Consensus Group on Transcranial Doppler in the Diagnosis of Brain Death*

Latin American Consensus on the use of transcranial Doppler in the diagnosis of brain death

Consenso Latinoamericano sobre el uso del Doppler transcraneal en el diagnóstico de muerte encefálica

ABSTRACT

Transcranial Doppler evaluates cerebral hemodynamics in patients with brain injury and is a useful technical tool in diagnosing cerebral circulatory arrest, usually present in the brain-dead patient. This Latin American Consensus was formed by a group of 26 physicians experienced in the use of transcranial Doppler in the context of brain death. The purpose of this agreement was to make recommendations regarding the indications, technique, and interpretation of the study of transcranial ultrasonography in patients with a clinical diagnosis of brain death or in the patient whose clinical diagnosis presents difficulties; a working group was formed to enable further knowledge and to strengthen ties between Latin American physicians working on the same topic.

A review of the literature, concepts, and experiences were exchanged in two meetings and via the Internet. Questions about pathophysiology, equipment, techniques, findings, common problems, and the interpretation of transcranial Doppler in the context of brain death were answered. The basic consensus statements are the following: cerebral circulatory arrest is the final stage in the evolution of progressive intracranial hypertension, which is visualized with transcranial Doppler as a "pattern of cerebral circulatory arrest". The following are accepted as the standard of cerebral circulatory arrest: reverberant pattern, systolic spikes, and absence of previously demonstrated flow. Ultrasonography should be used - in acceptable hemodynamic conditions - in the anterior circulation bilaterally (middle cerebral artery) and in the posterior (basilar artery) territory. If no ultrasonographic images are found in any or all of these vessels, their proximal arteries are acceptable to be studied to look for a a pattern of cerebral circulatory arrest.

Keywords: Brain death/diagnosis; Brain death/ultrasonography; Ultrasonography, Doppler, transcranial; Consensus

Conflicts of interest: None.

Submitted on November 26, 2013
Accepted on March 17, 2014

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DOI: 10.5935/0103-507X.20140035

INTRODUCTION

Transcranial Doppler (TCD) is a technique introduced by Aaslid in 1982,[1] widely used at present to evaluate cerebral hemodynamics in patients with brain injury.[2] This technique measures cerebral blood flow velocity in the major vessels of the base of the brain. In Latin America, transcranial Doppler has been used more frequently in recent years, including as an auxiliary technique in the diagnosis of brain death (BD).[3] Because TCD is a non-invasive real-time technique that is able to be performed at the bedside of the patient, it is ideal for serious, unstable, or difficult-to-transport patients. There are numerous studies that validate the usefulness of TCD in the diagnosis of cerebral circulatory arrest, usually present in patients with BD.[4,5]

The objective of this Latin American Consensus is to make recommendations regarding the indications, technique, and interpretation of the study of transcranial ultrasound in patients with a clinical diagnosis of BD and/or in patients whose clinical diagnoses present difficulties. However, protocols for the diagnosis of BD differ depending on the country or region of Latin America (and the world)[6] with respect to the indications and timing of certain confirmatory tests. Therefore, we consider it useful to generate standardized recommendations regarding how to perform and analyze TCD to confirm the diagnosis of BD to improve the reproducibility and comparison between studies in a multicenter setting.

Another equally important goal was to form a working group that would further consolidate knowledge and constructive ties between Latin American doctors working on the same topic. Although the issue in pediatrics is similar, the consensus focused on adults.

METHODOLOGY

For the consensus process, we used a method based on the "state of the art" Glaser approach.[7-10] A group of doctors, predominantly neurointensivists and neurologists, with experience in the use of TCD in this clinical setting conducted a review of the literature. The group was heterogeneous, composed of physicians with more than 20 years of experience in TCD and with published research articles as well as young physicians with internship experience at referral medical centers.

A search was conducted in different electronic databases (SCOPUS, PubMed and LILACS). The terms used in the search strategy were as follows: brain death, cerebral circulatory arrest and transcranial Doppler. The search languages included Spanish, Portuguese, English, and French according to the knowledge of the participants.

In the first step, 423 articles were found. Twenty-six doctors from eight Latin American countries with experience in this area reviewed these articles and categorized them according to their relevance. The bibliography was discussed and classified via internet discussion.

Multiple tables and lists were shared via the internet, including the following: (a) A data table of the participants, including the physicians' nationality, working hospital, specialty, previous experience in consensus, experience in literature searches, years of experience in TCD, and languages. (b) A list of bibliographic items, including a numbered list containing only the authors, titles, and sources (journal, year, and page number) of all the articles. According to the classification of each participant, a different color was given to each item according to their relevancy to the consensus, whether the abstract or the full article was available, and the language. In this manner, the bibliography was selected using (c) the chart features of each item; the original 423 articles were divided among participants into groups of 10 to 20 articles. The title, author, year, journal, and a summary of the article were included (classified as revision, review, or clinical case. Additionally, the study design, number of patients studied, and relevance to the consensus were included).

The first discussion meeting was conducted in Buenos Aires, Argentina in June 2012, in which the members of the consensus presented their findings and opinions. After the first meeting, participants were divided into groups of 2-3 members; groups were formed based on different levels of experience. Each group focused on answering questions about relevant aspects of the topic, and the information was shared via the Internet. With the responses of each group and the results of the respective literature reviews, opinions, and suggestions, the consensus coordinator prepared an initial manuscript. The manuscript was discussed at a second meeting in Buenos Aires in June of 2013. Prior to this second meeting, a new search of the literature published in the period between the two meetings was performed, and 71 additional articles were reviewed.

