Measuring lung water following major lung resection

Babu V. Naidu*, Vamsidhar B. Dronavalli, Pala B. Rajesh

Department of Thoracic Surgery, Heartlands Hospital, Bordesley Green East, Birmingham, B9 5SS, UK

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Abstract

Following the acute changes of lung resection surgery, does the ratio of intrathoracic blood volume (ITBV) to global end diastolic volume (GEDV) remain constant? If it does this could validate a single thermo dilution (STD) technique in the measurement of extravascular lung water index (EVLWI) in patients undergoing lung resection surgery. EVLWI was derived using both double dye technique (DDT) and single thermo dilution technique (STD) in four patients undergoing thoracotomy selected for major lung resection surgery. Regular measurements were made for up to 12 h after surgery. After the first two hours following lung resection surgery, the ratio of blood volume ITBV/GEDV shows little variation for up to 12 h. EVLWI measurements measured by STD correlate well with those of DDT. This preliminary study suggests that EVLWI measurements by STD could be used to measure changes in EVLW following major lung resection. An assessment of EVLW could be useful in early diagnosis, management and treatments of the devastating condition of postoperative acute lung injury.

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1. Introduction

Mortality following major lung resection in the UK remains largely unchanged over the last 20 years as reported in the National Thoracic Surgery Activity and Outcomes Report 2008 (Society for Cardiothoracic Surgery in Great Britain and Ireland). Up to 72% of these deaths are due to post-operative acute lung injury (PALI) [1]. Indeed fatal outcome following the development of PALI is reported between 50–100% [1, 2]. Suggested risk factors include increasing age [1], preoperative chemoradiotherapy [3], more extensive resection [1], impaired lymphatic drainage, ventilator associated barotrauma [2, 4, 5], and ischaemic reperfusion injury [6].

PALI, a non-cardiogenic pulmonary oedema shares clinical, radiological and histopathological characteristics with ARDS [7]. Whilst the aetiology is uncertain the high concentration of protein in the oedema fluid [8] and delayed presentation suggest this is an inflammatory mediated process. The condition may be exacerbated by excessive fluid administration [9] and changes in pulmonary vascular resistance [10, 11] but these factors are unlikely to be causal.

As with ARDS, the diagnosis of PALI is often delayed because clinical signs of pulmonary oedema present only once the extra vascular lung water (EVLW) rises over 7 ml/kg (ideal body weight) [12]. Therefore, any technique that could assess lung water would not only make the diagnosis of PALI early but might better guide fluid management of patients following lung resection.

*Corresponding author. Tel.: +44 121 424 3561; fax: +44 121 4241561.
E-mail address: babu.naidu@heartofengland.nhs.uk (B.V. Naidu).
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However, following lung resection the PTV and PBV change so this relationship is invalid. Using a double dye technique (DDT), both thermodilution and indocyanine green, it is possible to calculate each parameter because the indocyanine green stays within the circulation and does not enter EVLW. Hence its Mtt will measure ITBV. So it is possible to derive the new relationship between GEDV and ITBV. If this relationship remains constant throughout an individual patient’s postoperative period then a single thermodilution technique may be useful in measuring trends in EVLW following lung resection.

2. Methods

Three patients selected for elective major lung resection surgery for primary lung carcinoma at the Heartlands hospital were recruited and underwent EVLW measurements using the DDT and STD techniques as per protocol in this ethics approved study. During surgery a standardised anaesthetic protocol was used: ventilator settings of positive end expiratory pressure (PEEP) of 5 cm of H2O, induction and maintenance of anaesthesia with propofol and bilateral lung ventilation performed up until entry into the chest cavity. A central venous line was inserted in the anaesthetic room prior to onset of surgery. The COLD-Z machine was calibrated and set up as (COLD-Z, pulsiocath oximetrey thermodye dilution catheter)

2.1. EVLW measurements

The indocyanine indicator dye (1.5 mg/ml concentration, 1.5 ml + 0.15 ml/kg BW volume) was stored at 2–4 °C. Boluses were injected via a central line and thermo-dye dilution curves recorded. Measurements at each time point were performed in triplicate and the average values for ITBV, GEDV and EVLW from the two techniques were recorded.

3. Patients

A brief clinical summary of the three recruited patients:

Patient 1 was a 76-year-old male with a small peripheral non-small cell lung cancer (NSCLC) with an FEV, of 1.7 who underwent a left lower lobectomy. OLV time was 55 min and 2 l of intravenous fluid was administered over 12 h. Patient 2 was a 67-year-old male with a central NSCLC in the left hilum with an FEV, of 1.3 who underwent a left pneumonectomy. OLV time was 70 min and 3 l of intravenous fluid was administered over 12 h. Patient 3 was a 66-year-old male with a left upper lobe NSCLC with an FEV, of 1.6 who underwent a left upper lobectomy. OLV time was 130 min and 3.5 l intravenous fluid was administered over 12 h.

