

CASE REPORT / ПРИКАЗ БОЛЕСНИКА

Anesthesia for thyroid surgery in heart transplant patients – the first case study in Serbia

Nevena Kalezić¹, Jovan Jozić¹, Emilija Nestorović², Milan Jovanović³, Vladan Živaljević³¹University Clinical Center of Serbia, Centre for Anesthesiology and Resuscitation, Belgrade, Serbia;²University Clinical Center of Serbia, Clinic for Cardiology, Belgrade, Serbia;³University Clinical Center of Serbia, Clinic for Endocrine Surgery, Belgrade, Serbia**SUMMARY**

Introduction The number of patients in the world who have undergone heart transplantation is increasing, with better and longer survival rates, and therefore the number of patients who undergo various surgical interventions after transplantation is also increasing. This presents a challenge for anaesthesiologists.

Case outline A 45-year-old female patient underwent a total thyroidectomy due to suspected thyroid cancer. She had a heart transplant three years earlier. Preoperative preparation included evaluation of cardiac function, consultative examinations by a transplant cardiologist, laboratory and other diagnostic procedures, as well as a detailed analysis of all 20 medications that the patient uses in daily therapy. Common drugs were used for premedication and general endotracheal anaesthesia, with careful dose titration. Medicines were also prepared for the occurrence of heart rhythm disorders, bearing in mind that the heart is denervated, but there was no need for their use. The operation and postoperative course went smoothly and on the third postoperative day the patient was discharged from the hospital in good general condition.

Conclusion Preoperative preparation, anaesthesia, and postoperative treatment of this patient represented a challenge for our team, which was successfully overcome, considering that this is the first case of operative treatment of a patient with a transplanted heart in Serbia.

Keywords: thyroidectomy; transplanted heart; preoperative preparation

INTRODUCTION

Heart transplantation is the treatment of choice for decompensated heart failure that does not respond to conventional therapy, idiopathic dilated cardiomyopathy, and terminal ischemic heart disease. [1, 2] Since 1967, when Christian Bernard performed the first heart transplantation, a large number of those operations have been performed and it is constantly increasing. Only in the USA, over 3000 heart transplant operations are performed each year, while, according to the data of the International Society for Heart and Lung Transplantation in Europe, that number is around 1500–3000 annually [3]. Five-year survival rate after heart transplantation is over 72.5%, and 20-year survival is 21% [4]. Considering the increasing number of transplantations and life expectancy of those patients, the number of non-cardiac interventions performed on patients with previous heart transplantation is rising. In Serbia, the first heart transplant procedure was performed in 1995, when five patients were successfully operated on. The Heart Transplant Program was revived in 2013, and so far, 49 patients have been successfully surgically treated at the University Clinical Centre of Serbia (UCCS). To the best of our knowledge, apart from our patient, none of the others, previously mentioned patients, have yet undergone any other post-transplantation surgery, which certainly

represents a great challenge for us. Naturally, post-transplantation surgery requires the participation of the cardiologist involved in the post-transplantation monitoring program and an experienced team of anesthesiologists.

CASE REPORT

A female patient, 45 years old, was admitted to the UCCS Clinic for Endocrine Surgery for surgical treatment of the thyroid gland. In 2018, she underwent the heart transplantation procedure. Her heart problems began in 2005, when she received the seasonal flu vaccine, after which she developed a fever, malaise lasting four weeks, along with fatigue, angina pectoris, and dyspnea. Multiple chest X-rays were performed, as well as other examinations, but there were no signs of pneumonia nor cardiac decompensation. Her medical problems lasted two and a half years, while she was being treated with antibiotics under suspicion of chronic bronchitis. After the mentioned period, episodes of angina pectoris and dyspnea reappeared. Coronary disease was excluded by coronary angiogram examination. None of the branches of the coronary arteries showed significant stenosis in their proximal and distal parts. An echocardiogram revealed a pericardium filled with fluid, enlarged heart cavities, with severe reduction of the left ventricular

Received • Примљено:
December 5, 2022

Revised • Ревизија:
May 13, 2023

Accepted • Прихваћено:
May 16, 2023

Online first: May 19, 2023

Correspondence to:

Jovan JOZIĆ
Kneginje Zorke 40
11000 Belgrade, Serbia
jovan.jozic.jozo@gmail.com

systolic function with ejection fraction of the left ventricle (EF LV) of 17%, which led to a diagnosis of dilated cardiomyopathy. The next cardiac deterioration occurred in 2014 after a common cold, when she was treated conservatively, but due to her weakened heart and compromised hemodynamic stability, a pacemaker and defibrillator were implanted (single-chamber implantable cardioverter-defibrillator – ICD-VR). The heart transplantation was performed in 2018. The graft that was used was a healthy heart with normal anatomic characteristics and EF LV of 65%. During operation, the pacemaker and defibrillator were removed, but their wires couldn't be removed because one of them had fused with the vagal nerve, and the other one had been dislocated towards the right heart cavities where it is still located (Figure 1). Short- and long-term postoperative outcomes were uneventful (no form graft rejection, infections, allograft vasculopathy, nor malignancy).



Figure 1. The patient's chest X-ray

Regarding her comorbidities, our patient is obese (body weight = 99 kg, body height = 176 cm, body mass index = 32 kg/m²), has confirmed hyperlipidemia, arterial hypertension, and mild pulmonary hypertension. Since 2021, she has been treated for diabetes with intensive insulin therapy (short acting human insulin 6 + 8 + 8 IU before meals and intermediate acting human insulin 14 IU at 10 p.m.). She had COVID-19 on two occasions, once treated at home (in 2021) and the other time in the hospital (in 2022), both times with mild symptoms. She has not been vaccinated against the corona virus.

On June 22, 2022, she was admitted to the Clinic for Endocrine Surgery of the UCCS for operative treatment of the thyroid gland. A neck echotomographic examination verified a node in the left lobe of the thyroid gland about 4.5 cm in size of iso- to heteroechoic characteristics with the presence of intranodal vascularization. Fine-needle aspiration biopsy was performed and the obtained sample was analyzed. The result indicated an atypia of undetermined significance – Bethesda category III, which established the probability of thyroid cancer. Laboratory analyses (blood count, biochemistry, coagulation status) performed on the hospital admission day

showed no significant deviations from the reference values. N-terminal pro-B-type natriuretic peptide (NT pro-BNP) was 68 pg/mL before operation. Electrocardiogram (ECG) showed the presence of a biphasic p-wave with rhythm of 82 beats per minute. Chest radiography did not show any presence of consolidations and X-ray of cervical spine indicated degenerative changes in the form of uncarthrosis and reduction of the C5–C6 intervertebral space. Echocardiogram revealed an accelerated flow through the aortic valve, paradoxical movement of interventricular septum, EF LV of 70%, weaker longitudinal function of the right ventricle, severe tricuspid regurgitation, an indirectly assessed elevated systolic pressure in the right ventricle, and a wire visible in the right heart cavity.

Together with the transplant cardiologist who followed-up the patient after the transplantation, all 20 drugs that the patient uses on a daily basis were analyzed, in order to determine the optimal regimen, doses and timing for their application in the perioperative period, as well as possible interactions with medications that could be used during anesthesia (Table 1). She regularly took her therapy the day before surgery, and morning on the surgery day. Also, she received an antibiotic one hour before surgery (vancomycin 2 g intravenously), low molecular weight heparin (enoxaparin sodium 0.4 mL subcutaneously) two hours before surgery, gastro protective therapy (pantoprazole 20 mg orally), as well as her personal cardiology therapy (ivabradine 7.5 mg orally) and therapy for the regulation of pulmonary hypertension (sildenafil 20 mg).

For premedication, the patient received 5 mg of midazolam intramuscularly half an hour before surgery. During that period, she was under constant observation. In the meantime, in the operating room we prepared medications for possible intraoperative bradycardia (adrenaline in a dilution of 1:200,000) and tachycardia (amiodarone in a dilution of 1:4), as well as a defibrillator.

Non-invasive monitoring (ECG, pulse oximetry, noninvasive blood pressure, end-tidal CO₂, respiratory rate) was used intraoperatively. Before general endotracheal anesthesia (GEA) induction, the patient was preoxygenated with 100% oxygen (flow of 6 L/minute) for five minutes. During preoxygenation, she received 25 mg of hydrocortisone intravenously, in order to prevent acute adrenal insufficiency, bearing in mind that she regularly used glucocorticoids (prednisone) after transplantation.

