

DIAGNOSIS OF BRAIN DEATH - LITERATURE REVIEW

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Abstract: Introduction: In Brazil, the criteria for the diagnosis of brain death (BD) are defined by the Federal Council of Medicine (CFM) according to resolution 2,173/2017, which defines the condition as the complete and irreversible cessation of cerebral cortical functions and of the brainstem, in addition to the impossibility of maintaining life without artificial resources. **Objectives:** To present the current diagnostic criteria for BD and discuss the importance of accurate diagnosis of the condition. **Methods:** Literature review based on articles published in Portuguese, English and Spanish, between 2016 and 2021, from LILACS, SciELO and PUBMED databases. **Results:** The procedures for determining the EM must be initiated in all patients who present with non-perceptive coma, absence of supraspinal reactivity and persistent apnea, in addition to meeting certain prerequisites. It is mandatory to perform the following procedures to determine BD: two clinical exams, which confirm non-perceptive coma and absence of brainstem function; apnea test, which confirms the absence of respiratory movements after maximal stimulation of respiratory centers; complementary exam that proves the absence of brain activity. **Conclusion:** The CFM resolution provides great security to establish the diagnosis of BD by demanding that the required steps be carefully followed, in addition to determining that the evaluation be carried out by qualified and experienced professionals, as there can be no doubts or errors regarding to the determination of the ME. It is important to point out that the complementary exams are operator-dependent, which reinforces the importance of the report in these situations being done by a physician specialized in the method.

Keywords: “diagnosis”; “death”; “encephalic”.

INTRODUCTION

In Brazil, the criteria for the diagnosis of brain death (BD) are defined by the Federal Council of Medicine (CFM), which published, in December 2017, resolution 2,173/2017,¹ which defines the condition as complete and irreversible cessation. of cerebral cortical and brainstem functions, in addition to the impossibility of maintaining life without artificial resources.²

The criteria to determine the presence of BD must be performed in all patients who, as long as they meet some prerequisites, have the following suggestive signs: non-perceptive coma; absence of supraspinal reactivity; and persistent apnea.³

The diagnosis is difficult, needing to be made rigorously, as it is a moment of anguish for family members, who do not have knowledge about the subject,⁴ in addition to being essential to guarantee an unequivocal diagnosis, since it involves medical, ethical and legal principles. that are linked to organ donation for transplantation.^{1,5}

In order to confirm the diagnosis, a lack of response from the brainstem is necessary, and in Brazil, two physical examinations of the nervous system are mandatory to establish the diagnosis of BD. The apnea test is a mandatory test for this, being confirmatory if there is no spontaneous respiratory movements after stimulation of the respiratory center through hypercapnia in a value greater than 55 mmHg.⁵

It is worth noting that the diagnosis of BD is not only useful for the purpose of organ transplantation, being, in fact, necessary for every terminal patient, regardless of organ donation,⁶ because, as stated before, it involves medical, ethical and legal principles which also apply to the possible removal of this patient from the hospital bed, allowing the use of devices that could serve another patient who may still have their life preserved.

JUSTIFICATION

A better knowledge of the diagnostic criteria for brain death is essential, in order to know how to use them correctly, thus avoiding failures in future diagnoses and consequently the death of patients who could still be saved, if the condition were ruled out, in addition to, alternatively, freeing up new beds, after the BD is confirmed, for the care of new patients who need intensive medical care.

GOALS

PRIMARY OBJECTIVE

Conduct a comprehensive review on the topic of brain death.

SECONDARY OBJECTIVES

Present the current diagnostic criteria for brain death;

Discuss the importance of accurate diagnosis of the condition, in ethical and legal terms.

METHODS

This is a literature review study, which deals with the theme “diagnosis of brain death”. The discussion centers around the technical aspects that support the CFM Resolution 2,173/2017, a device that regulates the diagnosis of brain death in Brazil. For this purpose, a search for articles was carried out in the specific literature. The searches were carried out in the LILACS, SciELO and PUBMED databases.

