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COMMUNICATIONS

BRAIN DEATH DETECTION: THE ESSENTIALS

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Abstract

This article will elaborate the definition of brain death as well as the initial diagnostic assessment of patients suspected of brain death. We will explain the protocol for brain death detection as simple as possible, elaborating all diagnostic approaches available for proving brain death presence. Since, early recognition of symptoms that indicate potential brain death in the patient is of vital importance, the clinical assessment of patients suspected of brain death will be explained step by step in order to provide a simple but comprehensive guide for nurses, resident doctors and specialists that work in an Intensive Care Units where brain death is most commonly diagnosed and deceased donor are treated further on. Diagnosing brain death must be carried out according to all rules and protocols, to avoid any omission or error in making a very important and serious diagnosis. Close and frequent monitoring by the nurse and physicians is the most important toll beyond any others when we speak about early and on time brain death detection.

Keywords: *brain death; clinical assessment; diagnosis.*

Introduction

Brain death (BD) is a condition in which there is a complete and irreversible failure of the central nervous system - CNS. The most often encountered causes that lead to the occurrence of irreversible brain damage are severe neurotrauma, spontaneous brain hemorrhage, traumatic brain hemorrhage and anoxic hypoxic encephalopathy. In percentage terms, brain death the most often occurs due to cerebrovascular lesions (48%), craniocerebral injuries (32%), anoxic ischemic brain lesion (13%), brain tumors (4%) and other remaining causes in total of 3%. These patients are the most often treated in intensive care units, where the total number of deaths diagnosed with BD is 10-16%, and the total in all hospital institutions is 1-5% (1). Regarding the timely diagnosis and early detection of BD, a very important tool is the observation of patients

with the above-mentioned diagnoses upon admission to intensive care units. Every intensive care unit should have a transplant coordinator who would organize and manage the entire process together with the intensive care unit team, as well as the team that will perform the transplantation. Early recognition of symptoms that indicate potential brain death in the patient is of vital importance. In such cases, measures are immediately taken, primarily to save the injured person, and if, despite all efforts, brain death occurs, then the entire medical team should be focused on maintaining the vitality of the potential donor's organs until their successful explanations. Patients who have suffered massive brain injuries, most often during hospitalization, show symptoms that indicate extremely severe brain damage, which are the most often irreversible (1). Usually, at the first examination, these patients have a Glasgow Coma Scale of less than seven, which indicates a poor prognosis.

The Glasgow Coma Scale is used for neurological assessment of patients and is a sum of points from three components: ocular, vestibular and motor response. The total sum of these points is a very important diagnostic parameter. The minimum sum of these points is three, and the maximum is fifteen. A score of 0-12 points indicates moderate neurological impairment, while anything below 8 is considered a comatose state of the patient (2,3).

Scoring using the Glasgow Coma Scale:

1) Opening eyes
- Spontaneous (4 points)
- On command (3 points)
- With painful jaw (2 points)
- No response (0 points)

2) Speech function
- Spontaneous speech (5 points)
- Confused speech (4 points)
- Unintelligible words (3 points)
- Unintelligible voices (2 points)
- Inability to speak (1 point)

3) Motor function
- Follows command (6 points)
- Performs emphasized movement (5 points)
- Indicates pain (4 points)
- Flexion (3 points)
- Extension (2 points)
- No response (1 point)

During the examination, there may be asymmetry between the two sides of the body, and then the side that reacts more painfully is assessed (2).

Dilated and non-reactive pupils, absence of spontaneous respirations, as well as absence of reactions even in the most painful state, are the first symptoms that indicate brain death (2,3).

