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The validity of trans-esophageal Doppler ultrasonography as a measure of cardiac output in critically ill adults

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Abstract *Objective:* To determine the validity of the esophageal Doppler monitor (EDM) and echo-esophageal Doppler (Echo-ED) in measuring cardiac output in the critically ill. *Design:* Systematic search of relevant international literature and data synthesis. *Search strategy:* Literature search (1989–2003) using Ovid interface to Medline, Embase and Cochrane databases aimed at finding studies comparing EDM or Echo-ED cardiac output with that derived from simultaneous pulmonary artery thermodilution (PAC_{TD}) with Bland Altman measures of validity. *Patients:* Critically ill adults in operating departments or intensive care units. *Data synthesis:* Summary validity measures synthesized from Bland Altman analyses included pooled median bias and the median percentage of clinical agreement (PCA) derived from the limits of agreement. *Main results:* Eleven validation papers for EDM (21 studies) involving 314 patients and 2,400 paired measurements. The pooled median bias for PAC_{TD} versus EDM was 0.19 l/min (range –0.69 to 2.00 l/min) for cardiac output (16 studies), and 0.6% (range 0–2.3%) for changes in cardiac output (5 studies). The pooled median percentage of clinical agreement for PAC_{TD} versus EDM was 52% (interquartile range 42–69%) for cardiac output and 86% (interquartile range 55–93%) for changes in cardiac output. These differences in PCA were significant (p=0.03 Mann-Whitney) for bolus PAC_{TD} as the clinical "gold standard". We found an insufficient number of studies (2 papers) to assess the validity of Echo-ED. *Conclusions:* The esophageal Doppler monitor has high validity (no bias and high clinical agreement with pulmonary artery thermodilution) for monitoring changes in cardiac output.

Keywords Cardiac output · Trans-esophageal Doppler ultrasonography · Esophageal Doppler monitoring

Introduction

Estimation of cardiac output has a central role in the hemodynamic monitoring of critically ill and injured patients. Over the last three decades, the flow-directed balloon-tipped pulmonary artery catheter (PAC), and associated thermodilution technology, has become established as the bedside "gold standard" of cardiac output estimation in critical care medicine. However, with increasing concerns about the clinical utility and safety profile of the invasive PAC [1], alternative minimally invasive techniques for cardiac output estimation have emerged [2]. Trans-esophageal Doppler ultrasonography is one minimally invasive technique that can be used by the intensivist to estimate cardiac output in the critically ill. The technique and clinical use were first described in 1971 [3] and later refined in 1989 [4].

Two related esophageal Doppler technologies have emerged: the esophageal Doppler monitor (EDM, trade marked Cardio Q, previously ODM) and the echo-esophageal Doppler (Echo-ED, trade marked HemoSonic100, previously Dynemo3000). Both Doppler techniques determine the mean velocity of blood travelling through the descending thoracic aorta during ventricular systole. Left ventricular stroke volume, and hence cardiac output, is estimated from this mean systolic blood velocity measurement using a nomogram with EDM and using an M-mode echocardiographic estimate of aortic diameter with Echo-ED. The technical details and relative merits of these two techniques have been reviewed elsewhere [2, 5, 6].

Two recent semi-structured reviews have focused on the clinical utility of trans-esophageal Doppler ultrasonography [6] and how its accuracy compares with other minimally invasive techniques of cardiac output estimation [2]. However, central to any debate regarding the clinical utility of alternative technologies for hemodynamic monitoring is the question of validity: how well does a new technique estimate cardiac output compared with the established clinical "gold standard". No published reviews have addressed this issue systematically. Therefore, using peer-reviewed published clinical studies, we aimed to determine systematically the validity of both EDM and Echo-ED as measures of cardiac output in critical care compared with PAC_{TD} as the bedside "gold standard".

Methods

We designed a generic search strategy using the Ovid electronic interface (Table 1) to uncover any studies cited in Medline, Embase and the Cochrane databases relating to the clinical use of trans-esophageal Doppler ultrasonography. The search period commenced in 1989 because the first human validation study of the new generation esophageal Doppler systems was reported in this year [4]. The validity of comparing Doppler systems before this date is highly questionable [7]. The search strategy was performed in June 2003. Studies were limited to human use and to those with electronic abstracts so that the authors could readily appraise the results.

