Utility of esophageal Doppler as a minimally invasive hemodynamic monitor: a review

[Revue de l'utilité du Doppler œsophagien comme moniteur hémodynamique à effraction minimale]

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Purpose: The current bedside "gold standard" for cardiac output (CO) monitoring is thermodilution using a pulmonary artery catheter (PAC) but there is a number of risks associated with its use. The primary objective of this review was to evaluate the utility of esophageal Doppler (ED) as a minimally invasive monitor of CO.

Source: Medline literature search from 1966 to 2001 with citation review for studies comparing ED to PAC thermodilution for CO in perioperative and critically ill patients.

Principal findings: Twenty-five publications were identifed comparing ED and PAC measurement of CO in a broad range of patients. There was a good overall correlation between CO determined by ED and thermodilution (n = 18 studies, median R = 0.89, range 0.52 to 0.98) and minimal bias (n = 13, median -0.01, range 1.38 to 2 L·min^{-1}). The precision of ED was only fair overall as assessed by limits of agreement. The ED technique was found to be responsive in detecting changes in thermodilution CO and was reliable demonstrating both low intra- and inter-observer variation. ED was reportedly easy to insert after minimal training and was safe, with no significant complications identified.

Conclusion: ED is a practical, reliable, and valid device for measuring CO in perioperative and critically ill patients. Further studies with larger numbers of patients are needed to determine if the limited precision observed is inherent to the technique, the diagnoses of patients studied, or the small sample sizes.

Objectif : *La thermodilution avec un cathéter artériel pulmonaire (CAP) représente la référence actuelle en monitorage de chevet du débit cardiaque (DC), mais elle comporte certains risques. L'objectif principal de la présente revue était d'évaluer l'utilité du Doppler œsophagien (DO) comme moniteur du DC à effraction minimale.*

Source : *Nous avons procédé à une recherche dans Medline, pour la période de 1966 à 2001, et à une revue des citations pour les études comparant l'usage périopératoire du DO et de la thermodilution avec CAP pour le DC chez des patients gravement malades.*

Constatations principales : *Vingt-cinq articles traitaient de la comparaison des mesures du DC avec DO et CAP chez une grande diversité de patients. Une bonne corrélation globale a été notée entre le DC déterminé par le DO et la thermodilution (n = 18 études, R médian = 0,89, étendue de 0,52 à 0,98) et biais minimal (n = 13, médiane -0,01, étendue de 1,38 à 2 L·min^{-1}). La précision du DO n'a été que bonne dans l'ensemble comme l'ont montré les limites de la concordance. La technique du DO a été trouvée efficace, car elle détecte les modifications du DC noté par thermodilution, et fiable, puisqu'elle peut démontrer une faible variation intra-observateur et interobservateur. Les articles révèlent que le DO est facile à insérer, ne requérant qu'une formation minimale, et sans risque, ne présentant pas de complications significatives connues.*

Conclusion : *Le DO est un appareil de mesure périopératoire du DC pratique, fiable et valide pour des patients gravement malades. D'autres études auprès d'un plus grand nombre de patients demeurent nécessaires pour déterminer si la précision limitée qui a été observée est inhérente à la technique, aux diagnostics des patients étudiés ou aux échantillonnages de faible effectif.*

THE use of pulmonary artery catheters (PAC) for hemodynamic monitoring of perioperative and critically ill patients has become increasingly criticized.[1] Since the introduction of the flow-directed balloon-tipped PAC three decades ago by Swan *et al.* there has been an explosion in its use.[2] Despite concerns regarding its

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Dr. Laupland was supported by the 2000 Bayer Healthcare/Canadian Institutes of Health Research/Canadian Infectious Diseases Society Research Fellowship and a clinical fellowship award from the Alberta Heritage Foundation for Medical Research.

Accepted for publication September 27, 2001.

