Radical Lymphadenectomy Does Not Effect Intrathoracic Fluid Volume Changes After Lung Surgery

C Schröder, K Kuhn, P Macchiarini

Citation

Abstract
Objectives: The extent of lung tissue removal in thoracic surgery is known to have a large influence on postoperative edema. The relationship of radical lymphadenectomy and postop edema is controversial and investigated in this study.

Design: 32 patients undergoing lung resection (16 lobectomies, 3 sleeve lobectomies, 10 pneumonectomies, 3 carina resections) for cancer were randomized by type of lymphadenectomy (sampling or radical). Using trans-cardio-pulmonary thermodilution method (PiCCO™) intra thoracic blood volume index (ITBI), extra lung water volume index (ELWI), and cardiac index (CI), were determined pre- and postoperatively at 0, 12, 24, 36 and 48 hours. The influence of postoperative lung volume reduction was then mathematically corrected (ELWI-corr).

Results: ELWI-corr was significantly higher in bronchus sleeve resections within 12 hours in lobectomies (p=0.003) and pneumonectomies (p=0.031), whereas the ITBI remains stable in lobectomies, but decreased significantly within 48 hours in pneumonectomies (p=0.002) although clinical lung edema was not observed. No significant differences were found between sampling and radical lymphadenectomy (p>0.3). No significant changes were observed for CI and CVP between procedural or lymphadenectomy groups.

Conclusions: There were no differences in ELWI, CI and ITBI between lymph node sampling and radical lymphadenectomy. Bronchus sleeve procedures alone showed a drastic increase in ELWI. For each patient, ELWI needs to be normalized to the preoperative value and the postoperative lung volume (ELWI-corr). Anticipating significant lung edema, especially in sleeve resection patients, by monitoring ELWI-corr should improve the clinical outcome.

This work was orally presented at the 3rd EACTS/ESTS Joint Meeting September 2004, Leipzig, Germany

INTRODUCTION
Postoperative non-cardiac pulmonary edema is an often seen complication after thoracic surgery. Common diagnostics such as chest x-ray, central venous pressure and clinical findings do not show a high enough correlation with the intra-thoracic fluid status to guide adequate volume therapy [1,2,3].

Thermodilution method was developed and is well accepted in the therapy of the critically ill. Classically, the method is used in patients with sepsis and cardiac instability and it is commonly used in extensive cardiac, thoracic and abdominal operations [4,5,6]. There is only limited experience with lung resections and intrathoracic volume measurement in humans and a small number of studies using various animal models [7,8,9].

Our aim was to integrate this helpful tool in the sensitive field of thoracic surgery to obtain a method of early detection of volume overload, and to find out if parameters are altered by the amount of lung tissue removed. Furthermore we investigated the influence of operative procedures as sleeve resections and the type of lymph node dissection on the development of post-surgical lung edema.

MATERIAL AND METHODS

DEMOGRAPHICS
We studied 32 patients (mean age 62 years; 8 female) having elective lung resection between January 1st and September 30th 2000. IRB approval and written informed consent were obtained. All patients underwent either fiberoptic or rigid
bronchoscopy and had histology samples obtained preoperatively. Routine check-up consisted of thoracic imaging by standard chest x-rays and CT scans. Staging was completed by abdominal ultrasonography and cerebral CT scans. Where necessary, bone scans as well as ventilation and perfusion scintigraphies were performed for exact preoperative evaluation.

Inclusion criteria were patients suitable for surgery with pre- or intraoperatively staged non small cell lung carcinoma (NSCLC, n=28) with N0 or N1 disease on CT scan, biopsy bronchoscopy or mediastinoscopy. After surgery, by final pathology report, 4 cases turned out to have different types of histology (1 carcinoid, 1 SCLC “limited disease”, 1 benign lesion, 1 metastasis). 16 patients underwent lobectomies (11 upper lobe, 11 right sided), 3 sleeve lobectomies, 10 pneumonectomies (5 right sided) and 3 sleeve pneumonectomies. No preoperative chemo- or radiotherapy was performed in these patients.

Exclusion criteria were higher grades of pulmonary, cardiac, renal or arteriosclerotic diseases, aortic aneurysm and general contraindications against general anaesthesia or thoracotomy, as well as other malignant diseases. Vital capacity or FEV1 of less than 60% predicted value lead to exclusion.

