Role of Diagnostic Imaging Methods in Confirmation of Brain Death

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Learning objectives

To show how ancillary test can be crucial in quick determination of brain death (BD) especially in relation to organ transplant where time is of essence. Since Croatia has been among leading countries in the world in number of organ transplants per capita we also want to encourage discussion on methods for brain death determination since the methods have not been uniformly defined.
Background

Brain death is a clinical diagnosis as defined for the first time in 1968 [1]. In 1995 the American Academy of Neurology (AAN) defined practice parameters as guidelines for the management of patients with brain death [2]. Brain death criteria throughout the world revealed uniform agreement regarding the neurological examination with exception of the apnea test. Major differences between countries were present between presence of legal standards on organ transplantation, presence of practice guidelines for brain death for adults, number of physicians required to declare brain death, observational period or presence of required expertise of examining physicians. Only 40% of national practise guidelines require confirmatory testing. A mismatch between the practise parameters from the AAN and clinical practise at local hospitals was observed [3,4,5].

In Croatia confirmatory tests are obligatory and currently 6 ancillary tests (transcranial doppler (TCD), digital subtraction angiography (DSA), MSCT-angiography (MSCTA), electroencephalography (EEG), Technetium-99m hexamethylpropylene-amineoxime brain scan (Tc-HMPAO) and evoked potentials) are equally accredited. We conducted a retrospective study of patients diagnosed with BD in year 2012 in our hospital.

According to Croatian law [6], clinical neurological examination remains the standard to determine BD. Apnea test is a part of clinical neurological examination [7]. The performance of one confirmatory laboratory test is mandatory. Confirmatory tests should be performed after the observational period and the second clinical examination. The confirmatory test cannot replace the clinical examination or shorten the observational period.

1. Transcranial doppler is due to the bedside evaluation mostly preferred at our hospital. Neurosonology Research Group of the World Federation of Neurology created guidelines for the use of TCD for the determination of cerebral circulatory arrest in brain death confirmation, and these guidelines were adopted by the Croatian National Society [5]. Cerebral circulatory arrest can be confirmed if the following extra and intracranial Doppler sonographic findings have been recorded and documented both intra- and extracranially and bilaterally in two examinations at an interval of at least 30 min.: systolic spikes or oscillating flow in any cerebral artery recorded by bilateral transcranial insonation for anterior circulation, and any intracranial vertebral or basilar artery which is recorded by sub-occipital insonation for the posterior circulation. The diagnosis established by the intracranial examination must be confirmed by the extracranial bilateral recording of the common carotid arteries, internal carotid arteries and vertebral arteries.

2. DSA is classically considered to be the reference standard for imaging BD. Experience in this setting dates back to a paper published by Heiskanen in 1964 [8]. The currently accepted method of assessment is done with separate contrast injections performed in both common or internal carotid arteries, as well as in both vertebral arteries. Angiographic findings in brain death include lack of contrast opacification of
the internal carotid arteries beyond the supraclinoid segment, and filling of the vertebral arteries to, but not beyond their dural penetration. Despite cerebral angiography being considered the "gold standard" for determination of BD, there are many concerns with its use. Cerebral angiography requires specialized neuroradiologic expertise, it is an invasive test, its availability is not always immediate and the cost of examination is not low. Controversy also exists regarding the potential for iodineted contrast to damage transplantable tissues [9].

3. **MSCTA** has been increasingly employed to establish the diagnosis of BD in recent years since French authorities accepted the method to confirm the clinical diagnosis of BD. MSCTA is usually performed as CT angiography of the supraaortic and intracranial vessels. CTA technology is readily available 24 hours a day, 7 days a week and does not require the presence of a specialty-trained physician to perform. Spiral CT scans were performed on a 16-row multidetector scanner. The standard protocol consisted of an unenhanced CT study of the head, CT angiography of the cervical and intracranial vessels with application of 100 ml contrast agent into a cubital vein using an automated injector with a flow rate of 4ml/s and a late venous-phase of the scull. The MSCTA started automatically with the appearance of contrast agent in the aortic arch, the late-phase series was started manually one minute after the CTA was finished. Therefore, there is no consensus about the interpretation of CTA for brain circulatory arrest in Croatia, lack of opacification of the arteries above the carotid syphon and foramen magnum was classified as positive.

4. **Somatosensory evoked potentials (SEPs)** are generated by stimulation of afferent peripheral nerve fibers by either physiological or electrical means. Evoked potential (EP) tests measure the electrical activity of the brain in response to stimulation of specific sensory nerve pathways. Brain death is confirmed by bilateral absence of N20-P22 response with median nerve stimulation [10].
Fig. 1: CT, massive intracerebral haematoma.

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Imaging findings OR Procedure details

In our hospital TCD, DSA, MSCTA and evoked potentials were used to demonstrate BD. TCD was preferred due to bedside evaluation. In 31 out of 36 patients clinical diagnosis of BD was confirmed with ancillary test. TCD was positive in 13, MSCTA in 9, evoked potentials in 6 and DSA in 3 patients. MSCTA was repeated twice in three and three times in one patient. In 3 out of 11 patients, who underwent MSCTA, BD could not be confirmed because of residual brain flow. Two patients died during the observational period.

The study included 36 patients (15 females, 21 males), mean age 41 (range 17-79 years), with severe brain lesions that finally led to brain death. The causes were: neurotrauma (13 patients), massive aneurysmal subarachnoidal hemorrhage (10 patients), A-V malformation (2 patients), hypertensive parenchymal hemorrhage (9 patients) and ischemic stroke (2 patients). The mean time from clinical diagnosis to confirmation of brain death in regard to test was 180 minutes for TCD (shortest time 40 minutes), 480 minutes for MSCTA (shortest time 46 minutes) and 519 minutes for DSA (shortest time 153 minutes). Due to technical reasons DSA was performed only during working hours. In 31 out of 36 patients clinical diagnosis of BD was confirmed with ancillary test. TCD was positive in 13, MSCTA in 9, evoked potentials in 6 and DSA in 3 patients. MSCTA was repeated twice in three and three times in one patient. In 3 out of 11 (27%) patients, who underwent MSCTA, BD could not be confirmed because of residual brain flow. Two patients died during the observational period.
Fig. 1: CT, massive intracerebral haematoma.

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Fig. 2: CTA, coronal MIP reformation (patient with open skull defect) shows blood flow in both middle cerebral arteries.

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Fig. 3: CTA, sagittal MIP reformation, complete lack of cerebral blood flow.

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Fig. 4: CTA, transversal plane, absence of intracerebral vessel opacification with good filling of external carotid branches.

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Fig. 5: CTA, coronal plane, absence of intracerebral filling with patent external carotid circulation in patient with huge craniotomy.

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**Fig. 6:** DSA profile, lack of contrast opacification of the internal carotid artery with patent external carotid circulation.

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Fig. 7: DSA, carotid artery - absence of contrast filling of the internal carotid artery beyond the 3rd segment. Sedimentation of contrast media in common carotid artery.

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Conclusion

Although most countries agree upon the definition of BD, there is a discrepancy between the means by which it is determined. We find that confirmatory tests help in diagnosis and also shorten the time in which BD is established.

TCD is due to the bedside evaluation mostly preferred, but might have technical difficulties (no bone window in up to 10% of cases) and it is skill dependent. MSCTA is fast, it is usually available around the clock and is less invasive and less expensive than DSA [11]. In the countries where brain death cannot be determined by a single clinical observation, standardized protocol for MSCTA image analysis is needed (e.g. France accepted the 7-point CTA score for BD diagnosis in 1998).
References


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