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Pulmonary Edema Induced by Esophagectomy

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1. Introduction

Esophageal cancer is the seventh leading cause of cancer deaths worldwide (410,000 new cases annually)(1). Asian, Middle Eastern, and East African countries have a markedly higher incidence of esophageal cancer than other areas. In the United States, the incidence of adenocarcinoma of the distal esophagus and gastroesophageal junction has progressively increased to approximately 70% of all esophageal cancers over the last two decades. It affects mostly Caucasian men, and its pathogenesis is linked to gastroesophageal reflux disease (GERD) and the development of Barrett's esophagus. On the other hand, squamous cell carcinoma is responsible for 95% of all esophageal cancers worldwide. It arises from whole esophagus, from the cervical esophagus to the gastroesophageal junction, and spreads to the cervical, thoracic, and abdominal lymph nodes with relative ease because of the abundant and complex lymphatic network (2). Therefore, esophagectomy with extensive neck, thoracic, and abdominal lymph node dissection, the so-called "3-field lymph node dissection," is needed for curative surgery for esophageal squamous cell carcinoma (3). Though chemotherapy, radiotherapy, and combination therapy of both have been substantially developed as treatments for esophageal squamous cell carcinoma in recent years, these treatments are still inferior in survival rate and late toxicity compared to surgery (4).

Esophagectomy with 3-field lymph node dissection is one of the most invasive surgical procedures. This highly invasive surgery is currently still associated with high morbidity, despite improvements in surgical techniques and perioperative managements. A "cytokine storm" during and after esophagectomy induces severe hemodynamic changes involving loss of circulating blood volume and filling of the third space. Furthermore, extensive lymph node dissection and ligation or excision of the thoracic duct have a causal influence on mediastinal lymphostasis, which disturbs drainage of extravascular lung water (EVLW) from the lungs and causes pulmonary edema. Pulmonary edema may form the base of pulmonary complications such as atelectasis and pneumonia, the most common complications after esophagectomy.

Monitoring of EVLW in cases of critically ill patients with acute lung injury (ALI) or acute respiratory distress syndrome (ARDS) has proved to be very informative and useful for predicting outcome (5.6).

Based on these findings, we monitored perioperative changes in EVLW using the recently developed single transpulmonary thermodilution technique to determine whether EVLW correlates with respiratory function and predicts pulmonary complications. In this chapter, we expound on the importance of recognizing and monitoring EVLW during perioperative managements of esophagectomy for thoracic esophageal squamous cell carcinoma.

2. Extravascular Lung Water (EVLW)

EVLW is the amount of water that is present in the lungs outside of the pulmonary vasculature, put simply, the alveoli and interstitium of the lungs. Thus, EVLW is a quantitative term describing pulmonary edema. EVLW is expressed using the formulas described in **Fig.1**. Intrathoracic thermal volume (ITTV) is computed by multiplying cardiac output (CO) by mean transit time (MTt), which is the time when half of the indicator has passed the point of detection of the artery. Pulmonary thermal volume (PTV) is computed by multiplying CO by downslope time (DSt), which is the exponential downslope time of the thermodilution curve. Global end diastolic volume (GEDV) is calculated by subtracting PTV from ITTV. Intrathoracic blood volume (ITBV) is expressed as GEDV x 1.25. Finally, EVLW is calculated by subtracting ITBV from ITTV. Extravascular lung water index (EVLWI, EVLW/body surface area, ml/m^2) is a more precise parameter than EVLW and provides more accurate results, particularly in overweight patients.

