

Diagnosing Brain Death by CT Perfusion and Multislice CT Angiography

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Published online: 30 June 2009
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Abstract

Introduction Although the diagnosis of brain death (BD) is usually based on clinical criteria, in sedated patients, ancillary techniques are needed. This study was designed to assess the accuracy of cerebral multislice computed tomographic angiography (CTA) and CT perfusion (CTP) in diagnosing BD.

Methods Prospective observational study in 27 BD patients.

Results All patients were diagnosed as BD based on clinical and electroencephalogram findings. After BD diagnosis, CTP was performed followed by 64-detector multislice CTA from the aortic arch to the vertex. Images were reconstructed from 0.5 mm sections. In 24 patients, a lack of

cerebral blood flow (CBF) was detected by CTP, and CTA revealed luminal narrowing of the internal carotid artery in the neck and absence of anterior and posterior intracranial circulation (sensitivity 89%). CTA detected CBF exclusively in extracranial portions of the internal carotid and vertebral arteries. Two patients with anoxic brain injury and decompressive craniectomy showed CBF in the CTA such that the CTP results were considered false negatives, given BD had been confirmed by clinical and EEG findings, along with evoked potentials. In one clinically BD patient, in whom an alpha rhythm was detected in the electroencephalogram, CBF was only observed in the intracranial internal carotid with no posterior circulation noted. This patient was therefore considered exclusively brain stem dead.

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Conclusions The radiological protocol used shows a high sensitivity and excellent specificity for detecting the cerebral circulatory arrest that accompanies BD. As a rapid, non-invasive, and widely available technique it is a promising alternative to conventional 4-vessel angiography.

Keywords Brain death · Cerebral circulatory arrest · Cerebral computed tomographic angiography · Cerebral computed perfusion · Organ donor

Abbreviations

BAEP	Brainstem auditory-evoked potentials
BD	Brain death
BH	Brain hemorrhage
CBF	Cerebral blood flow
CBV	Cerebral blood volume
CTA	Computed tomographic angiography
CTP	Computed tomography perfusion
EEG	Electroencephalogram
GCS	Glasgow coma scale
ICP	Intracranial pressure
MCA	Middle cerebral artery
MIP	Maximum intensity projection
MTT	Mean transit time
ROI	Region of interest
SAH	Subarachnoid hemorrhage
SEP	Somatosensory-evoked potentials
SLST	Superior longitudinal sinus thrombosis
TBI	Traumatic brain injury
TCD	Transcranial Doppler ultrasonography
Tc99-HMPAO	Tecnecium 99-hexamethylpropylene amine oxime
VR	Volume rendering

Introduction

Brain death (BD) is defined as the irreversible loss of activity of all the neurological structures of both brain and brainstem. Its diagnosis is based on an exhaustive neurological examination [1–6], which should be conducted by physicians with experience in managing neurocritical patients. Declaring a patient brain dead has tremendous medical, ethical, and legal implications since it is on this determination that high-responsibility decisions are based, such as discontinuing support measures or the procurement of organs for transplant.

Besides a clinical diagnosis, there are several ancillary laboratory tests that may be mandatory depending on the country and/or corresponding legislation [7–9].

Electrophysiological tools such as evoked potentials, electroencephalogram (EEG) [10], and the Bispectral index [11, 12] are the mainstay for BD determination. However,

when the patient has been administered a sedative drug, techniques that assess cerebral blood flow (CBF) are required such as cerebral angiography, Tc99-HMPAO radionuclide angiography, Xenon-CT, or transcranial Doppler ultrasonography (TCD) [13–16]. Some of these methods have the drawback that not all hospitals can offer these tests 24 h a day, and others such as TCD require an appropriate sonic window and expert personnel.

More recently, cerebral angiography by computed tomographic angiography (CTA) has also been used to diagnose BD [17–21]. This widely available method can rapidly confirm a lack of CBF. However, few studies have evaluated the efficacy of the new multislice CT angiography instruments used in conjunction with computed tomographic perfusion (CTP) to diagnose BD [22–24].

The intracranial pressure (ICP) increase that occurs in the context of an intracranial pathology diminishes the cerebral perfusion pressure; in extreme situations, this pressure may be insufficient to maintain brain oxygenation and metabolism. When ICP exceeds the systolic arterial pressure of the patient, cerebral circulatory arrest occurs leading to BD.

The aim of the present study was to assess the use of CTA plus CTP to detect the cerebral circulatory arrest that occurs during BD.

Materials and Methods

This prospective clinical study was performed at the Intensive Care Medicine Unit of a teaching hospital. Preliminary results obtained in the first six patients of this series of 27 subjects have been previously published [24].

