# LABORATORY REPORT

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# Effect of Cardiac Output on Extravascular Lung Water Measurements Made with the Thermoconductivity Method

William H. Noble, M.D., F.R.C.P.(C), \* J. Colin Kay, A.I.M.L.T.+

The authors tested the effects of injectate temperature and of changing cardiac output on the measurement of lung water by the thermoconductivity technique (ETV<sub>L</sub>). Cardiac output in dogs was increased and decreased with isoproterenol and halothane, respectively. Post mortem extravascular lung water (pulmonary extravascular tissue weight [PETW]) was determined using a weighing technique. Cardiac output varied between 0.7 and 8.8 l/min and did not influence the ETV<sub>L</sub> measurement. The authors conclude ETV<sub>L</sub> measured by the thermoconductivity technique is not influenced by large changes in cardiac output. (Key words: Anesthetics, volatile: halothane. Heart: cardiac output. Lung: extravascular lung water. Measurement techniques: cardiac output; extravascular lung water. Sympathetic nervous system sympathomimetic agents: isoproterenol.)

TWO REPORTS HAVE described a false increase in extravascular lung water (ETV<sub>L</sub>) using the thermodye technique and the Edwards® computer when cardiac output is decreased in dogs by renal pedicle clamping or by an overdose of halothane.2 In contrast we have measured ETV<sub>L</sub> using the thermoconductivity technique in low cardiac output settings created by emboli and shock and found that cardiac output did not influence ETV<sub>L</sub>.3-5 However, cardiac output was not specifically lowered in these experiments. Furthermore, the thermoconductivity technique uses a room temperature injectate while the Edwards® computer technique uses an iced injectate. It is possible the higher thermal gradients created by the iced injectate account for the falsely increased ETV<sub>L</sub> by creating thermal indicator losses that do not occur with the smaller temperature gradients of the room temperature injectate.

We therefore measured  $ETV_L$  using the thermoconductivity technique in dogs in whom cardiac output had been increased with isoproterenol and decreased with halothane. To assess the effect of injectate temperature we used both room temperature and iced injectate.

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Address reprint requests to Dr. Noble.

#### Methods

Six dogs were initially anesthetized with pentobarbital 30 mg·kg<sup>-1</sup> and anesthesia was maintained with additional 50 mg doses as needed. They were intubated and ventilated at a tidal volume of 15 ml·kg<sup>-1</sup> and 12 breaths/min with 100% O<sub>2</sub> while in the supine position. A 2-mm OD Silastic® catheter containing a Veco‡ thermistor catheter (time constant 0.12 s) was floated into the pulmonary artery (PA) from the external jugular vein. Placement of the catheter tip just beyond the pulmonary valve was determined with pressure monitoring. A 2.5-mm OD catheter containing two stainless steel electrodes for blood electrical conductivity measurements and a Veco® thermistor catheter were advanced from the femoral artery to the aortic arch.<sup>3,4</sup> Pressures were recorded on a Beckman® six-channel recorder.

# DOUBLE-INDICATOR DILUTION TECHNIQUE

For each determination of ETV<sub>L</sub> 5 ml of either room temperature or iced 3% saline were injected into the PA. The midpoint of injection and the difference between injectate temperature in the PA and dog blood temperature were computed. Blood was withdrawn through the aortic sensing catheter at 43 ml·min<sup>-1</sup> and then immediately reinfused. Aortic blood conductivity and temperature changes were recorded.<sup>5</sup> Conductivity and thermodilution curves were integrated and corrected for recirculation by extrapolation to zero of the downslope exponential calculated between 80% and 40% of the curve peak. Cardiac output (Q) was computed using Hosie's formula of thermodilution.<sup>6</sup> Mean transit time (MTT) was computed by the equation:

$$MTT = \frac{\int_0^\infty \mathbf{t} \cdot \mathbf{c}(\mathbf{t}) dt}{\int_0^\infty \mathbf{c}(\mathbf{t}) dt}$$

where c(t) is the outflow electrical conductivity ( $E_C$ ) or temperature (T) in blood. Then, central blood volume (CBV) =  $\dot{Q}$  (MTT<sub>EC</sub>) and ETV<sub>L</sub> =  $\dot{Q}$  (MTT<sub>T</sub> – MTT<sub>EC</sub>)

<sup>\*</sup> Professor of Anaesthesia and Chief Anaesthetist.

<sup>†</sup> Chief Technician.

<sup>‡</sup> Victory Engineering Corporation, Springfield Avenue, New Jersey.

where  $MTT_T$  is mean transit time of the thermal indicator and  $MTT_{EC}$  is mean transit time of the change in electrical conductivity.  $ETV_L$  is expressed as ml of  $ETV_L$  per kg of dog weight.

The aortic and PA thermistors were calibrated immediately prior to the experiment over the entire range of the iced or room temperature injectate. When iced injectate was used, the injectate came from tubing placed in a slurry of ice. In both cases dog blood temperature and temperature of injectate were recorded from a thermistor at the tip and inside the PA catheter.

