

Lithium dilution cardiac output measurement: A clinical assessment of central venous and peripheral venous indicator injection*

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Objective: The lithium indicator dilution technique has been shown to measure cardiac output (CO) accurately by using central venous injection of lithium chloride (Li-CCO). This study aimed to compare the measurement of CO by using peripheral venous administration of lithium chloride (Li-PCO) with Li-CCO.

Design: Prospective, observational human study.

Setting: Surgical intensive care unit.

Patients: Thirty-one patients were studied after major surgery. All patients had arterial, central, and peripheral venous catheters. A total of 24 patients had pulmonary artery catheters.

Measurements: Serial measurements of Li-CCO and Li-PCO were made during hemodynamically stable conditions. CO was also measured using thermodilution (TDCO) when a pulmonary artery catheter was present. Data were analyzed by linear regression, the generalized estimating equation, and the comparison method described by Bland and Altman.

Main Results: There were 93 Li-CCOs, 93 Li-PCOs, and 216 TDCOs recorded. The ranges of COs were similar: Li-CCO, 2.36–11.52 L/min (mean, 5.22 L/min; n = 31); Li-PCO, 1.63–9.99 L/min

(mean, 5.22 L/min; n = 31), and TDCO, 3.28–10.4 L/min (mean, 5.75 L/min; n = 24). There was good linear correlation between Li-CCO and Li-PCO ($R^2 = .845$). The mean difference for Li-CCO–Li-PCO was very small and insignificant ($p = .97$), and the limits of agreement were acceptable (mean difference \pm SD, 0.0005 ± 0.64 L/min). The mean difference for Li-CCO–Li-PCO was smaller if the peripheral injection site was proximal rather than distal to the wrist ($p = .053$). Li-PCO and Li-CCO values were lower than simultaneously obtained TDCO measurements (Li-PCO–TDCO, -0.538 ± 0.95 L/min, $p = .003$; Li-CCO–TDCO, -0.526 ± 0.67 L/min, $p = .0001$).

Conclusions: Li-PCO gives a measurement that agrees well with Li-CCO. Accuracy of Li-PCO is probably improved if a proximal arm vein is used. Li-PCO provides accurate measurements of CO without the risks of pulmonary artery or central venous catheterization. (Crit Care Med 2002; 30:2199–2204)

KEY WORDS: cardiac output; measurement techniques; lithium dilution

Lithium dilution cardiac output measurement (LiDCO, London, UK) is a new clinical technique for measuring blood flow (1). Lithium chloride is injected as an intravenous bolus into a vein, and its concentration in arterial blood is then measured over time by a lithium-sensitive electrode attached to a peripheral arterial catheter. Cardiac output (CO) can be calculated by using an analytic algo-

rithm that calculates CO from the area under the lithium dilution curve. Lithium is an appropriate indicator because its plasma concentration is normally negligible, and as it does not bind to plasma or tissue proteins, there is minimal loss of indicator as it passes from the injection catheter through the heart and lungs (2). Furthermore, lithium has no significant toxicity in the doses used to make the measurements. Plasma concentrations of lithium achieved during CO measurement are <1% of the desired and therapeutic levels maintained during clinical therapy for treatment of mania with lithium carbonate (3).

Several studies have demonstrated that the lithium dilution method using central venous injection provides CO values that are in close agreement with simultaneously measured CO values obtained using other techniques of CO measurement (4, 5). If the lithium dilution technique could be performed accu-

rately by using a peripheral vein, then CO could be measured without the risks of central venous catheterization, thereby enhancing the clinical applicability of this measurement technique. Because minimally invasive CO measurement for intravascular volume optimization has been shown to be valuable even for patients who do not have central pressure monitoring (6), it seems important to determine whether lithium dilution CO can be measured without central venous catheterization.

In this study, we investigated whether the accuracy of the original lithium dilution CO method was influenced by the site of intravenous lithium injection. In a controlled clinical environment in postoperative patients, we compared CO measurement by peripheral vein administration of lithium (Li-PCO) to CO measurements by central venous administration of lithium (Li-CCO). In a subset of patients who had a pulmonary artery catheter in place, ther-

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modilution CO (TDCO) was used as an additional measurement of CO to compare with both lithium dilution techniques.

