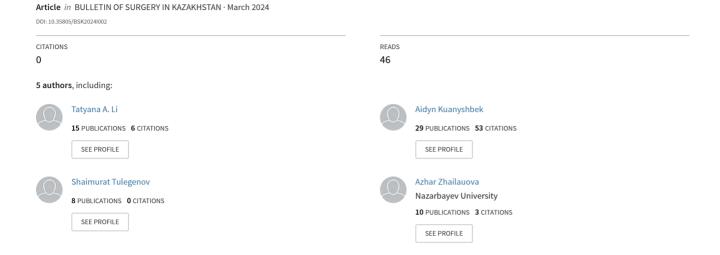
### THE STRATEGY OF MECHANICAL VENTILATION DURING CARDIOPULMONARY BYPASS AS A PREDICTIVE FACTOR FOR PULMONARY COMPLICATIONS IN THE INTENSIVE CARE UNIT



# THE STRATEGY OF MECHANICAL VENTILATION DURING CARDIOPULMONARY BYPASS AS A PREDICTIVE FACTOR FOR PULMONARY COMPLICATIONS IN THE INTENSIVE CARE UNIT

#### Author for correspondence: Tatyana Li –

Doctor of Cardiac Intensive Care Unit, Anaesthetist intensivist, Heart Center CF "University Medical Center," Turan Ave 38, Astana, Kazakhstan, E-mail: leeanestrean@gmail.com

#### Conflict of interest:

The authors declare no conflict of interests

#### Key words:

Mechanical ventilation, Cardiopulmonary bypass, Atelectasis Wachruschew I., Li T., Kuanyshbek A., Tulegenov S., Zhailauova A.

Heart Center, CF UMC, Astana, Kazakhstan.

#### **Annotation**

**Background.** Pulmonary complications are the second most common complication after cardiac surgery with cardiopulmonary bypass. Pulmonary atelectasis can occur from various intraoperative causes such as prolonged operation, time of anaesthesia more than 3-4 hours, use of a thoracic artery, use of cardiopulmonary bypass during surgery, lack of ventilation, haemotransfusion of 4 or more units of packed red blood cells in the perioperative period. Impact of mechanical venatilation during cardiopulmonary bypass still unknown.

**Methods**. Prospective, randomised study at one centre. Adult patients undergoing cardiac surgery with a pump by sternotomy for coronary artery disease were included.

Patients were randomised into two groups – one group receiving mechanical ventilation and one group receiving no ventilation during cardiopulmonary bypass. The main endpoint was Pa02/Fi02 as a marker for the quality of ventilation and perfusion measured. Secondary endpoints were postoperative pulmonary complications such as atelectasis and prolonged mechanical ventilation of more than 72 hours.

**Results**. 190 consecutive patients were included, 92 and 98 in each group. No significant difference was found in the PaO2/FiO2 ratio in the groups, p=0.591. A significant difference was found in the number of atelectasis during ultrasound investigation of the lungs in the non-ventilated group, p = 0.0001.

**Conclusion**. On-pump cardiac surgery without mechanical ventilation can lead to atelectasis of the lungs.

Қанның жасанды айналымы кезіндегі жүрек-өкпе ауа айналымының механикалық желдету жоспарының стратегиясы реанимация бөліміндегі өкпе асқынуларының болжамды факторы ретінде

#### Хаталысатын автор: Татьяна Ли -

кардиохирургиялық реанимация бөлімшесінің дәрігері, «Университет медициналық орталығы» жүрек орталығының дәрігер-анестезиологы, Тұран даңғылы, 38, Астана, Қазақстан, E-mail: leeanestrean@ gmail.com

#### Мудделер қақтығысы:

авторлар мүдделер қақтығысының жоқтығын мәдімдейді Вахрушев И., Ли Т., Қуанышбек А., Төлегенов Ш., Жайлауова А.

UMC КҚ Жүрек Орталығы, Астана Қазақстан

#### Түіндеме

**Өзектідігі.** Түйі нжасанды қан айналым кезіндегі қолданылатын кардиохирургиялық процедуралардан кейін өкпе асқынулары екінші орында тұр. Өкпе ателектазы операция себептерінен туындауы мүмкін, мысалы, ұзақ операция және анестезия

уақыты 3-4 сағаттан асатын жағдайда, кеуде артериясын қолдану, операция кезінде жасанды қан айналымын қолдану және механикалық желдетудің мүмкін еместігі, сондай-ақ периоперативті кезеңде 4 немесе одан да көп құты эритроциттерінен қан құюы. Жүрек-өкпе айналымы кезінде механикалық желдетудің әсері әлі белгісіз.

