REVIEW ARTICLE

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Noninvasive Cardiac Output Monitors: A State-of the-Art Review

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DESPITE IMPROVEMENTS in resuscitation and supportive care, progressive organ dysfunction occurs in a large proportion of patients with acute, life-threatening illnesses and those undergoing major surgery.[1-5] Recent data suggest that early aggressive resuscitation of critically ill patients may limit and/or reverse tissue hypoxia and progression to organ failure and improve outcome.[6] In a landmark study, Rivers et al[7] showed that a protocol of early goal-directed therapy reduces organ failure and improves survival in patients with severe sepsis and septic shock. Similarly, optimization of cardiac output (CO) in patients undergoing major surgery has been shown to reduce postoperative complications and the length of stay.[8-13] By contrast, excessive fluid resuscitation has been associated with increased complications, increased lengths of intensive care unit and hospital stay, and increased mortality.[14-17] These data suggest that fluid resuscitation should be titrated closely to minimize the risks of over- or under-resuscitation.[18]

Over the last 2 decades, the understanding of the complexities of shock has improved, and conventional approaches to resuscitation have come under increasing scrutiny. The traditional measured variables of resuscitation have included blood pressure, pulse rate, central venous pressure, and arterial oxygen saturation. These variables change minimally in early shock and are poor indicators of the adequacy of resuscitation.[19] Furthermore, the clinical assessment of CO and intravascular volume status are notoriously inaccurate.[20] With the increased recognition of the limitations of traditional methods to guide resuscitation, newer techniques have emerged that dynamically assess patients' physiologic response to a hemodynamic challenge.

In patients with indices of inadequate tissue perfusion, fluid resuscitation generally is regarded as the first step in resuscitation. However, clinical studies consistently have shown that only about 50% of hemodynamically unstable patients are volume responsive.[14] Therefore, the resuscitation of hemodynamically unstable patients requires an accurate assessment of the patients' intravascular volume status (cardiac preload) and the ability to predict the hemodynamic response after a fluid challenge (volume responsiveness). Fundamentally, the only reason to give a patient a fluid challenge is to increase the stroke volume (SV) (volume responsiveness). If the fluid challenge does not increase the SV, volume loading serves the patient no useful benefit and is likely to be harmful. Therefore, the measurements of SV and CO are fundamental to the hemodynamic management of critically ill and injured patients and unstable patients in the operating room. Both fluid challenges and the use of inotropic agents/vasopressors should be based on the response of the SV to either of these challenges. Until recently, continuous real-time CO monitoring required a thermodilution pulmonary artery catheter (PAC). During the past decade, several less invasive methods have been developed. These technologies are reviewed in this article.

Adolph Fick described the first method of CO estimation in 1870.[21] This method was the reference standard by which all other methods of determining CO were evaluated until the introduction of the PAC in the 1970s.[22] Despite its limitations, CO measurement with a PAC using the bolus thermodilution method has become the de facto gold standard for the measurement of CO and is the reference standard used to compare noninvasive technologies.[23,24] When assessing the reliability and clinical use of a noninvasive CO device, 2 factors are important: the accuracy of individual measurements compared with the reference standard and the ability to track changes in the SV and CO accurately and reproducibly after a therapeutic intervention. The latter is the most important factor when evaluating these devices because it directly impacts clinical decision making and therapeutic interventions. In most clinical situations, whether a cardiac index is 2.1 or 2.6 L/min/m^2 is not of great clinical importance; however, whether the change in the SV after a fluid bolus is 5% or 15% is of great clinical significance. The most frequently used analytic method for evaluating CO monitoring devices is the Bland-Altman method of plotting the bias against the mean CO and determining the limits of agreement (LOAs).[25] The percentage error is calculated as the ratio of 2 standard deviations (SDs) of the bias (LOA) to the mean CO and is considered clinically acceptable if it is below 30%, as proposed by Critchley and Critchley.[23] The Bland-Altman method only addresses how well the method

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being evaluated agrees with the reference method and fails to show whether the test method reliably detects changes in CO. Although the accuracy of noninvasive CO devices to measure trends in CO has not been standardized, a number of methods have been described in the literature, including the correlation coefficient, the Bland-Altman method, the 4-quadrant plot, and receiver-operator characteristic (ROC) curve analysis.[24]

CO AS MEASURED BY CARBON DIOXIDE REBREATHING

CO can be calculated by the CO_2 partial rebreathing technique using the modified Fick equation.[21] NICO (Respironics, Murraysville, PA) is a proprietary device that measures CO based on this principle. The CO_2 partial rebreathing technique compares end-tidal carbon dioxide partial pressure obtained during a nonrebreathing period with that obtained during a subsequent rebreathing period. The ratio of the change in end-tidal carbon dioxide and CO_2 elimination after a brief period of partial rebreathing (usually 50 seconds) provides a noninvasive estimate of the CO.[26] A limitation of the rebreathing CO_2 CO method is that it only measures pulmonary capillary blood flow (ie, the nonshunted portion of the CO). To calculate the total CO, intrapulmonary shunt and anatomic shunt factions (Qs/Qt) must be added to the pulmonary capillary blood flow. The NICO system estimates Qs/Qt using a shunt correction algorithm that uses oxygen saturation from pulse oximetry and the fractional concentration of inspired oxygen.

The CO_2 rebreathing technique has a number of significant limitations. Almost all the validation studies have been performed in patients undergoing anesthesia or in deeply sedated mechanically ventilated intensive care unit patients in whom the agreement with thermodilution CO has varied from "poor" to "acceptable."[27-32] In spontaneously breathing patients, the rebreathing period is associated with an increase in minute ventilation.[33] This reduces the accuracy of the CO determinations.[30,34] Furthermore, a low minute ventilation, high shunt fraction, and a high CO result in inaccurate measurements.[27,29,34] Considering the limitations of this technology and the potential inaccuracies, the routine use of the CO_2 rebreathing technique to guide fluid and vasopressor therapy cannot be recommended.

ESOPHAGEAL DOPPLER

The esophageal Doppler technique measures blood flow velocity in the descending aorta by means of a Doppler transducer (4-MHz continuous wave or 5-MHz pulsed wave according to the manufacturers) placed at the tip of a flexible probe. The probe is introduced into the esophagus of sedated, mechanically ventilated patients and then rotated so the transducer faces the descending aorta and a characteristic aortic velocity signal is obtained. The CO is calculated based on the diameter of the aorta (measured or estimated), the distribution of the CO to the descending aorta, and the measured flow velocity of blood in the aorta. Because esophageal Doppler probes are inserted blindly, the resulting waveform is highly dependent on correct positioning. The clinician must adjust the depth, rotate the probe, and adjust the gain to obtain an optimal signal.[35] Poor positioning of the esophageal probe tends to underestimate the true CO. There is a significant learning curve in obtaining adequate Doppler signals, and the correlations are better in studies in which the investigator was not blinded to the results of the CO obtained with a PAC.[36] A major limitation of esophageal Doppler monitoring is the assumption that a fixed percentage of the CO is directed to the head and descending aorta. Although this may be true in healthy volunteers, the present authors have shown that a disproportionate percentage of the increase in CO with fluid loading in hemodynamically unstable patients is directed into the carotid arteries.[37] Therefore, the increase in blood flow velocity in the descending aorta may not correlate well with the increase in the SV. Nevertheless, esophageal Doppler monitoring has use in aiding in the assessment of the hemodynamic status and guiding fluid therapy in the operating room.[10-12,38]

A completely noninvasive Doppler technology, the ultrasound CO monitor (USCOM, Sydney, Australia), uses transaortic or transpulmonary Doppler ultrasound flow tracings to calculate CO as the product of the SV and heart rate. The SV is calculated from a proprietary algorithm applying ultrasound principles of blood velocity–time integral (VTI) measurements in the ventricular aortic/pulmonary outflow tract. Studies comparing USCOM measurements of CO with those obtained by the standard thermodilution technique have shown mixed results.[39-42] The use of Doppler ultrasound to determine the cardiac index has several inherent technologic limitations. Potential sources of variation exist in the estimation of the aortic/pulmonary outflow tract area, the determination of the VTI, and the variability with operator-dependent measurements. With USCOM, the aortic/pulmonary outflow tract area is not measured directly but rather calculated from a proprietary anthropometric algorithm based on the subject's body height. The stroke distance is simply the distance a red blood cell travels per systolic stroke. This is measured as the VTI of the Doppler flow profile of each systolic stroke. Thus, the accuracy of the USCOM technology depends on obtaining accurate, reproducible VTI values. A precise VTI measurement requires a good flow signal and its correct interpretation, both of which are heavily dependent on the subject and the operator. An improper technique of poor Doppler ultrasound beam alignment with blood flow at the aortic/pulmonary outflow tract will lead to suboptimal VTI measurements. A further limitation of this technique is that it is not conducive to continuous monitoring.

