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MODERN CONCEPTS OF ARTIFICIAL LUNG VENTILATION DURING GENERAL ANESTHESIA IN CANCER PATIENTS: A LITERATURE REVIEW

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ABSTRACT

Relevance: *Among patients who have undergone extensive surgical interventions under general anesthesia with artificial ventilation (ventilator), various postoperative respiratory complications of an obstructive or restrictive nature are often found*

The study aimed to *generalize current data from systematic reviews, meta-analyses, and scientific publications on the use of preventive and therapeutic strategies for lung ventilation to improve the quality of anesthetic care for cancer patients.*

Methods: *The PubMed Electronic Database (NCBI) was searched to identify randomized controlled and prospective observational studies, systematic reviews, and meta-analyses, as well as scientific articles published in English between 2016 and 2023 that focused on the results of application and comparison of lung protective ventilation strategies with conventional mechanical ventilation in patients undergoing major and prolonged surgery.*

Results: *As a result of a comparison of data from a review of large-scale scientific studies and articles, a relationship was established between the use of a protective lung ventilation strategy with a low tidal volume (6-8 mL/kg of ideal body weight), in combination with individualized PEEP, periodic lung recruitment maneuvers and significant improvement in clinical outcomes, respiratory complications, early mortality and length of hospital stay in patients undergoing surgery.*

Conclusion: *Using protective lung ventilation during anesthesia during major surgical interventions reduces the incidence of postoperative pulmonary complications.*

Keywords: *modern concepts of mechanical ventilation, postoperative pulmonary complications, low tidal volume, individualized PEEP.*

Introduction: More than 230 million surgical interventions are performed annually in the world. Postoperative pulmonary complications are one of the most serious consequences that have a negative effect on treatment outcomes and post-surgical mortality [1].

Postoperative pulmonary complications occur in 11-33% of operated patients [2].

Large tidal volumes were initially recommended to prevent the occurrence of atelectasis and hypoxemia during general anesthesia for major abdominal and thoracic surgery [3].

According to many studies, during IVL, the alveolar epithelium was damaged due to mechanical overstretching and inflammatory cytokines were released, such as tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), IL-8 and 10, which contribute to the activation of macrophages and neutrophils. These cells produce large amounts of collagenase and elastase and release large amounts of active oxygen. All of these substances can directly or indirectly destroy alveolar epithelial cells or even vascular endothelial cells, resulting in damage to lung tissue [4].

In most studies, the primary outcome was the frequency of postoperative pulmonary complications defined as the combination of any respiratory infection, respiratory failure, pleural effusion, atelectasis, or pneumothorax following the European Perioperative Clinical Outcome consensus statement (Table 1) [5]. The length of stay in the hospital and the intensive care unit (ICU) and in-hospital mortality were also assessed [6].

Some large-scale studies utilized p/f index, arterial oxygen tension (PaO_2) and PCO_2 in arterial blood before, during, and after trachea extubation in ICU, $etCO_2$, dead-space fraction (Vd/Vt), and lung compliance as estimates of the use of protective lung ventilation during surgery [7].

The study aimed to generalize current data from systematic reviews, meta-analyses, and scientific publications on the use of preventive and therapeutic strategies for lung ventilation to improve the quality of anesthetic care for cancer patients.

Materials and Methods: The PubMed (NCBI) database was searched for randomized controlled trials (RCT) and prospective observational studies, systematic reviews, meta-analyses and scientific articles published in English from 2016 to 2023 and focusing mainly on the outcomes and comparison of lung protective ventilation strategies and conventional mechanical ventilation in patients undergoing extensive and prolonged surgical interventions. RCT and prospective observational studies, systematic reviews, meta-analyses and scientific articles on the use of a lung protective ventilation strategy during surgery in pregnant women, children and patients with underlying chronic lung diseases were excluded.

This analytical review included 11 systematic reviews and meta-analyses, 11 RCTs, 1 retrospective study, and 1 review of foreign recommendations.