Articles published between the years 2016 and 2021, written in Portuguese, English and Spanish, were selected. The descriptors used were “diagnosis”, “death” and “encephalic”, using the Boolean operator AND to gather the descriptors in the title and abstract. Articles that were not directly related to the proposed theme and that were not within the time and language parameters mentioned above were excluded.

RESULTS

The CFM resolution 2,173/2017 highlights the ethical and legal commitment that the health team, especially physicians, must have in identifying patients with clinical criteria for BD, so that this diagnosis can be established as quickly as possible. It must be noted that the neurological assessment of patients potentially presenting with BD is supported by a series of clinical criteria, with legal issues involving the initiation of procedures for the diagnosis of BD in patients who are in non-perceptive coma, absence of supraspinal reactivity and persistent apnea, even in the context of possible organ donation.^{7,8}

BD is defined as a permanent and irreversible loss of brain function due to a known and proven cause, capable of causing certain clinical manifestations. The diagnosis of BD must be absolutely certain and performed in a standardized way, with 100% specificity, leaving no doubts. Any uncertainty during the process makes the diagnosis impossible, and the evaluation process must be interrupted.⁸

In order to reach the diagnosis of BD, four steps must be completed, which will be described individually, namely: prerequisites; physical exam; apnea test; and complementary exams.⁸

PREREQUISITES

Presence of brain injury of known cause, irreversible and capable of causing a clinical picture.

The diagnosis of the lesion that caused the coma must be established by clinical examination and confirmed by complementary exams. Doubt as to the presence of an irreversible lesion or its cause prevents the determination of BD. Before starting the examinations for the determination of BD, a minimum period of observation of six hours must be respected, in a hospital environment,

after coma has been established, and a minimum of 24 hours, when the primary cause of the condition is hypoxic encephalopathy - ischemia after cardiorespiratory arrest or rewarming in therapeutic hypothermia.⁸

Absence of factors that could confound the clinical picture.

hydro electrolyte, acid-base or endocrine disturbance and exogenous intoxication:

The team responsible for the diagnosis of BD is the one who defines whether these abnormalities are capable of causing or worsening the clinical picture, leading to a picture suggestive of BD.⁸

Hypothermia (rectal, bladder or esophageal temperature below 35°C):

Brainstem reflexes can be abolished when there is severe hypothermia, becoming a confounding factor for the determination of ME. Therefore, body temperature must be corrected and maintained above 35°C.⁸

Drugs with central nervous system depressant action (NCDF) and neuromuscular blockers (NMB):

These drugs do not cause non-perceptive coma when they are used at therapeutic doses, not altering the procedures for determining ME;

When used in continuous infusion, at the usual doses for sedation and analgesia, in patients with normal renal and hepatic function and who are not undergoing hypothermia, it is necessary to wait four to five half-lives after discontinuing them;

It is necessary to wait for more than five half-lives of these drugs, after discontinuing them, in patients with hepatic and/or renal failure and in those undergoing hypothermia, as well as if higher than conventional doses are used. It is necessary to be sure that the drugs have been metabolized/eliminated and no longer have therapeutic action, according to calculations or by checking their serum levels;

In the situations mentioned above,

it is preferable to use complementary tests that assess cerebral flow, since the electroencephalogram (EEG) has its result altered with the use of these drugs.⁸

CLINICAL EXAMINATION

Eat non-perceptive.

