Does the Central Venous Pressure Predict Fluid Responsiveness? An Updated Meta-Analysis and a Plea for Some Common Sense*

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Background: Despite a previous meta-analysis that concluded that central venous pressure should not be used to make clinical decisions regarding fluid management, central venous pressure continues to be recommended for this purpose.

Aim: To perform an updated meta-analysis incorporating recent studies that investigated indices predictive of fluid responsiveness. A priori subgroup analysis was planned according to the location where the study was performed (ICU or operating room).

Data Sources: MEDLINE, EMBASE, Cochrane Register of Controlled Trials, and citation review of relevant primary and review articles.

Study Selection: Clinical trials that reported the correlation coefficient or area under the receiver operating characteristic curve (AUC) between the central venous pressure and change in cardiac performance following an intervention that altered cardiac preload. From 191 articles screened, 43 studies met our inclusion criteria and were included for data extraction. The studies included human adult subjects, and included healthy controls ($n = 1$) and ICU ($n = 22$) and operating room ($n = 20$) patients.

Data Extraction: Data were abstracted on study characteristics, patient population, baseline central venous pressure, the correlation coefficient, and/or the AUC between central venous pressure and change in stroke volume index/cardiac index and the percentage of fluid responders. Meta-analytic techniques were used to summarize the data.

Data Synthesis: Overall 57% ± 13% of patients were fluid responders. The summary AUC was 0.56 (95% CI, 0.54–0.58) with no heterogenicity between studies. The summary AUC was 0.56 (95% CI, 0.52–0.60) for those studies done in the ICU and 0.56 (95% CI, 0.54–0.58) for those done in the operating room. The summary correlation coefficient between the baseline central venous pressure and change in stroke volume index/cardiac index was 0.18 (95% CI, 0.1–0.25), being 0.28 (95% CI, 0.16–0.40) in the ICU patients, and 0.11 (95% CI, 0.02–0.21) in the operating room patients.

Conclusions: There are no data to support the widespread practice of using central venous pressure to guide fluid therapy. This approach to fluid resuscitation should be abandoned. (*Crit Care Med* 2013; 41:1774–1781)

Key Words: central venous pressure; fluid challenge; hemodynamic monitoring; meta-analysis; volume responsive

The cornerstone of treating patients with hypotension, hypoperfusion, and shock remains as it has been for decades, that is, IV fluids. A fluid optimization protocol based on maximizing perioperative stroke volume (SV) and cardiac output (CO) has been shown to reduce postoperative complications and length of stay in patients undergoing major surgery (1–5). Similarly, early aggressive resuscitation of critically ill patients may limit and/or reverse tissue hypoxia, progression to organ failure, and improve outcome (6–8). However, overzealous fluid resuscitation has been associated with increased complications, increased length of ICU and hospital stay, and increased mortality (9–13). Fundamentally, the only reason to give a patient a fluid challenge is to increase SV (volume responsiveness) with an increase in CO and oxygen delivery (6). If the fluid challenge *does not* increase SV, volume loading serves the patient no useful benefit and is likely to be harmful.

Despite limited scientific data, the central venous pressure (CVP) has been used for the last 50 years to guide fluid therapy (14). In 2008, we published a meta-analysis evaluating the ability of the CVP to guide fluid therapy (15). We demonstrated that the CVP was no better than flipping a coin in predicting fluid responsiveness and concluded that the "*CVP should not be used to make clinical decisions regarding fluid management.*" Despite this finding, the CVP continues to be recommended to guide fluid resuscitation (16, 17). Since the publication of our

*See also p. 1823.

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meta-analysis, the concept of fluid responsiveness has become well accepted, and a number of studies have been published investigating the role of various techniques to assess fluid responsiveness (6). Due to the ongoing recommendations in the Critical Care and Anesthesia literature to use the CVP to guide fluid therapy, we decided it was important to update our meta-analysis to include the most recent studies. We were curious to explore whether any of the more recent studies were able to demonstrate a role of the CVP in guiding fluid resuscitation. In addition, in our previous meta-analysis, all the studies were grouped together. We postulated that in the controlled environment of the operating room, the CVP may be more predictive of volume responsiveness than in hemodynamically unstable critically ill ICU patients. Furthermore, due to changes in cardiac performance following cardiac surgery, the CVP may be less reliable in these patients than in those patients undergoing noncardiac surgery. We therefore decided a priori to perform subgroup analysis according to the setting the study was performed (ICU or operating room) and the type of patient population (cardiac surgery vs noncardiac surgery patients) to make our finding more clinically relevant.

