Criteria and guidance

Criteria and practical guidance for determination of brain death in adults (BQCC version)

Brain Injury Evaluation Quality Control Centre of National Health and Family Planning Commission

Part I. CRITERIA FOR DETERMINATION OF BRAIN DEATH

I. Prerequisites of the determination
   A. The cause of coma is known.
   B. Exclusion of reversible coma.

II. Clinical diagnosis
   The clinical diagnosis of brain death should fulfill all the three conditions listed as follows:
   A. Deep coma.
   B. Absence of brainstem reflexes.
   C. No spontaneous respiration (depending on mechanical ventilation to maintain breath completely and apnea test to confirm no spontaneous respiration).

III. Confirmatory tests
   The diagnosis of brain death should fulfill at least two of the three confirmatory tests listed as follows:
   A. Short-latency somatosensory evoked potential (SLSEP) of median nerve shows that bilateral N9 and (or) N13 exist, while P14, N18, and N20 are absent.
   B. Electroencephalogram (EEG) shows electrical silence.
   C. Transcranial Doppler (TCD) sonography shows that the blood flows of intracranial anterior and posterior circulation demonstrate reverberating flow, small systolic spike, or absence of blood flow signal.

IV. Time of determination
   If the clinical diagnosis and confirmatory tests all fulfill the criteria of brain death, brain death can be determined for the first time. A repeat determination should be done 12 hours later after the first time, and if still all fulfill the determinative criteria, brain death will be confirmed at last.

Part II. PRACTICAL GUIDANCE FOR DETERMINATION OF BRAIN DEATH

Brain death is an irreversible loss of the whole brain function (including the brainstem). The determination of brain death is listed as follows.

I. Prerequisites
   A. The cause of coma is known
   Primary brain injury that can induce coma includes brain trauma, cerebral vascular disease, and etc. Secondary brain injury that can induce coma is mainly the anoxic encephalopathy resulting from cardiac arrest, anesthetic accident, drowning, asphyxia, and etc. In comatose patients, brain death of unknown reason cannot be determined.

B. Exclusion of reversible coma
   Reversible coma includes acute intoxication, such as carbon monoxide poisoning, alcoholic poisoning, sedative hypnotics poisoning, narcotic poisoning, antipsychotic drug poisoning, and muscle relaxant poisoning; hypothermia (bladder or rectal temperature ≤ 32°C); severe electrolyte and acid-base disturbance; and severe metabolism and endocrine disturbance, such as hepatic encephalopathy, uremic encephalopathy, hypoglycemic encephalopathy, or hyperglycemic encephalopathy.

II. Clinical evaluation
   A. Deep coma
   1. Examination and determination of the results: On pressing bilateral supraorbital incisure tightly with the thumb, respectively, or needling the face, there should not be any motor responses on face. The Glasgow Coma Scale is 3.

   2. Pitfalls:
      2.1. Any noxious stimulus should be limited in the region of head and face.
      2.2. Deep coma should not be judged rashly if trigeminal nerve or facial nerve damages exist.
      2.3. Stimulations below the neck may induce spinal reflexes. The spine cord below the foramen magnum may survive in brain death, so the spinal reflexes or and spinal automatic reflexes still exist. The spinal reflexes include all deep reflexes and pathological reflexes. The spinal automatic reflexes mostly related to the stimulating position, such as stimulating the neck, may trigger the rotation of the head; stimulating the upper limb may trigger flexion, extension, lift, pronation, and supination of the upper limb; stimulating abdomen may trigger contractions of abdominal wall muscle; and stimulating the lower limb may trigger its flexion and extension. Spinal automatic reflexes should be differentiated from spontaneous movements of limbs. Spinal automatic
reflexes are strictly related to the specific stimulating position, while spontaneous movements always occur unilateral without any stimulation. There should not be spontaneous movements of limbs in brain death.  
2.4. There should not be decerebrate rigidity, decorticate rigidity, and spasm in brain death.

B. Absence of brainstem reflexes

1. Pupillary light reflex

1.1. Examination: Observe pupillary contraction to a bright light in both eyes. First, illuminate one pupil with lateral light, observe the response of the ipsilateral pupil (direct pupillary light reflex), then examine the other. Illuminate one pupil, observe the response of the contralateral pupil (indirect pupillary light reflex), then examine the other. These examinations should be performed repeatedly.  
1.2. Determination of the results: No bilateral direct and indirect light reflexes are determined in the absence of pupillary light reflex.  
1.3. Pitfalls: Brain death patients mostly present bilateral mydriasis (>5 mm). However, small-sized or medium-sized pupils can be found in brain death. Therefore, the size of the pupil cannot be the essential condition in brain death. Some factors, such as ocular disease or trauma, may influence the determination of pupillary light reflexes, so the results should be analyzed carefully.

