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BRIEF REPORT

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Extravascular lung water and intrathoracic blood volume: double versus single indicator dilution technique

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Abstract *Objective*: The accuracy of single thermodilution was assessed in measuring extravascular lung water (EVLW) and intrathoracic blood volume (ITBV). *Design*: Single thermodilution ($_{ST}$) was prospectively compared with thermo-dye dilution ($_{TD}$) in 13 mechanically ventilated pigs using the Pulsion Cold Z-021 monitor. *Interventions*: Lung injury was induced with oleic acid injection. *Results*: $EVLWI_{TD}$ increased from 4.3 ± 1.4 to 11.3 ± 4.5 ml/kg ($p = 0.0014$) and $ITBV_{TD}$ decreased from 581 ± 66 to 540 ± 85 ml ($p = 0.039$) after induction of lung injury. $EVLW_{ST}$ was systematically overestimated (0.5–1 ml/kg) and $ITBV_{ST}$ was slightly underestimated (15–20 ml) when calculated automatically by the Pulsion Cold Z-021 monitor. This bias could be removed by adjusting two coefficients needed for the computation of $ITBV_{ST}$ and $EVLW_{ST}$ so that the following regression equations were obtained: $EVLWI_{ST} = 0.98 \cdot EVLWI_{TD} + 0.27$ ($r = 0.94$, $p < 10^{-6}$) and $ITBV_{ST} = 1.0 \cdot ITBV_{TD} + 0$ ($r = 0.87$, $p < 10^{-6}$). *Conclusions*: Single thermodilution allows estimation of ITBV and EVLW values with reasonable accuracy and therefore provides useful information about the cardiac preload and the severity of lung injury. However, automatic calculation of $EVLWI_{ST}$ and $ITBV_{ST}$ using the Pulsion Cold Z-021 might be biased. Therefore, researchers and clinicians should validate single thermodilution for the given settings, before employing this method to estimate EVLW and ITBV.

Key words Extravascular lung water · Intrathoracic blood volume · Thermodilution · Thermo-dye dilution

Introduction

The pulmonary extravascular thermal volume has been used in numerous clinical and experimental studies as a measure of extravascular lung water (EVLW). EVLW is a marker for the severity of lung injury, the knowledge of which may improve the outcome in some critically ill patients by guiding the volume therapy [1]. In vivo, EVLW is commonly measured with a combined thermo-dye dilution technique, but the indocyanine green (ICG) used for this technique is relatively expensive. Therefore, the accuracy of EVLW estimation by single thermodilution with a lung water monitor (Pulsion Cold Z-021) was studied. In addition, the intrathoracic blood volume (ITBV), which is an indicator of the circulating blood volume [2], was also compared with the single thermodilution versus the thermo-dye dilution technique.

Table 1 Hemodynamic parameters and extravascular lung water. Numbers are given as mean ± standard deviation. For measurements performed in triplicates the coefficient of variation [%] is given in parentheses. (*PAOP* pulmonary arterial occlusion pressure, Paw_{Mean} Mean airway pressure, *EVLWI* extravascular lung water index, *ITBV* intrathoracic blood volume, $_{TD}$ determined by thermo-dye dilution, $_{ST}$ determined by single thermodilution)

		Baseline		Lung injury	
PaO_2	[mmHg]	479 ± 63		98 ± 84	
Hb	[g/l]	84 ± 9		93 ± 9	
Heart rate	[bpm]	116 ± 26		129 ± 31	
MAP	[mmHg]	102 ± 15		87 ± 13	
CVP	[mmHg]	6 ± 2		9 ± 2	
PAOP	[mmHg]	6 ± 2		9 ± 3	
Paw_{Mean}	[cmH_2O]	5 ± 2		8 ± 2	
CO_{TD}	[l/min]	4.5 ± 1.0	(2.4 ± 1.5)	4.3 ± 1.0	(3.9 ± 2.8)
CO_{ST}	[l/min]	4.6 ± 1.1	(2.8 ± 1.4)	4.4 ± 0.8	(4.2 ± 2.5)
$EVLWI_{TD}$	[ml/kg]	4.3 ± 1.4	(8.2 ± 5.0)	11.3 ± 4.5	(8.4 ± 9.0)
$EVLWI_{ST}$	[ml/kg]	4.4 ± 2.2	(3.0 ± 3.0)	11.5 ± 4.6	(4.2 ± 2.5)
$ITBV_{TD}$	[ml]	581 ± 66	(3.3 ± 1.6)	540 ± 85	(4.6 ± 2.7)
$ITBV_{ST}$	[ml]	583 ± 120	(4.0 ± 2.0)	534 ± 102	(5.7 ± 3.0)