MATERIALS AND METHODS

After approval by the Institutional Review Board, we obtained informed consent and evaluated 31 patients. The study was performed in the surgical intensive care unit after completion of cardiac surgery (25 patients) or general surgery (six patients). All patients were mechanically ventilated during the study period. Patients underwent central and peripheral intravenous and arterial catheterization as standard care for their operative procedures. All patients had a 20-gauge radial arterial catheter and a peripheral intravenous catheter in the right or left arm (20-gauge, 18-gauge, 16-gauge, or 14-gauge catheter). All patients underwent central venous catheterization of the right internal jugular vein with an 8.5-Fr introducer sheath. Twenty-four patients had a 7.5-Fr pulmonary artery catheter placed through this sheath, and the remaining seven patients had a 16-gauge central venous catheter placed.

Lithium Dilution Cardiac Output

Details of the lithium dilution measurement system have been provided by other authors (1, 4, 5) and are summarized briefly below.

Indicator. The indicator is lithium chloride that comes packaged in a 10-mL glass ampoule. A dose of 0.3 mmol (2 mL) per injection was used in this study.

Sensor. The disposable lithium sensor consists of a polycarbonate flow-through cell containing the lithium-selective electrode. It has an eccentric inlet that causes the blood to swirl past the tip of the electrode. The electrode is made of polyurethane and has a central lumen. Silver-silver chloride paint coats the inside and the outside of the electrode, which is filled with a supporting reference material that provides a constant ionic environment. A wick, soaked in 0.9% sodium chloride when the cell is first primed, makes the connection between the blood in the cell near the electrode and the remote reference electrode. This ensures constancy of the reference voltage and avoids artifact from temperature changes. The membrane is made of polyvinyl chloride and contains a lithium ionophore that makes it selectively permeable to lithium ions. A correction is applied for plasma sodium because of relatively low selectivity of the membrane for lithium over sodium. The voltage from the sensor is logarithmically related to the plasma lithium concentration. The signal is amplified by an electrically isolated preamplifier, converted from an analog to digital signal, and recorded on computer.

Recording the Signal. A new sensor was used for each patient and attached to a three-

way stopcock positioned in the arterial pressure catheter manometer tubing approximately 10 cm from the radial arterial catheter. The sensor was prepared by flushing with 0.9% sodium chloride to soak the wick and remove all air bubbles. A battery-powered roller pump then controlled the flow of arterial blood over the lithium sensor at a rate of 4 mL/min while the sensor was automatically electronically recalibrated. An extension tube with an internal volume of 3 mL was connected to the central or peripheral intravenous catheter and primed with 0.9% sodium chloride before a bolus dose of lithium chloride was "parked" in the dead space of the tube, ready for injection. When the sensor recalibration gave a stable baseline voltage reading, the lithium chloride was flushed into the vein with 15 mL of sodium chloride to encourage rapid transportation into the central circulation. Arterial blood was drawn continuously over the lithium sensor at a controlled rate until the indicator was detected by the sensor. An indicator curve recorded the change in plasma concentration of lithium chloride. The roller pump was then stopped and the sensor flushed with 0.9% sodium chloride. Approximately 4 mL of blood was removed and wasted with each lithium-dilution measurement.

Derivation of CO. The indicator dilution curves were analyzed by the monitor, and CO was determined by validated mathematic analysis (2, 7). The primary circulation curve of the indicator was discriminated automatically from the secondary (or recirculation) curve by the method of Linton et al. (7). This is based on the theory of log-normal analysis to determine the integral of the primary curve (8). CO was then calculated from the formula (1):

$$\text{Cardiac output (L/min)} \quad [1]$$
$$= \frac{\text{Dose of lithium chloride (mmol)} \times 60}{\text{Area under the curve} \times (1 - \text{PCV})}$$

Area under the curve equals the integral of the primary curve ($\text{mmol} \cdot \text{L}^{-1} \cdot \text{sec}$), and PCV is the packed cell volume. Packed cell volume was calculated from the hemoglobin concentration: $\text{PCV} = \text{hemoglobin}/34$ (g/dL). Because lithium is distributed only in the plasma fraction of blood, a correction factor of $1 - \text{PCV}$ needs to be included to convert plasma flow into blood flow or CO.