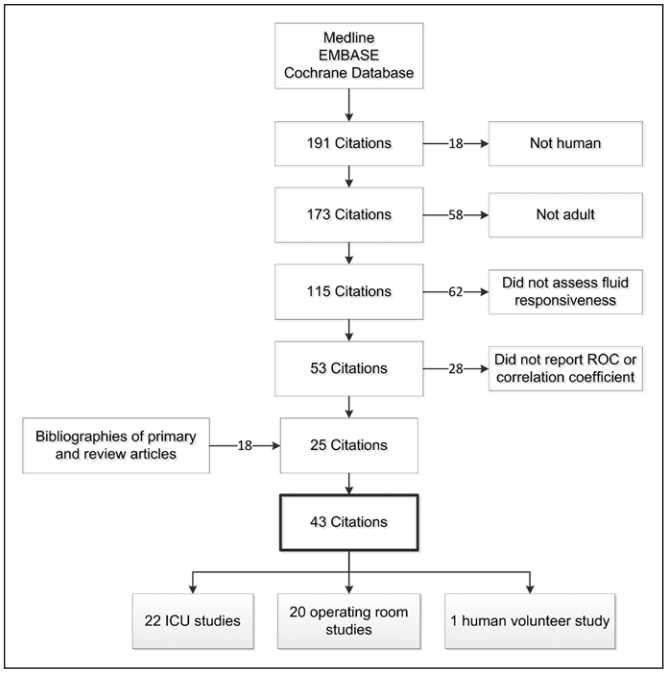

Figure 1. Flowchart of study selection. ROC = receiver operator characteristic.

METHODS

Identification of Trials

Our aim was to identify all relevant clinical trials that investigated the ability of the CVP to predict fluid responsiveness. Fluid responsiveness was defined as an increase in CO or SV following a preload challenge, usually a volume challenge or passive leg raising (PLR) maneuver. We restricted this analysis to human adults; however, there was no restriction as to the type of patient or the setting where the study was performed. We used a multimethod approach to identify relevant studies for this review. Both authors independently searched the National Library of Medicine's MEDLINE database for relevant studies in any language published from 1966 to June 2012, using the following Medical Subject Headings and keywords: CVP (explode) and fluid therapy or fluid responsiveness. In addition, we searched EMBASE and the Cochrane Database of Systematic Reviews. Bibliographies of all selected articles and review articles that included information on hemodynamic monitoring were reviewed for other relevant articles. This search strategy was done iteratively, until no new potential citations were found on review of the reference lists of retrieved articles. We performed this meta-analysis according to the guidelines proposed by the Quality of Reporting of Meta-analyses group (18).

Study Selection and Data Extraction

Only studies that reported the correlation coefficient or the area under the receiver operating characteristic curve (AUC) between the CVP and change in cardiac performance following a fluid challenge, PLR maneuver/postural change, or positive end-expiratory pressure challenge were included in this analysis. Both authors independently abstracted data from all studies using a standardized form. Data were abstracted on study design, study size, study setting, patient population, criteria used to define fluid responsiveness, type of fluid challenge, the primary technology being assessed, the correlation coefficients and AUC (including 95% CIs) for the CVP and fluid responsiveness, the percentage of patients responding to a fluid challenge, as well as the baseline CVP in the fluid responders and nonresponders.

