The effect of partial cross clamping administration on postoperative healing of pulmonary functions for coronary artery bypass graft operations

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ABSTRACT

الأهداف : عمل مقارنة بين العزل الجزئي للقلب عن الدورة الدموية باستخدام آلية التهوية الرئوية والعزل الكلي للقلب عن الدورة الدموية أثناء عملية طعم مجازة الشريان التاجي في المجازة القلبية الرئوية، ومدى تأثير ذلك على تنفس الرئتين .

الطريقة : أُجريت هذه الدراسة في قسم جراحة القلب في مركز الأبحاث والتدريب بمستشفى إيرزوروم، إيرزوروم، وقسم جراحة القلب في كلية أكدينيز الجامعي، أنطاليا، تركيا . شملت الدراسة 30 مريض ممن خضعوا لعملية طعم مجازة الشريان التاجي وذلك خلال الفترة من فبراير إلى أبريل 2007م . لقد قمنا بتقسيم المشاركين في الدراسة إلى مجموعتين وهما : المجموعة أ (العدد:15) وشملت المرضى الذين أُجريت لهم عملية العزل الكلي للقلب عن الدورة الدموية، والمجموعة ب (العدد:15) وشملت مرضى العزل الجزئي للقلب عن الدورة الدموية باستخدام آلية التهوية الرئوية .

النتائج : لقد قمنا بدراسة وظائف الرئة بعد العملية الجراحية وذلك اعتماداً على كل من : 1) معدل تأكسد غازات الدم في الشرايين، و2) نتائج مقياس التنفس . كما أننا قمنا بتسجيل التالي : الوقت المستغرق لعملية المجازة القلبية الرئوية وبتبني طريقتي العزل الجزئي للقلب والعزل الكلي للقلب عن الدورة الدموية، والوقت المستُغرق لنزع الأنبوب، وعدد وأنواع الطعوم، وعدد الأيام في غرفة العناية المركزة والمستشفى . أشارت نتائج الدراسة إلى أنه لم يكن هناك اختلافاً واضحاً بين المجموعتين عند تسجيل معدل التأكسد، وتفاصيل العملية الجراحية والبقاء في المستشفى . غير أننا لا حظنا اختلافاً واضحاً بين المجموعتين وذلك لصالح المجموعة ب بعد تسجيل نتائج مقياس التنفس وتأثير العزل الجزئي على وظائف الرئة التنفسية .

خاتمة : أظهرت هذه الدراسة بأن العزل الكلي للقلب عن الدورة الدموية وتوقف دوران الدم في الرئتين يعدان من الأسباب الرئيسية لحدوث المشاكل التنفسية في الرئتين وذلك اعتماداً على استجابة الالتهاب الرئوي أثناء عملية طعم مجازة الشريان التاجي .

Objectives: To compare partial cross clamping and mechanic pulmonary ventilation technique with total cross clamping utilization during cardiopulmonary bypass in coronary artery bypass graft operations in terms of pulmonary healing.

Methods: Between February and April 2007, isolated coronary artery bypass graft operation was performed for 30 patients in the Cardiovascular Surgery Department, Erzurum Regional Training and Research Hospital, Erzurum, and the Cardiovascular Surgery Department, Medical Faculty, Akdeniz University, Antalya, Turkey. The patients were divided into 2 groups; Group A (n=15) with total cross clamping, and Group B (n= 15) partial cross clamping and mechanic pulmonary ventilation in cardiopulmonary bypass.

Results: Postoperative pulmonary functions were studied in 2 main data; 1) the oxygenization rate of artery blood gas, and 2) spirometer results. Additionally, total cardiopulmonary bypass and total cross-clamping times, extubation times, numbers and types of grafts, days of intensive care unit treatment, and hospitalizations were recorded. There was no statistically significant difference between the 2 groups for oxygenization rate, and surgery hospitalization details. We observed a statistically significant difference with advantage in Group B in spirometric results in terms of healing of pulmonary functions.

Conclusion: Total cross clamping and circulatory arrest of the lungs are the main sources of postoperative pulmonary complications based on the pulmonary inflammatory response in coronary artery bypass surgery.

