Evaluation of a lithium dilution cardiac output technique as a method for measurement of cardiac output in anesthetized cats

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Objective—To evaluate the use of a lithium dilution cardiac output (LiDCO) technique for measurement of CO and determine the agreement between LiDCO and thermodilution CO (TDCO) values in anesthetized cats.

Animals—6 mature cats.

Procedure—Cardiac output in isoflurane-anesthetized cats was measured via each technique. To induce different rates of CO in each cat, anesthesia was maintained at > 1.5X end-tidal minimum alveolar concentration (MAC) of isoflurane and at 1.3X end-tidal isoflurane MAC with or without administration of dobutamine (1 to 3 µg/kg/min, IV). At least 2 comparisons between LiDCO and TDCO values were made at each CO rate. The TDCO indicator was 1.5 mL of 5% dextrose at room temperature; with the LiDCO technique, each cat received 0.005 mmol of lithium/kg (concentration, 0.015 mmol/mL). Serum lithium concentrations were measured prior to the first and following the last CO determination.

Results—35 of 47 recorded comparisons were analyzed; via linear regression analysis (LiDCO vs TDCO values), the coefficient of determination was 0.91. The mean bias (TDCO-LiDCO) was –4 mL/kg/min (limits of agreement, –35.8 to + 27.2 mL/kg/min). The concordance coefficient was 0.94. After the last CO determination, serum lithium concentration was < 0.1 mmol/L in each cat.

Conclusions and Clinical Relevance—Results indicated a strong relationship and good agreement between LiDCO and TDCO values; the LiDCO method appears to be a practical, relatively noninvasive method for measurement of CO in anesthetized cats. (*Am J Vet Res* 2005;66:1639–1645).

Hemodynamic monitoring of patients is essential to assess cardiac function, organ perfusion, and O_2 delivery and evaluate the effects of vasoactive, inotropic, and fluid treatments during anesthesia. The most valuable global indicator of cardiovascular function is **cardiac output (CO)** because it determines oxygen delivery, which is considered the end point of cardiopulmonary function. Monitoring the change in CO in response to treatments and anesthetic agents plays a key role in the management of human patients who are anesthetized or in an intensive care unit.[1] Unfortunately, a combination of indirect indices of cardiac performance such as heart rate and rhythm, pulse rate and quality, arterial blood pressure, central venous pressure, urine output, capillary refill time, and serum lactate concentration and base excess is often all that is available for cardiovascular assessment of patients in small animal practice. The use of a combination of these indirect indices of cardiac performance has been associated with inaccurate estimates of CO in human adults[2,3] and children,[1] which have resulted in suboptimal and even inappropriate interventions in human adults.[4-6] With regard to the currently available methods for CO measurement, the current cost of equipment, the technical difficulties associated with the equipment, the necessary instrumentation of the patient, and the invasiveness of the techniques have so far prevented their routine use in small animals, thereby restricting awareness of this important parameter among many researchers and clinicians. Measuring CO in physically small patients such as cats or small dogs is further complicated by the fact that most of the hardware needed to perform the measurement has not been adapted or validated for these smaller animals.

The use of a **thermodilution CO (TDCO)** technique was introduced to clinical practice in 1971, and it has since become the most popular technique with which to measure CO in humans[3] and other animals. It has also become an accepted gold standard against which other methods for the measurement of CO are compared.[7] The TDCO technique has many advantages. Specifically, once the animal is instrumented, the measurements can be performed quickly and repeatedly; the technique does not require the operator to have advanced technical or diagnostic skills and does not involve the withdrawal of blood; and the indicator involved is nontoxic, nonaccumulating, and nonrecirculating. Measurement of CO by use of the TDCO technique has been validated in cats against an in vitro system,[8] the direct Fick method and echocardiography,[9] and a radioactive microspheres technique.[10] Overall, the TDCO technique was found to be a consistent and dependable method for measurement of CO in cats in a research setting. Technical problems were easy to recognize, and the measurements could be performed repeatedly if needed. Unfortunately, the TDCO technique requires placement of a pulmonary artery catheter, which is an invasive procedure associated with complications.[11] Furthermore, insertion of the pulmonary artery catheter in cats is time consuming and relatively difficult to accomplish[9]; the procedure requires anesthesia, fluoroscopy, and dye injection. In addition, in phys-

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ically small species, introduction of the pulmonary artery catheter often requires the use of a jugular vein cutdown technique and ligation of the jugular vein following the removal of the catheter, which further increases the invasiveness of the procedure.

