

## Reduction of Apnea Test Time in an Extracorporeal Membrane Oxygenation-Dependent Potential Donor

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The diagnosis of brain death is essential for deceased donor organ transplantation. Currently, extracorporeal membrane oxygenation (ECMO) is used to increase the chance of survival of patients with severe cardiac and respiratory failure. Therefore, cases of ECMO-dependent potential donors are increasing. The apnea test (AT) is a mandatory component in the clinical determination of brain death. However, conventional AT is not easily applicable to ECMO-dependent potential donors because both the ventilator and ECMO play an important role in carbon dioxide elimination. Accordingly, different methods of AT from those used in routine procedures must be considered. We report here a case of conventional AT with time delay and two cases of AT within 3 minutes by adjusting sweep gas flow rate of ECMO in ECMO-dependent potential donors.

**Key Words:** Apnea test, Brain death, Extracorporeal membrane oxygenation

**중심 단어:** 무호흡검사, 뇌사, 체외막 산소공급

### INTRODUCTION

As organ transplants are increasing, brain death determination becomes more and more important. Brain death in a normothermic, non-drugged comatose patient with a known irreversible massive brain lesion and no contributing metabolic or hormonal derangements is declared when brainstem reflexes, motor responses are absent(1-3). Determination of brain death is essential for deceased donor organ transplantation. Apnea test (AT) is indispensable component in the clinical determination of brain death. AT is to prove the absence of respiratory control system reflexes in the brainstem when intense physiologic stimulation to breathe is pres-

ent(1). Nowadays extracorporeal membrane oxygenation (ECMO) is used to increase the chance of survival of patients with severe cardiac and respiratory failure(4). Therefore the number of ECMO-dependent potential donor is increasing. Conventional AT is not easily applicable in ECMO-dependent potential donor because both ventilator and ECMO play an important role in carbon dioxide elimination. However, there's very little data of AT in ECMO-dependent potential donor. We present three cases of AT in ECMO-dependent potential donor.

### CASE REPORTS

#### 1. Case 1

A 54-year-old woman was diagnosed acute aortic dissection, Stanford type A. When she arrived at emergency room, she was received venoarterial ECMO (VA-ECMO) as a rescue device. And then she underwent ascending aorta replacement. ECMO was started with 3,870 RPM and 0.7 fraction of inspired oxygen (FiO<sub>2</sub>), 4 L/min oxygen flow.

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She received continuous renal replacement therapy in intensive care unit and dopamine (4 µg/kg/min) was infused continuously. Postoperative 7 days after operation, AT was started because she was diagnosed with hypoxic brain damage. Routine AT starts to inhalation of 100% oxygen 10 minutes. And then disconnecting ventilator from the patient with 6 L/min of 100% oxygen via endotracheal tube. Next, we observe increase of partial pressure of arterial carbon dioxide (PaCO<sub>2</sub>) that is above of 50 mmHg, confirms spontaneous respiratory efforts was absent. If the patient has intact brainstem, spontaneous respiratory efforts develop early as the patient's PaCO<sub>2</sub> level increases. In first AT, PaCO<sub>2</sub> increase from 40.0 to 62.4 mmHg for 20 minutes and second AT, PaCO<sub>2</sub> increase from 36.3 to 55.4 mmHg for 15 minutes. After brain death determination, the patient's bilateral kidneys were successfully retrieved for donation.

## 2. Case 2

A 33-year-old woman suffering from systemic lupus erythematosus pericarditis and pulmonary artery hypertension presented for VA-ECMO due to sudden cardiac arrest. ECMO was started with 2,608 RPM and 0.8 FiO<sub>2</sub>, 4 L/min oxygen flow. During ECMO maintenance, vital signs were stable without any administration of inotropic drugs. On 6 days after ECMO insertion, AT was performed. Because carbon dioxide elimination is dependent on sweep gas flow rate of ECMO(5), we decreased sweep gas flow rate in process of AT. In first AT, we decreased sweep gas flow rate from 3.0 to 2.0 L/min and PaCO<sub>2</sub> increase from 44.1 to 60.2 mmHg for 3 minutes. On the next day, we carried out second AT, we reduced sweep gas flow rate from 4.0 to 1.0 L/min, PaCO<sub>2</sub> increase from 41.2 to 51.2 mmHg within 3 minutes. After brain death determination, the liver was successfully retrieved for donation.

