ANESTHETIC MANAGEMENT FOR IMPLANTATION OF TOTAL ARTIFICIAL HEART DEVICE: CASE SERIES

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ABSTRACT

The treatment of end-stage heart failure is heart transplant; however the majority of patients die due to deficiency of organ donation. Total artificial heart implantation made for the purpose of extending the life span and bridging to transplantation in patients with end-stage heart failure is a good option. We present our initial experiences in the anesthetic management of total artificial heart implantation cases performed in our institution.

Five out of seven patients (46.8±8.4 years) were taken to surgery with inotropic support. Four patients were diagnosed as dilated cardiomyopathy. Three patients were subject to cardiac arrest during the preoperative period and mechanical ventilation was applied for one of these patients. Intraoperative ketamine, midazolam, fentanyl, rocuronium were used in doses of 192±89 mg, 8±3.5 mg, 335±157 µg and 192±43 mg, respectively. Fresh donor blood, fresh frozen plasma, thrombocyte and erythrocyte suspension requirements were 2.1±1.6 unit, 2± 1.8 unit, 0.43±0.5 unit and 0.6± 0.9 unit, respectively. At least one complication developed in all of the patients; four patients who had sepsis and renal failure died and; 3 patients who were not subject to this complication were discharged from the hospital.

Total artificial heart implantation made for the purpose of bridging to transplantation for end-stage heart failure patients is a valuable option and its anaesthetic management is challenging. It is important that anesthesiologists have knowledge about the implanted device and the surgical procedure.

Keywords: *Artificial heart, heart-assist devices, postoperative complications, anesthetic agents, treatment outcome.* ***Nobel Med 2016; 12(2): 75-79***

TOTAL YAPAY KALP CİHAZI İMPLANTASYONUNDA ANESTEZİK YAKLAŞIM: OLGU SERİSİ

ÖZET

Son dönem kalp yetmezliğinin tedavisi kalp transplantasyonudur. Ancak hastaların çoğu organ bağışı eksikliği nedeniyle transplantasyon yapılamadan ölmektedir. Bu hastalarda ömrü uzatmak için, transplantasyona köprüleme amacıyla total yapay kalp implantasyonu yapılması iyi bir seçenektir. Biz bu makalede total yapay kalp implantasyonu uygulanan ilk hastalarımızdaki anestezi deneyimlerimizi sunuyoruz.

Yedi hastanın (46,8±8,4 yıl) beşi inotrop desteğinde operasyona alındı. Dört hasta dilate kardiyomiyopati tanısı almıştı. Üç hastada preoperatif dönemde kardiyak arrest öyküsü mevcuttu ve bunlardan birine mekanik ventilasyon uygulanmıştı. İntraoperatif ortalama ketamin, midazolam, fentanil, rokuronyum kullanımı sırasıyla 192±89 mg, 8±3,5 mg, 335±157 µg, 192±43 mg olarak gerçekleşti. Ortalama taze donör kanı, taze donmuş plazma, trombosit ve eritrosit süspansiyonu gereksinimi sırasıyla 2,1±1,6 Ü, 2± 1,8 Ü, 0,43±0,5 Ü ve 0,6± 0,9 Ü idi. Hastaların hepsinde en az bir komplikasyon gelişti. Dört hasta sepsis ve renal yetmezlikten ölürken; bu komplikasyonların gelişmediği üç hasta taburcu edildi.

Son dönem kalp yetmezliği hastalarında total yapay kalp implantasyonu transplantasyona köprüleme amacıyla iyi bir seçenektir ve anestezik yaklaşımı farklı özellikler içermektedir. Bu nedenle anesteziyologların implante edilecek cihaz ve cerrahi işlem hakkında bilgi sahibi olması önemlidir.

Anahtar kelimeler: Yapay kalp, kalp-destekleyici cihazlar, postoperatif komplikasyonlar, anestezik ajanlar, tedavi sonucu. **Nobel Med 2016; 12(2): 75-79**

INTRODUCTION

The treatment of final stage heart failure is heart transplant; however the majority of patients die due to deficiency of organ donation.[1-4] Right or left ventricular assist devices are implemented (VAD) for the purpose of bridging to transplantation in single sided heart failure and bi-level VAD or Total Artificial Heart (TAH) are implemented in bi-level heart failure. The anesthetic management of patients undergoing TAH implantation is challenging as patients are often in a critical general condition with multiple organ failure.[1-7] In this surgery, the patient's ventricles and all covers are excised and the device is implanted.[5-10] In this article, we aimed to present our anesthetic management for the initial seven TAH device implantation in our hospital.