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Coronary artery stenosis is the most frequent medical reason for clinical morbidity.[1] Acute myocardial infarction and arrhythmia are 2 main reasons for mortality among coronary arterial disease patients. Severe coronary atherosclerosis is generally treated with coronary artery bypass graft surgery. During coronary artery bypass graft, cardiopulmonary bypass associated complications occur in many systems and organs of the body. These life-threatening complications include lungs, brain, heart, kidneys, and intestines. Emergency, female gender, re-operation, low left ventricular contractility, simultaneous percutaneous transluminal coronary angioplasty, congestive heart failure, mitral deficiency, cerebro-vascular disease, chronic obstructive lung disease, and kidney failure increases the rate of operative mortality and morbidity.[2,3] Generally, the lungs are the most frequently affected organ system according to the ischemic period of cross clamping and the subsequent reperfusion injury. During the coronary artery surgery, polymorph nuclear cell accumulation, adhesion between neutrophils and pulmonary endothelium, free oxygen radical products, arachidonic acid and its products, neutrophil elastase activation are the cause of the pulmonary damage. In a routine coronary artery bypass graft operation, pulmonary ventilation and pulmonary circulation are ceased during cardiopulmonary bypass. In our opinion, this manipulation is the reason for pulmonary complications in the short and long term postoperative period. The aim of this study is to evaluate the effect of partial cross clamping and mechanical ventilation during the cardiopulmonary bypass procedure in elective coronary artery bypass graft operations on the postoperative pulmonary function recovery period.

Methods. Between February and April 2007, 30 elective coronary arterial bypass-grafting (CABG) patients were included in our study in the Akdeniz University Cardiovascular Surgery Department, Antalya, and the Erzurum Regional Training and Research Hospital Cardiovascular Surgery Department, Erzurum, Turkey. The Ethical committees of the 2 hospitals approved the study protocol, and all procedures were carried out in accordance with the Declaration of Helsinki. Excluding criteria were known chronic obstructive lung disease with nominal spirometer values, kidney disease, left ventricular dysfunction with an ejection fraction under 35%, re-operations, preoperative or postoperative neurological dysfunctions, and combined operations with artery disease or valve replacements. The patients were operated according to American College of Cardiology and American Heart Association. operation criteria.[1] All patients were operated under cardioplegic cardiac arrest. The 30 patients were studied in 2 groups. Group A (n=15) - total cross clamping (CCL), and Group B (n=15) - partial CCL with pulmonary ventilation. The purpose of partial CCL and continuity of lung perfusion and mechanical ventilation during cardiopulmonary bypass (CPB) procedure is a strategy to prevent ischemic injury and reperfusion harm that occurs with a conventional total CCL and CABG operations. In Group A, pulmonary blood flow and ventilation were arrested during the CPB period. In Group B, CCL was applied to the aorta alone, pulmonary flow and ventilation were maintained during CPB. During the CPB period, ventilation parameters consisted of tidal volume in 8 milliliters per kg, a respiratory rate of 10 per minute, with inspiratory oxygen fraction (FiO_2) 0.4 (40%), and positive end expiratory pressure for 5 centimeters H_2O. Routine preoperative evaluation contained routine blood test with cardiac panel, detailed physical examination, chest x-ray, transthoracic echocardiograms, spirometer tests, and coronary angiography. Transthoracic echocardiograms showed aortic diameter, thickness of inter-ventricular septum, valve functions, pulmonary artery pressure and left ventricular wall motion. Arterial blood gas was examined in all patients to estimate the partial pressure of O_2 and CO_2. Spirometer tests implied information of preoperative forced vital capacity (FVC) and forced expiratory volume (FEV_1). Supplementary data were recorded for age, gender, smoking history, and diabetes mellitus. In preoperative data, 2 groups were in a homogeneous distribution for medical status and history. Both groups obtained the same premedication before operation containing propofol 2-3 mg/kg, fentanyl citrate 10-15 microgram/kg, and pancuronium bromide 0.1 mg/kg. Following endo-tracheal intubation, anesthesia maintenance dose included propofol 2-5 mg/kg/h, and fentanyl citrate 5-10 microgram/kg/h intravenously. The sevoflurane was used for inhalation anesthesia. Lung ventilation was achieved within a degree of 0.4 $Fi0_2$. At this stage, an artery blood gas evaluation presented the oxygenization rate of the patient with partial pressure of oxygen in artery blood (PaO_2)/$Fi0_2$. Values fewer than 200 PaO_2/FiO_2 commented as an oxygenization defect depending on various reasons. The entire group of patients received a median sternotomy. After the left intermammarian artery dissection, non-domminat extremity radial artery excision and great saphenous vein harvesting, injection of heparin administered the activated clotted time to be over 400 seconds. Following pericardiectomy, aorta-caval cannulation performed. Maintaining 28°C of body core temperature, total CCL in Group A and partial CCL combined with pulmonary ventilation in Group B were applied. Cardiopulmonary bypass was accomplished with centrifugal pump and membrane oxygenator. For myocardial protection we used 3 steps of cardioplegia: 500 ml of normothermic blood cardioplegia, cold cardioplegia in 10 ml/per kg in 40 mm Hg pressure, and 500 ml of hot-shot cardioplegia before removal of the CCL. Additive cardioplegia doses were applied every 20 minutes of cardiac arrest. Coronary anastomoses were performed in total cardiac arrest. Following the removal of the CCL and protamine sulphate administration, proximal anastomoses were performed with a side clamp on the aorta. Following the hemostasis maneuvers, surgical drains were placed and the sternum closed. At this stage, an oxygenization rate was recorded for both groups. Study parameters include oxygenization rates after closure of the sternum, coronary graft types and numbers, pleura openings, times of CPB and total CCL. The oxygenization rate is defined as the ratio of PaO_2 to FiO_2 of mechanic ventilation. Patients were transported to the cardiovascular intensive care unit from the operation room. Oxygenization rates were measured at one and 5 hours of intubation. Following extubation, daily spirometer tests were performed on the patients to analyze forced vital capacity (FVC) and FEV1.