## 3. Case 3

A 54-year-old man was transported emergency room with sudden cardiac arrest and received VA-ECMO as a rescue device. ECMO was started with 2,271 RPM and 0.7 FiO<sub>2</sub>, 4 L/min oxygen flow. During ECMO maintenance, dopamine (4 µg/kg/min), norepinephrine (0.15 µg/kg/min), vasopressin (0.03 U/hr) were infused continuously. On 5 days after ECMO insertion, AT was performed. Method of

AT was same case 2. In first AT, we decreased sweep gas flow rate from 2.0 to 1.0 L/min and PaCO<sub>2</sub> increase from 45.0 to 61.5 mmHg for a minute and second AT, we reduced sweep gas flow rate from 4.0 to 2.0 L/min, PaCO<sub>2</sub> increase from 35.1 to 52.0 mmHg within 3 minutes. After brain death determination, the patient's organs including the liver and both kidneys were successfully retrieved for donation.

## DISCUSSION

The drive to breathe in the setting of an intense ventilatory stimulus (i.e., respiratory acidosis) is a critical marker of brainstem function. As a consequence, AT is an important component of brain death assessment. This procedure requires close monitoring of a patient as all ventilator support is temporarily removed and PaCO<sub>2</sub> levels are allowed to rise. A "positive" test is defined by a total absence of respiratory efforts under these conditions(1). General procedure of AT is to temporarily remove the ventilator. Since the support of respiration was stopped, the carbon dioxide would build up in the patient and AT can be successfully finished. However, increasing PaCO<sub>2</sub> is difficult in patients with ECMO because ECMO functions as elimination of carbon dioxide like a ventilator. Our patients used VA-ECMO that provides both respiratory and hemodynamic support, in contrast to veno-venous ECMO, which provides only respiratory support. Gas exchange occurs in the membrane oxygenator. Extracorporeal venous blood exposed to fresh gas (or sweep gas) that adds oxygen and removes carbon dioxide. Affecting factors of oxygenation and elimination of carbon dioxide are diffusion gradient, membrane surface area, fraction of delivered oxygen (FdO<sub>2</sub>), blood flow rate, fresh gas (sweep gas) flow rate(5). Oxygenation is influenced by the other four elements except the fresh gas flow rate and carbon dioxide elimination is dependent on sweep gas flow rate and is independent of blood flow rate. An increase in the sweep gas flow rate results in a decreased concentration of carbon dioxide in the fresh gas. This increases the diffusion gradient, promotes greater carbon dioxide elimination, and causes a decrease in the PaCO<sub>2</sub>(5). The first case used the conventional AT method. AT time was delayed because ECMO serves to remove car-

**Table 1.** Vital sign and PaO<sub>2</sub> during apnea test

Variable	Case 1	Case 2	Case 3
Mean blood pressure (mmHg)			
Primary apnea test	78→60	80→77	94→87
Secondary apnea test	96→101	77→64	86→96
Heart rate (beat/min)			
Primary apnea test	101→101	115→115	99→97
Secondary apnea test	101→101	101→104	97→96
PaO <sub>2</sub> (mmHg)			
Primary apnea test	213.0→137.5	134.2→87.5	491.0→344.5
Secondary apnea test	383.7→629.0	232.9→285.3	256.6→380.9

Abbreviation: PaO<sub>2</sub>, partial pressure of arterial oxygen.

bon dioxide. In the second and third cases, we were able to reduce AT time by diminishing the sweep gas flow rate of ECMO.

AT may cause a significant risk of complications such as hypotension, hypoxia, and even cardiac arrest. Therefore if a potential donor has hypotension and hypoxia, severe complications should be taken into consideration during AT(6). If condition of potential donor can't tolerate non-ventilation period, AT can be replaced by a transcranial Doppler or cerebral angiography. Transcranial Doppler can be brought to the bedside to demonstrate lack of brain blood flow(1). Usually there's no need to consider performing alternative test instead of AT in ECMO-dependent potential donor because ECMO provides respiratory and circulatory support. Table 1 shows that severe hypoxia and hypotension did not occur in all cases.

However, shortening the AT time can be of great significance in unstable patients. Considering high vasopressor requirement and frequent application of renal replacement therapy in ECMO-dependent potential donor, the reduction of AT time is essential. Furthermore, the patient's condition may deteriorate due to the time delay in attempting to perform alternative test if AT is not possible with conventional method.

In conclusion, we could increase PaCO<sub>2</sub> and reduce AT

time in ECMO-dependent potential donor by reducing sweep gas flow rate of ECMO and stopping the ventilation.

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