### POST MORTEM LUNG WATER ANALYSIS

Immediately before the animals were killed with an injection of KCl, 20 ml of blood was removed and heparinized. After the animals were killed, the lungs were removed, weighed, and homogenized. The equation and methods used to determine pulmonary extravascular tissue weight (PETW) have been presented. With this technique blood left in the lung was calculated using hemoglobin (Hb) as the indicator. Lung blood was then subtracted from the total weight, leaving PETW expressed as ml of extravascular tissue per kg of dog weight.

#### **EXPERIMENTS**

We measured ETV<sub>L</sub> at baseline cardiac output ( $\dot{Q}$ ) in each dog. The injectate temperature was alternated so that pairs of ETV<sub>L</sub> measurements were performed with both room and iced temperature injectate.  $\dot{Q}$  was then decreased by increasing the halothane concentration until systolic arterial blood pressure reached 60 mmHg.  $\dot{Q}$  was then increased by reducing halothane and by an infusion of isoproterenol at 15  $\mu$ g·kg<sup>-1</sup>·min<sup>-1</sup>.  $\dot{Q}$  was then again decreased by stopping isoproterenol and increasing inhaled halothane. Paired measurements (room temperature and iced injectate) of ETV<sub>L</sub> were made at each level of  $\dot{Q}$  and in the transition phase between  $\dot{Q}$ s. The last ETV<sub>L</sub> was always made with a low  $\dot{Q}$  so a comparison between the last ETV<sub>L</sub> and the post mortem PETW could be made.

## **STATISTICS**

Statistical analysis<sup>7</sup> between room and iced injectate results were carried out with a paired t test. The relationship between  $\dot{Q}$  and ETV<sub>L</sub> was analyzed using a linear regression in each dog. P < 0.05 was considered significant. Data are reported as mean  $\pm$  SD.

# Results

With the room temperature injectate, baseline ETV<sub>L</sub> was  $7.5 \pm 2.3 \text{ ml} \cdot \text{kg}^{-1}$ , and a final ETV<sub>L</sub> was  $7.4 \pm 1.8 \text{ ml} \cdot \text{kg}^{-1}$ . Post mortem PETW was  $6.1 \pm 1.1 \text{ ml} \cdot \text{kg}^{-1}$  so

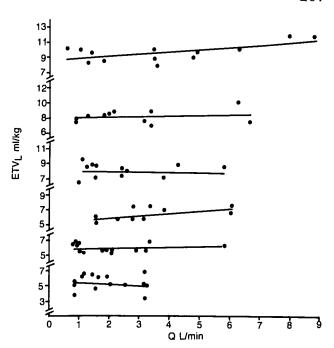


FIG. 1. The relationship between  $\dot{Q}$  ( $1 \cdot min^{-1}$ ) and  $ETV_L$  (ml of lung water per kg of dog weight) in all six dogs with room temperature injectate. The Y axis is broken to allow all data to be plotted in each dog.

the ratio of final ETV<sub>L</sub>/PETW was  $1.2 \pm 0.4$ . This compares with a ratio of  $1.5 \pm 0.3$  in other control dogs. Baseline  $\dot{Q}$  was  $3.7 \pm 1.0 \ l \cdot min^{-1}$  and  $\dot{Q}$  was varied between 0.7 and  $8.8 \ l \cdot min^{-1}$ .  $\dot{Q}s$  less than  $0.7 \ l \cdot min^{-1}$  could not be sustained.

When ETV<sub>L</sub> is plotted against  $\dot{Q}$  (fig. 1), the mean intercept is  $6.9\pm1.5~\text{ml}\cdot\text{kg}^{-1}$  (table 1), a value that agrees closely with our baseline ETV<sub>L</sub> measurement (7.5  $\pm$  2.3  $\text{ml}\cdot\text{kg}^{-1}$ ). ETV<sub>L</sub> was unaffected by changes in  $\dot{Q}$  in four dogs when either room temperature or iced injectate were used (figs. 1 and 2; table 1). Two of the dogs have slopes (0.33 and 0.29  $\text{ml}\cdot\text{kg}^{-1}\cdot\text{l}^{-1}\cdot\text{min}^{-1}$ ) that are statistically different from zero. However, tests for the homogeneity of the regression slopes for all six dogs indicate the slopes

TABLE 1. Regression Lines between Q and ETVL\*

	Room Temperature Injectate		Iced Injectate	
Dog No.	Slope	Y Intercept	Slope	Y Intercept
1	0.29†	8.56	0.63†	9.35
2	0.09	7.95	0.26	8.45
3	0.05	8.08	-0.31	11.41
4	0.33†	5.30	-0.02	7.24
5	0.03	5.83	0.41†	7.16
6	-0.15	5.63	-0.02	6.56
Mean ± SD	0.11 ± 0.17	6.89 ± 1.46	0.15 ± 0.34	8.36 ± 1.80

<sup>\*</sup> Same sequence top to bottom as in figs. 1 and 2.

