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EFFECTS OF MECHANICAL VENTILATION DURING CARDIOPULMONARY BYPASS ON POSTOPERATIVE PULMONARY COMPLICATIONS

UTICAJ MEHANIČKE VENTILACIJE U TOKU EKSTRAKORPORALNE CIRKULACIJE NA POSTOPERATIVNE PLUĆNE KOMPLIKACIJE

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Summary

Introduction. It is common practice in on-pump cardiac surgery to stop mechanical ventilation when extracorporeal circulation is started or to continue with low tidal volumes. The aim of this study was to investigate whether patients ventilated with low tidal volumes had a lower percentage of postoperative pulmonary complications compared to patients who were not ventilated during cardiopulmonary bypass. **Material and Methods.** This retrospective study included patients who underwent coronary artery bypass graft surgery over a period of 14 months. Patients with lung diseases and those with an ejection fraction < 30% were excluded from the study. **Results.** A total of 499 patients were included in the study. Of these, 398 were ventilated with low tidal volumes, while 101 patients were not ventilated during extracorporeal circulation. The groups did not differ in baseline characteristics, comorbidities, and intraoperative data. Pulmonary complications were equally prevalent in both groups (ventilated 16%, not ventilated 17.8%). The most frequent were the need for prolonged mechanical ventilation (ventilated 5.8%, not ventilated 5.9%), and pleural effusions (ventilated 4.8%, not ventilated 5.9%). The incidence of pneumonia was identical in both groups (2%). Other complications were less frequent. Duration of mechanical ventilation after surgery, stay in the intensive care unit, and in-hospital mortality did not differ significantly between the groups. **Conclusion.** Pulmonary complications after cardiac surgery are still common. The experience at our clinic showed that the choice of mechanical ventilation strategy during cardiopulmonary bypass does not affect postoperative pulmonary complications.

Key words: Cardiac Surgical Procedures; Cardiopulmonary Bypass; Respiration, Artificial; Lung; Risk Factors; Postoperative Complications; Treatment Outcome

Sažetak

Uvod. Uobičajena praksa kod *on-pump* kardiohirurških operacija jeste da se mehanička ventilacija pluća obustavlja kada se započne ekstrakorporalna cirkulacija ili se nastavlja niskim disajnim volumenom. Cilj ove studije bio je da ispita da li su pacijenti ventilirani niskim disajnim volumenom imali manji procenat postoperativnih plućnih komplikacija u odnosu na pacijente koji nisu ventilirani u toku ekstrakorporalne cirkulacije. **Materijal i metode.** Retrospektivna studija kardiohirurških pacijenata operisanih u periodu od 14 meseci. U studiju su uključeni samo pacijenti sa hirurškom revaskularizacijom miokarda. Iz studije su isključeni pacijenti sa plućnim bolestima i oni sa ejekcionom frakcijom < 30%. **Rezultati.** U studiju je uključeno ukupno 499 pacijenata. Od toga, 398 je ventilirano niskim disajnim volumenom dok 101 pacijent nije ventiliran u toku ekstrakorporalne cirkulacije. Grupe se nisu razlikovale po osnovnim karakteristikama, komorbiditetima i intraoperativnim podacima. Plućne komplikacije su bile podjednako zastupljene (ventilirani 16%, neventilirani 17,8%). Najučestalije su bile potreba za produženom mehaničkom ventilacijom pluća (ventilirani 5,8%, neventilirani 5,9%) i pleuralni izlivi (ventilirani 4,8%, neventilirani 5,9%). Učestalost pneumonije je bila identična u obe grupe (2%). Ostale komplikacije su bile manje učestalosti. Trajanje mehaničke ventilacije pluća nakon operacije, boravak u jedinici intenzivnog lečenja i intrahospitalni mortalitet nisu se značajno razlikovali po grupama. **Zaključak.** Plućne komplikacije nakon kardiohirurških operacija su i dalje česte. Iskustvo na našoj klinici je pokazalo da izbor strategije mehaničke ventilacije pluća u toku ekstrakorporalne cirkulacije ne utiče na plućne komplikacije.