2. Corneal reflex

2.1. Examination: Lift one upper eyelid, expose the cornea, touch the edge of the cornea lightly with a cotton swab, and observe whether there is a blink response. Then, examine the other side.  
2.2. Determination of the results: No bilateral blink is determined in the absence of corneal reflex.  
2.3. Pitfalls: The absence of corneal reflex should not be judged when there are weak retractions of the upper and lower eyelids, periorcular muscles, even without obvious blinks of eyes. Especially in conditions of ocular diseases or trauma and trigeminal nerve or facial nerve diseases, which may influence the determination of corneal reflex, the results should be analyzed carefully.

3. Oculocephalagric reflex

3.1. Examination: Hold the head in both hands with thumbs keeping the eyes open with the patient supine. Rapidly turn the head from one side to the opposite side and observe the movements of the eye. Then, examine the other side.  
3.2. Determination of the results: No eyeball movement to the opposite side when the head turns to left or right is determined in the absence of oculocephalic reflex.  
3.3. Pitfalls: In condition of extraocular muscles palsy, which may influence the determination of oculocephalic reflex, the results should be analyzed carefully. This examination should not be done when cervical vertebra trauma exists to avoid spinal cord injury.

4. Oculovestibular reflex

4.1. Examination: Put a kidney-shaped disk near the external auditory canal to avoid the water flowing out. Then, aspirate 20-ml saline (0–4°C) into a syringe, slowly irrigate this saline into one external auditory canal in 20–30 seconds, and maintain the eyelids separated at the same time. Observe whether there is nystagmus. Then, examine the other side.  
4.2. Determination of the results: Observe for 1–3 minutes after irrigation. No nystagmus is determined in the absence of oculovestibular reflex.  
4.3. Pitfalls: Any damage should be excluded from otoscopy before examination. If there is any damage, the examination should be prohibited. Clear up the blood clots or other obstructions in the ear canals before examination. When there are weak movements of eyeballs, the absence of oculovestibular reflex should not be judged even without obvious nystagmus. In condition of trauma on head or face, the hemorrhage or edema in the eyes may influence the judgment of oculovestibular reflex; the results should be analyzed carefully. This examination is different from the caloric tests used in otorhinolaryngology, which use cold water (20°C) or water at 7°C above and below body temperature to stimulate alternatively. The caloric tests used in otorhinolaryngology cannot be used to determine brain death.

5. Cough reflex

5.1. Examination: Stimulate the tracheal mucosa with an aspiration tube longer than artificial airway to elicit cough reflex.  
5.2. Determination of the results: No cough is determined in the absence of cough reflex.  
5.3. Pitfalls: If there are movements of chest or abdomen when stimulating, the cough reflex should not be determined.

The determination of brain death should fulfill the absence of all the above five brainstem reflexes. If some of the five brainstem reflexes cannot be fully performed, the confirmatory tests should be added.

C. Apnea

Apnea and depending on mechanical ventilator completely to maintain ventilation are necessary for brain death determination. Apart from the breathing movements of chest or abdomen by observations, apnea should be confirmed by the apnea test according to the strict procedures and methods as follows.

1. Prerequisites

1.1. Raise body temperature to a bladder or rectal temperature ≥36.5°C.  
1.2. Adjust vasopressors to a systolic blood pressure ≥90 mmHg or mean arterial pressure ≥60 mmHg.  
1.3. Preoxygenate for 10–15 minutes with 100% oxygen to an arterial partial pressure of oxygen (PaO₂) ≥200 mmHg.
1.4. Adjust the minute volume to an arterial partial pressure of carbon dioxide (PaCO$_2$) of 35–45 mmHg. If there is chronic hypercapnia, PaCO$_2$ might be above 45 mmHg.

2. Procedure
   2.1. Disconnect the patient from ventilator for 8–10 minutes.
   2.2. Place the oxygen tube into the level of carina through artificial airway and deliver 100% O$_2$ at 6 L/min.
   2.3. Observe the respiratory movements of chest or abdomen closely.
   2.4. Arterial blood gas was drawn to measure PaCO$_2$ at 8–10 minutes, and patient was reconnected to ventilator.

3. Determination of the results: If respiratory movements are absent and PaCO$_2$ is ≥60 mmHg or 20 mmHg over a baseline, apnea can be confirmed.

4. Pitfalls:
   4.1. Patients may present obvious decrease in blood oxygen saturation, blood pressure and heart rate, arrhythmia, and so on during this examination. Stop the examination at once when these symptoms occur and declare the failure of the test. To avoid the influence of the apnea test on confirmatory tests, this examination should be the last step for determining brain death.
   4.2. This test need at least two doctors (one monitors the breath, blood oxygen saturation, heart rate, cardiac rhythm, and blood pressure; the other manages the ventilator) and one nurse (manages the oxygen tube and draws arterial blood).

