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Endotracheal Cardiac Output Monitor

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Background: **The endotracheal cardiac output monitor (ECOM) is a new device that uses an endotracheal tube with multiple electrodes to measure cardiac output (CO). It measures the changes in electrical impedance caused by pulsatile blood flow in the aorta. The system was tested for safety and efficacy in 10 swine.**

Methods: **Swine (60–80 kg) were chronically instrumented with a transit time flow probe on the ascending aorta and vascular occluders on the vena cava and pulmonary artery. After a minimum recovery of 4 days, the animals were anesthetized and intubated with an ECOM endotracheal tube. CO measurements from the ECOM system were compared to transit time flow probe measurements using linear regression and Bland–Altman analysis. Three different inotropic states were studied: (1) baseline; (2) increased (dobutamine); and (3) decreased (esmolol). CO was changed at each inotropic state by impeding left ventricular filling with the vena cava or pulmonary artery occluders. CO values between 0 and 15 l/min were studied. Pigs were studied for 24 h consecutively.**

Results: **There was no deterioration of the impedance signal with time and no tracheal injury from the ECOM electrodes. There is a linear relationship between the ECOM and transit time flow probe CO between 0 and 15 l/min (slope = 0.94; intercept = 0.15 l/min; R^2= 0.77). The mean difference between the two measures (bias) is 0.15 l/min and the SD is 1.34 l/min. The limits of agreement are −2.53 to 2.82 l/min.**

Conclusion: **Endotracheal CO monitor is a promising technology that needs further evaluation in clinical trials. (Key words: Algorithm; bioimpedance; flow probe; pig.)**

CARDIAC output is a key physiologic parameter. Unfortunately, it is often difficult to measure without using invasive techniques with associated risk. Since its introduction, the pulmonary artery catheter has been considered the gold standard for the measurement of cardiac output (CO) in humans. Unfortunately, pulmonary artery catheters have been associated with serious complications.[1,2] Thoracic electrical bioimpedance (TEB) has been suggested as a possible noninvasive technique for the measurement of CO. The accuracy and reliability of TEB have been evaluated multiple times, with some studies demonstrating good correlation with thermodilution[3–7] and others with poor correlation.[6,8–15] TEB is not reliable in patients after cardiopulmonary bypass,[8,9] kidney transplants,[11] congestive heart failure,[16] pulmonary edema,[14] sepsis,[12] pregnancy,[15] abdominal surgery,[11,17] or critical illness.[13,14]

One of the limitations of TEB is the signal-to-noise ratio. TEB systems commonly use an alternating current (1–4 mA at 20–100 kHz) applied to the skin and have little control over the percentage of current passing through the vascular structures in the chest. Changes in the electrical impedance of the lungs with respiration change the percentage of the total current passing through blood-containing structures. Finally, treating all of the blood-containing structures in the chest as a single impedance to be measured does not allow separation of the signal into its various components. A technique that stabilizes the percentage of current delivered to the target structure and records the electrical impedance signals directly from that target structure may improve the accuracy and reliability of impedance-based measurement of CO.

The endotracheal CO monitor (ECOM) is a system that records the voltages produced by a current (2 mA at 100 kHz) delivered to the tracheal mucosa by electrodes on

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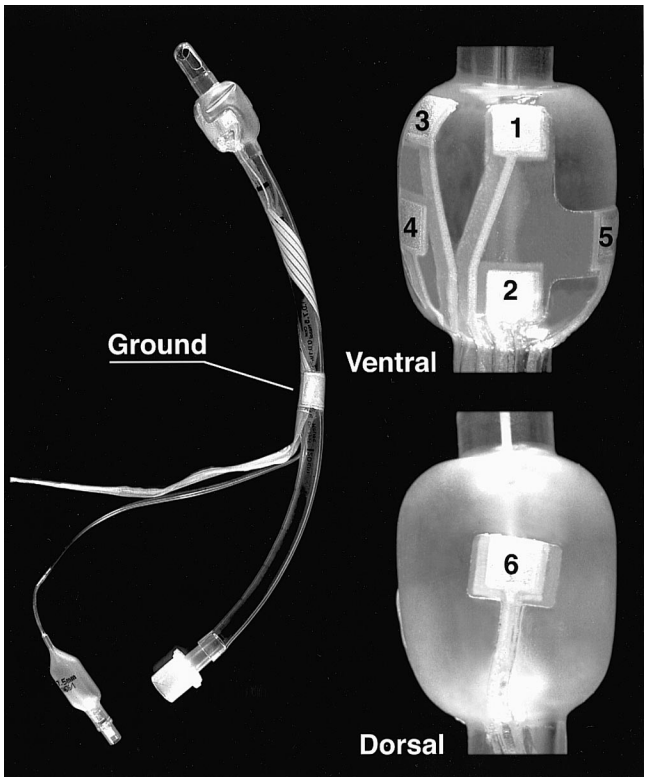

Fig. 1. Model 6-3D endotracheal tube with six electrodes on the balloon and one ground electrode on the shaft. (*Left*) The entire endotracheal tube showing the ground electrode on the shaft of the tube. (*Top right*) Ventral surface of the balloon with electrodes 1–5. (*Bottom right*) Dorsal surface of the balloon with electrode 6. Electrode 3 is the current source. Electrode pairs 1 and 2, 4 and 5, and 1 and 6 give the three orthogonal signals.

an endotracheal tube. The proximity of the ascending aorta and trachea allows the design of a device that can optimize the current delivery and signal recording from impedance changes in the ascending aorta. This study tested the safety, accuracy, time stability, and sources of variability of the ECOM system in 10 chronically instrumented swine.