**Әдістері**. бір орталықта перспективалық рандомизацияланған сынақ. Зерттеуге жүректің ишемиялық ауруы үшін стернотомия арқылы сорғыны пайдаланып жүрекке операция жасаған ересек пациенттер енгізілді.

Пациенттер екі топқа бөлінді яғни рандомизацияланды бірінші топқа механикалық желдету қолданылды да, ал екінші топқа жасанды қан айналымы кезінде механикалық желдету берілмеді. Негізгі соңғы көрсеткіш желдету және перфузия сапасының көрсеткіші ретінде PaO2/FiO2 болды. Екінші соңғы көрсеткіште операциядан кейінгі өкпе асқынулары болды, мысалы, ателектаз және 72 сағаттан астам уақыт бойы механикалық желдету кезіндегі асқынулар.

**Нәтижелері.** қатарынан 190 пациентті, әр топта 92 және 98 науқас қатысты. Топтарда PaO2/FiO2 қатынасында айтарлықтай айырмашылық табылған жоқ p=0.591. Өкпенің ультрадыбыстық зерттеуінен кейін механикалық желдетусіз өткен топтағы p = 0.0001 көрсетіп ателектаздар саныайтарлықтай жоғары болды.

**Қорытынды.** жасанды қан айналым кезіндегі операция, өкпенің механикалық желдетуінсіз өткен жағдайда өкпе ателектазының жиілігі едәуір жоғары болады.

#### Түйінді сөздер:

механикалық желдету, жасанды қан айналымы, ателектаз

## Стратегия механической вентиляции легких во время искусственного кровообращения как прогностический фактор легочных осложнений в отделении интенсивной терапии

### Вахрушев И., Ли Т., Куанышбек А., Тулегенов Ш., Жайлауова А.

Центр Сердца КФ UMC, Астана Казахстан

#### Аннотация

**Введение.** Легочные осложнения занимают второе место по распространенностипосле кардиохирургических операций с применением искусственного кровообращения. Ателектаз легочной ткани может возникнуть в результате различных причин, таких как длительная операция и анестезия, более 3-4 часов, выделение грудной артерии, искусственного кровообращенияи отсутствие искусственной вентиляции легких, а также массивные гемотрансфузии более 4 единиц эритроцитарной взвеси в периоперационном периоде. Влияние искусственной вентиляции легких во время искусственного кровообращения на осложнения послеоперационного периода до сих пор неясно.

**Материалы и методы.** Рандомизированное одноцентровое исследование. В исследование были включены взрослые пациенты, перенесшие открытую операцию на сердце с проведением искусственного кровообращения.

Пациенты были рандомизированы в две группы – одна группа с искусственной вентиляцией легких во время искусственного кровообращения, вторая без вентиляции во время искусственного кровообращения. Основной точкой измерения был индекс PaO2/FiO2 как показатель качества вентиляции и перфузии в легких. Вторичными показателями оценки были послеоперационные легочные осложнения, такие как ателектаз и длительная искусственная вентиляция легких более 72 часов.

**Результаты**. В исследование были включены 190 последовательных пациентов, 92 и 98 в каждой группе. Не было обнаружено существенной разницы в отношении PaO2/

#### Автор для корреспонденции: Татьяна Ли –

врач кардиологического отделения реанимации, врач-анестезиолог-реаниматолог, Кардиологический центр КФ «Университетский медицинский центр», пр. Туран, 38, Астана, Казахстан, E-mail: leeanestrean@gmail.com

#### Конфликт интересов:

Авторы заявляют об отсутствии конфликта интересов

#### Ключевые слова:

Искусственная вентиляция легких, искусственное кровообращение, ателектаз.

FiO2 индекса в группах, p=0.591. При ультразвуковом исследовании легких была выявлена достоверная разница в количестве ателектазов, большев группе без искусственной вентиляции легких, p = 0.0001.

**Заключение**. Операция на открытом сердце с применением искусственного кровообращения, без длительной вентиляции легких может привести к ателектазу легких.

#### Introduction

Cardiac surgery with cardiopulmonary bypass (CPB) is highly associated with complications. Acute lung injury is the second most common complication of CPB after the heart injury and ranges from mild pulmonary dysfunction to fatal acute lung injury. Following cardiac surgery, more than 30% of patients are reported to have significant respiratory impairment for at least one week after surgery.