Revision accepted January 16, 2002.

safety and lack of empiric evidence for benefit, it has become a standard of care for managing high-risk perioperative and critically ill intensive care unit (ICU) patients in many centres. In the 1990's a number of non-randomized cohort and case-control studies associating the use of PAC with increased mortality were published with increasing concern raised about its widespread use.[1,3,4]

Sandham and colleagues on behalf of the Canadian Critical Care Clinical Trials Group recently reported on a randomized controlled trial of PAC use in 1994 high-risk geriatric surgical patients.[5] They found no difference in the mortality rate (7.8% PAC *vs* 7.7% control) or length of hospitalization among patients treated with the aid of a PAC as compared to those managed without this device. However, patients randomized to PAC use showed a trend toward less renal impairment but suffered a significantly higher rate of procedural complications and pulmonary emboli. Although the results of this trial must be generalized cautiously to all high-risk perioperative and critically ill patients, this trial provides good evidence that PACs do not inherently increase mortality. However, it is not clear whether the potential advantages of less organ dysfunction and improved diagnostic certainty with PAC outweigh the significantly increased complications associated with its use.

Non-invasive or minimally invasive hemodynamic monitoring techniques may provide an alternative to the use of PAC. However, to be adopted, these techniques, at a minimum, need to demonstrate that they are safe and provide accurate hemodynamic information. A number of non-invasive or minimally invasive methods have been proposed and include esophageal Doppler (ED), transesophageal echocardiography, arterial waveform analysis, thoracic impedance, and modified Fick techniques.[6–8] ED is well suited to the perioperative or ICU environment because it is a relatively simple technique that does not require specialized training or complex equipment. The primary objective of this report was to perform a semi-structured, comprehensive review of the utility of ED as a minimally invasive measure of cardiac output (CO) in perioperative and critically ill adult patients. Since many critical care physicians and anesthesiologists may not be familiar with this technique, a brief review of theoretical and practical aspects of ED and its use as a cardiac preload measure is also presented.

ED: theoretical considerations

ED was first proposed as a minimally invasive hemodynamic measure in the 1970's and it has undergone significant technological advancement and clinical evaluation since.[9,10] Initially, suprasternal transthoracic ultrasound/Doppler probes were used for determining CO but they were not widely adopted because probe position instability limited their use for repeated measures over extended periods of time.[11] Esophageal probes were recognized to have two significant advantages over suprasternal probes. The first was that the smooth muscle tone of the esophagus is a natural means of maintaining the probe in position for repeated measures. The second was that the esophagus is in close anatomical proximity to the aorta so that signal interference from bone, soft tissue, and lung is minimized. Over the past three decades ED has evolved from an experimental technique to a relatively simple bedside procedure with the latest models incorporating both Doppler and echo-ultrasound in a single probe.

Determination of CO using ED is based on the following principles.[12] A Doppler flow probe is used to directly measure flow velocity (V_f). The cross sectional area of the aorta (CSA_a) is then determined either by ultrasonic measurement or estimated using published nomograms. Aortic blood flow (ABF) is then calculated based on the product of V_f and CSA_a. Because the ED probe measures ABF in the descending aorta, the measured ABF is always less than CO as a result of blood flow to aortic arch branches. Although it varies among patients and disease states, ABF is typically 70% of CO.[12] Therefore, ED probes directly measure ABF but only estimate CO.

There are a number of considerations regarding the accuracy of ED for estimating CO. First, turbulence arising from thoracic aortic aneurysms, intra-aortic balloon pumps, and aortic valve disease may affect the V_f profile and lead to invalid results. However, this is a theoretical concern that has not been adequately studied. Second, the assumption of a constant proportion of blood flow to the descending aorta may not be valid such as in the setting of aortic coarctation, aortic cross-clamp, acute bleeding, or pregnancy.[13,14] Finally, the CSA_a may vary considerably between patients and within the same patient in different disease states. Some ED models estimate CSA_a using nomograms based on patient gender, age, and body surface area or use a single transthoracic ultrasonic measure at the start of the study. In the former case, significant error in the actual aortic diameter may occur as a result of biological variation and in both cases error may arise from changing states of hydration, stress, vasoactive medication use, or from application of an aortic cross-clamp.[11,15,16] In an attempt to minimize this error, an echo-ED model that contains both a Doppler and ultrasound (M-mode) probe has been developed.[12]

With the echo-ED, real-time measurements of V_f and CSA_a are made and continuously measured ABF is displayed.

