BRAIN death (BD), which is defined as the irreversible cessation of all brain functions, is characterized by the arrest of cerebral circulation. The diagnosis of BD is based on clinical examination, while adjunctive tests may be used to verify cerebral circulatory arrest (CCA). In a previous report, we confirmed the accuracy of transcranial Doppler sonography (TCD) to confirm CCA in BD, but excluded subjects with absent temporal bone windows (ABW). This is a limitation of TCD, which occurs in about 10% of patients, precluding evaluation of the anterior cerebral circulation, thereby rendering TCD confirmation of CCA unfeasible. Hence, we evaluated whether the addition of the transorbital examination of the anterior cerebral circulation improved the accuracy of TCD to detect CCA in brain-dead patients. The findings of the extended TCD protocol were compared with angiography. Finally, we investigated whether reporting the sonographic and angiographic confirmation of CCA to relatives of brain-dead patients might improve their comprehension and/or satisfaction with the medical information.

**PATIENTS AND METHODS**

**Patients**

This prospective study was performed from 2004–2009 in a cohort of 90 consecutive intensive care unit (ICU) patients with clinically established BD. All patients were continuously monitored for...
systemic blood pressure, heart rate, intracranial pressure, \(P_{\text{aO}_2}\) and \(P_{\text{aCO}_2}\) to maintain steady-state conditions and to prevent hypotension (systolic blood pressure <110 mm Hg), bradycardia (heart rate <60 beats/min), and hypoxia (\(S_{\text{PO}_2}\) <95%). For all patients, the \(P_{\text{aO}_2}\) was maintained at 33–35 mm Hg throughout the study. Subjects were excluded from the study they underwent decompressive craniectomy or ventricular drain, exhibited an episode of hypoxia or hypotension during angiography or Doppler examinations, died within 48 hours of ICU admission, their family representatives refused to participate in the study, or no family members visited them within 5 days after their admission to the ICU.

Three patients were excluded because apnea tests could not be performed due to desaturation and arrhythmia, and 1 patient was excluded due to hypoxia during the Doppler measurements. Additionally, 2 subjects were excluded because they previously had undergone decompressive craniectomy: 1 subject because he died within 24 hours of admission, and 1 subject because she received no visits within the first 5 days following admission. Hence, the study included 82 patients, including 45 males with an overall age of 43 ± 19 years. They all displayed clinically diagnosed BD due to head injury (\(n = 55\) cases; 67%), subarachnoid aneurysmal hemorrhage (\(n = 19\); 23%), or cerebral infarction (\(n = 8\); 10%). The study, which conformed to the principles outlined in the Declaration of Helsinki, was approved by the Institutional Ethics Committee.

**Clinical Diagnosis of BD, Confirmatory Tests, and End-of-Life Family Conferences**

During their hospitalization and before the clinical diagnosis of BD, all subjects had undergone at least 1 TCD examination including a transorbital approach that had exhibited diastolic flow in the anterior and posterior cerebral circulation. During these examinations 11 patients were identified as cases with ABW.

BD was diagnosed clinically according to uniformly accepted criteria in all patients. Immediately after the clinical diagnosis of BD, all patients underwent TCD of the basilar and middle cerebral arteries with a transforaminal and transtemporal approach, respectively, as well as transorbital Doppler sonography (TOD) of the internal carotid arteries (ICAs).

If the initial TCD examination could not reveal CCA, the test was repeated every 30 minutes until CCA could be confirmed. However, 8 ± 6.5 hours following the clinical diagnosis of BD, Doppler confirmation of CCA was evident in all patients. Ultrasound examinations were performed with a Philips HD11XE system (Philips Medical Systems, Bothell, Wash, USA) according to the standard procedure in the literature.