Material and methods

Anesthesia

After approval of the local Animal Ethics Committee, 13 healthy pigs (weight 30 ± 4 kg) were premedicated with 40 mg azaperonum (Janssen, Belgium), then anesthesia was induced with atropine (0.04 mg/kg), tiletamin/zolazepam (6 mg/kg, Reading, Carros, France) and xylazin (2.2 mg/kg, Bayer, Leverkusen, Germany) im, followed by a constant infusion of 400 mg/h clomethiazole (Astra, Södertälje, Sweden), 150 µg/h fentanyl and 2.5 mg/h pancuronium for muscle relaxation. The animals were tracheotomized and mechanically ventilated. Ringer-acetate (1000 ml) was infused before baseline measurements, thereafter fluid replacement aimed at a stable systemic arterial blood pressure (~ $30\ ml \cdot kg \cdot h^{-1}$ after induction of lung injury).

An 18-gauge catheter and a thermistor-tipped fiberoptic catheter (Pulsiocath 4F FT PV 2024, Pulsion Medical System, Munich, Germany) were inserted via the carotid artery and advanced into the descending aorta for measurements of cardiac output (CO), EVLW and ITBV. A Swan Ganz catheter was introduced via the right external jugular vein. Blood gas samples were analyzed with ABL 300 and OSM 3 Hemoximeter (Radiometer, Copenhagen Denmark). Transpulmonary CO, ITBV and EVLW were determined in triplicate by injecting 8 ml ice-cooled indocyanine green (ICG) (ICG-Pulsion, Pulsion Medical System, Munich, Germany; 1 mg/ml) or by injecting 8 ml ice-cooled saline.

Study protocol

Baseline values were obtained after a 30-min stabilization period, after which lung injury was induced with oleic acid (0.1 ml/kg, Apoteksbolaget, Göterborg, Sweden) injected via a central venous catheter. Measurements were repeated 120 min after the induction of lung injury.

Calculation of ITBV and EVLW

The mean transit time (MTt) of a suddenly injected indicator bolus between the site of injection and the site of detection multiplied by the CO equals the total volume marked by the indicator [3]. The exponential downslope time (DSt) of the registered indicator curve multiplied by the CO corresponds to the largest individual volume marked by the indicator [4].With the thermo-dye (TD) dilution technique, $ITBV_{TD}$ and $EVLW_{TD}$ can thus be calculated as:

1. $ITBV_{TD} = CO \cdot MTt_{ICG,}$ where MTt_{ICG} is the mean transit time of indocyanine green
2. $EVLW_{TD} = (CO \cdot MTt_{Therm}) - ITBV_{TD}$, where MTt_{Therm} is the mean thermal transit time

Using the single thermodilution (ST) technique $CO \cdot MTt_{Therm}$ equals the intrathoracic thermoaccessible volume (ITTV) and CO · DStTherm is the pulmonary thermoaccessible volume (PTV), where DSt_{Therm} is the exponential thermal downslope time. $ITBV_{ST}$ and $EVLW_{ST}$ can consequently be estimated as:

3. $ITBV_{ST} = a \cdot (ITTV - PTV) + b$, where "a" and "b" are coefficients derived from linear regression analysis between $EVLW_{TD}$ and (ITTV – PTV)
4. $EVLW_{ST} = ITTV - ITBV_{ST}$

All data are presented as the mean ± standard deviation. Regression analyses were made with the least squares method. Parameters before and after the induction of lung injury were compared using a Wilcoxon signed rank test, with $p < 0.05$ as the level of significance.

Results

Oleic acid injection increased EVLWI ($p = 0.0014$), decreased ITBV slightly ($p = 0.039$) but did not affect CO (Table 1).