Figure 1 schematically depicts the evolution of the consensus. No other methodology was used, such as the Delphi method, because we wanted the consensus to focus on the Latin American reality and because another methodology would have involved the incorporation of the suggestions by experts outside of our region with different experiences. All consensus participants endorsed the recommendations presented in this paper. The following aspects were considered: pathophysiology, equipment, technique, findings, solutions to common problems, and interpretation.

RESULTS

1. Preliminary considerations: What is the alteration of cerebral blood flow in the brain-dead patient? Can cerebral blood flow be observed in a patient who is clinically brain-dead? Does the finding of preserved cerebral blood flow exclude the diagnosis of brain death? What is the pathophysiological significance of the pattern of cerebral circulatory arrest?

Patients develop brain death in a high percentage of cases due to severe and progressive intracranial

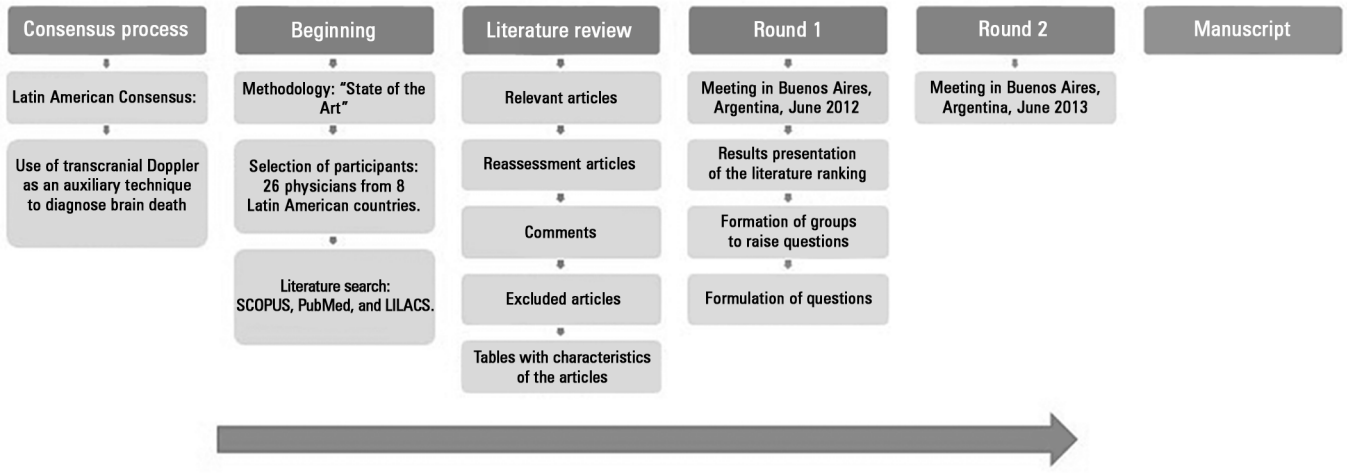

Figure 1 - Consensus process.

hypertension, decreased cerebral perfusion pressure, and global ischemia. However, it should be noted that there are cases of complete and irrecoverable absence of brain functions (i.e., brain dead) even in the presence of sustained cerebral blood flow. A clear example is reperfusion in a patient who has suffered a heart attack and is resuscitated too late. Under these circumstances, the patient's brain has been irreversibly damaged by global ischemia. However, the flow is restored, and for a time, persists. Therefore, the discovery of flow does not rule out BD.[11] However, if cardiorespiratory function in this patient is artificially maintained, dead brain cells generate edema and intracranial hypertension, eventually leading to decreased cerebral perfusion pressure (CPP) and finally the absence of flow. If the ultrasound study is repeated, eventually it will be possible see the pattern of cerebral circulatory arrest (Figure 2).

Cerebral circulatory arrest is the final stage in the evolution of progressive untreated or refractory to treatment intracranial hypertension (ICH). The decrease in CPP is accompanied by characteristic changes. The normal sonographic pattern of the arteries of the brain stem is continuous flow. The blood moves in a single direction within the vessel and is slowed during diastole and accelerated in systole without stopping (the flow velocity never reaches zero) or reversing direction. If intracranial pressure begins to rise, resistance opposes CBF and slows its flow. Flow initially slows more in diastole, which is the part of the cycle in which it moves with lower energy. The cardiogenic response is a stronger contraction,

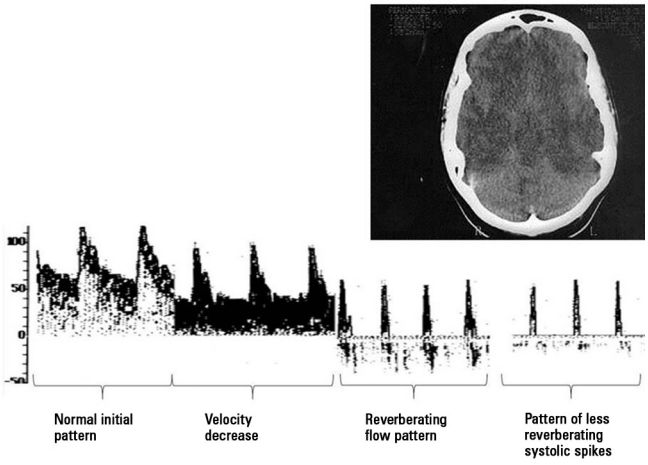

Figure 2 - A 19-year-old patient with asthma who experienced a cardiac arrest during an asthma attack; she was resuscitated via CPR. Admission GCS was 4 with initial brainstem reflexes; over 12 days, the Doppler pattern deteriorated, with all clinical neurological activity disappearing. The initial sonogram revealed normal flow velocity, evolving to slowing velocity, and cerebral circulatory arrest. Tomographic image post-CPR demonstrates diffuse anterior ischemia, as noted by the contrast "white cerebellum".

which increases systolic velocity; coincidentally, this also increases the pulsatility index (PI). The formula is as follows: PI=(SV-DV)/MV, SV: systolic velocity; DV: diastolic velocity; MV: mean velocity. This phenomenon is gradually accentuated.