Table 1 – Definition of postoperative respiratory complications according to the European consensus statement on perioperative clinical outcomes [5]

Complication	Definition
Respiratory infection	Patient has received antibiotics for a suspected respiratory infection and met one or more of the following criteria: new or changed sputum, new or changed lung opacities, fever, white blood cell count >12×10^9/л.
Respiratory failure	Postoperative PaO_2<8 kPa (60 mmHg) on room air, a PaO_2:FiO_2<40 kPa (300 mmHg) or arterial oxyhaemoglobin saturation measured with pulse oximetry <90% and requiring oxygen therapy.
Pleural effusion	Chest radiograph demonstrating blunting of the costophrenic angle, loss of sharp silhouette of the ipsilateral hemidiaphragm in upright position, evidence of displacement of adjacent anatomical structures or (in supine position) a hazy opacity in one hemithorax with preserved vascular shadows.
Atelectasis	Lung opacification with a shift of the mediastinum, hilum or hemidiaphragm toward the affected area, and compensatory over-inflation in the adjacent non-atelectatic lung.
Pneumothorax	Air in the pleural space with no vascular bed surrounding the visceral pleura.

Results: The conducted review of scientific publications, results of RCTs and prospective observational studies, systematic reviews, and meta-analyses that compared lung protective ventilation strategies and conventional mechanical ventilation in various surgical interventions (cardiac surgery, abdominal surgery, laparoscopic surgery, neurosurgery, spinal surgery, and thoracic surgery) showed that lung protective ventilation strategy during anesthesia that includes low tidal volume, optimal positive end-expiratory pressure (PEEP) and periodic lung recruitment maneuvers might improve intraoperative oxygenation of the body and pulmonary mechanics and reduce the incidence of early postoperative atelectasis [7-11].

A meta-analysis conducted by Yang et al. to compare mechanical ventilation with low tidal volume (n=521) and conventional lung ventilation (n=533) and their impact on the postoperative incidence of atelectasis, lung infection, acute lung injury (acute respiratory distress syndrome), and length of hospital stay, included 16 studies with a total of 1054 patients. The analysis revealed a statistically significant reduction in postoperative lung infection (OR (odds ratio) = 0.21, 95% CI (confidence interval) 0.09-0.50, P-value (significance level) = 0.0003), atelectasis (OR=0.36, 95% CI 0.20-0.64, P-value = 0.006), acute lung injury (OR=0.15, 95% CI 0.04-0.61, P-value = 0.008), and duration of hospital stay (mean difference = -2.08, 95% CI -3.95 to -0.21, P-value = 0.03) when using lung-protective ventilation (LTV, PEEP, recruitment maneuvers) compared with conventional ventilation during general anesthesia [12].

The use of lung-protective ventilation in surgical interventions through laparotomic access, as well as during laparoscopic abdominal and gynecological operations and robot-assisted laparoscopic prostatectomy, significantly reduces the incidence of postoperative pulmonary complications due to improved pulmonary function and intraoperative body oxygenation [13-16].

In an RCT by Liu et al., ventilation with a low tidal volume of 6-8 mL/kg ideal body weight (IBW), moderate PEEP-6, and periodic recruitment maneuvers (every 30 minutes in the study) improve pulmonary mechanics during anesthesia of more than 6 hours and reduce the development of postoperative respiratory complications (Figure 1) [17]. The researchers also reported an increase in static compliance of the lungs (Cstat) (Fig. 2) and a reduction in driving pressure (Figure 3) during lung-protective ventilation compared with conventional laparoscopic lung ventilation. Figures 2 & 3 provide mean ± standard deviation. The difference between the two groups was significant at p<0.05 [18].

Moreover, an RCT by Park et al. on the study of the parameters of protective ventilation of the lungs during laparoscopic operations in hepatobiliary surgery proved the positive effect of the lung recruitment maneuver on oxygenation. This might be due to optimal alveolar recruitment, improved regional pulmonary ventilation, and normalization of the ventilation-perfusion ratio, as evidenced by a decrease in the alveolar-arterial oxygen gradient ($AaDO_2$). The effect of PEEP was due to the maintenance of adequate alveolar gas exchange. Significance when compared with group R was P<0.05 (Figure 4) [9].