III. Confirmatory tests

A. Short-latency somatosensory evoked potential (SLSEP)

1. Environmental requirements:
   1.1. The environmental temperature should be controlled between 20°C and 25°C.
   1.2. Use separate power supply. Manostat can be used, if necessary.
   1.3. Suspend other medical machines that may interfere with evoked potential, if necessary.
2. Recording techniques:
   2.1. Designation of electrode locations: According to the international 10–20 system, place disc electrodes or disposable needle electrodes. C’3 and C’4: At 2 cm behind the positions of C3 and C4 in international 10–20 system. C’3 or C’4 is called C’c when stimulating the contralateral side. Fz and FPz: Fz is located at the center of forehead and FPz is located at the midpoint of frontal pole. Cv6 is located at the spinous process of the 6th cervical vertebra. CLi and CLc: At 1 cm above ipsilateral and contralateral side clavicles, respectively.
   2.2. The montage listed below requires at least four channels (recording electrode-reference electrode). Channel 1: CLi-CLc (N9); Channel 2: Cv6-Fz, Cv6-FPz, or Cv6-CLc (N13); Channel 3: C’c-CLc (P14, N18); and Channel 4: C’c-Fz or C’c-FPz (N20).
   2.3. Electrode impedance: ≤5 kΩ (recording electrodes and reference electrodes).
   2.4. Placement of the groundwire and impedance: at 5 cm above the stimulating point.
   2.5. Analysis time: 50 ms and 100 ms, if necessary.
   2.7. Average times: 500–1000.

3. Procedure
   3.1. Prepare the electromyography/evoked potential machine. Prepare disc electrodes or disposable needle electrodes.
   3.2. Start the machine, input the general information of patient, and get into the recording state.
   3.3. Place the recording electrodes and reference electrodes.
   3.4. Place the stimulating electrodes. Position of stimulating electrodes: 2 cm above the midpoint of wrist transverse striation, where the median nerve lies below. Generally, the stimulating current is between 5 mA and 25 mA. If the patient has skin edema at the electrode location or peripheral nerve diseases, the current might be increased properly. The stimulus intensity is appropriate to induce the muscles innervated by retraction of median nerve slightly, that is, the thumb flexes of about 1 cm. It should be kept unchanged during the examination. Stimulating parameters: The duration of stimulating square wave is 0.1–0.2 ms, up to 0.5 ms, if necessary. Frequency of stimulation: 1–5 Hz. Stimulate bilateral sides.
   3.5. At least 500–1000 averages for each time make the waveform stable and smooth. Record SLSEP at least 2 times on each side.

4. Determination of the results: It supports the determination of brain death that SLSEP shows bilateral N9 and (or) N13 exist, while P14, N18, and N20 are absent.

5. Pitfalls:
   5.1. Keep the patient’s skin temperature normal (hypothermia may induce prolongation of the latencies).
   5.2. Some factors, such as trauma or skin edema at the electrode locations, subclavian vein catheter, median nerve diseases, cervical cord lesion, or electromagnetic field interfere with environment and may influence the analysis of evoked potentials. The waveforms of SLSEP are for information only in the above conditions, and the brain death should be determined according to other confirmatory tests.

B. Electroencephalogram (EEG)

1. Environment conditions
   1.1. Use separate power supply. Manostat can be used, if necessary.
   1.2. Suspend other medical machines that may interfere with EEG, if necessary.
2. Parameter setting
   2.1. Place a minimum of eight scalp electrodes according
to the international 10–20 system: frontal pole Fp1, Fp2; central C3, C4; occipital O1, O2; temporal T3, T4, and reference electrodes at bilateral earlobes or mastoids. Place the grounding electrode at midpoint of frontal pole (FPz) and common reference electrode at median central point (Cz).

2.2. Inter-electrode impedances should be under 10 000 Ω but over 100 Ω, and electrode impedances should be matched on the whole.
2.3. Set the high-frequency filter between 30 Hz and 75 Hz, low-frequency filter at 0.5 Hz, and time constant at 0.3 second.
2.4. Sensitivity: 2 μV/mm.

3. Procedure
3.1. Prepare the EEG machine. Prepare disc electrodes or disposable needle electrodes.
3.2. Start the machine and input the general information of patient. Check the parameter setting. Calibration run should be made for 10 seconds before tracing. Input 10 μV square wave into amplifier. The sensitivity of each amplifier should be the same.
3.3. Place the recording electrodes.
3.4. A single recording should be at least 30 minutes.
3.5. Give somatosensory, auditory, or visual stimuli during tracing and observe the stimulus-related EEG reactivity.
3.6. Any interferences from outside, machine, or patient during tracing should be documented on the record in real time.
3.7. Electrocardiography tracing at the same time is essential.

4. Determination of the results: It supports the diagnosis of brain death that EEG shows electrical silence, that is, no EEG activity over 2 μV.