PULSE CONTOUR ANALYSIS

The concept of pulse contour analysis is based on the relation among blood pressure, SV, arterial compliance, and systemic vascular resistance (SVR).[43] The SV or CO can be calculated from the arterial pressure waveform if the arterial compliance and SVR are known. Although the 4 pulse contour systems that are available commercially use different pressure-volume conversion algorithms, they are based on this basic principle. These systems can be divided into 3 categories: (1) pulse contour analysis requiring an indicator dilution CO measurement to calibrate the pulse contour (ie, LiDCO System; LiDCO, Cambridge, UK; and PiCCO System; Pulsion, Munich, Germany), (2) pulse contour analysis requiring patient

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Table 1. Overview of the Pulse Contour-Based Hemodynamic Monitoring Devices[43]

System Characteristic	FloTrac System	PiCCO System	LiDCO System	PRAM
Arterial waveform analysis	SD of 2000 arterial waveform points	Area under the systolic portion of the arterial waveform	RMS method applied to the arterial pressure signal	Area under curve
Requirements	Peripheral or central arterial catheter	Central arterial catheter and subclavian or IJ CVC	Peripheral or central arterial catheter	Peripheral or central arterial catheter
Calibration	Uncalibrated/internal	Transpulmonary thermodilution	Lithium indicator dilution Manual	Uncalibrated/internal Automatic
Recalibration	Automatically		Manual	
Indicator	None	Saline	Lithium	None
Additional parameters		SVV	SVV, PPV, GEDV, EVLW, SVR	SVV, PPV
Advantages	Minimally invasive Operator independent Easy to use	Broad range of hemodynamic parameters More robust during hemodynamic instability	Minimally invasive More robust during hemodynamic instability	Minimally invasive
Disadvantages	Inaccurate especially in vasoplegic patients Does not accurately track changes in SV	More invasive	Requires lithium	Few validation studies

Adapted with permission.[43]

Abbreviations: CVC, central venous catheter; GEDV, global end-diastolic volume; EVLW, extravascular lung water; IJ, internal jugular; RMS, root mean square.

demographic and physical characteristics for arterial impedance estimation (ie, FloTrac System; Edwards Lifesciences, Irvine, CA), and (3) pulse contour analysis that does not require calibration or preloaded data (ie, MostCare System; Vyetech Health, Padua, Italy). Table 1 contrasts the characteristics of the 4 systems. In addition to measuring the SV, these systems report the SV variation (SVV) and/or pulse pressure variation (PPV). The SVV/PPV may be useful in predicting fluid responsiveness in select patient groups (see later).

An important factor when interpreting the CO measured by a pulse contour system is the site that the blood pressure is measured (ie, the radial *v* the femoral artery). Discrepancies among central and peripheral blood pressures have been described in a number of clinical circumstances, such as after cardiopulmonary bypass, in patients with septic shock treated with high-dose vasoconstrictors, and in patients during reperfusion after a liver transplant.[44] The differences in blood pressure among different sites may be large, and in conditions of intense vasoconstriction, the radial blood pressure may underestimate the true aortic blood pressure, giving a falsely low CO value. Furthermore, it has been shown that in volume-responsive patients there is selective redistribution of blood flow to the cerebral circulation with a significantly smaller percentage increase in blood flow in the brachial artery.[37] This may lead to a significant error when the radial pulse is used for pulse contour analysis.

Lithium Dilution and Pulse Contour Analysis

The LiDCO system combines pulse contour analysis with lithium indicator dilution for continuous SV and SVV monitoring. The arterial pressure waveform is interpreted as a continuous curve describing the volume of the arterial tree in arbitrary units (standardized volume waveform). The effective value (approximately 0.7 times the original amplitude) of this volume waveform is determined using the root mean square, a mathematic principle to calculate the magnitude of a varying quantity. The root mean square value is called "nominal SV" and is scaled to an "actual SV" using a patient-specific calibration factor.[43] This factor is derived from a lithium indicator dilution CO measurement and corrects for arterial compliance and variations among individuals. The lithium can be injected into a peripheral vein, and the doses do not exert pharmacologically relevant effects in adult patients. The LiDCO indicator dilution method has shown to be at least as reliable as other thermodilution methods over a broad range of CO in a variety of patients.[45-48] Recalibration should be performed after acute hemodynamic changes and after any intervention that alters vascular impedance.

Transpulmonary Thermodilution and Pulse Contour Analysis

The PiCCO monitoring system combines pulse contour analysis with the transpulmonary thermodilution CO (TPCO) to determine a number of hemodynamic parameters. The TPCO requires both central venous (internal jugular or subclavian) and central arterial (femoral artery) catheterization. TPCO measurements with PiCCO have been shown to be reliable in comparison with PAC thermodilution in broad groups of patients.[49,50] The continuous pulse contour SV is calculated from the area under the systolic portion of the arterial waveform. In addition, the shape of the arterial waveform (dP/dt), arterial compliance, SVR, and a patient-specific calibration factor are required for the calculation.[43,49] Arterial compliance is derived from the SVR and the shape of the diastolic part of the arterial waveform. The PiCCO monitor uses TPCO measurement for calibration of the algorithm. The PiCCO calibration appears to remain accurate within 6 hours of calibration even when the vascular tone has changed.[51] In addition, the thermodilution curve can be used to measure the global end-diastolic volume and extravascular lung water, a marker of pulmonary

edema.[49,52-54] The monitor also measures SVV/PVV, which has been shown to be predictive of fluid responsiveness.[55] In a randomized controlled trial, Mutoh et al[56] showed an improved clinical outcome for patients with subarachnoid hemorrhage randomized to a PiCCO-based hemodynamic algorithm as compared with the "standard of care," which used a PAC algorithm. Additional studies are required to evaluate the clinical benefit of this technology.

Pulse Contour Requiring Patient Demographic and Physical Characteristics and No Calibration

The FloTrac system consists of the FloTrac sensor and corresponding Vigileo monitor. The system is operator independent, needs no external calibration, and requires a peripheral arterial catheter only. The basic principle of the system is the linear relation between the pulse pressure and the SV. The SV is estimated using the following equation[43]: $SV = SD_{AP} \times \chi$. The arterial pressure waveform is sampled each 20 seconds at 100 Hz, which results in 2,000 data points. SD_{AP} is the standard deviation of these data points and reflects the pulse pressure. The factor χ represents the conversion factor that depends on arterial compliance, the mean arterial pressure, and waveform characteristics. The patient's vascular compliance is assessed using biometric values (ie, sex, age, height, and weight) according to the method described by Langewouters et al.[57] Waveform characteristics assessed are skewness (degree of asymmetry) and kurtosis (degree of peakedness) of the individual arterial pressure curve. Skewness and kurtosis represent changes in the arterial waveform, which should reflect changes in vascular tone. The factor χ is recalculated every minute and enables calculation of the SV without external calibration.

Because the system is operator independent, easy to use, needs no external calibration, and only requires a peripheral arterial catheter (usually the radial artery), the FloTrac system has found popular appeal and has been studied widely, particularly in the setting of cardiac surgery. To date, the accuracy of FloTrac has been evaluated in 45 studies[58-102]; these are summarized in Table 2. Studies evaluating the first-generation FloTrac showed poor agreement compared with intermittent thermodilution, which is the gold standard. Second-generation devices were purported to be more reliable; however, their accuracy remained clinically unacceptable. Furthermore, in patients with low SVR (eg, sepsis or liver failure), measurements were unreliable, with the bias being correlated with the SVR.[65,95,99,101] The data from Table 2 show that the percentage error is lower in cardiac patients as compared with other cohorts (37% ± 11% *v* 47% ± 11%, $p = 0.01$). The third-generation software claims to have overcome these problems. However, 6 recent validation studies evaluating this latest version do not show improved accuracy in comparison with older versions.[97-102] More problematic is the fact that the system does not track changes in the SV accurately after a volume challenge or after the use of vasopressors.[65,79,85,94,95,100,101,103] These limitations significantly restrict the clinical use of this device. The SVV may be useful in intraoperative fluid optimization in select noncardiac surgical patients.[104] However, in a cohort of medical patients, it was reported that the SVV was poorly predictive of volume responsiveness.[105] Takala et al[106] randomized 388 hemodynamically unstable patients to noninvasive monitoring with the FloTrac system for 24 hours or usual care (the control group). The main outcome measure was the proportion of patients achieving hemodynamic stability within 6 hours of starting the study. Surprisingly, the time to reach the predefined resuscitation goals was longer in the FloTrac group, with worse clinical outcomes in these patients.

Pulse Contour Requiring No Patient Data and No Calibration

The MostCare system uses the pressure recording analytic method (PRAM) to determine the SV.[107] PRAM measures the area under the curve of the arterial waveform. No external calibration or pre-estimated data are required. The morphology of the arterial waveform is analyzed to determine an internal calibration. This system uses high-time resolution by sampling the signal at 1,000 Hz, and it analyzes the whole cardiac cycle. The area under the pressure wave (P/t) is determined during the whole cardiac cycle. The PRAM methodology analyzes the pressure wave morphology and, in real time, identifies the diastolic phase from the dicrotic notch determination. The P/t is then divided into contributions from the diastolic phase and the systolic phase, with 2 impedances based on different characteristics. There are limited studies that have evaluated the accuracy of this system, with those published by the patent holder's group showing good results,[107-112] whereas independent studies have shown mixed results.[113-115]

Comparative Studies of the Pulse Contour Systems

A number of studies have been performed comparing the accuracy of the 3 major pulse contour systems (none has compared the MostCare system). Unfortunately, many of these studies suffer methodologic problems in terms of the gold standard used (thermodilution) and the sample size. Hadian et al[94] performed a cross-comparison of the CO and trending accuracy of the LiDCO, PiCCO, and FloTrac systems compared with intermittent PAC thermodilution.[94] In this study, the performances of the PiCCO and LiDCO systems were adequate and comparable, whereas that of the FloTrac system was suboptimal. Monnet et al[65] compared the changes in pulse contour–derived CO induced by a fluid challenge or norepinephrine in patients undergoing monitoring with the PiCCO or FloTrac systems. Although the PiCCO system accurately tracked the changes in volume- and norepinephrine-induced cardiac index (the area under the ROC curves = 0.878 and 0.924, respectively), the FloTrac system was less reliable (the area under the ROC curves = 0.564 and 0.541, respectively).