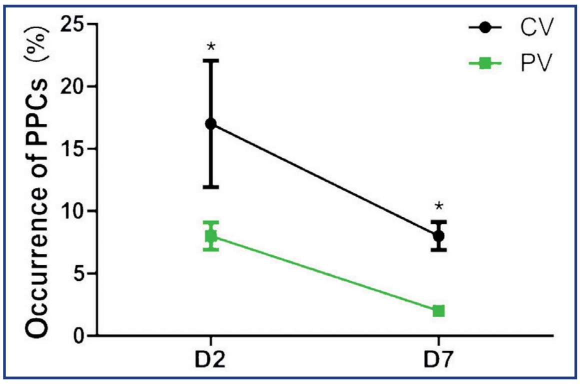
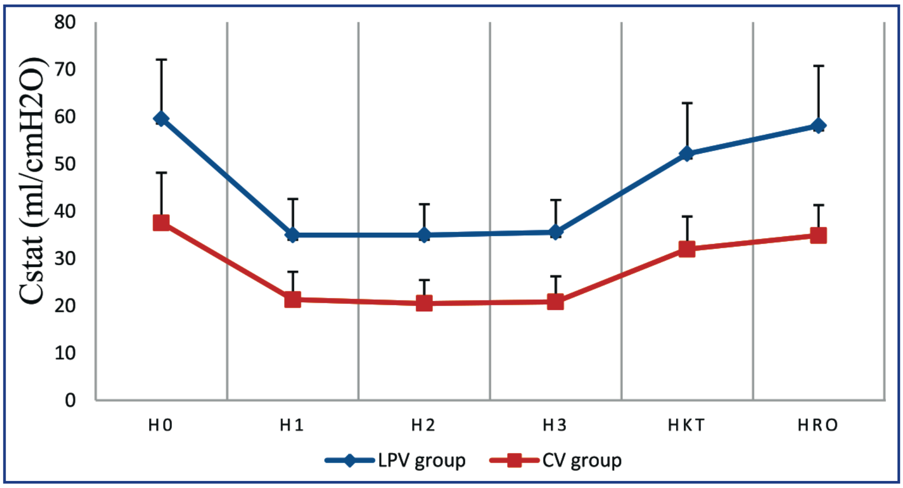
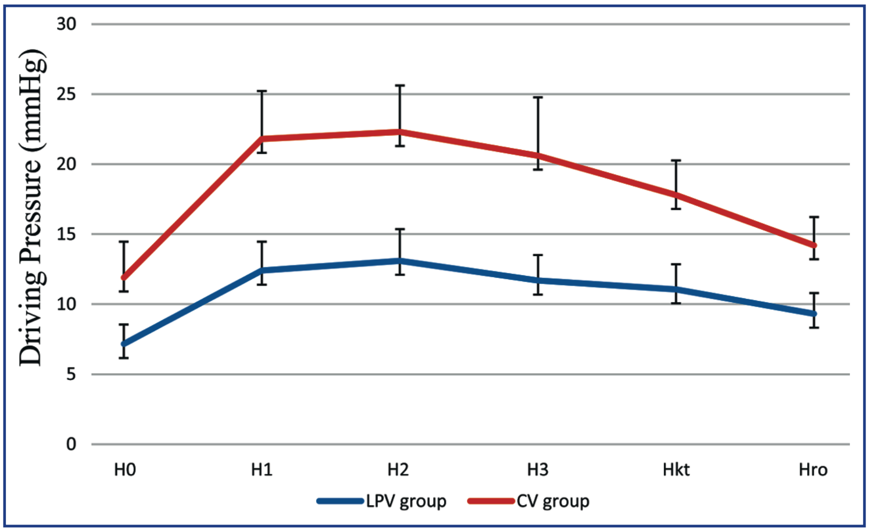


Figure 1 – Occurrence of postoperative pulmonary complications (PPCs) on day 2 (D2) and day 7 (D7) after surgery in patients with ventilation time longer than 6 h treated with protective ventilation (PV) and conventional ventilation (CV) [17]