Definition of Brain Death

A diagnosis of BD was made when there was severe structural injury, a GCS score of 3, lack of brainstem reflexes and findings in the atropine test (inability to achieve a 10% increase in heart rate following the administration of 0.04 mg/kg iv atropine sulfate), and apnea test (lack of spontaneous ventilation and final PaCO₂ ≥60 Torr or 7.98 KPa) in patients not under sedation nor showing significant metabolic alterations or hypothermia. Both clinical and ancillary tests were performed according to international recommendations [5].

Transcranial Doppler Ultrasonography

This examination was performed using a TCD ultrasound instrument (Smart Lite, Rimed, Israel). The protocol involved insonation of the anterior circulation via the temporal window: supraclinoid carotid artery and middle

cerebral artery (MCA); and of the posterior circulation through the occipital window: vertebral arteries and basilar artery. The presence of reverberating flow and systolic spikes was taken to denote cerebral circulatory arrest following the recommendations of the Task Force on Brain Death of the Neurosonology Research Group of the World Federation of Neurology [16]. The examination was considered complete when the two MCAs and posterior circulation at least could be insonated.

Electroencephalogram

The EEG was conducted for 30 min using a 10-channel recorder (Neurofax, Nihon Kohden, Japan) at maximal sensitivity to record responses to painful and light stimuli following the technical guidelines of the American Society of Electrophysiology [10]. A lack of cerebral neuroelectrical activity was taken to denote BD.

CT Protocol

Twenty-eight examinations were conducted in the 27 BD subjects (Patient 12 underwent 2 tests) using a multislice 64-detector tomographer (Aquilion 64 TSX-101 A/EC, Toshiba Medical Systems SA, Japan). Table 1 provides the time elapsed (in hours) between the clinical and EEG diagnosis and the CTP plus CTA study. The delays observed were the result of the availability of the CT equipment. After a non-enhanced CT, perfusion CT was immediately started followed by CTA. A non-ionic intravenous contrast medium Ioversol (Optiray 300 Ultrayect, Mallinckrodt Medical Imaging, Ireland) was administered via a central vein using an automatic injector (Optivantage, DH Mallinckrodt, Ireland). During the procedure, systolic arterial pressure was ≥ 100 mm Hg in all patients. Data acquisition was generally completed within 10 min. Image reconstruction and analysis required a further 10 min. Images were interpreted by experienced neuroradiologists.

CTP Technique

Four sections 8 mm in thickness were obtained. The first section was taken at the level of the basal ganglia. The bolus of contrast material (60 ml at a flow rate of 4 ml/s) was injected and subsequent changes in brain tissue attenuation were monitored during the transit time of approximately 5 s at high temporal resolution. The software requires placement of small regions of interest (ROIs) on one artery (MCA) and one vein (transverse sinus) to generate arterial input functions and venous outflow functions, respectively, for the deconvolution analysis. The semiautomatic postprocessing method used in our protocol delivers color maps

of mean transit time (MTT), CBF, and cerebral blood volume (CBV) in less than 1 min (Vitrea 2 perfusion program, version 3.9, Toshiba Medical Systems, Japan).

A lack of cerebral perfusion was recorded when no blood flow was detected; this is described by the software as an incapacity for automatic postprocessing of information, indicating null CBF, CBV, and MTT.

CTA Technique

A volumetric spiral CT examination was performed from the aortic arch to vertex. The scanning conditions were: 120 kv, 250 mA, 0.828 pitch factor, helical pitch 53, 0.5 s scan time, field of view (FOV) 320. We injected 80 ml of contrast material intravenously at a flow rate of 3.5 ml/s. For optimal timing, the bolus tracking method was used almost exclusively. After the start of contrast material injection, the software measures the attenuation values of a ROI within the aortic arch, and spiral scanning is automatically started as soon as the threshold of 100 HU (Hounsfield Units) is surpassed. The images were reformatted at a section thickness of 0.5 mm. After reformatting and inspection of cross-sectional images, 3D imaging was performed using the postprocessing procedures: maximum intensity projection (MIP), volume rendering (VR), and multiplanar reformatting (Work Station: Vitrea 2 version 3.9).

Image Analysis Two sets of vessels were examined in the CTA: (1) Extracranial vessels. We examined the extracranial portions of the vertebral arteries, primitive carotid arteries, and internal carotid arteries; (2) Intracranial vessels. Both the anterior and posterior circulations were analyzed. A lack of brain circulation was defined according to the Quality Standards Subcommittee of the American Academy of Neurology, as no intracerebral filling at the level of the carotid bifurcation or circle of Willis [5]. A lack of posterior circulation was indicated by contrast stop at the magnum foramen.

Statistical Analysis Descriptive data are expressed as the mean \pm standard deviation.