Upon further increase in ICP, all velocities are decreased, but always to a greater degree in diastole. There comes a time when the flow rate is zero in diastole. This corresponds to a "systolic peak" on the sonogram. This situation is represented by a sonogram of low flow

velocity and high pulsatility occupying the entire systole. When the ICP continues to rise and reaches the blood pressure (BP), diastolic flow is reverberant, i.e., moving very slowly in the systolic phase and in reverse direction in the diastolic phase. When the ICP reaches the mean arterial pressure (MAP), there are systolic spikes. When the ICP reaches the systolic blood pressure, flow is not observed in the vessels.[12] Later, we will further address the sonographic image of each pattern.

Some authors[13] disagree with the patterns of cerebral circulatory arrest being called "flow" patterns because they represent a 'stagnant' column, i.e., the blood does not "flow"; the genesis of the reverberating patterns and systolic spikes should, according to this hypothesis, include the percussive effect of cardiac systole on a thrombosed blood column.

In a series of 40 patients, Poularas et al. confirmed 100% concordance between the cerebral angiography and TCD in the diagnosis of cerebral circulatory arrest.[14]

The first consensus on the usefulness of TCD in cerebral circulatory arrest, published in 1998, emphasized the value of this technique in cases where the existence of sedative drugs prevented the execution of an EEG for the diagnosis of BD.[15] Petty published a study in 1990 with suggestions on their value and performance as well as data on sensitivity and specificity.[16]

In 2000, an update was published defining the effectiveness of the technique in different disorders and included the diagnosis of cerebral circulatory arrest as type B recommendation, class II evidence.[17] Since then, there have been several publications, including the 2004 guidelines of the American Neurological Association (Sloan et al.), in which a type A Class II evidence recommendation is made to confirm the diagnosis of BD by TCD.[3]

Regarding the specificity and sensitivity of the method, there are techniques that compare TCD with other flow surrogate methods that are related to the diagnosis of BD. The diagnosis of BD depends on which standard is used. In the case of Uruguay, where TCD is performed only if there is clinical diagnosis uncertainty (the most common use being the setting of depressant drugs, mainly thiopental), a CCA pattern was observed in 75% of 445 patients with clinical suspicion of BD.[18]

As will be discussed later in the text, a brain-dead patient may in certain circumstances exhibit sustained blood flow. Thus, the presence of cerebral blood flow in a clinically BD patient does not correspond to a false negative. However, the opposite is not true; the absence of cerebral blood flow for a given period inevitably accompanies the death of the brain and therefore the death of the individual.

One circumstance in which it is possible to observe normal flow and clinical BD that would correspond to a false negative in the diagnosis of BD is the misidentification of an extracranial vessel with normal flow-as intracranial flow. This is avoided with proper technique (topography of each window, window depth, and direction of the ultrasonic beam).

Consensus declaration

Cerebral circulatory arrest is the final stage in the evolution of progressive intracranial hypertension.

2. Is it mandatory to confirm the diagnosis of brain death with an ancillary study? What ancillary studies are available to the physician to support the diagnosis of brain death? For which patients should we be inclined toward certain technical methods?

The diagnosis of brain death is clinical. Diagnostic criteria vary in different countries, and even in some countries such as the USA, the protocols used vary in different states. According to the protocol, diagnosis should a) always be supported by a technical method or b) only applied in doubtful cases.

Confirmatory studies of brain death can be classified into the following:

a) Those that measure or evaluate cerebral blood flow: TCD, 4-vessel cerebral arteriography, digital subtraction angiography, multi-slice CT angiography, and angioscintigraphy with radiotracers. There are also nuclear medicine studies to assess cerebral blood flow, such as positron emission tomography or single photon emission tomography. In general, all have little practical applicability compared with TCD; they are limited by the high cost, the need to transport the patient, the inability of immediate assessment, and others.

Studies evaluating flow are of particular interest in the following:

Cases in which brainstem reflexes cannot be evaluated, which are primarily cases of maxillofacial injuries.

The existence of toxic CNS depressants.

Cases in which the apnea test cannot be completed.

Cases in which diagnosis cannot be delayed while waiting for the clearance of long-acting drugs.

What is sought with these methods is the absence of flow. The cessation of circulation in the adult brain for longer than 10 minutes (except in extreme hypothermia) causes irreversible damage to the brain tissue. Demonstration

of this by itself, independent of the etiology, allows for the diagnosis of brain death. When transcranial Doppler is used, evidence of the absence of useful flow is termed cerebral circulatory arrest.

b) Electrophysiological methods: electroencephalogram (EEG) and evoked potentials to assess the absence of multimodal encephalic function.

The main limitation of the use of ECG in these intensive patients is the presence of depressants of the central nervous system. EEG becomes useless when the absence of a function is due to reversible extrinsic causes, such as the use of central nervous system depressants and hypothermia.

Consensus declaration

TCD is a flow study. Studies evaluating flow are of particular interest in the following: cases in which brainstem reflexes cannot be evaluated, cases in which the apnea test cannot be completed, and cases involving CNS depressants.

3. What are the characteristics of transcranial Doppler equipment used for the diagnosis of cerebral circulatory arrest? Can transcranial color Doppler also be used?