**CARDIOPULMONARY MONITORING**

After induction of general anaesthesia by standardised means with electrocardiography, oxygen saturation and blood pressure monitoring using total intravenous anaesthesia (TIVA), a standard central venous line (Arrow™ International, Reading, Pennsylvania, USA) was introduced via the ipsilateral jugular vein. Central venous pressure was recorded. All patients were extubated immediately after surgery. Patients were routinely transferred from the ICU to regular wards after 48 hours.

**AGREEMENT DOUBLE AND SINGLE INDICATOR METHOD**

There has so far been a general recommendation against using the single indicator thermodilution method (PiCCOTM) in thoracic surgery. It was thought that pulmonary blood volume may be altered by the operation and thus lead to inexact values [10], because PiCCOTM does not measure pulmonary blood volume index (PBVI), but adds constantly 25% to global enddiastolic volume index (GEDI). In double indicator method (COLDTM), the data achieved are actual measured parameters. The indocyanin green is protein bound and stays strictly in the intravascular space, thus reflects unaltered data even during possible changes in factors like pulmonary blood volume. Since the double indicator method is a more invasive (large arterial introducer needed), risky (protein bound indicator may cause allergies and shock), technically more difficult and time consuming and, finally, more costly, the goal was to establish a single indicator method useful in lung resections. Agreement between PiCCOTM and COLDTM concerning cardiac index (CI) and GEDI was well investigated in the development of the PiCCOTM-system [11,12,24,25]. For comparison of ITBI and ELWI the first 9 patients underwent both double and single indicator methods.

**MEASUREMENT OF THORACIC FLUID VOLUMES**

Double indicator method (n=9) (COLDTM): A fiberoptic thermistor tipped catheter (Pulsiocath™, PV2023, Pulsion Medical Systems, Munich, Germany) was placed via the ipsilateral femoral artery by a 4 French introducer and positioned in the infrarenal aorta. The catheter was then connected to a double indicator computer device (COLD™ Z-021, Pulsion Medical Systems, Munich, Germany). In serial a single indicator computer device (PiCCOTM, Pulsion Medical Systems, Munich, Germany) was connected. 10 ml of cold indocyanin green (ICG-Pulsion™, Pulsion Medical Systems, Munich, Germany) mixed with cold (less than 8°C Celsius) normal saline were administered into the central venous line for the parallel measured of double and single indicator method.

Single indicator method (n=23) (PiCCOTM): A thermodilution catheter (Pulsiocath™, PV2014L08, Pulsion Medical Systems, Munich, Germany) was placed directly in the ipsilateral femoral artery. 20 ml of cold (less than 8°C Celsius) normal saline were administered into the central venous line for single indicator thermodilution method.

Cardiac index (CI), intrathoracic blood volume (ITBI) and extravascular lung water index (ELWI) were recorded [11,12,24,25]. To obtain more exact values than shown on PiCCOTM, with no decimals, we calculated the absolute EVLW values by dividing it by the patient’s weight in kilograms, obtaining a calculated ELWI. The PiCCOTM device calculated these data by mean transit time of the thermal indicator. ITBI is calculated by global enddiastolic volume index (GEDI) plus pulmonary blood volume index (PBVI). ELWI is intrathoracic thermo volume (“needle-to-needle”) minus ITBI.
RELATIVE CHANGES IN ITBI AND ELWI (ITBI-RELATIVE, ELWI-RELATIVE)

To receive the relative changes of ITBI and ELWI compared to the preoperative situations, the preoperative value for ITBI and ELWI were set to 100%. The postoperative change was given in percent changes at 0, 12, 24, 36 and 48 hours postoperatively for each single patient.

LUNG VOLUME ADJUSTED FOR ELWI-RELATIVE FOLLOWING SURGERY (ELWI-CORRECTED)

To account for the resected lung volume in thoracic surgery procedures we corrected the ELWI-relative to the predicted remaining lung volume following surgery. Based on anatomical data [13], depicted in Table 1, the ELWI-relative was transformed to ELWI-corrected using the term: ELWI-corrected (%) = ELWI-relative (%) / remaining lung volume (%) x 100.

Figure 1
Table 1: Estimated remaining lung volume in % following anatomical resection.

