

Turkish Neurological Society Diagnostic Guidelines for Brain Death*

“Brain death” is the loss of all activities of the parts of central nervous system that reside within the skull, that is, brain, brain stem and cerebellum, permanently without recovery. Turkish Neurological Society, in accordance with the public perception of brain death, accepts this concept as “total brain death”. Total brain death refers to the medical judgement that a person is dead.

Turkish Neurological Society’s brain death guideline is a scientific text. The society created this text during a workshop it organized and the guideline has been undersigned by the neurologists and academics listed below. This guideline is in accordance with “Organ and Tissue Extraction and Transplantation Law (29.05.1979, Volume: 2238 Official Newspaper. Date: 03.06.1979 Official Newspaper Volume: 16655)” and “Ministry of Health Organ and Tissue Transplantation Services Legislation (Official Newspaper 01.02.2012-28191) Supplement-1”.

The 11th item of the 02.01.2014 legislature number 2238 which states “The medical death condition that pertains this law is decided by a committee of 4 physicians including a cardiologist, a neurologist, a neurosurgeon and an anesthesiologist and reanimation specialist, using the state-of-the-art guidelines and methodologies available at that time in the nation”, has been changed and reformulated as. “The medical death is decided with the consensus between two physicians, one of them being either a neurologist or neurosurgeon, and the other being either an anesthesiologist and reanimation specialist or an intensive care doctor, using evidence-based medical guidelines”. Turkish Neurological Society requires an individual examination and a clinical evaluation by a neurologist for declaring of brain death and recommends neurology consultation for all cases. According to the Turkish Neurological Society guidelines, “Brain Death Diagnostic Process” comprises of several steps.

Satisfying the Prerequisites

The following prerequisites should be satisfied in order to start the diagnostic process:

1. The diagnosis of a disease or process capable of causing total brain death should be certain for the patient.
2. There should be neuroimaging evidence for irreversible, severe structural brain damage with computerized tomography or magnetic resonance imaging. The imaging procedure can be done in the advanced stages of the declaration process depending on the clinical status of the patient and the previous radiological findings if necessary.

3. The treatment options for the diseases or processes causing brain damage should be exhausted or there should be a lack of response to all available treatment attempts.

4. Systolic blood pressure should be exceeding the upper bounds for the specific age group; cases who are 18 years of age or older must have blood pressure ≥ 100 mmHg. The blood pressure prerequisite can be achieved with vasopressor support.

5. Central body temperature should be ≥ 36 °C (96.8 °F)

6. There should not be electrolyte imbalance or metabolic disruption severe enough to suppress brain stem reflexes. In situations where the contribution of electrolyte imbalance or metabolic disorders to the process are unclear, diagnosis of brain death can be made by using supporting tests evaluating cerebral blood flow.

7. The patient should be under the influence of sedatives, anesthetics, consciousness changing analgesics or neuromuscular blockers or similar drugs. If the levels of these drugs taken can be measured, ample time should be allowed for the serum levels of the drugs to drop below therapeutic threshold. If drug levels cannot be measured, and the kidney and liver functions are normal, the wait period should be 5 times the elimination half-life of the drug. When liver and kidney functions are not normal, waiting for 5 times the elimination half-life of the drug is impossible, or when prior use of such drugs is uncertain diagnosis of brain death can be made by using additional tests for cerebral blood flow.

8. Neurological examinations findings closely following events that may cause hypoxic ischemic acute brain damage, such as cardiopulmonary resuscitation, are not reliable for the diagnosis of brain death; in order to start evaluating the three main clinical signs of brain death (coma, loss of brain stem reflexes and apnea test), the wait period should be 24 hours and the examination findings should be supported with tests evaluating cerebral blood flow.

Evaluating the Main Signs of Brain Death

The three main clinical signs of brain death are coma, loss of brain stem reflexes and apnea test.

Coma

Glasgow coma scale score should be 3 (since vocalization cannot be assessed, actually 2-T). There should be no response to painful stimulation of supraorbital ridge or temporomandibular joint. There should be no response to painful stimulation besides

*These guidelines were prepared/approved by the undersigned neurologists and academics, and they represent the opinions of Turkish Neurological Society.

