Transthoracic echocardiography as predictor of fluid responsiveness in circulatory failure patients

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Abstract: Objectives: To evaluate role of tranthoracic echocardiography in prediction of fluid responsiveness in cirulatory failure patients. **Data Sources:** a literature search using MEDLINE, EMBASE and the Cochrane Database of Systematic Reviews for prospective studies with no restrictions. All materials accessible from these database to 2016 were included. **Study Selection:** a special search was conducted with the key words transthoracic echocardiography, fluid responsiveness & circulatory failure. Only full text articles in indexed journals were included. **Data Extraction:** The initial investigation exhibited 3138 articles of which 8 met the incorporation criteria. The articles discussed the role of Echocardiography in predicting fluid responsiveness. **Data Synthesis:** the main result of the review. Each study was reviewed independently; the data obtained were rebuilt in a new language according to the need of the researcher and arranged into topics through the article. **Results:** The predictive power of diagnostic accuracy of transthoracic echocardiography parameters changes with the respiratory cycle or passive leg raising in mechanically ventilated patients was strong throughout the articles reviewed. **Conclusion:** Transthoracic echocardiographic techniques accurately predict fluid responsiveness in critically ill patients who develop circulatory failure.

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1. Introduction:

The management of the critically ill patient to optimization the tissue oxygen delivery is an essential part in intensive care unit (ICU). Insufficient intravascular loading in the early resuscitation of acute sepsis results in tissue under perfusion, organ dysfunction, and acidosis. Excessive fluid administration has also been shown to be detrimental in the perioperative setting and in acute lung injury, prolonging both time on mechanical ventilation and time in intensive care [1], [2].

However, it has been reported 50 percent of patients do not exhibit the desired effect after fluid bolus [3] and more than half of patients have the risk of excessive fluid administration [4].

It is therefore essential to have reliable tools for predicting the efficacy of volume expansion (VE) and thus distinguishing patients who might benefit from VE from those in whom the treatment is likely to be inefficacious.

For the past 10 years, many studies have focused on the prediction of fluid responsiveness. Static hemodynamic indices (such as central venous pressure [CVP] or pulmonary artery occlution pressure [PAOP]) are demonstrated to be little value in predicting fluid responsiveness [5] [6].

Dynamic indices (such as stroke volume variation [SVV] or pulse pressure variation [PPV]), based on analysis of preload dependence, have been validated to predict fluid responsiveness [5] [7] [8] [9]. And now modern intensive care is increasingly concerned with the avoidance of unnecessary invasive procedures which contribute to patient morbidity either directly or more often through the associated risk of catheter related bloodstream infection [10].

So, invasive or mini- invasive methods are replacing by new methods focused on non-invasive. In mechanically ventilated patients who have no spontaneous respiratory effort, the change in intrathoracic. pressure has a cyclical effect on both the left and right heart. A rise in intrapleural pressure compresses the pulmonary vasculature and in turn causes compression of the venous inflow vessels and the heart itself. This reduces both right ventricular (RV) preload and left ventricular (LV) after load whilst conversely both RV afterload and LV preload are increased. These effects are accentuated by hypovolaemia implying variation in stroke volume with cyclical respiratory changes can be used to predict whether stroke volume will alter if preload is increased. This is the basis of the increasingly ubiquitous stroke volume variation monitoring systems but can also be examined using Doppler echocardiography of flow through valves, vessels, or outflow tracts. If the cross-section at the point of measurement can be visualized or accurately estimated, then the product of that area and the integral of the flow time curve (generated by the Doppler signal) is equal to the stroke volume.

Transthoracic echocardiography (TTE) is increasingly used for noninvasive hemodynamic assessment of critically ill patients since high quality images and Doppler signals are obtained with recent TTE equipment [11]. TTE provides clinicians with valuable information including stroke volume, left ventricular preload, and filling. The stroke volume can be easily obtained using the left ventricular outflow track Doppler method [12].

2. Material and Method

The guidance published by the Centre for Reviews and Dissemination was used to assess the methodology and outcomes of the studies. This review was reported in accordance with the Preferred Reporting Items for Systematic reviews and Meta-Analyses statement. The institutional review board and ethics committee of Menofiya University approved this study.

Search strategy:

An electronic literature search was carried out using Medline, EMBASE, CINAHL, and the Cochrane database of systematic reviews. The search terms used were ((fluid) OR (volume) OR (preload) OR (filling)) AND ((respons∗) OR (status) OR (assess∗)) AND (echocardiograph∗).