<table>
<thead>
<tr>
<th>Resection</th>
<th>Remaining lung volume (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left upper lobe</td>
<td>73.6</td>
</tr>
<tr>
<td>Left lower lobe</td>
<td>78.4</td>
</tr>
<tr>
<td>Left pneumonectomy</td>
<td>52.0</td>
</tr>
<tr>
<td>Right upper lobe</td>
<td>79.2</td>
</tr>
<tr>
<td>Right middle lobe</td>
<td>89.6</td>
</tr>
<tr>
<td>Right lower lobe</td>
<td>79.2</td>
</tr>
<tr>
<td>Right pneumonectomy</td>
<td>48.0</td>
</tr>
</tbody>
</table>

OPERATION PROCEDURE AND RANDOMIZATION

After placing the patient into the contralateral side position, a standard posterolateral thoracotomy was performed and radical excision of tumorous tissue by lobectomy or pneumonectomy. Patients were randomized in two groups at the time of data acquisition concerning the type of lymph node dissection: the “sampling” group with mediastinal lymph node sampling and the “radical” group with radical mediastinal lymphadenectomy by surgeons preference. Three patients received a bronchus sleeve procedure and 3 patients a sleeve pneumonectomy in combination with radical mediastinal lymphadenectomy in all 6 patients. At time of data analysis the results of these sleeve-resected patients were different from the non-sleeve resected patients.

A third group “radical with sleeve resection” was created by these patients data.

STATISTICAL ANALYSIS

Unless otherwise mentioned, all data are presented as means and standard error of the mean (SEM) for all variables. Continuous variables were checked for normality by plotting histograms. Variables that were not normally distributed were analysed using the Kruskal-Wallis test and the Mann-Whitney U test. Those that were normally distributed were assessed with a one-way analysis of variance and the Student’s t-test. Chi-square test for trend was used for non-normally distributed variables and Repeated Measures was used for normally distributed values and their changes over time. To prove agreement of ITBI and ELWI between COLD™ (a) and PiCCO™ (b) system, the Bland-Altman test was used requiring >95% of all measurement t differences to be inside the two standard deviation (SD) interval [14]. P values less than 0.05 were considered statistically significant. All tests were two-tailed. All statistical analyses were performed on a personal computer with the statistical package SPSS™ for Windows (Version 10.0, SPSS™, Chicago, USA).

RESULTS

AGREEMENT BETWEEN DOUBLE AND SINGLE INDICATOR METHOD (COLD™ AND PICCO™)

Nine patients underwent simultaneous double and single indicator method (COLD™ (a) and PiCCO™ (b)) to determine the degree of agreement between these systems. Bland-Altman testing showed significant agreement (>95% value differences within two SD) for all observed parameters, confirming prior studies in patients not undergoing lung resection surgery [1,11,12,24,25]. Lung surgery related results for ITBI and ELWI are shown in Figure 1, previously published, cardiac related parameters are not shown (CI, GEDI). We concluded that single indicator method (PiCCO™) delivers valuable data compared with the double indicator method (COLD™). Therefore the single indicator method alone was used in the remaining 23 patients.
Figure 2
Figure 1: Agreement between double and single indicator method (COLDÂ™ and PiCCOÂ™) Bland-Altman testing showed significant agreement (>95% value differences within two SD, n=48) for ITBI [A] and ELWI [B] between double (a=COLDÂ™) and single (b=PiCCOÂ™) indicator method systems (ITBI (COLDÂ™-PiCCOÂ™) mean 23.1 Â± 96.4 SD ml/m ; ELWI (COLDÂ™-PiCCOÂ™) mean Â–0.21 Â± 1.05 SD ml/kg).

GENERAL FINDINGS
The “sampling” group included 17 patients; the “radical” group -including the sleeve procedures- had 15 patients. No significant differences were seen between these groups concerning mean age 63 (52-75) years for the “sampling” group and 61 (41-72) years for the “radical” group. Vital capacity (92.3 ±13.3% SD versus 92.9 ±17.14% SD), FEV1 (84.6 ±12.9% SD versus 83.0 ±14.8% SD) pO2, pCO2, and SaO2 were not significantly different between groups and performed procedures. Changes in CI, GEDI and CVP were not significantly different between study groups (sampling versus radical) and performed procedures throughout the observation period.