TDCO

Bolus TDCO measurements were performed using 10 mL of 5% dextrose at room temperature injected through the proximal right atrial port of the pulmonary artery catheter. The dilution curves were recorded, and CO was calculated by a standard bedside monitor (Agilent, Andover, MA) using the Stewart-Hamilton equation. Thermal indicator injec-

tion was synchronized to the end-expiratory phase of the respiratory cycle.

Experimental Procedure

Before CO measurement, plasma hemoglobin and sodium concentrations were measured by standard laboratory analysis to provide the required correction factors for measurement of CO by lithium dilution. Once the patient was hemodynamically stable in the intensive care unit, three sets of CO measurements were recorded in rapid succession. Each of the three measurement sets consisted of the following: Li-CCO, Li-PCO, and in patients with a pulmonary artery catheter, TDCO in triplicate. This provided a total of three Li-CCO and three Li-PCO measurements for each of the 31 patients and an additional nine TDCO measurement for each of the 24 patients with a pulmonary artery catheter. Mean arterial blood pressure (MAP) and heart rate (HR) were recorded at the start and end of the study period. All CO measurements were retained in the data set and analyzed.

Statistical Analysis

An average value for Li-CCO, Li-PCO, and TDCO was calculated from the three measurement sets. The linear regression equations for Li-CCO vs. Li-PCO, Li-CCO vs. TDCO, and Li-PCO vs. TDCO were calculated by simple linear regression analysis using the least-squares method from the x-y plots. Using the method described by Bland and Altman (9) for assessing agreement between measurement techniques, the differences between Li-CCO and Li-PCO, Li-CCO and TDCO, and Li-PCO and TDCO were plotted against the mean values for these pairs. The bias (mean difference) and limits of agreement ($\text{bias} \pm 2 \text{ sd}$) were determined and used to summarize the level of agreement between methods. To provide a summary statistical analysis comparing the three CO measurement techniques, the generalized estimating equation was applied, owing to the repeated measures in individual subjects (10, 11).

RESULTS

All patients were men, 20 patients were white, and 11 patients were African-American. Other demographic variables are summarized in Table 1. The mean time to perform the three measurement sets in each patient was 37 mins (range, 21–89 mins). Individual patient HRs and MAPs ranged from 49 to 112 beats/min and 51 to 109 mm Hg, respectively. All patients were studied during hemodynamically stable periods, as indicated by the small changes in HR and MAP over

the study period. Changes in HR were minimal; 94% of patients had a change in HR of <10% (mean [SD] percentage change of 2% [$\pm 5.6\%$]). Changes in MAP were slightly greater; 87% of patients had a percentage change in MAP of <10% (mean [SD] percentage change of -4% [$\pm 15\%$]). The majority of patients (68%) had a small change in central venous pressure of <10% (mean [SD] percentage change of 3% [$\pm 27\%$]).

Three central and three peripheral lithium injections were performed in all 31 patients. Nine TDCOs were measured in each of the 24 patients with a pulmonary artery catheter. The total number of CO measurements was 402: 93 Li-CCOs, 93 Li-PCOs, and 216 TDCOs. No measurements of CO were excluded from analysis. The range of COs measured by the three techniques was similar: Li-CCO (2.36–11.52 L/min; mean, 5.22 L/min; n = 31), Li-PCO (1.63–9.99 L/min; mean, 5.22 L/min; n = 31), and TDCO (3.28–10.4 L/min; mean, 5.75 L/min; n = 24). Linear correlation between measurements of Li-CCO and Li-PCO, Li-CCO and TDCO, and Li-PCO and TDCO are shown in Figure 1. The R^2 value of the linear regression line x-y plot was highest for Li-CCO and Li-PCO (.84) and lowest for Li-PCO and TDCO (.64). Analysis of individual CO measurement sets using the generalized estimating equation showed no significant difference between CO measurement performed by Li-CCO vs. Li-PCO ($p = .97$), whereas CO measurement by TDCO was statistically different from Li-PCO ($p = .003$) and Li-CCO ($p < .0001$). Furthermore, the relationship between the three methods of CO measurement was consistent throughout the range of low, normal, and high CO (Fig. 1).

