrest and critical illness, such as Focused Intensive Care Echocardiography (FICE), Sonography in Hypotension and Cardiac Arrest (SHOC), Focused Echocardiography in Emergency Life Support (FEEL) or Rapid Ultrasound for Shock and Hypotension (RUSH); each taking around 5-6 minutes.

This article will focus on what fluid responsiveness is, why it is important and how echo may be used to assess it.

Frank-Starling relationships

If contractility and afterload are unaltered then an increase in venous return (preload) leads to increase in stroke volume (see figure 1). A saturation point is reached at the start of the flat section of the curve where further increases in preload do not increase stroke volume, at which point additional fluid loading increases oedema without benefit of increased stroke volume. Different illness and shock syndromes are associated with very different Frank-Starling curves, for example in septic shock the curve may be flatter than in health.

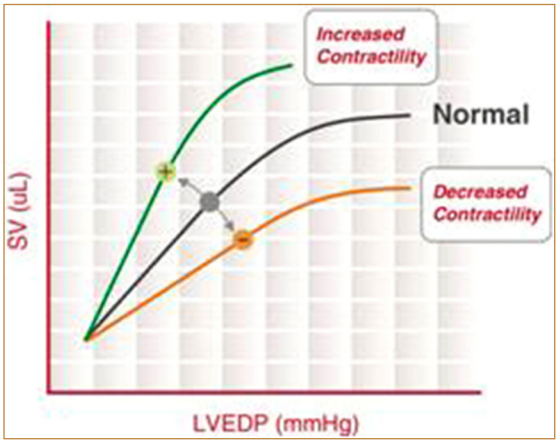


Figure 1. Frank-Starling curve: This work acts as the basic core principle for fluid responsiveness, however note the curve for each patient we treat is different and so identifying how much volume loading to give is not straight-forward.

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Clinicians have little knowledge of where each patient sits along Starling's curve, or the dose response curve for each fluid bolus, or the optimal point for fluid loading. Such knowledge is key to titrate fluid doses and ensure optimal increases in stroke volume with minimal increases in filling pressures risking tissue oedema. Patients who increase their stroke volume by 10% or more are (commonly) described as fluid responders, while those who do not are non-responders. In the latter, alternative means are sought to increase cardiac output, such as inotropy, if increases in organ oxygen delivery are required. If this is not the case then further fluid boluses risk oedema and fluid overload for no benefit.[2]

Shock Syndromes

Shock is a clinical manifestation of acute circulatory failure. Assessing the fluid status in critically ill and shocked patients can be extremely challenging. Features of each mechanism of shock can often co-exist making management of these patients even more difficult. Echo can be a useful adjunct in defining the aetiology of shock.

Both hypervolaemia and hypovolaemia have been shown to be harmful, with the former leading to interstitial oedema with compartment syndromes. A positive fluid balance is associated with increased days on a mechanical ventilator, renal failure and increased mortality.[3] Under-resuscitation (and therefore hypovolaemia) risks tissue hypoperfusion and organ dysfunction.

The 3 multi centre randomised control trials ProCESS,[4] ARISE[5] and ProMISe[6] all failed to demonstrate a significant reduction in mortality with early goal directed therapy (EGDT) in sepsis compared to usual care. The implications of this may be a re-emphasis that clinical judgment remains key in the management of these patients rather than adhering to strict targets, and that a "one size fits all" approach is not what is recommended.

The FEAST trial[7] demonstrated fluid bolus administration with saline or albumin increased absolute risk of death at 48 hours by 3.3% points and increased the risk of death and/or neurological sequelae by 4% points at 4 weeks, compared to those receiving standard care with no fluid bolus. This trial was conducted in children with febrile illness (around half with malaria) in Kenya, Tanzania and Uganda. The relevance of these findings to the acute medicine adult population in developed countries remains unknown (a UK Paediatric trial is currently underway). However it is clear that fluid therapy has impact on outcomes.

No suitably powered RCT has assessed the role of stroke volume guided fluid administration as a resuscitation goal. This may prevent fluid overload by identifying fluid non-responders and may offer optimised fluid loading in responders.