Condition characterized by permanent unconsciousness, with deprivation of supraspinal motor response to intense painful stimuli in the supraorbital region, on the trapezius and on the nail bed of the four limbs. Behavioral responses such as decerebrate (limb extension) or decortication (spastic flexion of the upper limbs) nullify the diagnosis of BD.⁸

Occasionally, deep tendon reflexes, limb movements, opisthotonos or trunk flexion, shoulder adduction/shoulder elevation, sweating, flushing, or tachycardia may be noted during stimulation or spontaneously. These signals mean that there is still marrow activity – by marrow release! –, not annulling the diagnosis of ME.⁸

Cadaveric movements after the diagnosis of BD can cause doubts to family members about the patient's death. Electrophysiological studies found the presence and increase of spinal reflexes after BD, and it is important to emphasize that their presence does not invalidate the diagnosis. The explanation for these phenomena is that the loss of normal spinal cord inhibition that occurs at rest by the brainstem, telencephalon and diencephalon develops, releasing the spinal cord to react reflexively. Therefore, in ME spinal cord reflexes are common, since there is no central inhibition.⁶

A classic example is the Lazarus sign, in which there is a sudden flexion of both upper limbs on the chest, and even flexion of the trunk may occur. This reflex movement is produced at the spinal cord level, unrelated to brainstem activity or brain activity. This movement must

not be confused with decortication posture.⁶

Absence of brain stem reflexes.

Absence of the photomotor reflex: When performing light stimulation with the aid of a flashlight, the pupils must not respond, remaining fixed. However, they may present irregular contours and variable and asymmetrical diameters.⁸

Absence of corneal-palpebral reflex: When directly stimulating the lower lateral corner of the cornea, dripping cold saline solution or using a cotton ball soaked in saline or distilled water, the normal reflex will not be observed, that is, the normal response of blink of an eye.⁸

Absence of the oculocephalic reflex (“doll eyes”): When performing a rapid movement of the head in a lateral and vertical direction, the normal deviation of the eyes will not occur, that is, the eyes will follow the movement of the head. This test must not be performed on patients with suspected or confirmed cervical spine injury.⁸

Absence of the vestibulo-caloric reflex: In this exam, otoscopy must first be performed to verify the absence of tympanic perforation or occlusion of the external auditory canal by cerumen. The test is performed with the head in a supine position, elevated to 30°, irrigating the external auditory canal with 50 to 100 ml of cold water (around 5°C) with the aid of a syringe. The absence of deviation of the eyes must be observed for one minute. There must be a minimum interval of three minutes before the test is performed between each ear canal.⁸

Absence of cough reflex: When stimulating the trachea with the aid of a suction cannula, there must be no cough or reflex bradycardia.⁸

APNEA TEST

It is mandatory to perform the apnea test for the diagnosis of BD, which is determined

by the absence of spontaneous respiratory movements after the maximum stimulus of the respiratory center (located in the brainstem) through hypercapnia, with the PaCO₂ value greater than 55 mmHg.⁸

Adult patients must have a body temperature (esophageal, bladder, or rectal) above 35°C, arterial oxygen saturation above 94%, and systolic blood pressure (SBP) greater than or equal to 100 mmHg or mean arterial pressure (MAP) greater or equal to 65 mmHg. Children under 16 must have the SBP and MAP values described in Table 1.⁸

Age	Blood Pressure (BP)	
	Systolic BP (mmHg)	Mean BP (mmHg)
Up to 5 incomplete months	60	43
From 5 months to 2 incomplete years	80	60
From 2 to 7 incomplete years	85	62
From 7 to 15 years	90	65

Table 1. SBP and MAP values required for the diagnosis of BD in children under 16 years of age.

Technique.

Ventilation with 100% FiO₂ for at least 10 minutes to ideally reach a PaO₂ equal to or greater than 200 mmHg and PaCO₂ between 35 and 45 mmHg);

Place digital oximeter and collect initial arterial blood gases (by arterial catheterization);

Disconnect the patient from mechanical ventilation;

Establish continuous flow of O₂ through an intratracheal catheter, located at the level of the carina (6L/min), or T-tube (12L/min) or through CPAP (up to 12 L/min + up to 10 cm H₂O pressure);

Observe the presence of any respiratory movement for eight to ten minutes. Predict an

increase in PaCO₂ of 3 mmHg/min in adults and of 5 mmHg/min in children, to estimate the necessary ventilation disconnection time;

Collect arterial blood gases at the end of this time;

Reconnect mechanical ventilation.⁸

Test interruption.