They are the most often first noticed by the nurse who participates in the treatment of the patient. When the first symptoms characteristic for brain death are observed, medical examinations should be immediately started to prove existence of brain death. In the meantime, emphasis is placed on hemodynamic maintenance and perfusion of organs and tissues in the potential donor. The process itself from undertaking investigative methods to prove brain death to organ explantation should last from 12-24 hours. After proving the presence of brain death in the patient, according to the legal rules of the country, the doctor who is responsible for treating the patient should inform the family about the patient's health condition and explain the possibility of organ donation, and thus the possibility of saving another human life. Attention must be paid to legal and medical regulations, and everything must take place without any legal or ethical lapses.

Brain Death Detection Methods

According to the World Brain Death Project, every patient that will be treated as a possible organ donor because of BD should have a previously established neurologic diagnosis that can lead to an irreversible and complete loss of all brain functions. All clinical conditions and diseases that can confound the clinical examination and may mimic BD should be excluded prior to establishing the final diagnosis (4). There are generally three steps used for the successful and on-time detection of potential organ donors. They are:
1) Administrative method - involves monitoring of all patients that are admitted in the intensive care units.
2) Presence of a coordinator for assessing a potential donor - Every brain-dead patient is a potential donor. The coordinator is always guided by the answers to the following questions:
-Who is a potential donor?
(Severe brain injuries: brain hemorrhages, neurotraumas, cerebrovascular stroke, anoxic ischemic brain lesion);
-What pathological changes are there?
(Severe brain injuries, Glasgow coma < 7);
-Where is it the most often found?
(Emergency centers, intensive care units, neurosurgical centers).
3) Connection with other centers - Ensuring more successful mutual communication and cooperation, to timely prove brain death in the patient, maintain hemodynamic stability of the donor and evaluate the donor. For on-time recognition of potential donors and proof of brain death in the patient, there must be a perfect protocol. The protocol should consist of: a team, a member of which is directly responsible for recognizing and monitoring the health condition of the potential donor; protocol for facilitating recognition and identification of a potential donor and mutual cooperation of the entire medical team. The existence of a professional and educated team, responsible for identification, maintaining hemodynamic stability and good perfusion of

the organs of the potential donor, as well as the existence of an organized and trained team for explantation and implantation of the transplant, are key factors for successful transplantation. The need for organ transplantation is increasing significantly, and the largest number of donated organs are obtained from deceased organ donors who were diagnosed with brain death. Therefore, timely recognition and diagnosis of brain death in a potential organ donor is of immense importance. The success of transplantation as the entire process depends on the early recognition of the potential donor, whose clinical picture is most often recognized in the first 24 hours of admission to the ICU (Intensive Care Center), and 25% of them are recognized in the first 48 hours or more. A qualified team of intensivists, neurosurgeons and neurologists perform the first clinical examination of the potential donor, while the neurologist and nephrologist are responsible for conducting instrumental tests to prove brain death. There are two basic concepts of brain death: whole brain death and brainstem death. Whole brain death - In this case, there is an irreversible cessation of the functions of the cerebellum and cerebellum, as well as the brainstem. In the case of whole brain death, a clinical examination and instrumental tests are required to establish an accurate diagnosis. In case of Brainstem death there is an irreversible loss of consciousness and spontaneous breathing. Only a clinical examination can prove the absence of the brainstem activity.

Diagnosing Brain Death

Brain death is a condition in which there is an irreversible loss of all brain functions, including brainstem functions. The function of other organs, due to their possible explantation, can be preserved for a short time with the help of various medications and mechanical support. Brain death occurs because of an increase in intracranial volume, which the most often occurs due to brain edema or due to the presence of a collection or obstruction that impedes the circulation of cerebrospinal fluid. With the increase in intracranial pressure, blood circulation to the brain gradually slows down until it stops completely. When brain death occurs, the condition is irreversible and circulatory death occurs quickly. The most common causes that lead to brain death are stroke, brain hemorrhage, or severe traumatic injuries to the head and brain. The diagnosis of brain death takes place in four stages:
I. Existence of prerequisites for establishing a diagnosis of brain death. Prerequisites that must exist in order to make a decision to approach procedures for diagnosing brain death are:

- the patient is in a comatose state,
- the patient does not have spontaneous breathing,
- knowledge of the exact cause of brain damage,
- brain damage is irreversible.