Propofol (160 mg) was used for GEA induction, rocuronium bromide at a dose of 0.8 mg/kg was used for intubation and muscle relaxation. The patient was intubated using a video laryngoscope (GlideScope; Verathon, Bothell, WA, USA). To maintain anesthesia, a gas mixture of sevoflurane (2 vol%), oxygen (50%) and air (50%) was used. For analgesia, diluted fentanyl (1:4) was used in intravenous bolus doses, starting before induction, up to a total dose of 150 µg. Sugammadex was used to reverse the neuromuscular block in a dose of 4 mg/kg.

During the procedure, hemodynamic parameters remained stable. Initial arterial tension was 123/74 mmHg, and heart rate was 80 beats per minute. The highest measured value of arterial tension was 130/75 mmHg, and

Table 1. Drugs, doses, and timing of their use

Drug name	Drug group	Drug dose	Timing
Furosemide	Diuretic	40 mg	8 a.m.; 6 p.m.
Amlodipine	Antihypertensive	2.5–5 mg	12 p.m.
Sildenafil	Antihypertensive	20 mg	8 a.m.; 4 p.m.; 12 a.m.
Ivabradine	Antiarrhythmic	5 mg	8:15 a.m.
Human insulin*	Antidiabetic	6 + 8 + 8 IU	before meals
Human insulin**	Antidiabetic	14 IU	10 p.m.
Prednisone	Corticosteroid	5 mg	8:15 a.m.
Mycophenolic acid	Immunosuppressant	1000 mg	10 a.m.; 10 p.m.
Tacrolimus	Immunosuppressant	3 mg	10 a.m.; 10 p.m.
Rosuvastatin	Statin	10 mg	10 pm
Trimethoprim-sulfamethoxazole	Antibiotic	800/160 mg	Tuesdays, Thursdays, and Sundays at 10 a.m.
Pantoprazole	Gastro Protection	40 mg	7:30 a.m.; 7:30 p.m.
Bromazepam	Anxiolytic	1.5–3 mg	optionally
Potassium chloride	Supplement	1 bag, each 3rd day 2 bags	9 a.m.
Calcium carbonate	Supplement	1000 mg	8:30 a.m.
Vitamin C	Supplement	1000 mg	9 a.m.
Vitamin D ₃	Supplement	2000 IU	8 p.m.
Folic acid	Supplement	5 mg	10 a.m.
Iron	Supplement	1000 mg	7:30 a.m.
Magnesium	Supplement	375 mg	8:15 a.m.; 8:15 p.m.

*short-acting;

**intermediate acting

heart rate 80 beats per minute. The operation (total thyroidectomy) lasted 50 minutes and was uneventful. The patient was extubated on the operating table, after all conditions were met (consciousness presence, performing all instructions, adequate motor response, spontaneous respiration with a frequency of 12 breaths per minute, oxygenation > 95%, hemodynamically stable). She was transferred to the Coronary Care Unit (CCU) for 24-hour monitoring by a cardiologist. In the CCU she received her own cardiac, immunosuppressive, and other chronic therapy. The concentration of tacrolimus in the blood was in the therapeutic range postoperatively. Postoperative value of NT pro-BNP was 75 pg/mL. The patient was transferred to the surgical ward 24 hours after the operation, and on the third postoperative day she was discharged from the hospital with therapy recommendations. The postoperative period was uneventful. No arrhythmias were detected during the perioperative period.

This case report was approved by the institutional ethics committee, and written consent was obtained from the patient for the publication of the case report.

DISCUSSION

The number of heart transplantations worldwide is constantly rising; the success of this surgical procedure is greater with higher post-transplant survival rate, and experiences with non-cardiac surgeries of those patients are increasing [5]. However, here in Serbia we cannot claim that we have excessive numbers and experience with such patients. To the best of our knowledge, this was the first case of a patient with previous heart transplant undergoing

non-cardiac surgery, so the challenge for our anesthesia team was even greater.

Numerous physiological factors within previous heart transplant patients must be taken into account during the preoperative preparation and GEA, such as the denervation of the transplanted heart, the number and influence of other medications those patients use on a daily basis (e.g., the interaction between immunosuppressants and anesthetics), the possibility of the graft rejection, proper perioperative pain therapy, and the possibility of infection [6].