CPB is a mandatory component of cardiac surgery and enables the maintenance of adequate body perfusion and oxygenation. Physiologically, the cardiopulmonary system should be partially bypassed during CPB and completely bypassed under aortic cross-clamping to create a bloodless and immobile surgical field.<sup>4,5</sup> On pump heart surgery, factors such as CPB, hypothermia, the surgical intervention, anaesthesia, medications, massive transfusions can cause diffuse lung injury.6 During CPB, the lungs receive less blood from bronchial arterial flow, which leads to ischaemia. The absence of pulsatile flow during CPB causes several changes in the lungs that lead to increased severity of inflammation.8 There are several methods to prevent lung injury, improve gas exchange and reduce the increase in inflammatory responses during CPB, but the role of mechanical ventilation is still unclear. 9,10

Atelectasis is a common pulmonary complication in patients undergoing cardiac surgery with cardiopulmonary bypass and an important cause of postoperative hypoxaemia.11 Various reasons have been put forward to explain why patients undergoing on-pump cardiac surgery experience alveolar collapse. These include a relaxed diaphragm compressing the caudal parts of the lower lobes, surgical manipulations of pulmonary structures and depressurisation of the respiratory system during CPB to enable better visualisation of the surgical field. Although most of the mechanisms causing intraoperative lung collapse disappear when patients wake up and begin spontaneous breathing, postoperative atelectasis and hypoxemia may persist for several days.<sup>6</sup> Recent publications have shown that the best mechanical ventilation strategy during open-heart surgery with a pump is still unclear.<sup>12</sup> While some studies suggest a positive impact on oxygenation and systemic inflammatory response, the actual clinical effect of ventilation during cardiopulmonary bypass is controversial. Moreover, the results of these studies can't be consistently interpreted due to literature biases.<sup>13</sup>

#### Materials and methods

This is a prospective, randomised study conducted in patients undergoing elective on-pump CABG due to coronary arteries disease (CAD) from September till December 2023. Method of randomization:simple computer-generated random numbers (odd and even numbers).

Patients were recruited from a single regional healthcare centre in Kazakhstan. The study included all adult patients aged ≥18 years that underwent cardiac surgery with CPB. Patients were randomised into two groups – one group receiving low tidal volume (LTV) mechanical ventilation and one group receiving no ventilation during CPB.

Mechanical ventilation strategy: Immediately after intubation, mechanical ventilation was started in volume-controlled ventilation mode with initial parameters VT 5-7 ml/kg, PEEP – 5-10 cmH20. Immediately after initiation of CPB modes of mechanical ventilation in the LTV group – VT 3-5 ml/kg, PEEP – 5-8 mm H20, frequency – 7-10 per minute. In the second Non-ventilated (NV) group, ventilation was stopped in standby mode. The original ventilation parameters were restored after weaning from CPB.

The main endpoint was Pa02/Fi02 as a marker for the quality of ventilation and perfusion measured in the ICU in the immediate postoperative period. Secondary endpoints were postoperative pulmonary complications such as pulmonaryatel-

ectasis and prolonged mechanical ven- Medical Center." tilation of more than 72 hours. Atelectasis was diagnosed using the US method jection), and the shunt was measured in the arterial blood gases (ABG). Patients in primary parameters.

ABG were measured several times just before intubation on spontaneous breathing with atmospheric 02, during CPB (they were not included because of extracorporeal oxygenation), immediately after admission to the ICU after surgery and 24, 48, 72 hours after surgery in the ICU.

Chest X - ray were conducted routinely (not more than 10 days before surgery). COPD, emphysema, fibrosis was combined in the meaning - pulmonary pathology.

#### Ethicalapproval.

This study was conducted in strict accordance with the principles outlined in the Helsinki Declaration. Before commencing the research, approval was to the study, 92 of them were included obtained from the Local Bioethics Committee of the Corporate Fund "University NV group.

#### Statistical analysis

For continuous variables, the arith-(more than 3 B-lines in the lateral pro- metic mean, standard deviation (SD), median and range were calculated. For binary or categorical variables, abboth groups were comparable in terms of solute and relative frequencies (n, %) were calculated. To assess the differences between the groups, standard independent-samples t-tests were performed using pooled analyses for equal variances and Satterthwaite analyses for unequal variances. P values of <0.05 were taken to indicate significance. To determine whether the means of two datasets are different from each other the Z test was used. The Z score is used to assess the significance of an individual data point within a distribution, while the Odds Ratio and the Chi-Square test are used to analyse the association between variables in different contexts.