II. Exclusion of reversible causes - Conditions that may give a clinical picture like brain death or challenge the diagnosis of the same are:

- a state of hypothermia < 35 degrees Celsius,

- intoxication with drugs: benzodiazepines, antiepileptics, anesthetics, barbiturates or alcohol,
- hypotension with systolic pressure <80mm Hg,
- metabolic and endocrinological conditions: myasthenia gravis, hepatic encephalopathy.

First, in these situations, the first step is to correct the current condition, then proceed to conduct instrumental tests that prove circulatory arrest of the brain (3).

III. Clinical examination

1. Pupil status - In order the pupils to be defined as non-reactive, all diseases and medications that would cause the pupils to be in such state must be excluded. A condition in which the pupils are moderately or completely dilated, in a neutral position, where there is an absence of photo motor reflex, as well as ocular movement, is considered a positive test for brain death.
2. Corneal reflex - absence of spontaneous blinking, where the stimulus is stronger than in conscious patients.
3. Trigeminal nerve - with strong stimulation in the area of innervation of the trigeminal nerve, the reaction is absent.
4. Oculocephalic reflex - This test is not performed in patients with cervical injuries. Method of performance - by holding the eyelids open, the patient's head is abruptly rotated to one side, the head is held in that position for 3-4 seconds and then the head is abruptly rotated to the other side. In a deceased patient, the eyes follow the movement of the head. In patients with brain death, there is an absence of the oculocephalic reflex.
5. Oculovestibular test - Method of performance - the patient's head is raised by 30 degrees and 50ml of cold water is introduced into the ear canal with a plastic catheter. In patients with brain death, there is an absence of any eye movement. For an accurate result, attention must be paid to the possible existence of an ear injury, the presence of blood or cerumen in the ear canal. Also, during treatment with sedatives, anticonvulsants, in the presence of previous ear diseases, as well as in the case of a fracture of the temporal bone, the result may be false.
6. Pharyngeal reflex - Method of performance - with a spatula, the root of the tongue and the back of the throat are stimulated. In patients with brain death, the pharyngeal reflex is absent.
7. Tracheal reflex - This is the last reflex to disappear in patients with brain death. Method of performance - with a suction catheter, through the endotracheal tube, the trachea is stimulated. In patients with brain death, the tracheal reflex is absent.
8. Muscle atony.
9. Atropine test - Method of performance - atropine is administered intravenously at a dose of 0.04mg/kg body weight. A positive test is considered when the acceleration of the heart rate is not greater than 10% of the initial heart rate.
10. Apnea test - This test is performed last. It proves the absence of spontaneous respirations during the disconnection from the respirator. The patient should be disconnected from the respirator for a time interval that would result in a sufficient increase in CO_2 in the atrial blood, which would provoke the neurons of the respiratory center. The apnea test can be performed with and without the help of a respirator.

o Without the help of a respirator - The patient is ventilated for 10-20 minutes with 100% oxygen. $PaCO_2$ should be 5.3kPa (40mmHg) or higher before disconnecting from the respirator. After disconnecting the patient from the respirator, oxygen is introduced at 6 l/minute through a catheter in the endotracheal tube. Wait until $PaCO_2$ reaches 8.0kPa (60mmHg).

o Without a respirator - The ventilation mode should be CPAP, PEEP 10-12cmH_2O, FiO_2

- monitoring oxygenation and capnography,
- monitoring the arterial blood pressure through invasive monitoring,
- with each apnea, the module should be returned to CPAP,
- depending on the initial values, after 5-10 minutes, a reading of CO_2 is taken on the capnography at the end of expiration,
- when CO_2 reaches a value of 50mmHg, arterial blood is taken for analysis of $PaCO_2$ and PaO_2,
- every 2 minutes, arterial blood is taken for analysis until $PaCO_2$ reaches a value of 60mmHg,
- upon detection of spontaneous respirations, saturation lower than 85%, PaO_2 <65mmHg, systolic pressure lower than 65mmHg or cardiac arrhythmia, the test is stopped.