Statistical analysis. The data are expressed as proportions, or as mean ± standard deviation. Differences in categorical variables were analyzed by 2 analyses. Differences in continuous variables were analyzed by Student t tests. Overall survivals were determined by the Kaplan-Meier method; the estimated probability is shown together with the standard deviation. Statistical modeling and testing were performed using S-PLUS statistical software (Math Soft, Cambridge, MA, USA). Results were considered significant if *p* values were less than 0.05.

Results. In our study, the parameters were collected in 3 phases: preoperative, intra-operative, and postoperative periods. Age, gender, smoking history, hypertension, diabetes mellitus, and spirometer test with FVC and FEV_1 were determined as the preoperative period. Oxygenization rate with sternal closure (PaO_2/FiO_2), pleurotomy side and quantity, CABG type and quantity, duration of total cross clamp and cardiopulmonary bypass (minutes) was evaluated in the intra-operative period. In the postoperative period, oxygenization rates at the first and fifth hour in the intensive care unit, extubation time (hours), days in the intensive care unit and hospitalization, and daily spirometer test with FVC and FEV_1 was assessed.

The preoperative demographic data were similar in both study groups, as shown in **Table 1**. Both groups consisted of 2 female patients to 13 male patients. Smoking history was evaluated in years of tobacco use. Diabetes mellitus was treated with anti-diabetic drugs in 6 patients for Group A, and 5 patients for Group

Table 1 - Preoperative comparison of parameters.

Preoperative parameter	Group A (mean)	Range	Group B (mean)	Range	*P*-value
Age	60.30	48-74	59.20	49-69	>0.05
Gender (F/M)	2/13		2/13		>0.05
LVEF (%)	59.47	45-70	60.20	55-70	>0.05
Smoking (years)	19.47	15-45	19.21	12-50	>0.05
FVC (%)	81.05	53.7-101	83.62	52.6-116.3	>0.05
FEV_1 (%)	95.35	55-114	96.92	58-130	>0.05
DM	6/15		5/15		>0.05
HT	9/15		10/15		>0.05

M/F - male/female, LVEF - left ventricular ejection fraction, FVC - forced vital capacity, FEV_1 - forced expiratory volume in first second, DM - diabetes mellitus, HT - hypertension

Table 2 - Recorded intra-operative data between groups.

Intra-operative parameters	Group A	Group B	*P*-value
OR	346.62 (222.6-509.8)	427.29 (171-716)	>0.05
TCPB (minutes)	120.33 (96-180)	111.3 (65-155)	>0.05
TCC (minutes)	64.67	59.07	>0.05
CABG	3	2.73	>0.05
LIMA	15	15	>0.05
VSM	12	13	>0.05
RA	8	6	>0.05
Pleurotomy	13	13	>0.05
Unilaterally	12	11	>0.05
Bilaterally	1	2	>0.05

OR - oxygenization rate (PaO_2/FiO_2), TCPB - cardiopulmonary time, TCC - cross clamp time, CABG - coronary artery bypass graft, LIMA - left intermammarian artery, VSM - vena saphena magna, RA - radial artery

Table 3 - Postoperative detail of results.