Because of the invasiveness and complications associated with the TDCO technique, there remains interest in the development of new, less invasive methods for measurement of CO. Considerable work has been done to validate noninvasive methods to measure CO in veterinary patients, but very little attention has been focused on smaller animals such as cats. In search for an "ideal" CO measurement technique, the **lithium dilution CO (LiDCO)** method was developed. The LiDCO technique is an indicator dilution method that does not require placement of a pulmonary artery catheter. The indicator, lithium chloride (LiCl), is injected in the right atrium and detected in a peripheral artery by use of a sidestream lithium sensor. The CO value is calculated from a concentration-over-time curve. Validation studies of the LiDCO technique against TDCO, transpulmonary thermodilution, electromagnetic flow-probe, and transesophageal Doppler echocardiographic techniques have been reported for children,[12] human adults,[13] pigs,[14] horses,[15] dogs,[16] and foals.[17] In all the comparisons, there was, in our opinion, substantial agreement between LiDCO and other measurement techniques. The relative noninvasiveness and ease of instrumentation of the LiDCO method make it particularly suitable for use in veterinary research and clinical settings, and the method is now frequently used to measure CO in veterinary research settings.[a-c] However, none of these studies have so far addressed whether this technique is applicable and accurate for use in physically small species. Although this technique has been used in human infants that weighed as little as 2.6 kg, that investigation[12] did not involve collection of repeated measurements over a wide range of CO rates. Disadvantages of the LiDCO technique include blood loss associated with the required blood withdrawal associated with each CO determination; the indicator, lithium, has potential toxic effects[18] and does accumulate; and the method carries a certain degree of invasiveness because of the need for central venous and arterial catheters. The purpose of the study reported here was to evaluate the use of a LiDCO technique for measurement of CO and determine the agreement between LiDCO and TDCO values in anesthetized cats.

Materials and Methods

Animals—The study was approved by the Animal Care Committee of the University of Guelph. Six mature purpose-bred domestic shorthair cats that weighed 3.0 to 5.4 kg were used in this study. Food was withheld from the cats for 12 hours before the experiment, but water was available ad libitum.

Instrumentation—After premedication with medetomidine hydrochloride[d] (10 to 20 µg/kg of body weight, IM), anesthesia was induced with isoflurane in oxygen administered via a face mask. The cats were intubated, and anesthesia was maintained with isoflurane delivered in oxygen (200 mL/kg/min) via a coaxial, nonrebreathing anesthetic circuit; breathing was spontaneous for the duration of the instrumentation period. Having been intubated, the cats were given atipamezole hydrochloride[e] (50 to 100 µg/kg, IM) to reverse the effect of medetomidine. Instrumentation included placement of a 20-gauge, 1.5-inch catheter in the cephalic vein, a 20-gauge, 1.5-inch catheter in the right femoral artery, a 4-F thermistor-tipped TD catheter[f] in the right jugular vein, and a 4-F straight flush catheter[f] in the left jugular vein. With fluoroscopic guidance, the TD catheter was positioned in the pulmonary artery using a modified 6-F catheter[g] curved at its distal end as an introducer. Correct positioning of the right atrial and pulmonary artery catheters was confirmed by injection of contrast agent into the catheters during fluoroscopic monitoring and by examination of their respective pressure waveform displayed on a monitor.[h] Correct positioning of the TD catheter in the pulmonary artery during the experimental period was confirmed by periodic examination of the pressure waveform. A balanced electrolyte solution was infused through the cephalic venous catheter at a rate of 5 mL/kg/h for the duration of the experiment. Once the instrumentation was completed, the cats were mechanically ventilated at a rate of 10 to 18 breaths/min and a tidal volume of 10 to 15 mL/kg to maintain the **end-tidal carbon dioxide concentration ($EtCO_2$)** between 30 and 45 mm Hg, as measured by a sidestream gas analyzer.[h]

Measurement of CO—A computer[j] was used to determine TDCO measurements as previously described.[9,16] The computation constant for the computer was adjusted for a 4-F TD catheter, an injectate at room temperature (23° to 25°C), and an injection volume of 1.5 mL of 5% dextrose in water, as specified in the operation manual.[19] All TDCO measurements were initiated at end expiration but without inducing apnea. As recommended, TDCO measurements were repeated until 3 consecutive values with a difference of ≤ 10% were obtained.[20] The mean of these 3 values was used for the comparison with the LiDCO value.