Basic Physiology

Assessing intravascular volume status with bedside echo can help to identify those shocked patients who need to improve their stroke volume in order to improve their cardiac output:

Cardiac output = Heart rate x Stroke volume

An increase in cardiac output can therefore improve the delivery of oxygen to the tissues (DO_2) providing there are no shunts and there is normal tissue organ extraction:

$DO_2 = CO \times Ca0_2$

Where CO is the cardiac output and $Ca0_2$ is the arterial oxygen content.

Preload, contractility and afterload are the determinants of cardiac output. Many clinicians use surrogates of preload to assess fluid responsiveness. In the ICU, central venous pressure (CVP) and pulmonary artery occlusion pressure (PAOP) have historically been used as estimates of right ventricular (RV) and left ventricular (LV) preloads. These are known as static parameters – those that are assessed at a point in time as compared to those that look at heart-lung interactions, known as dynamic indices. Static parameters are poor predictors of fluid responsiveness.[8]

Role of echo

Echo is easily used, and is a safe tool to assess cardiac function, volaemic status and fluid responsiveness in the shocked patient. However there is a high degree of operator dependence, so the more experience a clinician has in this skill the better for more accurate assessment. Clinicians need not perform a detailed assessment but focus the study on the clinical questions at hand, hence the term focussed echo. Simple and quick visual assessments and basic parameters can be obtained in the ED, AMU and the wards which can help guide fluid management. Due to time constraints and labour intensiveness, echo cannot be used for continuous haemodynamic analysis however it can be used repeatedly and rapidly to check response to therapy (such as before and after a fluid bolus).

Hypovolaemia on echo

The echo appearances of hypovolemia are one of a small, hyperkinetic fast beating heart, providing previous biventricular function is normal.

Other features include LV cavity end-systolic obliteration, known as a "kissing ventricle". In the parasternal short axis view, looking at the LV at papillary muscle level, one can obtain reduced LV end-diastolic (less than $5.5cm^2/m^2$) and systolic areas. Reduced end-systolic and end-diastolic dimensions of the cardiac chambers are noted, with reduced volumes best seen in the apical four chamber view.

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Hypovolaemia v Sepsis on Echo

Hypovolaemic and distributive shock can present with similar hyperdynamic echo appearances, and frequently co-exist. In hypovolaemia stroke volumes are reduced, which can be identified as a reduced RV outflow tract velocity-time integral (VTI) in the parasternal short axis view, or a reduced LV outflow tract VTI seen in the apical five chamber view. VTI is the red cell mass ejected each systole and thus corresponds to stroke volume. Measurement is made using Pulse wave Doppler.

Hyperdynamic LV

Hyperdynamic left ventricular ejection fraction (HDLVEF) is defined by the American College of Cardiology (ACC) as an ejection fraction of greater than 70%. This can particularly be seen in septic and hyper-adrenergic states, in which there is increased contractility due to increased circulating catecholamines.

HDLVEF may be a non-specific finding but has significance. Paonessa et al found that critically ill patients with HDLVEF had increased 28-day mortality compared to those with normal left ventricular ejection fraction (NLVEF).[9]

IVC variability

The venous capacitance system contains roughly two thirds of the intravascular volume. The IVC is best visualised in the subcostal view, with the probe placed anteriorly below the xiphoid process in the longitudinal plane.

IVC size decreases in hypovolaemia, and increases with increasing right sided pressure, including fluid overload.

The IVC diameter predicts central venous pressure in spontaneously breathing and mechanically ventilated patients.[10-12] The IVC and SVC drain into the right atrium and so can be a valuable tool in assessment of right atrial compliance. The American Society of Echocardiography (ASE) guidelines state that an IVC diameter of less than 2.1cm with collapsibility of greater than 50% is synonymous with a low CVP of 3 mmHg. A high CVP (15 mmHg) can be estimated with a dilated IVC of greater than 2.1cm that has less than 50% respiratory collapse.[13] However a systematic review concluded that CVP had little or no role in volume assessment.[8]

Essentially, a very small collapsing IVC in a shocked patient suggests fluid tolerance as opposed to a dilated fixed IVC which could be a sign of fluid intolerance (i.e. fluid administration may be harmful).