Study selection:

The search was limited to "human" and "English language." Only full-text articles in indexed journals were included. Reviews, chapter, case reports, reference network and studies published in abstract form were excluded. We included only studies with adult patients admitted in ICU. Articles were collected by one reviewer and crosschecked by another reviewer and references of included papers were examined to identify other studies of interest.

Between investigators, there are inevitable differences in the choice of stroke volume or cardiac output, the volume of fluid given, the duration over which the fluid load was given, and the type of fluid given.

Data extraction:

Information from each qualified review had freely extracted in copy utilizing an information accumulation frame to catch data on study attributes, mediations, quantitative outcomes detailed for every result of intrigue. Conclusion, remarks on each review had made.

As a result of heterogeneity in the gathered information, it had unrealistic to perform meta-examination. Critical information had gathered, then an organized survey had performed with the outcomes arranged.

Quality assessment:

The Standards for Reporting of Diagnostic Accuracy (STARD) initiative developed a guide for assessing the quality of reporting of studies of diagnostic accuracy [13]. In this review, the STARD score was adapted to judge the quality of the investigation in each article selected.

A 19-point score was devised using 19 of the 25 STARD criteria. Each criterion was assigned one point and the overall score divided into categories: poor (score 0–10), adequate (11–15), and good (16–19). The results of the selected studies were not meta-analysed due to the heterogeneity of methodologies, as well as the differences in patient selection, modes of ventilation and definition of fluid response. There was insufficient data for the construction of summary receiver-operator characteristic (SROC) curves or for the calculation of *Q* star statistics, and the simple average of sensitivity and specificity data is not an informative approach. Furthermore, the usage of a fixed effects model such as SROC would be expected to produce exaggeratedly high levels of reported accuracy for a test that is to be put to use in the complex environment of the critically ill patient [14].

3. Results:

*Eight studies were included for review***.** *The quality scores ranged between 13 and 15, indicating an adequate standard throughout.*

Assessment of Fluid Responsiveness Using Transaortic Stroke Volume Increment to Passive Leg Raising. Important differences between studies were evident in the study protocols. Maizel et al. [15] and Pr`eau et al. [16] used a 30 to 45 degree leg raise from the supine position where all others started with the patient semirecumbent at 30 to 45 degrees before tilting the bed until the patient was supine with legs raised.

These two methods have been shown to result in different volumes of caudal surge of blood which potentially affects the validity of the test. Maizel et al. [15] had no second baseline measurement prior to fluid delivery. In all studies, the pretest baseline measurements of stroke volume were similar before the passive leg raise and before the assessment of a response to fluid bolus. All studies showed good sensitivity (77 to 100 percent) and specificity (88 to 99 percent) using a threshold of 10 to 15 percent increment of stroke volume or cardiac output.

Strikingly, stroke volume change with PLR predicted the correct response to volume expansion in 16 of the 18 patients with arrhythmia. [17].

Assessment of Fluid Responsiveness Using Transaortic Stroke Volume Variation with Respiration.

A single study by Biais et al. looked at the use of stroke volume variation for prediction of fluid responsiveness [18]. In this study, stroke volume variation measured across the aortic valve was used to predict a fluid response which was delivered as a 20mL/kg/m2 bolus of 4% albumin. Stroke volume variation was calculated using the formula:

$$SVV = \frac{(SV_{max} - SV_{min})}{SV_{mean}} \quad (1)$$

All patients were receiving mandatory ventilation and had no spontaneous respiratory effort.

The area under the receiver operator characteristic (ROC) curve was used to ascertain a threshold of nine percent stroke volume variation as being the most useful for discerning responders from nonresponders. Using this cut-off, there was excellent sensitivity and specificity (100 and 88 percent, resp.).

Assessment of Fluid Responsiveness through Respiratory Variation of IVC Diameter. Two studies by Barbier et al. and Feissel et al. used respiratory variation of the diameter of the IVC to predict fluid responsiveness [18, 20]. Both studies included only mechanically ventilated patients, without spontaneous respiratory effort. Each study compared the maximum and minimum diameter of the IVC just distal to the hepatic vein: *D*max and *D*min, respectively.

Both studies expressed the distensibility of the IVC as a percentage index.