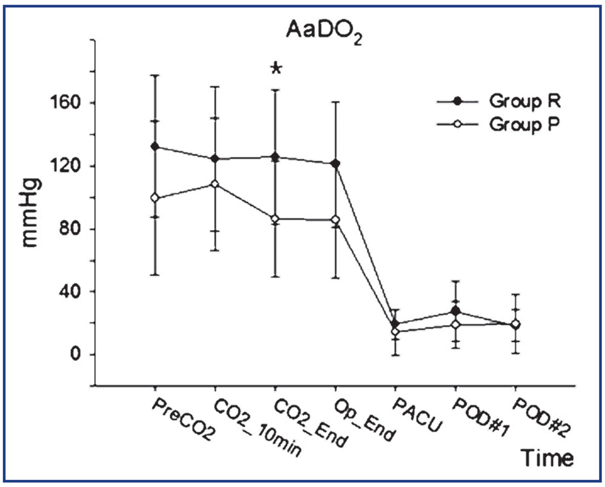
Abbreviations (axis X): H0 (after intubation), H1 (30 min after pneumoperitoneum), H2 (1 h after pneumoperitoneum), H3 (2 h after pneumoperitoneum), Hkt (10 min after pneumoperitoneum stopped), Hro (before extubation)

Figure 2 – Changes in intraoperative pulmonary static compliance (Cstat) in the groups with protective ventilation (LPV) and conventional ventilation (CV) [18]



Abbreviations (axis X): H0 (after intubation), H1 (30 min after pneumoperitoneum), H2 (1 h after pneumoperitoneum), H3 (2 h after pneumoperitoneum), Hkt (10 min after pneumoperitoneum stopped), Hro (before extubation)

Figure 3 – Intraoperative driving pressure in the groups with protective ventilation (LPV) and conventional ventilation (CV) [18]



*Legend: Axis Y – Pressure (mm Hg). Axis X – Time: PreCO2: after the anesthetic induction; CO2_10 min: 10 min after pneumoperitoneum; CO2_20 min: 20 min after pneumoperitoneum; CO2_end: end of pneumoperitoneum; Op_end: operation end; PACU: post-anesthesia care unit; POD#1: postoperative 24 h; POD#2: postoperative 48 h *P \ 0.05 compared with group R*

Charts – Group R: Conventional ventilation with alveolar recruitment maneuver (ARM) group; Group P: protective lung ventilation group;

Figure 4 – Oxygenation of the patients with AaDO2 [9]

Standard $AaDO_2$ in a healthy person is 10 to 40 mm Hg. It also depends on venous shunting due to hypoxic pulmonary vasoconstriction. At venous blood bypass above 30-35%, an increase in the oxygen fraction in the inhaled mixture does not lead to a noticeable increase in the partial pressure of oxygen in the body and is accompanied by a significant increase in $AaDO_2$ – above 100-200 mm Hg.

Patients after cardiac surgical interventions involving opening (often bilateral) of the pleural cavities, operations on the heart, switched off from the blood circulation, in conditions of hyperkalemia, using a heart-lung machine, are more prone to postoperative pulmonary atelectasis [19].