Pulse Contour Analysis and Dynamic Preload Indices

A number of studies, mainly those performed in a controlled setting in the operating room, have shown that the PPV derived from the analysis of the arterial waveform and the SVV derived from pulse contour analysis are predictive of fluid responsiveness.[55] The principles underlying this technique are based on the physiologic changes that occur during positive-pressure ventilation.[116] Intermittent positive-

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Table 2. Accuracy of the FloTrac/Vigileo System

Author	Year	Version Setting	Reference Method		Data Points	Bias	LOA[21]	% Error[19]
Chakravarthy[54]	2007	1.01	Cardiac	PAC	438	0.15	0.66	13
De Waal[55]	2007	1.01	Cardiac	PAC	184	0	—	33*
Manecke[56]	2007	1.01	Cardiac	PAC	295	0.55	1.96	39*
McGee[57]	2007	1.01	Various-ICU	PAC	561	0.2	2.38	43
Zimmerman[58]	2008	1.01	Cardiac	PAC	192	0.1	2.90	48*
Marque[59]	2009	1.01	Cardiac	PAC-CCO	33	−0.1	1.68	31*
Ostergaard[60]	2009	1.01	Cardiac	PAC	50	−0.5	1.87	48
Monnet[61]	2010	1.01	Sepsis-ICU	PiCCO	160	−0.2	5.4	61
Opdam[62]	2006	1.03	Cardiac	PAC	218	0	2.28	45*
Sander[63]	2006	1.03	Cardiac	PAC	108	0.6	2.80	54
Breukers [64]	2007	1.03	Cardiac	PAC	56	−0.14	2.00	31
Mayer[65]	2007	1.03	Cardiac	PAC	244	0.46	1.15	46
Sander[66]	2008	1.03	Cardiac	PAC	84	0.1	2.20	46*
Cecconi[67]	2010	1.03	Various-ICU	PAC	203	−1.1	3.70	55
Button[68]	2007	1.07	Cardiac	PAC	150	0.25	2.27	54
Cannesson[69]	2007	1.07	Cardiac	PAC	166	−0.26	1.74	38
Sakka[70]	2007	1.07	Sepsis-ICU	PiCCO	72	0.5	4.60	68
Mehta[71]	2008	1.07	Cardiac	PAC	96	−0.27	0.44	29
Staier [72]	2008	1.07	Cardiac	PAC	120	0	1.42	36
Compton[73]	2008	1.07	Various-ICU	PiCCO	324	0.68	1.94	59
Bias[74]	2008	1.07	OTLTx	PAC	400	0.8	2.70	43
Eleftheriadis[75]	2009	1.07	Cardiac	PAC	96	0.4	1.70	34
Ham[76]	2010	1.07	Cardiac	PAC-CCO	6492	−0.1	4.40	46
Hofer[77]	2010	1.07	Cardiac	PAC	156	0.2	2.10	42*
Jo[78]	2010	1.07	Cardiac	PAC	250	−0.07	0.67	26
Slagt[79]	2010	1.07	Sepsis-ICU	PAC	86	−1.6	3.20	48
Junttila[80]	2011	1.07	ICH-ICU	PAC	407	1.5	3.90	58
Haenggi [81]	2011	1.07	Post-CA	PAC	395	0.23	1.28	34
Saraceni [82]	2011	1.07	Various-ICU	PAC	141	−0.18	4.72	67*
Vetrugno[83]	2011	1.07	Cardiac	PAC	360	−0.5	1.70	37
Prasser[84]	2007	1.1	Cardiac	PAC	158	0.01	1.63	26
Della Rocca [85]	2008	1.1	OTLTx	PAC	126	0.95	2.82	26
Mayer[86]	2008	1.1	Cardiac	PAC	282	0.19	0.60	24
Senn[87]	2009	1.1	Cardiac	PiCCO	200	−0.15	1.60	29
Biancofiore[88]	2009	1.1	OTLTx	PAC	290	1.3	2.80	54
Zimmerman[89]	2009	1.1	Cardiac	PAC	138	0.04	2.13	42*
Hadian[90]	2010	1.1	Cardiac	PAC	110	0.43	3.37	59
Krejci[91]	2010	1.1	OTLTx	PAC	97	−1.78	2.78	69
Slagt[79]	2010	1.1	Sepsis-ICU	PAC	73	−1.2	2.30	32
Mutoh[92]	2009	1.1	SAH-ICU	PiCCO	179	0.57	1.00	25
Biancofiore[93]	2011	3.02	OTLtx	PAC	200	0.38	2.33	52
De Backer[94]	2011	3.02	Sepsis-ICU	PAC	401	0	2.20	30
Metzelder [95]	2011	3.02	SAH-ICU	PiCCO	158	0.9	2.50	30
Phan[96]	2011	3.02	Cardiac	PAC	44-0.21	1.13	47	
Monnett[97]	2012	3.02	Various-ICU	PiCCO	60	0.5	3.7	54
Su[98]	2012	3.02	OTLx	PAC	3234	−0.8	4.8	75

Abbreviations: PiCCO, transpulmonary thermodilution; Post-CA, post–cardiac arrest; OTLx, orthotopic liver transplant; ICH, intracerebral hemorrhage; SAH, subarachnoid hemorrhage; PAC-CCO, pulmonary artery catheter continuous cardiac output; ICU, intensive care unit.

*Percentage error calculated form data reported in the study.

pressure ventilation induces cyclic changes in the loading conditions of the left and right ventricles. Mechanical insufflation decreases the preload and increases the afterload of the right ventricle. The reduction in the right ventricular preload and the increase in the right ventricular afterload both lead to a decrease in right ventricular stroke volume, which is at a minimum at the end of the inspiratory period. The inspiratory reduction in right ventricular ejection leads to a decrease in left ventricular filling after a phase lag of 2 or 3 heartbeats. Thus, the left ventricular preload reduction may induce a decrease in the left ventricular SV, which is at its minimum during the expiratory period. The cyclic changes in the right ventricular and left ventricular SV are greater when the ventricles operate on the steep rather than the flat portion of the Frank-Starling curve. Therefore, the magnitude of the respiratory changes in the left ventricular SV is an indicator of biventricular preload dependence. A PPV/SVV of greater than 12% to 13% has been reported to

be predictive of volume responsiveness.[55] It should be noted that in this systematic review, the predictive area under the ROC curve for the PPV was significantly greater than that for the SVV ($p < 0.001$).[55] This may be related to the fact that a number of assumptions are made in the calculation of the SV (by pulse contour analysis). However, the PPV usually is measured directly from the arterial pressure tracing using advanced digital software. This suggests that the PPV may be the preferred arterial waveform–derived variable when dynamic indices are used for hemodynamic monitoring. This finding is supported by the study of Renner et al[117] in pediatric patients undergoing cardiac surgery in whom the PPV was highly predictive of fluid responsiveness, whereas the SVV, the central venous pressure, and the global end-diastolic volume index could not distinguish between fluid responders and nonresponders. The SVV/PPV measured by the LiDCO system has been shown to be accurate for the assessment of fluid responsiveness.[55,118,119] In a randomized controlled trial by Pearse et al,[120] a significant reduction in complications and a median stay in the hospital were reported in high-risk surgical patients treated with LiDCO-based goal-directed therapy.

Cannesson et al[121] studied the PPV in 413 patients during general anesthesia and mechanical ventilation using the "gray zone" approach. They identified a range of PPV values between 9% and 13% for which fluid responsiveness could not be predicted accurately. Numerous factors hinder the accuracy of PPV monitoring, most notably ventilator-patient dyssynchrony, arrhythmia (particularly atrial fibrillation), low-tidal-volume ventilation, altered chest wall and pulmonary compliance, pulmonary hypertension, and increased intra-abdominal pressure.[122-126] In routine clinical practice both in the operating room and the intensive care unit, dynamic preload indices may be poor predictors of volume responsiveness.[37,127]

THORACIC BIOIMPEDANCE

Standard bioimpedance systems apply a high-frequency electric current of known amplitude and frequency across the thorax and measure changes in voltage (amplitude of the returning signal compared with the injected signal). The ratio between voltage and current amplitudes is a measure of transthoracic direct current resistance (more generically referred to as impedance [Zo]), and this varies in proportion to the amount of fluid in the thorax. The instantaneous rate of the change of Zo is believed to be related to the instantaneous blood flow in the aorta. Therefore, the SV is proportional to the product of maximal rate of the change of Zo (dZo/dt_{max}) and ventricular ejection time (VET). Early studies showed a poor agreement between thoracic electrical bioimpedance (TEB) and thermodilution CO.[128-130] In addition, the accuracy of TEB worsened as the degree of volume overload increased.[131] Newer-generation devices using upgraded computer technology and refined algorithms to calculate CO have produced improved results.[132-134] However, a poor correlation between TEB-derived CO and that determined by thermodilution in the setting of a cardiac catheterization laboratory was reported.[130] In the Bioimpedance CardioGraphy (BIG) substudy of the ESCAPE heart failure study, there was a poor agreement among TEB and invasively measured hemodynamic profiles.[135] Bioimpedance has been found to be inaccurate in the intensive care unit and other settings in which significant electric noise and body motion exist and in patients with increased lung water.[131,136,137] Furthermore, this technique is sensitive to the placement of the electrodes on the body, variations in patient body size, and other physical factors that impact on electric conductivity between the electrodes and the skin (eg, temperature and humidity).[130,138]

BIOREACTANCE

Because of the limitations of bioimpedance devices, newer methods of processing the impedance signal have been developed. The most promising technology to reach the marketplace is the NICOM device (Cheetah Medical, Portland, OR), which measures the bioreactance or the phase shift in voltage across the thorax. The human thorax can be described as an electric circuit with a resistor (R) and a capacitor (C), which together create the thoracic impedance (Zo). The values of R and C determine the 2 components of impedance, which are (1) amplitude (a), the magnitude of the impedance (measured in ohms); and (2) phase (phi), the direction of the impedance (measured in degrees). The pulsatile ejection of blood from the heart modifies the value of R and the value of C, leading to instantaneous changes in the amplitude and the phase of Zo. Phase shifts can occur only because of pulsatile flow. The overwhelming majority of thoracic pulsatile flow stems from the aorta. Therefore, the NICOM signal is correlated almost wholly with aortic flow. Furthermore, because the underlying level of thoracic fluid is relatively static, neither the underlying levels of thoracic fluids nor their changes induce any phase shifts and do not contribute to the NICOM signal. The NICOM monitor contains a highly sensitive phase detector that continuously captures thoracic phase shifts, which together result in the NICOM signal (Fig 1).

