Apnea tests in the determination of brain death in patients treated with extracorporeal membrane oxygenation (ECMO)

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Abstract

Extracorporeal Membrane Oxygenation (ECMO) is a well-established method of support in patients with severe respiratory and/or circulatory failure. Unfortunately, this invasive method of treatment is associated with a high risk of neurological complications including brain death. Proper diagnosis of brain death is crucial for the termination of futile medical care. Currently, the legal system in Poland does not provide an accepted protocol for apnea tests for patients on ECMO support. Veno-arterial ECMO is particularly problematic in this regard because it provides both gas exchange and circulatory support. CO₂ elimination by ECMO prevents hypercapnia, which is required to perform an apnea test. Several authors have described a safe apnea test procedure in patients on ECMO. Maximal reduction of the sweep gas flow to the oxygenator should maintain an acceptable haemoglobin oxygenation level and reduce elimination of carbon dioxide. Hypercapnia achieved via this method should allow an apnea test to be conducted in the typical manner. In the case of profound desaturation and an inadequate increase in the arterial CO₂ concentration, the sweep gas flow rate may be increased to obtain the desired oxygenation level, and exogenous carbon dioxide may be added to achieve a target carbon dioxide level. Incorporation of an apnea test for ECMO patients is planned in the next edition of the Polish guidelines on the determination of brain death.

Key words: brain death, diagnostics, apnea test; organ donor; extracorporeal circulation; ECMO

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The extracorporeal membrane oxygenation (ECMO) method uses extracorporeal circulation, a technique that is used in cardiac surgery, for the treatment of acute heart failure and/or respiratory distress. The first reports of the effectiveness of this method date to the 1970’s [1]. In Poland, the ECMO system was used as a supplementary therapy for acute respiratory distress syndrome for the first time by the team of Roman Przybylski, MD and Adam Grzybowski, MD in Silesian Centre for Heart Diseases in Zabrze in 1998 [2]. Currently, ECMO is used in intensive care systems for adults as well as children, and the availability of this method in Poland is continuously growing.

The modern ECMO system consists of an oxygenator with an integrated heat exchanger, a centrifugal pump, system of medical gas delivery with a mixer, temperature controller and system of drains and cannulas (Fig. 1).

Depending on the location of cannula insertion and the range of support, two types of ECMO can be performed: veno-venous (VV-ECMO) and veno-arterial (VA-ECMO).

In the VV-ECMO system, two venous cannulas are used, which are commonly inserted into the femoral vein and the internal jugular vein. Venous blood is obtained through the femoral cannula, and then oxygenated blood is delivered to the cannula placed in internal jugular vein between the superior vena cava and the right atrium. Integrated, double-lumen, inflow-outflow venous cannulas that can be inserted through any central vein are currently available. The use of a VV-ECMO system results in venous blood oxygenation, and this blood is subsequently is pumped by the right ventricle into the pulmonary circulation. VV-ECMO only ensures support of pulmonary gas exchange in cases in which there is no possibility of improvement based solely on mechanical
ventilation. Blood is oxygenated, and carbon dioxide is eliminated. An adequate cardiovascular system is an essential prerequisite for the use of this method.

The VA-ECMO system allows the support of not only gas exchange but also cardiovascular system function. This system contains one or, more commonly, two venous cannulas (inflow), and the arterial cannula is inserted to the femoral artery or subclavian artery (peripheral ECMO). Sometimes the VA-ECMO system is placed directly into the right atrium and ascending aorta (AAo) (central ECMO). This system is commonly used for short-term support in patients who have undergone cardiac surgery due to acute perioperative heart failure, but it could also be used when the insertion of a peripheral cannula is problematic or impossible. The configuration of venous cannulas in both the VV-ECMO and VA-ECMO systems is similar; therefore, in the case of heart failure development, VV-ECMO can possibly be converted into VA-ECMO by the insertion of an additional arterial cannula and simply exchanging the drain setup.

Regulation of the ECMO system is based on controlling the blood flow, which is regulated by the pump speed, composition of the gas mixture, gas flow through the oxygenator and the temperature of the heat exchanger. The use of ECMO requires appropriate anticoagulation therapy, which could cause haemorrhagic complications.

Current indications for ECMO very wide and include acute respiratory distress and/or heart failure in adults as well as in children. ECMO is used after conventional therapies are exhausted; however, the main prerequisite for the use of ECMO is reversibility of the disease. In recent years, the ECMO system has also been used in the treatment of cardiac arrest as ECMO-supported cardiopulmonary resuscitation (E-CPR) and in the treatment of patients with severe hypothermia to perform controlled warming of the patient and support of the cardiovascular and respiratory systems. Use of the ECMO system during the last AH1N1 influenza pandemic [3, 4] contributed to the popularization this method in Poland and led to higher availability for patients through central purchases of medical equipment by the Ministry of Health.

Unfortunately ECMO is an invasive procedure that produces a relatively high risk of complications. Neurological adverse events have been observed in more than 30% of patients treated with this method, and brain death (BD) is possible in up to 20% of patients [5]. In children treated with E-CPR, the percentages of neurological complications and BD were 22% and 11%, respectively [6].