In an RCT in patients with hypoxemia after heart surgery in an ICU in Brazil (December 2011-2014) by Costa Leme et al., the use of an intensive lung recruitment strategy was associated with less severe pulmonary complications and improved survival among hospitalized patients compared to moderate lung recruitment strategy (Figures 5 & 6). Figure 5 shows the severity of postoperative pulmonary complications: grade 0 represents no symptoms or signals; grade 1, one of the following: dry cough, abnormal lung findings and temperature 37.5°C or higher with normal chest radiograph, or dyspnea without other documented cause; grade 2 means two of the following: productive cough, bronchospasm, hypoxemia ($SPO_2 \leq 90\%$) at room air, atelectasis with gross radiological confirmation (concordance of 2 independent experts) plus either temperature higher than 37.5°C, or abnormal lung findings, hypercarbia ($PaCO_2$>50 mm Hg) requiring treatment; grade 3 is one of the following: pleural effusion resulting in thoracentesis, pneumonia, pneumothorax, extended noninvasive ventilation, or reintubation lasting less than 48 hours; grade 4 means reintubation or invasive mechanical ventilation for 48 hours or more; and grade 5 – death before hospital discharge. In the intensive strategy group, the patients underwent three lung recruitment cycles (60 sec each), comprised of PEEP 30 cm H_2O, pressure ventilation, inspiratory pressure 15 cm H_2O, respiratory rate 15 per minute, inspiratory time 1.5 seconds, and FiO_2 0.40. During the intervals (60 sec) between the recruitment cycles and further the patients were ventilated or pressure-controlled with controlled driving pressure to obtain a VT of 6 mL/kg body weight, an inspiratory time of 1 second, PEEP of 13 cm H_2O, and a minimum respiratory rate to maintain $PaCO_2$ between 35- and 45-mm Hg. No hemodynamic instability was observed during the recruitment maneuver [20].

In addition to the benefits of applying the lung protective ventilation concept, Wang et al. proved that a low tidal volume in combination with an appropriate can inhibit the release of inflammatory cytokines such as tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), interleukin-10 (IL-10). There are several publications on the impact of various artificial lung ventilation regimens on inflammatory cytokines in elderly patients after gastric and colonic surgery under general anesthesia (Table 2) [4, 21].

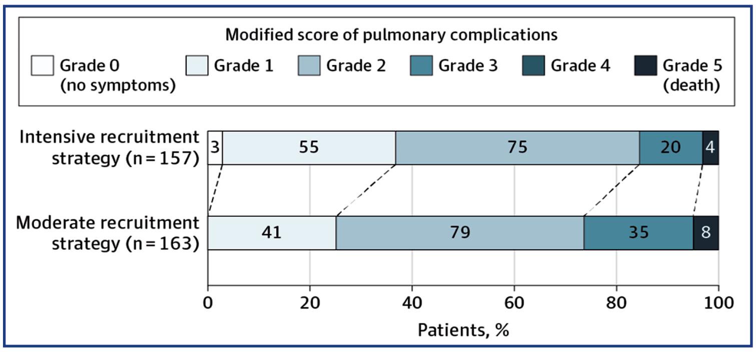


Figure 5 – Modified stratification of early postoperative complications [20]