#### Results

A total of 190 patients were enrolled in the LTV group and 98 patients in the

LTV group, Chiz-sta-P value NV group, N=98 N=92 squared tistic Age, (years) 62±9.63 1.953 59±11.40 0.052\*Gender, n (%) Female 44 (44.9%) 52 (56.5%) 1.270 0.260 Male 54 (55.10%) 40 (43.48%) 1.228 0.268 BMI, m<sup>2</sup> 29.7± 4.12 4.125 0.0001\* 27.4±3.56 \_ Comorbidity, n (%) 27 (27.55%) 22 (23.91%) 0.775 Stroke 0.082 34 (36.96%) 0.268 0.604 MI history 42 [42.86%] 31 (31.63%) 32 (34.78%) 0.792 Diabetes 0.069 Surgery timings, median (range), minutes CBP time 88.5±38.2 92.0±27.56 0.38 0.56 Aortic cross 59.5±25.92 61.0±27.44 0.50 0.54 clamp time Baseline levels, median (range) Pa02/Fi02 422.6 ±164.6 409.53±170.12 0.538 0.591 4.975 0.0001\* F shunt 0.15±0.05 0.12 ±0.03 Haemoglobin 139.0±11.6 132.0±8.54 0.632 0.09 Haematocrit 42.0±6.71 39.0±5.12 0.174 0.32 Chest X Rav 17 (17.36%) 14 (15.21%) 0.025 0.874 pathology

\* z test statistical significance P≤0.05. LTV – Low tidal volume, NV – non ventilated, MBI – body mass index, CBP – cardiopulmonary bypass, MI history - myocardial infarction history

Demographics and initial laboratory characteristics

Table 1. The characteristics were generally similar in both groups.

Before surgery, Pa02/Fi02 F-shunt parameters were numerically in the normal range. Chest X-ray before surgery had revealed pulmonary pathologies

The demographic data is shown in due to chronic lung disease in 14 (15.21%) of patients. More than 1/3 of the patients had a history of comorbidity conditions such as type 2 diabetes, ischemic stroke and acute myocardial infarction. The postoperative ICU data with primary and secondary outcomes are shown in Table 2.

Table 2. Primary and secondary outcomes in the intensive care unit

	NV group (n= 98)	LTV group (n=92)	OR	z-sta- tistic	P value
PEEP intraop. period (cmH20)	0	7.38 ±2.12	-	-	-
Pa02/Fi02	312±155.4	328.64±170.6	-	0.704	0.482
PC02	45.8±19.2	39.5±12.54	_	2.659	0.008*
Fshunt	0.45±0.1	0.19±0.06	_	21.558	0.0001*
Pulmonary complications (%)					
Atelectasis signs (US)	30 (32.61%)	6 (6.52%)	6.32ª	3.877	0.0001*
Recruitment manoeuvre	35 (38.04%)	11 (11.96%)	4.09°	3.667	0.0002*
Mechanical ventilation more than 72 hours	15 (15.3%)	12 (13.04%)	1.20	0.446	0.655

<sup>\*</sup> z test statistical significance P<0.05

PEEP intraoperative period - Positive end-expiratory pressure intraoperative period, LTV – low tidal volume, NV – non-ventilated, US – ultrasound.

No significant difference was found between the groups for the primary endpoint Pa02/Fi02 ratio (p=0.482).

A significant difference was found for the F-shunt indicator 0.19±0.06 vs  $0.45\pm0.1$  with a p-value < 0.0001.

Mean paCO2 level in the immediate postoperative period was higher in the NV group although without significant statistical difference. In the non-ventilated group, there were more detected signs of pulmonary atelectasis during US30 (32.61%) vs.6 (6.52%), OR=6.32, 95%CI [2.49;16.07], z-statistic 3.877, P value <0.0001. The recruitment manoeuvre shortly after ICU admission was performed in 11 (11.96%) of patients in the LTV group and in35 (38.04%) of patients in the NV group, which was a significant difference between the groups, OR=4.09, 95%CI [1.92;8.68], z-statistic 3.667, P value 0.0002. In addition, the importance of the F-shunt was significantly higher in the NV group 0.45±0.1 vs 0.19±0.06 (p value < 0.0001), substantiating the presence of venous blood shunt in the lung due to pulmonary atelectasis.

proximately the same in both groups at 12 (13.04%) and 15 (15.3%) and was not significant, P value 0.655.