CASES

After obtaining approval of Ethical Committee, seven patients who underwent TAH implantation (Syncardia CardioWest Total Artificial Heart System; Syncardia Systems, Inc, Tucson, Arizona) between September 2010-June 2013 were retrospectively analysed. Preoperative characteristics, intraoperative hemodynamic and respiratory parameters, anesthetic drugs, blood products, durations of mechanical ventilation, hospital and intensive care were recorded. The patient and surgical data are presented as mean values ± standard deviation.

Invasive arterial pressure, electrocardiogram (ECG), central venous pressure (CVP), body temperature, urine output and intraoperative trans-esophageal echocardiography (TEE) and respiratory parameters were monitored for all patients. Anesthesia induction was ensured with ketamine (1-2 mg kg^{-1}), midazolam (30-50 µg kg^{-1}), fentanyl (1-2 µg kg^{-1}) and rocuronium (1 mg kg^{-1}); maintenance of anesthesia was ensured with volatile anaesthetics (sevoflurane and desflurane 0.5-1 MAC), propofol infusion (1 mg kg^{-1} $hour^{-1}$), midazolam and fentanyl in bolus doses.

Due to the long procedures, requirement for numerous catheter attempts and open sternum, meropenem 1 g every eight hours and teikoplanin 400 mg every twelve hours was started. Antibiotics were revised according to antibiogram. Prior to cannulation 400 unit kg^{-1} heparin was used and end of the CPB it was completely neutralized by protamine sulfate. After the implantation, the decision for sternal closure was made based on whether pulmonary veins and caval veins were compressed or not. All of our patients were transported to the intensive care unit with open chests, taking into consideration the possibility of inflow obstruction, hemorrhage and cardiac tamponade. The patients with stable general condition were taken for sternal closure at a later date. Systemic anticoagulation was initiated with intravenous heparinization (activated partial thromboplastin time, 50-55 sec) at postoperative 24^{th} hour. According to coagulation parameters 100 mg acetylsalicylic acid was administered and increased to 300 mg day^{-1} as antithrombotic drug during the early postoperative period. After with drawal of chest tubes, oral anticoagulation with warfarin sodium was targeted to an international normalized ratio of 2 to 3.

Five out of seven patients (46.8±8.4 years, 84.8±7.5 kg) were taken to surgery with inotropic support (one patient was supported with intra-aortic balloon pump). There was systemic disease in 5 patients, cigarette smoking in 4 patients, and a history of cardiac surgery in 3 patients. Three of our patients were subject to cardiac arrest. Mechanical ventilation was required in the preoperative period for only one patient. The average arterial blood pressure was 80±6 mmHg, heart rate was 90±23 pulse min^{-1}, CVP was 18±8 mmHg and systolic pulmonary artery pressure (sPAP) was 55±16 mmHg.

Intraoperative ketamine, midazolam, fentanyl, rocuronium were used in doses of 192±89 mg, 8±3.5 mg, 335±157 µg and 192±43 mg, respectively. Fresh donor blood, fresh frozen plasma, thrombocyte and erythrocyte suspension requirement were 2.1±1.6 unit, 2±1.8 unit, 0.43±0.5 unit and 0.6±0.9 unit, respectively. Two patients were transported into intensive care without inotrope, 4 patients were backed by only noradrenaline and one patient was backed by dual inotrope (Dopamine and noradrenaline). The patients were taken to sternum closure surgery at postoperative 62±29 (30-120) hours. Tamponade or revision due to bleeding occurred in four patients before sternum closure surgery. At least one complication was seen in all of the patients; respiratory complications in 6 patients, neurological complications in 2 patients, renal complications in 4 patients (dialysis was required), gastrointestinal complications in 4 patients, sepsis in 4 patients and multiple organ dysfunction syndrome (MODS) in 6 patients. Four patients with sepsis and renal failure died; 3 patients who were not subject to this complication were discharged from hospital (Table).

Table. Perioperative values of the patients

Patient	**1**	**2**	**3**	**4**	**5**	**6**	**7**
Age (year)	47	57	39	47	51	33	54
Weight (kg)	85	76	74	93	90	92	84
BSA (kg m^{-2})	2.0	1.92	1.90	2.13	2.07	2.16	2.02
Diagnosis	DCMP	DCMP	ICMP	Device	DCMP	DCMP	VA
LVEF (%)	20	20	20	10	25	20	40
RVEF (%)	40	30	30	35	30	20	55
MAP (mm Hg)	73	80	78	75	90	83	86
HR (beat min^{-1})	78	105	110	85	86	120	50
CVP (mm Hg)	12	26	20	21	12	32	8
sPAP (mm Hg)	45	85	60	50	60	53	32
PCWP (mm Hg)	31	32	30	32	35	33	14
Ketamine (mg)	270	325	100	150	150	250	100
Midazolam (mg)	6	3	12	5	8	12	10
Fentanyl (µg)	500	500	500	250	200	150	250
Rocuronium (mg)	170	200	160	150	200	190	280
CBP (min)	258	270	264	360	252	317	248
Anesthesia (min)	540	450	420	585	480	600	420
Dev.Time (day)	14	770	665	146	13	36	511
Outcome	**Exitus**	**Disch**	**Disch**	**Exitus**	**Exitus**	**Exitus**	**Disch**

