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CASE REPORT

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# Anesthesia management of a patient who had twice heart transplantations

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**Abstract**

Heart retransplantation is a rare situation. 100-120 patients are retransplanted annually worldwide, which is 2-4 % of all adult heart transplants. Here we present anesthetic management of a case, who had heart retransplantation and needs a hysterectomy operation. After a careful preoperative evaluation, including coronary angiography, echocardiography, and detailed blood analysis, she had a hysterectomy operation. She was discharged from the hospital without any complications. Heart transplant recipients have some unique problems. They have a denervated heart, so the medications used during the operation may have altered pharmacodynamics. These patients take immunosuppressant agents, which may have some serious side effects. They should be evaluated carefully for their cardiovascular status, their comorbidities, and the medications they use, during the perioperative period. Also, cooperation with the patient's cardiac transplant team is very important during the entire period.

**Keywords:** Heart retransplantation, non-cardiac surgery, anesthesia

## Introduction

Heart retransplantation is a very rare situation. But retransplantation of the heart is still controversial. As survival rates of retransplanted patients are lower than primary transplantations, it is debatable to transplant to a patient who had heart transplantation before, instead of a patient waiting for a heart on the waiting list. When survival rates of retransplanted patients are investigated closely, it is observed that the mortality rates are higher in the early period after retransplantation, and survival rates are significantly higher after 1 year [1]. Patients may need retransplantation because of cardiac allograft failure secondary to acute rejection (19%), primary graft failure (17%), and coronary artery vasculopathy (CAV) (55%) [1]. But retransplantation for CAV has the best prognosis, almost similar to primary transplantation [2].

As organ transplantation operations become more frequent, patients with end-stage organ failure life expectancy are prolonged. Patients, who had organ transplantation operation, may have to be operated for various reasons after transplantation. For these reasons, anesthetists must have information about this new group of patients. Anesthetists must know about their pathologies as well as their medications used for immunosuppression after transplantation. In this case report, we wanted to discuss what anesthesiologists should pay attention to in such patients, in which we present a hysterectomy operation performed on a patient who had undergone two heart transplants.

## Case Presentation

42 years old female patient had a heart transplantation operation twice. She had first heart transplantation (7 years ago) because of postpartum dilated cardiomyopathy. She had retransplantation (2 years ago), because of cardiac allograft failure secondary to coronary artery vasculopathy (CAV). After retransplantation, she had menometrorrhagia causing severe iron deficiency anemia. This condition was not related to her heart retransplantation or her medications. She has been taking oral Ferrum drugs for the past two years. She has been in

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gynecology follow-up for the last two years. But they weren't successful with medical therapy so they planned a hysterectomy operation. Coronary angiography was performed preoperatively and coronary arteries were found atherosclerotic but without any stenosis. The ejection fraction was 70%, with normal left ventricle systolic function, first-degree mitral regurgitation, 1-2 degree tricuspid regurgitation, and pulmonary arterial pressure 55 mmHg at preoperative transthoracic echocardiography. Her hemoglobin level was 8,8 g/dl so two packs of erythrocyte suspension were given preoperatively. And her hemoglobin level raised to 9,6 g/dl. Her leukocyte count was 5520 per mm3 and was within the normal range (Table 1). The cardiovascular team checked her tacrolimus blood level before surgery. She wasn't taking any steroid therapy, since steroid therapy was ceased one year after her second transplantation operation. Her kidney and liver functions were within the normal range. Her preoperative medication consisted of isosorbide-5-mononitrate, tacrolimus, and mycophenolate mofetil as immune suppressants, sulfamethoxazole-trimethoprim as an antibiotic, Ferro glycocoll as oral Ferrum therapy, and low molecular weight heparin. In her physical exam, she was ASA III, 167 cm long, and 77 kg weight and had no pathologic finding. In the operating room, the patient was monitored with electrocardiography (ECG), peripheric oxygen saturation (pulse oximetry), and invasive arterial pressure monitoring via the right radial artery. We did not use a central venous catheter, as this was an ordinary operation and the patient's preoperative echocardiography stated that the allograft was in a good condition. We did not want to raise the infection risk by the central venous catheter. And we did not apply further invasive monitorization techniques. We paid maximum attention to sterility during all procedures. Before anesthesia induction, her arterial pressure was 170/95 mmHg, heart rate: 98 per minute and SpO2 levels were 99. The patient was premedicated with 2 mg of iv midazolam. 0,5 mg/kg lidocaine, 0,3 mg/kg fentanyl, 3 mg/kg pentothal and 0,8 mg/kg rocuronium was given for anesthesia induction. After oral endotracheal intubation 0,1 mg/kg midazolam was added to increase the depth of anesthesia. 50% oxygen and air mixture and sevoflurane were given for the maintenance of anesthesia. Ventilatory settings were adjusted as 6 ml.kg-1 tidal volume and 13 per min respiratory rate. During operation peak airway pressures were between 22-19 cm H2O, EtCO2 levels were between 28-30 and SpO2 levels were 98. Blood gas samples were analyzed hourly and all values were within the normal range. Before surgical incision, intravenous 1 gr cefazolin was given as antibiotic prophylaxis. Urine output was monitored with a urine catheter during operation. The operation lasted for two hours, 1500 ml isotonic solution was given and her urine output was 650 ml during operation. Arterial blood pressure was about 140/80 mmHg and heart rate was around 70 per min during operation. IV nitroglycerin ınfusion was given for high blood pressure at the beginning of anesthesia induction and then stopped. No erythrocyte or fresh frozen plasma infusion was needed. Hysterectomy and salphingoooferectomy were performed on the patient. The patient was transferred to the cardiovascular intensive care unit after the operation, under sedation. Her vital signs were; 152/80-mmHg blood pressure, 77 per min heart rate, and SpO2 level 99 when she arrived at the cardiovascular ICU. Two hours later, she was extubated without any need for a reversal for neuromuscular blockade. On the second postoperative day, blood tacrolimus levels were checked and adjusted her immunosuppressive therapy. She has transferred the regular ward and discharged from the hospital on the same day.