Table 1 Generic search strategy using the Ovid interface to access Medline, Embase and Cochrane databases between the beginning of 1989 and June 2003

Set	Search history
1	(Oesophageal ad. Doppler).tw
2	(Esophageal adj Doppler).tw
3	(Transoesophageal adj Doppler).tw
4	(Transesophageal adj Doppler).tw
5	1 or 2 or 3 or 4
6	Limit 5 to abstracts
7	Limit 6 to human
8	Limit 7 to year = Jan 1989–June 2003

We hand-searched all abstracts returned from each database in turn to find every prospective study comparing paired estimates of cardiac output (or cardiac index) derived from pulmonary artery catheter thermodilution (PAC_{TD}) and trans-esophageal Doppler ultrasound during adult patient management. The full text manuscripts of these studies were retrieved and appraised. We only included those studies that were designed to test the newer generation esophageal Doppler systems (EDM or Echo-ED). Furthermore, we only included studies using the Bland and Altman method for assessing agreement between two methods of clinical measurement [8]. We considered validity studies involving EDM and Echo-ED separately, and we further separated studies reporting on absolute measurements of cardiac output and those reporting change in cardiac output over time.

We defined and calculated two summary validity measures: "pooled median bias" and "percentage of clinical agreement". The (pooled) median bias and range were determined from the distribution of mean bias results from the studies included [6]. Furthermore, using the standard errors published, we calculated the precision of the bias for each study (95% confidence intervals of bias). In addition, we decided that the clinically acceptable limits of agreement for cardiac output estimation for each study would be ±15%, based on reports of repeatability of the bedside "gold standard" method (PAC_{TD}) [4, 9, 10]. We then calculated the number of paired measurements that were within our clinically acceptable limits of agreement (i. e. within ±15% of mean bias) for every study [9, 11] and we called this number the percentage of clinical agreement (PCA), expressed as a percentage of the total number of paired data in each study. Therefore, PCA indicated what percentage of paired measurements could be considered clinically interchangeable for each study. We did not produce composite bias and limits of agreement for the studies included because we did not expect to have ready access to the unpublished original data from each study. Furthermore, we did not include conference or meeting abstracts because of the difficulties in appraising the methods and results reported in this way.

Results

Our search strategy produced 198 original papers in the Medline database, 204 in Embase and 20 in the Cochrane databases. As expected, there was a good deal of overlap between the results from each database, with Embase incorporating all studies discovered in the Medline and the Cochrane databases. Using our inclusion criteria, we found 11 validation papers (reporting 21 studies) for EDM (Table 2) and 2 papers (reporting 3 studies) for Echo-ED (Table 3). These studies involved 314 patients with over 2,400 paired measurements for EDM, and 46 patients with 462 paired measurements for Echo-ED. No studies compared EDM and Echo-ED with PAC_{TD} within the same protocol.

When considering PAC_{TD}-versus EDM-estimated cardiac output, the pooled median bias from the nine papers (16 studies) that reported on absolute cardiac output was 0.19 l/min (range –0.69 to 2.00 l/min). The precision of bias (95% confidence intervals for bias) was either reported (rarely) or could be calculated from the standard errors of bias published in each study. Precision of bias overlapped zero (no bias) in 9 of these 16 studies, while the rest suggested an underestimation of absolute cardiac

Table 2 Summary of studies regarding the validity of esophageal Doppler monitoring (*EDM*) estimation of cardiac output compared with pulmonary artery catheter thermodilution (*PAC_{TD}*). Bias (with ** for 95% confidence intervals of bias not incorporating zero) and limits of agreement (*LOA*) were calculated using the Bland and Altman method in each case. The percentage of clinical agreement (*PCA*) was estimated for each study