Unlike many of the other devices reviewed in this article, NICOM is totally noninvasive. This system consists of a high-frequency (75 kHz) sine wave generator and 4 dual-electrode "stickers" that are used to establish electric contact with the body (Fig 2).[139] Within each sticker, 1 electrode is used by the high-frequency current generator to inject the high-frequency sine wave into the body, whereas the other electrode is used by the voltage input amplifier. Two stickers are placed on the right side of the body, and 2 stickers are placed on the left side of the body. The stickers on a given side of the body are paired, so the currents are passed between the outer electrodes of the pair, and voltages are recorded from between the inner electrodes. Thus, a noninvasive CO measurement signal is determined separately from each side of the body, and the final noninvasive CO measurement signal is obtained by averaging these 2 signals. The system's signal processing unit determines the relative phase shift ($\Delta\Phi$) between the input and output signals. The peak rate of change of Φ ($d\Phi/dt_{max}$) is proportional to the peak aortic flow during each beat. The SV is calculated from the following formula: $SV = C \times VET \times d\Phi/dt_{max}$, where C is a constant of proportionality and VET is determined from the NICOM and electrocardiographic signals. Unlike bioimpedance, bioreactance-based CO measurements do not use the static impedance (Zo) and do not depend on the distance between the electrodes for the calculations of SV,

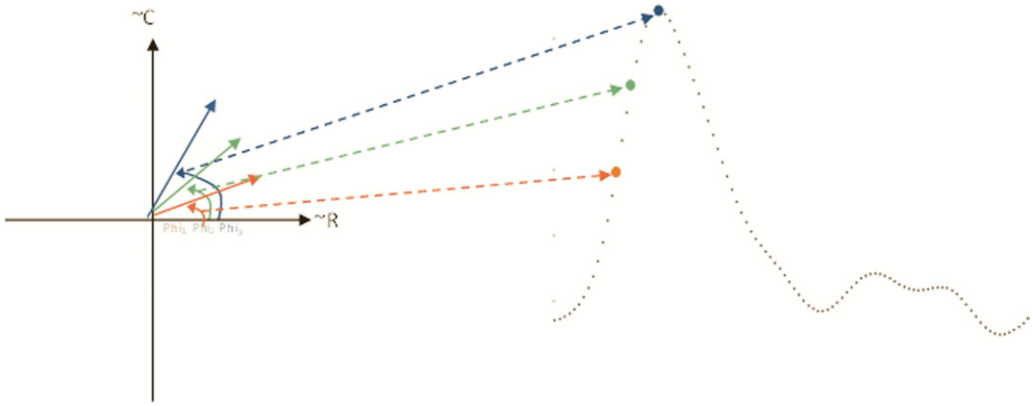

Fig 1. Pulsatile changes in thoracic volume induce phase shifts that are detected continuously by the NICOM's phase-detection mechanism and captured in the form of the NICOM signal. (Color version of figure is available online.)

both factors that reduce the reliability of the result.[139] NICOM averages the signal over 1 minute, therefore allowing "accurate" determination of CO in patients with arrhythmias.

The CO as measured by bioreactance has been shown to be highly correlated with that measured by thermodilution and pulse contour analysis.[139-144] Squarra et al[143] compared the NICOM system with PAC-derived CO in 110 patients after cardiac surgery. The reported bias was +0.16 L/min; the LOA was ±1.04 L/min with a relative error of 9%. The precision of the NICOM system was better than that of thermodilution, with the device being able to track changes in CO accurately. In a study of 3 intensive care units (70 patients), Raval et al[140] reported a bias of −0.09 L/min and an LOA of ±2.4 L/min, with the NICOM system closely tracking changes in the thermodilution CO. Rich et al[142] performed right-heart catheterization in 24 patients with pulmonary hypertension. Simultaneous CO measurements were performed using thermodilution, NICOM, and the Fick methods at baseline and after adenosine vasodilator challenge. CO measured by the NICOM system was significantly more precise than that of thermodilution (3.6% ± 1.7% *v* 9.9% ± 5.7%, $p < 0.001$). Bland-Altman analyses revealed a mean bias and LOA of −0.37 ± 2.6 L/min and 0.21 ± 2.3 L/min, respectively. The adenosine challenge resulted in a similar mean increase in CO with each method. The accuracy of NICOM was assessed in hemodynamically unstable intensive care unit patients and healthy volunteers after passive leg raising (PLR) and fluid challenges (intensive care unit patients) using carotid and brachial arterial Doppler ultrasound flow (mL/min) as the reference technique. In a previous study,[37] almost 100% concordance was found be-

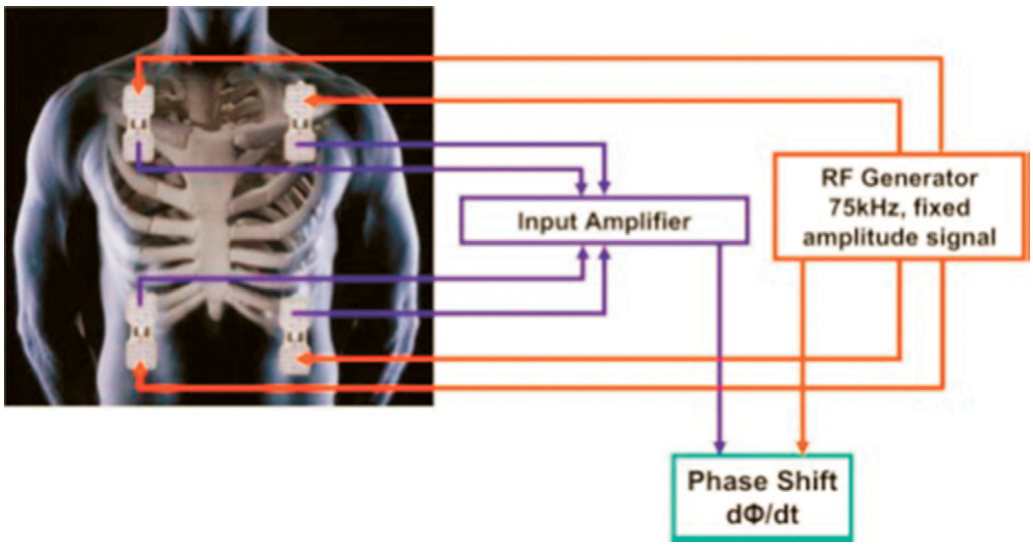

Fig 2. The NICOM system and its connection to the body. Four double-electrode stickers are placed around the thorax. A high-frequency current is passed between the 2 outer electrodes, and the resulting voltages are recorded between the 2 inner electrodes. The relative phase shift (Φ) and rate of change of phase ($d\Phi/dt$) between these signals are determined and used in the calculations of the SV. RF, radiofrequency. (Reproduced with permission from the American Physiological Society.[139]) (Color version of figure is available online.)

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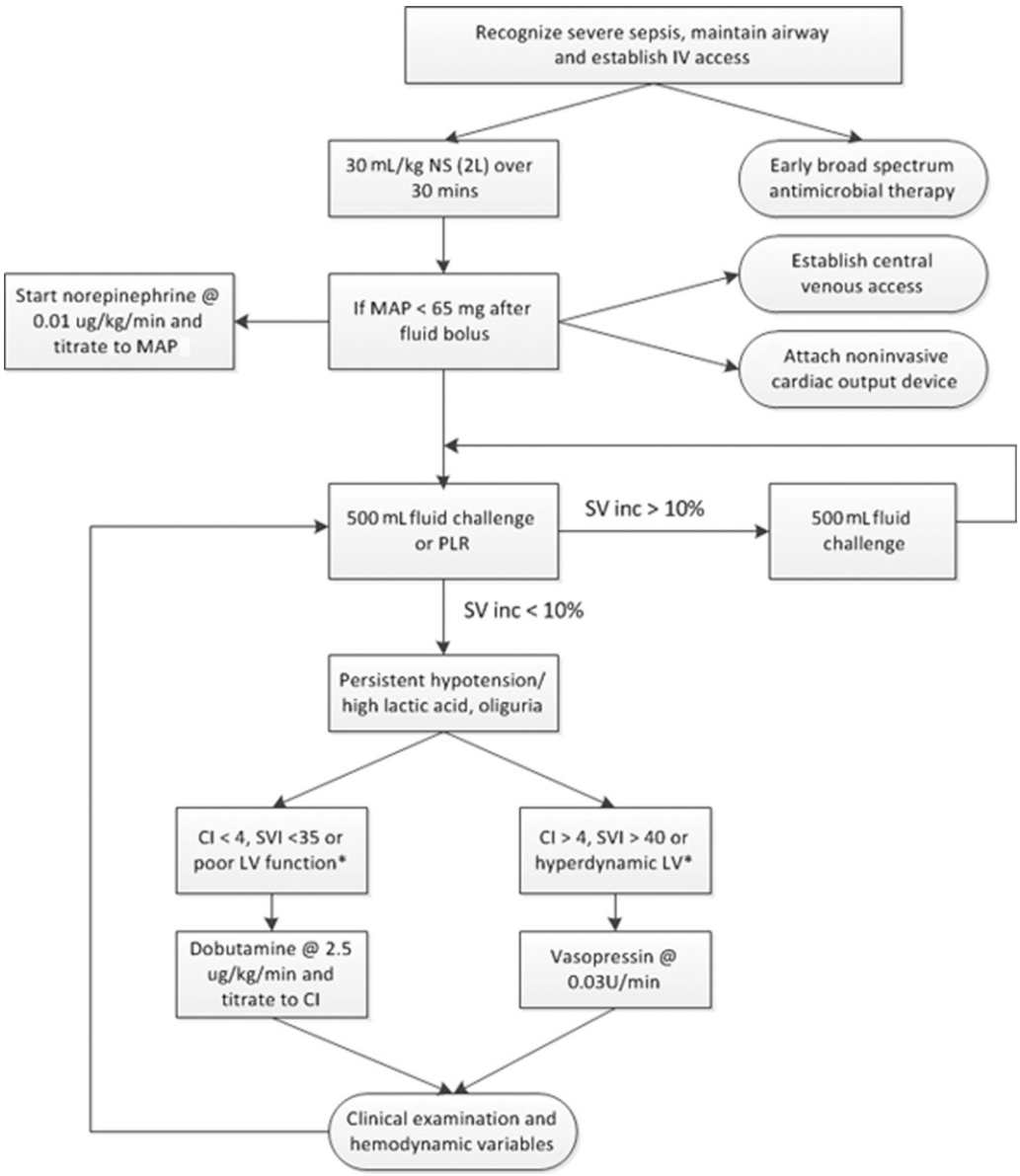

