Evaluation of Pulsed Doppler Common Carotid Blood Flow as a Noninvasive Method for Brain Death Diagnosis: A Prospective Study

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Among the main causes for the relatively small number of organ donors, the delay in the diagnosis of brain death plays a major role. This prospective study was designed to evaluate whether pulsed Doppler mean and phasic common carotid blood flow (CCBF) combined with arterial and jugular venous blood gases could rapidly and specifically establish a diagnosis of brain death. CCBF was measured by an 8 MHz pulsed Doppler flowmeter, allowing measurement of the vessel diameter via a double transducer probe, which fixed the ultrasonic incidence angle. From an initial series of patients (n = 28) with an established diagnosis [brain death n = 14; severe coma with a Glasgow Coma Scale (GCS) less than 7, n = 14], the results of the logistic regression analysis process yielded the most discriminating parameters for brain death diagnosis: end-diastolic velocity (V_{ed} − 1.4 vs. 12.7 cm/s; t = 7.67, P = 0.001) and blood flow (Q_{ed} − 13.6 vs. 121.4 ml/min). These parameters were then tested in a blind fashion on a second series of 28 comatose patients (GCS = 7). They resulted in correct diagnosis (brain death n = 14 or severe coma n = 14) for all patients. Brain death diagnosis was confirmed by clinical signs, EEG, and/or angiography. From the analysis of the overall population (n = 56), a value of Qed of less than 31.4 ml/mn indicates brain death. The authors conclude, that pulsed Doppler measurements of CCBF represent an early, low cost and noninvasive technique, the results of which may prompt legally accepted procedures, which in turn would reduce the delay required before brain death is diagnosed. Moreover, this technique could help in deciding on discontinuation of active therapy in severely injured patients. (Key words: Artery, common carotid: blood flow. Brain: coma evaluation; death. Measurement technique: pulsed Doppler flowmetry.)

AN INCREASED NUMBER of successful organ transplantations requires more donor organs, which in turn requires shorter delays before brain death is diagnosed. This

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delay is often extended because of ethical problems[1] or difficulties in interpreting the data during hypothermia and/or barbiturate infusion.[2,3]

Although the concept of brain death is controversial,[4] it is generally considered as the equivalent of cessation of cerebral blood flow,[3,4] which can be assessed by radionuclide imaging or cerebral arteriography.[4,5] However, these techniques require the transport of patients whose vital signs are unstable and whose lungs are being mechanically ventilated and furthermore cannot be performed in all medical centers. The ideal method to diagnose brain death and the absence of cerebral blood flow should be noninvasive, easy to perform by an intensivist, inexpensive, quantitative, sensitive, and specific and be able to be performed at the bedside. This has led to an attempt to use Doppler velocity measurements of extracranial[6,7] or intracranial[8] vessels, or both.[9] Because none of these studies has evaluated the Doppler sensitivity and specificity, the present study was designed to test pulsed Doppler common carotid blood flow (CCBF) measurement as an index of mean hemispheric perfusion[10] for brain death diagnosis. This technique has been extensively used to measure arterial diameter, sectional blood velocity, and blood flow in superficial vessels.[10-14]

Two questions were considered: 1) Are the common carotid flow patterns different in brain death and severe coma patients? 2) Are these patterns specific and sensitive enough to confirm the diagnosis of brain death?

Materials and Methods

PATIENTS

From December 1982 to November 1986, 56 patients suffering from neurologic or neurosurgical disorders and divided in two series were studied.

Study 1. Twenty-eight patients (36 ± 4 yr) with an established diagnosis (brain death or severe coma) were studied. Patients with hypothermia (core temperature below 32.2° C), drug intoxication, and severe metabolic disorders were excluded in this first phase. In all cases com-

puted tomographic (CT) scan and/or angiography were performed as a diagnostic procedure. All therapeutic procedures were attempted before the study. According to the recommendations of the current literature,[2,15,16] the criteria of brain death were as follows: 1) absence of cerebral functions: deep coma with lack of cerebral receptivity and responsiveness; 2) absence of brain stem functions: apnea, dilated pupils, absence of cephalic reflexes, i.e., corneal, gag, cough and sucking reflexes; and 3) electrocerebral silence on two successive EEG.

A diagnosis of brain death was established before instituting the protocol for 14 patients of the 28, defining group 1.

Group 2 consisted of the 14 remaining patients in severe coma assessed by a Glasgow Coma Scale (GCS)[17] < 7 but who did not manifest the criteria of brain death.

The discriminant pulsed Doppler parameters determined from the first step of the study were tested in a prospective diagnostic manner in a second population of patients (study 2).