Barbier et al. used a "distensibility index" calculated by

$$\frac{(D_{max} - D_{min})}{D_{min}} \quad (2)$$

whereas Feissel et al. corrected the mean of the two values:

$$\frac{(D_{max} - D_{min})}{0.5(D_{max} + D_{min})} \quad (3)$$

Barbier et al. showed a sensitivity and specificity of 90 percent using a cut-off distensibility index of 18 percent to indicate fluid responsiveness. Feissel et al. demonstrated a correspondingly high positive and negative predictive value, 93 and 92 percent, respectively, using an IVC diameter variation of 12 percent (20).

4. Discussion:

This review shows that TTE is a highly discriminative test for the prediction of the stroke volume or cardiac output response to volume loading in critically ill patients, thus highlighting the potential for expansion of its role in quantitative assessment. Importantly, TTE techniques appear useful in patients with spontaneous respiratory effort and those with arrhythmias: this is in contrast to many of the techniques that involve invasive monitoring which have been shown to be inaccurate in these situations [21].

Table 1: Characteristics of studies selected.

Study	Technique	Selection	Ventilation	Rhythm	Volume and type	Time (min)	Response criteria
Barbier et al.	IVC DI	Shock (sepsis) and acute lung injury	All mand	Any	7m L/kg colloid	**30**	>15% CO TTE
Feissel et al.	Δ*D*IVC	Shock (sepsis)	All mand	Any	8mL/kg colloid	**20**	>15% CO TTE
Lamia et al.	PLR	Shock (sepsis or hypovolaemia)	All spont	Regular SR or AF	500mL crystalloid	**15**	>15% SV TTE
Maizel et al.	PLR	Shock (unspecified)	All spont	Regular SR	500mL crystalloid	**15**	>15% CO TTE
Biais et al.	PLR	Shock (sepsis or haemorrhage)	All spont	Any	500mL crystalloid	**15**	>15% SV TTE
Biais wt al.	SVV	Post-operative (liver surgery)	All mand	Regular SR	20 mL/kg/m2 colloid	**20**	>15% CO TTE
Thiel et al.	PLR	Shock (unspecified)	Mixed	Any	500mL crystalloid or colloid	**Unspecific**	>15% SV TTE
Pr´eau et al.	PLR	Shock (sepsis or acute pancreatitis)	All spont	Regular SR	500mL crystalloid	<30	>15% SV TTE

Selection: inclusion criteria summary, PLR: passive leg raising, spont: spontaneous respiratory effort whether or not on mechanical ventilation, mand: ventilator giving mandatory breaths only and patient fully adapted to ventilator, SR: sinus rhythm, AF: atrial fibrillation, TTE: transthoracic echocardiography, SV: stroke volume, CO: cardiac output, Δ*D*IVC change in IVC diameter adjusted by the mean (see text), IVC DI: IVC distensibility index (see text), and unspec: unspecified time.

Table 2: Collated results of all included studies.

Study	Predictive test	Threshold	Resp %	AUC (ROC)	Sens	Spec	PPV	NPV
Lamia et al.	PLR SVI or CO rise	≥12.5%	**54**	0.96 ± 0.04	**77**	**99**		
Maizel et al.	PLR CO rise PLR SV rise	≥12% ≥12%	**50**	0.90 ± 0.06 0.95 ± 0.04	**63**	**89** **89**	**85** **83**	**76** **73**
Biais et al.	PLR SV rise	≥13%	**67**	0.96 ± 0.03	**69**	**80**		
Thiel et al.	PLR SV rise	≥15%	**46**	0.89 ± 0.04	**100**	**93**	**91**	**85**
Pr´eau et al.	PLR SV rise PLR dVF rise	≥10% ≥8%	**41**	0.90 ± 0.04 0.93 ± 0.04	**81**	**90**	**86**	**90**
Biais et al.	SVV	≥9%	**47**	0.95	**86**	**80**	**75**	**89**
Barbier et al.	IVCDI	≥18%	**41**	0.91 ± 0.07	**86**	**88**		
Feissel et al.	Δ*D*IVC	≥12%	**41**		**90**	**90**	**93**	**92**

Threshold: cut-off between responders and nonresponders, Resp: proportion responding to fluid load, AUC (ROC): area under the receiver-operator curve, Sens: Sensitivity, Spec: Specificity, PPV: positive predictive value, NPV: negative predictive value, *r*: correlation coefficient, PLR: Passive leg raising, SI: single investigator/reader, CO: cardiac output, SV: stroke volume, dVF: change in femoral artery velocity as measured by Doppler, SVI: stroke volume index, LVEDAI: left ventricular end-diastolic area, *E/Ea*: mitral *E*-wave velocity/mitral annulus *E* velocity measured by tissue Doppler, Δ*D*IVC: change in IVC diameter (*D*) as calculated by (Dmax − Dmin)/0.5(Dmax + Dmin), IVC DI: IVC distensibility index calculated by (Dmax − Dmin)/Dmin.