Fig 3. (A) The protocol for early goal-directed resuscitation of patients with sepsis. (B) The protocol for hemodynamic optimization in the operating room.

tween fluid responsiveness as determined by carotid flow and the NICOM system.[37] Benomar et al[145] showed that the NICOM system could predict fluid responsiveness accurately from changes in CO during PLR. As part of goal-directed perioperative therapy in patients undergoing major surgery, Waldron et al[146] compared fluid responsiveness with an esophageal Doppler monitor and the NICOM system. Notwithstanding the limitations of esophageal Doppler monitoring (as discussed previously), there was a good agreement between these technologies. In this study, hemodynamic variables were not displayed by the esophageal Doppler monitor for 7.8% measurements as compared with 3.7% for the NICOM monitor.

It should be noted that electrocautery interferes with the NICOM signal. However, as long as the device receives a single for at least 20 seconds within a minute, the CO can be determined. When electrocautery is on for more than 40 seconds in a given minute, the CO for that minute is not displayed. NICOM assessment of the CO can be performed in ventilated and nonventilated patients alike; can compute the CO in patients with atrial and ventricular arrhythmias; is very easy to set up with a high degree of acceptability by nursing staff; and can be performed seamlessly in the emergency room, intensive care unit, and operating room. Additional studies with this device are required to confirm the accuracy, reliability, and versatility with this device and to show improved patient outcomes. Figure 3A and B are algorithms using the NICOM monitor that were developed

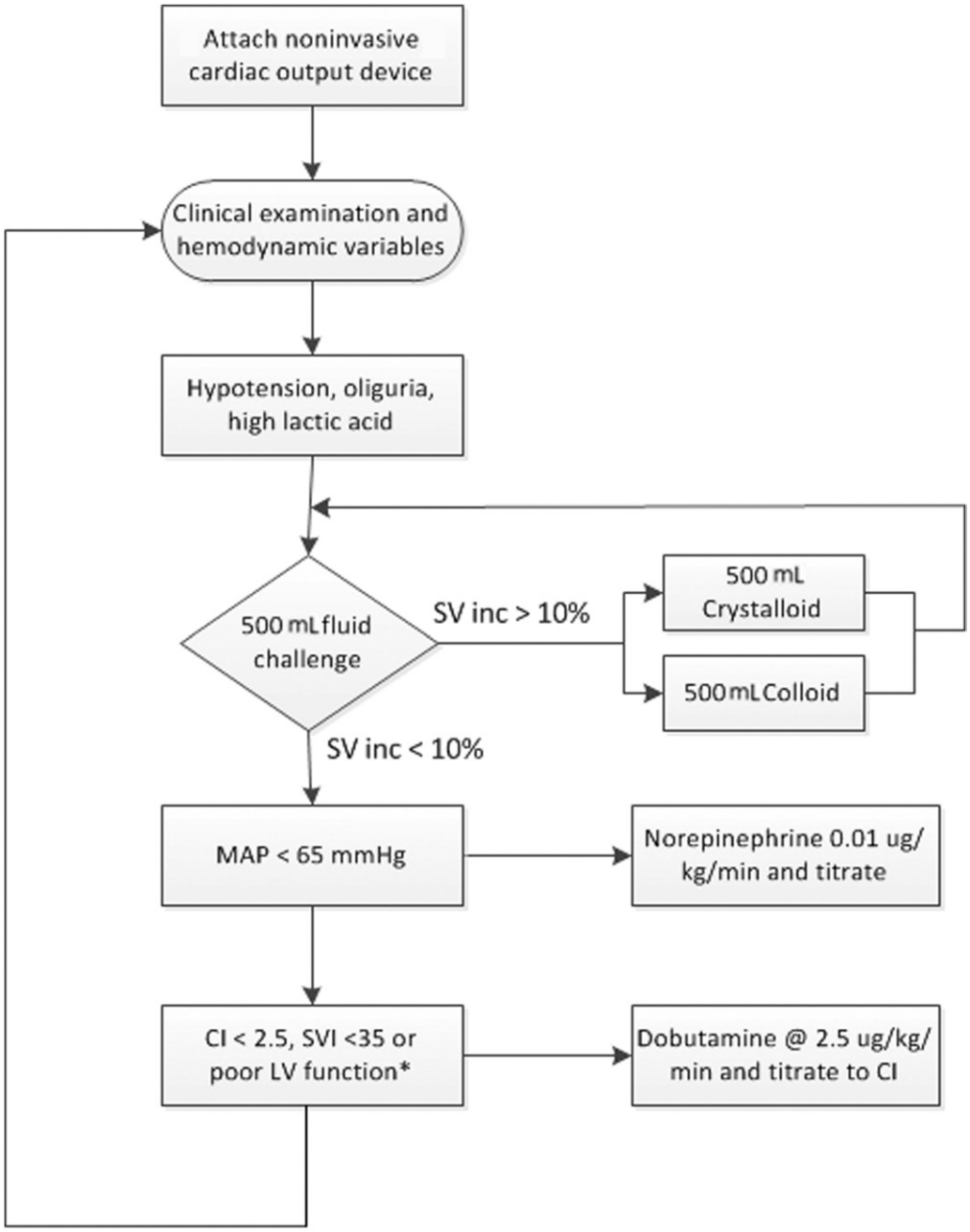

Fig 3. (Cont'd)

for the hemodynamic management of septic patients and those in the operating room.

ECHOCARDIOGRAPHY

Although echocardiography traditionally is not considered a monitoring device, both transthoracic and transesophageal echocardiography provide invaluable information on both left and right ventricular function, which is crucial in the management of hemodynamically unstable patients.[147,148] In addition, a number of dynamic echocardiographic parameters that are based on changes in venacaval dimensions or cardiac function induced by positive-pressure ventilation or PLR appear to be highly predictive of volume responsiveness.[147]

CONCLUSIONS

Although no device is perfect, a number of noninvasive methods to determine the CO in a broad range of patients and settings are now available. The major use of these devices is to optimize fluid resuscitation by determining the patients' re-

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sponse to a PLR maneuver or a fluid challenge. It is important to stress that there are very little data showing that any of these monitoring devices improve patient outcome. In reality, outcomes are changed by the correct interpretation of the data that monitors provide and then instituting the appropriate therapeutic intervention(s). Furthermore, physicians should not blindly follow algorithms and bundles but rather should embrace the patient's clinical, hemodynamic, laboratory, and radiographic data to chart a course based on the integration and correct interpretation of these data.