ED: practical considerations

Probe placement

The ED probe is placed via the oral or nasal route and may be left *in situ* for days to weeks.[17] The ideal probe tip location is at the level between the fifth and sixth thoracic vertebrae because at that level the aorta is adjacent and parallel to the esophagus.[18] This location is achieved by superficially landmarking the distance to the third sternocostal junction anteriorly and is approximately 30 to 40 cm in the average adult. After insertion, the ED probe is then rotated on its axis to achieve an optimal signal prior to taking measurements. Contraindications to ED use include known esophageal anatomical abnormalities such as malformations, tumours, strictures or varices, recent esophageal or upper airway surgery, or acute esophagitis. Because of the mild discomfort associated with placing the probe (comparable to insertion of a nasogastric or orogastric drainage tube) and maintaining it in fixed position, patients monitored with an ED require adequate sedation.

Safety and ease of use

ED appears to be associated with few complications and minimal training is required to insert and achieve an adequate signal in most patients. Although not formally timed in studies, ED has been reported to typically take less than five minutes to place and obtain a clear signal.[17,19,20] Two studies have formally evaluated the role of experience on the quality of results and found that approximately ten to 12 patients were required for an operator to develop consistent efficiency and accuracy.[21,22] No major adverse events related to the use of ED were reported in any of the literature included in this review. Furthermore, one author has anecdotally reported no significant complications with his use of ED in more than 500 patients.[17]

ED as a valid measure of CO

Search strategy

CO determination by thermodilution using a PAC is the current bedside "gold standard" method and has been shown to be comparable to other valid measures including the Fick and dye dilution techniques.[23] Since PAC thermodilution cardiac output (CO_{TD}) is the most widely used standard, a Medline search from 1966 to February 2001 was conducted to identify published studies comparing CO_{TD} and ED CO (CO_{ED}) or ABF in perioperative and intensive care patients. Search terms included PAC, Swan Ganz catheterization, ED, and Doppler echocardiography. Studies were limited to English language, human, and age > 12 yr. Abstracts were screened and full-length articles were retrieved for all relevant studies. Review articles and bibliographies of identified studies were searched in an attempt to identify other studies missed by the Medline search strategy.

Measures of agreement

In this review the parameters of Bland and Altman were chosen in preference to the product-moment correlation coefficient (R) to assess agreement between CO_{TD} and CO_{ED} or ABF.[24] The product-moment correlation coefficient is merely a measure of the degree of linear association between the two methods and is a poor measure of agreement or the degree to which the two techniques measure the same absolute value. In Bland–Altman analysis, the difference between the two measures (CO_{TD}–CO_{ED}) is plotted against their mean [½(CO_{TD} + CO_{ED})]. The mean difference or "bias" is a measure of how well the two techniques agree on average.[25] A measure of precision or range of agreement for a given individual is expressed as the 95% "limits of agreement". This is calculated as the bias ± two standard deviations of the differences. Practically, if 95% limits of agreement (LOA) are within clinically acceptable limits the two techniques may be used interchangeably.[24]

Identified studies

A total of 25 full-length articles and abstracts were identified that fulfilled the search criteria and are shown in the Table. Nineteen reports evaluated ED[13,14,21,22,26–39] and six[16,20,40–43] assessed echo-ED CO_{ED}/ABF *vs* PAC CO_{TD} respectively. However, one data set was published twice,[42,43] and one abstract that was more than five years old was excluded from review based on journal policy.[44] No studies were identified that directly compared ED CO/ABF with echo-ED CO/ABF. The identified studies varied considerably in patient population and in quality (Table). Twelve studies were from Europe, nine from the United States, one from Australia, and one from South Africa. There was a broad range of patients enrolled including perioperative (cardiac, aortic reconstructive, and general surgery) and medical and surgical ICU patients. The studies were generally small with a median of 20 (range 9 to 60) patients. It is not practical to report a detailed critical appraisal of each of the study methodologies in this review. However, despite its importance to the validity of their results, it is notable that only a minority of the studies described an adequate blinding process.[13,26,28,29,39] Furthermore, a number of