DIFFERENCES BETWEEN LOBECTOMIES AND PNEUMONECTOMIES
Looking at differences between performed procedures (lobectomies, n=19; pneumonectomies, n=13) independently of the type of lymph node dissection, there were significant (p=0.032) changes throughout the 48 hours period postoperatively concerning the relative ITBI including the sleeve procedures. The values for pneumonectomies were predominately lower throughout the observation period (Figure 2A) showing that these cases were consistently carried out with less volume substitution. The relative ELWI decrease was procedure specific, with a mean decrease of 11.7% seen after lobectomy and 33.6% after pneumonectomy (p=0.006). There were no statistically significant changes found throughout the postoperative observation period within the same procedure group (Figure 2B).

Figure 3
Figure 2: ITBI relative and ELWI relative differences by type of lung resection

[43x799]Radical Lymphadenectomy Does Not Effect Intrathoracic Fluid Volume Changes After Lung Surgery

4 of 8
Radical Lymphadenectomy Does Not Effect Intrathoracic Fluid Volume Changes After Lung Surgery

was corrected by the anatomical lung volume resection (Table 1).

INFLUENCE OF SAMPLING AND RADICAL LYMPHNODE DISSECTION

No significant changes (p>0.3) in ITBI relative and ELWI corrected were observed throughout the 48 hours study period in lobectomies (Figure 3A+B) and pneumonectomies (Figure 4A+B).

Figure 4

Figure 3: Lobectomies: ITBI relative and ELWI corrected

[A] Relative ITBI was not different between sampling or radical lymphnode dissection and radical with sleeve resection lobectomies. Corrected ELWI was significantly increased in sleeve resected cases within the first 12 hours of observation compared to non-sleeve procedures (p=0.031). No significant changes in corrected ELWI were observed between sampling and radical lymphnode dissection.

Figure 5

Figure 4: Pneumonectomies: ITBI relative and ELWI corrected

[A] Relative ITBI was significantly decreased throughout the observation period of 48 hours in sleeve pneumonectomies (p=0.002) compared to non-sleeve procedures. Corrected ELWI increased in all pneumonectomy cases after surgery. Sleeve resected cases peaked at a mean of 175 ±21% normalized to the preoperative value (100%), resulting in a significant increase with in the first 12 hours after sleeve pneumonectomy (p=0.031) compared to non-sleeve procedures. Between 24 and 48 hours following pneumonectomy a slight increase in ELWI corr. was observed in all groups, showing no significant differences between groups. Comparing early ITBI and ELWI results, sleeve pneumonectomies showed a high potential to accumulate lung water even in a setting of significantly lower ITBI.

INFLUENCE OF SLEEVE RESECTION PROCEDURES

In sleeve lobectomies the relative ITBI was not different compared to non sleeve lobectomies (Figure 3A) and ranged in the mean between 93-116% of the preoperative value. A significant increase in corrected ELWI was observed in sleeve resected patients with in the first 12 hours of observation compared to non sleeve procedures (sampling
and radical combined \(p=0.003\). The values for lung volume corrected ELWI in the sleeve resected group was found to be a mean of 169 ±47% postoperatively and 175 ±40% at 12 hours, a significant increase compared to the values in the non sleeve resected group, which ranged between 105-133% (Figure 3B).

The findings in sleeve pneumonectomies were similar to the findings in sleeve lobectomies. Throughout the observation period of 48 hours, the relative ITBI was significantly decreased in patients who underwent sleeve pneumonectomies \(p=0.002\). ITBI relative values ranged between 59-85\% of the preoperatively measurements, where as non sleeve resected patients showed stable postoperative values within the first 24 hours of observation (95-106\%) and even slight increases in relative ITBI for the following time period (100-116\%) (Figure 4A). The corrected ELWI increased in all pneumonectomy cases after surgery. For non sleeve resected cases, an increase of the mean value to 130-136\% was observed. Compared to these values, sleeve resected cases peaked at a mean of 175 ±21\% normalized to the preoperative value (100\%). This extreme rise of corrected ELWI within the first 12 hours after pneumonectomy in sleeve resected cases was significant compared to the non sleeve resected cases \(p=0.031\).