Postoperative parameters	Group A	Group B	*P*-value
OR 1	231.23 (103-392)	211.42 (94-446)	>0.05
OR 5	267.55 (120.3-417)	258.88 (138.4-417.2)	>0.05
Extubation (minutes)	540 (300-1380)	457 (300-1080)	>0.05
ICU (day)	2.8 (2-5)	2.73 (2-6)	>0.05
Hospitalization (day)	6.33 (5-9)	6.55 (5-9)	>0.05

OR1 - oxygenization rate (PaO_2/FiO_2) of first hour, OR 5 - oxygenization rate (PaO_2/FiO_2) of fifth hour, ICU - intensive care unit

Table 4 - Daily recorded postoperative FVC and FEV1 with calculated mean values of Group A and Group B.

Days	Group A FVC (%)	FEV1 (%)	Group B FVC (%)	FEV1 (%)	*P*-value
1	25.13 (14-32)	21.87 (55-114)	39.73 (31-53)	44.47 (30-65)	<0.05
2	27.80 (16-39)	24.27 (16-41)	49.40 (39-64)	52.23 (39-71)	<0.05
3	34.12 (17-44)	31.67 (20-42)	54.87 (39-64)	58.73 (40-77)	<0.05
4	41.47 (30-52)	40.33 (30-56)	59.47 (50-76)	63.47 (54-85)	<0.05
5	47.47 (29-57)	47.0 (31-60)	63.80 (56-74)	69.0 (58-90)	<0.05

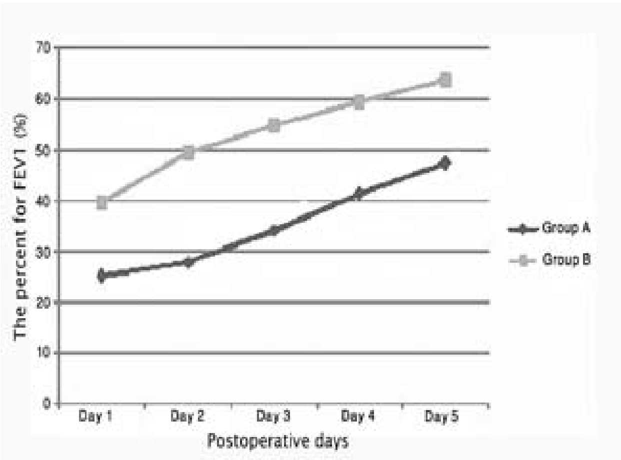

Figure 1 - A graphical illustration depicting postoperative FVC results. The increase in percentile values of FVC was higher in group B than group A during postoperative days. This result was statistically significant.

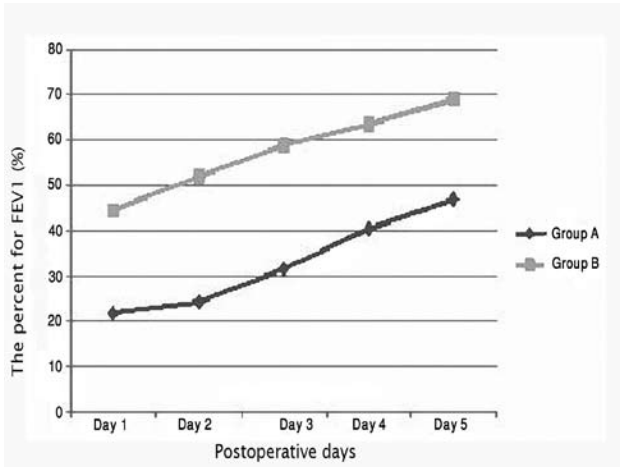

Figure 2 - Graphical summary of postoperative FEV_1 results. The increase in percentile values of FEV_1 was higher in group B than group A during postoperative days. This result was statistically significant.