Methods

Endotracheal Tube Design

A custom-built 7.5-mm endotracheal tube was designed with six electrodes on the balloon and one on the shaft (model 6-3D; Imagyn, Newport Beach, CA; fig. 1). The shaft electrode is a 15-mm-wide band that serves as a ground. Electrodes were composed of a conducting ink on a plastic backing. The plastic backing was then glued onto a 7.5-mm endotracheal tube (Euromedical Industries Sdn. Bhd., Penang, Malaysia). The electrode surface is smooth and atraumatic to the tracheal mucosa. The field current is produced between balloon electrode 3 and the ground electrode on the shaft of the tube. Three orthogonal pairs of sensing electrodes (1 and 2, 4 and 5, 1 and 6) on the balloon are used to measure three impedance signals (DZ_x, DZ_y, DZ_z). DZ is the change in impedance with time. The three-dimensional impedance field is calculated from these three measurements:

$$DZ_{3-D} = \sqrt{DZ_x^2 + DZ_y^2 + DZ_z^2}$$

Tube electrocardiogram is measured between balloon electrodes and the shaft ground. A 15-cm extension was placed on the 7.5-mm, 31-cm-long tube to allow use in a pig. The tube was designed by the Veterans Affairs Medical Center and manufactured by ACT Medical Inc. (Newton, MA).

Electronic Design

Custom-built electronics (Rivertek Medical Systems, St. Paul MN) were designed that produced a sinusoidal current source at a set frequency (100 kHz). The electronics measured three impedance signals, three-lead surface electrocardiogram (right and left forelimb, left hindlimb), and internal electrocardiogram and recorded it on a lap-top computer at 400 samples per second (Dell PC 66 MHz Portable, Round Rock, TX). Simultaneous recordings of the aortic flow (Transonics Transit Time flow meter HT 206; Transonics Systems, Inc., Ithaca, NY) and arterial pressure (Model OM; Electronics for Medicine, White Plains, NY) were recorded with the impedance signals. The impedance system was designed and manufactured by Rivertek Medical Systems Inc. Custom software was written to analyze the impedance signals (Rivertek Medical Systems Software in C++, Borland International, Scotts Valley, CA; Veterans Affairs Medical Center Software in LabVIEW, National Instruments Corporation, Austin, TX).

Algorithm Design

During the design process for this study, tests of the standard algorithms used for impedance systems were performed: Kubicek[18] (equation 1) and Bernstein-Sramek[19] (equation 2).

$$SV_K = \rho\frac{L^2}{Z_0^2} \times (DZ)_{Max}(RVET) \quad (1)$$

The Kubicek formula consists of three basic components multiplied together to obtain the stroke volume

(SV_K). The parameter for the conversion of impedance measurements from ohms-seconds to milliliters is given by $\rho(L^2/Z_0^2)$, where ρ is the blood conductivity in ohms-centimeters, L is the length of the conducting material, and Z_0 is the steady-state impedance. The maximum magnitude of the change in impedance with time is given by DZ_{Max}, where $DZ = Z(t) - \overline{Z(t)}$. RVET is the right ventricular ejection time. The Kubicek formula simplifies to a parameter $[\rho(L^2/Z_0^2)]$ times an approximation of the integral of the impedance signal (DZ) over the ejection time (RVET). Many of the impedance algorithms have this basic form.

The Bernstein-Sramek[19] formula (equation 2) for stroke volume (SV_{BS}) has the same basic form:

$$SV_{BS} = \frac{VEPT}{Z_0} \times (dZ/dt_{max}) \times (VET) \qquad (2)$$

where VEPT is the volume of electrical participating tissue, calculated as $\delta[(0.17H)^3]/4.25$, where δ is a scaling factor relating height in centimeters (H), observed weight, ideal weight, and β, the relative blood volume index. ρ, the blood resistivity, has been eliminated by assuming that it a constant (135 Ω-cm). VET is the ventricular ejection time. dZ/dt_{Max} is the rate of change of impedance during systole. Z_0 is the basal thoracic impedance. The basic form is simply a correction factor times the amplitude of the signal times the ejection time.

In preliminary design work, these formulas were found to be inadequate with both surface impedance and endotracheal impedance measurements. A new formulation of the Kubicek formula (equation 1) was derived that used a Simpsons integral from the start of ejection to the end of ejection rather than a Gaussian integral with a single time step. This new formulation has been described as the Shmulewitz algorithm[20] (equation 5). The Shmulewitz algorithm repeated the basic form of the Kubicek and Bernstein-Sramek algorithm design. There was the assumption of a linear relationship between the impedance-derived measure of stroke volume and true stroke volume as in equation 3:

$$y = mx + b \qquad (3)$$

Instead of the simple integral used in the Kubicek and Bernstein-Sramek algorithms, a true integral of the change in impedance signal (DZ) was used.

$$SV = m \times \int_{BET}^{EET} DZdt + b \qquad (4)$$

where SV is the stroke volume and m is the slope of the relationship between the stroke volume calculated in ohms-seconds and true stroke volume in milliliters. The units of m are (milliliter)/(ohms-seconds) and are derived from an empirical fit of the Shmulewitz integral to the true stroke volume. The lumped parameter (m) recognizes that the physical model relating a change in measured impedance to a change in CO is not fully understood. The parameter (m) is derived empirically. DZ is the change in the impedance with time. The intercept of the linear relationship is given by b. EET is the end ejection time, and BET is the beginning of ejection time. There is no parameter (L) for electrode spacing because the interelectrode distances are fixed by tube design, and their effect is lumped into the parameter, m. Fortunately, when tested in animals, the intercept (b) has always been zero, and equation 4 simplifies into equation 5 (the Shmulewitz algorithm):

$$SV_{Shmulewitz} = m \times \int_{BET}^{EET} DZdt \qquad (5)$$

Endotracheal impedance measurements analyzed with this new equation have a linear relationship, with a zero intercept between the stroke volume calculated from the impedance signal and that measured by the transit time flow probe. Unfortunately, the slope of this relationship (m) varies between subjects and with tube position. This variation in the calibration factor between patients has been found in other impedance systems, requiring some form of calibration.[21,22]

In an effort to eliminate the need for calibration between patients and with changes in endotracheal tube position, a multiparameter algorithm based on the Shmulewitz algorithm as well as a series of other terms derived from the impedance signal was developed. The Shmulewitz algorithm was converted into a three-dimensional algorithm using three orthogonal impedance recordings (DZ_x, DZ_y, DZ_z; equation 6). The subscripts x, y, or z denote the x, y, or z directions, respectively.