DCMP: Dilated cardiomyopathy, **ICMP:** ischemic cardiomyopathy, **Device:** device exchange, **VA:** malign ventricular arrhythmia, **BSA:** body surface area, **LVEF:** left ventricular ejection fraction, **RVEF:** right ventricular ejection fraction, **MAP:** mean arterial pressure, **CVP:** central venous pressure, **sPAP:** systolic pulmonary artery pressure, **PCWP:** pulmonary capillary wedge pressure, **CPB:** cardiopulmonary bypass, **Anesthesia:** anesthesia time, **Dev. Time:** device support time, **Disch:** discharge, **HR:** heart rate.

DISCUSSION

Total artificial heart is a kind of VAD applied in biventricular heart failure. The weight of these devices is 150 gr and each ventricle can constitute 70 ml stroke volume and cardiac outflow that is close to 9 litres in one minute without elevating central venous pressure over 15 mmHg. These devices are implemented most frequently to patients who are subject to biventricular heart failure, arrhythmias resistant to ventricular, ventricular defects which cannot be repaired, and to patients who are subject to ventricular failure after mechanical cover. They result in an increase in systolic arterial pressure, improvement in perfusion pressure of end-organs and a decrease in CVP.[5-10]

The management of anesthesia for implantation of ventricular supportive devices is challenging due to coexisting diseases and repeated surgical procedures. The patients are taken to surgery with diverse drugs like diuretics, beta-blockers, antiaritmics and anticoagulants. Anesthesiologists must deal with hemodynamic changes during induction and bleeding problems executed after cardiopulmonary bypass.[2] It is unavoidable that these hemodynamic changes and bleeding problems occur in patients who are subject to TAH implantation surgery. Induction and maintenance of anesthesia for TAH implantation are similar to those for VAD implantation surgery, however the patients' general situation may be worse (as cardiogenic shock) and they may be backed by inotropic agents.[2]

All of our patients were using antiaggregants (acetylsalicylic acid), anticoagulants (sodium warfarin), diuretics (furosemide, spironolactone, and hydrochlorothiazide), beta-blockers (Metoprolol suksinat) or anti-arrhythmic agents (amiodarone). Antiaggregants and anticoagulants caused increased usage of blood products and diuretics caused hypotension after induction and intraoperative oliguria. Difficulty in arterial and central vein catheterization was experienced in 3 patients who had medical history of cardiac surgery beforehand. Ultrasonography could be a good option for patients in whom catheterization difficulty is expected and for patients who are subject to bleeding diathesis.

Vasodilatation effect of induction agents, blockage of the sympathetic system, transition from spontaneous breathing into breathing with positive pressure, and hemodynamic instability must be expected after induction of anaesthesia. Usage of angiotensin converting enzyme (ACE) inhibitor deepens hypotension after induction; therefore vasoactive agents may be used in these patients to balance systemic vascular resistance.[3,4] Etomidate is an induction agent used commonly however it may cause adrenal insufficiency. Propofol constitutes hypotension through its negative inotropic effect. Fentanyl can be used between the ranges of 50-100 µg kg^{-1}, however it must be titrated if bradycardia develops.[4] Rocuronium has become the most popular agent in cardiac surgery recently. Hypoxia and hypercapnia must be avoided, as they may cause pulmonary hypertension, and tidal volume should be between the ranges of 6-8 ml kg^{-1}. Positive end-expiratory pressure (PEEP) application must be implemented carefully as it may worsen right ventricular insufficiency.

Ketamine, midazolam and fentanyl were used as induction agents for the purpose of minimizing hemodynamic changes in our patients. Ketamine ensured continuation of sympathetic activity and thus bradycardia that is based on high-dose fentanyl was avoided. Propofol and sodium pentothal were not used due to their myocardial depression effects. Although etomidate is the agent that effects hemodynamic at the least, it was not used as it did not exist in our hospital's pharmacy. The finding that the induction time was longer in our study compared with normal patients is an expected result, as all induction agents were titrated due to low ejection fractions. Despite this, hypotension (under 60 mm Hg) developed in 3 patients in our study. Ephedrine 10 mg was used to treat hypotension in two patients, while low dose adrenaline (5 µg) was used in one patient. Noradrenaline infusion (0.1 µg kg^{-1} dk^{-1}) was started for one patient upon development of hypotension during CPB.