B. None of our patients required insulin preoperatively. Intra-operative oxygenization rates were calculated following closure of the sternum and before leaving the operation room. Total CPB and total CCL time, CABG number, and types with pleurotomy are summarized in **Table 2**. Radial artery harvesting from the non-dominant extremity, and right internal mammary artery (IMA) application was not performed. Values less than 200 were accepted as a finding of pulmonary deterioration in relation to oxygenization rate. The CABG quantities for each patient were 3 in Group A, and 2.73 for Group B. All patients received IMA graft for the left anterior descending artery. Non-dominant extremity radial artery used in 8 patients in Group A, and in 6 patients for Group B. The Modified Allen test was applied before radial artery harvesting in each case. Pleurotomy is a complication that mostly occurs during the preparation of IMA. This situation affects the postoperative pulmonary functions negatively. In Group A, 13 cases developed a pleurotomy, and in one case bilaterally. Pleurotomy occurred in 13 patients in Group B with 2 cases bilaterally. There was no a difference between patients in relation to intra-operative parameters.

Postoperative data included days in the intensive care unit and hospitalization, oxygenization rates at the first and fifth hours in the intensive care unit, and extubation times for Group A and Group B, as summarized in **Table 3**. Intensive care unit stays were similar in both groups. There was no difference between patients in relation to postoperative parameters. At the same time, daily spirometer studies were performed for 5 days postoperatively. For each recording of spirometers, including FVC and FEV_1, patient was asked to repeat the test 3 times. The highest values were recorded as the result of the spirometer test on that particular day. Patients were seated during the spirometer test to optimize the position of the thorax and diaphragm. Group A and Group B's spirometer results are summarized in **Table 4**. Calculated mean FVC values and FEV1 data were higher in group B compared with group A, and this difference was statistically significant in both parameters (p<0.05). Graphical comparison of postoperative daily FCV data for Groups A and B are shown in **Figure 1**. Graphical comparison of postoperative daily FEV1 data for Group A and B are shown in **Figure 2**. Generally, there was no significant difference in preoperative demographic data, intra-operative oxygenization rates, operative characteristics, and postoperative findings other than spirometric tests. However, FEV1 and FCV values were higher for the first 5 days in group B, and this difference was statistically significant.

Discussion. In CABG surgery, a CCL can be administered in 2 different ways; total CCL or partial CCL. A total CCL occludes both the aorta and common pulmonary artery without allowing any flow from the heart to the aorta and common pulmonary artery to the lungs. A partial CCL occludes only the aorta and allows flow from the right chambers of the heart to the lungs during the CPB period.

Coronary artery bypass graft related pulmonary injury has been well known since the early years of this procedure.[4] Pulmonary deterioration is mainly caused by pulmonary ischemia during CPB and reperfusion injury afterwards.[5,6] Despite the effort of several pulmonary protection strategies, the lungs still are the most vulnerable tissue during open-heart surgery. Pulmonary parenchyma is perfused in 2 ways in regular physiology; the pulmonary artery system, and the bronchial artery system. A widespread anastomosis vascular net connects these 2 vessel systems. In a normal hemodynamic status, the bronchial artery system carries 1-3% load of pulmonary perfusion. During CPB, a total CCL occludes the pulmonary artery system flow. Thus, pulmonary parenchyma perfusion depends only on bronchial artery flow in the CPB period. Following removal of CCL, the blood flow through the pulmonary parenchyma triggers a cascade of inflammatory reactions with reperfusion ischemia. The great amounts of pro-inflammatory cytokines, polymorph nuclear cell accumulation, free oxygen radicals, arachidonic acid and its products, reactive cell accumulation and activation, proteolytic enzymes and neutrophil elastase activation cause the secondary pulmonary deterioration.[7] In this pathophysiology, leaks from the intravascular area to parenchyma, reduced pulmonary elasticity, loss of surfactant integrity and quantity, and degradation of oxygen transport results in pulmonary edema, atelectasis, postoperative pneumonia, and "pump lung."