TABLE Summary of studies for ED CO

Study population (year)	*Modalities compared*	*Number of patients (paired measurements)*	*Results*	*Limitations*	*Reference*
ICU, Lyon, France (1985)	Echo esophageal Doppler (ED) *vs* thermodilution cardiac output (CO_{TD})	21 (300)	R = 0.98	Not blinded, no Bland-Altman (BA) analysis	(42, 43)
Cardiac surgery, Boston, USA 1986	ED (Ultracom, Lawrence Medical Systems, Camarillo USA) *vs* CO_{TD}	16 (372)	R = 0.92	Not blinded, no BA analysis, small study	(32)
Elective surgery, Seattle, USA (1987)	ED (Ultracom) *vs* CO_{TD}	23 (420)	R = 0.67 overall, after the first ten patients R = 0.85. Bias (limits of agreement, LOA) -0.16 (-0.97, 0.65) $L \cdot min^{-1}$	Not blinded, results statistical analysis not well described	(22)
Cardiovascular surgery, Stanford, USA (1988)	ED (Lawrence 3000, Lawrence Medical Systems) *vs* CO_{TD}	9 (25)	R = 0.68 Bias -0.1 $L \cdot min^{-1}$	Not blinded, small study, LOA reported inconsistently in article	(35)
Surgical or ICU patients, London UK (1989)	ED (prototype) *vs* CO_{TD}	38 (238)	Percent bias (LOA) for changes in CO_{TD} 0.6% (-13.5%, 14.7%)	No R between CO_{TD} and ED or BA analysis reported, not blinded	(36)
Elective surgery, Los Angeles, USA (1989)	ED (Ultracom) *vs* CO_{TD}	14 (246)	R = 0.75 Bias -1.38 $L \cdot min^{-1}$	Not blinded, small study	(30)
Postcardiac surgery ICU, Zurich, Switzerland (1990)	ED (Accucom I, Datascope Corp. Paramus, USA) *vs* CO_{TD}	23 (96)	R = 0.55	Not blinded, no BA analysis	(37)
Noncardiac surgery, New Haven, USA	ED (Accucom I and II) *vs* CO_{TD}	43 (923)	Accucom I: R = 0.72, bias (LOA) -0.4 (-2.9, 2); Accucom II R = 0.91, bias (LOA) -0.2 (-1.6, 1.2) $L \cdot min^{-1}$	Exact values for BA analysis not reported (estimated from graphs), not blinded	(33)
Cardiac surgery, Sydney, Australia (1991)	ED (Lawrence 3000) *vs* CO_{TD}	11 (106)	Bias -1.0 LOA (-4.6, 2.6) $L \cdot min^{-1}$.	Small study, not blinded	(38)
Abdominal aortic surgery, New Haven, USA	ED (Accucom II) *vs* CO_{TD}	39 (489)	Baseline R = 0.94, X-clamp R = 0.72, postclamp R = 0.88. Approx. Bias (LOA) baseline -0.3 (-1.7, 1.1), X-clamp 0.7 (-1.9, 3.3), postclamp -0.1 (-1.6, 1.4) $L \cdot min^{-1}$.	Exact values for BA analysis not reported (estimated from graphs)	(13)
Postop cardiac surgery patients Zurich, Switzerland (1993)	ED (Accucom II) *vs* CO_{TD}	16 (140)	R = 0.52, bias (LOA) -0.37 (-3.8, 3.0) $L \cdot min^{-1}$.	Not blinded, small study	(34)

