ROLE OF TRANSCRANIAL DOPPLER SONOGRAPHY IN CONFIRMATION OF BRAIN DEATH

M. HELMI AFIFI* (MD), MOUSTAFA M. MOUSTAFA** (MD)
Department of ICU* and Radiology**, KFSH (Buraidah, Saudi Arabia)
*Assistant Prof. of Anesthesia & ICU, Menoufiya Faculty of Medicine
**Assistant Prof. of Radiology, Assuit Faculty of Medicine

ABSTRACT
The aim of the study was to determine the specificity and sensitivity of Transcranial Doppler Sonography (TCD) as a confirmatory test for diagnosis of brain death and to assess the possibility of adding this test to the protocol for diagnosis of brain death in ICU.

TCD examination was done in 20 patients (group I) with brain death confirmed either by clinical assessment and EEG (17 patients) or by clinical assessment alone (3 patients). The clinical diagnosis of brain death was performed, according to the Saudi Ministry of Health approved protocol which included lack of response to stimulation and absence of brain stem reflexes (pupillary to light, corneal, oculocephalic, oculovestibular, gag and cough). The clinical assessment was repeated after at least 6 hours. EEG was done, if possible and was reported by the neurologist on call. Apnea test was done after the second clinical documentation of brain death was completed. TCD studies of the ophthalmic arteries, middle cerebral arteries and basilar artery were carried out. A characteristic TCD flow pattern of reversed diastolic flow or short systolic spikes, in at least two cerebral arteries, was seen in 17 patients (85% sensitivity). TCD examination of 24 comatose patients who were not brain dead (group II) did not reveal the same characteristic pattern in any of those cases (100% specificity).

Conclusion: TCD is a highly specific and sensitive non-invasive tool that can be included in the protocol for diagnosis of brain death as a rapid bedside confirmatory test in patients proven clinically to be brain dead. The described TCD patterns of brain death should be elicited in 2 or more of the cerebral arteries.

INTRODUCTION
Nowadays, brain death is the most widely accepted criterion for death, both legally and medically. It is defined as the irreversible cessation of brain function, even though blood continues to circulate to rest of the body. The diagnosis of brain death has become an important issue because of its relation with possible organ transplant or removal of life support measures. It is essentially a clinical diagnosis which includes three cardinal findings: coma or unresponsiveness, absence of brain stem reflexes and apnea. However, objective confirmatory tests are needed if clinical criteria cannot be reliably evaluated e.g. due to drugs, hypothermia or facial trauma, or due to some ethical or legal considerations.

Confirmatory tests either document the absence of neuronal activity e.g. EEG or evoked potentials or the absence of cerebral perfusion as cerebral angiography, radionuclide scanning as well as transcranial Doppler sonography (TCD). Confirmatory tests that are included in the Saudi Ministry of Health protocol for the diagnosis of brain death are flat EEG or absence of blood flow by cerebral angiography. However, EEG is time consuming and supporting staff is not always available. Also, considerable artifacts can limit its interpretation. Angiography, although considered as the most reliable to demonstrate absence of cerebral circulation, is expensive, invasive and requires patient transporting.

A relatively simple, non-invasive way to determine changes in cerebral circulation occurring in brain death is the use of TCD. Since its advent by Aaslid in 1982, a number of authors have demonstrated specific patterns characteristic of cerebral circulatory arrest consisting of reversed diastolic flow or small systolic spikes. The aim of the study is to determine the specificity and sensitivity of TCD as a confirmatory test for diagnosis of brain death and to assess the possibility of adding this test to the protocol for diagnosis of brain death in ICU.

MATERIALS AND METHODS
Study included 44 comatose patients admitted to ICU in King Fahd Specialist Hospital, Buraidah, Saudi Arabia during the period from August 2001 to November 2002. The different causes of coma are shown in Table (1). 37 patients were males and ages were between 6 months and 95 years (mean 33.8 y) (Table 2). All patients were mechanically ventilated with PaCO2 between 35-45 mmHg and PaO2 >70 mmHg. Patients were divided into 2 groups: Group I included 20 patients where TCD was done for confirmation of brain death already documented either by clinical assessment and EEG or by clinical assessment alone. In Group II, TCD was done for 24 comatose patients who were not clinically brain dead.