Data Analysis

Studies were subgrouped according to the location where the study was performed (ICU or operating room) and the type of patient population (cardiac surgery vs noncardiac surgery patients). Summary data are presented as means (± standard deviations) and percentages as appropriate. Meta-analytic techniques were used to summarize the data. The random effects models using Comprehensive Meta-analysis 2.0 (Biostat, Englewood, NJ) were used to determine the summary AUC and correlation coefficients. Summary effects estimates are presented with 95% CIs. We assessed heterogeneity between studies using the Cochran Q statistic (19), with a p value of less than or equal to 0.10 indicating significant heterogeneity (20), and I^2 with suggested thresholds for low (25%–49%), moderate (50%–74%), and high (> 75%) values (21, 22).

RESULTS

A flow diagram outlining the search strategy and study selection is illustrated in **Figure 1**. Forty-three studies met the inclusion criteria for this meta-analysis (23–65). The details of these studies are provided in **Table 1**. Overall 2,105 fluid responsiveness maneuvers were performed in 1,802 patients. Twenty-two studies were performed in ICU patients (four cardiac surgery patients), and 20 studies (13 cardiac surgery patients) were

TABLE 1. Characteristics of the Studies Included in Meta-Analysis

Author	Year	Patients	No. of Patients	Method
ICU				
Calvin et al (23)	1981	Various	28	PAC
Reuse et al (24)	1990	Various	41	PAC
Wagner and Leatherman (25)	1998	Various	25	PAC
Michard et al (26)	2000	Sepsis	40	PAC
Reuter et al (27)	2002	CABG	20	PiCCO
Barbier et al (28)	2004	Sepsis	20	TEE
Kramer et al (29)	2004	CABG	21	PAC
Marx et al (30)	2004	Sepsis	10	PAC, PiCCO
Perel et al (31)	2005	Vascular surgery	14	TEE
De Backer et al (32)	2005	Various	60	PAC
Osman et al (33)	2007	Septic	96	PAC
Magder and Bafaqeeh (34)	2007	CABG	66	PAC
Wyffels et al (35)	2007	CABG	32	PAC
Auler et al (36)	2008	CABG	59	PAC
Muller et al (37)	2008	Various	35	PiCCO
Huang et al (38)	2008	ARDS	22	PAC, PiCCO
Garcia et al (39)	2009	Various	38	Flotrac (Edwards Life-Sciences, Irvine, CA)
Thiel et al (40)	2009	Various	89	Doppler
Garcia et al (41)	2009	Various	30	Flotrac
Moretti and Pizzi (42)	2010	SAH	29	PiCCO
Muller et al (43)	2011	Various	39	TTE
Lakhal et al (44)	2011	ARDS	65	PAC/PiCCO
Operating room				
Berkenstadt et al (45)	2001	Neurosurg	15	PiCCO
Rex et al (46)	2004	CABG	14	PiCCO/TEE
Preisman et al (47)	2005	CABG	18	TEE, PiCCO
Hofer et al (48)	2005	CABG	40	PAC, PiCCO
Wiesenack et al (49)	2005	CABG	20	PiCCO
Solus-Biguenet et al (50)	2006	Hepatic	8	PAC, TEE
Cannesson et al (51)	2006	CABG	18	TEE
Lee et al (52)	2007	Neurosurg	20	TEE, Doppler
Cannesson et al (53)	2007	CABG	25	PAC
Belloni et al (54)	2008	CABG	19	PAC, TEE
Biais et al (55)	2008	OTLTx	35	PAC, TEE