$ITBV_{TD}$ and (ITTV – PTV) demonstrated a significant linear relationship with a coefficient of correlation (r) of 0.87 ($p < 10^{-6}$), the regression equation being: $ITBV_{TD} = 1.73 \cdot (ITTV - PTV) - 7.7$. In Eq. 3 "a" was therefore substituted by 1.73 and "b" by –7.7, which differs from the values used by the Pulsion Cold Z-021 (hu-

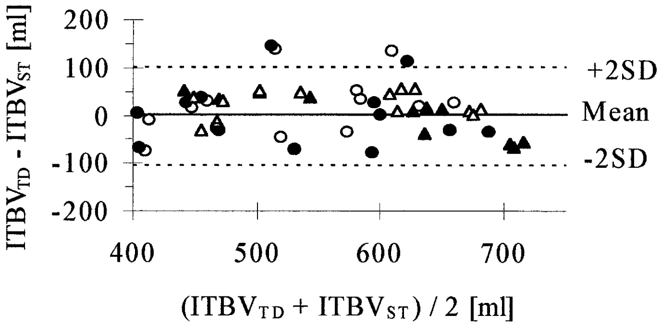

Fig. 1 Intrathoracic blood volume before and after induction of lung injury. Intrathoracic blood volume (ITBV) before (▲, △) and after (●,○) induction of lung injury. The x-axis shows the mean of ITBV measurements by single thermodilution and thermo-dye dilution before and after induction of lung injury. The y-axis shows the difference of ITBV between both methods. ▲ and ●: calculation of $ITBV_{ST}$ with coefficients "a" and "b" corrected for the present data set. △ and ○: calculation of $ITBV_{ST}$ with coefficients "a" and "b" as determined by the manufacturer of the Pulsion Z-021. The mean ± 2SD are calculated for the solid symbols (▲, ●). ($_{TD}$ measured by thermo-dye dilution, $_{ST}$ measured by single thermodilution)

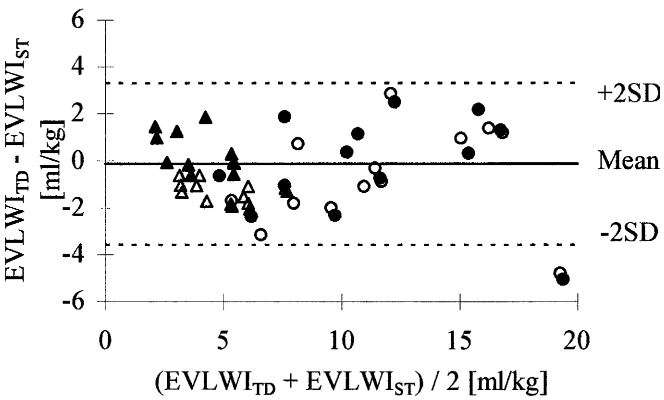

Fig. 2 Extravascular lung water index before and after induction of lung injury. The x-axis shows the mean of the extravascular lung water index (EVLWI) before (▲, Δ) and after (●, ○) induction of lung injury as assessed by single thermodilution and thermo-dye dilution. For further explanations see Fig. 1

mans: a = 1.16, b = 86; pigs: a = 1.30, b = 0; [5]). Consequently, $ITBV_{ST}$ calculated with the coefficients of the manufacturer (a = 1.30, b = 0) resulted in a slight underestimation (15–20 ml) as compared to thermo-dye dilution. Figure 1 shows $ITBV_{TD}$ and $ITBV_{ST}$ calculated with both sets of coefficients before and after oleic acid injection [6]. $EVLWI_{ST}$ was linearly correlated to $EVLWI_{TD}$ ($r = 0.94$, $p < 10^{-6}$) according to the equation: $EVLWI_{ST} = 0.98 \cdot EVLWI_{TD} + 0.27$. However, a bias of 0.5–1 ml/kg was found, if "a" and "b" were not corrected for the present data set. Figure 2 shows EVLWI before and after the induction of lung injury. The differences of CO measurements between saline and ICG injections were minimal (0.0 ± 0.1 l/min at baseline and 0.1 ± 0.2 l/min after the induction of lung injury).

Discussion

This study shows that single thermodilution allows a reasonable estimate of EVLWI and ITBV. An injection of cold saline alone can thus provide valuable information about the cardiac preload and the severity of lung injury.