Author, date and country	Patient group	Cardiac output measurements	Key results	Study comments
Singer M et al. 1989, England [4]	60 adults; 14 sedated and mechanically ventilated general ICU and 46 during cardiothoracic surgery	PAC_{TD} vs EDM prototype, 238 paired readings during standard care (range 1.5–10 l/min) with 200 changes in cardiac output used for analysis (–72.6% to 125.4%)	Bias: 0.6% LOA: –13.5 & 14.7% PCA: 96%	Confidence intervals for bias reported as crossing zero Bias and LOA reported for percentage change of cardiac output during standard cardiovascular interventions and not absolute values
Singer M and Bennett D 1991, England [12]	43 adults sedated and mechanically ventilated on general ICU	PAC_{TD} vs EDM prototype, 49 paired readings of change in cardiac output during pre-load manipulation	Bias: 0.6% LOA: –16.4 & 17.6% PCA: 91%	We calculated confidence intervals for bias as crossing zero Bias and LOA reported for percentage change of cardiac output during cardiac pre-load manipulation and not absolute values
Klotz KF et al. 1995, Germany [13]	6 adults sedated and mechanically ventilated during abdominal aortic surgery	EDM vs PAC_{TD}		We calculated all confidence intervals for bias as not crossing zero, suggests underestimation of cardiac output by EDM throughout
		(a) pre-aortic clamp (n=55 paired readings, mean cardiac output 4.73 l/min)	Bias: –0.96 l/min** LOA: –3.24 & 1.33 l/min PCA: 46%	Authors speculate that increase bias during cross-clamping of the aorta suggest that EDM underestimates cardiac output compared with PAC_{TD}.
		(b) during clamp (n=75 paired readings, mean cardiac output 3.71 l/min)	Bias: –1.51 l/min** LOA: –2.99 & -0.02 l/min PCA: 54%	This could be the result of a change in distribution of cardiac output away from the lower body due to cross-clamping but no independent measurements were made to confirm this
		(c) post-clamp (n=65 paired readings, mean cardiac output 5.02 l/min)	Bias: –1.47** LOA: –3.79 & 0.86 l/min PCA: 48%	
Keyl C et al. 1996, Germany [14]	24 adults sedated and mechanically ventilated during coronary artery bypass graft surgery	EDM vs PAC_{TD}:		Confidence intervals for bias reported as crossing zero in each study
		(a) post induction (n=24 paired readings, cardiac output range 2.0–6.8 l/min)	Bias: 0.38 l/min LOA: –1.70 & 2.50 l/min PCA 42%	No repeated measures were used in these analyses, thereby limiting the potential for introducing systematic bias. The methodology described here represents the correct use of the Bland and Altman technique for assessing the agreement between two methods of clinical measurement
		(b) after knife to skin (n=24 paired readings, cardiac output range 2.6–7.0 l/min)	Bias: 0.48 l/min LOA: –2.30 & 3.30 l/min PCA: 68%	
		(c) post-sternotomy (n=24 paired readings, cardiac output range 2.9–7.8 l/min)	Bias: 0.69 l/min LOA: –2.20 & 3.60 l/min PCA: 40%	
		(d) change (b-a), range –12 to +65% change in cardiac output	Bias: 2.3% LOA:-42 & 47% PCA: 50%	
		(e) change (c-b), range –30 to +40% change in output	Bias: 6.8% LOA: –29 & 43% PCA: 60%	
Krishnamurthy B et al. 1997, Northern Ireland [15]	16 adults sedated and mechanically ventilated under-going elective coronary revascularization	PAC_{TD} vs EDM:		We calculated confidence intervals for bias as crossing zero in each study
		(a) 11 patients with no re-focusing of ultrasound beam throughout operative period (n=513 paired readings, cardiac output range 2.4–8 l/min)	Bias: 0.79 l/min LOA: –2.20 & 3.80 l/min PCA 40%	Investigator blinded
		(b) 5 patients with re-focusing of beam before each reading (n=285 paired readings, cardiac output range 3.0–7.4 l/min)	Bias: 0.14 l/min LOA: –0.58 & 0.85 l/min PCA: 97%	Results suggest re-focusing of ultrasound beam improves validity of Doppler technique compared with PAC_{TD}