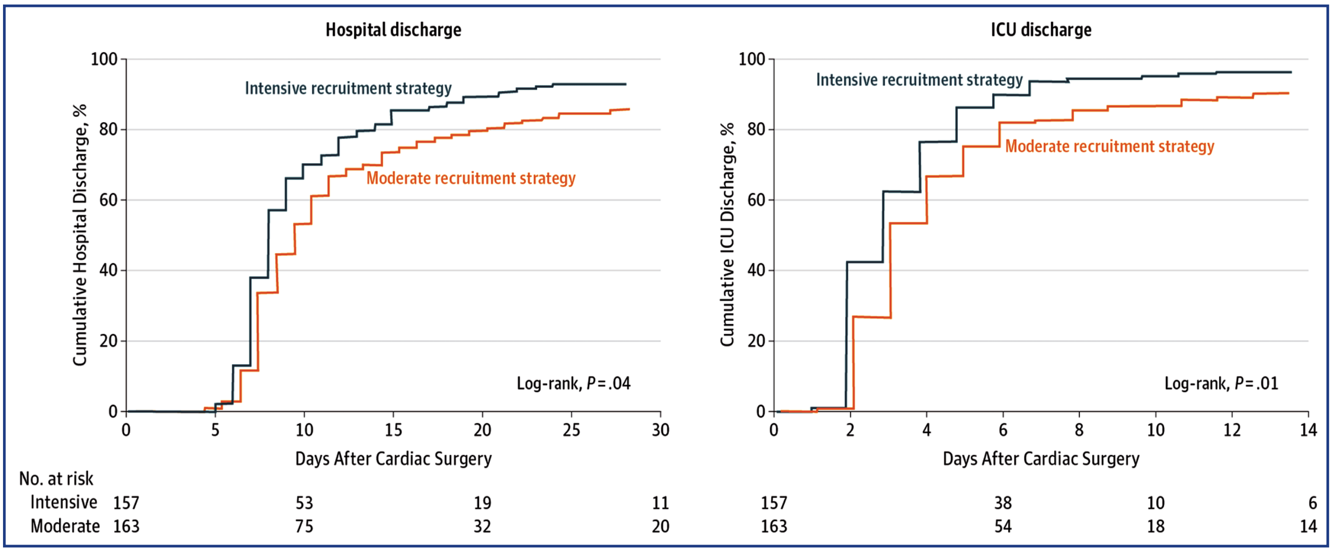


Figure 6 – Kaplan-Meier survival analysis for time to hospital discharge and Intensive Care Unit discharge among patients after cardiac surgery

Table 2 – Comparison of serum inflammatory factor levels before and after operation between the two groups (mean ± SD) [4]

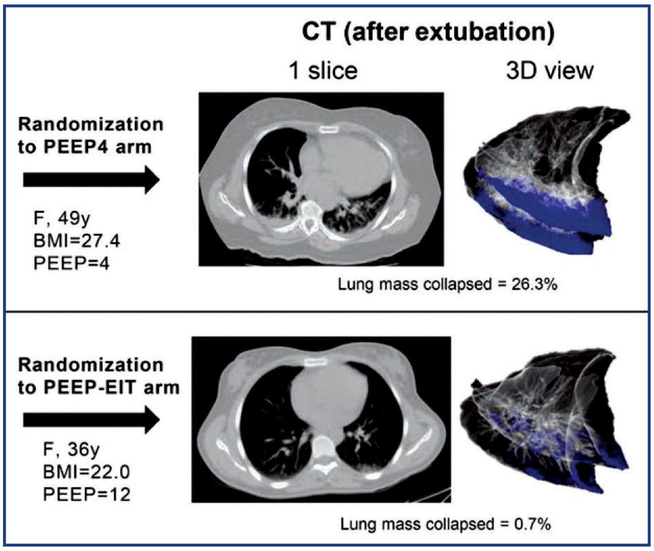
Group	TNF-α (ng/mL)		IL-6 (pg/mL)		IL-10 (pg/mL)	
	Preoperative	4 h after operation	Preoperative	4 h after operation	Preoperative	4 h after operation
Group A (n=60)	43.26±6.80	76.65±8.77	47.14±5.50	56.94±7.30	34.62±5.10	29.51±4.75
Group B (n=60)	45.10±6.55	89.28±12.64	45.03±6.28	69.71±10.38	36.36±6.15	25.83±5.08
value t	-1.510	-6.359	1.958	-7.795	-1.687	4.099
value P	0.134	0.000	0.053	0.000	0.094	0.000

Notes:
TNF-α – tumor necrosis factor-α; IL – interleukin;
Group A – tidal volume 6.0 mL/kg + PEEP 5.0 cm H_2O;
Group B – VT 6.0 mL/kg IBW + PEEP (8.0 cmH_2O);
P value – 0.09.

Though the protective role of more physiological tidal volume was established at 6-8 mL/kg IBW, additional protection provided by PEEP remains unclear. The authors suggested that individually titrated PEEP during anesthesia may improve lung function during and after surgery.

In recent years, it has been proven that a more rational approach to lung ventilation during anesthesia may change the incidence of postoperative pulmonary complications [22]. Thus, Pereira et al. showed that individualized PEEP measurements could reduce postoperative atelectasis measured by electrical impedance computed tomography (PEEP-EIT) while improving intraoperative oxygenation of the body and reducing the driving pressure level (Figure 7) [23].