Cardiac output assessment

Stroke volume variation

Echo can be used for assessment of cardiac output. Information is needed regarding the cross sectional area of the left ventricular outflow tract (LVOT) and the velocity of blood flow (more specifically the velocity time integral, VTI) across the LVOT, as explained below:

Cardiac output = Heart rate x Stroke Volume
Stroke Volume = LVOT area x LVOT VTI
= Pi x (LVOT diameter/2)^2 x LVOT VTI

The LVOT diameter is measured in systole in the parasternal long axis view. The VTI is assessed using pulsed wave Doppler analysis of the LVOT in the apical 5 chamber view. It can be traced out on the echo machine. Measured in centimetres, normal values are between 15-25 cm. The VTI provides information regarding the velocity of blood flow across the time period of systole.

Multiplying the heart rate by the stroke volume will obtain the cardiac output. As the area of the LVOT is assumed to not change acutely and be fairly constant, the LVOT VTI can be used as a surrogate measurement of stoke volume.

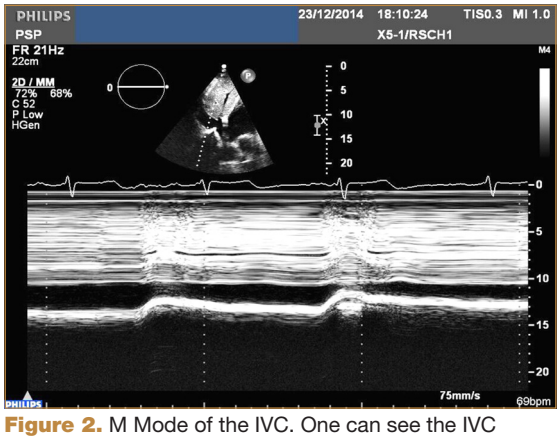


Figure 2. M Mode of the IVC. One can see the IVC diameter varying with respiration, in this the IVC size is normal with > 50% collapse with respiration.

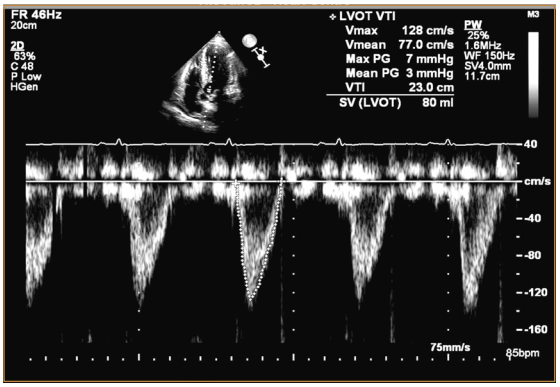


Figure 3. LVOT VTI assessment. LVOT VTI assessment. Obtained using Pulse Wave Doppler through the LVOT in the apical 5 chamber view. The VTI here is normal measuring 23 cm (normal range 15-25 cm).

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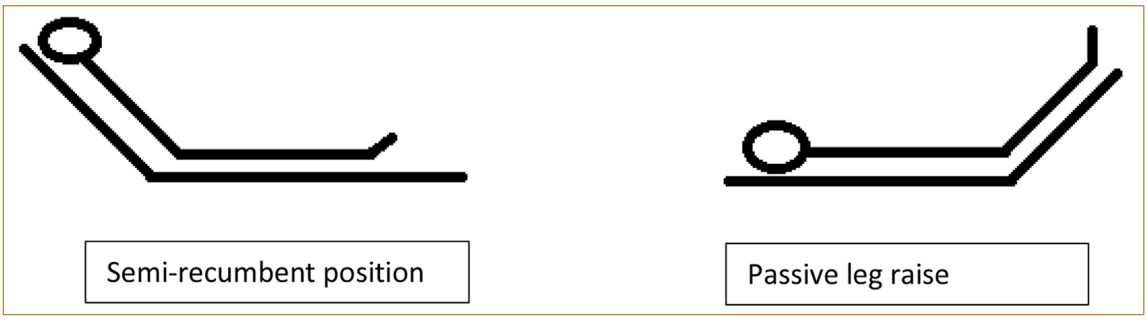


Figure 4. Passive Leg Raise. The patient's legs are raised up to 45 degrees from the semi-recumbent position.

Passive leg raise

Passive leg raise (PLR) is a reversible manoeuvre that mimics a fluid challenge, without the potential harmful effects of fluid administration. Its acts by transiently relocating around 300 ml venous blood from the legs and splanchnic reservoir to the intrathoracic compartment. This results in an increase in RV preload.[14-19] If the RV is responsive to preload, right heart cardiac output increases resulting in an increase in LV preload. If the LV is preload responsive, the increased filling results in an increased stoke volume and so cardiac output is increased. PLR has been used to detect whether patients are fluid responsive as the LV stroke volume will not increase if either chamber is not preload responsive. It is one of very few techniques validated in spontaneously ventilating patients and so is useful outside the intensive care environment.