The test must be interrupted in case of arterial hypotension (SBP less than 100 mmHg or MAP less than 65 mmHg), cardiac arrhythmia or significant hypoxemia, requiring arterial blood gas analysis and reconnecting the patient to the respirator. If the final PaCO₂ is lower than 56mmHg, the test must be repeated after hemodynamic stability has been achieved.⁸

Interpretation of results.

Positive test (presence of apnea): absence of respiratory movements, with final PaCO₂ greater than 55mmHg;

Inconclusive test: absence of respiratory movements, with final PaCO₂ lower than 56 mmHg;

Negative test (absence of apnea): existence of respiratory movements, with any value obtained in PaCO₂.⁸

Alternative ways of performing the apnea test.

There are some patients in whom it is not possible to obtain a persistent increase in PaCO₂ without concomitant hypoxia. In these cases, an apnea test with another method is allowed, for patients who cannot support the disconnection of the ventilator:

Connect a "T" piece to the orotracheal tube and couple the patient to a CPAP (continuous positive airway pressure valve) with a pressure of 10 cm of H₂O and a flow of O₂ at 12 L/minute;

Carry out the apnea test in equipment specific for non-invasive ventilation (NIV), and which has a connection with supplementary oxygen flow. Set the device in CPAP mode, with a pressure of 10cm of

H₂O and an O₂ flow between 10-12L/minute. Ventilators that do not have CPAP mode must not be used, as they can cause hypoxemia.⁸

A review study demonstrated that it is possible to perform the apnea test in adults under extracorporeal membrane oxygenation (ECMO) in cases of suspected BD. Control is performed by *sweep adjustments*. flow and, in cases of hemodynamic instability, maintenance of the blood flow value on ECMO.^{9,10}

COMPLEMENTARY EXAMS

It is mandatory to carry out complementary exams, in order to prove, in an indisputable way, the absence of brain blood perfusion, electrical activity or brain metabolic activity, thus having a diagnostic confirmation of BD. The exams that can be performed are explained below:

Cerebral angiography: must reveal the absence of intracranial flow, analyzing the internal carotid and vertebral arteries. Technically, such a failure is defined by the absence of opacification of the internal carotid arteries, at least above the ophthalmic artery and the basilar artery;

Electroencephalogram: proves cortical electrical inactivity or electrical silence in the brain (absence of brain electrical activity with a potential greater than 2 μV);

Transcranial Doppler ultrasound: demonstrates the absence of brain blood flow, through the presence of reverberant diastolic flow and small systolic peaks in the initial phase of systole;

SPECT brain scintigraphy: It is a single-photon emission computed tomography associated with radioisotope material, in which the absence of perfusion or brain metabolism is verified.⁸

The most indicated complementary exams are those that assess the presence of cerebral perfusion, such as cerebral angiography and

transcranial Doppler ultrasound, as these exams do not undergo alterations resulting from the previous use of CNS depressant drugs. There may be a situation where there is blood perfusion or brain electrical activity due to the persistence of some residual focal brain activity; in these cases, if there is an evolution to ME, the repetition of the exams a few hours or days later will demonstrate the absence of residual activity. Anyway, it is important to highlight that it is possible to use only one complementary exam compatible with ME for its determination.⁸

Transcranial Doppler ultrasound stands out for being a method applicable at the bedside, portable, non-invasive, easily reproducible by the operator, which does not require contrast, is more economical, and is not affected by drugs that act on the CNS, being it is inevitable that intensivists will gradually increase their use for the diagnosis of BD in the near future, precisely because of these advantages.¹¹