Regarding the use of a lung protective ventilation strategy during anesthesia for major thoracic interventions against the background of one-lung ventilation, in 4 large-scale meta-analyses among 16 trials, the authors came to the same conclusion that driving pressure – oriented ventilation with low tidal volume with PEEP and periodic recruitment maneuvers – reduces the Vd/Vt by 5.9%. It also increases arterial oxygen tension (PaO_2) – the lung recruitment maneuver increases blood PaO_2 by 82 mm Hg and PEEP by 30 mm Hg; improves lung compliance by 4.3 mL/cm H_2O; and reduces the incidence of postoperative pulmonary complications (Figure 9) [7, 24].



Abbreviations: BMI, body mass index; CT, computed tomography

Figure 7 – Examples of EIT images (at PEEP-EIT and PEEP of 4 cm H2O) and CT images (after extubation) of two patients: top – a patient randomized for PEEP4 arm; bottom – a patient randomized for PEEP-EIT arm. One axial slice of the lung computed tomography and 3D reconstruction of the lungs show the collapsed lung in blue (areas between –200 to +100 UH)

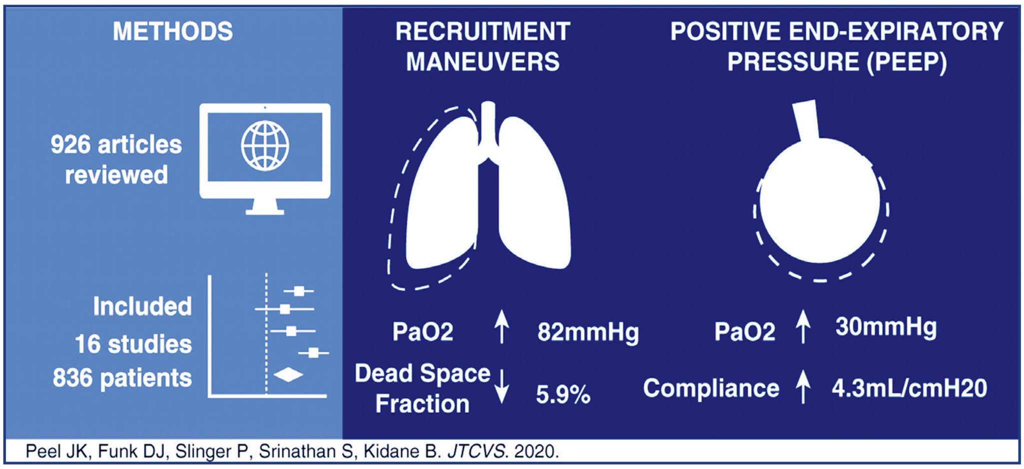


Figure 9 – PEEP and recruitment maneuvers during one-lung ventilation and their positive effect on lung function [7]

Conclusion: Our analysis of the modern strategy for applying lung protective ventilation during anesthesia in long and extensive surgical interventions showed that this approach effectively reduces the incidence of postoperative pulmonary complications. All detected publications evidenced a positive impact of lung protection methods on the course of the surgical and postoperative period. The simplicity of protection principles enables routine use of this methodology in anesthesiologic practice.

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АҢДАТПА

ОНКОЛОГИЯЛЫҚ НАУҚАСТАРДА ЖАЛПЫ АНЕСТЕЗИЯ КЕЗІНДЕ ӨКПЕНІҢ ЖАСАНДЫ ЖЕЛДЕНУІНІҢ ЗАМАНАУИ ТҰЖЫРЫМДАМАЛАРЫ: ӘДЕБИЕТКЕ ШОЛУ

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Өзектілігі: *Өкпенің жасанды вентиляциясы (ЖЖЖ) арқылы жалпы анестезиямен кең көлемді хирургиялық операциядан өткен пациенттер арасында обструктивті немесе рестриктивті сипаттағы әртүрлі операциядан кейінгі тыныс алу жолдарының асқынулары жиі кездеседі.*

Зерттеудің мақсаты *– онкологиялық науқастарға анестезиялық көмек көрсету сапасын арттыру мақсатында жүйелі шолулар мен мета-талдаулардың ағымдағы деректерін, өкпе вентиляциясының профилактикалық және емдік стратегияларын қолдану жөніндегі ғылыми деректерді жалпылау.*