TABLE *continued*

Study population (year)	*Modalities compared*	*Number of patients (paired measurements)*	*Results*	*Limitations*	*Reference*
Cardiac surgery, Belfast, Northern Ireland (1997)	ED (ODM II, Doptek) *vs* continuous CO_{TD}	11 Group I (probe not readjusted) 5 Group II (probe readjusted)	Bias (LOA) for Group I = 0.8 (-2.2, 3.8) and Group II = 0.14 (-0.58, 0.85) $L{\cdot}min^{-1}$	Small study	(29)
ICU patients, Nimes, France	ED (ODM I) *vs* CO_{TD}	11 (107) training, 49 (320) evaluation	Training and evaluation R = 0.53 and R = 0.89, bias (LOA) 1.2 (-2.0, 4.4) and 0.1 (-2.1, 2.3) $L{\cdot}min^{-1}$ respectively	Unclear if adequate blinding in evaluation phase	(21)
Medical ICU, Paris, France Paris, France) *vs* CO_{TD}	Echo-ED (Dynemo-3000, Sometec Inc.,	20 (80)	R = 0.80	Not blinded, no BA analysis	(41)
Medical ICU, Nice, France (1998)	Echo-ED (Dynemo-3000) *vs* CO_{TD}	22 (60)	R = 0.92	BA analysis not reported	(16)
3 ICUs in Paris, France (1998)	ED (ODMI) *vs* CO_{TD}	46 (136)	R = 0.95, bias (LOA) 0.24 (-1.56, 2.04) $L{\cdot}min^{-1}$		(39)
Cardiac or abdominal surgery, Stuttgart, Germany (1998)	Echo-ED (Dynemo 3000) *vs* CO_{TD}	48 (171)	R = 0.90	No BA analysis, not blinded, abstract publication	(20)
Surgical ICU Detroit, USA (1998)	ED (EDM, Deltex Medical Inc.) *vs* CO_{TD}	10	R = 0.92	No BA, analysis, not blinded, abstract publication, small study	(27)
ICU, Bobigny, France (1999)	ED (ODM II) *vs* continuous CO_{TD}	10 (145)	Bias (LOA) -0.01 (-0.97, 0.96) $L{\cdot}min^{-1}$	Small study	(26)
3 Surgical ICUs in New Orlean's USA (1999)	ED (Deltex) *vs* CO_{TD}	14 (118)	R = 0.77	Not blinded, no BA analysis, small study	(31)
Off pump cardiac surgery, Stuttgart, Germany (1999)	Echo-ED (Dynemo 3000) *vs* CO_{TD}	10 (50)	R = 0.89 Bias (LOA) 0.77 (-0.49, 2.03) $L{\cdot}min^{-1}$	Not blinded, abstract publication, small study	(40)
Preeclampsia, Cape Town, South Africa	ED *vs* CO_{TD}	17	Bias (LOA) 2.0 (-1.0, 5.0) $L{\cdot}min^{-1}$	Not blinded, type of ED and ABF correction factor not specified, small study	(14)
Elective cardiac surgery, Dallas, USA (2000)	ED (Deltex) *vs* CO_{TD} *vs* direct aortic flow probe	34 (160)	R = 0.77 for ED-CO *vs* flow probe comparable to CO_{TD}	Did not report correlation or agreement directly with CO_{TD}	(28)

ICU = intensive care unit; ABF = aortic blood flow.

the studies were limited because they only reported correlation coefficients and did not perform Bland–Altman analysis of their results.[24]

CO_{ED} vs CO_{TD}

In general, the studies showed good correlation between the ED derived ABF or CO and CO_{TD}. In the 18 studies that reported the correlation coefficient, the median was 0.89 (range 0.52 to 0.98). There was a tendency for a higher correlation to be observed with the newer generations of ED and echo-ED (Table). Among the 13 studies that reported a measure of bias, the median was -0.01 (range -1.38 to 2) $L \cdot min^{-1}$. It is not possible to estimate composite LOA without the raw data from each of the studies. Boulnois and Pechoux[12] pooled three studies[16,20,41] of echo-ED and found among 90 (311 matched measurements) patients a correlation coefficient of 0.89, bias of 0.06 $L \cdot min^{-1}$, and LOA -2.21 to 2.33 $L \cdot min^{-1}$.