Results

Study Population

The study subjects were 27 patients (17 men, 10 women of mean age 49.7 ± 16.8 years) admitted to our ICU from May 2006 to July 2008 who progressed to BD. The study was authorized by Ethic's committee approval. Consent for clinical research was obtained from the relatives of each

Table 1 Patient characteristics ($n = 27$)

Patient	Age (years)	Sex	Diagnosis	CTA	CTP	EEG	TCD	Time (hours) CD to CTA/CTP EEG to CTA/CTP	Further findings
1	76	F	TBI	—	—	—		4	
								3	
2	67	M	TBI	—	—	—	—	2	
								1	
3	50	M	SAH	—	—	—	—	2	
			DecompC					1	
4	56	F	SAH + CA	—	—	—	—	2	
								1	
5	36	F	SAH	—	—	—	—	5	
			DecompC					4	
6	34	M	TBI	—	—	—	I (R MCA, L MCA)	2	
			Multiple skull fractures					1	
7	24	F	SAH + CA	—	—	—	—	5	
								4	
8	67	M	BH	—	—	—	INP	3	
								2	
9	55	F	CA	+	+	—	+	4	Evoked potentials (—)
								3	TCD at 14 h (—)
10	25	F	SLST	—	—	—	INP	3	
								2	
11	37	M	TBI	—	—	—		3	
								2	
12	70	M	TBI	+	+	—	I (R MCA)	2	At 16 h
			Burst fracture					1	CTA (—)
			DecompC						CTP (—)
13	31	M	TBI	—	—	—	I (L MCA)	3	
			DecompC					2	
14	78	F	BH	—	—	—	I (L MCA)	4	
								3	
15	53	M	TBI	—	—	—	—	2	
			DecompC					1	
16	74	M	BH	—	—	—	INP	3	
								2	
17	50	M	TBI + CA	+ only ICA	+	+		5	
			Multiple skull fractures					1	
18	47	M	CA	—	—	—	—	1	
								<1	
19	35	M	Meningitis	—	—	—		1	
								<1	
20	23	M	TBI	—	—	—		1	
								<1	
21	72	F	SAH	—	—	—		2	
								1	
22	47	F	TBI	—	—	—	INP	4	
								2	

Table 1 continued

Patient	Age (years)	Sex	Diagnosis	CTA	CTP	EEG	TCD	Time (hours) CD to CTA/CTP EEG to CTA/CTP	Further findings
23	54	M	TBI	—	—	—	—	2	
								1	
24	36	M	TBI	—	—	—		5	
			Multiple skull fractures					2	
25	38	M	CA	—	—	—		4	
								1	
26	63	M	TBI	—	—	—	I (L MCA)	2	
								1	
27	45	F	CA	—	—	—		3	
								1	

F Female, *M* Male, *TBI* traumatic brain injury, *decompC* decompressive craniectomy, *SAH* subarachnoid hemorrhage, *BH* brain hemorrhage, *CA* cardiac arrest, *SLST* superior longitudinal sinus thrombosis, *CTA* computed tomographic angiography, *CTP* cerebral perfusion computed tomography, *ICA* internal carotid artery, *EEG* electroencephalogram, *TCD* transcranial Doppler ultrasonography (*I* incomplete, insonated arteries between parentheses, *MCA* middle cerebral artery, *INP* insonation not possible), *CD* clinical diagnosis, \pm presence or absence of cerebral blood flow or electrical activity

patient. The mean time elapsed from ICU admission to BD was 5.2 ± 5.5 days. On admission, all the participants had severe neurological damage and a Glasgow coma scale (GCS) ≤ 8 . Intracranial pressure was monitored in 9 (33%) patients and in 5 (19%) a decompressive craniectomy was performed. The causes of BD were: traumatic brain injury (TBI, $n = 14$), subarachnoid hemorrhage (SAH, $n = 4$), brain hemorrhage (BH, $n = 3$), cerebral anoxia ($n = 4$), superior longitudinal sinus thrombosis (SLST, $n = 1$), and meningitis ($n = 1$). Two patients with TBI and one with SAH suffered cardiac arrest before admission to the ICU. Brainstem auditory-evoked potentials (BAEP) and somatosensory-evoked potentials (SEP) were recorded in Patient 9 (see Table 1).

Clinical Diagnosis

All patients fulfilled the clinical prerequisites and criteria for BD in the neurological examination including: lack of motor response to pain stimulation, lack of brainstem reflexes, and the results of the atropine and apnea tests interpreted according to international recommendations. At the time of examination, no patient was hypothermic or under treatment with sedatives.

Electroencephalogram

In no patient was electrical brain activity detected except in Patient 17 who showed a predominating alpha rhythm. This activity persisted in the 3 EEGs performed over 48 h and ceased in the fourth EEG.

Transcranial Doppler

A TCD scan was performed in 18 (67%) of the 27 patients. However, only in 9 (50%) was a complete exam possible including the detection of oscillatory flow or systolic spikes as criteria for cerebral circulatory arrest [16] both in the anterior and posterior circulation. In 5 patients (28%), the TCD was incomplete (signals were detected in one or both MCAs but the posterior circulation could not be insonated). In the remaining 4 patients (22%), no artery could be insonated.