The LiDCO values were determined by use of a commercial LiDCO computer.[j] In brief, the sensor[k] for blood LiCl measurements was attached to the side port of a 3-way valve that was connected to the femoral artery catheter, and the sensor and the computer were prepared as described in the operation manual.[21] The inlet port of the sensor was attached to the femoral artery catheter, and the outlet port was attached via tubing to a collection bottle with the tubing passing through a flow-regulator pump. When the pump was activated, it withdrew blood from the femoral artery and forced the blood across the sensor at a constant rate (4 mL/min) into the collection bottle. Injection of LiCl[l] involved placing the compound into an extension set with a volume of 2.5 mL that was attached to the straight flush catheter of the left jugular vein. The dose of LiCl chosen to measure CO in cats was 0.005 mmol/kg, extrapolated from results of previous studies[12,16] in dogs and humans and as advised by the manufacturer's technical personnel. Preliminary experiments in which doses of 0.15 mmol of LiCl/mL (normal dilution of the indicator) were used involved administration of very small injectate volumes that were error prone and produced inconsistent results. As a result, for the present study, the commercially available LiCl solution was diluted from a concentration of 0.15 mmol/mL to a concentration of 0.015 mmol/mL with saline (0.9% NaCl) solution to make the volume of the LiDCO injectate comparable to the volume of the TDCO injectate. A so-called park and ride method was used to ensure that all of the LiCl bolus entered the right atrium after injection. This involved first placing the LiCl indicator bolus (1.0 to 1.8 mL) in the extension set. Then, after updating the blood hemoglobin and sodium concentrations on the computer, the regulator pump was started just enough to draw blood from the femoral artery into the sensor, at which point the pump was stopped to minimize the volume of blood withdrawn. Once a steady baseline was attained on the computer, the injection

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dial on the computer was pushed and the regulator pump was turned on to draw blood at the normal rate through the sensor. In a preliminary study,[m] it was determined that the total volume of blood withdrawn per determination was decreased to 4 to 5 mL by use of this method. When the injection dial was pressed, a manual count of 6 seconds was instituted. At the 6-second mark, the LiCl previously parked in the injection set was injected into the right atrium with a 3-mL bolus of saline solution. After collection of the curve data, the regulator pump was stopped when the computer indicated to do so. As recommended by the manufacturer, a single LiDCO determination was obtained at each sampling interval.

Hemodynamic parameters (heart rate; respiratory rate; mean, systolic, and diastolic arterial pressures; $EtCO_2$; and **end-tidal isoflurane concentration [Etiso]**) and core body temperature were recorded before each comparative TDCO and LiDCO determination. A disposable transducer attached to the femoral artery catheter provided systolic, mean, and diastolic arterial blood pressure measurements. Heart rate was recorded from the ECG,[h] and core body temperature was measured by use of the thermistor of the pulmonary artery catheter. All variables, except core body temperature, were recorded from a multiparameter monitoring unit[i] that was calibrated prior to the experimental period. The blood hemoglobin and sodium concentrations were measured, and a complete blood gas analysis[n] was performed prior to the first LiDCO determination at each level of hemodynamic function; blood samples were collected from the femoral artery catheter.

For each cat, serum lithium concentration was measured in blood samples collected before and after the study by use of a flame photometer.[o] The limit of detection of the assay is 0.10 mmol/L.

