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● *Review*

ULTRASONOGRAPHIC MEASUREMENT OF THE RESPIRATORY VARIATION IN THE INFERIOR VENA CAVA DIAMETER IS PREDICTIVE OF FLUID RESPONSIVENESS IN CRITICALLY ILL PATIENTS: SYSTEMATIC REVIEW AND META-ANALYSIS

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Abstract—Respiratory variation in the inferior vena cava (⊿IVC) has been extensively studied with respect to its value in predicting fluid responsiveness, but the results are conflicting. This systematic review was aimed at investigating the diagnostic accuracy of ⊿IVC in predicting fluid responsiveness. Databases including Medline, Embase, Scopus and Web of Knowledge were searched from inception to May 2013. Studies exploring the diagnostic performance of ⊿IVC in predicting fluid responsiveness were included. To allow for more between- and within-study variance, a hierarchical summary receiver operating characteristic model was used to pool the results. Subgroup analyses were performed for patients on mechanical ventilation, spontaneously breathing patients and those challenged with colloids and crystalloids. A total of 8 studies involving 235 patients were eligible for analysis. Cutoff values of ⊿IVC varied across studies, ranging from 12% to 40%. The pooled sensitivity and specificity in the overall population were 0.76 (95% confidence interval [CI]: 0.61–0.86) and 0.86 (95% CI: 0.69–0.95), respectively. The pooled diagnostic odds ratio (DOR) was 20.2 (95% CI: 6.1–67.1). The diagnostic performance of ⊿IVC appeared to be better in patients on mechanical ventilation than in spontaneously breathing patients (DOR: 30.8 vs. 13.2). The pooled area under the receiver operating characteristic curve was 0.84 (95% CI: 0.79–0.89). Our study indicates that ⊿IVC measured with point-of-care ultrasonography is of great value in predicting fluid responsiveness, particularly in patients on controlled mechanical ventilation and those resuscitated with colloids. (E-mail: zh_zhang1984@hotmail.com) **© 2014 World Federation for Ultrasound in Medicine & Biology.**

Key Words: **Fluid responsiveness, Ultrasonography, Variation in inferior vena cava, Critical illness, Mechanical ventilation, Meta-analysis.**

INTRODUCTION

Fluid management is crucial in the treatment of critically ill patients, particularly for those with acute circulatory failure. Accumulating evidence suggests that either hypovolemia or fluid overload can lead to poor clinical outcomes, including prolonged mechanical ventilation, higher mortality, renal dysfunction and impairment in oxygenation (Alsous et al. 2000; Boyd et al. 2011; Corrêa et al. 2012; Murphy et al. 2009). Therefore, many investigators have explored reliable techniques or biomarkers in the goal of predicting fluid responsiveness in critically ill patients. The goal of fluid resuscitation is to maintain sufficient tissue perfusion while avoiding significant interstitial edema. The Frank-Starling principle states that the greater the volume of blood entering the heart during diastole, the greater is the volume of blood ejected during systole (Saks et al. 2006). This phenomenon, termed *fluid responsiveness*, is one of the most reliable parameters in the decision on whether additional fluid can be given. Many parameters, for example, central venous pressure, pulse pressure variation and stroke volume variation, have been evaluated with respect to their utility in fluid management, using fluid responsiveness as the reference standard (Saugel et al. 2013; Suehiro et al. 2012; Yang et al. 2013).

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However, because of the invasiveness and time involved placing a central venous catheter and making the measurement, these indices are of limited use in emergency departments and general wards.

More recently, bedside point-of-care ultrasonography has gained popularity; its advantages include non-invasiveness, rapid diagnosis and low cost (Au and Vieillard-Baron 2011; Royse et al. 2012). Respiratory variation in inferior vena cava diameter (ΔIVC) has been extensively investigated for its usefulness in the evaluation of volume status. However, these studies involved heterogeneous populations, and the results are conflicting. To clarify these mixed results, we carried out this systematic review, with the hypothesis that ΔIVC as measured by bedside ultrasonography performs well in predicting fluid responsiveness in critically ill patients.

METHODS

Searching strategy and study selection

We searched the Medline, Embase, Scopus and Web of Knowledge databases from inception to May 2013. There was no language restriction. The searched item consisted of terms related to volume status (including central venous pressure, fluid responsiveness, volume status, right atrial pressure) and terms related to inferior vena cava (IVC).

Study selection was performed in two phases. Phase 1 comprised screening for titles and abstracts, and phase 2, review of the full texts of studies obtained in phase 1. References in review articles were manually searched for potential relevant studies. Studies investigating the diagnostic accuracy of ΔIVC in predicting fluid responsiveness were included. Exclusion criteria were (i) studies measuring IVC with techniques other than ultrasonography; (ii) studies using central venous pressure or right atrial pressure as the reference standard, because these static parameters have been found to be unreliable for monitoring volume status (Marik et al. 2008); (iii) studies that did not report the diagnostic performance of ΔIVC; (iv) experimental studies involving animals. Two reviewers independently employed the searching strategy; disagreement was settled by a third opinion at the conclusion of each phase.

Important information was abstracted from the included articles in a standardized form by two reviewers. Abstracted data included the name of the first author, publication year, study population, exclusion criteria, sample size, respiratory pattern, site of IVC measurement, formula for the calculation of ΔIVC, definition of fluid responsiveness and volume expansion strategy.

Quality assessment

Included studies were assessed for their report quality based on the Quality Assessment of Diagnostic Accuracy Studies (QUADAS) protocol (Whiting et al. 2003). Spectrum bias was thought to be present when patients with low-quality images or patients who refused to participate in the study were excluded, because we felt that exclusion of these patients could potentially bias the results. The reference standard was considered to be correct when fluid responsiveness was defined as an increase in stroke volume index, cardiac output or cardiac index, irrespective of the techniques used for measurement. Disease progression bias was thought to be absent if cardiac performance was assessed immediately after fluid challenge. Partial verification bias occurs when some of the study participants do not receive confirmation of the diagnosis by the reference standard. Differential verification bias occurs when not all of the index test results are verified by the same reference standard. Description of index test was adequate if the study explicitly described the formula used to obtain ΔIVC, and description of reference standard was considered to be adequate if the study explicitly described the method used to evaluate fluid responsiveness. Un-interpretable/intermediate test results refer to cases with low-quality ultrasound image.

Statistical analysis

Studies reporting estimates of sensitivity and specificity were included in meta-analysis. Between-study variation was expected to be significant because of large variations in the calculation of ΔIVC, patients and disease cohorts, study settings and reference standards. Therefore, we adopted a hierarchical regression model for meta-analysis of studies reporting diagnostic accuracy (hierarchical summary receiver operating characteristic), which allowed for more between- and within-study variability than other fixed effect approaches (Rutter and Gatsonis 2001). Pooled statistics, including sensitivity, specificity, diagnostic odds ratio, positive likelihood ratio and negative likelihood ratio, were reported. To account for significant variations in area under the receiver operating characteristic (AUROC), we adopted a random effects model to pool AUROCs by using the method of DerSimonian and Laird, with the estimate of heterogeneity from the Mantel-Haenszel model (DerSimonian and Kacker 2007). All statistical analyses were performed using Stata 11.2 (College Station, TX, USA). A two-tailed $p < 0.05$ was considered to indicate statistical significance.

RESULTS

Our initial search identified 275 citations, 235 of which were excluded by inspection of the title and