Bland-Altman plots comparing the three methods of CO measurement are shown in Figure 2 (mean values of Li-PCO, Li-CCO, and TDCO for each patient). The mean bias and limits of agreement between the three methods are summarized in Table 2. There was no overall bias between Li-CCO and Li-PCO (Fig. 2A and Table 2). In contrast, TDCO measurements were greater than both lithium dilution methods, with a bias of approximately 0.5 L/min. Limits of agreement between methods were narrowest for Li-CCO–TDCO and widest for Li-PCO–TDCO.

Eight patients (25.8%) received lithium injection into a vein distal to the wrist, and 23 (74.2%) received injections

Table 1. Patient demographics

	Age	Height	Weight	Hgb	Na ⁺
Mean	62.9	178	88.9	10.0	135.9
SD	11.3	6.5	19.0	1.6	2.4
Range	42–80	168–191	57–137	7.4–14.3	132–143
Units	Years	cm	Kilograms	g/dL	mmol/L

Hgb, hemoglobin.

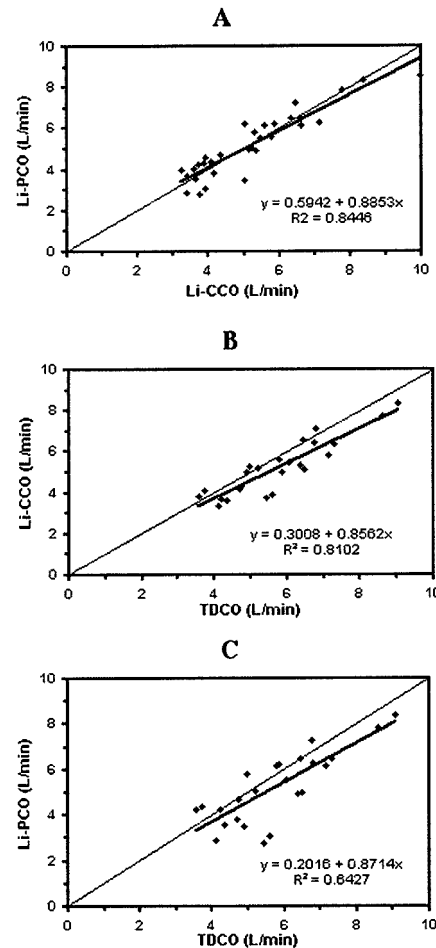


Figure 1. Comparison of cardiac output measurements, with x-y plots and linear regression for average values of each patient. *Li-CCO*, lithium dilution cardiac output by central injection; *Li-PCO*, lithium dilution cardiac output by peripheral injection; *TDCO*, thermodilution cardiac output.

proximal to the wrist. The R^2 values of the Li-CCO–Li-PCO x-y plots and the limits of agreement by Bland-Altman analysis showed differences between the two sites of injection (Fig. 3 and Table 3). The limits of agreement between Li-CCO and Li-PCO were much wider when the lithium indicator was injected distal to the wrist. Analysis of individual CO measurement sets using the generalized estimating equation showed a marginal differ-