$$SV_{3D-Shmulewitz} = \left[\left(m_x \times \int_{BET}^{EET} DZ_x dt\right)^2 + \left(m_y \times \int_{BET}^{EET} DZ_y dt\right)^2 + \left(m_z \times \int_{BET}^{EET} DZ_z dt\right)^2\right]^{1/2} \qquad (6)$$

We also developed a three-dimensional form of the

maximum of the first derivative [$(dDZ/dt)_{MAX}$] of the change in impedance:

$$SV_{3D-Diff} = \left[\left[m_{xD}\frac{dDZ_x}{dt}MAX\right]^2 + \left[m_{yD}\frac{dDZ_y}{dt}MAX\right]^2 + \left[m_{zD}\frac{dDZ_z}{dt}MAX\right]^2\right]^{\frac{1}{2}} \quad (7)$$

Equation 7 derives its form from a three-dimensional version of the Bernstein-Sramek algorithm. There is a correlation between the ECOM signal (DZ), the integral of the signal ($\int_{BET}^{EET} DZdt$), and the differential [$(dDZ/dt)_{MAX}$] of the signal and true CO. However, none of the individual correlations is robust enough to provide an invariant relationship between the parameter and true CO without calibration across animals. There is also information in timing parameters derived from the signal: ejection time, duration of decay of signal, time to peak of first derivative, and so on.

Step-wise multiple linear regression,[23] with all of the parameters that individually correlated with stroke volume, was used to fit the impedance parameters to the transit time flow probe measurements of CO (SAS Version 6.12, SAS Institute, Cary, NC). The multiparameter model was able to stabilize the slope of the relationship between impedance-derived measurement of CO and true CO (liters/minute) across animals. The multiparameter model does not rely on height, weight, hematocrit, or blood conductivity and is derived empirically.

Calibration

No changes in the algorithm were permitted between animals. There are no subject-specific parameters (height, weight, surface area, conductivity) in the algorithm. The empiric fit of the algorithm provides the calibration. The algorithm will need to be calibrated before use in humans.

Chronic Animal Preparation

Approval was obtained from the Institutional Animal Care and Use Committee at the Veterans Affairs Medical Center. Female swine (60–80 kg) were sedated with ketamine (25 mg/kg intramuscularly). Mask induction with isoflurane was then followed by intubation with an endotracheal tube (6.0 ID, 30-cm length). A 20-gauge catheter was placed in an ear vein for intravenous fluids. Prophylactic antibiotics were administered (cefazolin 1 g intravenously before incision followed by cephalexin 500 mg orally twice daily for 5 days). The animal was ventilated with 100% oxygen and isoflurane to maintain anesthesia. A left thoracotomy was performed under sterile conditions. A Transonics transit time flow probe (TTFP; model 28A, Transonic Systems, Inc.) was placed on the ascending aorta, and vascular occluders (In Vivo Metric, Healdsburg, CA)[24] were placed on the vena cava and pulmonary artery. The flow probe cable and occluder lines were tunneled to the animal's back. The thoracotomy was closed, and air was evacuated with a chest tube. The animals were given ketorolac (30 mg intravenously) followed by buprenorphine (0.3–0.6 mg intramuscularly every 8 h for 5 days) for postoperative pain. The animals were allowed to recover for at least 4 days.

Experimental Preparation

Previously instrumented swine were sedated with ketamine (25 mg/kg intramuscularly), and anesthesia was induced *via* mask with isoflurane. A 20-gauge, 48-mm catheter was placed in an ear vein for intravenous fluids. Prophylactic antibiotics were given (cefazolin 1 g intravenously every 8 h). Animals were intubated with the custom-built endotracheal tube (model 6-3D) at a depth of 44 cm to the tip of the snout. The tube was secured in place and marked to allow the identification of movement or rotation. Anesthesia was maintained with 100% oxygen and isoflurane. The animal's neck was then opened using a sterile technique. A 16-gauge, 57-mm catheter was placed in the internal jugular vein for drug and fluid infusions. Arterial pressure was measured with a 16-gauge, 57-mm catheter in the common carotid artery (Abbott Critical Care Systems Model 42,558-01 Disposable Pressure Transducer, Abbott Laboratories, Abbott Park, IL; Monitor Model OM, Electronics for Medicine). The neck was closed. A suprapubic bladder catheter was placed using sterile technique for urinary drainage.

Data Collection

The ECOM system electronics functioned continuously for 24 h in each pig, and CO was calculated beat by beat. Data were recorded in 45-s blocks at 400 samples per second. Data recorded included the impedance measurements from the endotracheal tube, arterial pressure, and ascending aortic flow from the TTFP. Two types of files were created: occlusion and baseline files. Occlusion files had a dramatic change in the CO caused by inflating the inferior pulmonary artery and/or vena caval occluders. CO could change from 15 to 0 l/min and

return to preocclusion levels in 45 s. Baseline files were steady-state files in which the CO was stable during the 45 s. The CO could be any value from 0 to 15 l/min, but it was constant during a baseline file.

Cardiac output was also altered with infusions of esmolol (0.1–1.0 $mg \cdot kg^{-1} \cdot min^{-1}$) and dobutamine (5–20 $\mu g \cdot kg^{-1} \cdot min^{-1}$). Combinations of drugs (esmolol or dobutamine) and occlusions (pulmonary artery and/or vena cava) produced COs between 0 and 15 l/min. A set of data (two baseline measurements and two occlusions) were collected each hour for 24 h consecutively. Data from high (dobutamine infusions) and low (esmolol infusions) inotropic states were obtained once during the 24-h data collection period.