#### Discussion

The issue of mechanical ventilation has been a subject of debate for over three decades. The MECANO study by Nguyen, Lee S., et al, a single-center randomised clinical trial conducted on patients undergoing cardiac surgery, found no significant difference in the primary endpoint, which was a composite measure of postoperative mortality and pulmonary complications. In our study, the Pa02/Fi02 index also did not differ between groups. 14

The same opinion was in the study conducted by Zhang et al., 413 adult patients undergoing elective cardiac surgery with CPB were observed. The study examined non- ventilation or low tidal volume (VT) ventilation at 30% or 80% FiO2. The study concluded that the continuation of low VT ventilation did not offer any significant advantage over no ventilation during CPB, in relation to the The need for prolonged mechanical incidence of PPCs during hospital stay ventilation for various reasons was ap- after the surgery. However, due to the

<sup>°</sup> OR - Odds ratio; OR>1 means that the event is directly related and has a chance of occurring in the first group

limitations in the study's design, the au- management were carried out according thors were unable to draw a strong conclusion on the effects of the application of low VT ventilation at 30% on the severity of pulmonary complications. 15

conducted systematic review and meta-analysis, Chi et al., 2017, continued ventilation during CPB showed a prominent increase of Pa02/Fi02 index in versus the patients whose ventilation support was turned off. This discrepancy could be explained from the standpoint of a reduced number of patients participating in the current research. Moreover there was some data in favour of mechanical ventilation during CPB.<sup>16</sup>

There is evidence from studies that the use of continuous mechanical ventilation during CPB can have significant clinical benefits. These benefits include improved oxygenation and reduced inflammation, which ultimately leads to less lung injury. A recent meta-analysis of 16 clinical trials also showed that mechanical ventilation during surgery resulted in a reduced shunt fraction and an increase in oxygenation immediately after weaning from CBP. The analysis also concluded that maintaining MV throughout the entire duration of extracorporeal circulation could reduce the CPB-related inflammatory response and tissue damage.12

that the strategy of low tidal volume ventilation with a PEEP of more than 5 cm H20 during CPB may be beneficial to avoid the formation of atelectasis in the lung tissue. In addition, we were forced to apply strict ventilation parameters with high inspiratory pressure in the ICU due to pulmonary atelectasis in the postoperative period. In this study, we observed a correlation between preserved mechanical ventilation with PEEP and atelectasis formation in the postoperative period.

#### Limitations.

There are some limitations to this study. Small number of patients, a single-centre study, all of the perioperative (GrantNo.AP19677596).

to our hospital's clinical practice.

#### Conclusion

Maintaining a low tidal volume and PEEP during CPB may be beneficial for pa-However, according to the recently tients undergoing CABG cardiac surgery. In our opinion, it is a mandatory measure to maintain a PEEP of 5 to 10 during CPB in patients with excessive body weight.

What is already known on this toppatients receiving ventilation support ic: After cardiopulmonary bypass, patients are at risk of developing pulmonary complications such as pulmonary atelectasis and edema. Atelectasis, the collapse of alveoli, can occur due to the reabsorption of air from the alveoli during periods of reduced lung volume. Pulmonary edema may develop as a result of increased capillary permeability and fluid retention.

> What this study adds: Determination of the effect of mechanical ventilation with positive PEEP to pulmonary atelectasisformation in the postoperative period still unknown and the benefit for cardiac surgery patients is to preserve mechanical ventilation during cardiopulmonary bypass.

> Acknowledgements: The team of authors expresses gratitude to the staff of the intensive care unit of our hospital.

Authors' Contributions: Sh.T.: Study conception and design, surgeries, revising discussion section of the manu-In our study we have obtained data script. A.K.: Study design, data analysis, and interpretation, revising discussion section of the manuscript. A.Zh.: Data acquisition, analysis, and interpretation; surgeries, revising results section of the manuscript. I.W.: Data collection, drafting, revising results section.T.L.: Study conception and design, overall responsibility of the study, data analysis and interpretation. All authors have approved the final version of the article.