As changes in cardiac output may be transient, a fast response device to determine cardiac output pre and post leg raise is crucial. TTE is therefore an invaluable tool to assess this. A stroke volume increase of 12-15% following a PLR indicates a patient is responsive to the fluid challenge.

PLR can be used on the AMU as a safe "fluid challenge" provided there is a bedside assessment of stroke volume to see if a patient is fluid responsive. Importantly, PLR can be used in spontaneously breathing patients and in the presence of arrhythmias. However PLR is limited and should not be used in patients with intra-abdominal hypertension and in those following surgery or a fracture.[20] Also one should use caution with this technique in severe hypovolaemia as, due to reduced blood flow to the legs, PLR can be falsely negative.

Measuring LVOT VTI variation following a PLR can give a visual and quantifiable assessment of fluid responsiveness in the acute medical patient. However bear in mind this can be time consuming on the acute take and there are several limitations to this method which one should be aware of before interpreting any results obtained.

Monnet and Teboul have described the 5 rules that should be used when performing PLR.[21] These are highlighted in the table above:

	Pitfalls using LVOT VTI with PLR
1	Adequate echo windows are needed to obtain accurate measurements. This may not always be achievable in the critically ill patient.
2	Misalignment of the PW Doppler in the LVOT can lead to underestimation of velocities, and so in turn stroke volume. A 15° change in angle induces a 5% measurement error.
3	Inaccurate measurement of the LVOT diameter can significantly over and under-estimate the stroke volume. This is because the LVOT area= Pi x (LVOT diameter/2)^2 . Measuring the stroke volume this way is time consuming and so, as mentioned, VTI can be used as a surrogate assessment for stroke volume.
4	Deep breathing can cause the cardia to move, meaning it is often difficult to be sure that the PW Doppler remains in the same place in the LVOT throughout the respiratory cycle. This can result in VTI variation due to respiration rather than true hypovolaemia.
5	VTI variation with PLR can require two people at the bedside (the physician performing the echo) and one person elevating both legs. Not only is this time consuming but it may not always be practical to perform in the fast paced environments of the ED or AMU. One way around this is to perform the PLR with an electronic hospital bed that allows for head and leg elevation.
6	Echo is not a tool for continuous assessment of cardiac output and so serial VTI assessments need to be performed to gauge changes in stroke volume in the single patient over a period of time. This, again, is time consuming and may not always be feasible.
7	In patients with right heart failure, stroke volume variations are affected by the increase in RV impedance during inspiration. Hence, giving a fluid bolus in these patients may only increase the RV filling pressure but may not reach the LV, and so no increase in LV SV will be seen. Indeed, this may result in detrimental effects to the patient. This effect can be especially noted in severe RV failure in patients who are mechanically ventilated.

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Rule	Criteria
1	PLR should begin from the semi-recumbent position, not from the supine position. This mobilises venous blood from the splanchnic reservoir, further affecting preload.
2	PLR affects must be assessed by measuring cardiac output, not blood pressure.
3	Effects of PLR can dissipate after 1 minute, hence cardiac output assessment must detect short term changes. Echo can do this.
4	Measurement of cardiac output should be done before and during PLR, but also after once in a semi-recumbent position to see if cardiac output lowers back to baseline.
5	Avoidance of factors that enhance adrenergic stimulation (such as coughing, pain and awakening) should be done prior to PLR testing.

The Right Ventricle

The RV is a high volume and low pressure chamber. The size of the RV is significantly affected by the loading conditions, especially afterload as seen in massive PE. A low RV preload state can be seen on echo as a small RV at end diastole. It is imperative to check both the LV and RV are small in size when diagnosing hypovolaemia.

Acute RV failure is not an uncommon finding and is an important one to recognise. Changes in physiology such as hypoxaemia, hypercapnia and acidaemia can all increase RV afterload. Important causes in the AMU patient include acute respiratory distress syndrome (ARDS) and particularly pulmonary embolism (PE).

