Abstract: The cardiopulmonary bypass, or heart-lung machine is one of the biggest medical inventions in the mid-20th century and the advances in cardiac surgery would not have been possible without this contrivance. Nevertheless, it is not without its share of side-effects, with post-perfusion acute lung injury being among one of the most severe and life-threatening complications. We report a case of 65-year-old female patient diagnosed with left main and three-vessel coronary artery disease and admitted for an elective coronary artery bypass grafting (CABG). Triple bypass grafting procedure was performed. After weaning from bypass, the patient developed severe pulmonary edema with calculated Murray score of 4 points suggesting ECMO (extracorporeal membrane oxygenation) as the only salvage procedure. Peripheral venoarterial ECMO was implanted. After 5 days the mechanical support was withdrawn with full pulmonary recovery. Innovative cardiopulmonary bypass circuit and techniques, lung-protective mechanical ventilation strategies, ECMO etc. are amid possibilities to avoid this potentially lethal complication.

Keywords: Cardiac surgery, cardiopulmonary bypass, lung injury, pulmonary edema, ECMO.

INTRODUCTION
Since the beginning of use of the so-called “heart-lung machine” for the cardiac surgery procedures it has been recognized that the CPB is associated with wide range of complications such as: hemolysis, air embolism, clotting, systemic inflammatory response, post-perfusion acute lung syndrome with acute respiratory distress syndrome (ARDS). The latter is cause for severe pulmonary parenchymal shunting with fluid sequestred in the alveoli, consolidation and atelectasis preventing gas exchange. Despite the recently success of protective mechanical ventilation strategies in lowering mortality and ongoing efforts to discover other effective interventions the treatment of these conditions remains a challenge and require quick thinking and perfect team work, especially when happens in the operating theatre.

CASE PRESENTATION
We present a case of 65-year-old lady admitted with clinical symptoms of dyspnea and shortness of breath. The patient denied a family history of cardiovascular diseases. PCI was done demonstrating 70% aorto-ostial LMCAD combined with three-vessel coronary artery disease: 70% stenosis of the left anterior descendant artery (LAD), occluded circumflex artery (RCX) and 80% stenosis of the right coronary artery (RCA). The patient was referred to our institution for surgical treatment as the best option for this case.

At admission the 12-channel electrocardiogram (ECG) showed sinus rhythm, R-wave progression in leads V1 to V4 as well as left axis deviation. The trans-thoracic echocardiography demonstrated left ventricle ejection fraction of 48%, aortic root diameter: 24mm, aortic bulbus: 33mm, ascending aorta (AA): 28mm. Aortic, mitral and tricuspid valves were without deviations. The laboratory test results (Table 1) apart from blood glucose, cholesterol and triglycerides were within the normal ranges.

| Hemoglobin      | 137 g/l |
|-----------------|---------|
| Hematocrit      | 0.40 L/l|
| Erythrocytes    | 4.73 g/l|
| Leucocytes      | 8.5 g/l |
| Platelets       | 204 G/l |
| Total cholesterol| 5.3 mmol/l |
| Triglycerides   | 2.39 mmol/l|
| Total protein   | 79 g/l  |
**Table 1: Laboratory test results;**

The chest X-ray on admission (Figure 1) demonstrated inflated lungs bilaterally without infiltrative changes and cardiomegaly. The calculated body mass index (BMI) was 36.4 and EuroSCORE II (European System for Cardiac Operative Risk Evaluation) of the patient was 2.53%.

![Figure 1: Chest X-ray on admission;](image)

The patient was operated in an elective manner. General anesthesia was inducted with propofol 1-3mg/kg, fentanyl 3-5 µg/kg and suxamethonium chloride 1mg/kg. The anesthesia was maintained with Sevoflurane and intermittent boluses of fentanyl every 30mins. Muscle relaxation was maintained with pipecuronium 0.04mg/kg. Typical cannulation of the AA and right auricle was performed and CPB was instituted. Cold blood cardioplegic solution was used and administered in antegrade and retrograde fashion. Triple CABG was performed: left internal thoracic artery (LIMA) to the LAD artery and saphenous venous grafts to the RCA and RCX arteries. The CPB was discontinued without catecholamine support. The total CPB and cross-clamp time were 53min. and 37min. respectively.