Patient 9 was the only one to show CBF with high mean velocities recorded in every artery examined both in the anterior and posterior circulation.

The sensitivity obtained for diagnosing BD by TCD was low (44.4%). Patient 9 showed CBF and this result was considered a false negative. In the remaining cases, this low sensitivity was essentially due to the difficulty of obtaining a signal and conducting a complete study.

Radiology

A lack of cerebral perfusion and CBF was confirmed in all patients except in Patients 9 and 12, whose radiology findings were considered false negatives for a diagnosis of brain death, and in Patient 17.

CTP

With the exception of the patients mentioned, no blood flow was detected, preventing the automatic postprocessing of information by the software. Irrespective of the ROI

selected, since there was no contrast agent filling of arteries, it was not possible to obtain a color map and thus determine CBF, CBV, or MTT.

CTA

In all subjects, the extracranial portions of both carotid arteries, vertebral arteries, and the external carotid artery and its branches could be observed, confirming transit of the contrast medium and an adequate technique.

In the anterior circulation, we observed luminal narrowing of the internal carotid arteries in the neck, and detected the contrast stop below or at the level of the internal carotid bifurcation, with no filling of the intracerebral circulation (Figs. 1, 2, 3, 4a). In the posterior circulation, the contrast medium did not extend beyond the

foramen magnum; no flow was observed in the intracranial vertebral arteries (Fig. 4b).

The sensitivity obtained for the radiological study was 89%. The clinical characteristics of the 27 patients and results of the ancillary tests are provided in Table 1. Given the particular features observed in the CTP plus CTA study, Patients 9, 12, and 17 are described below in more detail.

Patient 9

This patient is a 55-year-old woman who suffered cardiac arrest while trying to hang herself. After cardiopulmonary resuscitation, she was admitted with a GCS 3. On the third day of admission, BD was confirmed by clinical examination, EEG, and brainstem auditory-evoked potentials and median nerve somatosensory-evoked potentials tested

Fig. 1 CTA revealing the lack of blood flow in the brain. 3D-image reconstruction. *Fine arrows* point to the superficial temporal artery, a branch of the external carotid artery. *Thick arrow* indicates the site of craniectomy

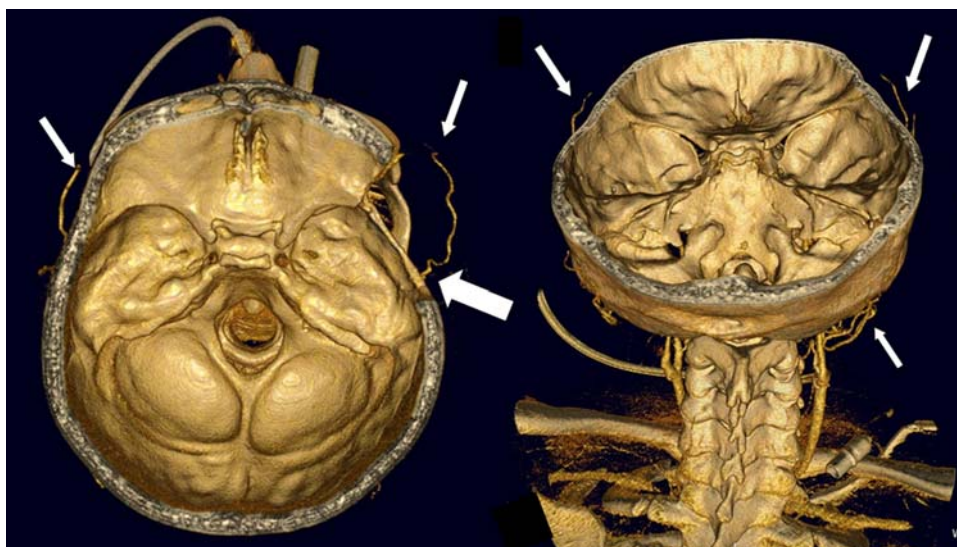


Fig. 2 Autotracing revealing the progressive narrowing of the internal carotid artery of the neck. 3D-image reconstruction in which the contrast medium stop (*thick arrows*) can be observed. *Fine arrows* point to the different branches of the external carotid artery