Using single thermodilution, ITBV and EVLWI are not obtained directly, but are derived from the measurements of CO, ITTV and PTV using Eqs. 3 and 4, respectively. The coefficients "a" and "b" in Eq 3 are computed using linear regression analysis between $ITBV_{TD}$ and (ITTV-PTV) and affect the calculation of $ITBV_{ST}$ **and** $EVLW_{ST}$. For the present data "a" and "b" differed markedly from the values used by the manufacturer of the Pulsion Cold Z-021 [5]. Consequently, the Pulsion Cold Z-021 overestimated $EVLWI_{ST}$ (0.5–1 ml/kg) and underestimated $ITBV_{ST}$ (15–20 ml) systematically, whereas no such bias occurred following correction of "a" and "b". Differences of "a" and "b" may be due to different detection sites of the thermo-dye dilution curves (e.g. descending aorta versus femoral artery), because this affects the thermoaccessible volume (ITTV) between the site of injection and the site of detection. In addition, the coefficients might not only vary among different species [5] but possibly also among different breeds of laboratory animals. Therefore, clinicians and researchers should establish the values of the coefficients "a and b" for the given settings before sole use of the single thermodilution technique.

The precision of $ITBV_{ST}$ and $EVLWI_{ST}$ measurements was acceptable considering a standard deviation of $ITBV_{TD}–ITBV_{ST} = \pm 56$ ml (Fig. 1) which is similar to previously reported data [7], and of $EVLWI_{TD} – EVLWI_{ST} = \pm 1.7$ ml/kg. After oleic acid injection only the scatter of $ITBV_{TD} – ITBV_{ST}$ increased, but not that of $EVLWI_{TD} – EVLWI_{ST}$. This might be explained by the difficulty in calculating MTt_{Therm} accurately in cases of large distribution volumes [8]. MTt_{Therm} directly affects the calculation of $ITBV_{ST}$, while EVLW is more or less proportional to PTV ($CO \cdot DSt_{Therm}$).

Ideally, thermodilution and thermo-dye dilution should be compared simultaneously. In this study measurements were done sequentially, but during stable hemodynamic conditions. Since CO was always determined by thermodilution whether or not ICG was used, differences of CO between the two sets of measurements reflect changes of the hemodynamic state and random noise, but are not related to the single thermodilution or thermo-dye dilution technique. The CO differences between the two sets of measurements averaged

1.5 ± 3.9 % and thus do not explain the differences of EVLWI and ITBV observed between the two methods.

Use of indocyanine green makes the thermo-dye dilution technique relatively expensive and repeated measurements performed in triplicate considerably increase both the cost of hemodynamic monitoring of critically ill patients as well as research. In conclusion, the single thermodilution technique with the Pulsion Cold Z-021 provides additional information for estimating EVLWI and ITBV for the same price as a standard hemodynamic monitoring.

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References

1. Eisenberg PR, Hansbrough JR, Anderson D, Schuster DP (1987) A prospective study of lung water measurements during patient management in an intensive care unit. Am Rev Respir Dis 136: 662–668
2. Lichtwarck-Aschoff M, Zeravik J, Pfeiffer UJ (1992) Intrathoracic blood volume accurately reflects circulatory volume status in critically ill patients with mechanical ventilation. Intensive Care Med 18: 142–147
3. Meier P, Zierler KL (1954) On the theory of indicator-dilution method for measurement of blood flow and volume. J Appl Physiol 6: 731–744
4. Newman EV, Merrel M, Genecin A, Monge C, Milnor WR, McKeever WP (1951) The dye dilution method for describing the central circulation. An analysis of factors shaping the time-concentration curves. Circulation 4: 735–746
5. Pulsion Medical Systems: User's Manual Pulsion Cold Z-021 Version 5.X. 1995.
6. Bland JM, Altman DG (1986) Statistical methods for assessing agreement between two methods of clinical measurement. Lancet I: 307–310
7. Buhre W, Bendyk K, Weyland A, Kazmaier S, Schmidt M, Mursch K, Sonntag H (1998) Assessment of intrathoracic blood volume. Thermo-dye dilution vs single-thermodilution technique. Anaesthesist 47: 51–53
8. Wallin CJ, Rosblad PG, Leksell LG (1997) Quantitative estimation of errors in the indicator dilution measurement of extravascular lung water. Intensive Care Med 23: 469–475