**Table 1.** Laboratory values and echocardiography findings

| | Preoperative | Postoperative |
|---|---|---|
| **Hb (12-16 g/dL)** | 8.6 | 9.6 |
| **ALT (0-33 U/L)** | 4 | 8 |
| **AST (0-32 U/L)** | 13 | 17 |
| **BUN (6-20 g/dL)** | 10 | 13 |
| **Glucose (74-106 mg/dL)** | 109 | 110 |
| **Tacrolymus (µg/L)** | 7.6 | 8.6 |
| **Echocardiography** | ejection fraction was 70%, normal left ventricle systolic function, 1° mitral regurgitation, 1-2° tricuspit regurgitation, pulmonary arterial pressure 55 mmHg | ejection fraction was 65-70%, normal left ventricle systolic function, 1° mitral regurgitation, 1-2° tricuspit regurgitation |

## Discussion

Evaluations of immune-suppressive agents and surgical techniques have led to an increase in early and late survival of heart transplants. The median survival after primer heart transplantation has raised to 12,5 years. And if the heart recipient survives the first year, the average survival time has risen to 14,8 years [3]. Heart retransplantation is a rare and controversial situation. Retransplantation is controversial because the short term and long term survivals are lower than primary transplantation [2]. But patients retransplanted for coronary artery vasculopathy (CAV) after one year from primary transplantation have similar survival rates with primary transplantations [2]. Complications

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like graft failure, rejection, and CAV can be seen after one year from primary transplantation. Although treatments like aggressive immunosuppressive therapy, percutaneous transluminal coronary angiopathy, coronary artery bypass grafting, valve repairments, temporal or long term mechanical circulatory assist devices had been tried, the most effective and permanent treatment of these complications is retransplantation [1]. But retransplantation is still rare. Rizvi et al reported in a systematic review that, 7,446 patients had primary heart transplantation and 345 of them had retransplantation [1]. In the 2017 ISHLT report retransplantation rate was reported as 6% [4]. Barghash et al. reported in their review that 100-120 patients had retransplantation annually worldwide indicating 2-4% of all adult heart transplants. All these reviews have similar conclusions that; in the early period after retransplantation, patients have higher mortality rates compared to primary transplantation. This is an expected result because early mortality is mostly because of acute rejection and patients with acute rejection tend to be critically ill, intubated, and under medical or mechanical support, which raises the mortality rate. But retransplantation for CAV after one year from the primary transplantation has better and almost similar long-term survival rates with primary transplants [1,2,5,6]. But retransplanted patients are exposed to immunosuppressive therapy for longer times, which may cause higher infection and malignancy rates after transplantation leading to similar but still higher mortality rates when compared with primary transplantation.