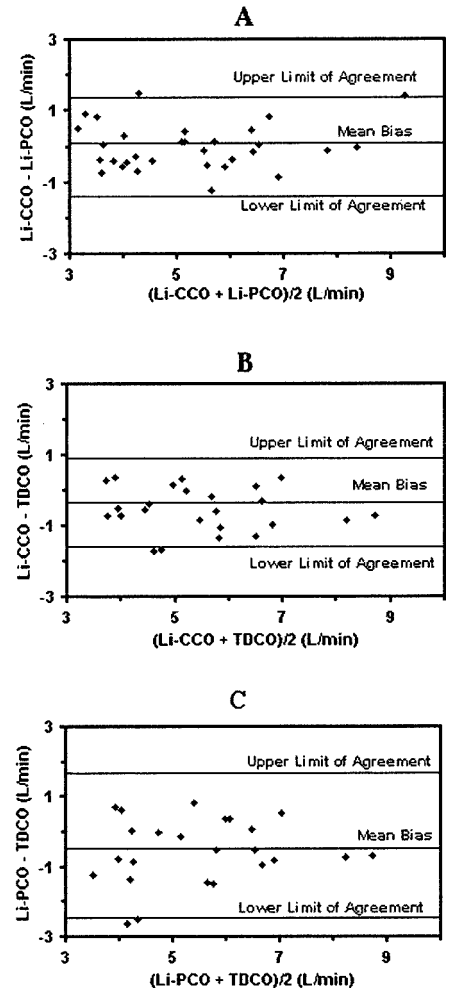


Figure 2. Bland-Altman plots showing the difference between cardiac output measurements as a function of the average between methods, using mean measurement values for each patient. *Li-CCO*, lithium dilution cardiac output by central injection; *Li-PCO*, lithium dilution cardiac output by peripheral injection; *TDCO*, thermodilution cardiac output.

ence in the agreement between peripheral and central lithium dilution methods as a function of the site of peripheral lithium injection ($p = .053$).

Various error messages of “long appearance time,” “peak concentration low,” “positive drift of lithium dilution sensor,” and “unusual shape of curve” were displayed frequently by the computer during lithium

Table 2. Bias, sd, and upper and lower limits of agreement for lithium dilution cardiac output by central injection (Li-CCO), lithium dilution cardiac output by peripheral injection (Li-PCO), and thermodilution cardiac output (TDCO) as a function of the average between methods, using mean measurement values for each patient

	Mean Bias	SD	Upper Limits	Lower Limits
Li-CCO-Li-PCO	0.005 ^a	0.64	1.29	-1.28
Li-CCO-TDCO	-0.526 ^b	0.63	0.73	-1.78
Li-PCO-TDCO	-0.538 ^c	0.95	1.35	-2.43

^aLi-PCO equals Li-CCO by GEE ($p = .97$); ^bLi-CCO not equal to TDCO by GEE ($p < .0001$); ^cLi-PCO not equal to TDCO by GEE ($p = .003$). All data are L/min.