Experimental protocol—In each cat, 3 conditions of hemodynamic function were induced; the comparison between LiDCO and TDCO values was performed for each condition. A high rate of CO was induced via infusion of dobutamine hydrochloride (1 to 3 µg/kg/min) through the cephalic venous catheter and maintenance of a light plane of anesthesia (Etiso, approx 2% [1.3× the **minimum alveolar concentration [MAC]**).[22] An intermediate rate of CO was induced via maintenance of a light plane of anesthesia without administration of dobutamine (Etiso, approx 2% [1.3× MAC]). A low rate of CO was induced via maintenance of a deep plane of anesthesia (Etiso > 2.4% [1.5× MAC]). The order in which the 3 hemodynamic function conditions were applied to each cat was randomized according to a complete block design. No attempt was made to ensure that the CO rates were identical for each cat. The CO measurements were performed when the cats had reached a stable plane of hemodynamic function (after at least 15 minutes of stabilization), as determined by heart rate, arterial blood pressure, Etiso, and $EtCO_2$. Hemodynamic stability was defined as changes in heart rate, mean arterial pressure, Etiso, and $EtCO_2$ that were all < 15% during collection of the LiDCO and TDCO measurements for comparison. At each level of hemodynamic function, at least 2 comparisons between LiDCO and TDCO values were made. Two sequences of data collection were used to measure CO within a level of hemodynamic function:

LiDCO (1) – TDCO (3) : TDCO (3) – LiDCO (1), or
TDCO (3) – LiDCO (1) : LiDCO (1) – TDCO (3).

Each cat was randomly assigned to one of those sequences by the flip of a coin, and all the measurements on each cat were performed in the same sequence; each sequence was applied to 3 cats.

Statistical analyses—The data were analyzed as cardiac index and reported as milliliters per kilogram per minute. An ANOVA for repeated measures was performed by use of a statistical software package[p] to account for the effects of cats, methods of CO determination (TDCO and LiDCO), hemodynamic function conditions (high, intermediate, and low rates of CO), period, and carryover on the cardiac index. Carryover controls for the possibility of any residual effect of the previous treatment. Statistical significance was set at a value of $P \leq 0.05$. A linear regression analysis was performed on the comparisons between the TDCO and LiDCO values. A Bland-Altman analysis[23-25] was done on the comparisons between the TDCO and LiDCO values, and the mean bias (with 60% confidence interval) and limits of agreement (mean bias ± 1.96 SD of the differences) were calculated to quantify and graphically represent the degree of agreement between the 2 methods. A coefficient of concordance was calculated as an additional measure of agreement between the 2 methods.

Results

Forty-seven comparisons were collected from 6 cats. Thirty-five data pairs were available for comparison; 12 of the 47 (25.5%) data pairs were excluded from analysis because of excessive hemodynamic variability during data collection, as defined by the experimental protocol. The mean ± SD cardiac index associated with the LiDCO technique was 109 ± 41 mL/kg/min, and the mean cardiac index associated with the TDCO technique was 105 ± 49 mL/kg/min. The linear regression equation was as follows:

LiDCO value = 0.795(TDCO value) + 0.025,

and the coefficient of determination (r^2) was 0.91 (**Figure 1**). The mean bias (TDCO-LiDCO) was –4 mL/kg/min with limits of agreement of –35.8 to 27.2 mL/kg/min (**Figure 2**). The concordance coefficient was 0.94. Overall, LiDCO measurements generally overestimated TDCO measurements at lower CO values, and TDCO measurements generally overestimated LiDCO measurements at higher CO values. For all cats, the serum lithium concentration before the experiment and after the CO determinations (ie, after 8 to 10 LiCl injections/cat) was below the limit of detection of the assay.

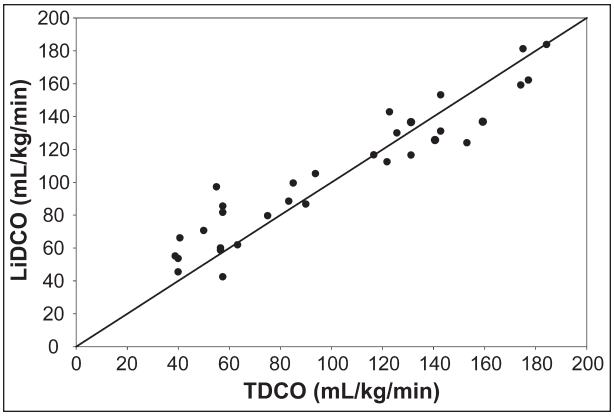

Figure 1—Plot of cardiac index measurements obtained in 6 isoflurane-anesthetized cats by use of lithium dilution cardiac output (LiDCO) and thermodilution cardiac output (TDCO) techniques. The regression equation is LiDCO equals 0.795(TDCO) plus 0.025; coefficient of determination (r^2) is 0.91.