Between 24 and 48 hours following pneumonectomy a slight increase was observed in all groups, with mean ranges of 125-148\%, showing no significant differences (Figure 4B). A summary observation comparing early ITBI and ELWI results in Figure 4 showed the high potential in sleeve pneumonectomies to accumulate lung water in a setting of even significant lower intrathoracic blood volume.

**DISCUSSION**

**AGREEMENT BETWEEN DOUBLE AND SINGLE INDICATOR METHOD**

In this study we confirmed the high correlation between the COLD\(\text{TM}\) and PiCCO\(\text{TM}\) system readouts \([1,11,12,20,24,25]\). Focusing on the parameter regarding intrathoracic volume changes (ITBI, ELWI), we were able to show that the PiCCO\(\text{TM}\) system is a useful tool in detecting non-cardiac lung edema after lung surgery.

**TECHNICAL AND ANATOMICAL PRECAUTIONS**

The raw values computed by the PiCCO\(\text{TM}\) system for ITBI and ELWI were subject to large interindividual variation \([12,24,112]\). To account for these individual settings a preoperative value was needed to normalize the postoperative values accordingly. We calculated “relative” ITBI and ELWI values for normalization, shown in the paper in %-values. At the bedside situation in the ICU a taped preoperative value printout next to the PiCCO\(\text{TM}\) monitor allowed a quick rough estimation of the “relative” values.

Since the PiCCO\(\text{TM}\) system primarily was developed for cardiac monitoring the calculation of the lung volume is a fixed value based on weight & height \([1,12,20,25]\). To account for the reduced lung volume the postoperative relative ELWI was corrected for the anatomical amount of remaining lung volume after surgery. This seemed to be a critical point in data interpretation. For example: the preoperative ELWI was 8 ml/kg, a pneumonectomy was performed and the postoperative value is again 8 ml/kg. This does not depict stable conditions, but rather shows, at a postoperative predicted ELWI of 4 ml/kg, there is double the amount of lung water in the remaining lung, a condition which would result in severe clinical symptoms unless treated. A calculated lung volume adaptation is essential.

Based on lung physiology it is given that pulmonary blood volume index (PBVI) would not significantly change with lung removal surgery. Even in a pneumonectomy the PBVI remains stable, since pulmonal arteries are vessels with a very high potential of volume uptake without significant intraarterial pressure alterations. The total cardiac output is driven into the remaining pulmonal system. Therefore the ITBI remains stable and does not need lung volume adaptation compared to ELWI \([12,17,19,117]\).

**TYPE OF LYMPHADENECTOMY**

As postoperative non-cardiac lung edema is a well-known complication of thoracic surgery, we tried to determine whether the type of lymphadenectomy plays a role in this phenomenon. We could not find any significant differences between lymph node sampling and ipsilateral radical mediastinal lymphadenectomy. We could not find any physiologic contradiction against routine radical lymphadenectomy, which is strongly recommended \([18,19]\).

**SLEEVE RESECTION**

We observed independent of performed procedures (lobectomy or pneumonectomy) a highly significant increase in lung water (ELWI corr.) in the early postoperative phase in the patients that underwent bronchus sleeve procedures. The values reached substantial levels, up to double the amount of preoperative lung water, even though the early ITBI was significantly decreased. Sleeve pneumonectomies showed the high potential to accumulate lung water. Reasons
could be the interrupted lymphatic drainage \[16,18,20\]. Reexpansion, intraoperative manipulation and reperfusion injury are factors that influence non-cardiac intrapulmonary fluid volumes, but cannot be prevented during surgery \[17,21,22\].

**CORRESPONDENCE TO**

Carsten Schröder, MD
Dept. of Thoracic and Vascular Surgery,
Heidehaus Hospital (Hannover Medical School)

Current Address: 3448 Merrick Drive, Lexington, KY, 40502, USA Tel: +1 859-608-5154 Fax: +1 859-258-4296 E-mail: dr_c_schroeder@yahoo.com

**References**

Author Information

Carsten Schröder, M.D.
Department of Vascular and Thoracic Surgery, Hannover Medical School, Heidehaus Hospital

Karsten Kuhn, M.D.
Department of Vascular and Thoracic Surgery, Hannover Medical School, Heidehaus Hospital

Paolo Macchiarini, M.D., Ph.D.
Department of Vascular and Thoracic Surgery, Hannover Medical School, Heidehaus Hospital