Equipment specifications

TCD requires an equipment with a pulsed Doppler transducer emitter of 2MHz. Sample volume studied may be variable with a transmission potential (intensity or amplitude) of 100mW/cm^2 (the intensity of an ultrasound beam is the energy per unit area expressed in milliwatts per square centimeter, (mW/cm^2); ultrasound intensities lower than 100mW/cm^2 may be used)[19] and sound filters. It should be possible to increase or decrease the transmission power of the ultrasound depending on the window used.

From a technical point of view, approximately 5-15% of patients do not exhibit adequate temporal bone windows; this prevents the evaluation of the middle cerebral arteries. The ability to evaluate the cerebral arteries also depends on operator experience.

Transcranial color Doppler (TCCD) or transcranial color-coded duplex ultrasonography (TCCS) can also be used in these cases.[20] This technique combines the B mode analysis of the frequency spectrum with that of the pulsed mode, which differs from transcranial Doppler because it adds the two-dimensional representation of the brain parenchyma and intracranial vascular structures in real time. TCCS is more accurate in imaging the vascular anatomy of even small arterial and venous branches. TCCS enables the correction of the insonation angle between the ultrasound beam and the blood flow direction, enabling a more accurate flow velocity calculation. In the context of temporal hyperostosis, TCCS helps differentiate between an absence of vascular signal and a lack of permeability of the window, as a poorly-permeable temporal window does not allow the visualization of the vessel and cannot visualize parenchymal structures in mode B.

TCCS exhibits high sensitivity for weak flows if the energy or power mode is used. A disadvantage of TCCS is that it takes longer to handle the keyboard during insonation, and the transducer is somewhat heavier.[21,22] The limitations of this method to pass through difficult windows are similar to those of TCD.[23]

Consensus declaration

Both conventional TCD and TCCD can be used for the diagnosis of CCA.

4. What is the correct technique and what are the clinical conditions necessary to perform a Doppler study seeking to confirm or rule out cerebral circulatory arrest? How and where does one measure? How long is insonation performed for each window?

Clinical conditions

It is essential to know the patient's blood pressure to avoid false positives in the presence of hypotension. TCD cannot validate cerebral circulatory arrest with systolic/diastolic arterial blood pressures lower than 90/50mmHg or mean arterial blood pressures lower than 60 mmHg.

Three sectors should be studied: two anterior symmetrical sectors, both right and left middle cerebral arteries (MCAs), and the posterior basilar artery (BA) or both vertebral arteries (VA).[24]

Useful access

Anterior sector

The temporal window is used to study the middle cerebral artery bilaterally. The temporal window is formed by the region extending superior to the zygomatic arch, anterior to the tragus and posterior to the lateral commissure of the ipsilateral eye. The temporal window may be anterior, middle, or posterior. Different patients differ in the part of the window that is permeable to

ultrasound. In fact, a percentage of individuals, between 5 and 15% in different studies, exhibit temporal windows with no permeability to ultrasound.[1,25,26] Because of this technical limitation, the absence of signals during the performance of TCD is not considered a diagnostic pattern of cerebral circulatory arrest unless a study was previously conducted demonstrating that the windows are permeable to ultrasound. The temporal window becomes impermeable to ultrasound as age increases. The group with the lowest ultrasound permeability of the temporal window consists of older women. The group of patients in brain death is predominately composed of young males whose temporal window is often permeable to ultrasound. The middle cerebral artery is found between 45 and 55mm depth. If the MCA is not found at these depths, the search can go as deep as 60-65mm.

The ultrasonic beam is directed slightly upward in all cases at an angle of approximately 10° to 20°. The beam is directed slightly backwards if the anterior temporal window is used, slightly forward if the posterior temporal window is used, and only slightly upward if the average temporal window is used.

The intensity emitted initially should be equal to 100mW/cm^2 but can be raised up to 400mW/cm^2 to increase the equipment detection power for cases in which the signal becomes difficult to detect. The registration of each artery should be maintained for at least 30 seconds, registering the bilateral middle cerebral arteries and the basilar artery. If detection must be achieved through the orbital window to look at the internal carotid sinus (see below), the power must be decreased to 10mW/cm^2 to avoid damage to the ocular structures.

Posterior sector

In the case of the posterior sector, the occipital or transforaminal window is used. This window is at the level of the foramen magnum, and the ultrasonic beam direction is from here to the base of the nose. Sonography is performed at a depth between 80 and 100mm when searching for the basilar artery. Ringelstein reported the union of the vertebral arteries to form the basilar artery and the bifurcation of the latter were found at depths of 84+/-8 and 108+/-8mm, respectively.[27] Other authors report somewhat lower values, 58.8 and 66.6 mm in men and women for the start of the basilar artery and 90.0 and 80.4 at the termination, respectively.[28] The position of these patients can be varied to perform sonography through the occipital window. It is necessary to know which cervical movements can be performed; in the absence of contraindications, lateral flexion or decubitus supine position with the head lateralized to the opposite side of the transducer should be used, with a small pillow or pad used to flex the head, leaving a space for the hand holding the transducer. Alternatively, forward flexion of the head in the decubitus supine position can be used.

It should be noted that a position change can trigger hemodynamic changes ranging from hypertension to irreversible cardiac arrest and neurological or spinal reflexes (opisthotonos, triple flexion, reflex of Lazarus).

Insonation can be performed on the dorsal decubitus position without moving the head; in this case, the insonation is performed laterally, down and into the mastoid. It is possible to perform insonation of both vertebral arteries instead of the basilar artery. If both arteries have reverberating flow or spikes (and similar patterns also exist simultaneously anteriorly), cerebral circulatory arrest is diagnosed.