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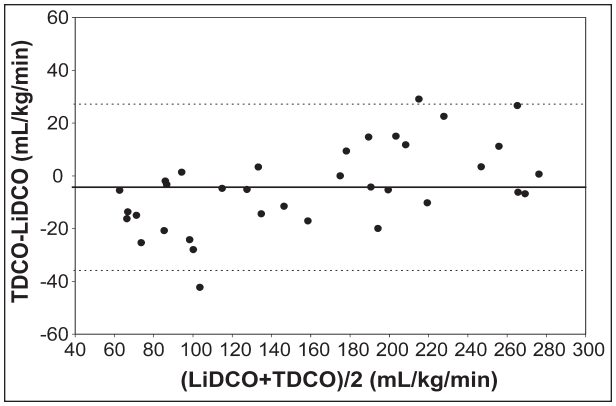

Figure 2—Bland-Altman plot of cardiac index measurements obtained in 6 isoflurane-anesthetized cats by use of LiDCO and TDCO techniques. Each point represents a paired observation (n = 35 datum points). Mean bias for the comparison of LiDCO and TDCO is –4 mL/kg/min (limits of agreement, –35.8 to 27.2 mL/kg/min). The solid horizontal line indicates the mean bias, and the dotted horizontal lines indicate the limits of agreement (ie, mean bias ± 1.96 SD).

Discussion

Evaluation of the accuracy, reliability, and precision of anesthesia monitoring techniques is an active area of veterinary and human research. Not only does a new measurement technique have to be proven accurate, precise, and reliable by use of a standard technique as a reference, the applicability and usefulness of the new measurement technique must be evaluated. A standard technique, usually a technique considered to be a gold standard, is traditionally used to validate a new technique, and an appropriate statistical method must be chosen to determine correlation (association) and agreement between the measurements obtained by use of the gold standard and the new method. The choice of a gold standard may prove to be difficult, especially when evaluating CO measurement techniques, because of the inherent variability of each method and the inability to absolutely confirm values for any method. Also, when comparing 2 methods of measuring CO (especially when the 2 methods are not applied simultaneously as was the case in the present study), one must keep in mind that CO is dynamic and varies on a beat-to-beat basis. We chose the TDCO technique as our reference method because it has been validated in cats[9,10] and because it is the most often used CO measurement technique in feline cardiovascular research. In addition, the TDCO technique proved to be the most practical method to use, compared with other methods such as the direct Fick method.[9] Although the instrumentation of the cats for TDCO measurement was time consuming (requiring approx 1 hour to complete), the TDCO measurements themselves were easy, simple, and fast to perform. Furthermore, because the TDCO indicator is nontoxic and does not accumulate, the measurements could be repeated numerous times.

To the authors' knowledge, this is the first study to investigate the use of the LiDCO technique in cats. The agreement between LiDCO and TDCO values (based on the concordance coefficient and the Bland-Altman analysis) in the present study was good. To compare the agreement between LiDCO and TDCO values in cats with the agreement found between LiDCO and TDCO values in other species, we assessed the ratio of the mean bias to the mean cardiac index. In the present study, the ratio of the mean bias to the mean cardiac index was 3%, whereas in other studies,[13,15] this ratio ranged from 4% to 12%. Therefore, the mean bias determined in our study compares favorably with the bias determined in other studies to validate the LiDCO technique. However, the bias value must be interpreted with caution as it is the mean of differences between TDCO and LiDCO measurements. The limits of agreement determined in the present study were wide, and the Bland-Altman plot analysis revealed some dispersion around the bias. Increasing the number of comparison would certainly have improved the reliability of the statistical analysis and might have narrowed the limits of agreement. Unfortunately, the number of comparisons used for analysis in the present study was small because 12 of 47 data pairs had to be excluded because of hemodynamic instability during the measurement period; this instability was largely due to variation in heart rate and blood pressure. On the basis of criteria used in other studies,[16,17] we had defined hemodynamic stability in our study as variation of < 15% in heart rate, mean arterial blood pressure, $EtCO_2$, and Etiso within the measurement of a comparison. Despite taking several steps to minimize hemodynamic variability, we still had to eliminate a large portion of the data because of this factor.