The clinical examination is performed in two stages (2). The first examination includes: examination of the pupils, corneal reflex, trigeminal reflex, oculocephalic reflex, oculovestibular reflex, pharyngeal reflex, tracheal reflex, muscle atony and atropine test. After 24 hours, the clinical examination is repeated, including the apnea test. After obtaining a positive clinical examination for brain death, instrumental tests are performed on the potential donor (2,3.7).

IV. Instrumental tests

Instrumental tests are used to examine the bioelectric activity and blood circulation in the brain. These tests should be non-invasive, reliable, precise, fast and economical, be performed without transporting the patient and be easily interpreted by the doctor working in the intensive care unit (5-9).

1. Selective brain panangiography - This examination can detect several findings that are compatible with brain death: complete cessation of arterial contrast and absence of venous filling, cessation of cerebral circulation in the Circle of Willis and significantly slow arterial-venous time. A delay greater than 15 seconds is not compatible with brain function. The biggest disadvantage of this procedure is the transportation of the patient to the X-ray machine intended for angiography.
2. Radionuclide scintigraphy - A highly sensitive technique, independent of previous drug administration and the current clinical condition of the patient, performed using 123 and Tc99m.
3. Transcranial Doppler sonography - This technique examines blood circulation through the brain and monitors possible circulatory arrest. It is suitable for repeated performance due to the possibility of performing it at the patient's bedside.

4. Evoked Somatosensory Potentials - This test examines the visual, auditory, and somatosensory pathways using light, auditory and electrical stimulus at different frequencies. Hypothermia can give false results with visual stimulus. Chronic deafness, temporal bone fractures, and eardrum or middle ear injuries can give false results with auditory testing. When examining sensory pathways, false results can be obtained if there is peripheral nerve damage.
5. EEG - With this recording, which lasts about 30 minutes, no brain-generated bioelectrical activities are detected in the event of brain death. In some cases, due to the presence of cardiac activity, it is possible to record electrical activity. All conditions that compromise the clinical examination also compromise the EEG examination.
At the Clinic for Anesthesia, Resuscitation and Intensive Care (CARIC), in the period from 2021-2023, there were a total of 12 cadaveric donors. In the intensive care unit at CARIC, in 2021, a total of nine cadaveric donors were recorded. In 2022, there was only one cadaveric donor. In 2023, a total of two cadaveric donors were recorded. The cause of brain death in seven of them was intracerebral hemorrhage and subarachnoid hemorrhage in severe polytrauma, while in the remaining five, the cause was spontaneous brain bleeding. At the Clinic for Neurosurgery, in the period from 2021-2023, a total of seven cadaveric donors were recorded. In the intensive care unit of the Clinic of Neurosurgery, a total of 318 patients died from spontaneous intracerebral hemorrhage and subarachnoid hemorrhage in the period from 2021 to 2023. Seven of these patients were processed as potential donors. A ruptured aneurysm was the cause of the cerebral hemorrhage in 71.4%, and in the remaining 28.6% the cause was a hypertensive crisis. As previously was noted in the literature, cerebrovascular events and neurotrauma were the most frequent cause of death according to our experience as well. Diagnosis of brain death was established in the ICU from an anesthesiologist, following the above-described protocol step by step in a multidisciplinary collaboration with nurses, ICU stuff and interventional radiologist.

Conclusion

Diagnosing brain death must be carried out according to all rules and protocols, to avoid any omission or error in making a very important and serious diagnosis. Regarding the fact that most of the cases of BD diagnosis are met in the ICU, systematic approach of clinical and instrumental examination is needed in order to establish clear diagnosis of BD. Close and frequent monitoring by the nurse and physicians is the most important tool beyond any others when we speak for early and on time brain death detection.

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