After weaning from CPB the patient developed acute deterioration of the respiratory function with development of severe hypoxic respiratory failure, acute pulmonary edema and severe right heart failure (Figure 2). The arterial blood-gas analyses (Table 2) demonstrated severe gas exchange impairment. The calculated Murray lung injury score was 4 which suggested immediate ECMO implantation.

| Time (min) | PaO₂ | PCO₂ | O₂ sat. |
|-----------|------|------|---------|
| 13:05     | 67.8 | 40.2 | 92%     |
| 13:20     | 45.3 | 47.5 | 81%     |
| 13:30     | 38.8 | 56.4 | 69%     |
| 14:00 ECMO| 92   | 37.9 | 92.4%   |
| 14:30     | 153  | 27.9 | 99.9%   |
| 15:00     | 274  | 25.2 | 100%    |
| 16:00     | 307  | 29   | 99.9%   |
| ECMO-Ex 5 days later | 111 | 33.6 | 98.8% |
Peripheral venoarterial ECMO was implanted via right femoral vein and artery. In the postoperative period numerous toilet bronchoscopies and airway lavages were performed for atelectasis prevention. In the following days the respiratory function improved substantially and the patient was extubated on the postoperative day (POD) 3. The ECMO support was discontinued and explanted on the POD 5.

Table 2: Blood gas analyses before and after ECMO implantation and explantation.

| PaO$_2$/FiO$_2$ | 75.3 | 45.3 | 38.8 | 102.2 | 170 | 304.4 | 341 | 246 |
|----------------|------|------|------|-------|-----|-------|-----|-----|
| BE             | -9.7 | -3.6 | -3.8 | -2.6  | -2.3| -1.9  | -2.1| -1.3|

Figure 2: Extravascular fluid causing foam coming out of the endotracheal tube;

Figure 3: Chest radiograph on POD 3;

Figure 4: Chest X-ray on POD 7;
The total intensive care unit stay was 10 days. The stay in the postoperative department was uneventful and the patient was discharged on POD 16 on medical therapy with acetylsalicylic acid 100mg/daily, rosuvastatin 10mg/daily, perindopril 5mg/twice daily, metoprolol 50mg/twice daily and the individualized insulin scheme. One month after the operation the patient is doing well without any complaints or remarks.

DISCUSSION
Post-perfusion lung syndrome represent only 1-2% of all cardiac surgery complications but with mortality rates 40-90% depending on different institutions. Moreover, once confirmed the probability of developing multiple-organ system failure(MOSF) is approximately 70% which makes it very rare yet very lethal diagnosis. Although they differ in severity of development ARDS and post-perfusion lung syndrome have the same mechanism of triggering the systemic inflammatory processes. The contact between blood and the artificial CPB circuit activates leucocytes, platelets, coagulation, fibrinolytic, kinin-bradkinin and complement system. During reperfusion the circulating protease released by leucocytes, the free radicals and intestinal endotoxin translocation cause increased pulmonary microvascular permeability, alveolar macrophage activation and release of inflammatory mediators such as tumor necrosis factor-α, interleukin 6 and 8, superoxide dismutase etc. resulting in lungs being the first targeted organ. The breakdown of type IV collagen which is one of the main constituent of the basement membrane produces significant levels of 7S protein which together with procalcitonin levels are markers of severe lung injury. Is the CPB only responsible for the severe pulmonary edema? The causes can be many. If the reason was cardiac failure due to perioperative myocardial infarction we should expect elevated cardiospecific enzymes as well as ECG changes. Intraoperative trans-esophageal echocardiography should be routinely used to monitor the myocardial, valve function and regional wall motion abnormalities after weaning from CPB as well as after anesthesia induction to exclude anesthesia-related cardiac depression or pulmonary edema. The graft patency can be easily confirmed with ultrasound flowmetry or via PCI. The vast majority of cardiac surgery patients are polymorbid and many of them require pre- or intraoperative blood products transfusion. Transfusion-related acute lung injury(TRALI) can cause severe bilateral pulmonary edema, hypoxemia and be indistinguishable from ARDS. The symptoms usually begin 1 to 4 hours after transfusion and majority of the patients improve within 48 to 96 hours. Regarding the graft choice, there are no absolute contra-indications to perform a total arterial revascularization, and it is always preferred if possible. According to Vazhev, which published data from patients operated using entirely arterial grafts for revascularization with 93% long-term survival and 0% cases of graft occlusion confirmed with PCI. However, we choose to use LIMA only instead of BIMA because of the patient’s obesity as well as because of the insulin-dependent diabetes. Many medications can induce pulmonary toxicity. Amiodarone is one of the most frequently used antiarrhythmic drugs. Being an iodine-containing compound it can accumulate in the lungs and cause wide range of symptoms from subtle to severe life-threatening lung injuries. Regarding cases with severe noncardiogenic pulmonary edema causing refractory life-threatening hypoxemia, the usage of ECMO is always an option and in many of the cases is a lifesaving procedure, as it was in our case. Whether or not the CPB itself is responsible for postoperative lung dysfunction still remains controversial, and it needs many further investigations regarding this particular topic. But one thing is clear – an early diagnosis and timely treatment are absolutely crucial for the patient’s best outcome.

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