REFERENCES

1. Sakr Y, Dubois MJ, De Backer D, et al: Persistent microcirculatory alterations are associated with organ failure and death in patients with septic shock. Crit Care Med 32:1825-1831, 2004
2. Dewar D, Moore FA, Moore EE, et al: Postinjury multiple organ failure. Injury 40:912-918, 2009
3. Cohn SM, Nathens AB, Moore FA, et al: Tissue oxygen saturation predicts the development of organ dysfunction during traumatic shock resuscitation. J Trauma 62:44-55, 2007
4. Patila T, Kukkonen S, Vento A, et al: Relation of the sequential organ failure assessment score to morbidity and mortality after cardiac surgery. Ann Thorac Surg 82:2072-2078, 2006
5. Lobo SM, Rezende E, Knibel MF, et al: Early determinants of death due to multiple organ failure after noncardiac surgery in high-risk patients. Anesth Analg 112:877-883, 2011
6. Shapiro NI, Howell MD, Talmor D, et al: Implementation and outcomes of the multiple urgent sepsis therapies (MUST) protocol. Crit Care Med 34:1025-1032, 2006
7. Rivers E, Nguyen B, Havstad S, et al: Early goal-directed therapy in the treatment of severe sepsis and septic shock. N Engl J Med 345:1368-1377, 2001
8. Lopes MR, Oliveira MA, Pereira VO, et al: Goal-directed fluid management based on pulse pressure variation monitoring during high-risk surgery: A pilot randomized controlled trial. Crit Care 11:R100, 2007
9. Polonen P, Ruokonen E, Hippelainen M, et al: A prospective, randomized study of goal-oriented hemodynamic therapy in cardiac surgical patients. Anesth Analg 90:1052-1059, 2000
10. Gan TJ, Soppitt A, Maroof M, et al: Goal-directed intraoperative fluid administration reduces length of hospital stay after major surgery. Anesthesiology 97:820-826, 2002
11. Wakeling HG, McFall MR, Jenkins CS, et al: Intraoperative oesophageal Doppler guided fluid management shortens postoperative hospital stay after major bowel surgery. Br J Anaesth 95:634-642, 2005
12. Noblett SE, Snowden CP, Shenton BK, et al: Randomized clinical trial assessing the effect of Doppler-optimized fluid management on outcome after elective colorectal resection. Br J Surg 93:1069-1076, 2006
13. Hamilton MA, Cecconi M, Rhodes A: A systematic review and meta-analysis on the use of preemptive hemodynamic intervention to improve postoperative outcomes in moderate and high-risk surgical patients. Anesth Analg 112:1392-1402, 2011
14. Boyd JH, Forbes J, Nakada T, et al: Fluid resuscitation in septic shock: A positive fluid balance and elevated central venous pressure increase mortality. Crit Care Med 39:259-265, 2011
15. Maitland K, Kiguli S, Opoka RO, et al: Mortality after fluid bolus in African children with severe infection. N Engl J Med 364: 2483-2495, 2011
16. de-Madaria E, Soler-Sala G, Sanchez-Paya J, et al: Influence of fluid therapy on the prognosis of acute pancreatitis: A prospective cohort study. Am J Gastroenterol 106:1843-1850, 2011
17. Rosenberg AL, Dechert RE, Park PK, et al: Review of a large clinical series: Association of cumulative fluid balance on outcome in acute lung injury: A retrospective review of the ARDSnet tidal volume study cohort. J Intensive Care Med 24:35-46, 2009
18. Bundgaard-Nielsen M, Secher NH, Kehlet H: "Liberal" versus "restrictive" perioperative fluid therapy—A critical assessment of the evidence. Acta Anaesthesiol Scand 53:843-851, 2009
19. Marik PE, Baram M, Vahid B: Does the central venous pressure predict fluid responsiveness? A systematic review of the literature and the tale of seven mares. Chest 134:172-178, 2008
20. Saugel B, Ringmaier S, Holzapfel K, et al: Physical examination, central venous pressure, and chest radiography for the prediction of transpulmonary thermodilution-derived hemodynamic parameters in critically ill patients: A prospective trial. J Crit Care 26:402-410, 2011
21. Fick A: Ueber die Messung des Blutquantums in den Herzventrikeln. Sitzungsber PhysiologischMedizinosche Ges Wuerzburg 2:16, 1870
22. Swan HJ, Ganz W, Forrester J, et al: Catheterization of the heart in man with use of a flow-directed balloon-tipped catheter. N Engl J Med 283:447-451, 1970
23. Critchley LA, Critchley JA: A meta-analysis of studies using bias and precision statistics to compare cardiac output measurement techniques. J Clin Monit Comput 15:85-91, 1999
24. Critchley LA, Lee A, Ho AM: A critical review of the ability of continuous cardiac output monitors to measure trends in cardiac output. Anesth Analg 111:1180-1192, 2010
25. Bland JM, Altman DG: Statistical methods for assessing agreement between two methods of clinical measurement. Lancet i:307-310, 1986
26. Jaffe MB: Partial CO2 rebreathing cardiac output – Operating principles of the NICO system. J Clin Monit Comput 15:387-401, 1999
27. Rocco M, Spadetta G, Morelli A, et al: A comparative evaluation of thermodilution and partial CO2 rebreathing techniques for cardiac output assessment in critically ill patients during assisted ventilation. Intensive Care Med 30:82-87, 2004
28. Nilsson LB, Eldrup N, Berthelsen PG: Lack of agreement between thermodilution and carbon dioxide-rebreathing cardiac output. Acta Anaesthesiol Scand 45:680-685, 2001
29. van Heerden PV, Baker S, Lim SI, et al: Clinical evaluation of the noninvasive cardiac output (NICO) monitor in the intensive care unit. Anaesthesiol Intensive Care 28:427-430, 2000
30. Odenstedt H, Stenqvist O, Lundin S: Clinical evaluation of a partial CO2 rebreathing technique for cardiac output monitoring in critically ill patients. Acta Anaesthesiol Scand 46:152-159, 2002
31. Binder JC, Parkin WG: Noninvasive cardiac output determination: Comparison of a new partial-rebreathing technique with thermodilution. Anaesthesiol Intensive Care 29:19-23, 2001
32. Kotake Y, Moriyama K, Innami Y, et al: Performance of noninvasive partial CO2 rebreathing cardiac output and continuous thermodilution cardiac output in patients undergoing aortic reconstruction surgery. Anesthesiol 99:283-288, 2003
33. Tachibana K, Imanaka H, Takeuchi M, et al: Effects of reduced rebreathing time, in spontaneously breathing patients, on respiratory effort and accuracy in cardiac output measurement when using a partial carbon dioxide rebreathing technique: A prospective observational study. Crit Care 9:R569-R574, 2005
34. Tachibana K, Imanaka H, Takeuchi M, et al: Noninvasive cardiac output measurement using partial carbon dioxide rebreathing is less accurate at settings of reduced minute ventilation and when spontaneous breathing is present. Anesthesiol 98:830-837, 2003
35. Lefrant JY, Bruelle P, Aya AG, et al: Training is required to improve the reliability of esophageal Doppler to measure cardiac output in critically ill patients. Intensive Care Med 24:347-352, 1998

ARTICLE IN PRESS

36. Valtier B, Cholley BP, Belot JP, et al: Noninvasive monitoring of cardiac output in critically ill patients using transesophageal Doppler. Am J Respir Crit Care Med 158:77-83, 1998

37. Marik PE, Levitov A, Young A, et al: The use of NICOM (bioreactance) and carotid Doppler to determine volume responsiveness and blood flow redistribution following passive leg raising in hemodynamically unstable patients. Ann Crit Care 2012 (in press)

38. Sinclair S, James S, Singer M: Intraoperative intravascular volume optimisation and length of hospital stay after repair of proximal femoral fracture: Randomised controlled trial. BMJ 315:909-912, 1997

39. Tan HL, Pinder M, Parsons R, et al: Clinical evaluation of USCOM ultrasonic cardiac output monitor in cardiac surgical patients in intensive care unit. Br J Anaesth 94:287-291, 2005

40. Thom O, Taylor DM, Wolfe RE, et al: Comparison of a suprasternal cardiac output monitor (USCOM) with the pulmonary artery catheter. Br J Anaesth 103:800-804, 2009

41. Boyle M, Steel L, Flynn GM, et al: Assessment of the clinical utility of an ultrasonic monitor of cardiac output (the USCOM) and agreement with thermodilution measurement. Crit Care Resusc 11:198-203, 2009

42. Chand R, Mehta Y, Trehan N: Cardiac output estimation with a new Doppler device after off-pump coronary artery bypass surgery. J Cardiothorac Vasc Anesth 20:315-319, 2006

43. Montenij LJ, de Waal EE, Buhre WF: Arterial waveform analysis in anesthesia and critical care. Curr Opin Anaesthesiol 24:651-656, 2011

44. Camporota L, Beale R: Pitfalls in haemodynamic monitoring based on the arterial pressure waveform. Crit Care 14:124, 2010

45. Bein B, Worthmann F, Tonner PH, et al: Comparison of esophageal Doppler, pulse contour analysis, and real-time pulmonary artery thermodilution for the continuous measurement of cardiac output. J Cardiothorac Vasc Anesth 18:185-189, 2004

46. Mora B, Ince I, Birkenberg B, et al: Validation of cardiac output measurement with the LiDCOTM pulse contour system in patients with impaired left ventricular function after cardiac surgery. J Anesth 66: 675-681, 2011

47. Garcia-Rodriguez C, Pittman J, Cassell CH, et al: Lithium dilution cardiac output measurement: A clinical assessment of central venous and peripheral venous indicator injection. Crit Care Med 30: 2199-2204, 2002

48. Linton R, Band D, O'Brien T, et al: Lithium dilution cardiac output measurement: A comparison with thermodilution. Crit Care Med 25:1796-1800, 1997

49. Oren-Grinberg A: The PiCCO monitor. Int Anesthesiol Clin 48:57-85, 2010

50. Holm C, Mayr M, Horbrand F, et al: Reproducibility of transpulmonary thermodilution measurements in patients with burn shock and hypothermia. J Burn Care Rehabil 26:260-265, 2005

51. Hamzaoui O, Monnet X, Richard C, et al: Effects of changes in vascular tone on the agreement between pulse contour and transpulmonary thermodilution cardiac output measurements within an up to 6-hour calibration-free period. Crit Care Med 36:434-440, 2008

52. Fernandez-Mondejar E, Rivera-Fernandez R, Garcia-Delgado M, et al: Small increases in extravascular lung water are accurately detected by transpulmonary thermodilution. J Trauma 59:1420-1423, 2005

53. Kozieras J, Thuemer O, Sakka SG: Influence of an acute increase in systemic vascular resistance on transpulmonary thermodilution-derived parameters in critically ill patients. Intensive Care Med 33:1619-1623, 2007

54. Katzenelson R, Perel A, Berkenstadt H, et al: Accuracy of transpulmonary thermodilution versus gravimetric measurement of extravascular lung water. Crit Care Med 32:1550-1554, 2004

55. Marik PE, Cavallazzi R, Vasu T, et al: Dynamic changes in arterial waveform derived variables and fluid responsiveness in mechanically ventilated patients. A systematic review of the literature. Crit Care Med 37:2642-2647, 2009

56. Mutoh T, Kazumata K, Ishikawa T, et al: Performance of bedside transpulmonary thermodilution monitoring for goal-directed hemodynamic management after subarachnoid hemorrhage. Stroke 40: 2368-2374, 2009

57. Langewouters GJ, Wesseling KH, Goedhard WJ: The static elastic properties of 45 human thoracic and 20 abdominal aortas in vitro and the parameters of a new model. J Biomech 17:425-435, 1984

58. Chakravarthy M, Patil TA, Jayaprakash K, et al: Comparison of simultaneous estimation of cardiac output by four techniques in patients undergoing off-pump coronary artery bypass surgery—A prospective observational study. Ann Card Anaesth 10:121-126, 2007