Inclusion Criteria	Mechanical Ventilation	Other Comparator	Challenge	r-ΔSV	Area Under the Receiver Operator Characteristic Curve
SV	N	–	250 cc Colloid	0.16	–
CI	Y	RVEDVI	300 cc Colloid	0.21	–
SV > 10%	Y	RVEDVI	500 cc Colloid	0.44	–
CI > 15%	Y	PPV	500 cc Colloid	–	0.51
SVI > 15%	Y	SVV	500 cc Colloid	–	0.42
CI > 15%	Y	IVC-collapse	7 mL/kg Colloid	0.17	0.57
CI > 12%	Y	PPV	500 cc Colloid	0.13	0.49
CI	Y	SVV, ITBVI	500 cc Colloid	0.41	–
CI > 15%	Y	SVV	7 mL/kg colloid	0.27	–
CI > 15%	Y	SVV	500 cc Colloid	–	0.54
CI > 15%	Y	–	500 cc Colloid	–	0.58
CI > 0.3%	Y	–	350 cc Colloid	0.36	–
CI > 15%	Y	PPV	500 cc Colloid	0.16	0.6
CI > 15%	Y	PPV	20 mL/kg LR	–	0.58
SVI > 15%	Y	ITBVI	500 cc Colloid	–	0.68
CI > 15%	Y	SVV, PPV	500 cc Colloid	–	0.42
SVI > 15%	Y	Brachial artery velocity	500 cc Colloid	–	0.64
SV > 15%	Y	PLR	PLR	–	0.52
SVI > 15%	N	Valsalva	500 cc Colloid	–	0.51
CI > 15%	Y	SVV, IVC-collapse	7 mL/kg Colloid	–	0.66
VTI > 15%	Y	PPV/VTI	500 cc Colloid	–	0.61
CO > 10%	Y	PPV	500 cc Colloid	–	0.63
SV > 5%	Y	SVV	100 cc Colloid	0.05	0.493
SVI > 5%	Y	PPV, ITBVI	Head up-down	0.3	–
SV > 15%	Y	SVV	250 cc Colloid	–	0.61
SVI > 25%	Y	SVV, GEDV	10 mL/kg Colloid	0.02	0.54
SVI > 20%	Y	PPV	7 mL/kg Colloid	0.34	–
SVI > 10%	Y	PPV, LVEDA	250 cc Colloid	–	0.63
CO > 15%	Y	LVSA	PLR	0.23	0.27
SVI > 10%	Y	PPV, Doppler	7 mL/kg Colloid	–	0.54
CI > 15%	Y	PVI, PPV	500 cc Colloid	0.28	0.57
CI > 15%	Y	PPV	7 mL/kg Colloid	0.08	–
CO > 15%	Y	SVV	20 mL × BMI colloid	–	0.64

(*Continued*)

TABLE 1. (*Continued*). Characteristics of the Studies Included in Meta-Analysis

Author	Year	Type of Patients	No. of Patients	Method
Hofer et al (56)	2008	CABG	40	PAC, Flotrac
de Waal et al (57)	2009	CABG	18	PiCCO
Cannesson et al (58)	2009	CABG	25	PAC
Zimmerman et al (59)	2010	Ab-surg	20	Flotrac
Desebbe et al (60)	2010	CABG	21	PAC
Desgranges et al (61)	2011	CABG	28	PAC
Shin et al (62)	2011	OTLTx	33	PAC, Flotrac
Broch et al (63)	2011	CABG	81	PiCCO
Cannesson et al (64)	2011	Various	413	PAC/PiCCO
Volunteers				
Kumar et al (65)	2007	Healthy volunteer	12	Echocardiography

SV = stroke volume, PAC = pulmonary artery catheter, RVEDVI = right ventricular end-diastolic volume index, PPV = pulse pressure variation, CABG = coronary artery bypass graft, PiCCO = transpulmonary thermodilution, Pulsion Medical Systems (Feldkirchen, Germany), SVI = stroke volume index, SVV = stroke volume variation, TEE = trans-esophageal echocardiography, IVC = inferior vena cava, ITBV = intrathoracic blood volume index, ARDS = acute respiratory distress syndrome, PLR = passive leg raise, SAH = subarachnoid hemorrhage, CI = cardiac index, TTE = trans-thoracic echocardiography, VTI = velocity time integral, CO = cardiac output, GEDV = global end-diastolic volume, LVEDA = left ventricular end diastolic area, LVSA = left ventricular surface area, PVI = pleth variability index, PEEP = positive end-expiratory pressure, OTLTx = orthotopic liver transplant.

performed in the operating room. In addition, a single study that evaluated the hemodynamic response to fluid loading in healthy volunteers was also included. Most of the studies used an increase of stroke volume index (SVI) or cardiac index (CI) of 15% following a 500 cc fluid challenge (usually a tetrastarch) to define fluid responsiveness.