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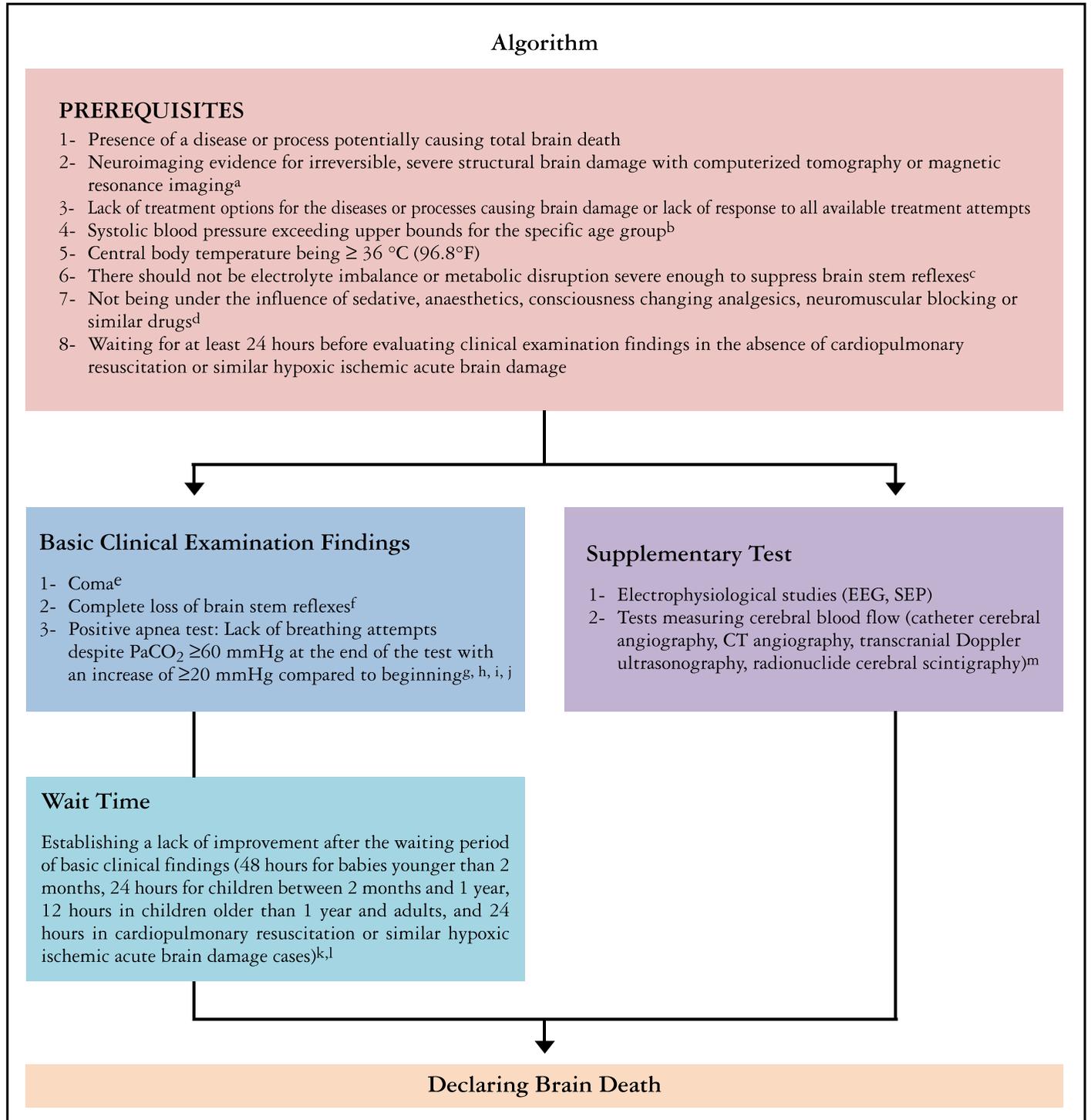
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spinal reflexes and automatisms. Sweating, blushing, tachycardia, fever, sustaining normal blood pressure without medication or presence of sudden spikes, presence of reflexes below foramen magnum (deep tendon reflex, Babinski sign, surface reflexes, Lazarus and similar complex spinal reflexes and automatisms etc.) or lack of diabetes insipidus development do not rule out brain death diagnosis.

Total Loss of Brain Stem Reflexes

Pupils should be at midline and fully dilated (4-9 mm) and unresponsive to bright light. Painful stimulation applied on suborbital ridge or temporomandibular joint and four extremities should not elicit any facial response (in bulbar muscles including facial and orofacial muscles). Cornea reflex should be absent. Oculocephalic and oculo-vestibular reflexes should be completely



absent. Gagging, coughing, sucking and rooting reflexes should be completely absent.

Apnea Test

Apnea test is conducted and documented by a specialist as required by the law. Physicians and consulting branches should not conduct or repeat apnea test separately, but instead aim for a

single, diagnostic apnea test for the comatose patients who also satisfy all conditions for lacking brain stem reflexes.

Before apnea test, it should be ensured that the body temperature is $\geq 36^{\circ}\text{C}$ (96.8°F), blood pressure is above the lower limit for the age group and the patient was given no medication that interferes with breathing capacity. pH and PaCO₂ in pre-test arterial blood gas sample should be within normal levels but in cases where hypercarbia due to lung pathologies, such as chronic

^aImaging may also be conducted during more advanced stages of declaration.

^bSystolic blood pressure should be ≥ 100 mmHg in cases 18 years and older. Blood pressure precursor may be established with vasopressor support.

^cWhen the contributions of electrolyte imbalance or metabolic disorders to the process are unclear, diagnosis of brain death can be made by using additional tests for cerebral blood flow.

^dIf the levels of these drugs taken can be measured, ample time should be allowed for the serum levels of the drugs to drop below therapeutic threshold. If drug levels cannot be measured, and the kidney and liver functions are normal, the wait period should be 5 times the elimination half-life of the drug. When liver and kidney functions are not normal, waiting for 5 times the elimination half-life of the drug is impossible, or when prior use of such drugs is uncertain diagnosis of brain death can be made by using additional tests for cerebral blood flow.