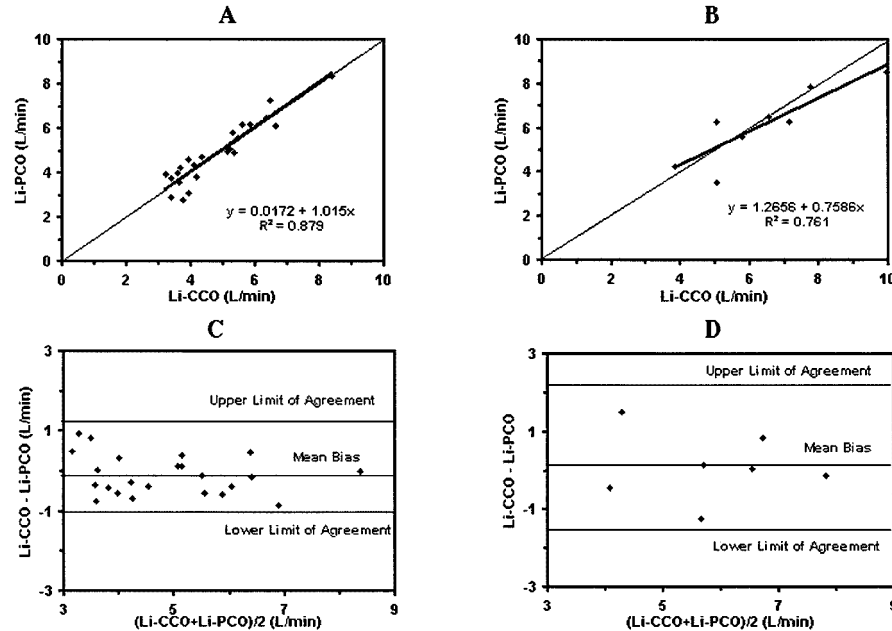


Figure 3. Cardiac output measurements by lithium dilution, comparing peripheral and central indicator injection. Lithium injection proximal to the wrist (A) and lithium injection distal to the wrist (B). Bland-Altman plots for lithium injection proximal to the wrist (C) and distal to the wrist (D). Li-CCO, lithium dilution cardiac output by central injection; Li-PCO, lithium dilution cardiac output by peripheral injection.

Table 3. Bias, sd, and upper and lower limits of agreement for lithium dilution cardiac output by central injection (Li-CCO) and lithium dilution cardiac output by peripheral injection (Li-PCO) for lithium injections proximal and distal to the wrist

	Mean Bias	SD	Upper Limits	Lower Limits
Li-CCO-Li-PCO (proximal to wrist)	-0.09	0.49	0.90	-1.08
Li-CCO-Li-PCO (distal to wrist)	0.27	0.94	2.15	-1.59

All data are L/min.

dilution CO measurements. A minority (26%) of Li-CCO measurements displayed an error message, the most common being "appearance time too long." In contrast, the majority (71%) of Li-PCO measurements displayed one or more of these messages. Visual inspection of lithium dilution curves from individual patients showed that Li-PCO curves were wider, had a lower peak, shallower upstroke, and increased appearance time compared with those of Li-

CCO. This effect was exaggerated the more peripheral the site of lithium injection (Fig. 4). Despite these frequent alerts, all measurements were included in the analysis, and no curves were discarded because of error messages (see Discussion).

DISCUSSION

Our results show a close agreement between Li-CCO and Li-PCO. There is no

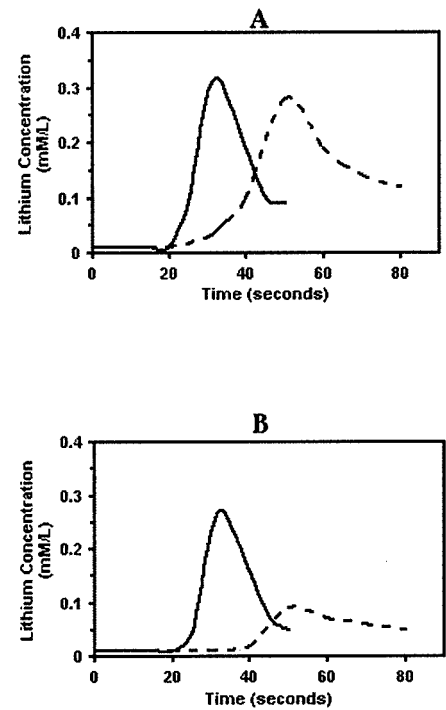


Figure 4. Lithium indicator dilution curves for lithium dilution cardiac output by central injection (Li-CCO, bold line) and lithium dilution cardiac output by peripheral injection (Li-PCO, dashed line) from a patient with peripheral lithium injection (A) proximal to the wrist (Cardiac output values for Li-CCO, 5.2 L/min, and Li-PCO, 5.1 L/min, were similar, and there were no error messages for either.) and (B) distal to the wrist (Cardiac output values for Li-CCO, 7.1 L/min, and Li-PCO, 6.3 L/min, were similar. There were error messages for the Li-PCO curve but not for the Li-CCO curve.).

significant bias between the two techniques, and the limits of agreement are narrow. This suggests that Li-PCO can provide an accurate measure of CO, confirming preliminary reports by others using a porcine model (12) and a human experimental protocol comparing antecubital and central intravenous injections of lithium (13). In addition, our results show that Li-PCO more closely approximates Li-CCO when peripheral injections of lithium are proximal to the wrist, suggesting that the peripheral injection method should be used with more proximal arm veins.