Ključne reči: Kardiohirurške procedure; kardiopulmonalni bajpas; mehanička ventilacija; pluća; faktori rizika; postoperativne komplikacije; ishod lečenja

Introduction

About 1.5 million cardiac surgeries are performed annually around the world [1]. Despite great progress in surgical technique and perioperative anesthetic management, cardiac surgeries are accompanied by numerous postoperative complications, caused both by the surgical procedure itself, and by numerous unfavorable characteristics of the patients (age, comorbidities) [2]. After cardiovascular complications, postoperative pulmonary complications (PPCs) are the most common complications in cardiac surgery, occurring in up to 40% of patients [3]. They are associated with prolonged stay

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Abbreviations

PPCs – postoperative pulmonary complications
ICU – intensive care unit
MV – mechanical ventilation
TV – tidal volume
PEEP – positive end-expiratory pressure
CPB – cardiopulmonary bypass
PaO_2 – arterial oxygen partial pressure
FiO_2 – fractional inspired oxygen
$PaCO_2$ – partial pressure of carbon dioxide
CABG – coronary artery bypass graft
IQR – interquartile range

in the intensive care unit (ICU), prolonged hospitalization, and increased mortality [3–7].

Mechanical ventilation (MV) is an integral part of cardiac surgery. It is certainly a risk for the development of PPCs. In the last two decades, introduction of lung protective ventilation, which includes low tidal volume (TV), low plateau and driving pressure, recruitment maneuvers, and adequate positive end-expiratory pressure (PEEP), has contributed to the reduction of pulmonary complications in surgery patients [8, 9]. However, on-pump cardiac surgery is performed in conditions of cardiopulmonary bypass (CPB), which is responsible for systemic inflammatory response and oxidative stress, leading to pulmonary ischemia-reperfusion injury [4, 10, 11]. Other factors also contribute to the development of complications, including the patient's respiratory function, type of surgery, pain after sternotomy, anesthesia protocol, and use of blood and blood products [4, 12]. The CPB completely takes over the role of the heart and lungs and enables smooth surgical work, so the question arises whether MV is necessary during that period. International guidelines for CPB management recommend the use of PEEP (recommendation class IIa), as well as ventilation during CPB (recommendation class IIb), due to lung protection [13]. However, these are low-grade recommendations, mainly due to different study results. In practice, the dilemma of applying the MV during CPB still remains. The usual practice is not to ventilate the lungs or to ventilate with low TV. A study that included 69 cardiac surgery centers in Italy showed that in as many as 75% of centers, ventilation stops during CPB [14].

The results of some studies showed that CPB without MV is associated with decrease in the arterial oxygen partial pressure (PaO_2) to fractional inspired oxygen (FiO_2) ratio, arterial blood pH, static pulmonary compliance, as well as increase in partial pressure of carbon dioxide ($PaCO_2$), pulmonary shunt, and alveolar-arterial oxygen gradient [15]. One meta-analysis showed that MV during CPB may improve post-CPB oxygenation and gas exchange in patients undergoing cardiac surgery, altough long-term outcomes are unknown [16]. On the other hand, some randomized studies and meta-analyses showed that maintaining a low TV did not reduce the incidence of PPCs compared to a strategy in which no ventilation was performed during CPB [5, 6, 17–19].

The aim of this study was to investigate whether patients ventilated with low TV with the use of PEEP after coronary artery bypass graft (CABG) surgery have a lower percentage of PPCs compared to patients who were not ventilated during CPB.

Material and Methods

The retrospective study was conducted at the Clinic of Cardiovascular Surgery of the Institute of Cardiovascular Diseases of Vojvodina in Sremska Kamenica in the period from October 1, 2021 to December 1, 2022. The study was approved by the Ethics Committee of the Institute of Cardiovascular Diseases of Vojvodina (No. 2115-1/4). The study included patients who were admitted for CABG surgery. Only patients undergoing elective surgery were included in the study. Patients with chronic lung diseases and patients with an ejection fraction < 30% were excluded from the study. The first group (group V) included patients who were ventilated during CPB (TV 3 ml/kg predicted body weight, PEEP 5 cm H_2O, respiratory rate 10 - 12/min, FiO_2 0.6 - 0.7). The second group (group NV) included patients who were not ventilated during CPB.

All patients underwent surgery under general endotracheal anesthesia. As premedication, they received midazolam 3.75 - 7.5 mg orally. Midazolam, sufentanil, propofol, and rocuronium bromide were used to induce anesthesia. After intubation, the lungs were mechanically ventilated with a 50/50 oxygen/air mixture. Anesthesia was maintained with sevoflurane, analgesia with continuous infusion of sufentanil, while neuromuscular relaxation was maintained with intermittent administration of rocuronium bromide. The following monitoring was used perioperatively: electrocardiography, pulse oximetry, continuous arterial pressure, arterial gas analysis, central venous pressure, body temperature, and diuresis. Medial sternotomy approach was used in all patients. After surgery, patients were transferred to the ICU, where sedation with propofol continued, until the conditions for extubation were met.