Laboratory Studies

Temperature, endotracheal cuff pressure (Mallinkrodt Medical Digital P-V Gauge, St. Louis, MO), electrolytes (Na, K, iCa), *p*H, glucose, and hematocrit (i-STAT EC6+; I-STAT Corporation, Princeton, NJ), ρ, and blood conductivity (Leycom Sigma 5, Rijnburgerweg, The Netherlands) were measured every hour. Arterial blood gases (*p*H, carbon dioxide partial pressure, oxygen partial pressure, bicarbonate, total carbon dioxide, base excess, oxygen saturation) were measured as needed (i-STAT G3+, I-STAT Corporation).

Pathology

Tests of the effects of direct-current cardioversion and electrocautery were performed at the end of the 24-h data collection period to evaluate the possibility of tracheal injury from the electrodes.[25] The animal was externally direct-current cardioverted three times with 360 J. The chest was then opened using electrocautery. The entire length of trachea was opened longitudinally from the superior end to the carina, and the position of the endotracheal tube balloon was marked with a suture. The tracheal mucosa was visually inspected, photographed, and saved in 10% formalin.

Data Analysis

In developing an empiric model using either multiple linear regression, neural networks, or adaptive filtering, it is important to separate training data from test data. Data files were analyzed in two separate groups. The occlusion files (those with changes in CO) were analyzed to develop the empiric algorithm between the ECOM CO (CO_{ECOM}) and TTFP CO (CO_{TTFP}). Separate baseline files with different mean COs were analyzed to test the algorithm. Linear regression and Bland–Altman analysis[26] between CO_{TTFP} and CO_{ECOM} are presented for the group (10 animals) and for individual animals. The Bland–Altman analysis for the error with changes in systolic pressure, hematocrit, blood conductivity, and time were calculated. Blood conductivity was changed with dextrose 50% (300 ml) and 3% sodium chloride solutions (500 ml). Systolic pressure was changed with dobutamine, esmolol, and occlusions.

Results

Nine of the 10 animals studied completed the entire 24-h protocol. One animal developed signs consistent with a diagnosis of malignant hyperthermia (MH) diagnosed by hypercarbia (carbon dioxide partial pressure = 78 mmHg), metabolic acidosis (*p*H 7.30 with base excess −14), hyperkalemia (potassium = 8.8 mM), muscle rigidity, fever (108.5°F), and, finally, ventricular tachycardia, which progressed to ventricular fibrillation and death 14 h into the protocol. Treatment with dantrolene was not attempted. Gross examination revealed that the muscles were white, and the animal was completely rigid. Data from the animal with a presumed diagnosis of MH (pig no. 3) was included with that from the other nine animals.

Gross Examination of the Tracheal Mucosa

None of the nine animals that survived for 24 h showed evidence of tracheal mucosal injury from the balloon electrodes. There was slight hyperemia of the tracheal mucosa in the pattern of the balloon but no indication of electrical burns, abrasions, or injury from the balloon electrodes. The animal with a presumed diagnosis of MH (pig no. 3) had a 4-mm-diameter hematoma in the tracheal mucosa at the level of the balloon. The hematoma was not related to an electrode, merely the endotracheal balloon. There was no sign of burns, erosion, or other injury from the balloon.

Correlation and Bland–Altman Analysis of CO_{TTFP} and CO_{ECOM}

Figure 2 shows an impedance recording during release of the vascular occluders. Figure 3 is a comparison of CO_{ECOM} and CO_{TTFP} from the 29,657 heart beats recorded during occlusion runs from the 10 animals during the 24-h recording period. There is a linear correlation between CO_{ECOM} and CO_{TTFP} (R^2 = 0.84; table 1). The intercept is 0.00 l/min, and the slope is 0.99. Figure 4 shows the difference between CO_{ECOM} and CO_{TTFP} plot-