Our results are consistent with those of Jonas et al. (13), who showed a small bias (0.13 ± 0.8 L/min), good limits of agreement, and excellent correlation ($R^2 = .99$) between central and peripheral lithium methods. The slight difference in results could be explained by variations in study design and data analysis. We stud-

ied three times as many patients (31 vs. 10) and performed fewer measurements in each patient (3 vs. 5). Most importantly, we made our measurements over as brief a time period as possible (mean, 37 mins vs. 60 mins). A shorter period improves the likelihood of obtaining stable hemodynamic conditions. This is reflected in the minor changes that we report in HRs and MAPs between the start and completion of the measurement sets. We did not limit our peripheral lithium injections to the antecubital fossa veins, and we used suitable superficial venous access from the elbow to the hand, which represents normal clinical practice. Although our patients were not randomized to have lithium injected either proximal ($n = 23$) or distal ($n = 8$) to the wrist, our analyses suggest that this may influence CO measurement. The limits of agreement between Li-PCO and Li-CCO were wider if a vein below the wrist was used, and we recommend that Li-PCO injections should be through venous access above the wrist.

Our data suggest that the lithium CO methods remain accurate across a wide range of COs. Jonas et al. (13) found that when CO exceeded 10 L/min, Li-CCO was higher than Li-PCO ($p < .0025$), possibly either because of overestimation of the primary area of the Li-PCO curve caused by recirculation of lithium or underestimation of the primary Li-CCO curve caused by slow sensor response. Similarly, Kurita et al. (12) found that agreement of CO measurement was worse between Li-PCO and electromagnetic flowmetry when they tested Li-PCO under hyperdynamic conditions in pigs. We did not see variability in the level of agreement between Li-CCO, Li-PCO, and TDCO over a wide range of CO (1.63–11.52 L/min). Consequently, our data suggest that the lithium methods remain accurate in both high and low CO states.

In 24 patients, a pulmonary artery catheter was used for peri-operative monitoring, and in this group, we could compare Li-CCO and Li-PCO with TDCO. Bias analysis showed that TDCO measurement of CO was different (greater) by approximately 0.5 L/min compared with either Li-CCO or Li-PCO. Linton et al. (4) found a slightly smaller bias and better limits of agreement for Li-CCO vs. TDCO (-0.25 ± 0.46 L/min). These authors compared mean values of five CO measurements in each patient, whereas we compared the mean values of three measurements, and

this may have artificially improved the agreement seen in their study.

Although Li-PCO and Li-CCO both yield CO values that are different from TDCO, this does not mean that the COs derived by the lithium methods are less accurate. Using electromagnetic flowmetry as the reference method, Li-CCO had less variation and better repeatability than TDCO in a porcine model (5). The same group compared Li-CCO, TDCO, and Li-PCO with the same reference standard and showed that the agreement between Li-PCO and electromagnetic flowmetry was equivalent to that of TDCO and electromagnetic flowmetry (12).

TDCO measurement is known to have limitations (14), and comparisons of sequential TDCO readings may have an inherent variability of 20% (15). Different algorithms for the analysis of thermal vs. lithium indicator curves could contribute to the bias and disagreement between techniques. More significantly, TDCO measures CO over several heartbeats and one respiratory cycle (~10 secs), whereas the lithium dilution methods measure CO over many heartbeats and several respiratory cycles (~30 secs). We standardized TDCO measurement to the end of expiration to provide more repeatable measurements of CO (15). We were aware, however, that CO may be overestimated in patients receiving positive pressure ventilation when the thermal indicator injection occurs during end-expiration (16). Moreover it is clear that the CO value measured by TDCO varies as much as 25%, depending on the time of indicator injection during the respiratory cycle (17). Lithium dilution measurement obviates this problem because the indicator curve is generated over multiple respiratory cycles. Consequently, we believe, like others (4, 5), that the lithium dilution methods may provide a more accurate average CO as compared with thermodilution measurements. Because pulmonary artery catheters allow measurement of cardiac filling pressures and mixed venous oxygen saturations, they may still be required for monitoring some patients with severe cardiopulmonary disorders.