Time in each window

The registration of each artery should be maintained for at least 30 seconds, registering the bilateral middle cerebral arteries and the basilar artery or the vertebral arteries. The study should be repeated after 30 minutes.

Consensus declaration

Perform insonation of anterior and posterior circulation vessels under acceptable hemodynamic conditions.

The pattern of CCA should be maintained over time.

5. What patterns are accepted for the diagnosis of cerebral circulatory arrest?

Images

The pattern of cerebral circulatory arrest is given by any of the three findings listed below: a) Reverberant flow, also called “to and fro” oscillating motion, is characterized by a spectrum of two-phase flow velocities, with equivalent components of inward and outward flow such that the net result is zero average velocity. This pattern was reported by Hassler in 1988 and 1989 and by Powers in 1989.[24,29] The pattern was interpreted as a systolic-diastolic oscillation of the column due to blood flow distal to the obstruction. The direction of flow in the vessel studied is the same as that of normal flow in the systolic phase and contralateral in the diastolic phase (Figure 3, central sonogram of the

top row and the two sides of the bottom row, and Figure 4, sonogram of the right) (Figures 3 and 4). b) Systolic spikes, very short sonograms with a duration lower than 200ms, appearing at the beginning of the systolic phase without a flow signal in the remainder of the cycle, and a systolic velocity not higher than 100cm/s. (Figure 4, left sonogram). c) The third pattern is the disappearance of a previously detected flow. In this case, no image can be obtained through a bone window previously demonstrated to be permeable to ultrasound, meaning a real flow abscence. In cases of reverberating flow and systolic spikes, flow is minimal or oscillating and is not effective. These findings were initially described only in the arteries of the anterior sector but quickly began to be included in descriptions of the posterior.[24]

These features are considered confirmatory when they are described in the following three sectors: 1 and 2) left and right anterior sectors and 3) posterior sector (either basilar artery or both vertebral arteries).[5,30,31]

The record for each artery should be maintained for at least 30 seconds. The study must be repeated after 30 minutes to check whether the pattern persists. This persistance rules out that the circulatory arrest could be caused by a transient wave of intracranial hypertension.[32,33] In the event that the sonograms are very small and unclear, the consensus group recommended examination without the envelope of the maximum velocities because it can produce confusing images in these cases.

Consensus declaration

The three following patterns are accepted as cerebral circulatory arrest: reverberant flow, systolic spikes, disappearance of a previous registered flow.

6. What solution can be sought when no sonogram can be found through a temporal window? What if no image is found in through the occipital window?

When there is an absence of a temporal window, increased transmission power ultrasound should be used. If an unclear image is obtained, the gain should be increased (such as by placing an amplifier).

If there is a lack of a sonographic image despite these changes, one must accept the following: a) the window has no permeability to ultrasound; or b) there is no signal. In all cases, the physician must ask if there was a preliminary examination demonstrating the permeability of the window

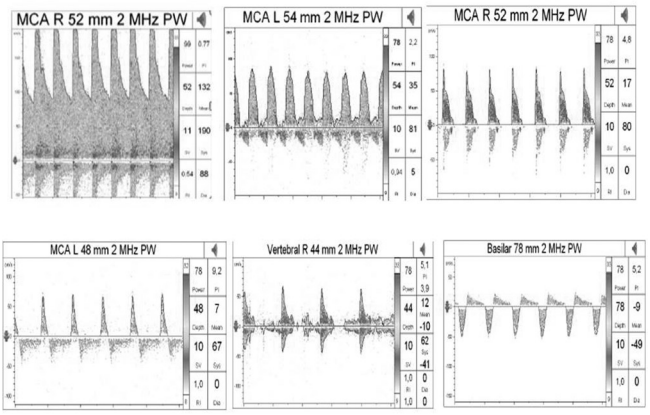

Figure 3 - Two repeated studies over time in a patient with clinical brain death. In the top row, the left central sonogram and the center belong to the first study; the other sonograms belong to the second study. MCA - middle cerebral artery; R - right; L - left. The right middle cerebral artery (left sonogram of the top row) shows normal velocity and pulsatility blood flow, and continuous flow during the arterial pulse. These findings rule out rules out the diagnosis of cerebral circulatory arrest. The left middle cerebral artery (central sonogram of the top row) demonstrates a reverberating flow pattern, but a unilateral finding does not constitute cerebral circulatory arrest of the three sectors needed to support a diagnosis of brain death. After repeating the test (the remaining 4 sonograms), the flow pattern of the right middle cerebral artery has worsened; a unidirectional peak occupies approximately half of the cycle (systolic peak), these sonograms are not systolic spikes, because their duration is longer. The reverberant pattern in the left middle cerebral artery persists, showing lower velocities. The basilar artery has a shimmering pattern. The right vertebral artery exhibits systolic peaks with some ipsilateral flow during diastole. Together, these sonograms do not constitute a pattern of cerebral circulatory arrest of the three territories; thus, the right middle cerebral artery visualization should be repeated. When corroborating reverberating flow in the basilar artery, the vertebral artery should not be included in the assessment because the distal vessel provides sufficient evidence of the hemodynamic status of each sector studied.