Әдістері: *PubMed электронды дерекқорында (NCBI) рандомизацияланған бақыланатын және перспективалық бақылау зерттеулерін, жүйелі шолулар мен мета-талдауларды, сондай-ақ 2016 және 2023 жылдар аралығында ағылшын тілінде жарияланған, өкпенің қорғанысты желдету және ауыр және ұзақ хирургиялық операцияға ұшыраған науқастарда әдеттегі механикалық желдету арқылы қорғаныс желдету стратегиялары және оның нәтижелеріне салыстыруға бағытталған ғылыми мақалаларды анықтау үшін іздестірілу жүргізілді.*

Нәтижелері: *Кең көлемді ғылыми зерттеулер мен мақалаларды шолу деректерін салыстыру нәтижесінде өкпенің қорғаныш вентиляциясының стратегиясын қолдану мақсатында тыныс алу көлемі төмен (6-8 мл/кг идеалды дене салмағына), жекелендірілген PEEP, өкпені мезгіл-мезгіл жинау маневрі жасалынған жағдайда клиникалық нәтижелердің айтарлықтай жақсаруы, тыныс алу жолдарының асқынулары, ерте өлім-жітім және хирургиялық операция жасалған науқастарда ауруханада болу ұзақтығы азайғаны анықталды.*

Қорытынды: *Ірі хирургиялық араласулар кезінде анестезия кезінде өкпенің қорғанышты желденуі тұжырымдамасын қолдану операциядан кейінгі өкпе асқынуларының жиілігін төмендетеді.*

Түйінді сөздер: *механикалық желдетудің заманауи тұжырымдамалары, операциядан кейінгі өкпелік асқынулар, тыныс алудың төмен көлемі, жекеленген оң экспираторлық қысым.*

АННОТАЦИЯ

СОВРЕМЕННЫЕ КОНЦЕПЦИИ ИСКУССТВЕННОЙ ВЕНТИЛЯЦИИ ЛЕГКИХ ВО ВРЕМЯ ОБЩЕЙ АНЕСТЕЗИИ У ОНКОЛОГИЧЕСКИХ ПАЦИЕНТОВ: ОБЗОР ЛИТЕРАТУРЫ

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Актуальность: *Среди пациентов, перенесших обширные оперативные вмешательства под общей анестезией с искусственной вентиляцией легких, нередко встречаются различные послеоперационные респираторные осложнения обструктивного или рестриктивного характера.*

***Цель исследования** – обобщить актуальные данные систематических обзоров, мета-анализов и научных публикаций о применении профилактических и лечебных стратегий вентиляции легких с целью повышения качества оказания анестезиологической помощи онкологическим пациентам.*

Методы: *Был проведен поиск в электронной базе данных PubMed (NCBI), для выявления рандомизированных контролируемых и проспективных обсервационных исследований, систематических обзоров и мета-анализов, а также научных статей, опубликованных на английском языке с 2016 по 2023 годы, в которых основное внимание уделялось результатам применения и сравнения стратегий защитной вентиляции легких при традиционной механической вентиляции у пациентов, перенесших обширные и длительные оперативные вмешательства.*

Результаты: *В результате сопоставления данных проведенного обзора крупномасштабных научных исследований и статей установлена взаимосвязь между использованием стратегии защитной вентиляции легких с низким дыхательным объемом (6-8 мл/кг идеальной массы тела), в сочетании с индивидуализированным показателем положительного давления в конце выдоха, периодическими маневрами рекрутмента легких и значительным улучшением клинических исходов, уменьшением количества осложнений со стороны дыхательной системы, сокращением ранней летальности и продолжительности пребывания в стационаре у пациентов, перенесших хирургические вмешательства.*

Заключение: *Применение концепции защитной вентиляции легких во время анестезии, при обширных оперативных вмешательствах снижает частоту развития послеоперационных легочных осложнений.*

Ключевые слова: *современные концепции искусственной вентиляции легких (ИВЛ), послеоперационные легочные осложнения, низкий дыхательный объем (ДО), индивидуализированный показатель положительного давления в конце выдоха (ПДКВ).*

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