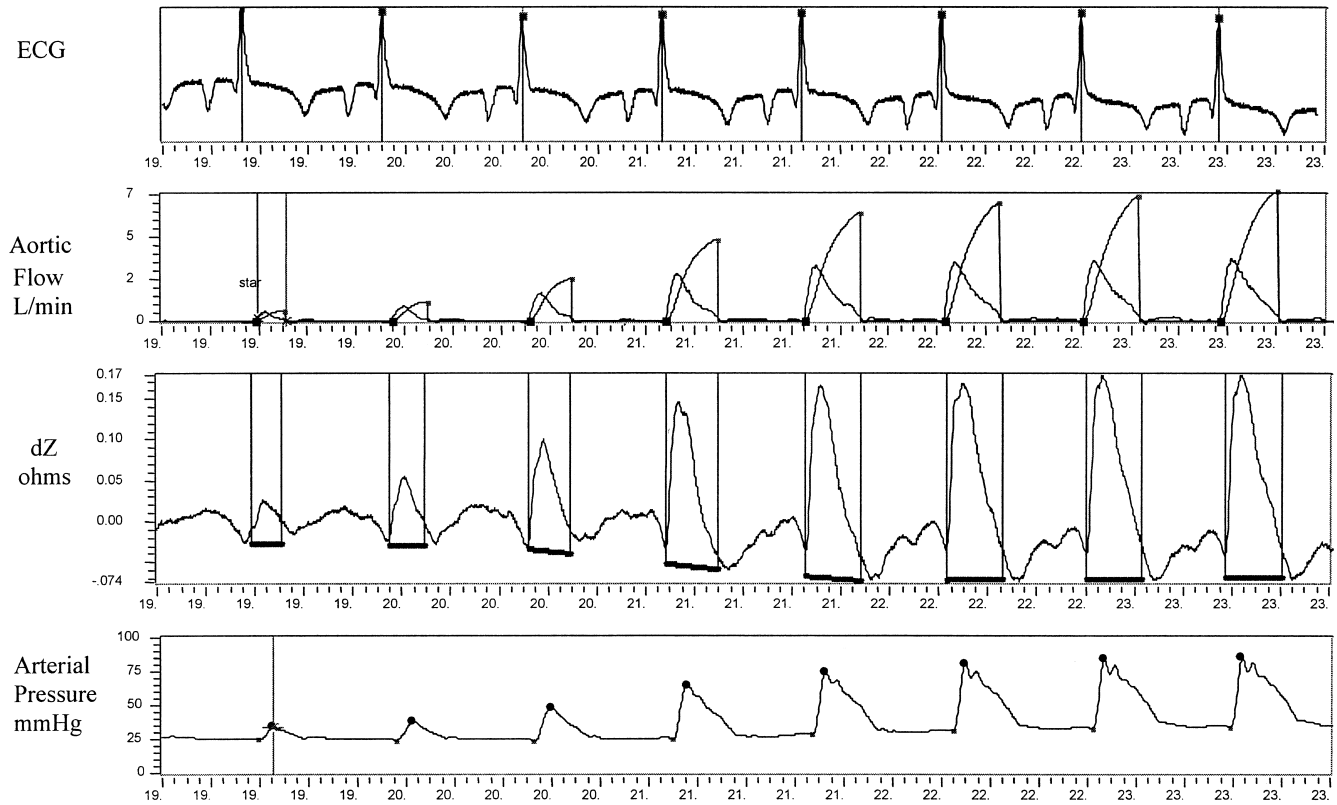

Fig. 2. Data recorded during release of the vascular occluders on the inferior vena cava and pulmonary artery. The top trace is the electrocardiogram derived from the endotracheal tube electrodes. The R wave is identified by a square and a vertical line. The second trace is aortic flow (liters/minute) measured by the transit time flow probe. The curve ending in a small square is the integral of transit time flow probe flow and gives stroke volume. The third trace is the change in impedance with time (DZ) measured in ohms. The trace between the two vertical lines corresponds to the aortic flow. The last trace is arterial pressure in millimeters mercury.

ted against the average of the two measurements (Bland–Altman).[26] COs between 0 and 15 l/min were measured. The mean CO_{TTFP} for occlusion files was 5.9 ± 3.0 l/min, whereas it was 5.9 ± 2.9 l/min for ECOM. The mean difference (bias) between CO_{ECOM} and CO_{TTFP} simultaneously measured COs was 0.01 ± 1.14 l/min, yielding a limit of agreement (bias + 2 SD) of −2.28 to 2.27 l/min for the occlusion data. Bland–Altman plots for individual animals are shown in figure 5 with the R^2, slope, intercept, bias, and limits of agreement for each animal detailed in table 2.

The 91,684 heart beats (obtained from the same 10 animals and same 24-h collection period) recorded during baseline runs (constant CO during the data collection period) were tested in the ECOM algorithm. The R^2 for the baseline files was 0.77. The slope was 0.94, and the intercept was 0.58 l/min. The mean CO_{TTFP} was 6.8 ± 3.1 l/min compared with a mean CO_{ECOM} of 6.6 ± 3.0

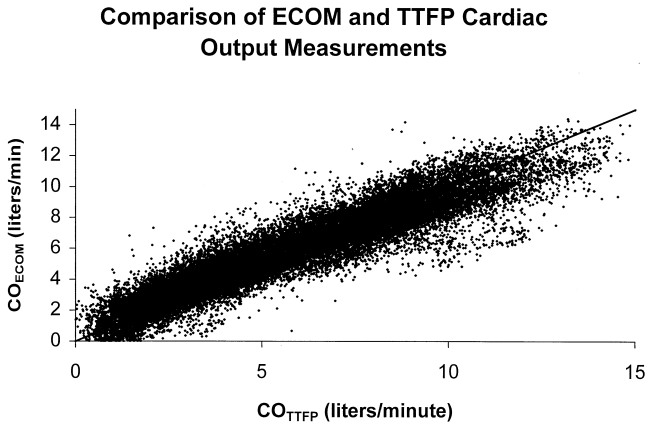

Fig. 3. Plot of cardiac output calculated from the endotracheal cardiac output monitor system and the transit time flow probe from 29,657 heart beats recorded during occlusion runs from the 10 animals during the 24-h recording period. The relationship is linear (R^2 = 0.84; slope = 0.99; intercept = 0.0).

Table 1. Results of Analysis of Occlusion and Baseline Files in 10 Pigs

	Occlusion Files	Baseline Files
Mean CO_{TTFP} (l/min)	5.9 ± 3.0	6.8 ± 3.1
Mean CO_{ECOM} (l/min)	5.9 ± 2.9	6.6 ± 3.0
Slope of regression of CO_{TTFP} *vs.* CO_{ECOM}	0.99	0.94
Intercept of regression (l/min)	0.00	0.58
R^2	0.84	0.77
Mean difference (Bias) (l/min)	0.01	0.15
SD of Bias (l/min)	1.14	1.34
Limits of agreement (Bias ± 2 SD of Bias) (l/min)	−2.28 to 2.27	−2.53 to 2.82

CO_{TTFP} = cardiac output as measured by transit time flow probe; CO_{ECOM} = cardiac output as measured by endotracheal cardiac output monitor.

l/min. The bias was 0.15 ± 1.34 l/min for a limit of agreement of −2.53 to 2.82 l/min.

We also plotted mean difference (fig. 6) between CO_{ECOM} and CO_{TTFP} as function of systolic pressure, hematocrit, blood conductivity, and time. The mean systolic arterial pressure was 82 ± 24 mmHg (range, 23–180 mmHg). Mean hematocrit was 25 ± 3% (range, 19–35%). Mean blood conductivity (ρ) was 124 ± 16 Ω-cm (range, 83–157 Ω-cm). We found no systematic effect of these variables on the error.

Discussion

The ECOM system is able to measure stroke volume and CO in anesthetized swine with limits of agreement of −2.53 to 2.82 l/min. There was no systematic error with changes in systolic pressure, hematocrit, blood conductivity, or time. There was no evidence of serious injury from the electrodes on the endotracheal tube or from the application of current to the tracheal mucosa from 24 h of continuous use. The ECOM system is a new method for measuring CO from impedance signals.