Within 3 ± 2 hours after TCD confirmation of CCA, all subjects underwent 4-vessel angiography as previously described. Following angiographic confirmation of CCA, the family’s consent was obtained for organ donation by a committee consisting of an intensive care consultant, a neurologist, a cardiologist, a neurosurgeon, and an anesthesiologist. In this series, 12 patients (14.5%) became organ and tissue donors. All confirmatory tests were performed by experienced observers who were blinded to the patient’s identity.

In all cases, an end-of-life family conference was held within 12 hours after the confirmation of CCA. All conferences were timed and were performed in person by the director of the ICU. Using a sealed envelope technique, the 82 families were randomly allocated into 2 groups. The families of group A (\(n = 41\)) had BD described as an irreversible arrest of brain function diagnosed exclusively by clinical examination. The families of group B (\(n = 41\)) had BD described as an irreversible arrest of brain function diagnosed clinically and characterized by CCA, as established by means of TCD and angiography. Thereafter, 1 member of each family—either the patient’s designated surrogate or the person who ranked highest in the hierarchy for surrogate decision-making—was interviewed by an independent investigator, who assessed the member's comprehension of the diagnosis and prognosis of his or her relative. Poor comprehension was defined as a failure to understand any of the above 2 components, and adequate comprehension was defined as understanding any combination of these components. “I don’t know” answers were taken as indicating absence of comprehension. Additionally, in a modified version of the Critical Care Family Needs Inventory (CCFNI) questionnaire, the family representative entered his or her age, gender, and relationship to the patient, and replied to 14 items, each of which received a score between 1 (indicating extreme satisfaction) and 4 (indicating extreme dissatisfaction). Thereafter, the satisfaction score was calculated as the sum of the scores of the previous items, with the lowest score being 14 (extreme satisfaction) and the highest being 56 (extreme dissatisfaction).

**Statistical Analysis**

Cohen’s \(\kappa^{12}\) was used to verify agreement between TCD and angiography. Comparisons of categorical and continuous variables between the 2 randomized groups were performed with Pearson chi-square and Student t tests for independent samples, respectively, whereas comparisons of satisfaction were performed with the nonparametric Mann-Whitney test. All results are expressed as mean values ± standard deviations, except satisfaction scores, which were expressed as medians (range). \(P\) values of less than .05 were regarded as significant. All data were stored on a spread sheet (Excel 2003; Microsoft, Seattle, Wash, United States), with analyses performed using a commercially available statistical package (MedCalc 8.0; MedCalc Software, Mariakerke, Belgium).

**RESULTS**

Both angiography and TCD verified CCA in all cases. The agreement between the 2 methods was 100% (\(\kappa = 1\)). The mean time from admission to the ICU until BD diagnosis was 21.5 ± 9 days. The mean time between a clinical diagnosis of BD and TCD detection of CCA was 45 ± 10 minutes. In 68 (83%) cases CCA was confirmed by the initial TCD examination, and in 14 (17%) cases by a second TCD examination. In the 11 subjects with ABW, CCA was confirmed using the transforaminal and transorbital recordings. The addition of TOD of the ICAs enabled 15.5% more cases of CCA to be diagnosed by means of TCD.

In all patients angiography confirmed CCA by demonstrating an absence of filling of the intracranial arteries (Fig 1). TCD verified CCA (Fig 2) by exhibiting the following flow patterns: (1) brief systolic forward flow or systolic spikes and diastolic reversed flow (\(n = 38\); 46.5%), (2) brief systolic forward flow or systolic spikes and no diastolic flow (\(n = 19\); 23%) or (3) no demonstrable flow (\(n = 25\); 30.5%).

All families agreed to complete the submitted questionnaire. Groups A and B were similar in terms of age, gender, and relationship to the patient. The mean duration of the end-of-life conferences was 25.5 ± 7 minutes in the families of group A and 24.5 ± 6 minutes in the families of group B (\(P = .47\)). The difference in the hospitalization period
between patients of family groups A and B was not significant (22.5 ± 9 days vs 20.5 ± 8.5 days; P = .37). Twenty-seven (66%) participants of group A and 35 (85.5%) of group B demonstrated adequate comprehension of the patient’s diagnosis and/or prognosis (χ² = 4.23; P = .04). Participants in group B displayed significantly lower CCFNI scores than those in group A (25 [range, 15–42] vs 36 [range, 17–52]; P = .0002), indicating better satisfaction. Three group A patients and 9 group B patients (χ² = 3.51; P = .06) became organ and tissue donors.