The following parameters were also examined in all patients: demographic data (age and sex), height, weight, body mass index (BMI), comorbidities (arterial hypertension, previous myocardial infarction, cerebrovascular accident, smoking, dyslipidemia, diabetes, chronic kidney disease), ejection fraction before surgery, and European System for Cardiac Operative Risk Evaluation (EuroScore II). Intraoperative variables included: cross-clamp time and CPB time. Postoperatively, the duration of MV and the number of days in the ICU were recorded. Of particular importance was the monitoring of PPCs: prolonged MV (≥ 24 h), pleural effusion, pneumonia, pneumothorax, respiratory failure, reintubation, and bronchospasm. We also compared in-hospital mortality between groups.

We used descriptive statistical measures: arithmetic mean, standard deviation, median, quartiles, frequency, and percentile. The t-test for independent samples and the Mann-Whitney U test were used to

Table 1. Baseline patient characteristics and intraoperative data
Tabela 1. *Osnovne karakteristike pacijenata i intraoperativni podaci*

	Group V *Grupa V*	Group NV *Grupa NV*	p *p*
Patients No./*Pacijenti Br.*	398	101	
Male No. (%)/*Muškarci Br. (%)* Female No. (%)/*Žene Br. (%)*	292 (73.4) 106 (26.6)	81 (80.2) 20 (19.8)	0.199
Age (years) mean ± SD/*Starost (godine) srednja vrednost ± SD*	65.5 ± 7.8	66.6 ± 8.3	0.238
Weight (kg) median (IQR)/*Težina (kg) medijana (IQR)*	80 (72 - 90)	82 (72 - 92)	0.494
Height (cm) median (IQR)/*Visina (cm) medijana (IQR)*	171 (163 - 176)	171 (165 - 176)	0.548
Body mass index (kg/m^2) median (IQR) *Indeks telesne mase (kg/m^2) medijana (IQR)*	27.6 (25.4 - 30.8)	27.8 (25.6 - 30.4)	0.823
Ejection fraction (%) mean ± SD *Ejekciona frakcija (%) srednja vrednost ± SD*	53 (46 - 59)	53 (44 - 58)	0.667
Hypertension No. (%)/*Hipertenzija Br. (%)*	339 (85.2)	87 (86.1)	0.876
Hyperlipoproteinemia No. (%)/*Hiperlipoproteinemija Br. (%)*	250 (62.8)	65 (64.4)	0.818
History of myocardial infarction No. (%)/*Infarkt miokarda u istoriji Br. (%)*	161 (40.4)	37 (36.6)	0.497
History of cerebrovascular accident No. (%)/*Cerebrovaskularni događaj u istoriji Br. (%)*	26 (6.5)	9 (8.9)	0.388
Diabetes mellitus No. (%)/*Dijabetes melitus Br. (%)*	140 (35.2)	39 (38.6)	0.562
Chronic kidney disease No. (%)/*Hronična bubrežna insuficijencija Br. (%)*	36 (9.0)	8 (7.9)	0.845
Smokers No. (%)/*Pušači Br. (%)*	200 (50.2)	52 (51.5)	0.911
EuroScore II/*EuroSkor II*	1.15 (0.8-1.9)	1.27 (0.85-1.92)	0.432
Intraoperative data/*Intraoperativni podaci*			
Aortic cross-clamp time (min) mean ± SD *Trajanje aortne kleme (min) srednja vrednost ± SD*	54.7 ± 20.0	54.8 ± 14.1	0.935
Cardiopulmonary bypass time (min) mean ±SD *Trajanje ekstrakorporalne cirkulacije (min) srednja vrednost ± SD*	62.0 ± 21.7	63.3 ± 24.4	0.618

Legend: EuroScore II - The European System for Cardiac Operative Risk Evaluation; IQR - interquartile range; Group V - patients ventilateds during CPB; Group NV - patients not ventilated during CPB
Legenda: EuroScore II – Evropski sistem za procenu operativnog rizika u kardiohirurgiji; IQR – interkvartalni raspon; Grupa V – pacijenti ventilirani niskim disajnim volumenom; Grupa NV – pacijenti koji nisu ventilirani u toku ekstrakarpalne cirkulacije; SD – standardna devijacija

compare the mean values of two variables. The association of categorical variables was examined using the χ^2 test for contingency tables and Fisher's exact test. A value of $p < 0.05$ was taken as statistically significant. Statistical analyses were performed using IBM SPSS Statistics for Windows, version 19.0 (IBM Corp., Armonk, NY, USA).