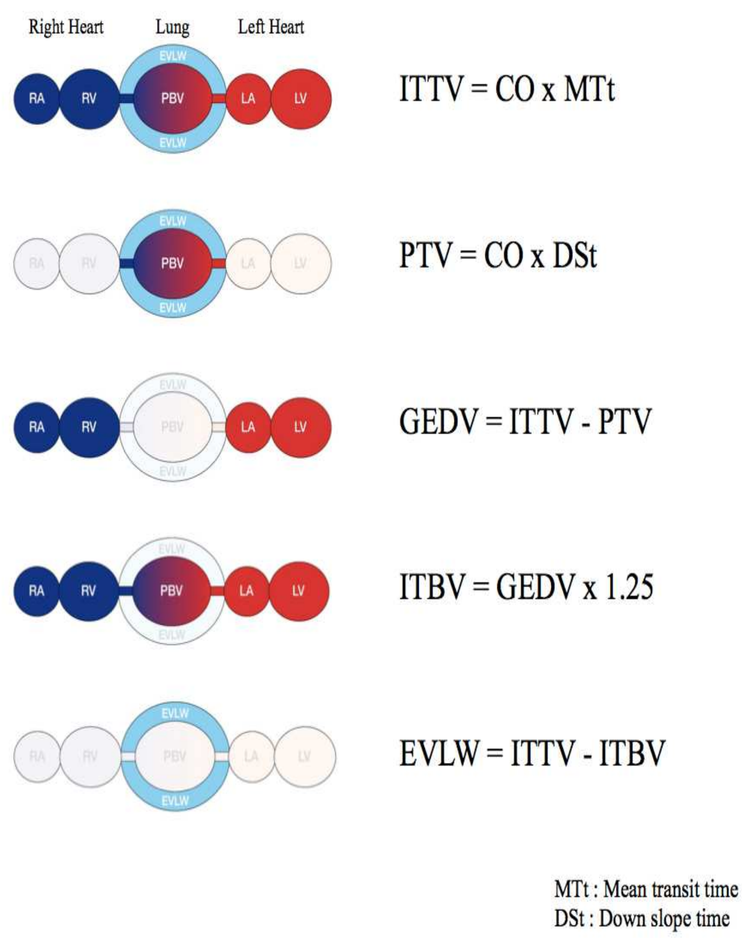

Fig. 1. EVLW and other parameters such as intrathoracic thermal volume (ITTV), pulmonary thermal volume (PTV), global end diastolic volume (GEDV), and intrathoracic blood volume (ITBV) are described with these formulas.

3. PiCCO

PiCCO (Pulsion Medical Systems, Munich, Germany, http://www.pulsion.com) is a less invasive advanced hemodynamic monitoring system employing the single transpulmonary thermodilution technique **(Fig.2)**. It requires only a standard central venous catheter and a femoral, axillary, brachial, or radial artery catheter (but not a pulmonary artery catheter). This system enables monitoring of cardiac function, vascular tone, and fluid distribution, including EVLW. EVLW and EVLWI are automatically calculated after a bolus infusion of cold saline via the central venous catheter. As mentioned above, monitoring EVLW using this system in critically ill patients with ALI/ARDS has proved to be very informative and useful for predicting outcome. The current PiCCO2 system is employed for management of patients not only with ALI / ARDS but also septic shock, burns, major surgery, and cardiac surgery, among others.