Responsiveness

Five studies specifically quantified ED's ability to detect changes in CO_{TD}. Studies typically defined a significant change in CO_{TD} as at least a 12–15% difference from baseline as per Stetz *et al.*[23] Valtier *et al.* found good agreement between changes in CO_{TD} and CO_{ED} R = 0.9, bias 0 $L \cdot min^{-1}$, LOA -1.7 to 1.7 $L \cdot min^{-1}$).[39] Cariou and colleagues calculated a sensitivity of 75% and specificity of 95% for echo-ED to detect a 13% change in CO_{TD} in medical ICU patients.[41] In patients undergoing aortic reconstructive surgery, Perrino found that ED detected changes of 15% CO_{TD} with a sensitivity of 89% without and 79% during cross-clamping of the aorta.[13] Two studies calculated percent bias (LOA) for changes in CO_{TD} of 0.6% (-13.5%, 14.7%) and -0.66% (-20.1%, 18.8%).[34,36] Penney *et al.* found that CO_{ED} correctly tracked CO_{TD} changes in 13 of 16 women with pre-eclampsia but they did not quantify the magnitude.[14] Kumar and colleagues reported similar results in 11 of 14 anesthetized surgical patients.[30]

Reliability

Six studies assessed the reproducibility of ED both between (inter-observer) and within (intra-observer) operators.[16,30,32,36,39,43] Inter-observer variability was assessed with echo-ED in two studies with 11 and 22 patients that found differences with repeated measures in stable patients to be 0.75% and 3.3% respectively between two operators blinded to each other's findings.[16,43] Intra-observer variability as assessed by calculating the coefficient of variation in four studies was 8%, 5.7%, 3.8%, and 3.3% for ED as compared to 12%, 8.3%, 6.2%, and 4.6% for thermodilution respectively.[16,32,36,39]

Applicability

The proportion of patients for whom a successful insertion and signal was obtained was 97% among the 558 patients included in this review. This rate, however, refers to those patients that were enrolled in the studies and does not necessarily reflect the applicability rate of consecutive patients presenting to the operating room or ICU. Reasons cited for ED failure included interference from a nasogastric tube, lung disease and particularly adult respiratory distress syndrome requiring high levels of positive end-expiratory airway pressure, and poor signal quality or inability to maintain a stable signal for unspecified reasons.[13,16,20,21,30,33,37]

ED for preload assessment

Although CO is the most valuable hemodynamic parameter, assessment of ventricular filling is also believed to be important in management of perioperative and critically ill patients. Unlike the use of PAC thermodilution for CO determination, there is unfortunately no bedside gold standard for determining optimal ventricular filling. In the absence of a good measure, the pulmonary capillary wedge pressure (PCWP) using a PAC is commonly used. However, the PCWP is subject to a number of technical, disease related, and interpretation problems and its validity has not been proven in critically ill human beings.[45,46] ED waveform analysis has been increasingly evaluated as a method for determining optimum cardiac preload. A detailed description of ED V_f waveform shape analysis is beyond the scope of this article, but it has been reviewed extensively by Singer.[17] The key preload parameter of interest is the flow time, that is the time required from start of waveform upstroke to return to baseline. Since the flow time is heart rate dependent it is typically corrected (FT_c) by dividing the flow time by the square root of the cycle time (normal range approximately 330 to 360 msec).[17] Few studies have attempted to evaluate the FT_c as a preload measure and are detailed in the following two paragraphs.

Singer and Bennett investigated FT_c as a measure of ventricular filling by placing an ED and a PAC in 43 mechanically ventilated ICU and cardiothoracic surgery patients in London, UK.[47] After baseline measures, the patient's ventricular filling was manipulated either by increasing it with *iv* fluid loading if hypovolemic (PCWP < 8 mmHg) or by decreasing it with *iv* nitrates if either normovolemic (PCWP 8–20 mmHg) and hypertensive or hypervolemic (PCWP > 20 mmHg). Patients who had decreased preload from intraoperative hemorrhage were also followed. They observed a matched increase in PCWP and FT_c with fluid loading

among all 18 patients with hypovolemia. Similarly, all normovolemic patients had a concordant decrease in PCWP and FT_c. However, while the PCWP decreased in all 12 hypervolemic patients, the FT_c increased initially in 11/12 patients (reflecting optimal CO) prior to decreasing. Thus, FT_c appears to be a useful measure to direct optimal ventricular loading.