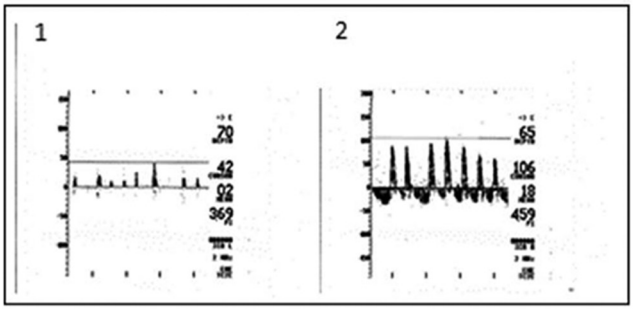

Figure 4 - A 65-year-old male patient with chronic atrial fibrillation, anticoagulation, cerebellar infarction with hemorrhagic transformation, hydrocephalus, external shunt, fever, venous sinus thrombosis, and multiple bilateral infarcts. GCS 3 without brainstem reflexes and without sedation for 24 hours. Mean arterial pressure 100mmHg. Transcranial Doppler does not demonstrate temporal window sonograms. Reverberating flow and systolic spikes at the right (1) and left (2) carotid syphon and basilar artery (not shown) are consistent with the diagnosis of brain death.

in which no image is now found. If this is the case, the second test ensures that the previously existing flow has disappeared, i.e., that there is now absence of flow in the vessel studied. It is preferable that both tests were performed by the same operator. c) If there is no history that allows us to state that the

window is permeable to ultrasound, we cannot confirm nor rule out anything with respect to the flow at that particular vessel. It is possible to solve this problem by studying the flow in the proximal vessels. In the case of a cerebral circulatory arrest pattern in a proximal vessel, we can conclude that in the distal region, there will be no flow. For the temporal window, if there is no image, a possible solution that is used frequently is looking for a carotid sonogram at the level of the carotid sinus through the orbital window.[34-37] Sonographic findings of cerebral circulatory arrest permit to conclude that the flow in the MCA (intracranial vessel, terminal branch of the internal carotid artery (ICA)) is equal to or worse than the flow observed in the carotid. However, the MCA could receive flow through the contralateral collateral circulation MCA or the posterior cerebral communicating arteries.[38] This is not the case because the diagnosis of cerebral circulatory arrest requires a confirmation of a circulatory arrest pattern in all territories (bilateral anterior and posterior). A finding of reverberating flow or spikes on a carotid sinus should be accompanied by the same findings in the contralateral anterior and in the posterior circuit.

Finally, we must insist that the study of the orbital window should only be performed when a sonogram cannot be obtained through the temporal window.[38-40]

In the case of the occipital window, if there is no flow in the basilar artery, vertebral arteries can be insonated through the same window, at a lower depth. If both vertebral arteries exhibit cerebral circulatory arrest patterns, it can be assumed that the flow in the BA is equal or worse.

Because of the difficulty in changing the position of the head of some patients, the physician may choose to perform insonation on both vertebral arteries instead of the BA. In cases in which both arteries exhibit a pattern of systolic spikes or reverberating flow in association with a similar pattern in both middle cerebral arteries, cerebral circulatory arrest is diagnosed.

It is possible to validate the pattern of cerebral circulatory arrest through an extracranial vessel only if it contains a pattern of reverberating flow or spikes. If there is an absence of flow or a different flow pattern, the pattern cannot be validated, and the study results are inconclusive.

Figure 5 presents the diagnostic algorithm of cerebral circulatory arrest (CCA).

Consensus declaration

In the absence of any ultrasound image in either MCA or BA, its proximal vessels: (ipsilateral internal carotid artery initially at the carotid siphon o secondarily at the neck, or both vertebral arteries, respectively) are acceptable for a diagnosis of CCA.

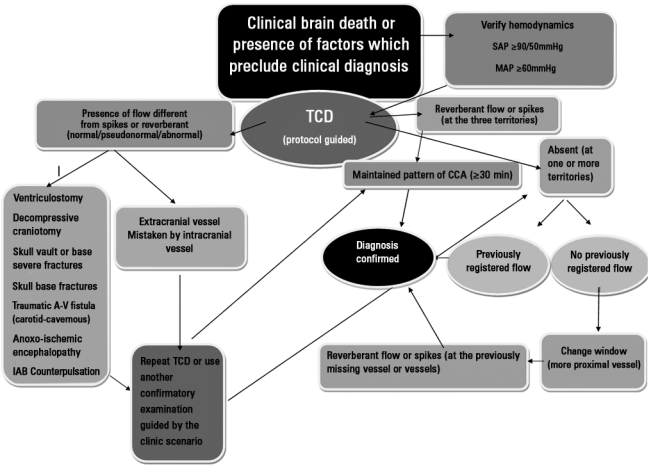

Figure 5 - Algorithm demonstrating the different routes to reach the diagnosis of cerebral circulatory arrest in a patient with a clinical diagnosis of brain death or factors that prevent or hinder the clinical diagnosis. SAP - systolic arterial pressure; MAP - mean arterial pressure; TCD - transcranial Doppler; CCA - cerebral circulatory arrest.

7. Which situations can confound the interpretation of transcranial Doppler records in cerebral circulatory arrest? In which cases can an ultrasound pattern of cerebral circulatory arrest be detected while the patient is not clinically brain dead? Are these considered false positives?

Clinical brain death and CCA are parallel phenomena that may not always coincide at the time of presentation, especially when the source of brain death is primarily infratentorial. This temporal asynchrony between the two phenomena leads to the concept of BD as an integrated and multi-phenomenological process. Therefore, to avoid misinterpretation, it is desirable that both clinical and instrumental phenomena that determine BD are simultaneous so that it is possible to establish the diagnosis of cerebral circulatory arrest with certainty.