After heart transplantation, the graft tissue has its own sinoatrial node, which is completely denervated and independent of the host's autonomic nervous system, so in those patients we can expect the following: a lack of baroreceptor reflex, no response to carotid sinus massage, a change in the heart frequency as a postural change, and the lack of reaction to Valsalva maneuvers [7, 8]. It is also known that after heart transplantation, due to vagal denervation and increased sensitivity of the graft myocardium to circulating catecholamines, episodes of arrhythmias and blockages (such as the first-degree atrioventricular block) can occur, which are usually detected after the transplant surgery [9]. Having that in mind, the use of atropine in case of intraoperative bradycardia would not be effective, and the use of beta-blockers in case of intraoperative tachycardia is not advised because of their wide range of cardiopulmonary effects and it can also cause potential total blockade of the heart muscle [10]. Considering these facts, our team was prepared to respond to potential rhythm changes with solutions of amiodarone and adrenaline. Some authors recommend verapamil for tachycardia and vasopressors (noradrenaline, dobutamine) for bradycardia treatment [11, 12].

Unlike in the non-heart transplant patients, reversing neuromuscular blockade with neostigmine and atropine in heart transplant patients remains a topic for further scientific research. It is also known, from the available scientific literature, that meta-analysis had been performed and proved that a smaller number of adverse reactions occur when using sugammadex compared to anticholinesterase drugs; therefore, we decided to reverse the neuromuscular block using sugammadex [3].

Signs of graft rejection must always be ruled out preoperatively, because scientific evidence showed that patients who undergo a surgical procedure and have proven indicators of graft rejection have a higher morbidity compared to those in whom rejection is excluded [13]. For these reasons, a heart muscle biopsy was performed preoperatively in our patient to rule out signs of rejection reaction.

It is better to avoid invasive procedures whenever possible because the risks of various complications (including

infection) outweigh the benefits that invasive monitoring can provide, so we decided to use non-invasive monitoring because we assessed that it was an operation with low intraoperative risk and that the patient was stable in terms of comorbidities, thus reducing the risk of infection [14]. This proved to be a good strategy because the patient was hemodynamically stable throughout the operation.

In conclusion, the patient who had a heart transplant four years earlier underwent total thyroidectomy under suspicion of thyroid cancer under general endotracheal anesthesia. In cooperation with the transplant cardiologist, she was well pre-operatively prepared for the operation. She tolerated the operation and GEA well and was discharged from the hospital on the third postoperative day in good condition. This is the first case of operative treatment of a patient with a transplanted heart in Serbia.

Conflict of interest: None declared.