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ⁱIn the event that apnea test prerequisites are not satisfied or the test is terminated for any reason before the target PaCO₂ levels are achieved, tests evaluating cerebral blood flow can be used to proceed with the declaration process.

^jIf the patient shows any spontaneous breathing attempt during apnea test, brain death is ruled out for the case (apnea test negative) and the test is terminated immediately.

^kIn the second examination following waiting period, it is sufficient to observe coma and the continuing lack of brain stem reflexes; repeating apnea test is not necessary.

^lIn cases where three main findings in the first examination are congruent with brain death diagnosis, it is not required to complete the waiting period when tests evaluating cerebral blood flow demonstrate the lack of cerebral blood flow.

^mIn the event that brain stem reflexes cannot be examined or the examination is under question, apnea test prerequisites are not satisfied or the test itself cannot be completed, electrolyte deficiency in the coma condition cannot be proven, effects of sedative or similar drugs cannot be estimated or it is impossible to wait 5 times the elimination half-life of these drugs, in post-cardiopulmonary resuscitation or similar hypoxic ischemia cases or 1 year of age or younger cases, the supplementary test should be about assessing cerebral blood flow. In cases who are 2 months old or younger, there should be two supplementary tests, at least one of them assessing cerebral blood flow.

obstructive pulmonary disease, cannot be alleviated, 20 mmHg offset rule should be applied to the initial state in order to accept apnea test as positive. Patient should be ventilated with 100% oxygen for 5-10 minutes. After supplying sufficient amount of oxygen, the patient should be detached from the mechanical ventilator and 6-8 L/minute oxygen should be supplied through an insert going through intubation/tracheotomy tube into the level of carina. During the test, patient's spontaneous breathing effort and heart rate, blood pressure and oxygen saturation should be monitored. Eight minutes after detaching the patient from the ventilator, if the target PaCO₂ level was not yet achieved, the test should be extended and the blood gas should be sampled every 2 minutes; in such cases the test is terminated when the desired PaCO₂ is achieved.

For a positive apnea test (suggesting brain death), PaCO₂ should be ≥ 60 mmHg at the end of the test and the patient should not have had breathing attempts despite the PaCO₂ level was increased ≥ 20 mmHg beyond its starting level.

If the patient shows any spontaneous breathing attempt during apnea test, brain death is ruled out for the case (apnea test negative) and the test is terminated immediately.

Apnea test should be terminated immediately in the event that the patient shows hemodynamic disturbance or hypoxemia. It is recommended that a blood gas sample is collected right before terminating the test in order to see if PaCO₂ level had reached the target value. If the test is terminated before PaCO₂ reached to the criterion level due to hemodynamic disturbance or any reason, the result of the apnea test is recorded as unknown (incomplete or inconclusive). In this situation, apnea test should be repeated after satisfying proper conditions. In the event that the prerequisites of apnea test cannot be completed or the test is terminated without reaching the target PaCO₂ level, the declaration process can proceed with the use of supplementary tests evaluating cerebral blood flow.

Waiting (Observation) Period

In order to satisfy the criterion of irreversibility, the main indicators of brain death should be proven to remain unchanged through the specified period (the wait period) after they were documented. This duration should be 48 hours for babies

younger than 2 months, 24 hours for children between 2 months and 1 year, 12 hours for children 1 year of age and adults, and 24 hours for cases with cardiopulmonary resuscitation or similar hypoxic ischemic acute brain damage. Neurological examination is repeated at the end of wait period by the specialists who first conducted the procedure. It is sufficient to demonstrate coma and the absence of brain stem reflexes persist uninterruptedly in this second examination but there is no need for repeating the apnea test.

Supplementary Test

Brain death clinical diagnosis should be supported with tests showing cerebral blood flow or brain electrical activity. Turkish Neurological Society accepts electroencephalography, sensory evoked potentials, transcranial Doppler ultrasonography, radionuclide cerebral scintigraphy (such as SPECT), CT angiography and catheter cerebral angiography as supplementary tests.

In the event that brain stem reflexes cannot be examined or the examination is under question, apnea test prerequisites are not satisfied or the test itself cannot be completed, electrolyte deficiency in the coma condition cannot be proven, effects of sedative or similar drugs cannot be estimated or it is impossible to wait 5 times the elimination half-life of these drugs, in post-cardiopulmonary resuscitation or similar hypoxic ischemia cases or 1 year of age or younger cases, the supplementary test should be about assessing cerebral blood flow. In such circumstances Doppler ultrasonography (minimum four systems), radionuclide cerebral scintigraphy (showing also the brain stem), CT angiography (arterial and venous phases) and catheter cerebral angiography can be used. In cases 2 months old or younger, two supplementary tests should be used and at least one of them should assess the cerebral blood flow. International and, if available, national norms should be used for the supplementary and diagnostics tests, and this should be documented on the case level.

A patient going through the process of brain death should be followed and monitored very closely regardless of organ donor status. When brain death takes place, the next step which is the preservation of organs should involve a multidisciplinary approach.