4. Analysis

Statistical analysis was performed using SPSS 15 software. Bland–Altman analysis was used to show the difference in EVLW measurements between the STD and DDT techniques. The mean values for the ratio of GEDV:ITBV at numerous time points were compared and the variability of this ratio calculated for each patient.

5. Results

In all three patients immediately following surgery, the ratio of GEDV:ITBV changed (Fig. 2) and continued to do so for the first two hours after surgery. However, for each patient, following these early changes the ratio showed little variability for the following 12 h (Table 1).

STD under estimated EVLW compared to DDT techniques in the pneumonectomy patient by 40 ± 10% (mean ± S.D.) and in the patient following left lower lobectomy by 5 ± 8%, respectively. However, in the patient following left upper lobectomy, STD over estimated EVLW compared to DDT

Further measurements were performed in recovery and at regular intervals up to 12 h following surgery.

Fig. 1. Schematic representation of all the vascular/fluid compartments within the chest cavity through which an indicator injected into a central vein may distribute. Indocyanine green distributes into ITBV whilst thermal indicator distributes into ITTV.

Fig. 2. Graph demonstrating the change in ratio of GEDV:ITBV for each patient during and following surgery for up to 12 h. Time points are from closure of thoracotomy. Time point –2 represents measurements in the anaesthetic room prior to onset of surgery.
techniques by $40\pm49\%$. The wider variation in reading in this last patient is explained by the marked variation in GEDV/ITBV ratio (Fig. 2).

From the Bland–Altman analysis the mean difference (MD) between EVLWI STD and EVLWI DDT for each patient and their limits of agreement were as follows:

Patient 1 – Left lower lobectomy – MD = $-0.31$ ml/kg limits of agreement = $1.07$ ml/kg to $-1.69$ ml/kg.

Patient 2 – Left pneumonectomy MD = $-1.96$ ml/kg limits of agreement = $-0.63$ ml/kg to $-3.29$ ml/kg.

Patient 3 – Left upper lobectomy MD = $0.68$ ml/kg limits of agreement = $2.85$ ml/kg to $-1.5$ ml/kg.

6. Discussion

Two hours following major lung resection surgery, the GEDV/ITBV ratio seems to reach a new constant with minimal variation for up to $12$ h postoperatively. The single dye technique tends to under or over estimate EVLWI values measured by double dye techniques in a consistent fashion for an individual patient. From the Bland–Altman analysis, the range of difference is not clinically significant between the two techniques. We cannot calculate the precision of this estimate of agreement and repeatability because all three cases are fundamentally different. In this small preliminary study, we also make the assumption that the thermodilution technique of COLD and PICCO techniques are comparable as done by the original validatory studies [13].

Waller et al. studied lung water following major lung resection using lung scintigraphy [14]. They showed a $4\%$ increase of overall lung to heart ratio to technetium radio-labelled albumin activity following pneumonectomy. As the authors point out, the technique is cumbersome and does not take into account changes in pulmonary blood volume. In animal studies, there is good correlation between gravimetric and EVLW, as assessed by STD and DDT techniques. Difference in findings between our study and others may perhaps be explained by species differences, the shorter follow-up and ventilation of animals during measurements.

The dogma of fluid restriction following pneumonectomy may have detrimental effects. However, a conservative strategy of fluid management may improve lung function, and shorten duration of mechanical ventilation and intensive care in patients who develop acute lung injury [15]. Hence it may be possible that to improve the outcome of PALI with this strategy especially if we can make the diagnosis early. Absolute cut-off values of EVLWI may be difficult to interpret because of the difficulty in predicting the change in GEDV/ITBV ratio. We suggest that a $50\%$ increase from baseline of EVLWI measured by PICCO might trigger this conservative fluid strategy. EVLWI measurements by PICCO will need to be validated as a predictor of the development of PALI in a much larger trial, as will the efficacy of such fluid strategies. This preliminary study suggests that PICCO could be used to measure changes in EVLW following major lung resection. An assessment of EVLW could be useful in early diagnosis, management and treatments of the devastating condition of PALI.

### Table 1

<table>
<thead>
<tr>
<th>Surgery</th>
<th>Mean ITBV/GEDV</th>
<th>Mean ITBV/ S.D.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left upper lobectomy</td>
<td>$1.36\pm0.08$</td>
<td>$1.15\pm0.05$</td>
</tr>
<tr>
<td>Left lower lobectomy</td>
<td>$1.23\pm0.03$</td>
<td>$1.15\pm0.05$</td>
</tr>
<tr>
<td>Left pneumonectomy</td>
<td>$1.15\pm0.05$</td>
<td>$1.15\pm0.05$</td>
</tr>
</tbody>
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Fig. 3. Bland–Altman analysis. The difference in EVLWI measurements between the two techniques is plotted against the mean EVLWI in ml/kg. The solid line represents $2$ S.D. from the mean of differences between values of EVLWI obtained from the two techniques.
References