In traditional thoracic bioimpedance (TEB), current is applied to the skin from electrodes placed at the level of the neck and at a level below the xyphoid process.[18] The thorax is treated as a single resistive element.[18,19] Any change in impedance not associated with respiration represents a change in conductor volume.[27] The signal is a composite of the impedance of the entire chest, which contains multiple structures that change their conductor volume with the cardiac cycle.[28] For example, in TEB, changes in lung volume or lung water can dramatically effect the signal-to-noise ratio and accuracy of the measurement.[6,14,29] Some systems model the chest and are affected by height, weight, and body habitus.[15,19,30]

The ECOM system, in contrast to TEB, applies the current and measures the resulting voltage directly from the tracheal mucosa. The ECOM electrodes are positioned to get as close as possible to the ascending aorta and measure the impedance signal in three dimensions. The signal obtained closely matches the shape and appearance of the ascending aortic flow waveform. The endotracheal electrodes are positioned to obtain as pure an ascending aortic flow signal as possible. Flow signals from the superior vena cava, right atrium, left atrium, and pulmonary artery are avoided by electrode design. The ECOM 6-3D tube is designed to maximize the aortic signal and minimize impedance signals from other vascular structures.

The ECOM algorithm uses the empiric fit between a number of impedance parameters and the measured CO in an effort to reduce the variability across animals. There are several improvements in this algorithm over previous impedance algorithms. The use of a Simpsons integral is an improvement over the Gaussian integral with a single time step (equations 1 and 2) because the measurement of ejection time is not critical. In a single-step Gaussian integral, the full amplitude of the signal DZ_{Max} or dZ/dt_{Max} is multiplied by the ejection time. Errors in the ejection time are critical with a Gaussian integral. In a Simpsons integral, the value of DZ at the end of ejection is small, and errors in the ejection time are multiplied by a number close to zero and therefore become nonsignificant (fig. 2). The three-dimensional algorithm helps to stabilize the correlation with changes in electrode position relative to the aorta. The empiric fit

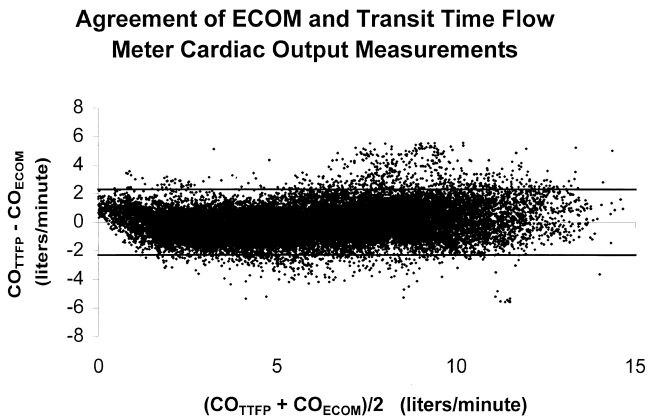

Fig. 4. Plot of the difference between cardiac output measured from the endotracheal cardiac output monitor and the transit time flow probe systems plotted against the average of the two measurements (Bland–Altman) for 29,657 heart beats recorded during occlusion runs from the 10 animals during the 24-h recording period. ± 2 SD are plotted (2 SD = 2.3 l/min).