Clearly, the clinician should be very cautious with fluid therapy in a patient with a dilated RV. Administration of fluid may worsen the shocked state of the patient with acute cor pulmonale so it is important to detect for signs of this before deleterious fluid therapy. Focused echo assessment can answer this question.

The more dilated the RV the less likely the patient's heart is to tolerate fluid administration, although note that in some patients with mild to moderate RV failure and dilatation they may be responsive to cautious fluid therapy. Some patients with chronic pulmonary hypertension may also be fluid responsive and more thorough stroke volume optimisation and assessment will be needed to titrate fluid loading in these particular cases. In patients with features of chronic pulmonary hypertension a key finding would be the presence of RV hypertrophy of > 5mm, best visualised in the subcostal view.

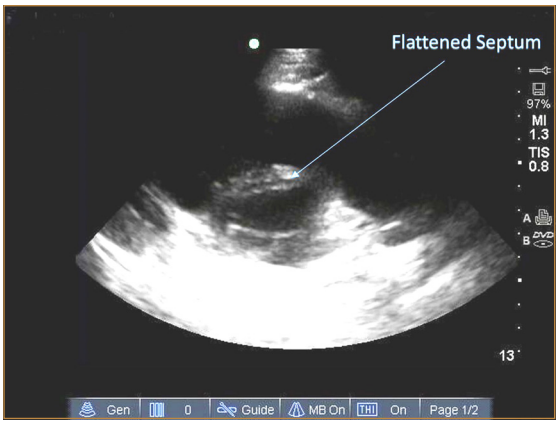


Figure 5. Parasternal Short Axis View: Showing a dilated RV with septal flattening. This is suggestive of RV pressure or volume overload.

A dilated RV and a small D shaped LV indicates severe RV pressure-volume overload. This is an absolute contra-indication to fluid therapy and it is important to recognise this on echo.

When to think about stopping fluid therapy

As mentioned, over-zealous fluid therapy impacts on patient outcomes. The key for the acute physician is to identify any signs on echo that suggest fluid intolerance, meaning that further fluid administration may be harmful to the patient. Signs to look out for include:

	Signs of an overloaded LV
1	High Left Ventricular End Diastolic Area (LVEDA) >20cm^2 (obtained in parasternal short axis view)
2	Reduced LV ejection fraction
3	Fixed inter-atrial septum to right. This is suggestive of raised LA pressure
4	LA enlargement (in the absence of significant MV disease)
5	Upstream effects, which can be seen as an Interstitial syndrome on lung ultrasound

	Signs of an overloaded RV
1	RV dilatation
2	RV systolic dysfunction
3	Small, D-shaped LV. This indicates ventricular inter-dependence.
4	Dilated IVC with no variability. This suggests a high RAP
5	Upstream effects, such as deranged LFTs on blood tests. Dilated hepatic veins on US is suggestive of hepatic congestion, this can be visualised on the subcostal view when assessing for IVC size.

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Conclusions

Assessing the aetiology of shock and whether a patient is fluid responsive is key to successful management. It is imperative to use several variables when assessing this. Bedside echocardiography is arguably the single most useful diagnostic tool available to achieve this. The advantage of echo is that it is non-invasive and is a method that assesses changes in volume, pressure and flow on both sides of the heart. Adequate training and maintenance of operator skills are important in order for it to be of routine and safe use in the management of the haemodynamically unstable patient. The increasing use of FICE and POCUS in training should enable extension of skills for fluid assessment at the bedside to be an achievable one for acute physicians.

Competing interest

none

MCQs

Regarding fluid status assessment:

1. Clinical examination is a good predictor of response to a fluid challenge
2. Static parameters are useful guides to assess for fluid responsiveness
3. Hypovolaemia on 2D echo presents as small chambers with walls closely opposed at end systole, a rapid heart rate and an empty collapsing IVC
4. A dilated IVC may indicate right heart failure
5. Hyperdynamic LV systolic function indicates an LV ejection fraction >70%

Regarding fluid responsiveness:

1. A stroke volume increase of >15% post PLR indicates fluid responsiveness
2. PLR can be used in arrhythmias and in spontaneously breathing patients, making this a viable option in the acute medical patient
3. Normal VTI values range between 5-10cm
4. A dilated RV with a D shaped septum is a contra-indication to further fluid therapy
5. Low LV filling pressures are associated with diastolic dysfunction

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