Table 2 Summary

Author, date and country	Patient group	Cardiac output measurements	Key results	Study comments
Colbert S et al. 1998, France [9]	18 adults sedated and mechanically ventilated under-going orthoptic liver transplantation	PAC_{TD} vs EDM, 234 paired readings during standard intra-operative care, range of cardiac output 5.9–10.1 l/min	Bias: 0.07 l/min LOA: –4.10 to 4.23 l/min PCA: 44%	We calculated confidence intervals for bias as crossing zero Repeated paired measures used for each analysis may introduce systematic bias to results
Lefrant JY et al. 1998, France [16]	60 adults sedated and mechanically ventilated during standard care on a general ICU	PAC_{TD} vs EDM:		EDM appears to underestimate cardiac output c.f. PAC_{TD} during training of the operator, but not so following training; we calculated confidence intervals for bias as supporting this
		(a) 11 patients in "training group" during learning curve of operators (n=107 paired readings, cardiac output range 4.0–13.1 l/min)	Bias: 1.20 l/min** LOA: –2.00 & 4.44l/min PCA 58%	Independent operators for the two techniques (? blinded)
		(b) 49 patients in "evaluation group" following training period (n=320 paired readings, cardiac output range 2.0–14.8 l/min)	Bias: 0.10 l/min LOA: –2.10 & 2.30 l/min PCA: 70%	
Valtier B et al. 1998, France [10]	46 adult sedated and mechanically ventilated during standard ICU care; 3 centers, 1 medical and 2 surgical	PAC_{TD} vs EDM: (a) 136 paired readings, cardiac output range 1.55–15.0 l/min	Bias: 0.24 l/min** LOA: –1.56 & 2.04 l/min PCA: 74%	EDM appears to underestimate cardiac output c.f. PAC_{TD} (a); we calculated confidence intervals for bias as supporting this
		(b) 88 paired changes, change in cardiac output range –4.0 to +9.0 l/min	Bias: 0.00 l/min LOA: –1.70 & 1.70 l/min PCA: 86%	No bias existed for changes in cardiac output (b) Blinded independent operators
Baillard C et al. 1999, France [17]	10 adults sedated and mechanically ventilated during standard care on a general ICU	PAC_{TD} vs EDM, 145 paired readings, cardiac output range 2.4–13 l/min	Bias: –0.01 l/min LOA: –0.97 & 0.96 l/min PCA: 98%	We calculated confidence intervals for bias as crossing zero Blinded independent operators
Penny JA et al. 2000, South Africa [18]	17 adult women on obstetric HDU with pre-eclampsia	EDM vs PAC_{TD}, 2–4 sets of paired readings separated by several hours (n= unspecified)		
		Paired readings from 17 women, cardiac output range 3.0–12.2 l/min	Bias: –2.00 l/min** LOA: –5.00 & 1.00 l/min PCA: 50%	Bias suggests that EDM tends to underestimate cardiac output in these patients c.f. PAC_{TD}; we calculated the confidence intervals for bias as supporting this
Leather HA and Wouters PF, 2001, Belgium [19]	14 male adults, prostatectomy under general + lumbar epidural anesthesia	EDM vs PAC_{TD}, 3 paired readings (n=42) (a) before epidural anesthesia (range 3.0–7.0 l/min)	Bias: –0.89 l/min** LOA: –-2.67 & 0.88 l/min PCA 62%	Bias reported as indicating underestimation of cardiac output by EDM in (a) and overestimation in (b). We calculated the confidence intervals for bias as supporting this in (a) but not in (b)
		(b) after epidural anesthesia (range 4.0–9.0 l/min)	Bias: 0.55 l/min LOA: –3.21 & 4.30 l/min PCA: 38%	

Table 3 Summary of studies regarding the validity of echo-esophageal Doppler (*Echo-ED*) estimation of cardiac output compared with pulmonary artery catheter thermodilution (PAC_{TD}). Bias (with ** for 95% confidence intervals of bias not incorporating zero) and limits of agreement (*LOA*) were calculated using the Bland and Altman method in each case. The percentage of clinical agreement (*PCA*) was also estimated from the available information in each study