Although TTE does not provide continuous monitoring which can be managed by nursing staff at the bedside, in reality, most clinical questions regarding fluid management arise intermittently. With equipment close at hand the time taken for a focussed TTE assessment rarely takes more than few minutes [22]. In addition, much of the data derived from pulmonary artery catheter measurement can be obtained using TTE, obviating the need for an invasive monitor that has been shown not to alter outcome [23]. The techniques of IVC diameter assessment, trans-aortic stroke volume variability with respiration and stroke volume increment with passive leg raising all provided strong predictive ability for response to a fluid bolus. The area under ROC curves was greater than 0.9 in all articles that presented the statistic. Although a clear threshold value for discriminating responders from nonresponders seems intuitively advantageous, clinicians are adept at coping with non-discriminatory results and using them to inform decisions made on the basis of the whole clinical picture. None of the three TTE techniques is convincingly the best and if possible all three should be used to minimize the impact of their limitations. On occasion, this may not be achievable for a number of reasons. Local pain or delirium may preclude all or part of a TTE exam in a small minority of cases. In the 260 scans attempted within the studies selected, just 13 could not be performed for these reasons making this a well-tolerated procedure in the main. Thoracic or abdominal wounds may sometimes make views impossible to achieve. Obesity or rib prominence can also make TTE acoustic windows difficult to obtain but it is rare that at least a single usable view cannot be obtained in an individual. In the reviewed studies, only nine of the 260 attempted scans were abandoned due to difficulty with anatomy. Additionally, the applicable techniques will depend on the presence or absence of mechanical ventilation or dysrhythmias. For example, in a patient with atrial fibrillation who is fully ventilated, transaortic Doppler assessment is inaccurate but subcostal measurement of the IVC diameter variation can be safely used.

Clinical Application.

The concept of "wet" and "dry" intensive care units has long been debated. The apparent benefits of goal-directed aggressive fluid resuscitation in the early stages of sepsis must be balanced with evidence for reduced morbidity when "restrictive" fluid regimes are used [24]. The literature lacks agreement on definitions of "wet" and "dry," or "liberal" versus "restrictive" fluid protocols, and consequently, it is difficult to be certain of applicability to a particular setting. Brandstrup provided compelling evidence in colorectal surgical patients and the ARDSNET group in the subset of acute lung injury, but there is a paucity of further evidence [2, 25]. It is important to recognize that this review neither allows assumptions about the longevity of the response to fluid, nor the value of a continuous fluid infusion thereafter. It also follows that a forecast suggesting the patient will be fluid responsive in no way guarantees the safety of a delivered bolus in terms of increasing extravascular lung water or worsening regional organ oedema and function.

The literature contains a growing body of work on optimising haemodynamics using other echocardiographic parameters, beyond simple measures of contractility and structural pathology. Patterns of flow across the mitral valve and tissue velocity of the annulus have proved useful, principally when assessed in combination. Tissue velocity, particularly that measured close to the mitral valve annulus, assessed using Doppler imaging (TDI) provides an accurate estimation of diastolic function of the left ventricle irrespective of preload changes [26,27]. Pulmonary artery occlusion pressure can be estimated by a number of methods, chiefly by tissue Doppler imaging but also by examining the pattern of movement of the interatrial septum [28]. Subtleties of the sonographic representation of interlobular septa can be used to assess extravascular pulmonary water and also correlate with pulmonary artery occlusion pressure [29]. An assessment using as many parameters as possible will provide valuable information at many stages of the patient's stay whether in managing the acute and unstable periods, or when weaning from the ventilator is troublesome [30]. Although detailed examination of the heart requires an experienced echocardiography practitioner, there is an increasing acceptance of the value of focussed echocardiographic assessments to answer common clinical questions arising in critical illness. This has arisen in tandem with the emergence of a number of courses and training programmes centred on evaluation of the critically ill patient by those less experienced in echocardiography. Jensen showed that with only limited training, a diagnostic transthoracic window was achieved 97 percent of the time when used in the evaluation of shock [20]. In the UK, a consultation process to provide a training template and curriculum for focussed echocardiography in critical care is currently underway [31].