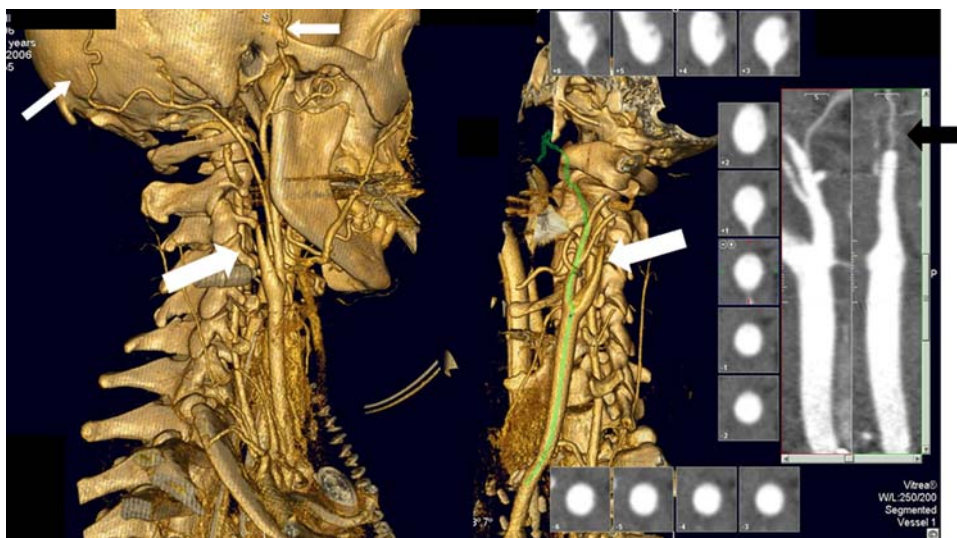


Fig. 3 Images showing blood flow in the carotid arteries. **a** 3D-image reconstruction and maximum intensity projection (MIP) images showing narrowing of the cervical portion of the internal carotid artery (*thick arrows*). **b** Note the adequate contrast filling of the branches of the external carotid artery (*fine arrows*) and lack of filling of the intracranial circulation

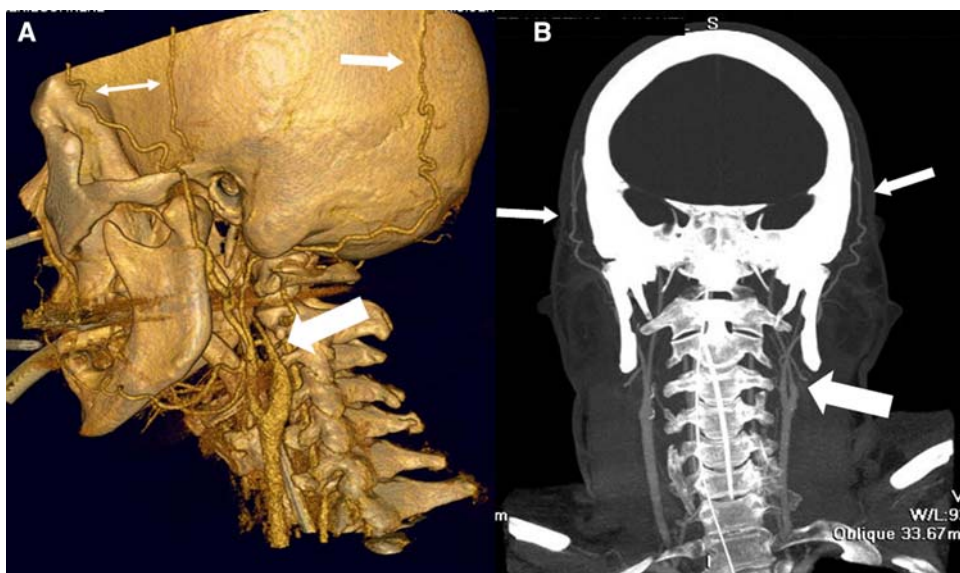


Fig. 4 Images showing the carotid siphon and lack of intracranial blood flow. **a** Postprocessing maximum intensity projection (MIP) images showing narrowing of the contrast medium in the carotid siphon and coronal projection multiplane reconstruction. **b** Note the extracranial course of the vertebral arteries filled with contrast medium and lack of intracranial blood flow