DISCUSSION

CCA is an imperative feature of BD. Cerebral blood flow tests are widely advocated to confirm the findings of clinical examinations. Angiography remains the gold standard of these tests, but is laborious. Therefore, a preliminary bedside confirmation of CCA and BD are disassociated, at least for a limited time. Therefore, a preliminary bedside confirmation of CCA may avoid untimely transfer of the brain-dead patient to the imaging department. TCD is a noninvasive highly specific method to detect CCA, but it is not feasible for patients with ABW. We investigated whether the addition of the transorbital examination of the anterior cerebral circulation improved the accuracy of TCD to detect CCA in brain-dead patients.

Angiography and TCD using a transorbital approach exhibited perfect agreement to detect CCA in all of our patients, a finding that confirmed and extended our previous results. In agreement with previous authors, the transorbital approach detected cessation of flow in the anterior cerebral circulation in all patients of our series, including the 11 subjects with ABW. In the latter cases, the confirmation of CCA would not be feasible by standard TCD, thus the implementation of TOD enabled detection of 15.5% more cases of CCA.

TOD demands a high level of technical expertise. Localizing the ICA through the orbital structures and the optic foramen is not as easy as localizing the major cerebral arteries via the transtemporal approach. Pitfalls may occur if an orbital vessel is wrongly addressed as the carotid siphon. In addition, TOD recordings should be interpreted with caution because there have been reports of clinically brain-dead patients in whom TOD demonstrated persistent diastolic flow in the ICAs, thereby providing a false-negative result. In such cases repeated TOD examinations are recommended to safely establish CCA. Finally, TOD may be difficult to perform in cases of ocular trauma.

End-of-life family conferences are considered to be a demanding but important part of ICU practice. It is difficult for relatives to conceive that a patient who breathes, although with mechanical assistance, and has a heartbeat—a state synonymous to life for many—is actually dead. Similarly, it is difficult for the medical staff to explain to relatives that the brain of the patient has sustained an irreversible injury and is no longer functioning and that physical death will soon follow, thus organ transplantation might be beneficial. A satisfactory explanation of BD may help families accept the death of their relative, promote the grieving process, and possibly ease the decision for organ donation. Hence, we investigated whether reporting the
angiographic and sonographic confirmation of CCA to families of brain-dead patients improved their comprehension and satisfaction with the medical information. Based on previous studies, we assessed the effectiveness of medical information in terms of comprehension and satisfaction, observing both factors to be significantly improved in relatives of group B, a finding that probably resulted from the additional medical information they received. This result was not the primary end point of our study, but could comprise the objective of future research. It is of note that a marginally higher, although not significant, transplantation rate was observed among patients in the above group. However, the rather small number of cases do not allow safe conclusions to be drawn at this point.

We have to underline that the confirmation of BD is strictly a clinical diagnosis. However, TCD may be used in the neuromonitoring of patients progressing toward brain tamponade because it can detect CCA with accuracy. The implementation of the transorbital approach may be particularly useful in elderly subjects and in females who more frequently exhibit ABW, but could also be of assistance in other patients to confirm the findings of the transtemporal approach. Finally, tests that confirm CCA may offer families additional information regarding the end-of-life situation of their relatives, thereby improving their comprehension and satisfaction with the medical care provided in the critical setting.

REFERENCES


Fig 2. TCD of the right middle cerebral artery (A) and TOD of the ipsilateral internal carotid artery (B) demonstrating systolic spikes in the patient of Fig 1.