Basal PEEP (4-5 cm H_2O) was applied for all of the patients, and no hemodynamic derangements were seen related to PEEP usage. Mechanical ventilation parameters were arranged to achieve $PaCO_2$ 30-40 mm Hg and PaO_2 levels above 70 mm Hg. Intraoperative hypoxia and hypercapnia were not seen except the one who developed hypoxemia after CPB. This problem was solved through deep tracheal aspiration and usage of higher PEEP and FiO_2 levels. Hypoxemia in our patient was attributed to coexisting lung infection.

Copeland *et al.* founded that 86% of their patients were male and the average ages of their patients was 51 in their study including 81 patients.[5] In their study, 53% of the patients had the diagnosis of ischemic cardiomyopathy; cardiac arrest was reported in 37% of the patients, mechanical ventilation in 43% of the patients and intra-aortic balloon pump in 32% of the patients. The investigators stated that pulmonary artery pressure (mPAP), pulmonary capillary wedge pressure (PCWP) and central venous pressure (CVP) were 41, 30, 20 mm Hg, respectively. Transplantation was implemented in 79% of the patients. The investigators stated that the factors related to mortality after implantation were smoking, history of mediastinal operation and having decided to implement TAH during CPB. The investigators did not determine the relationship between occurrences of right heart failure (high CVP, high sPAP and pulmonary vascular resistance, low cardiac index) and sepsis (mechanical ventilation support, occurrence of increased bilirubin and creatinine levels). The investigators stated that smoking was the only independent risk factor according to multivariate analysis.

Roussel *et al.* reported that 95% of the 42 patients in their series were male (average age: 45,7±9,5 years) and heart transplantation was implemented in 71,5% of the cases. 6 In their study, assist device support times were 1- 292 days (average 101±86 days); 6 patients (50%) died due to MODS, 2 patients died due to sepsis, 2 patients died due to respiratory distress syndrome, one patient died due to alveolar haemorrhage and one patient died due to technical reasons. Infection was determined during assist device support in 35 patients (85%). Reexploration and bleeding occurred in 54.7% of the patients.

El-Banayosy *et al.* stated that 88% of the 42 patients in their study were male (average age: 51±13 years) and all patients were taken to surgery with maximum inotropic support.[7] In their study, surgical bleeding occurred in 21% of the patients and surgical re-exploration was required in 9 patients (19%). Acute renal failure occurred in 15% and liver failure in 26% of the patients. In their study, 21 patients died due to MODS and 1 patient died due to technical reasons.

Torregrossa *et al.* founded that the average age was 50± 1.57 years and assist device support times were 554 days (range 365-1373) in a multi-centered series containing 47 patients.[8] Systemic infection occurred in 53% of patients, driveline infection in 27%, thromboembolic events in 19% and bleeding-related complications in 14%. Infections and hemorrhagic events have been identified as the primary causes of death.

In our study, intraoperative oliguria was seen in three patients; volume load was reduced through intraoperative ultrafiltration in these patients for whom

adequate diuresis could not be provided through furosemide treatment. The patients' ages, genders and the average CVP and PAP values showed similarity with the other studies, however no relationship was determined between smoking and mortality. All of the patients who were subject to sepsis or renal failure during the postoperative period died. In our study, assist device support times were longer when compared with other studies, however heart transplantation could not be implemented in any of the patients.

CONCLUSION

TAH implantation made for the purpose of bridging to transplantation is a good option for patients in whom inotropic therapy failed or in cases where left ventricular assist device implantation is not possible. The anesthetic management of patients undergoing TAH implantation entails specific characteristics. The surgical procedure is more complicated, surgical times are longer, transfusion requirements are higher, the general condition of the patients are worse, preoperative inotropic support requirements are higher and as a result the complication rates are higher than in other cardiac surgery patients. It is important that anesthesiologists have knowledge about the assist devices that will be implanted and the characteristics of the surgical procedure as these facilitate the anesthetic management.

*This article was presented in 10th Congress of Turkish Transplantation Centers Coordination Association executed in Bodrum between the dates of 15-18 October 2014.

*The author declares that there are no conflicts of interest.

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DELIVERING DATE: 11 / 08 / 2015 • **ACCEPTED DATE:** 03 / 11 / 2015

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