The good agreement between Li-CCO and Li-PCO suggests that the theory and assumptions made by Linton et al. (1) in determining CO by lithium dilution are valid, regardless of the site of lithium injection. These assumptions include instantaneous indicator injection, perfect mixing, and constant flow rate. In many

of our Li-PCO measurements, the shape of the lithium indicator curve was consistent with the indicator arriving at the heart as a bolus, with little loss of indicator in the peripheral venous system. Figure 4A graphically represents the similarity of the Li-CCO and Li-PCO dilution curves recorded in the one patient where the peripheral intravenous injection was made in a forearm vein. This similarity in curve appearance was not always present. In contrast, in a patient in whom Li-PCO measurements were made via a vein on the back of the hand, the shapes of the peripheral and central indicator curves were quite different (Fig. 4B). In general, the more distal the injection, the more distorted the indicator curve. This may explain the different bias and limits of agreement between Li-PCO and Li-CCO when the lithium was injected proximal or distal to the wrist.

Others have investigated the influence of peripheral indicator injection site on CO measurement by using indicator dye dilution (18–21). Two sources of error have been suggested as the cause of distorted indicator dilution curves after peripheral injection. The indicator could be trapped between the injection site and the central circulation, causing an overestimate of CO, or it could be slowly released into the central circulation, resulting in recirculation artifact and underestimation of CO. We believe that when lithium was administered below the wrist, it arrived into the central circulation as an infusion rather than a bolus. More than 70% of our Li-PCO indicator curves were accompanied by computer-generated error messages. The importance of the shape of the indicator curve and existence of error messages remain unclear in clinical practice. Analysis of our data did not show any alteration in the significance of our results if we included or excluded measurements that generated error messages. We have therefore not excluded any measurements of CO in our results. In clinical practice, however, it would seem reasonable to question the validity of very distorted Li-PCO curves. If the lithium dilution method is to be used routinely with peripheral lithium injections, new error limits will be needed to be included in the CO computer software.

Lithium dilution CO measurement has a number of technical limitations that must be considered. The lithium dilution CO methods require accurate measurements of serum sodium and hemoglobin. As our patients were studied in the early postoperative period, fluctua-

Lithium dilution by peripheral injection provides accurate measurements of cardiac output without the risks of pulmonary artery or central venous catheterization.

tions of these blood values may have occurred between the time of blood sampling and CO measurement. If the true hemoglobin is lower than the value entered into the CO computer, the CO will be artifactually increased by approximately 4% per 1 g/dL hemoglobin. The dose of lithium injected into the patient with each measurement (0.3 mmol) is small and unlikely to have any pharmacologic effect. The maximum recommended dose (3 mmol per 24 hrs) would need to be exceeded many times before effects of the drug are seen. Recent improvements in sensor technology and signal-to-noise ratio have allowed smaller (0.1–0.15 mmol) doses of lithium chloride to be used successfully (4, 12), which will increase further the margin of safety. Of note, lithium dilution CO measurement cannot be used in patients receiving oral lithium therapy because the lithium sensors have a logarithmic response and would underestimate the change in plasma lithium concentration if the starting level were too high.

CONCLUSION

In summary, Li-PCO provides a new method of CO measurement that agrees well with Li-CCO and TDCO techniques. To achieve the most accurate CO measurement with peripheral lithium injection, we recommend that Li-PCO be performed using an injection site proximal to the wrist. Although there is a difference in agreement between these three

methods of CO measurement, we feel that these are acceptable differences. It has been estimated that limits of agreement of $\pm 28\%$ are clinically acceptable when comparing CO measurement methods (22). Our results meet these stated limits of agreement. Li-PCO can be considered as an alternative method of CO measurement, with certain advantages. It avoids the risk of pulmonary artery catheterization (23) and central venous cannulation, and it is quick to perform (13). Furthermore, Li-PCO may have a valuable application as an intermediate diagnostic test in the operating room or intensive care unit in higher risk patients in whom knowledge of cardiac output could determine the need for more invasive hemodynamic monitoring, particularly central venous or pulmonary artery catheterization.

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