The clinical diagnosis of brain death was performed according to the Saudi Ministry of Health approved protocol (Fig.2). The tests were done by 2 physicians, one of them was the intensivist (first investigator, M. H. Afifi), and the other was the treating physician. The tests were repeated after at
least 6 hours. Clinical assessment included lack of response to stimulation and absence of brain stem reflexes (pupillary to light, corneal, oculocephalic, oculovestibular, gag and cough). Preconditions included the presence of irreversible brain damage, absence of spontaneous breathing and a period more than 6 hours after initial insult. Exclusion criteria for clinical documentation included hypothermia (core temp. <35.5 °C), untreated shock (BP< 90/50 mmHg), and metabolic or endocrinal causes of coma. Blood test was done if significant levels of sedatives, narcotics or depressants were suspected. EEG was done if possible and was reported by the neurologist on call. Apnea test was done after the second clinical assessment was completed. This test was done as follows: every patient was ventilated with 100% O₂ for 10 minutes. Ventilation was adjusted to keep PCO₂ within normal range. Ventilator was disconnected for 10 minutes while supplying endotracheal O₂ flow of 6 l/min. Test was considered positive when no respiratory efforts occurred and PaCO₂ was >60 mmHg.

TCD examination was performed by Logic 500 system (GE, USA) with a pulsed phased array 3.5 MHz Doppler probe. It was done by the second investigator (M. Moustafa) who was blind to the patient clinical assessment of brain death. Bilateral TCD studies of the ophthalmic arteries (OA), middle cerebral arteries (MCA) and basilar artery (BA) were carried out and recorded on hard copy single coated x-ray films. Transorbital approach (13) was used for OA, transtemporal approach (11) for MCA while midline suboccipital approach (11) was used for BA.

The patterns of reversed diastolic flow (oscillatory waveform) or short systolic spikes (Fig.1) were considered to be specific for circulatory arrest if they conformed to the following conditions (recommended by Hadani et al)(7):
The above mentioned TCD patterns were present in at least 2 cerebral arteries ( one on either side of anterior circulation or one artery in anterior circulation in addition to basilar artery).
Absence of signal from a vessel was regarded as a sign of flow cessation only if typical TCD patterns were seen in other vessels.
Signals with stable waveforms typical for circulatory arrest were recorded from each vessel for at least 3 minutes and the total duration of TCD examination was 30 minutes.

RESULTS

All patients in group I (20 patients) met the criteria of brain death at the time TCD was performed. In 17 cases, brain death was diagnosed by both clinical assessment and flat EEG (85%). In 3 cases, EEG was not performed (technician was not available).

A characteristic TCD pattern consisting of either reversed diastolic flow or short systolic spikes (Fig. 3,4), was found in 17 patients in brain death group ( 85% sensitive) but in non of group II non-brain death patients (100% specific). In the remaining 3 patients in group I, brain death was confirmed both clinically and by flat EEG but TCD flow pattern was normal in 1 case (5%) while no TCD signal could be obtained from any cerebral artery in 2 cases (10%). This means that TCD was insensitive in 15% of brain death patients. Table 3 shows summary of TCD pattern results in both studied groups.

**Figure 1: Typical TCD changes with increasing ICP (Huttemann et al).**

![Figure 1: Typical TCD changes with increasing ICP (Huttemann et al).](image-url)
Table (1): Causes of coma

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Group I</th>
<th>Group II</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head injury</td>
<td>13</td>
<td>12</td>
</tr>
<tr>
<td>Brain tumor</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Cerebrovascular accidents</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Hydrocephalus with VP shunt</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Near drowning</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Sudden Infant Death Syndrome</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Subarachnoid hemorrhage</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Arteriovenous malformation</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Septicemia</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Total (number)</td>
<td>20</td>
<td>24</td>
</tr>
</tbody>
</table>
Table (2): Age and sex

<table>
<thead>
<tr>
<th></th>
<th>Group I</th>
<th>Group II</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr.): range</td>
<td>0.5-70</td>
<td>1.5-95</td>
<td>0.5-95</td>
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<tr>
<td>Mean</td>
<td>31.7</td>
<td>35.2</td>
<td>33.8</td>
</tr>
<tr>
<td>Pedia. (&lt;12yr.): No</td>
<td>4</td>
<td>3</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>20 %</td>
<td>12.5 %</td>
<td>15.9 %</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>16 / 4</td>
<td>21 / 3</td>
<td>37 / 7</td>
</tr>
<tr>
<td>Total (No.)</td>
<td>20</td>
<td>24</td>
<td>44</td>
</tr>
</tbody>
</table>

Table (3): Summary of TCD pattern results.