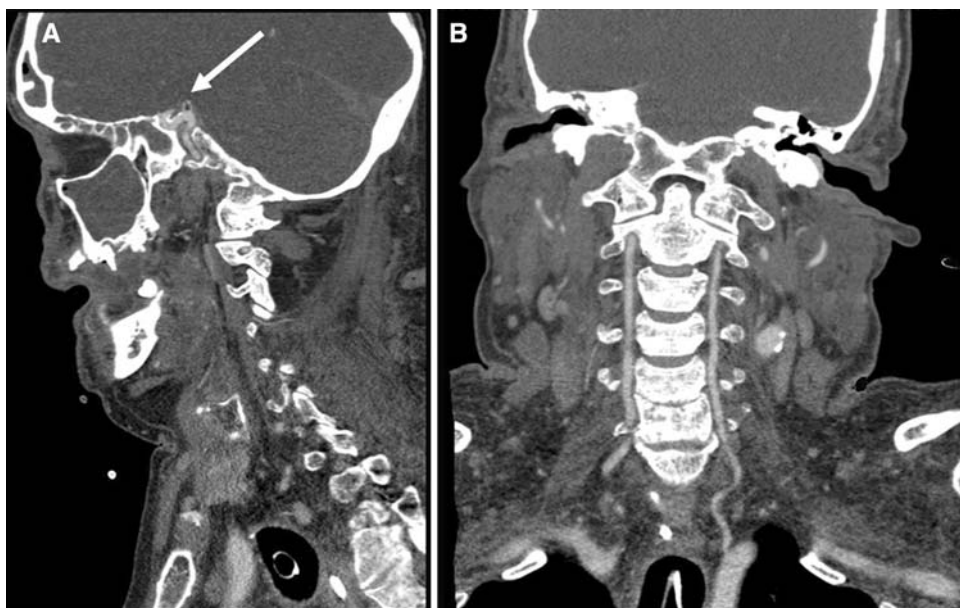


Fig. 5 CTA and CTP images for Patient 9. CTA shows the presence of both anterior and posterior intracranial blood flow. The image shows both carotid arteries, their intracranial branches, vertebral arteries, and basilar artery. The CTP scan indicates markedly reduced CBF with increased MTT at the level of the posterior circulation and right temporal lobe

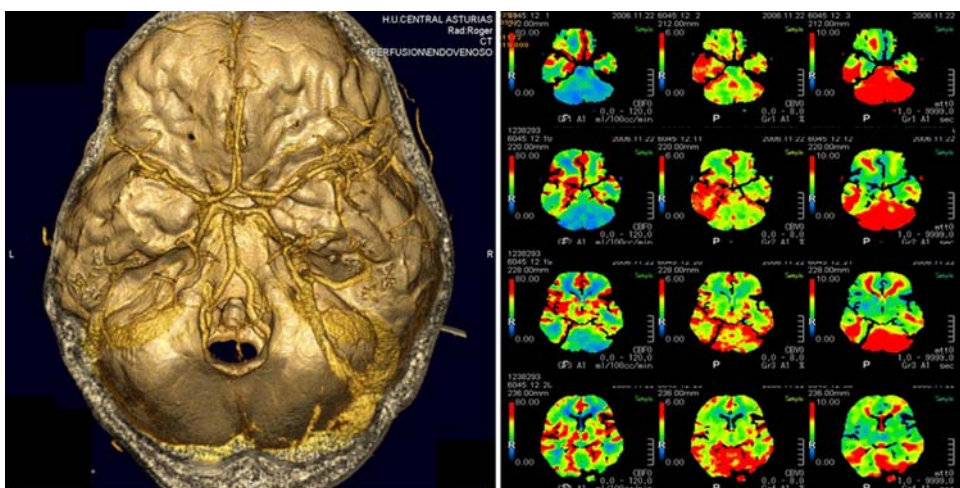
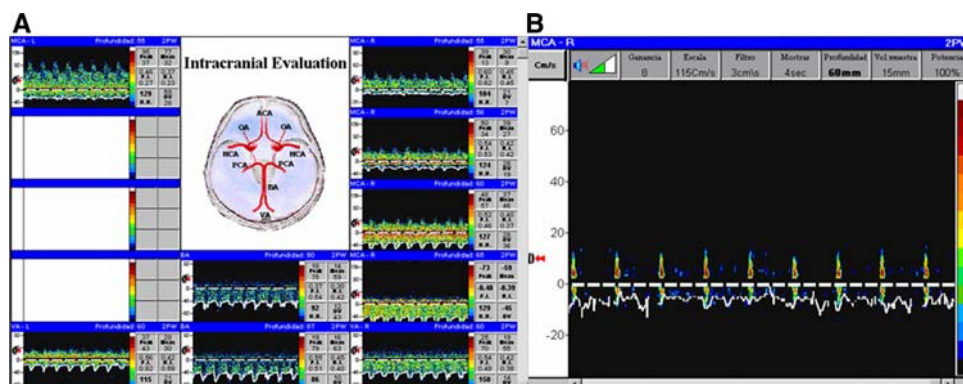


Fig. 6 TCD images for Patient 9. **a** TCD shows the presence of CBF in the vertebral arteries, basilar artery, and the middle cerebral arteries insonated at different depths. **b** TCD of the MCA performed 14 h later showing systolic spikes



following standard procedures. CTA showed flow through the intracranial carotid and vertebral arteries. Given the presence of arterial filling, the CTP color map could be acquired which indicated an elevated MTT and considerably reduced CBF and preserved CBV (Fig. 5). TCD revealed blood flow in the anterior and posterior circulation with slightly elevated mean velocities and a normal pulsatility index; 14 h later, the TCD showed a pattern of systolic spikes (Fig. 6).