#### **Funding**

This research is funded by the Science Committee of the Ministry of Science and Higher Education of the Republic of Kazakhstan «SUCCESS in ICU»

#### References

1. Monaco F, Di Prima AL, Kim JH, et al. Management of Challenging Cardiopulmonary Bypass Separation. J Cardiothorac Vasc Anesth. Jun

- 2020;34(6):1622-1635. doi:10.1053/j. jvca.2020.02.038
- Zheng XM, Yang Z, Yang GL, Huang Y, Peng JR, Wu MJ. Lung injury after cardiopulmonary bypass: Alternative treatment prospects. World J Clin Cases. Jan 21 2022;10(3):753-761. doi:10.12998/wjcc.v10.i3.753
- Kaufmann K, Heinrich S. Minimizing postoperative pulmonary complications in thoracic surgery patients. Curr Opin Anaesthesiol. Feb 01 2021;34(1):13-19. doi:10.1097/ACO.000000000000000945
- Wahba A, Milojevic M, Boer C, et al. 2019 EACTS/EACTA/EBCP guidelines on cardiopulmonary bypass in adult cardiac surgery. Eur J Cardiothorac Surg. Feb 01 2020;57(2):210-251. doi:10.1093/ejcts/ezz267
- Akhtar MI, Gautel L, Lomivorotov V, et al. Multicenter International Survey on Cardiopulmonary Bypass Perfusion Practices in Adult Cardiac Surgery. J Cardiothorac Vasc Anesth. Apr 2021;35(4):1115-1124. doi:10.1053/j.jvca.2020.08.043
- 6. Sanfilippo F, Palumbo GJ, Bignami E, et al. Acute Respiratory Distress Syndrome in the Perioperative Period of Cardiac Surgery: Predictors, Diagnosis, Prognosis, Management Options, and Future Directions. J Cardiothorac Vasc Anesth. Apr 2022;36(4):1169-1179. doi:10.1053/j. ivca.2021.04.024
- 7. Jiang F, Jiang X, Jia R. Research on the Mechanisms of Lung Injury in Cardiopulmonary Circulation (CPB). MEDS Clinical Medicine. 2022;3(5):5-11.
- O'Neil MP, Alie R, Guo LR, Myers ML, Murkin JM, Ellis CG. Microvascular Responsiveness to Pulsatile and Nonpulsatile Flow During Cardiopulmonary Bypass. Ann Thorac Surg. Jun 2018;105(6):1745-1753. doi:10.1016/j.athoracsur.2018.01.007
- 9. Mowery NT, Terzian WTH, Nel-

- son AC. Acute lung injury. Curr Probl Surg. May 2020;57(5):100777. doi:10.1016/j.cpsurg.2020.100777
- 10. Nteliopoulos G, Nikolakopoulou Z, Chow BHN, Corless R, Nguyen B, Dimarakis I. Lung injury following cardiopulmonary bypass: a clinical update. Expert Rev Cardiovasc Ther. Nov 2022;20(11):871-880. doi:10.108 0/14779072.2022.2149492
- 11. Tanner TG, Colvin MO. Pulmonary Complications of Cardiac Surgery. Lung. Dec 2020;198(6):889-896. doi:10.1007/s00408-020-00405-7
- Bignami E, Andrei G. Pro: Mechanical Ventilation During Cardiopulmonary Bypass in Adult Cardiac Surgery. J Cardiothorac Vasc Anesth. Jan 10 2024;doi:10.1053/j.jvca.2024.01.004
- 13. Weingarten N, Schraufnagel D, Plitt G, Zaki A, Ayyat KS, Elgharably H. Comparison of mechanical cardio-pulmonary support strategies during lung transplantation. Expert Rev Med Devices. Oct 2020;17(10):1075-1093. doi:10.1080/17434440.2020.1841630
- 14. Nguyen LS, Estagnasie P, Merzoug M, et al. Low Tidal Volume Mechanical Ventilation Against No Ventilation During Cardiopulmonary Bypass in Heart Surgery (MECANO): A Randomized Controlled Trial. Chest. May 2021;159(5):1843-1853. doi:10.1016/j.chest.2020.10.082
- 15. Zhang MQ, Liao YQ, Yu H, et al. Effect of ventilation strategy during cardiopulmonary bypass on postoperative pulmonary complications after cardiac surgery: a randomized clinical trial. J Cardiothorac Surg. Oct 30 2021;16(1):319. doi:10.1186/s13019-021-01699-1
- Chi D, Chen C, Shi Y, et al. Ventilation during cardiopulmonary bypass for prevention of respiratory insufficiency: A meta-analysis of randomized controlled trials. Medicine (Baltimore). Mar 2017;96(12):e6454. doi:10.1097/MD.00000000000006454