<table>
<thead>
<tr>
<th>TCD pattern</th>
<th>Group I (n=20)</th>
<th>Group II (n=24)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oscillating or short systolic spikes in ≥ 2 arteries</td>
<td>17</td>
<td>-</td>
</tr>
<tr>
<td>Non-obtainable signal from any artery</td>
<td>2</td>
<td>-</td>
</tr>
<tr>
<td>Normal flow pattern in all arteries</td>
<td>1</td>
<td>24</td>
</tr>
</tbody>
</table>

Figure 3: TCD pattern demonstrating reversed diastolic flow and short systolic spikes in right and left ophthalmic arteries (a-c), and basilar artery (d-f).
DISCUSSION

The TCD flow patterns seen in brain death patients occur as intracranial pressure (ICP) rises above mean arterial pressure leading to cerebral circulatory arrest. Initially, there is decrease in diastolic velocity followed by disappearance of the diastolic flow (fig.1). These changes may be reversible if reduced within a short time. With further development of circulatory arrest, oscillating patterns with retrograde diastolic flow, short systolic spikes and absent TCD signal succeed one another in progression towards the state of brain death. These TCD findings were confirmed in previous studies by four vessel angiography and radionuclide scanning. In our study, these patterns were seen, in at least 2 cerebral arteries, in 17 patients in group I. The characteristic TCD patterns were not found in any of the 24 patients in group II, all of them were not clinically brain dead. These results confirm the previous reports that use of TCD for confirming brain death is 100% specific with no false positive results. However, Hassler et al using continuous TCD monitoring, reported transient reversal of diastolic flow when ICP exceeded the systemic arterial pressure in comatose patients who were not clinically brain dead. Therefore, to avoid false positive results, we should not use TCD alone to diagnose brain death in patients who do not meet the clinical criteria. Also, the characteristic TCD signals should be detected in more than one artery as explained in the Methods, to avoid false positive results due to local cessation of blood flow in one of the cerebral arteries.

The sensitivity of TCD in confirmation of brain death was 85% as 3 cases in group I were considered to be falsely negative due to the absence of the characteristic TCD patterns although brain death was confirmed both clinically and by flat EEG. In 2 of them, there was no signal from any cranial artery but this was not considered as confirmation of brain death to avoid false positive results as it may occur if ultrasound beam is unable to penetrate the skull e.g. due to anatomic variations of bone and ossification, anatomic variations in circle of Willis or technical problems of examination. We met only one case of brain death in group I with preserved normal TCD flow pattern in all examined arteries. It was a case of electric shock with fall from height and an acute subdural hematoma was surgically evacuated. Preservation of forward diastolic flow could be explained by the presence of skull defect due to craniotomy. A number of reports showed preservation of forward diastolic flow in clinically and EEG confirmed brain death in cases with low ICP e.g. due to ventricular drain or open skull fracture or in cases where there is no persistent elevation of ICP e.g. anoxic post arrest brain damage. The discrepancies in sensitivity between...
our study and other authors (91.2-100%)\(^7\) can be due to differences in the number of studied patients or number of examined arteries. In the present study, TCD was performed as one time test. The use of serial TCD examination could improve sensitivity.

As pediatric patients were included in both studied groups starting from 6 months, the current results, in agreement with previous reports\(^6,22,23\), can be extrapolated to this population and TCD can be used for confirmation of brain death in infants and children.

This study demonstrates that TCD has the advantage of being accurate, non-invasive confirmatory test for clinical assessment of brain death with no false positive results. Also, it is helpful at times when supporting staff is unavailable for other methods of confirmation such as EEG or imaging studies. In comparison with EEG, TCD is easy to interpret with no artifacts and it was proved by many authors to be not affected by sedative or depressant drugs which may render EEG unreliable.\(^7,9,10\) Cerebral angiography, although considered a gold standard, has some drawbacks that makes it almost inapplicable in clinical practice. Cost is high, needs specialized personnel and technology, patient must be transported outside ICU connected to ventilators and inotropic infusions, and finally contrast media can be deleterious especially to kidneys.\(^3,10\) Recent studies\(^7,10\) in relatively large groups of patients demonstrated that TCD ultrasonography is effective in early detection of cerebral circulatory arrest, especially in presence of CNS depressant drugs, and can reduce the time to confirm brain death. This can reduce the duration of suffering for the relatives. It can also decrease the number of potential organ donors lost and to preserve a better function of retrieved organs.

In spite of these reports, TCD has not been included into the protocols for brain death in this country and in many institutes.\(^7,10\) As the machine is available in most hospitals and many ICUs, this can be partly explained by lack of clinical experience. However, the American Academy of Neurology (AAN) has accepted TCD as a reliable procedure for confirmation of brain death.\(^17\) In Germany TCD has been accepted as confirmatory test for brain death since 1991.\(^21\) The usefulness and guidelines for use of TCD as part of brain death protocol was documented by the Task Force Group on cerebral death of the World Federation of Neurology.\(^24\)

In conclusion, in agreement with the previously published studies, this study proves that TCD is a highly specific and sensitive method for confirmation of brain death in adults and children. It proves the validity of including TCD in protocols for diagnosis of brain death as a rapid bedside confirmatory test. To avoid false positive results: 1) It should be restricted to patients proved clinically to be brain dead. 2) The described TCD patterns of brain death should be elicited in 2 or more of the cerebral arteries. 3) Use of serial TCD examination can improve sensitivity.

REFERENCES