Patient 12

A 70-year-old man with TBI consisting of a burst fracture of the skull cap and base, subdural hematoma, and a large cerebral edema was admitted with a GCS 5. The subdural hematoma was evacuated and a decompressive craniectomy performed. Forty-eight hours after admission, a clinical exam indicated BD although the oculovestibular, photomotor, and corneal reflexes of the left eye could not be determined because of destruction of the facial bone at this level. In the TCD, only the right MCA could be insonated showing a pattern of systolic spikes. The CTP indicated cerebral perfusion, and in the CTA, the persistence of CBF through the intracranial carotid and vertebral arteries was detected. Cerebral circulatory arrest was confirmed 16 h later in a further CTP plus CTA.

Patient 17

This patient was a 50-year-old man with severe TBI consisting of a burst fracture of the skull cap and base who suffered loss of encephalic mass and underwent resuscitation for cardiac arrest. On admission, his GCS was 3. A clinical diagnosis of BD was made 24 h after admission. In this case, despite some electrical activity observed in the EEG, we decided to pursue a radiological study since the clinical findings indicated BD. The CTP indicated cerebral perfusion and the CTA revealed CBF only via the intracranial internal carotid arteries and a lack of circulation in the posterior fossa. The EEG showed electrical activity

consisting of alpha waveforms in three recordings. 48 h after the CTA, the EEG signal was isoelectric. Another CTA could not be performed and the diagnosis of BD was based on the clinical and EEG findings.

Discussion

A timely confirmation of BD is important since it allows for withdrawing support measures avoiding the unnecessary use of resources, and may also help optimize the procurement of organs for transplant.

In routine clinical practice, the greatest diagnostic challenge arises from the use of sedative agents, which invalidate the clinical examination and the EEG [25, 26]. In these cases, the physician has to use a test that determines CBF. The traditional gold standard has been the 4-vessel cerebral angiography. However, this technique has certain drawbacks that have limited its routine use: it is invasive, costly, and of limited availability since it requires a neuroradiology room with expert staff. In our study, the diagnosis of BD was based on the findings of a clinical examination, EEG, and TCD. We did not compare our data to the results of 4-vessel cerebral angiography because of the characteristics of our patient series and the fact that this instrument is not permanently available at our center. In an attempt to avoid these shortcomings, the use of CTA has been recently proposed. Dupas et al. [17] examined 14 BD subjects through CTA performed in two stages, 20 and 54 s after iv injection of the contrast agent. They compared the results of the CTA with the clinical diagnosis, EEG, and conventional cerebral angiography. Next, the authors established a radiological score based on seven BD criteria, which included a lack of opacification in pericallosal arteries, terminal arteries of the cortex, great cerebral vein, and internal cerebral veins. Based on a study of 15 BD patients subjected to two-phase CTA, Leclerc et al. [18] proposed that a lack of visualization of cortical branches of the MCA and internal cerebral vein were the best criteria for diagnosing BD.

In a study performed on 43 BD patients subjected to EEG, conventional angiography and two-phase CTA, Combes et al. [19] used the radiological score of Dupas [17]. Only in 30 cases BD was confirmed by the two angiography methods. In the remaining 13 patients, the CTA indicated some extent of cerebral perfusion, obtaining a sensitivity of 69.7%. Using the same protocol of two-phase CTA, similar findings have been reported by other authors. Thus, Quesnel [20] obtained a sensitivity of 52.4% and Brocas [21] noted that some patients required up to 4 successive CTA to make the diagnosis. These authors consider the sensitivity obtained unacceptable and given the high number of false negatives recommend that some sort of international consensus be reached to interpret CTA. All these studies involved the use of the two-phase CTA procedure with 3–4 detector CT instruments to determine the radiological score of Dupas [17] and lacked cerebral perfusion assessment or 3D reconstruction of images.

In contrast, the diagnosis of cerebral circulatory arrest that accompanies BD using the latest generation multislice CT technique including 3D-image reconstruction and CTP has only been described in a few reports [22–24, 27] and a low number of patients but with excellent results.

The main problem with CTA is the detection of CBF in some BD subjects. One of the reasons for the presence of CBF is that the ICP does not exceed the cerebral perfusion pressure. This occurs in patients whose skull is open because of multiple skull fractures, ventricular drainage, or decompressive craniectomy [28–32]. It may also be seen in patients with anoxia following cardiac arrest [33]. Normal CBF is 50–60 ml/100 g/min. When flow drops below 35 ml/100 g/min neuronal protein synthesis ceases, when ≤ 20 ml/100 g/min synaptic transmission is modified and no activity appears in the EEG, and when < 10 ml/100 g/min irreversible damage and neuronal death occur [34]. After being resuscitated from cardiac arrest, CBF may be partly restored since the ICP is not so elevated as to cause cerebral circulatory arrest, yet the hypoxic neuronal damage incurred during the time of cardiac arrest prevents the recovery of brain functions. The same occurs in an open skull situation in which a small amount of blood is able to enter the brain but flow is insufficient to maintain neurological functions. This persistence of some CBF could explain the two false negative results obtained in our patient series (Patient 12 and Patient 9).