Author, date and country	Patient group	Cardiac output measurements	Key results	Study comments
Nuan-Yen Su et al. 2002, Taiwan [11]	24 adults sedated and mechanically ventilated during coronary artery bypass graft surgery	PAC_{TD} vs Echo-ED		Bias in both cases is small and we calculated confidence intervals for bias as crossing zero. LOA was much smaller when using continuous PAC_{TD}
		(a) 12 patients using standard PAC_{TD} (bolus thermodilution). 185 paired readings (range 2.1–9.4 l/min)	Bias: 0.11 l/min LOA: −2.13 & 2.35 l/min PCA: 45%	Reproducibility of different PAC_{TD} techniques assessed using plots of standard deviation against mean cardiac output suggested significantly better reproducibility for continuous PAC_{TD}
		(b) 12 patients using new PAC_{TD} (continuous thermodilution). 192 paired readings (range 2.4–9.2 l/min)	Bias: 0.05 l/min LOA: −0.93 & 1.03 l/min PCA: 82%	
Jaeggi P et al. 2003, Switzerland [20]	22 adults sedated and mechanically ventilated on ICU immediately post-cardiac surgery	Echo-ED vs bolus PAC_{TD} 85 paired readings (mean cardiac index 2.72 l/min per m^2)	Bias 0.23 l/min per m^2 ** LOA: –1.4 to 1.8 l/min per m^2 PCA: 40%	Note cardiac index results reported Confidence intervals for bias were reported and did not cross zero, suggesting that Echo-ED overestimated cardiac index c.f. bolus PAC_{TD}

output by EDM (Table 2). The limits of agreement from each of these studies reporting on absolute cardiac output were assessed to be above the ±15% threshold in all but two papers (three studies) [15, 16]. These three latter studies involved continuous PAC_{TD}, while bolus PAC_{TD} had been used as the gold standard in all of the others. Therefore, the median percentage of clinical agreement between PAC_{TD} and EDM was 52% (interquartile range 42–69%) for all the studies reporting on absolute cardiac output estimation (n=16) and 50% (interquartile range 43–65%) when considering those studies that used bolus PAC_{TD} as the clinical gold standard (n=13).

Four papers (5 studies) [4, 10, 12, 14] from Table 2 considered the validity of EDM in monitoring trends in cardiac output rather than absolute values. The pooled median bias when monitoring change was 0.6% (range 0–2.3%). The precision of the bias was either reported or could be calculated from each study, and it overlapped zero (no bias) in every case. All of the studies that reported on trend monitoring used the bolus PAC_{TD} as the clinical gold standard and the median percentage of clinical agreement between PAC_{TD} and EDM was 86% (interquartile range 55–93%). Therefore, when comparing the median percentage of clinical agreement (PCA) figures from the studies that used bolus PAC_{TD} as the clinical gold standard, EDM performs significantly better as a trend monitoring device than for absolute cardiac output estimation (86% vs 50%, p=0.03: Mann-Whitney U test).

Only two papers (involving 3 studies) reported on PAC_{TD}- versus Echo-ED-estimated absolute cardiac output using the Bland Altman methodology (Table 3) [11, 20]. In one paper, the bias and limits of agreement appeared to depend on the thermodilution technique employed, with improved performance of Echo-ED apparent when a continuous PAC_{TD} technique was used instead of bolus PAC_{TD} [11]. However, both papers reported a poor percentage of clinical agreement (46% and 40%) when using bolus PAC_{TD} as the clinical gold standard. No studies compared PAC_{TD} with Echo-ED during trend monitoring of cardiac output.

Discussion

The validity of trans-esophageal Doppler ultrasonography as a measure of cardiac output has been investigated in a range of general intensive care and surgical patients. The majority of these validity studies have been performed using the esophageal Doppler monitor (EDM), with only two articles reporting on Echo-ED. Pooled results suggested that there was minimal systematic bias (underestimation) when estimating absolute cardiac output using EDM compared with pulmonary artery catheter thermodilution techniques (PAC_{TD}), and no systematic bias when estimating changes in cardiac output. Where underestimation of cardiac output by EDM was reported in individual studies, it was always for absolute estimation. The evidence was less convincing from the small number of studies using Echo-ED, with one study indicating that Echo-ED overestimated cardiac index compared with PAC_{TD}, and no studies reporting on the validity of Echo-ED in monitoring change of cardiac output during patient management.

