Introduction:
Acute lung injury (ALI) and the adult respiratory distress syndrome (ARDS) are responsible for the vast majority of respiratory-related death after thoracic surgery (1). There has been reported an overall prevalence rate of 2.2-4.2 % post-thoracotomy ALI/ARDS in patients undergoing lung resection (2, 3).

The concept of “lung protective ventilation” includes the use of low-tidal volumes, positive expiratory pressure (PEEP) and limitation of maximum inspiratory pressure (4, 5). There is a clear correlation between positive inspiratory pressure and mortality: the lower the level of maximum inspiratory pressure, the better the outcome (6).

However, the implementation of lung-protective concepts is frequently limited by a therapeutic dilemma: A reduced oxygenation often requires high end-expiratory pressure which limits carbon dioxide elimination with subsequent risk of severe hypercapnia. Hyperkapnia results in pulmonary and cardiac vasoconstriction, peripheral arterial and cerebral vasodilation, increased cardiac output, delivery from catecholamines, reduction of renal perfusion and triggers respiratory drive with the pathophysiological consequence of organ damage (myocardial insufficiency, renal failure, restriction of liver/intestinal circulation).

Therefore, in such cases of severe hypoxemia and hypercapnia the use of extracorporeal lung ventilatory support might be indicated (7, 8).

ECMO:
The modern era of extracorporeal membrane oxygenation (ECMO) for adults with ARDS was pioneered by Bartlett and colleagues in 1972 (9). In a recent multicenter randomized controlled trial (CAESAR trial), ECMO treated patients with ARDS had a 6 month survival benefit compared to non-ECMO treated patients (10).

ECMO can be inserted in veno-venous (VV) configuration in case of respiratory failure with severe hypoxemia (not responding to mechanical ventilation and lung protective strategies) or can be used as veno-arterial (VA) configuration (providing both respiratory and cardiac support).

In the last two decades, cannulae have improved flow dynamics allowing percutaneous insertion with the Seldinger technique into femoral and jugular vessels which is the standard of ARDS centers (11). Percutaneous insertion is associated with less bleeding complication.
as well as lower risk of infection. In order to facilitate this high flow, the placement of large catheters is indicated (> 20 French or larger).

**Criteria for ECMO indication (12):**

\[ \text{PaO}_2/\text{FiO}_2 < 80 \text{ mmHg}, \ \text{PIP} > 35 \text{ mmHg (first 24 hours)} \]

**Fast-Entry:**

\[ \text{PaO}_2/\text{FiO}_2 < 50 \text{ mmHg}, \ \text{PIP} > 35 \text{ (over 2 hours)} \]

Hypoxia is treated by increasing both the ECMO flow rate and FIO\(_2\) of the ECMO circuit, **not by altering the FIO\(_2\) and PEEP on the ventilator.** Elimination of CO\(_2\) depends on gasflow over the membrane and **not by increasing the respiratory rate on the ventilator.**

**Weaning criteria ECMO:**

\[ \text{FiO}_2 < 0.4, \ \text{PaO}_2 > 80 \text{ mmHg} \]

Target ventilator settings: PEEP ± 12 cm H\(_2\)O, PIP < 30 cm H\(_2\)O, Vt: 4-6 ml/kg

Respiratory rate spontaneous: -5/5/min

Weaning procedure includes the reduction of blood flow (0.5 l/min) every 12 hours to minimal blood flow of 0.5-1 l/min and the reduction of gas flow and F\(_2\)O\(_2\) over membrane.

ECMO trial off: gas flow 0.5-1 L/min over 15 min: if criteria fulfilled, discontinuation of ECMO.

Due to the fact, that current devices are coated with heparin, only a low level of systemic anticoagulation is necessary to prevent clotting of the cannulae, tubing and oxygenator (activated partial thromboplastin time (APTT) 50-70 s, high flow systems (5-7 l/min: 50 s). In case of heparin-induced thrombocytopenia (HITT), argatroban seems to be an alternative for anticoagulation on ECMO (13).

The most common complications associated with ECMO are life-threatening thrombosis and excessive bleeding caused by coagulaopathy (14). Furthermore, despite the use of ECMO in acute respiratory and cardiac failure increases survival, but may on the same time cause damage to the brain (15). Changes in cerebral blood flow and the use of heparin may contribute to both hemorrhagic and nonhemorrhagic intracranial lesions. Hypoxia is thought to be one of the most important factors developing cerebral injury (16). In addition, ECMO therapy itself can cause cerebral injury (16). Systemic insults and hypoxia can disrupt cerebral autoregulation, leaving the cerebral microcirculation vulnerable to changes in systemic blood pressure. Hypotension can result in ischemic cerebral damage and hypertension can cause cerebral hyperemia and increase the risk of cerebral hemorrhage. During VA ECMO, cerebral perfusion is mainly nonpulsatile which may lead to diffuse brain edema (17). The risk is reduced in VV-ECMO, in which the cerebral perfusion is pulsatile (17).

**Novalung (iLA)**

iLA was first described by Pott and colleagues (18) in 1951. In 1999, the iLA as the first pumpless mode for CO\(_2\) removal was developed and applied in a patient (20).
The iLA device is a pumpless arterio-venous shunt with carbon dioxide elimination as primary function owing to the arterial inflow blood. The principle is simple diffusion. The iLA is a low pressure-gradient device designed to operate without a mechanical pump. Based on this principle, adequate mean arterial blood pressure is mandatory. The preferred access sites are the femoral vessels by percutaneous cannulation using Seldinger’s technique. The major limitation of this device is that patients with primary oxygenation disorder may not sufficiently benefit from the pumpless iLA mode in terms of oxygenation.

**Criteria for iLA (Novalung) indication (12):**

- \( \text{PaCO}_2 > 80 \text{ mmHg} \); \( \text{PIP} > 35 \text{ cm H}_2\text{O} \); \( \text{pH} < 7,2 \) and \( \text{PaO}_2/\text{FiO}_2 > 80 \text{ mmHg} \)

**Weaning criteria iLA:**

- RASS 0/-1
- \( \text{F}_1\text{O}_2 < 0.4 \), \( \text{PaCO}_2 < 60 \text{ mmHg} \), \( \text{PIP} < 30 \text{ H}_2\text{O} \), \( \text{Vt: 4-6 ml/kg} \),
- Respiratory rate spontaneous – 5/min

**Weaning procedure:**

- Reducing \( \text{O}_2 \) flow iLA in steps of 1l/min
- iLA flow < 2 l/min over 6 h without gas flow
- iLA trial off: criteria fulfilled: discontinue iLA

The iLA can be used for \( \text{CO}_2 \) removal in cases of severe hypercapnia and acidosis in order to avoid the injury of mechanical support. However, apart from several indications (bridging to lung transplant, respiratory failure after lung resection, bronchopleural fistulas etc.) no outcome data are currently available.

Ischemic complications of the lower limb were reported to be associated with the large cannulation size for the arterial cannulation (17 French). As smaller cannulae (13 and 15 F) have become available, the ischemic complication rate has markedly decreased (21).

**Multimodal therapeutic approach:**

The concept of extracorporeal ventilatory therapy is part of the multimodal approach of the ABCDE- bundles (22): This means, daily assessment of the level of sedation, analgesia and delirium detection, as well as early spontaneous breathing (decreasing intrapulmonary shunt and intrathoracic pressures) (22, 23, 24).

**References:**