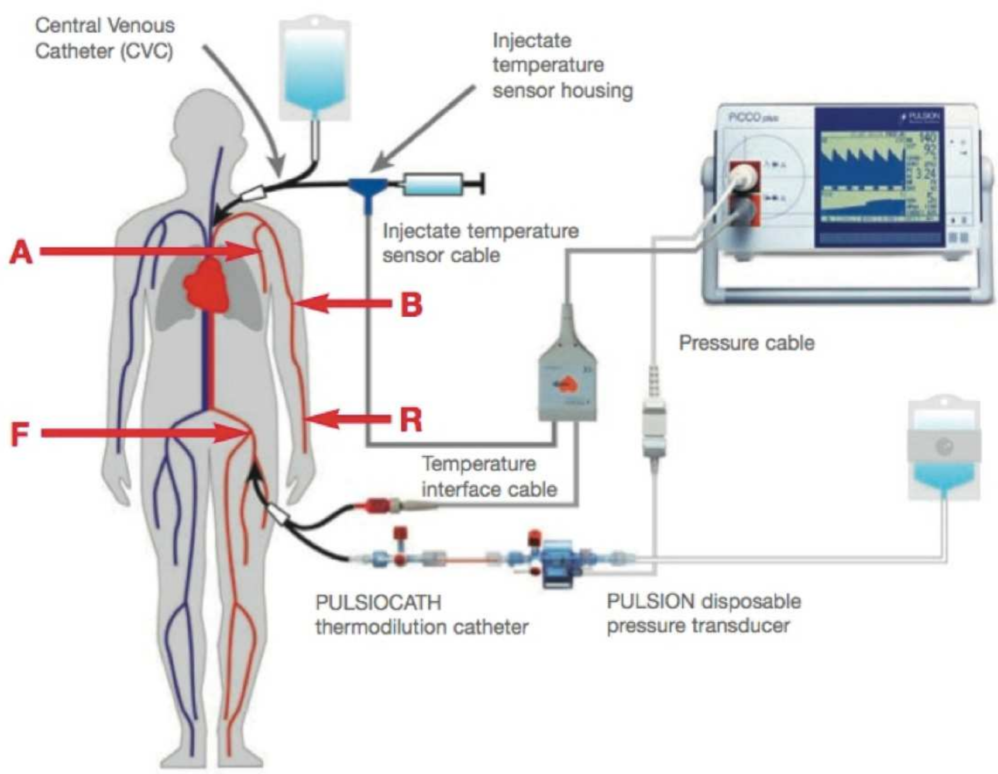

Fig. 2. General outline of the PiCCO system, which requires only a standard central venous catheter and a femoral, axillary, brachial, or radial artery catheter, but not a pulmonary artery catheter.

4. EVLW monitoring predicts pulmonary complications after esophagectomy

To determine whether EVLW correlates with respiratory function and predicts pulmonary complications after esophagectomy, we enrolled 23 patients with thoracic esophageal cancer in a prospective observational clinical trial (8). Informed consent was obtained from all patients.

All of these patients underwent esophagectomy with extensive lymph node dissection and reconstruction involving insertion of a gastric tube via the posterior mediastinal route. They were also monitored perioperatively using PiCCO from the day prior to surgery through postoperative day (POD) two. Our standard operative procedure is right transthoracic esophagectomy and resection of the lesser curvature with dissection of the mediastinal (involving the periesophageal region and areas around trachea and bilateral main bronchus), the abdominal (involving the perigastric region and areas around the celiac axis), and the bilateral neck lymph nodes (areas around common carotid artery, internal jugular vein and transverse cervical artery), the so-called "three-field lymph node dissection". Following surgery, the extubation criteria for the intratracheal tube were PaO_2 >100 Torr with a <40% inspired fraction of oxygen (FiO_2), forced vital capacity >800 ml, and no pulmonary complications. Based on these extubation criteria, the tracheal tubes were removed from 11 patients on the morning of POD one (extubation group); the remaining 12 patients remained intubated (intubation group). The respiratory Index was calculated using the following equation: respiratory index = $(PAO_2 - PaO_2)/PaO_2$, where $PAO_2 = [(760 - 47$ (atmospheric pressure)) x $FiO_2 - PaCO_2/0.8]$. The respiratory index essentially reflects the ability to oxygenate the lung.

In all patients, EVLW correlated significantly with the respiratory index ($r = 0.638$, $p < 0.0001$) at all measurement points after surgery (**Fig. 3**). The changes in EVLW and respiratory index during the perioperative period in the extubation and intubation groups are shown separately in **Fig.4**. In the extubation group, EVLW was clearly reduced immediately after surgery ($p = 0.0068$), but it recovered to preoperative levels within 12 h after surgery and remained at that