The relatively high risk of serious neurological complications, which consequently could lead to BD, requires the formulation and official approval of protocols for formal confirmation of BD. The current Ministry of Health announcement from July 17, 2007 regarding the criteria and modes of confirmation of permanent and irreversible cessation of brain functions [7] does not include a procedure for BD confirmation in patients treated with ECMO. In these patients, the evaluation of neural reflexes in areas supplied by brain stem nerves could be performed; however, conducting the apnea test (AT) in the recommended mode is not possible.

The medical community is convinced that performing an AT in patients treated with ECMO is extremely difficult. In countries where an AT is not mandatory for the confirmation of BD, there are reports of cases in which this test was not performed simply due to its complexity [8]. The current Ministry of Health announcement precisely presents the protocol for performing an AT, but elimination of CO2 through the ECMO system does not allow this test to be performed in the specified mode. The modern oxygenators are highly efficient, and disconnection from a ventilator does not significantly change the gasometric parameters of arterial blood.

The content of paragraph I of the Ministry of Health announcement, Note I, states that “The aim of the examination is to evaluate the ability to respond to the strongest respiratory stimulus, e.g., increasing the carbon dioxide level in the body. Apnea in the human body is characterized by a lack of reaction to an increase in the PaCO2 value to at least 60 mm Hg (7.9 kPa). Therefore, the test is performed correctly if the PaCO2 value is increased to at least 60 mm Hg (7.9 kPa), and the gain is at least 20 mm Hg (2.6 kPa)” Therefore, the formulation of a safe mode to obtain the mentioned gasometric parameters in patients treated with ECMO is of crucial importance.

The AT is more complex in patients treated with VA-ECMO. Reduction of blood flow through the VA-ECMO system...
significantly decreases support of the cardiovascular system and could lead to haemodynamic instability. Interruption of the gas supply to the oxygenator has been described in the literature [9], but in the case of VA-ECMO, it results in a shunt of unoxygenated venous blood to the arterial system and subsequent hypercapnia as well as hypoxemia, which could contribute to destabilization of the general state of the patient while performing the test.

Eliminating of CO₂ through the ECMO system depends on the volume of blood flowing through the oxygenator and the presence of CO₂ in the gas mixture as well as the speed of its flow through the oxygenator and the type of oxygenator [10]. The substitution of the gas mixture flowing into the oxygenator with oxygen with a simultaneous reduction of the sweep gas flow rate in the oxygenator leads to hypercapnia without significant hypoxemia. Several reports have been published that indicate that the sweep gas flow rate in adults could be safely decreased to the approximately 0.5 L min⁻¹ [11], while in small children, the flow value could be decreased to 0.1 L min⁻¹ [12]. For practical reasons, the sweep gas flow rate in the oxygenator should be decreased to the lowest value that does not lead to a significant decrease in the arterial blood saturation. In the case that these actions do not result in an increase in the partial pressure of CO₂ in the arterial blood and further reduction of gas flow leads to excessive decreases in oxygenation, exogenic CO₂ with the appropriate flow along with oxygen could be added to the oxygenator.

When arterial blood samples are obtained for gasometric tests, it should be noted that the reversed cephalad flow of blood in the descending aorta, caused by the femoral cannula of the VA-ECMO system together with the left ventricle ejection, could lead to mixing of blood with different gasometric parameters in the aorta. The partial gas pressure values and saturation of arterial blood samples obtained for tests from different locations could be significantly different. Therefore, obtaining arterial blood samples for gasometric tests from both radial arteries and choosing the sample with lower partial pressure of carbon monoxide as the referential sample is justified. This method is used because the brain stem is vascularized by vertebral arteries and branches of the subclavian arteries, and the gasometric parameters mentioned above should not significantly differ from those established in the radial arteries.

In practice, conducting an AT in a patient treated with VA-ECMO does not differ from the procedure described in the Ministry of Health announcement, with the exception of increasing the CO₂ pressure and the prevention of hypoxia. Nevertheless, it should be considered that gas exchange is generated by the ECMO pump and occurs mainly in the oxygenator rather than in the patient’s lungs. An AT could be performed by disconnecting the ventilator and oxygen insufflation or using hypoventilation with oxygen alone.

Performing an AT in a patient treated with VV-ECMO is significantly easier. There are no haemodynamic consequences of decreasing the blood flow through the ECMO system. Selective interruption of gas flow through the oxygenator is tantamount to stopping the support with the ECMO system because venous blood is only pumped within the venous system and does not undergo gas exchange. It could even be stated that the VV-ECMO system makes performing an AT easier because the appropriately established VV-ECMO parameters enable arbitrary control of the partial gas pressure in the patient’s arterial blood.

The use of ECMO in Poland for the treatment of severe hypothermia could become more common in the future [13]. In the case of E-CPR with the ECMO system, this technique could be used to induce therapeutic hypothermia. It is important to note that the pharmacokinetics and pharmacodynamics of drugs are altered at decreased temperatures, and after normothermia is achieved, this could lead to unpredictable serum concentrations, in the absence of laboratory evaluations, of the drugs that influence respiratory functions. Premature performance of the AT after normothermia is achieved could result in erroneous results [14, 15].

Utilization of ECMO will be likely become more widespread in the near future. With the growing number of patients treated with the ECMO method, the number of complications, including BD, will also increase. An appropriate diagnosis of BD and termination of futile treatment in these cases is extremely important for the families and medical staff. An AT could also be of great importance in cases in which organs are used for transplantation. In the next planned amendment of the BD diagnosis criteria, it is predicted that issues involving the use of new medical technologies, including treatment with ECMO, will be addressed.

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