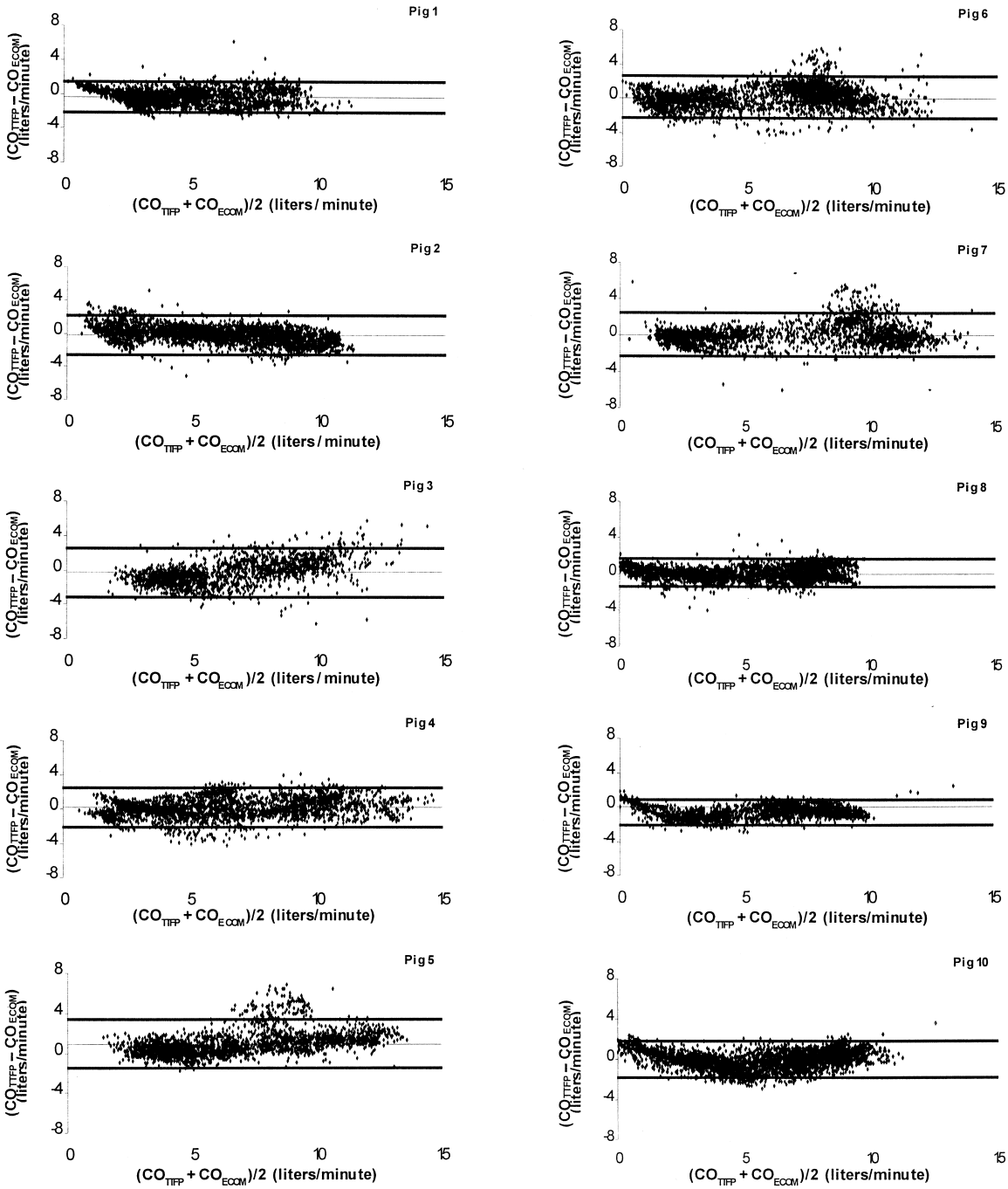

Fig. 5. Plot of the difference between cardiac output measured from the endotracheal cardiac output monitor and the transit time flow probe systems plotted against the average of the two measurements (Bland–Altman) for the 10 individual pigs during the 24-h recording period. ± 2 SD are plotted. See table 2 for specifics of R^2, slope, intercept, bias, and limits of agreement. Pig no. 3 died of a presumed diagnosis of malignant hyperthermia after 14 h.

Table 2. Number of Beats Collected, R^2, Slope, Intercept, Bias, and Limits of Agreement of Individual Pigs

	Occlusion Files							Baseline Files						
Pig No.	No. of Beats	R^2	Slope	Intercept (l/min)	Bias (l/min)	Bias − 2 SD	Bias + 2 SD	Beats	R^2	Slope	Intercept (l/min)	Bias (l/min)	Bias − 2 SD	Bias + 2 SD
1	2,518	0.86	0.95	0.61	−0.37	−2.13	1.40	8,460	0.76	0.94	−0.24	−0.62	−3.08	1.84
2	3,745	0.97	1.09	−0.44	−0.25	−2.57	2.07	9,267	0.83	0.66	1.7	−0.82	−3.90	2.26
3	1,999	0.93	0.85	1.15	−0.32	−3.11	2.47	7,229	0.75	0.95	0.03	−0.34	−3.29	2.62
4	2,896	0.97	0.95	0.25	0.13	−2.17	2.42	8,186	0.86	0.95	0.65	0.29	−2.32	2.90
5	2,694	0.96	0.90	0.18	0.95	−1.45	3.35	11,113	0.84	1.01	1.09	1.15	−1.55	3.86
6	3,384	0.96	0.95	0.20	0.16	−2.34	2.66	5,179	0.83	0.87	1.25	0.44	−1.96	2.84
7	2,596	0.97	0.96	0.22	0.06	−2.33	2.45	9,084	0.87	0.97	0.77	0.55	−1.92	3.03
8	3,480	0.98	0.98	0.02	0.14	−1.39	1.68	8,510	0.90	0.96	0.60	0.43	−1.23	2.10
9	2,429	0.98	0.98	0.45	−0.65	−2.11	0.81	13,104	0.92	1.08	−0.61	−0.05	−2.11	2.00
10	3,913	0.97	0.99	0.09	−0.05	−1.83	1.73	11,519	0.92	1.08	−0.19	0.31	−1.35	1.97
Average		0.95	0.96	0.27	−0.02	−2.14	2.10		0.85	0.95	0.51	0.13	−2.27	2.54
SD		0.04	0.06	0.41	0.43	0.51	0.72		0.06	0.12	0.74	0.59	0.88	0.63

between the multiple impedance parameters and the measured CO recognizes the fact that there is no simple physical model relating the impedance signal and CO; there are simply two highly correlated signals.

Accuracy

A key question to any new system for the measurement of CO is accuracy. There is a linear relationship between CO_{ECOM} and CO_{TTFP} measurements between 0 and 15 l/min (slope = 0.94; intercept = 0.15; R^2 = 0.77). For this empirically derived algorithm in this group of 10 pigs, the mean difference between the two measures (bias) is 0.15 l/min, and the SD is 1.34 l/min. The limits of agreement (bias ± 2 SD) are −2.53 to 2.82 l/min. The mean bias in individual animals was 0.13 ± 0.59 l/min. The TTFP and ECOM device measure the ascending aortic flow, not true CO, because coronary blood flow is not measured. Ascending aortic flow = CO − coronary blood flow. Coronary blood flow is 4–5% of CO. The empiric fit will need to be established in humans before clinical use.

New systems for CO measurement are commonly compared to pulmonary artery thermodilution measurements. Because development and testing of the ECOM system required multiple CO measurements, we compared ECOM measurements to the TTFP measurements. The TTFP measurements had many advantages over thermodilution. TTFP was more accurate (± 10%)[31] than thermodilution (± 20%).[32] TTFP allowed multiple comparisons of both steady-state and transient stroke volumes. We were able to make 121,341 measurements of stroke volume in 10 experiments. This number of comparisons would be impossible with thermodilution technology. Finally, TTFP allowed direct measurement of ascending aortic arch flow, which made design of the ECOM system possible.

Comparison to Other Impedance Measurements

A 1992 metaanalysis of surface bioimpedance systems found an R = 0.82 (R^2 = 0.67) but found lower correlations with patients in the intensive care unit.[33] The ECOM system has an R^2 of 0.77, a bias of 0.15, and a limit of agreement of −2.53 to 2.82 l/min (table 1). There is one theoretical and one experimental study of esophageal impedance electrodes. No one has previously attempted to measure impedance from endotracheal electrodes. The theoretical model suggests that accurate impedance-based measurements of CO are impossible because the signal from motion of the internal organs will be more important than volume changes in affecting the esophageal impedance signal.[34] Despite this theoretical result, Balestra *et al.*,[35] in a clinical study, found excellent correlations (R^2 = 0.98), small bias (0.05 ± 0.26 l/min), and small errors (−0.55 to 0.45) between thermodilution and intraesophageal impedance measurements. In contrast to these results with esophageal electrodes, they found very poor correlations (R^2 = 0.55), large bias (1.99 ± 2.20 l/min), and large errors (−2.32 and 6.30 l/min) between thermodilution and surface impedance measurements.[35] We tried to compare the ECOM system to a transthoracic bioimpedance system (TEB; BioZ.com, CardioDyanmics International Corporation, San Diego, CA) in a chronically instrumented pig. We found no correlation between TEB and TTFP measurement of CO.