Results

In the above-mentioned period, a total of 551 on-pump CABG surgeries were performed. Fifty-two patients were excluded from the study due to an ejection fraction < 30% or chronic lung disease. A total of 499 patients were included in the study. **Table 1** shows that during CPB, 398 patients were ventilated with low TV (group V), while there were 101 patients in the group without MV (group NV).

The groups did not differ significantly in basic demographic and anthropometric characteristics, comorbidities, ejection fraction, and EuroScore II. Both groups included mostly male patients. The average age in group V was 65.5 years, while in group NV it was 66.6 years. The average value of the ejection fraction was identical in both groups (53%). The leading comorbidity was hypertension, which was present in 85.2% of group V and 86.1% of group NV. The second most frequent comorbidity was hyperlipoproteinemia (group V 62.8%, group NV 64.4%). Diabetes mellitus and previous myocardial infarction were present in a significant percentage. Smokers accounted for half of the patients in both groups. Other comorbidities were present in a smaller percentage.

Intraoperative data were not significantly different between the two groups. The duration of the aortic clamp was 54.7 minutes in the group of ventilated patients and 54.8 minutes in patients without MV. The average duration of CPB was 62 minutes in group V and 63.3 minutes in group NV.

The primary outcomes and PPCs are shown in **Table 2**. They did not differ significantly between the groups. The most frequent were the need for prolonged MV (V 5.8%, NV 5.9%), and pleural effusions (V 4.8%, NV 5.9%). The frequency of pneumonia was identical in both groups (2%). Pneumothorax occurred in 1.8% of patients in group V and in 2% of patients in group NV. Other PPCs occurred in a smaller percentage.

Table 3 shows that patients in both groups were ventilated for an average of 10 hours after surgery

Table 2. Primary outcomes
Tabela 2. *Primarni ishodi*

	Group V *Grupa V*	Group NV *Grupa NV*	p *p*
Prolonged mechanical ventilation No. (%)/*Produžena mehanička ventilacija Br. (%)*	23 (5.8)	6 (5.9)	1.000
Pleural effusion No. (%)/*Pleuralni izliv Br. (%)*	19 (4.8)	6 (5.9)	0.613
Pneumonia No. (%)/*Pneumonija Br. (%)*	8 (2.0)	2 (2.0)	1.000
Pneumothorax No. (%)/*Pneumotoraks Br. (%)*	7 (1.8)	2 (2.0)	1.000
Respiratory failure/*Respiratorna insuficijencija Br. (%)*	3 (0.8)	2 (2.0)	0.267
Reintubation No. (%)/*Reintubacija Br. (%)*	3 (0.8)	0	0.877
Bronchospasm No. (%)/*Bronhospazam Br. (%)*	0	0	–

Legend: EuroScore II - **The European System for Cardiac Operative Risk Evaluation; IQR - interquartile range; Group V - patients ventilateds during CPB; Group NV - patients not ventilated during CPB**
Legenda: EuroScore II – Evropski sistem za procenu operativnog rizika u kardiohirurgiji; IQR - interkvartalni raspon; Grupa V - pacijenti ventilirani niskim disajnim volumenom; Grupa NV – pacijenti koji nisu ventilirani u toku ekstrakarpalne cirkulacije; SD – standardna devijacija

Table 3. Secondary outcomes
Tabela 3. *Sekundarni ishodi*

	Group V *Grupa V*	Group NV *Grupa NV*	p *p*
ICU intubation time (h) median (IQR) *Trajanje mehaničke ventilacije pluća u JIL (h) medijana (IQR)*	10 (8 - 12)	10 (8 - 12)	0.896
ICU length of stay (days) median (IQR)/*Boravak u JIL (dani) medijana (IQR)*	1 (0.9 - 1.1)	1 (0.9 - 1.1)	0.405
In-hospital mortality No. (%)/*Intrahospitalni mortalitet Br. (%)*	11 (2.8)	1 (1.0)	0.474

Legend: ICU – intensive care unit; IQR - interquartile range; Group V - patients ventilateds during CPB; Group NV - patients not ventilated during CPB
Legenda: *JIL – jedinica intenzivnog lečenja; IQR – interkvartilni raspon, Grupa V – pacijenti ventilirani niskim disajnim volumenom; Grupa NV – pacijenti koji nisu ventilirani u toku ekstrakarpalne cirkulacije*

which they spent in the ICU. In the ventilated group, 11 patients died (2.8%), and in the group of patients without MV, 1 patient died (1%).