Patient 17 was a case of cerebral anoxia in an open skull produced by a burst fracture but cannot be considered a false negative since the CTA revealed a lack of flow in the posterior circulation, obviously supporting the clinical diagnosis of BD. Given our angiographic findings, we consider this a case of *brain stem death*, and clearly different to the two false negatives (Patients 9 and 12) in whom we detected posterior and anterior circulation yet no

electrophysiological responses (isoelectric EEG and no evoked BAEP or SEP responses). The presence of CBF in the intracranial internal carotid arteries explains the initial persistence of electrical activity in the EEG. This agreement between the electrophysiological and angiographic findings adds strength to the sensitivity of CTA. In Spain as in many other countries, the accepted concept of BD is one of *whole brain death*. Hence, in cases of intratentorial disease, besides the clinical exam, a laboratory test demonstrating the lack of function of the cerebral hemispheres is mandatory [9]. This patient initially classified as *brain stem dead* was subsequently diagnosed as BD and legally declared dead when the EEG was isoelectric.

With the exception of the two false negative diagnoses mentioned, CTA plus CTP was able to identify the lack of cerebral perfusion and intracranial circulation and showed good correlation with the clinical and EEG findings. Using the clinical exam as the reference standard, the sensitivity obtained for this protocol was 89%. If we were to consider as a control group all the CTAs performed daily in neurocritical patients, the specificity of our CTA/CTP procedure would be 100% since obviously a lack of CBF has never been described in patients other than BD subjects. The sensitivity of TCD compared to CTA is much lower due to an inability to adequately insonate all the intracranial circulation.

Our findings indicate that CTP plus multislice CT angiography is able to demonstrate the lack of intracranial blood flow that exists in BD subjects. Our radiological protocol showed a high sensitivity and a wide safety margin for diagnosing BD. This technique would be indicated in especially diagnostically challenging patients such as those under treatment with sedatives, with severe facial damage, or metabolic alterations. It may be also useful when considering organ donation since it avoids delays in managing the potential donor. Although the patients included in our study were not sedated, their lack of CBF precludes the possibility of any neurological activity such that this criterion of a confirmed lack of blood flow in the brain will always determine an unequivocal diagnosis of brain death even in sedated patients [22, 35].

One of the main limitations of CTP is that it does not examine the entire encephalic parenchyma. Although CTP formed part of our radiological protocol, in view of the results obtained we consider that CTP would not really be necessary and has the added drawbacks of lengthening the examination time and increasing the amount of contrast agent needed. In effect, this procedure has been eliminated from our routine clinical practice.

Among the limitations of the CTA/CTP procedure, we should consider the possibility of false negatives, the need to transfer the patient to a radiology room, a need for modern CT devices and a need to administer contrast

medium. The latter is considered a risk factor for impaired kidney function, although it has been reported that the use of contrast causes no nephrological damage that could invalidate the use of the kidney for transplant [35].

Among its benefits, we should mention that CTA is inexpensive, rapid, non-invasive, easy to perform, and available at any time. In addition, CTA lacks the limitations inherent to 4-vessel cerebral angiography and shows improved sensitivity over 2-phase CT angiography [17–21]. Although we did not compare our protocol with these types of angiography, because of the excellent images provided by the new generation multislice CT instruments, we view this procedure as an interesting alternative to conventional 4-vessel angiography or 2-phase CT angiography.

Finally, despite the good results obtained here, the low number of patients examined to date and few published reports determine a need for further studies to confirm our observations.

Conclusions

Although the diagnosis of brain death is essentially based on clinical findings, in sedated patients an ancillary test is needed to confirm the absence of CBF. In this study, CT perfusion plus multislice CT angiography emerged as a technique capable of diagnosing brain death with a sensitivity of 89% and a diagnostic safety margin of 100%, since it identifies a lack of intracranial circulation. In situations of an open-skull or anoxia false negatives may be obtained. Given this technique is rapid, non-invasive, and widely available, we feel it is an interesting alternative to conventional 4-vessel angiography or two-phase CT angiography.

Acknowledgments The authors thank the medical and technical staff of the Radiology and Intensive Care Medicine units of the Hospital Universitario Central de Asturias, Oviedo, Spain for their help in managing the patients. The study was conceived by DE, who along with JO participated in its design and coordination and helped draft the manuscript. LM, DP, JA, GA, LC, AB and FC helped manage the brain-dead patients and also contributed to drafting and critically revising the manuscript. The images were acquired, processed and interpreted by PV, EM, AM and RL. All the authors read and approved the final manuscript.

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