Two other studies have been undertaken to try to assess FT_c as a measure of ventricular filling. DiCorte *et al.* in a blinded fashion compared pulmonary artery diastolic (PA_d) pressure and FT_c by ED to end-diastolic short-axis area (EDA) as measured by transesophageal echocardiography in 20 patients undergoing coronary bypass surgery.[28] They found a modest correlation between FT_c and EDA (R = 0.49) and a poor correlation with PA_d pressure and EDA (R = 0.10). Although this provides some evidence that FT_c may be a better measure of preload than PA_d it is not a clinically relevant comparison because PCWP is virtually always used in preference to PA_d. Madan and colleagues conducted a study among 14 surgical ICU patients comparing ED with PAC.[31] They found a better correlation between FT_c (R = 0.52) and CO_{TD} than with PCWP (R = 0.2) and CO_{TD}. Further study is needed to define the role of FT_c based optimization of ventricular filling.

ED driven protocols

Improved patient outcome?

In assessing any new technology or treatment an important criteria for its adoption is whether it can be shown to decrease morbidity and/or mortality. Two studies have shown improved outcomes with the use of ED perioperatively.[48,49] Sinclair *et al.* conducted a randomized controlled trial with 40 geriatric patients undergoing fractured hip repair under general anesthesia in London, UK.[49] All patients had an ED inserted but were randomized to either an intraoperative volume optimization protocol (goal FT_c > 350 msec and optimized stroke volume) *vs* usual care. Anesthesiologists were blinded to ED values but not to the *iv* volume administered. Protocol patients received significantly more fluid, had higher mean FT_c and CO values, but had similar blood pressure and heart rates compared to controls intraoperatively. Protocol patients had significant reductions in the main outcome measures of median time to be declared fit for discharge of ten *vs* 15 days and length of hospitalization of 12 *vs* 20 days as compared to control respectively (P < 0.05 for both). An important potential limitation of this study is that protocol patients may have been recognized (unblinded) based on the increased amount of fluids given and possibly discharged earlier.

In the other study by Mythen *et al.*, a prospective, randomized, open study was conducted with 60 elective cardiac surgery patients in London, UK.[48] The control patients received usual care and the treatment patients were given repeated boluses of 6% hydroxyethyl starch to maximize stroke volume based on ED and central venous pressure. Compared to control, the treatment group had a lower incidence of gut hypoperfusion as measured by gastric intramucosal pH < 7.32 (7% *vs* 56%, P < 0.001), less major complications (zero *vs* six patients, P = 0.01), and shorter mean lengths of ICU (one *vs* 1.7 days, P = 0.023) and overall hospital stay (6.4 *vs* 10.1 days, P = 0.011). The main limitation of this study is that it was not blinded and knowledge of the patients' treatment allocation may have influenced either management or ascertainment of outcome. Furthermore, as with the Sinclair study, the authors did not adequately describe a mechanism by which protocol patients would be able to be discharged earlier. Despite the limitations of these two studies, they are important contributions to the ED literature because they showed improvements in clinical outcomes with ED usage.

Summary and conclusions

ED is a minimally invasive technique that has a good safety profile, is easy to use, and requires only minimal training. When compared to the current bedside gold standard of bolus CO_{TD} using a PAC in a broad range of perioperative and critically ill patients, ED was found to be reliable, responsive to changes, and have good agreement with low bias in the majority of studies. However, wide limits of agreement were observed with ED in several studies raising concerns about the precision of this technique. Further clinical investigation with larger numbers of varied patients is required to determine if the limited precision observed is inherent to the technique, related to patients' diagnoses, or is simply a function of the small study sample sizes used. It is unlikely that ED will replace PAC at present because of the concerns regarding limited precision and reduced applicability. However, use of ED may lead to a reduction of the number of patients undergoing invasive monitoring with its associated risks. Future clinical investigations will hopefully further define its role in optimization of ventricular filling and in improving the outcome of perioperative and critically ill patients.

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