In the present study, there was a strong correlation (r^2 = 0.91) between the LiDCO and the TDCO measurements. Correlation is a measure of linear relationship or association and should not be substituted for agreement.[23] The measure of linear relationship identified in our study also compares favorably with findings of similar studies[9,12,14,15,17] in which different CO measuring techniques were compared. In a study[9] in cats in which the TDCO, direct Fick, and echocardiographic techniques were compared over a wide range of CO rates, the correlation coefficient between the Fick and TDCO measurements was 0.86 (r^2 = 0.74); the correlation coefficient between the echocardiographic and TDCO measurements and between the Fick and echocardiographic measurements was 0.71 (r^2 = 0.50) and 0.67 (r^2 = 0.45), respectively. In comparison studies involving LiDCO and TDCO measurements in pigs[14] and horses,[15] correlation coefficients were 0.93 (r^2 = 0.86) and 0.95 (r^2 = 0.90), respectively. In similar studies in children[12] and neonatal foals,[17] the r^2 values were 0.96 and 0.99, respectively.

There are numerous potential factors that contribute to the discrepancy between TDCO and LiDCO measurements in the present study. True changes in CO that developed in the short time interval between the sequential TDCO and LiDCO measurements could have contributed to the observed differences between the CO values obtained via the 2 techniques. It is also possible that while performing either technique, CO was altered in a positive or negative direction (although we have no evidence of such an occurrence). Although we might have minimized the impact of variations in CO during the measurement period by defining hemodynamic stability on the basis of a percentage change in the reference method (TDCO technique) measured at the beginning and at the end of a given set of comparisons, the coefficient of variation of replicate TDCO measurements is in the order of 10%.[19] Hence, we decided to use heart rate

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and blood pressure as the determinants. In addition to true differences in CO between measurements, errors (either technical in nature or inherent in the technique) could have contributed to the discrepancy in CO measurements observed between the 2 techniques. In the present study, the injection of both indicators was performed at the end of expiration; this is the usual practice for TDCO assessments and is intended to minimize the variability in respiration-related alterations in venous return and in respiration-related pulmonary artery thermistor temperature measurements.[26,27] In humans, the temperature change in the pulmonary artery increases at end-expiration during spontaneous respiration but decreases during intermittent positive-pressure ventilation, and TDCO measurements are underestimated during spontaneous breathing and overestimated during intermittent positive-pressure ventilation.[27] These temperature fluctuations should not affect LiDCO measurements. Measurement of right ventricular CO can vary by as much as 50% during the respiratory cycle.[27] Although reproducibility of consecutive measurements improves when the bolus injections are made at the same phase of the respiratory cycle, it can be argued that true CO is better estimated by making numerous injections throughout all phases of the respiratory cycle and then averaging the values.[19,26] The actual timing of the injection then becomes a trade-off between accuracy and reproducibility with the TDCO technique.

High background serum lithium concentrations reduce the ability of the LiDCO system to differentiate the next LiCl injection from the background serum lithium concentration.[16,21,28] A theoretical serum lithium concentration of 0.2 mmol/L has been set by the manufacturer; higher serum concentrations could interfere with the accuracy of the LiDCO system as a result of the background buildup of serum lithium.[21] Theoretically, after frequent LiDCO determinations within a short period or a high total number of determinations, the serum lithium concentration could increase sufficiently to interfere with the accuracy of the LiDCO measurement, leading to an underestimation of the curves and overestimation of CO.[16,28] In a study[28] in dogs, LiDCO values increased as background serum lithium concentration increased. The authors of that study concluded that this error was not clinically relevant at a serum lithium concentration of 0.1 mmol/L and modestly clinically relevant at a concentration of 0.4 mmol/L, based on the linear regression analysis of the relation between serum lithium concentration and the agreement between TDCO and LiDCO values. In the present study, background serum lithium concentrations were unlikely to have contributed to an error because low serum concentrations were detected in the cats at the end of the study period. Furthermore, it was also found in dogs that an increase in serum lithium concentration did not affect the agreement between LiDCO and TDCO values.[28]