Limitations.

This review was restricted to the specific question of fluid response. In reality, echocardiographic assessment of the critically ill aims to gain as complete a picture as possible of the cardiovascular state. Ideally, this should also involve a full structural study in addition to inspection of left ventricular filling state and perhaps even ultrasonic examination of the lungs.

Furthermore, studies using transoesophageal echocardiography (TOE) were not selected for this review and, although it would seem intuitive that flow or diameter measurements techniques taken with one kind of echocardiography could be safely extrapolated to another, this ignores the differing technical restrictions of each technique. Transoesophageal echocardiography has its own growing evidence base for its application in intensive care and clearly where it is available provides invaluable haemodynamic information to inform clinical decisions.

A significant limitation of this review is the small size of the study groups since only a single study included more than 40 patients [32]; this is typical of studies of diagnostic accuracy. Meta-analysis was not performed, due to the heterogeneity of the methods and patient characteristics. In addition due to the similarity of the sensitivity and specificity data, it was felt that further statistical analysis would not add useful information. It is conspicuous that only one article reported on the time between the initial predictive test and the subsequent assessment of a response to a fluid bolus [16]. Patients with haemodynamic instability can undergo rapid changes in cardiovascular parameters mandating that the period between the predictive and confirmatory tests should be as short as possible. The amount of fluid used, the type used, and the rate at which it was given all impact upon the response test in these studies. Unfortunately, there is no agreed formulation for a standard fluid load although almost all studies use approximately the same formulation.

Although no specific details were given about the qualifications of the echocardiography operator or reader most studies inferred they were experienced. Furthermore, blinding of the operator or reader, to the measurements taken after volume loading was rare and this is, therefore, a source of observer bias within the data.

Intraobserver variability was considered by the majority of studies and attempts were made to measure it with variable success. An intuitively more useful measurement of reproducibility was achieved by examining the variability of repeated measurements of distensibility by Feissel et al. [20]. This showed a greater degree of intraobserver concordance at 3.4 percent.

Any concern about the reproducibility of observations should however be viewed in the context of the consistent results achieved throughout the reviewed studies which is unlikely to have arisen by chance.

Of note, whilst the effects of varying tidal volumes on echocardiographic parameter assessment are minimal, the impact of raised intra-abdominal pressure and of different positive end expiratory pressure is largely unstudied [33].

Future Developments.

The clinical question that was not addressed in any of the articles was that of the "real-world" value of echocardiographic approaches to assessing fluid responsiveness. The studies reviewed do not provide us with information about translation into effects on morbidity or mortality, nor is there yet such a current evidence base in the literature. This evidence may well originate in the context of future investigation into the dilemma of conservative versus liberal fluid management. Transpulmonary microsphere contrast has already been shown to dramatically improve volumetric assessment and its use in the critically ill would intuitively improve the clinical utility of the modality still further [34]. Three dimensional echo remains in its infancy within the intensive care unit but the promise of increased, automated volumetric accuracy, and improved diagnostic clarity will also undoubtedly be examined in the near future [35, 36].

Conclusion:

Transthoracic echocardiography is becoming a powerful noninvasive tool in the daily care of the critically ill. This review brings together the evidence for employing TTE to predict fluid responsiveness. Assuming there is equipment and local expertise TTE is a repeatable and reliable method of predicting volume responsiveness in the critically ill. Transaortic stroke volume variation with the respiratory cycle, stroke volume difference following passive leg raising, and IVC diameter changes with respiration all provide good prediction of the likelihood of a response to a fluid bolus. The techniques can be used individually to address the needs of different patients and in combination to triangulate clinical information where uncertainties may occur. The studies reviewed form a robust platform of physiological data on which to base further studies involving larger numbers of patients which engage with clinically relevant outcomes, such as inotrope use, blood pressure, length of stay, and time to weaning from mechanical ventilation. Improved access to clinician-echocardiographers through a defined training process will facilitate such clinical studies and give patients access to accurate noninvasive information in answer to the daily clinical conundrum of fluid responsiveness.

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