Discussion

Pulmonary complications are very common after cardiac surgery. Most of these complications are not severe, but when a severe complication does occur, patients' lives may be in significant danger [20]. The aim of this study was to investigate whether MV with a low TV leads to a lower incidence of PPCs compared to the non-ventilated group during CPB. The study showed that there were no statistically significant differences in postoperative outcomes between the ventilated and non-ventilated groups. In the group that was ventilated with a low TV, pulmonary complications occurred in 16% of patients, and in the non-ventilated group in 17.8% of patients. The need for prolonged MV, pleural effusions, and pneumonia were the most common pulmonary complications in both groups.

John and Ervine used TV 5 ml/kg in their randomized, controlled study [21]. Their patients were exclusively non-smokers, while we included this group of patients in the research. They concluded that the time spent on MV was significantly reduced in the ventilated group, which indicates potential benefits of ventilation during CPB. However, their research included a total of 23 patients divided into 2 groups, which significantly decreased the power of the study. Davoudi et al. concluded that the group ventilated with continuous low TV (3 ml/kg, respiratory rate 12/min, PEEP 5 cmH_2O, and FiO_2 1.0) had better oxygenation after CPB, as well as better pulmonary function, which caused a reduction in the time at MV [22].

Recent studies have not found a significant difference between different MV strategies. A large, randomized study (MECANO study) included 1501 patients [5] who required valvular surgery, patients with chronic lung diseases and patients with heart failure, while our research excluded this category of patients due to the associated factors. In subjects who were ventilated with TV 3 ml/kg, frequency 5/min, and PEEP 5 cmH_2O, no reduction in PPCs was observed compared to the group of non-ventilated patients. The most frequent PPCs were pneumonia, need for respiratory support after 2 days, and reintubation. However, a post-hoc analysis of the same study, but in patients who underwent isolated CABG surgery, showed a lower percentage of PPCs in the group of patients in whom MV with a low TV was used, which may support the hypothesis that CABG procedures benefit more from ventilation strategy than other types of cardiac procedures [3].

The VENICE International Cohort Study, conducted in 9 countries, analyzed 676 patients and showed that PPCs were equally present in the group ventilated with low TV as in the group without MV

[4]. The same result was ontained by a meta-analysis conducted by Chi et al. [15]. An observational study examined the impact of continuing MV during CPB on functional residual lung capacity and it did not show a difference compared to the group of patients in whom ventilation was discontinued [23].

A comparative study from 2019 attempted to find out whether ventilation during CPB has an effect on postoperative pulmonary dysfunction [24]. The research included 66 patients divided into 3 groups: a group with pressure-controlled ventilation, a group with volume-controlled ventilation, and a control group of non-ventilated patients. The study showed that there were no significant differences in the PaO_2, $PaCO_2$, and PaO_2/FiO_2 ratios, nor were there significant differences observed on the chest X-rays among these three groups. In their study, Zhang et al. concluded that maintaining a low TV during CPB has no significant advantage in reducing the incidence of PPCs compared to a non-MV strategy among a non-ventilated group and two ventilated groups, with one group being ventilated with TV 3 - 4 ml/kg, respiratory frequency 10 - 12/min, PEEP 5 - 8 cm H_2O, and FiO_2 0.3, and the second group having the same ventilation parameters with FiO_2 0.8 [6]. Unlike our study, which included only patients who were admitted for CABG surgery, this study included predominantly patients who required valvular surgery (> 80%). The leading three PPCs were pleural effusion, atelectasis, and respiratory infection. The duration of MV in ICU was longer in all three groups compared to our study (non-ventilated 14.5 hours; ventilated FiO_2 0.3 15.5 hours; ventilated FiO_2 0.8 16 hours), while the length of stay in ICU was 3 days. Hospital mortality was similar to our results.

Conclusion

Pulmonary complications after cardiac surgery are still common. Experience at our clinic showed that the choice of mechanical ventilation strategy during cardiopulmonary bypass does not affect postoperative complications. Despite several studies done in the last decade, we still have no clear ventilation strategy for patients during cardiopulmonary bypass. Randomized, well-designed, and large multicenter studies with different tidal volumes, fractional inspired oxygen, and positive end-expiratory pressure are needed to provide stong recommendations.

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