With improved long-term survival, whether primary or retransplanted, living allograft recipient population has increased and therefore an increased chance that they may require non-cardiac surgery for any reason. Anesthesiologists must be aware of the physiological and pharmacological problems of allograft denervation and the intense immunosuppressive therapy of these patients [7-9]. Immunosuppressant agents can cause anemia, leucopenia, and thrombocytopenia as well as elevated postoperative infectious complications, delayed wound healing, adrenal insufficiency, hypertension, and interactions with anesthetic agents and antibiotics [10]. In the perioperative period, if immunosuppressant agents are ceased to avoid these complications than there will be a risk of rejection of the allograft. So it is advised that oral immunosuppressant agents should be continued in the perioperative period [10]. But if the patient will not be able to take oral drugs in the first postoperative day, then a transition of immunosuppressive therapy to methylprednisolone should be considered. But as we expected our patient will be able to take oral intake on the first postoperative day, we did not change our immunosuppressive therapy. During the perioperative period, maximum attention should be paid to sterility and this will reduce the infectious complications. No special antibiotic is needed for prophylaxis. Antibiotics recommended by guidelines for the surgery should be given to the patient for antibiotic prophylaxis [10]. Our patient did not have leucopenia. We paid maximum attention to sterility during the operation period and gave appropriate antibiotics before surgical incision for antibiotic prophylaxis. Immunosuppressant agents were given to the patient by the patient's treating cardiac transplant team, according to immunosuppressant agents' blood level in the perioperative period. We did not observe any complications related to immunosuppressive therapy. Tacrolimus, an immunosuppressive agent from the group of calcineurin inhibitors, which was used by our patient, may harm renal function. Blood creatinine levels should be checked in the preoperative period. And again renal damage caused by intraoperative hypervolemia must be prevented by appropriate intravascular volume therapy [10]. Our patient's preoperative creatinine levels were within the normal range. A sufficient amount of blood packs and freshly frozen plasma packs were prepared preoperatively, to be prepared for any hemorrhage during operation. Urine output measurements were within the normal range during the operation. Mycophenolate was the other immunosuppressive agent, which was used by our patient. Mycophenolate has lower post-transplant malignity rates and acute and chronic rejection rates. And it shouldn't be decreased preoperatively. But close monitoring of leucopenia/neutropenia is needed [10].

Preanesthetic evaluations of patients with cardiac transplantation have some differences. Transplanted hearts are denervated. In a transplanted heart, sympathetic, parasympathetic, and sensorial innervation have been lost, but intrinsic cardiac mechanisms are preserved. This situation makes the heart dependent on the Starling-volume relation. Optimization of preload is necessary for the maintenance of stroke volume. We provided this preload by crystalloid infusion. And again parasympathetic tonus loss causes higher cardiac rates while resting. On the contrary, tracheal intubation, shallow anesthesia, pain, hypervolemia, and stressful situation do not cause tachycardia response. So adequate pain release during the procedure is crucial [11]. We provided this by additional intravenous fentanyl during operation. It must be kept in mind that, there will be a change in response to some certain drugs. Epinephrine can increase cardiac contractility. But, atropine is ineffective to increase heart rate, and when neostigmine is administered as a neuromuscular blocker reversal agent, at the end of the surgery, it can lead to bradycardia and asystole. And again denervation of the heart and intrinsic conduction anomalies can usually cause arrhythmias. Our patient's initial heart rate was 98 per minute and it was around 70 per minute during operation. We didn't observe any arrhythmia. The patient was transferred to the cardiac intensive care unit at the end of the operation. During the transfer, the patient was sedated. We did not give neostigmine to reverse the muscle relaxant. The patient was extubated at the intensive care unit after full recovery from anesthesia and muscle relaxant.

Any anesthetic agent can be used for anesthesia induction to the patients with normal preoperative echocardiographic results; we used thiopental for anesthesia induction and the addition of midazolam and sevoflurane were used for anesthesia maintenance.

Also, coronary artery vasculopathy must be considered in the

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preoperative evaluation of patients who had heart transplantation previously. Cardiac allograft vasculopathy is the major impediment to long-term survival after heart transplantation [7]. This vasculopathy causes, coronary artery disease by progressive and diffuse intimal hyperplasia [5]. Especially before elective non-cardiac surgery, coronary arteries must be checked by coronary angiography. Our patient had diffuse intimal hyperplasia without any stenosis at her preoperative coronary angiography. Lastly, retransplanted allograft recipients have longer cumulative exposure to immunosüppressive therapy, so their risks of infection and malignancies are increased [6]. Extra precautions must be taken into account when retransplanted patients are in operation.

## Conclusion

Today, as the number of heart transplantation and retransplantation operations increases and also life expectancy of the heart recipients increase, anesthetists are to deal with different kinds of patients. Even if the transplanted heart function is normal, we must keep in mind that these patients have different properties and we must pay attention to the drugs they use. Especially, retransplanted patients are exposed to immunosuppressive therapy for longer times, it must be kept in mind that, infection and malignancy risks are increased. Also, preoperative and postoperative assessments should be done in cooperation with the patient's treating cardiac transplant team.

**Conflict of Interests**
*The authors declare that there is no conflict of interest in the study.*

**Financial Disclosure**
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**Patient Informed Consent**
*The patient was informed about the administration of anesthesia and recording of data.*

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