For TDCO measurements in the present study, a thermal indicator at room temperature was used to minimize the effect of indicator injection on heart rate and CO and provide an injection volume that could be more easily measured. Heart rate has been shown to decrease during injection of the TDCO indicator, and this change in heart rate may be less after injection of a room-temperature solution than an iced solution.[9,29] Also, in the present study, a small volume (1.5 mL) of 5% dextrose in water was used to minimize the short-term increase in stroke volume caused by the bolus injectate. The temperature and volume of injectate were also chosen to ensure that there was a thermal signal of 0.5°C in the pulmonary artery, as recommended.[19]

With indicator dilution methods, indicator loss is reflected by overestimation of CO. Lithium injectate loss through the lungs is an unlikely contributor to the discrepancy in measurements between techniques. Results of studies[30,31] conducted in adult humans have indicated that the pulmonary loss of LiCl was < 4%, and this loss was deemed to be unimportant. To the authors' knowledge, no such information is available for smaller patients. In physically small animals such as rats, the TDCO technique consistently overestimates CO, compared with values determined by use of other reference methods (especially at low CO rates), and the degree of indicator loss appears to be of greater magnitude in smaller individuals.[32] It is hypothesized that the amount of cold indicator administered is proportionally greater in physically small animals than in larger animals because their vessel walls are thinner and surface area-to-volume ratio is greater. These factors would increase diffusion of heat,[32,33] although the distance between the injection site and the pulmonary artery is shorter in smaller animals than it is in larger animals, which partially offsets the greater thermal indicator loss in smaller animals. A low CO rate also implies longer transit time for the thermal indicator; this increases the contact time between the indicator and the vessel walls, thereby increasing heat diffusion and loss of indicator.[32] In another study[9] in cats in which CO values obtained via the Fick method typically overestimated TDCO values, the authors hypothesized that the cooling effect on the catheter associated with sequential repeat injections would result in an underestimation of CO because of its effect on the computation constant and that this latter effect might be greater than that associated with indicator loss. In rabbits at high CO rates, aortic TDCO values overestimated CO values obtained by use of an aortic electromagnetic flow probe and Doppler flowmeter.[33] In our study, LiDCO measurements typically overestimated TDCO values at lower CO rates and TDCO measurements typically overestimated LiDCO values at higher CO rates. These findings could have resulted from a combination of the aforementioned contributors to the discrepancy between techniques.

In the present study, the quality and reliability of the lithium sensor were a concern, as many sensors had to be replaced during the study period because of an unsteady baseline, as indicated by the computer. As such, sensor quality could have affected the accuracy of the LiDCO measurements, although the built-in verification system should have minimized the impact of defective or inaccurate sensors. Nevertheless, sensor reliability has been suggested as a source of error in a previous study[16] involving the LiDCO technique. Unfortunately, to date, no studies have specifically assessed the accuracy or reliability of the commercially available lithium sensors in different species. Sudden pump battery failure has also been a problem that has resulted in incomplete time-concentration curves.[15] We

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avoided this by using a new battery for each cat, and in theory, irregular blood flow through the sensor would be recognized by the software and the curve would be rejected.[12]

Lithium toxicosis is a potential concern following the injection of many boluses of LiCl in a relatively short period of time. This concern would apply to many research designs that involve numerous CO determinations. According to Davenport,[34] cats are more sensitive to lithium than rats or dogs. The dose of injectate used in the present study was chosen by extrapolation of data from a human pediatric study[12] and on recommendations of the manufacturer's technical personnel. The serum lithium concentration in all blood samples assessed in the present study was < 0.1 mmol/L, which is < 1.6 to 4.6 mmol/L, the concentration range associated with toxic effects in cats.[18] Only 2 blood samples were analyzed for serum lithium concentration per cat: a sample collected prior to LiDCO procedures and a sample collected after administration of 8 to 10 bolus injections of LiCl (each dose, 0.005 mmol of LiCl/kg). We did not measure serum lithium concentration during the validation study; it is possible that at some point during the experiment, the serum lithium concentrations were > 0.1 mmol/L because lithium redistributes to extravascular compartments rapidly. However, it is unlikely that the serum concentrations would have reached toxic levels.