Infrequently, records can be found compatible with CCA while the patient continues to exhibit some clinical sign of neurological activity, including corneal reflex, extensor reactivity, etc., which refutes the clinical diagnosis of BD weak breathing.[41] This phenomenon has also been described in pediatric patients with reverberating flow. Another group analyzed 12 patients and described one patient who presented with a pattern of CCA with breathing preserved.[42] A study by our group identified a case of preserved corneal reflex in

16 patients with cerebral circulatory arrest patterns. Several of these papers are from a first period in which the study of the posterior portion was not required for the diagnosis of cerebral circulatory arrest.[43]

The meta-analysis by Monteiro described patients with cerebral circulatory arrest and weak breathing for several hours that inevitably evolved to BD.[44] Since 1998, different consensus groups have noted that the pattern of cerebral circulatory arrest in both MCAs may precede the loss of function at the level of the brainstem. The importance of studying the posterior circulation is emphasized.[15] A Chilean study evaluated 53 patients, including 25 in cerebral circulatory arrest.[45] The study described a patient who was breathing at the time of cerebral circulatory arrest. The patient completed the BD criteria at 24 hours. All patients described in this work inexorably developed BD at varying times within 24 hours. None were described as false positive. These scenarios have been reported in the literature with a frequency of approximately 1/100. They are interpreted as cases of imminent brain death. To our knowledge, there are no reports of patients who have survived in these conditions. These situations reaffirm that the two conditions are not exactly simultaneous.

The situations in which we can observe patterns of circulatory arrest that do not imply or do not match clinical brain death include cases of hypotension, sudden and transient elevations in ICP (spontaneous A waves or sudden active bleeding, such as in the initial rupture of a brain aneurysm[33]) and incomplete study, e.g., the evaluation of the superior circuit only.

We must insist on the following: 1) good systemic hemodynamics; 2) an examination for a period of at least 30 minutes, because the plateau waves last 15 minutes or less; and 3) an evaluation of the three sectors.

In other cases, the clinical diagnosis is made, but Doppler patterns of cerebral circulatory arrest are not yet observed due to the lack of synchronization between the two processes. In such circumstances, the diagnostic accuracy of TCD to confirm BD decreases. However, a large percentage of these patients will eventually exhibit a pattern of cerebral circulatory arrest.

These cases include the presence of ventriculostomy, decompressive craniectomy, opening of the calvarium, skull base fracture, traumatic arteriovenous fistula, anoxic-ischemic encephalopathy, and the use of intra-aortic balloon counterpulsation. The latter preserves diastolic flow, therefore the balloon has to be put in stand by mode if possible to diagnose by means of TCD the real cerebral hemodinamic situation.

In an as-of-yet unpublished study conducted by members of this consensus (GH, CP, GF, LM), 36 patients with decompressive craniectomy with clinically suspected BD were described in whom a complete clinical diagnosis was not possible due to different factors (depressant drugs, inability to perform an apnea test, etc.). In the first study, a CCA pattern was found in 43% of cases (14 patients). Of the 22 for which CCA was not initially verified, the study was repeated in seven patients, and CCA was detected in three patients. Of the remaining four patients, the study was repeated in two, and one of them exhibited a CCA pattern in the third study, and the other in the fourth.

Finally, it was verified that 19 patients exhibited CCA in the initial group of 34 patients, although there were 15 cases in which the study was never repeated. Thus, despite the fact that decompressive craniectomy may sustain flow, more than half of the patients with DC whose clinical status worsened to clinical diagnosis or high suspicion of brain death exhibited CCA.

Consensus declaration

There are situations (loss of hermeticity of the skull) that delay the onset of the CCA. However, a large percentage of these patients progress to CCA; therefore, the study involves no contraindications, but its repetition over time becomes peremptory for the diagnosis of such evolution.

8. What is the practical significance of circulatory arrest in both sectors separately? Is it ethically sound that either or both situations allow organ donation, thereby gaining time and optimal donor conditions? What degree of irreversibility is possible in both situations?

In patients with focal lesions, there may exist interhemispheric pressure gradients[46] between supra and infratentorial regions.[47] In the first years after the introduction of TCD, typical alterations of cerebral circulatory arrest became known, including several papers reporting only anterior (supratentorial) arrest. Subsequently, it was found that patients could have anterior circulatory arrest with the preservation of posterior flow and the existence or recovery of brain stem reflexes, which eliminated the clinical diagnosis

of BD;[37] this was interpreted as a false positive for the diagnosis of BD but was actually an incomplete study. Thereafter, different consensuses groups began requiring the study of posterior (basilar artery or both vertebral arteries) vessels in addition to the bilateral anterior sections.[37]

In patients examined with TCD, it is common to observe that the pattern of CCA is not presented simultaneously in all territories. The usual behavior is to repeat the study until the pattern is displayed and appears in all three sections; this observation supports the diagnosis of BD.

In countries where the criteria of brainstem death are accepted as death of the individual, it would be consistent to accept a pattern of circulatory arrest in the basilar artery or both vertebral arteries as supporting the clinical diagnosis of BD. In these cases, the presence of irreversible posterior circulatory arrest (CA) could save time and allow for better donors. We did not find any articles in the research literature that specifically focused on this topic. We have not found any work that attempts to validate the diagnosis of circulatory arrest BD through only the basilar artery in countries or regions that accept the criterion of brain stem death as the criterion of death. This type of study is very difficult to perform because often there is doubt in the clinical diagnosis of BD due to the presence of CNS depressant drugs involved in the therapeutics of intracranial hypertension. However, given the collateral circulation in the brain via the circle of Willis, the possibility exists that the distal portion of the basilar artery receives blood from the anterior sector; if this circulation is present, the brain stem can be perfused simultaneously to an absent circulation in the initial portion of the basilar artery. In our opinion, therefore, the pattern of CCA in just the basilar artery cannot be accepted as conclusive of brain stem absence of flow.