59. de Waal EE, Kalkman CJ, Rex S, et al: Validation of a new arterial pulse contour-based cardiac output device. Crit Care Med 35:1904-1909, 2007

60. Manecke GR, Jr, Auger WR: Cardiac output determination from the arterial pressure wave: Clinical testing of a novel algorithm that does not require calibration. J Cardiothorac Vasc Anesth 21:3-7, 2007

61. McGee WT, Horswell JL, Caldeeron J, et al: Validation of a continuous, arterial pressure-based cardiac output measurement: A multicenter, prospective clinical trial. Crit Care 11:R105, 2007

62. Zimmermann A, Kufner C, Hofbauer S, et al: The accuracy of the Vigileo/FloTrac continuous cardiac output monitor. J Cardiothorac Vasc Anesth 22:388-393, 2008

63. Marque S, Cariou A, Chiche JD, et al: Comparison between Flotrac-Vigileo and bioreactance, a totally noninvasive method for cardiac output monitoring. Crit Care 13:R73, 2009

64. Ostergaard M, Nielsen J, Nygaard E: Pulse contour cardiac output: An evaluation of the FloTrac method. Eur J Anaesthesiol 26:484-489, 2009

65. Monnet X, Anguel N, Naudin B, et al: Arterial pressure-based cardiac output in septic patients: Different accuracy of pulse contour and uncalibrated pressure waveform devices. Crit Care 14:R109, 2010

66. Opdam HI, Wan L, Bellomo R: A pilot assessment of the FloTrac cardiac output monitoring system. Intensive Care Med 33:344-349, 2007

67. Sander M, Spies CD, Grubitzsch H, et al: Comparison of uncalibrated arterial waveform analysis in cardiac surgery patients with thermodilution cardiac output measurements. Crit Care 10: R164, 2006

68. Breukers RM, Sepehrkhouy S, Spiegelenberg SR, et al: Cardiac output measured by a new arterial pressure waveform analysis method without calibration compared with thermodilution after cardiac surgery. J Cardiothorac Vasc Anesth 21:632-635, 2007

69. Mayer J, Boldt J, Schollhorn T, et al: Semi-invasive monitoring of cardiac output by a new device using arterial pressure waveform analysis: A comparison with intermittent pulmonary artery thermodilution in patients undergoing cardiac surgery. Br J Anaesth 98:176-182, 2007

70. Sander M, Spies CD, Foer A, et al: Cardiac output measurement by arterial waveform analysis in cardiac surgery—A comparison of measurements derived from waveforms of the radial artery versus the ascending aorta. J Int Med Res 36:414-419, 2008

71. Cecconi M, Dawson D, Casaretti R, et al: A prospective study of the accuracy and precision of continuous cardiac output monitoring devices as compared to intermittent thermodilution. Minerva Anestesiol 76:1010-1017, 2010

72. Button D, Weibel L, Reuthebuch O, et al: Clinical evaluation of the FloTrac/Vigileo system and two established continuous cardiac output monitoring devices in patients undergoing cardiac surgery. Br J Anaesth 99:329-336, 2007

ARTICLE IN PRESS

73. Cannesson M, Attof Y, Rosamel P, et al: Comparison of FloTrac cardiac output monitoring system in patients undergoing coronary artery bypass grafting with pulmonary artery cardiac output measurements. Eur J Anaesthesiol 24:832-839, 2007

74. Sakka SG, Kozieras J, Thuemer O, et al: Measurement of cardiac output: A comparison between transpulmonary thermodilution and uncalibrated pulse contour analysis. Br J Anaesth 99:337-342, 2007

75. Mehta Y, Chand RK, Sawhney R, et al: Cardiac output monitoring: Comparison of a new arterial pressure waveform analysis to the bolus thermodilution technique in patients undergoing off-pump coronary artery bypass surgery. J Cardiothorac Vasc Anesth 22:394-399, 2008

76. Staier K, Wiesenack C, Gunkel L, et al: Cardiac output determination by thermodilution and arterial pulse waveform analysis in patients undergoing aortic valve replacement. Can J Anaesth 55:22-28, 2008

77. Compton FD, Zukunft B, Hoffmann C, et al: Performance of a minimally invasive uncalibrated cardiac output monitoring system (Flotrac/Vigileo) in haemodynamically unstable patients. Br J Anaesth 100:451-456, 2008

78. Biais M, Nouette-Gaulain K, Cottenceau V, et al: Cardiac output measurement in patients undergoing liver transplantation: Pulmonary artery catheter versus uncalibrated arterial pressure waveform analysis. Anesth Analg 106:1480-1486, 2008

79. Eleftheriadis S, Galatoudis Z, Didilis V, et al: Variations in arterial blood pressure are associated with parallel changes in FlowTrac/Vigileo (R)–derived cardiac output measurements: A prospective comparison study. Crit Care 13:R179, 2009

80. Hamm JB, Nguyen BV, Kiss G, et al: Assessment of a cardiac output device using arterial pulse waveform analysis, Vigileo, in cardiac surgery compared to pulmonary arterial thermodilution. Anaesth Intensive Care 38:295-301, 2010

81. Hofer CK, Button D, Weibel L, et al: Uncalibrated radial and femoral arterial pressure waveform analysis for continuous cardiac output measurement: An evaluation in cardiac surgery patients. J Cardiothorac Vasc Anesth 24:257-264, 2010

82. Jo YY, Song JW, Yoo YC, et al: The uncalibrated pulse contour cardiac output during off-pump coronary bypass surgery: Performance in patients with a low cardiac output status and a reduced left ventricular function. Korean J Anesthesiol 60:237-243, 2011

83. Slagt C, Beute J, Hoeksema M, et al: Cardiac output derived from arterial pressure waveform analysis without calibration vs. thermodilution in septic shock: Evolving accuracy of software versions. Eur J Anaesthesiol 27:550-554, 2010

84. Junttila EK, Koskenkari JK, Ohtonen PP, et al: Uncalibrated arterial pressure waveform analysis for cardiac output monitoring is biased by low peripheral resistance in patients with intracranial haemorrhage. Br J Anaesth 107:581-586, 2011

85. Haenggi M, Barthelmes D, Ulmer H, et al: Comparison of non-calibrated pulse-contour analysis with continuous thermodilution for cardiac output assessment in patients with induced hypothermia after cardiac arrest. Resuscitation 82:423-426, 2011

86. Saraceni E, Rossi S, Persona P, et al: Comparison of two methods for cardiac output measurement in critically ill patients. Br J Anaesth 106:690-694, 2011

87. Vetrugno L, Costa MG, Spagnesi L, et al: Uncalibrated arterial pulse cardiac output measurements in patients with moderately abnormal left ventricular function. J Cardiothorac Vasc Anesth 25:53-58, 2011

88. Prasser C, Trabold B, Schwab A, et al: Evaluation of an improved algorithm for arterial pressure-based cardiac output assessment without external calibration. Intensive Care Med 33:2223-2225, 2007

89. Della Rocca G, Costa MG, Chiarandini P, et al: Arterial pulse cardiac output agreement with thermodilution in patients in hyperdynamic conditions. J Cardiothorac Vasc Anesth 22:681-687, 2008

90. Mayer J, Boldt J, Wolf MW, et al: Cardiac output derived from arterial pressure waveform analysis in patients undergoing cardiac surgery: Validity of a second generation device. Anesth Analg 106: 867-872, 2008

91. Senn A, Button D, Zollinger A, et al: Assessment of cardiac output changes using a modified FloTrac/Vigileo algorithm in cardiac surgery patients. Crit Care 13:R32, 2009

92. Biancofiore G, Critchley LA, Lee A, et al: Evaluation of an uncalibrated arterial pulse contour cardiac output monitoring system in cirrhotic patients undergoing liver surgery. Br J Anaesth 102:47-54, 2009

93. Zimmermann A, Steinwendner J, Hofbauer S, et al: The accuracy of the Vigileo/FloTrac system has been improved – Follow-up after a software update: A blinded comparative study of 30 cardiosurgical patients. J Cardiothorac Vasc Anesth 23:929-931, 2009

94. Hadian M, Kim HK, Severyn DA, et al: Cross-comparison of cardiac output trending accuracy of LiDCO, PiCCO, FloTrac and pulmonary artery catheters. Crit Care 14:R212, 2010

95. Krejci V, Vannucci A, Abbas A, et al: Comparison of calibrated and uncalibrated arterial pressure-based cardiac output monitors during orthotopic liver transplantation. Liver Transpl 16:773-782, 2010

96. Mutoh T, Ishikawa T, Nishino K, et al: Evaluation of the FloTrac uncalibrated continuous cardiac output system for perioperative hemodynamic monitoring after subarachnoid hemorrhage. J Neurosurg Anesthesiol 21:218-225, 2009

97. Biancofiore G, Critchley LA, Lee A, et al: Evaluation of a new software version of the FloTrac/Vigileo (version 3.02) and a comparison with previous data in cirrhotic patients undergoing liver transplant surgery. Anesth Analg 113:515-522, 2011

98. De Backer D, Marx G, Tan A, et al: Arterial pressure-based cardiac output monitoring: A multicenter validation of the third-generation software in septic patients. Intensive Care Med 37:233-240, 2011

99. Metzelder S, Coburn M, Fries M, et al: Performance of cardiac output measurement derived from arterial pressure waveform analysis in patients requiring high-dose vasopressor therapy. Br J Anaesth 106:776-784, 2011

100. Phan TD, Kluger R, Wan C, et al: A comparison of three minimally invasive cardiac output devices with thermodilution in elective cardiac surgery. Anaesthesiol Intensive Care 39:1014-1021, 2011

101. Monnet X, Anguel N, Jozwiak M, et al: Third-generation FloTrac/Vigileo does not reliably track changes in cardiac output induced by norepinephrine in critically ill patients. Br J Anaesth 108: 615-622, 2012