5. Pitfalls:
5.1. EEG machine used in the determination of brain death must match the request parameters.
5.2. Sedatives and anesthesia usage may influence the analysis of EEG; the result is for information only, and the determination of brain death should be based on other confirmatory tests.
5.3. Trauma or edema at the location of placing electrodes may influence the analysis of EEG; the result is for information only, and the determination of brain death should be based on other confirmatory tests.

C. Transcranial Doppler (TCD)
1. Environmental conditions: No special.
2. Equipments: Transcranial Doppler machine, with 2 MHz pulse-wave Doppler probe.
3. Parameter setting:
   3.1. Set an appropriate output power.
   3.2. Set the sampling volume: 10–15 mm.
   3.3. Adjust the gaining intensity: Adjust the gaining intensity according to the legibility presented by frequency spectrum.
3.4. Adjust the speed scale plate: Make the frequency spectrum completely presented on the screen with an appropriate size. Adjust the baseline: Make both of the upper and lower frequency spectrums completely presented on the screen.
3.5. Adjust the signal-noise ratio: Make the frequency spectrum clearly presented and decrease the noise as low as possible.
3.7. Set the Doppler frequency filtering wave: A state of low filtering frequency (<50 Hz).

4. Checking positions:
4.1. Temporal window: To detect the middle cerebral artery (MCA), place the probe at the area between the superciliary arch and the upper ear edges with supine body position.
4.2. Occipital window or perioccipital window: To detect the vertebral artery (VA) and basilar artery (BA), place the probe at foramen magnum just below the occipital tuberosity or near foramen magnum with supine body position (head has been raised) or lateral decubitus.
4.3. Ocular window: To detect the contralateral MCA and ipsilateral internal carotid artery (ICA) siphon, place the probe at the region of closed upper eyelid with supine body position.

5. Recognition of the arteries:
5.1. MCA: Through the temporal window, where the depth is between 40 mm and 65 mm, the direction of blood flow signal in systolic period is toward the probe. Or through the opposite ocular window, where the depth is more than 70 mm, the direction of blood flow signal is away from the probe. Common carotid artery compression test can confirm MCA, if necessary.
5.2. VA: Through the occipital window or the perioccipital window, where the depth is between 55 mm and 80 mm, the direction of blood flow signal in systolic period is away from the probe.
5.3. BA: Through the occipital window or perioccipital window, where the depth is between 80 mm and 120 mm, the direction of blood flow signal in systolic period is away from the probe.

6. Determination of the results:
6.1. Determination of the vessels: bilateral MCAs are the main judged vessels in anterior circulation. BA is the main judged vessel in posterior circulation.
6.2. Determination of the blood flow frequency spectrum:
   (i) Reverberating flow: Both the forward flow signal in systolic period (F) and the reverse flow signal in diastolic period (R) occur in the same cardiac cycle, and the direction of flowing index (DFI) is <0.8.
DFI is defined as DFI = 1 – R/F.

(ii) Small systolic spike in early systole: A single-way forward flow signal in early systolic period, duration is less than 200 ms, and velocity is less than 50 cm/s.

(iii) Absence of blood flow signal.

6.3. Determination of frequency: Check twice with an interval of 30 minutes.

It supports the determination of brain death that TCD shows that both the intracranial anterior circulation and the intracranial posterior circulation demonstrate one of the blood flow frequency spectrums mentioned above.

7. Pitfalls:

7.1. When temporal window is suboptimal, absent, or not accessible (not good enough to penetrate sound waves), choose ocular window to detect contralateral MCA and ipsilateral syphon segment of ICA.

7.2. If the blood flow signals are not so clear or even without any signals through temporal window for the first time, poor penetrability of the temporal window and the artifacts from manipulation should be excluded. The result is for information only, and the determination of brain death should be based on other confirmatory tests.

7.3. Some factors, such as ventricular drainage and cranial decompression, may influence the results. The results are for information only, and the determination of brain death should be based on other confirmatory tests.

7.4. If systolic peripheral arterial pressure is <90 mmHg, blood pressure should be raised before checking TCD.

D. Sequence of confirmatory tests

The recommendation sequence of the confirmatory tests is SLSEP, EEG, and TCD. At least two tests should fulfill the determination criteria of brain death.

IV. Procedures for determination

The determination of brain death can be considered to consist of three steps. First, the clinical evaluation of brain death fulfills the criteria (deep coma, absence of brain stem reflexes, and no spontaneous respiration). Second, the confirmatory tests, at least two of three confirmatory tests fulfill the criteria. Finally, the apnea test confirms apnea. If all the three steps mentioned above fulfill the criteria, brain death could be determined.

V. Personnels of determination

At least two physicians take part in the determination of brain death. Furthermore, they should be practitioners engaged in clinic work for more than 5 years.

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