In our experience,[m] the estimated volume of blood loss per LiDCO measurement in cats is 4.6 mL. This estimated volume does not include the volume of blood withdrawn for measurement of hemoglobin and sodium concentrations before LiDCO determinations. As expected, the volume of blood withdrawn from a cat associated with the LiDCO technique can be substantial and limits the number of measurements that can be performed on a cat without appropriate replacement therapy. The blood withdrawal provided by the peristaltic pump is constant, regardless of the size of the patient. With the LiDCO technique, the amount of blood loss is negligible for larger animals but is notable for smaller animals such as cats. The volume of blood loss during a LiDCO determination has been determined in few studies involving the LiDCO technique; Kurita et al[14] reported blood loss of 2.6 mL/LiDCO determination and Linton et al[12,13] reported a blood loss of approximately 3 mL/LiDCO determination. Unfortunately, those authors do not report how they measured that volume. In our experience, these reported blood volumes seem low because an interval of at least 30 seconds (during which 2 mL of blood is withdrawn) is needed after starting to draw blood into the sensor to establish a stable baseline, and then blood withdrawal continues from the time the CO determination is actually started until the time-concentration curve is completed (another interval of at least 30 seconds). There are a number of hypothetical solutions to limit the blood loss for small-sized patients. One solution would be the modification of the lithium sensor to make it an in vivo sensor (ie, the sensor would be introduced into the artery) so that blood would not have to be withdrawn from the artery at all. Another potential change to the sensor would be to modify its coating to allow the blood withdrawn from the artery to be returned to the cat. With the use of commercially available sensors, blood that has been in contact with the sensor cannot be returned to the patient because of bioincompatibilty.[12] The sensor could also be modified to make it smaller to allow less blood into the housing of the lithium-sensitive electrode. Also, adapting the peristaltic pump and the LiDCO system for a slower withdrawal rate (without prolonging the measuring time) would decrease the blood loss and make this CO monitoring system more suitable for use in physically small patients.

The main advantage of the LiDCO method, compared with the TDCO method, is that the instrumentation for LiDCO is easier and less invasive for the animal and the CO determination can be made more rapidly. Nevertheless, the LiDCO technique is associated with a certain level of invasiveness, particularly when used on small patients such as cats. Arterial catheters are difficult to insert and are not easy to maintain in cats; central venous catheters are certainly more difficult to insert in cats, compared with dogs and horses, and may require a cutdown procedure for placement. Because central venous and arterial lines are part of standard instrumentation for anesthesia and care of critically ill dogs and horses in intensive care units, use of the LiDCO system does not require additional instrumentation in those species under those circumstances; however, this does not apply to cats. The concern regarding the central venous line could be avoided by use of a peripheral catheter for LiCl injection because injection at a peripheral venous site correlates well with injection at a central venous site in dogs[16] and humans.[35] However, although TDCO measurements can be performed repeatedly and rapidly, the operator of the LiDCO system must wait at least 5 minutes between measurements to account for lithium recirculation,[21] making the LiDCO technique unsuitable for assessment of rapid changes in CO. To achieve maximum accuracy, repeating a LiDCO measurement requires analyzing an additional blood sample for serum sodium and hemoglobin concentrations, which increases the volume of blood withdrawn from the patient and requires administration of additional LiCl. Therefore, there are many steps involved in measuring CO by use of the LiDCO technique, and many technical errors can easily be introduced during LiDCO determinations.

For the assessment of CO in cats, the advantages of the LiDCO technique are its accuracy, the ease and rapidity of instrumentation of the patient, and the avoidance of pulmonary artery catheterization. Blood loss during measurement and the time and manipulations required to obtain measurements are major drawbacks to its use in physically small patients, and the need for an arterial catheter also limits the use of the LiDCO technique in cats in a clinical setting. Although the LiDCO measurements compared favorably with those obtained by use of the TDCO technique in the present study, further work needs to be done to validate a noninvasive technique to measure CO that will be more suitable than the LiDCO system for use in cats and in other physically small animals.

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