<sup>†</sup> Slope significantly different from zero.

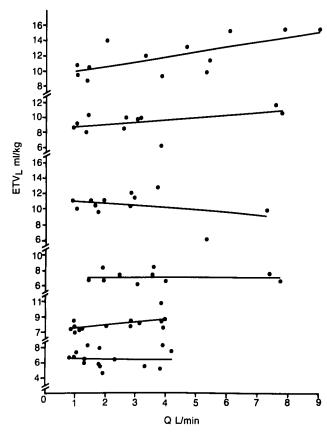


FIG. 2. The relationship between  $\dot{Q}$  ( $l \cdot min^{-1}$ ) and ETV<sub>L</sub> ( $ml \cdot kg^{-1}$ ) in all six dogs with iced injectate.

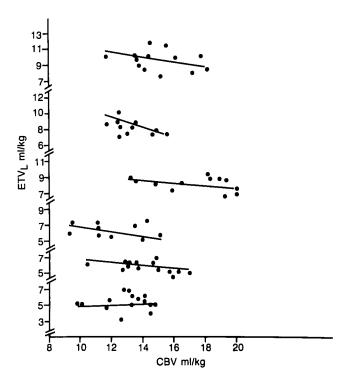


FIG. 3. The relationship between CBV (ml·kg $^{-1}$ ) and ETV<sub>L</sub> (ml·kg $^{-1}$ ) in all six dogs with room temperature injectate.

are not significantly different from one another.<sup>8</sup> The mean slope for all six dogs indicates for every  $1 \cdot min^{-1}$  increase in  $\dot{Q}$ , measured ETV<sub>L</sub> increases an average of  $0.1 \, ml \cdot kg^{-1}$  if room temperature injectate is used, and  $0.2 \, ml \cdot kg^{-1}$  if iced injectate is used. Figure 3 shows that changes in CBV resulting from the pharmacologic manipulation of  $\dot{Q}$  do not change ETV<sub>L</sub>. This was true when room temperature or iced injectate was used.

When iced injectate was used,  $\dot{Q}$  was increased 0.3  $\pm$  0.6 l·min<sup>-1</sup>, ETV<sub>L</sub> by 1.6  $\pm$  1.7 ml·kg<sup>-1</sup>, and the MTT difference between thermal and conductivity indicator was 0.6  $\pm$  1.7 s above the room-temperature injectate values.

## Discussion

The interventions of this experiment did not alter lung water because: 1) final ETV<sub>L</sub> (7.4  $\pm$  1.8 ml · kg<sup>-1</sup>) was not different than baseline ETV<sub>L</sub> (7.5  $\pm$  2.3 ml · kg<sup>-1</sup>); and 2) PETW (6.1  $\pm$  1.1 ml · kg<sup>-1</sup>) was not different than previous control dogs (5.9  $\pm$  0.9 ml · kg<sup>-1</sup>). Therefore, large alterations of Q did not affect the amount of water in the lungs. For example, a halving of Q from baseline in these dogs (3.7  $\pm$  1.0 l·min<sup>-1</sup>) would reduce ETV<sub>L</sub> by <0.2 ml · kg<sup>-1</sup>. This is within the error of the technique and is not clinically important. Alterations in CBV found in this experiment do not alter ETV<sub>L</sub>. These data support our previous work wherein we found that large variations in Q and CBV do not affect ETV<sub>L</sub>, and differ from results of Fallon et al., <sup>2</sup> who found that at low Q, ETV<sub>L</sub> measured with the Edwards® computer was increased.

We tested the hypothesis that these divergent results could be accounted for by the differences in injectate temperature. While we found differences in ETV<sub>L</sub> between iced and room temperature injectate, these differences were small and do not account for the divergent results. A second difference between the two techniques is the intravascular indicator used (Na in the thermoconductivity and indocyamine dye in the thermodye technique used by Fallon et al.2). Dye is sensed outside the body, resulting in a difference in the catheter transit time between the sensing of the thermal and dye indicators. A correction for the difference in catheter transit times must be used. (Catheter transit time differences between indicators do not exist in the thermoconductivity technique because both indicators are sensed at the same point.) How Q influences the thermodye measurement will depend on how the correction for catheter transit time is made. The final difference between the two techniques is the method of analysis of the indicator dilution curves. At the extremely low Q produced in these experiments, indicator dilution curves are low in amplitude, prolonged, and difficult for a computer to analyze. Because we did not perform a direct comparison of the two techniques,

we cannot resolve why the thermodye technique has been found to be inaccurate at low  $\dot{Q}$ .

In conclusion, large variations in  $\dot{Q}$  (0.7 to 8.8 l·min<sup>-1</sup>) and CBV (9.4 to 20.0 ml·kg<sup>-1</sup>) do not affect the accuracy of the ETV<sub>L</sub> measurement when it is measured with the thermoconductivity technique.

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