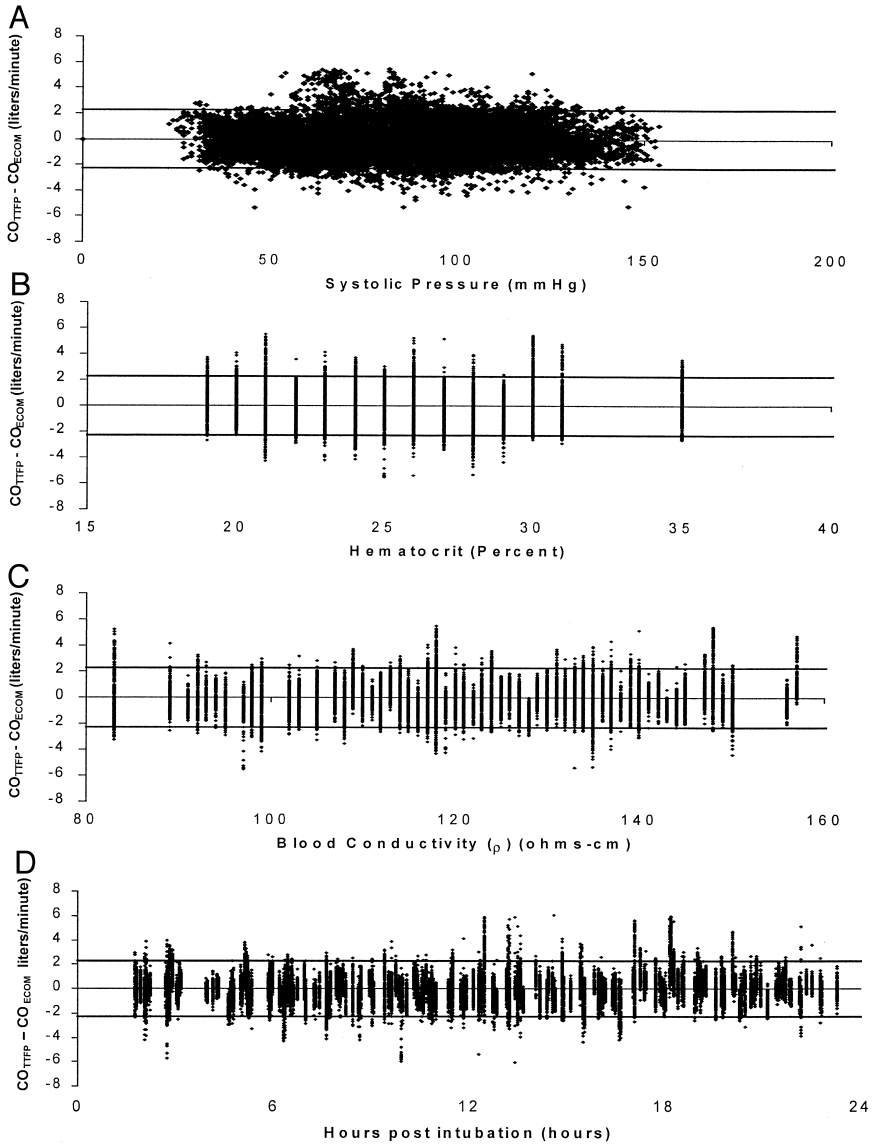

Fig. 6. Plot of the difference between cardiac output measured from the endotracheal cardiac output monitor and the transit time flow probe systems plotted against systolic arterial pressure (*A*), hematocrit (*B*), and blood conductivity (*C*), and duration of intubation (*D*).

Pathology

One goal of this trial was to assess the likelihood that the ECOM tube and electronics would injure the tracheal mucosa. Endotracheal tubes were left in place with the ECOM system running in anesthetized animals for 24 h to model prolonged clinical use of endotracheal tubes. The tubes were atruamatic to the tracheal mucosa. Electrosurgical cautery and direct-current defibrillation had no observed effect on the tracheal mucosa. The one animal that had signs of tracheal mucosal injury died of a presumed diagnosis of MH at 14 h. The injury was not associated with the balloon electrodes. The animal with the presumed diagnosis of MH was the only one with signs of tracheal injury. The ECOM system worked during the development of MH, and data from this animal were included in the analysis.

Limitations

The ECOM system has been developed and tested in swine. Human and porcine anatomy are different. We attempted to use swine with similar weights (60–80 kg), tracheal dimensions (1.5–2.5-cm diameter), and aortic dimensions (2–3 cm) to adult humans to reduce this limitation. However, the empirically fit algorithm will need to be adjusted for use in humans. Because the tracheal mucosa produces mucous and fluid, the ECOM

electrodes, algorithm, and electronics have been designed to reduce the effects of fluid and mucous accumulation. In this trial, the signal was stable for 24 h despite mucous accumulation, but the signal may deteriorate with prolonged intubation. The ECOM endotracheal electrodes must touch the tracheal mucosa. If the endotracheal balloon folds and the electrodes do not touch the mucosal surface, there is no signal. The ECOM algorithm is designed to compensate for loss of contact of one or two electrodes. If the patient has very stiff lungs with resulting high airway pressures, and the endotracheal balloon has a low pressure in it, multiple electrodes will lift off the tracheal wall, and signal will be lost. When the airway pressure decreases on the next ventilatory cycle, the electrodes will regain contact, and the signal will return.

Summary

A new system for the measurement of CO has been developed and tested in swine. The ECOM system provides a continuous measurement of CO derived from impedance measurements from electrodes on an endotracheal tube. ECOM is a promising technology that needs further evaluation in clinical trials.

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