REFERENCES

1. Tezcan B, Saylan A, Bolukbası D, Koculu R, Karadeniz U. Use of Sugammadex in a Heart Transplant Recipient: Review of the Unique Physiology of the Transplanted Heart. *J Cardiothorac Vasc Anesth.* 2016;30(2):462–5. [DOI: 10.1053/jjvca.2015.06.009] [PMID: 26409923]
2. Bhagra SK, Pettit S, Parameshwar J. Cardiac transplantation: indications, eligibility and current outcomes. *Heart.* 2019;105(3):252–60. [DOI: 10.1136/heartjnl-2018-313103] [PMID: 30209127]
3. Yuki K, Scholl R. Should we Routinely Reverse Neuromuscular Blockade with Sugammadex in Patients with a History of Heart Transplantation? *Transl Perioper Pain Med.* 2020;7(2):185–9. [PMID: 32039284]
4. Wilhelm MJ. Long-term Outcome Following Heart Transplantation: Current Perspective. *J Thorac Dis.* 2015;7(3):549–51. [DOI: 10.3978/j.issn.2072-1439.2015.01.46] [PMID: 25922738]
5. Fuchs M, Schibilsky D, Zeh W, Berchtold-Herz M, Beyersdorf F, Siepe M. Does the heart transplant have a future? *Eur J Cardiothorac Surg.* 2019;55(Suppl 1):i38–i48. [DOI: 10.1093/ejcts/ezz107] [PMID: 31106338]
6. Choudhury M. Post-Cardiac Transplant Recipient: Implications for Anaesthesia. *Indian J Anaesth.* 2017;61(9):768–74. [DOI: 10.4103/ija.IJA_390_17] [PMID: 28970636]
7. Navas-Blanco JR, Modak RK. Perioperative Care of Heart Transplant Recipients Undergoing Non-Cardiac Surgery. *Ann Card Anaesth.* 2021;24(2):140–8. [DOI: 10.4103/aca.ACA_130_19] [PMID: 33884968]
8. Haberbusch M, De Luca D, Moscato F. Changes in Resting and Exercise Hemodynamics Early After Heart Transplantation: A Simulation Perspective. *Front Physiol.* 2020;11:579449. [DOI: 10.3389/fphys.2020.579449] [PMID: 33240102]
9. Manolis AA, Manolis TA, Apostolopoulos EJ, Apostolaki NE, Melita H, Manolis AS. The role of the autonomic nervous system in cardiac arrhythmias: The neuro-cardiac axis, more foe than friend? *Trends Cardiovasc Med.* 2021;31(5):290–302. [DOI: 10.1016/j.tcm.2020.04.011] [PMID: 32434043]
10. Shah K, Kobashigawa J. Complications After Heart Transplantation in Adults: an Update. *Current Emergency and Hospital Medicine Reports. Cardiovascular Care.* 2019;7(2):27–35. [DOI: 10.1007/s40138-019-00180-7]
11. Lescroart M, Pequignot B, Janah D, Levy B. The medical treatment of cardiogenic shock. *J Intensive Med.* 2023;3(2):114–23. [DOI: 10.1016/j.jointm.2022.12.001] [PMID: 37188116]
12. Neethling E, Moreno Garijo J, Mangalam TK, Badiwala MV, Billia P, Wasowicz M, et al. Intraoperative and Early Postoperative Management of Heart Transplantation: Anesthetic Implications. *J Cardiothorac Vasc Anesth.* 2020;34(8):2189–206. [DOI: 10.1053/jjvca.2019.09.037] [PMID: 31753746]
13. Moaveni DM, Cohn JH, Hoctor KG, Longman RE, Ranasinghe JS. Anesthetic Considerations for the Parturient After Solid Organ Transplantation. *Anesth Analg.* 2016;123(2):402–10. [DOI: 10.1213/ANE.0000000000001391] [PMID: 27285002]
14. Chen SY, Wu ZF, Yang MT, Lai HC, Hung NK. Is Analgesia Nociception Index Monitor Suitable for Post Heart Transplant Patients under General Anesthesia? *J Med Sci.* 2020;40(5):248–50. [DOI: 10.4103/jmedsci.jmedsci_197_19]

Анестезија за операцију штитасте жлезде код болесника са трансплантираним срцем – приказ првог случаја у Србији

Невена Калезић¹, Јован Јозић¹, Емилија Несторовић², Милан Јовановић³, Владан Живаљевић³

¹Универзитетски клинички центар Србије, Центар за анестезиологију и реаниматологију, Београд, Србија;

²Универзитетски клинички центар Србије, Клиника за кардиологију, Београд, Србија;

³Универзитетски клинички центар Србије, Клиника за ендокрину хирургију, Београд, Србија

САЖЕТАК

Увод Све је већи број пацијената у свету којима је трансплантирано срце, са све бољим и дужим преживљавањем, па самим тим расте и број пацијената који се после трансплантације подвргавају различитим хируршким интервенцијама. То представља изазов за анестезиологе.

Приказ болесника Болесница старости 45 година подвргнута је тоталној тироидектомији због сумње на карцином штитасте жлезде. Код болеснице је три године раније учињена трансплантација срца. Преоперативна припрема укључивала је евалуацију срчане функције, консултативне прегледе трансплантационог кардиолога, лабораторијске и друге дијагностичке процедуре, као и детаљну анализу свих 20 медикамената које болесница користи у свакодневной терапији. За премедикацију и општу ендотрахеалну

анестезију коришћени су уобичајени лекови, уз пажљиво титрирање доза. Припремљени су и медикаменти за случај појаве поремећаја срчаног ритма имајући у виду да је срце денервисано, али није било потребе за њихову примену. Операција и постоперативни ток су протекли уредно и трећег постоперативног дана болесница је отпуштена из болнице у добром општем стању.

Закључак Преоперативна припрема, анестезија и постоперативно лечење ове болеснице представљали су изазов за наш тим, који је успешно савладан, с обзиром на то да је ово први случај оперативног лечења пацијента са трансплантираним срцем у Србији.

Кључне речи: тироидектомија; трансплантирано срце; преоперативна припрема