This consensus has not considered ethical factors due to the large variability in the diagnostic criteria of death in different countries. Independent of the diagnostic criteria of brain death, the presence of *regional* circulatory arrest has a very poor neurological functional outcome, as observed in the hemispheric infarction by carotid occlusion, malignant infarction of the middle cerebral, or poor outcome criterion in the CA of the MCA subsequent to thrombolysis (TIBI 1).[48]

Consensus declaration

Regardless of whether the accepted diagnostic criterion for BD is that of "whole-brain death" or "brainstem death", TCD supports the diagnosis of brain death only when vessels exhibit anterior and posterior CA patterns.

9. What training and experience are required to perform and report a study of cerebral blood flow with transcranial Doppler in the context of ancillary examination in the diagnosis of brain death?

To ensure the diagnosis of cerebral circulatory arrest to support the legal diagnosis of BD, the physician must be properly trained, familiar with their performance and interpretation. Each country or region may certify these doctors differently, but this consensus group recommends a minimum of 50 TCD studies conducted in neurocritical patients and 20 diagnoses of cerebral circulatory arrest.

All TCD studies must be documented and controlled by a an experienced professional, and the individual must pass a written examination on clinical pathophysiology, the diagnostic protocol of BD, and the physical principles of transcranial Doppler.

Consensus declaration

A minimum number of documented studies, approval by a tutor, and a theoretical test is recommended.

CONCLUSIONS

In an attempt to standardize the methodology of transcranial Doppler in Latin America, the present work presents consensus opinions of a group of experienced Latin American physicians intention to standardize when and how to use this technique to aid the diagnosis of the cerebral circulatory arrest that often accompanies brain death. A consensus statement by all members was issued for each point that was considered.

Cerebral circulatory arrest is the final stage in the evolution of progressive intracranial hypertension, the most common etiology of brain death.

If transcranial Doppler reveals a diffuse pattern of cerebral circulatory arrest, the diagnosis of brain death may be supported. The reverberant pattern of systolic spikes and the absence of flow shown previously are accepted as the standard of circulatory arrest by

transcranial Doppler. To support the diagnosis of brain death, transcranial Doppler must show one of these three patterns of cerebral circulatory arrest maintained over time in the anterior arteries (bilateral middle cerebral arteries) and posterior (basilar artery). Insonation must be performed under acceptable hemodynamic conditions in the bilateral anterior and posterior sector. In cases in which ultrasonographic imaging of either one or both middle cerebral arteries or basilar artery is not possible, the vessels proximal to them (ipsilateral internal carotid siphon or both intra- and extracranial vertebral, respectively) are acceptable for the diagnosis of cerebral circulatory arrest.

There are situations (loss of hermeticity of the braincase) that delay the onset of cerebral circulatory arrest; however, a percentage of these patients progress to cerebral circulatory arrest. Therefore, repeated use of TCD is critical for the diagnosis of this evolution.

Both conventional transcranial Doppler and transcranial color Doppler ultrasound can be used for the diagnosis of cerebral circulatory arrest.

Regardless of whether the diagnostic criteria of brain death accepted is "death of the whole brain" or "death of the brainstem", a diagnosis of brain death is supported when the vessels of the anterior (bilaterally) and posterior circulation exhibit a pattern of cerebral circulatory arrest.

A minimum number of documented studies are recommended that must be made by a physician, together with a theoretical test, to qualify for performing the diagnosis of cerebral circulatory arrest to support the legal diagnosis of brain death.

RESUMEN

El Doppler transcraneal evalúa la hemodinámica cerebral en el paciente neurocrítico. Se destaca su aporte como técnica auxiliar en el diagnóstico del paro circulatorio cerebral, que habitualmente presenta el paciente en muerte encefálica. Este Consenso Latinoamericano se conformó por un grupo de 26 médicos con experiencia en el uso de Doppler transcraneal en el contexto de muerte encefálica. El propósito de este consenso es realizar recomendaciones en relación a las indicaciones, técnica e interpretación del estudio de la ultrasonografía transcraneal en el paciente con diagnóstico clínico de muerte encefálica o en aquel paciente cuyo diagnóstico clínico presenta dificultades; formar un grupo de trabajo que permita profundizar conocimientos y consolidar lazos entre médicos latinoamericanos trabajando en el mismo tema.

Se revisó la literatura, se intercambiaron conceptos y experiencias en dos encuentros presenciales y vía Internet. Se contestaron preguntas sobre fisiopatología, equipo, técnica, hallazgos, problemas frecuentes e interpretación del Doppler transcraneal en el contexto de muerte encefálica. Las declaraciones fundamentales del consenso son: El paro circulatorio cerebral es la última etapa en la evolución de la hipertensión intracraneana progresiva, donde se visualiza con el Doppler transcraneal un "patrón de paro circulatorio cerebral". Se acepta como patrón de paro circulatorio cerebral: patrón reverberante, espigas sistólicas y ausencia de flujo previamente evidenciado. Se debe insonar - en condiciones hemodinámicas aceptables - sector anterior bilateralmente (arterias cerebrales medias) y sector posterior (arteria basilar). De no encontrarse ninguna imagen ultrasonográfica en éstas, las arterias proximales (carótida interna ipsilateral en sifón o ambas vertebrales respectivamente) son aceptables para el diagnóstico de paro circulatorio cerebral.

Descriptores: Muerte encefálica/diagnóstico; Muerte encefálica/ultrasonografia; Ultrasonografía Doppler transcraneal; Consenso

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