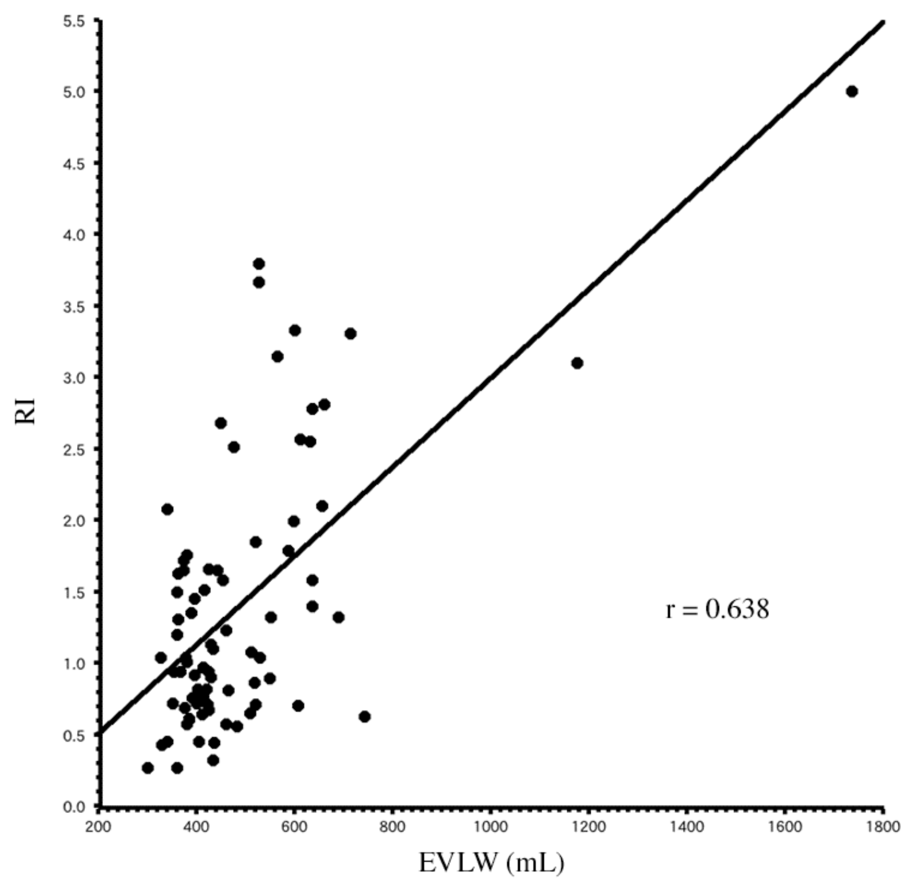

Fig. 3. EVLW correlated significantly with the respiratory index (RI) ($r = 0.638$, $p < 0.0001$) at all measurement points after esophagectomy.

level through POD two. By contrast, in the intubation group, both EVLW and respiratory index were elevated 12 h after surgery and were even higher 24 h after surgery. All of the patients in the extubation group recovered with no pulmonary complications, whereas four patients (33%) in the intubation group developed pneumonia or atelectasis that required artificial respiration managements. In all four patients that developed pulmonary complications, an increase in EVLW preceded their onset.