The EDM relates descending aortic blood flow velocity to total left ventricular cardiac output using a nomogram utilizing age, height and weight [4, 5]. This assumes a fixed relationship between blood flow to the branches of the aortic arch compared with the descending aorta under different conditions, and that descending aortic dimensions are constant throughout systole. The minimal systematic bias for absolute cardiac output estimation and the absence of bias for estimation of changes, in a variety of critically ill patients, provides evidence of the effectiveness of this nomogram and the validity of the related assumptions.

The calculations of percentage of clinical agreement suggested that EDM performs better as a trend monitor of cardiac output during patient management. This is not a disadvantage for EDM because it is the evolution of cardiac output rather than a single value that is most helpful for hemodynamic monitoring in critical care. There were too few studies to make a valid assessment of Echo-ED in this regard.

For the small number of studies involving continuous rather than bolus PAC_{TD}, we discovered that the limits of agreement tended to be narrower, resulting in a higher percentage of clinical agreement. One study showed a considerable improvement in the limits of agreement for Doppler estimated absolute cardiac output when using continuous, as opposed to bolus, PAC_{TD} within the same protocol [11].

These particular studies raise an important issue when comparing devices that purport to measure the same parameter. Bland and Altman state that the repeatability of two methods of measurement limit the amount of agreement which is possible [8]. If one method has poor repeatability (i.e. there is considerable variation in repeated measurements on the same subject), the agreement between the two methods is also bound to be poor. When the old method is the more variable, even a new method which is perfect will not agree with it. If both methods have poor repeatability, the problem is even worse. For example, from the studies in Table 2, two reported on the intra-observer variability for repeated absolute cardiac output determination [4, 10] by calculating the coefficient of variation for pulmonary artery bolus thermodilution as 6.2% and 12%, and for EDM as 3.8% and 8%, respectively. This suggests that the repeatability of bolus PAC_{TD} is indeed worse than that for EDM and that the limits of agreement do not necessarily reflect entirely on the performance of EDM in estimating cardiac output. Recent evidence suggests that continuous PAC_{TD} has better repeatability than bolus measurements and may be a better bedside “gold standard” [11, 21, 22, 23]. The majority of studies reviewed here report on bolus PAC_{TD} and so it is possible that they will have underestimated the validity of trans-esophageal Doppler techniques in estimating cardiac output.

The validation studies that we uncovered were generally performed on small numbers of patients using repeated measurements, with reports of operator-blinding techniques often missing. The possibility for systematic bias in these studies cannot be discounted. Furthermore, we have not reported summary measures of validity based on the original raw data but from the summary statistics of the studies in each paper. However, we have included for analysis all studies appraised, including a study that shows the need for a training period with the use of Doppler techniques [16] and a study that confirms the need for re-focusing of the probe before any formal assessment of cardiac output is made [15]. Inclusion of these studies will tend to underestimate the validity measurements.

We recommend that any future validity studies extended to other groups of critically ill adult and pediatric patients should pay special attention to study design; in particular operator-blinding and careful use of the Bland-Altman methodology. Furthermore, continuous pulmonary artery thermodilution techniques may be considered a more appropriate clinical “gold standard”. Finally, we would encourage more studies to determine the validity of Echo-ED for estimating cardiac output before any meaningful conclusions can be made about the value of M-mode ultrasonography for trans-esophageal Doppler cardiac output monitoring.

In conclusion, our systematic study includes the best available clinical evidence for assessing the validity of cardiac output estimation by trans-esophageal Doppler ultrasonography. When estimating absolute values of cardiac output, we have shown that EDM has minimal bias but limited clinical agreement with pulmonary artery thermodilution estimates. However, this agreement will be affected by the accuracy of the thermodilution-derived data. In addition, EDM has high validity (no bias and high clinical agreement) for monitoring changes in cardiac output during the management of critically ill patients in both operating rooms and intensive care units. We found an insufficient number of studies to assess the validity of Echo-ED in estimating cardiac output.

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