The risk of pulmonary complications after open-heart surgery range between 35-76%.[8] Furthermore, pulmonary complications are strongly associated with postoperative mortality and morbidity. Postoperative pulmonary distress is still a major problem for cardiac surgeons despite the developments of surgical technique and technical material of the cardiopulmonary circuit. As a catastrophic result of the pulmonary deterioration perspective, acute respiratory distress syndrome, and correlated multi-organ dysfunction are reported with a mortality rate of 91-96%. One surgical strategy against pulmonary complications and deterioration is partial CCL and pulmonary ventilation during CPB. Other strategies may include a filtration system in the cardiopulmonary circuit, as in the Drew Anderson Technique;[9] an open pulmonary circuit to room air during CPB with pulmonary perfusion, systemic medications of corticosteroids and neutrophil elastase inhibitors, deep hypothermia, and high cervical anesthesia.[10-12] These strategies have positive and negative aspects and need to be investigated with further studies. Various studies have reported the profound effect of pulmonary preservation on preoperative survival and recovery after CABG surgery with CPB. Increases in the incidence of significant pulmonary complications following CABG operations have a significant impact on the eventual patient outcome, so that in-hospital mortality rates for these patients may range from 4-24%. In the present study, we compared an alternative CPB strategy to reduce lung injury with partial CCL and mechanic pulmonary ventilation. Sievers et al[13] studied a variation of our technique. In 24 adult open-heart surgery cases, pulmonary perfusion and ultra filtration during CPB were examined. They divided patients into 3 groups, conventional CPB without pulmonary perfusion and ultra filtration (Group I, n= 7), with pulmonary perfusion alone (Group II, n= 9), and with ultra filtration (Group III, n= 8). Study parameters included plasma and bronco-alveolar fluid leukocyte integrity, lung injury markers (elastase proteinase inhibitor complex with Alfa macroglobulin) and oxygenization index (PaO_2/FiO_2). Clinical data with extubation time, intensive care unit period, and study parameters were significantly better in Group III. Sievers et al[13] advocated additive anti-inflammatory medication to improve results. In our patient series, no significant difference occurred in oxygenization rates between the 2 groups. Group B results were slightly better, but this difference introduced no statistically difference with analyses. Extubation times were similar for both groups. In addition, no significant difference occurred for intensive care unit stays and the hospitalization period between groups. In our opinion, partial CCL and mechanic ventilation during CPB may not improve the in-hospital treatment interval. The CABG operations with CPB present severe deterioration in spirometric tests postoperatively. In a study reported, the spirometric tests improved at the postoperative day 15 (14). Taggard et al[15] investigated postoperative FVC and FEV_1 parameters after coronary CABG surgery. They reported a healing interval for pulmonary functions within 6 days to 6 weeks regardless of the gender of the patient and to CPB durations. Taggard's study results are in parallel with the present study. They observed the most significant deterioration in the first postoperative day for FVC and FEV_1, similar to our results. The FVC results were decreased almost to one fourth compared with the preoperative measurement. FVC values recovered in following postoperative days for group A and group. The FVC values were seriatim recovered for group A and group B. Nevertheless, the recovery rates were significantly higher in group B undergoing partial CCL and mechanical ventilation compared with group A. In group B, fifth day FVC results were close to the preoperative values compared with Group A's outcome. A similarity was observed for FEV_1 results in favor of Group B. The FEV_1 results followed a similar pattern to the FVC. The most significant decline occurred at the first postoperative day for both groups. In Group A, at the fifth postoperative day, the FEV_1 values were less than the half of the preoperative value. Thus, the results demonstrate a serious pulmonary parenchyma injury. In group B, the FEV_1 values on the fifth day were significantly closer to the preoperative values compared with group A, and this difference was statistically significant. Furthermore, some other postoperative conditions are also reported as associated with deterioration of pulmonary function such as IMA grafts, pleurotomy, postoperative pleural fluid collections, diaphragm dysfunction with elevation and re-intubation in several articles.[9,10,14] In our study, these parameters were homogeneous for both groups including re-intubation numbers, IMA grafts, and other phrenic nerve related complications. A significant statistical difference was not observed for oxygenization rate results between both groups. Recent studiesreport the oxygenization rate as a clear and potent indicator for pulmonary function for intubated patients.[5-7,9-11] Limitations of this prospective study include the lack of a wider quantity of patient population. However, we specifically aimed to homogenize our cases in 2 groups as to eliminate possible reasons other than cross clamp application during surgery. As a matter of fact, our patient number was limited as a result of our effort to homogenize our 2 groups from different surgical techniques. On the other hand, some constant factors as surgical management practice of individual surgeon on operations may interfere with our results. Nevertheless, we believe that this investigative aspect of cross clamp related to postoperative healing on pulmonary functions may lead further investigations on pulmonary tissue inflammatory response agents after cardiopulmonary bypass period.

In conclusion, we strongly advocate partial CCL with pulmonary ventilation during CPB for CABG, especially for patients with impaired preoperative pulmonary function. Partial CCL and continuity of ventilation improve pulmonary recovery and postoperative quality of life of the patients. Despite our results, we believe that there is a need more advanced and detailed studies associated with this subject.

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