102. Su BC, Tsai YF, Chen CY, et al: Cardiac output derived from arterial pressure waveform analysis in patients undergoing liver transplantation: Validity of a third generation device. Transplant Proc 44: 424-428, 2012

103. Lorsomradee S, Lorsomradee S, Cromheecke S, et al: Uncalibrated arterial pulse contour analysis versus continuous thermodilution technique: Effects of alterations in arterial waveform. J Cardiothorac Vasc Anesth 21:636-643, 2007

104. Benes J, Chytra I, Altmann P, et al: Intraopeartive fluid optimization using stroke volume variation in high risk surgical patients: Results of prospective randomized study. Crit Care 14:R118, 2010

105. Machare-Delgado E, DeCaro M, Marik PE: Inferior vena cava variation compared to pulse contour analysis as predictors of fluid responsiveness: A prospective cohort study. J Intensive Care Med 26:116-124, 2011

106. Takala J, Ruokonen E, Tenhunen JJ, et al: Early noninvasive cardiac output monitoring in hemodynamically unstable intensive care

ARTICLE IN PRESS

patents: A multicenter randomized controlled trial. Crit Care 15:R148, 2011

107. Romano SM, Pistolesi M: Assessment of cardiac output from systemic arterial pressure in humans. Crit Care Med 30:1834-1841, 2002

108. Scolletta S, Romano SM, Biagioli B, et al: Pressure recording analytical method (PRAM) for measurement of cardiac output during various haemodynamic states. Br J Anaesth 95:159-165, 2005

109. Franchi F, Silvestri R, Cubattoli L, et al: Comparison between an uncalibrated pulse contour method and thermodilution technique for cardiac output estimation in septic patients. Br J Anaesth 107:202-208, 2011

110. Calamandrei M, Mirabile L, Muschetta S, et al: Assessment of cardiac output in children: A comparison between the pressure recording analytical method and Doppler echocardiography. Pediatr Crit Care Med 9:310-312, 2008

111. Giomarelli P, Biagioli B, Scolletta S: Cardiac output monitoring by pressure recording analytical method in cardiac surgery. Eur J Cardiothorac Surg 26:515-520, 2004

112. Scolletta S, Miraldi F, Romano SM, et al: Continuous cardiac output monitoring with an uncalibrated pulse contour method in patients supported with mechanical pulsatile assist device. Interact Cardiovasc Thorac Surg 13:52-56, 2011

113. Paarmann H, Groesdonk HV, Sedemund-Adib B, et al: Lack of agreement between pulmonary arterial thermodilution cardiac output and the pressure recording analytical method in postoperative cardiac surgery patients. Br J Anaesth 106:475-481, 2011

114. Maj G, Monaco F, Landoni G, et al: Cardiac index assessment by the pressure recording analytic method in unstable patients with atrial fibrillation. J Cardiothorac Vasc Anesth 25:476-480, 2011

115. Zangrillo A, Maj G, Monaco F, et al: Cardiac index validation using the pressure recording analytic method in unstable patients. J Cardiothorac Vasc Anesth 24:265-269, 2010

116. Michard F, Teboul JL: Using heart-lung interactions to assess fluid responsiveness during mechanical ventilation. Crit Care 4:282-289, 2000

117. Renner J, Broch O, Duetschke P, et al: Prediction of fluid responsiveness in infants and neonates undergoing congenital heart surgery. Br J Anaesth 108:108-115, 2012

118. Geerts B, de Wilde R, Aarts L, et al: Pulse contour analysis to assess hemodynamic response to passive leg raising. J Cardiothorac Vasc Anesth 25:48-52, 2011

119. Wyffels PA, Sergeant P, Wouters PF: The value of pulse pressure and stroke volume variation as predictors of fluid responsiveness during open chest surgery. J Anesth 65:704-709, 2010

120. Pearse R, Dawson D, Rhodes A, et al: Early goal-directed therapy after major surgery reduces complications and duration of hospital stay: A randomised controlled trial. Crit Care 9:R687-R693, 2005

121. Cannesson M, Le MY, Hofer CK, et al: Assessing the diagnostic accuracy of pulse pressure variations for the prediction of fluid responsiveness: A "gray zone" approach. Anesthesiol 115:231-241, 2011

122. Jacques D, Bendjelid K, Duperret S, et al: Pulse pressure variation and stroke volume variation during increased intra-abdominal pressure: An experimental study. Crit Care 15:R33, 2011

123. Mahjoub Y, Pila C, Friggeri A, et al: Assessing fluid responsiveness in critically ill patients: False-positive pulse pressure variation is detected by Doppler echocardiographic evaluation of the right ventricle. Crit Care Med 37:2570-2575, 2009

124. Muller L, Louart G, Bousquet PJ, et al: The influence of the airway driving pressure on pulsed pressure variation as a predictor of fluid responsiveness. Intensive Care Med 36:496-503, 2010

125. von Ballmoos MW, Takala J, Roeck M, et al: Pulse-pressure variation and hemodynamic response in patients with elevated pulmonary artery pressure: A clinical study. Crit Care 14:R111, 2010

126. Lakhal K, Ehrmann S, Benzekri-Lefevre D, et al: Respiratory pulse pressure variation fails to predict fluid responsiveness in acute respiratory distress syndrome. Crit Care 15:R85, 2011

127. Lansdorp B, Lemson J, van Putten MJ, et al: Dynamic indices do not predict volume responsiveness in routine clinical practice. Br J Anaesth 108:395-401, 2012

128. Raaijmakers E, Faes TJ, Scholten RJ, et al: A meta-analysis of three decades of validating thoracic impedance cardiography. Crit Care Med 27:1203-1213, 1999

129. Bowling LS, Sageman WS, O'Connor SM, et al: Lack of agreement between measurement of ejection fraction by impedance cardiography versus radionuclide ventriculography. Crit Care Med 21:1523-1527, 1993

130. Marik PE, Pendelton JE, Smith R: A comparison of hemodynamic parameters derived from transthoracic electrical bioimpedance with those parameters obtained by thermodilution and ventricular angiography. Crit Care Med 25:1545-1550, 1997

131. Critchley LA, Calcroft RM, Tan PY, et al: The effect of lung injury and excessive lung fluid, on impedance cardiac output measurements, in the critically ill. Intensive Care Med 26:679-685, 2000

132. Sageman WS, Riffenburgh RH, Spiess BD: Equivalence of bioimpedance and thermodilution in measuring cardiac index after cardiac surgery. J Cardiothorac Vasc Anesth 16:8-14, 2002

133. Gujjar AR, Muralidhar K, Banakal S, et al: Noninvasive cardiac output by transthoracic electrical bioimpedence in post-cardiac surgery patients: Comparison with thermodilution method. J Clin Monit Comput 22:175-180, 2008

134. Spiess BD, Patel MA, Soltow LO, et al: Comparison of bioimpedance versus thermodilution cardiac output during cardiac surgery: Evaluation of a second-generation bioimpedance device. J Cardiothorac Vasc Anesth 15:567-573, 2001

135. Kamath SA, Drazner MH, Tasissa G, et al: Correlation of impedance cardiography with invasive hemodynamic measurements in patients with advanced heart failure: The bioimpedance CardioGraphy (BIG) substudy of the evaluation study of congestive heart failure and Pulmonary Artery catheterization effectiveness (ESCAPE) trial. Am Heart J 158:217-223, 2009

136. Raue W, Swierzy M, Koplin G, et al: Comparison of electrical velocimetry and transthoracic thermodilution technique for cardiac output assessment in critically ill patients. Eur J Anaesthesiol 26:1067-1071, 2009

137. Engoren M, Barbee D: Comparison of cardiac output determined by bioimpedance, thermodilution, and the Fick method. Am J Crit Care 14:40-45, 2005

138. Wang DJ, Gottlieb SS: Impedance cardiography: More questions than answers. Curr Cardiol Rep 8:180-186, 2006

139. Keren H, Burkhoff D, Squara P: Evaluation of a noninvasive continuous cardiac output monitoring system based on thoracic bioreactance. Am J Physiol 293:H583-H589, 2007

140. Raval NY, Squara P, Cleman M, et al: Multicenter evaluation of noninvasive cardiac output measurement by bioreactance technique. J Clin Monit Comput 22:113-119, 2008

141. Squara P, Rotcajg D, Denjean D, et al: Comparison of monitoring performance of bioreactance vs. pulse contour during lung recruitment maneuvers. Crit Care 13:R125, 2009

142. Rich JD, Archer SL, Rich S: Evaluation of noninvasively measured cardiac output in patients with pulmonary hypertension. Am J Respir Crit Care Med 183:A6440, 2011

143. Squara P, Denjean D, Estagnasie P, et al: Noninvasive cardiac output monitoring (NICOM): A clinical validation. Intensive Care Med 33:1191-1194, 2007

144. Heerdt PM, Wagner CL, DeMais M, et al: Noninvasive cardiac ouput monitoring with bioreactance as an alternative to invasive instrumentation for preclinical drug evaluation in beagles. J Pharmacol Toxicol Methods 64:111-118, 2011

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145. Benomar B, Ouattara A, Estagnasie P, et al: Fluid responsiveness predicted by noninvasive bioreactance-based passive leg raise test. Intensive Care Med 36:1875-1881, 2010

146. Waldron NH, Miller TE, Nardiello J, et al: NICOM versus EDM guided goal directed fluid therapy in the perioperative period. Anesthesiology 115:A680, 2011

147. Levitov A, Marik PE: Echocardiographic assessment of preload responsiveness in critically ill patients. Cardiol Res Pract 2012: 819696, 2012

148. Salem R, Vallee F, Rusca M, et al: Hemodynamic monitoring by echocardiography in the ICU: The role of the new echo techniques. Curr Opin Crit Care 14:561-568, 2008