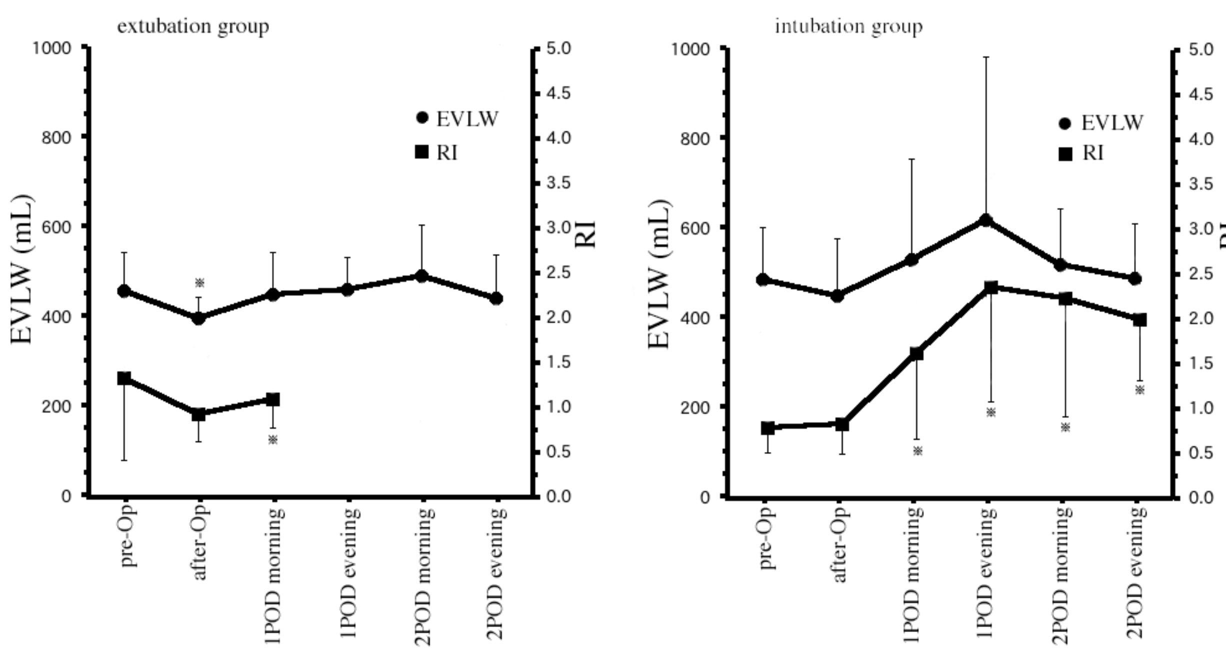

Fig. 4. The changes in EVLW and the respiratory index (RI) during the perioperative period in the extubation and intubation groups. In the intubation group, both EVLW and respiratory index were elevated 12 h after surgery and were even higher 24 h after surgery.

5. Conclusion

We have shown that EVLW measured using the PiCCO system reflects the level of postoperative pulmonary edema induced by esophagectomy with extended lymph node dissection. Patients who showed no significant postoperative changes in EVLW or respiratory index recovered without pulmonary complications. By contrast, those patients who showed an increase in EVLW on POD one showed a substantial increase in their respiratory index, and some developed pulmonary complications. Measurement of the EVLW using the PiCCO system thus proved to be a useful method for monitoring the pulmonary edema and was predictive of the pulmonary complications that subsequently occurred. This PiCCO system enables us to begin early managements of patients who develop pulmonary edema following esophagectomy with extensive lymph node dissection.

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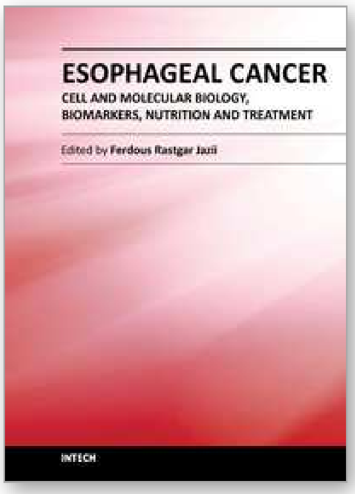

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Esophageal Cancer illustrates recent achievements and investigations in the esophageal tumorigenesis from different perspectives. Readers find mechanisms involved in esophageal tumorigenesis, cellular, molecular, genetic, epigenetics, and proteomics, their relevance as the novel biomarkers and application in esophageal cancer diagnosis and therapy. The book covers detailed effect of nutritional factors in addition to ethanol metabolic pathway in the inhibition of retinoic acid metabolism and supply. Diagnosis, classification, and treatment of esophageal cancer, application of both surgical and non surgical methods as well as follow up of the disease are described in detail. Moreover readers are endowed with especial features of esophageal cancer such as multiple early stage malignant melanoma and pulmonary edema induced by esophagectomy, the two features that received less attention elsewhere in literature.

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