AUC data were available for 33 studies and correlation data for 20 studies. Overall 57% ± 13% of patients were fluid responders, with 52% ± 11% of ICU patients being fluid responders as compared to 63% ± 15% of patients in the operating room. The mean baseline CVP was 8.2 ± 2.3 mm Hg in the fluid responders and 9.5 ± 2.2 mm Hg in the nonresponders. The summary AUC was 0.56 (95% CI, 0.54–0.58), with no heterogenicity between studies (Q statistic $p = 0.9$, $I^2 = 0\%$). The summary AUC was 0.56 (95% CI, 0.52–0.60) for those studies done in the ICU and 0.56 (95% CI, 0.54–0.58) for those done in the operating room. Similarly, the summary AUC was 0.56 (95% CI, 0.51–0.61) for the cardiac surgery patients and 0.56 (95% CI, 0.54–0.58) for the noncardiac surgery patients. The summary correlation coefficient between the baseline CVP and the delta SVI/CI was 0.18 (95% CI, 0.1–0.25), being 0.28 (95% CI, 0.16–0.40) in the ICU patients, and 0.11 (95% CI, 0.02–0.21) in the operating room patients.

DISCUSSION

This study confirms and extends the findings of our previous meta-analysis, namely, that the CVP is unable to predict fluid responsiveness among a broad range of patients in various clinical settings. A review of cardiac physiology would lead one to the same conclusion as the premise that the CVP (or pulmonary artery occlusion pressure) is a measure of preload responsiveness is seriously flawed. The CVP is believed to be an indicator of right ventricular end-diastolic volume index (RVEDVI). The RVEDVI in turn is believed to be an indicator of preload responsiveness. Both of these assumptions are incorrect, resulting in a cascading error of logic. Due to the curvilinear shape of the ventricular pressure-volume curve, there is a poor relationship between ventricular filling pressure and ventricular volume (preload). This relationship is further disturbed by diastolic dysfunction and altered ventricular compliance that is characteristic of critical illness. Furthermore, clinical studies have clearly demonstrated that ventricular volumes (RVEDVI, left ventricular end-diastolic area, global end-diastolic volumes) are unable to predict fluid responsiveness (25, 46, 52, 54, 66).

The origins of CVP monitoring can be traced back to Hughes and Magovern (14), who in 1959 described a complicated technique for right atrial pressure monitoring. These authors intermittently measured blood volume (using radioactive serum albumin) and hourly urine output, blood pressure, respiratory rate, and pulse rate in 25 postthoracotomy patients. Without providing any summary data or statistical testing, they made the remarkable conclusion that "right atrial pressure is an accurate and sensitive recording of the effective circulating blood volume" and that "the adequacy and rate of treatment are accurately reflected by the right atrial pressure monitor, and two cases are presented to substantiate the same."

Inclusion Criteria	Mechanical Ventilation	Other Comparator	Challenge	r-ΔSV	Area Under the Receiver Operator Characteristic Curve
SV > 25%	Y	SVV, PPV	Head up-down	–	0.29
SVI > 12%	Y	PPV, SVV	10 mL/kg Colloid	–	0.57
CI > 15%	Y	SVV	500 cc Colloid	–	0.53
SVI > 15%	Y	SVV/PVI	7 mL/kg Colloid	0.18	0.55
CI < 15%	Y	PVI	10 cm PEEP	–	0.25
CI > 15%	Y	PVI	500 cc Colloid	–	0.48
CI > 15%	Y	SVV	10 mL/kg Colloid	0.11	0.57
SVI > 15%	Y	PVI, PPV	PLR	0.12	0.6
CO > 15%	Y	PPV	500 cc Colloid	–	0.57
	N	Various	3,000 Crystalloid	0.32	–

The technique of CVP monitoring was further popularized by Wilson and Grow (67) and soon became routine in patients undergoing thoracic surgery. Based on these anecdotes, CVP became the standard tool for guiding fluid therapy, initially in the operating room and then in the ICU and emergency department.

In conclusion, there are no data to support the widespread practice of using CVP to guide fluid therapy. This approach to fluid resuscitation is without a scientific basis and should be abandoned.

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