Studies show that brain computed tomography has 100% sensitivity for the diagnosis of BD, which is superior compared to computed tomography angiography, which had an accuracy of 86% and 96.3% in two different studies, both compared with the brain computed tomography. For the diagnosis of ME, CT angiography results may, in some cases, show intracranial filling, leading to misdiagnosis.¹²⁻¹⁴

SECOND CLINICAL EXAMINATION

It must be performed by another physician, using the same techniques used in the first clinical examination, and the repetition of the apnea test is unnecessary, if it was positive (absence of respiratory movements in the presence of hypercapnia).⁸

The interval between the two clinical examinations must be at least one hour in patients aged 2 years and over. In patients aged 2 to 24 months, the interval is 12 hours. In

patients with 7 days to 2 incomplete months, the interval is 24 hours.⁸

MEDICAL TEAM

To be able to evaluate patients with suspected BD, the physician must have at least one year of experience in assisting patients in coma, have followed up or performed at least ten diagnoses of BD and have carried out specific training that meets the standards determined by the Council. Federal Medicine.⁸

Each hospital is responsible for appointing the qualified team to carry out clinical and complementary exams to determine BD, and forwarding the information to the State Transplant Center (CET). In the absence of a doctor indicated by the hospital, it will be up to the CET of your Federative Unit to indicate this professional.⁸

It must be noted that clinical and complementary exams are operator-dependent. Thus, in order to avoid failures, the second clinical examination must be performed by another physician, who does not belong to the local transplant team, in addition to, necessarily, one of the evaluating physicians must be a specialist in the area of intensive medicine, emergency medicine, neurology or neurosurgery.⁶

COMMUNICATION TO FAMILY MEMBERS

The patient's family or legal guardian must be communicated clearly and evidently, without any doubts about the patient's serious scenario, explaining what brain death is and what tests are necessary to diagnose it.⁸

The follow-up of a doctor close to the patient's family is allowed to observe the procedures for determining the BD, as long as it does not imply a delay in the times of the necessary exams.⁸

It is known that there is still difficulty in

understanding the concept of brain death, as there is a lack of understanding on the part of family members, inexperience of the teams to carry out complementary exams and incorrect approaches, repressing family members to authorize a possible donor.¹⁵

The necessary clarifications must be provided to family members, differentiating the state of brain death from the state of coma, helping them to understand the difference, explaining that BD is irreversible brain damage, in which there is no chance of returning to life.¹⁵

Upon receiving the news of the BD, the family members have different feelings, such as sadness, crying, anger, insecurity, pain. Therefore, it is very important that the professionals involved know how to approach the family during the moment of mourning, helping to accept and adapt to the feeling of loss, mainly through good communication.¹⁵

ORGAN TRANSPLANTATION

Only family members or legal guardians can make decisions regarding organ donation.

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Most potential organ donors are young victims of trauma from external causes, and traumatic brain injury is one of the main causes of the evolution of critical patients to brain death.¹⁶

As is well known, the diagnosis of BD is essential to start the entire process involved in the possible performance of organ and tissue transplantation. Its delay leads to a lower effectiveness and quality of the transplant, in addition to maintaining the occupation of beds in the intensive care unit by patients without therapeutic possibilities.¹⁶

CONCLUSION

The CFM Resolution on which the present work is based provides great security for establishing the diagnosis of brain death,

by demanding that the required steps be carefully followed, in addition to determining that the evaluation be carried out by qualified and experienced professionals, as they do not doubt that doubts may persist or errors may occur regarding the determination of the ME. It is important to point out that the complementary exams are operator-dependent, which reinforces the importance of the report in these situations being done by a physician specialized in the method.

The protocol is complex, but fundamental for correct diagnoses, which helps in the medical approach with the patient's family regarding the acceptance of death and the possible consent of organ donation, since the moment of giving the news of the death of the loved one and even addressing the issue of organ donation is something very delicate, often not being well accepted by family members due to the moment of pain and suffering.

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