Study 2. Based on the previously obtained Doppler parameters (series 1), 28 patients (37 ± 4 yr) suffering from severe coma (GCS < 7) were classified according to presence or absence of brain death. For all patients confirmation of brain death was made by repeated EEG and/ or angiography criteria. For patients with severe metabolic disorders, drug intoxication, or hypothermia, EEG was not used as a confirmatory test. In these cases (n = 6) classification of brain death was assessed only by clinical signs and angiography.

In both series Doppler measurements were performed when systolic arterial blood pressure (radial artery catheter or noninvasive method) was >80 mmHg.

COMMON CAROTID BLOOD FLOW MEASUREMENT

In the first eight patients in series 1 carotid blood flow measurements were performed on both vessels. Because results for a given patient did not differ more than 6%, additional measurements were made only on one side.

Carotid blood flow was obtained with a bidimensional pulsed Doppler system, operating at a frequency of 8 MHz as previously described, with a recurrent frequency of 64.8 kHz.[9-14] Because the velocity during diastole was low, it should be noted that the resolution of this apparatus was 0.1 kHz (1.9 cm/s). In addition to the pulsed emission, two fundamental features allowed measurement of diameter and blood velocity of the common carotid artery: a bidimensional recording of the Doppler signals and a range-gated time system of reception. The former was obtained with a probe containing two transducers, with an angle of 120 degrees between them so that when Doppler signals recorded by each transducer were equal in absolute value, the incidence angle of each ultrasonic

beam with the vessel axis was 60 degrees.[12,14] With the latter it was possible to select the time delay from the emission and the duration of the reception and to convert these times echographically into the depth and the width of the Doppler sample volume.[12,14] Using a pedal incorporated with the apparatus, it was possible to automatically vary the depth and the width of the sample volume by incremental or decremental steps of 0.4 mm. To determine the arterial diameter, the width of the measurement volume was reduced to the smallest convenient value with sufficient reflected energy (about 0.4 mm); its depth from the transducer was progressively increased step by step. This was continued across the lumen of the artery, which permitted recording of velocities of the different stream lines involved in the arterial flow. Thus, the first and the last Doppler signals recorded when crossing the vessel corresponded to the proximal and distal arterial walls, respectively. The difference in depth between these two signals represented the systolic internal arterial diameter. To take into account the ultrasonic incidence angle, a correction was made by multiplying this difference by sine 60 degrees (60 degrees being the incidence angle between the ultrasonic beam and the vessel axis). Common carotid diameter was expressed in centimeters with an error of less than 8% and a reproducibility of 5 ± 3%.[12,14]

Once the arterial diameter was determined, the velocity of the entire arterial blood column was measured (V_m). The width of the measurement volume was thus increased to the value of arterial diameter; its depth from the transducer was adjusted to be equal to the distance between the proximal arterial wall and the skin. Common carotid blood velocities were expressed in centimeters per second and arterial flows were calculated as the product between blood velocities (V_m) and arterial section (S) calculated from the diameter (S = II D^2/4).

Application to common carotid artery. The pathway of the common carotid artery was determined by palpation of the neck. An ultrasonic gel was used as a coupling medium between the probe and the skin. The Doppler signal was monitored by a loudspeaker and continuously recorded at 50 mm/s paper speed on a multichannel recorder, once the probe position was correct. Mean time for measurements was 5 ± 2 min. For one operator repetitive measurements were reproducible with an error of ±4%. Four investigators (C.L., D.P., A.P., S.B.) performed measurements, and interobserver variations averaged 6 ± 1% (SD).

From beat-by-beat cross-sectional blood flow velocity curves, the peak systolic (V_s) and the end-diastolic (V_{ed}) velocities were manually measured. To minimize the influence of mechanical ventilation, each value represented the mean of ten successive cardiac cycles.[18] Then, using V_{ed} end-diastolic blood flow (Q_{ed}) was computed as explained because it correlated well with hemispheric blood flow.[19] In each tracing the presence or absence of an end-
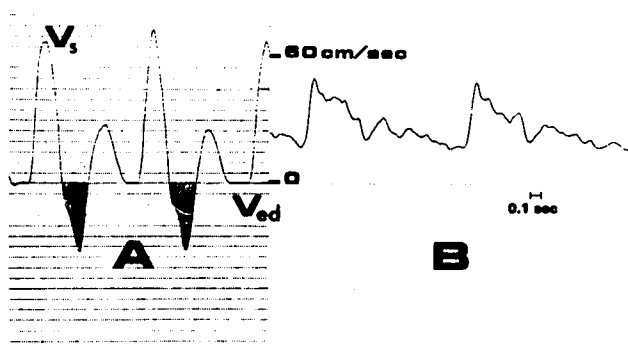
FIG. 1. Typical velocity curves obtained in a case of brain death (A) with end-systolic reverse flow and in one case of severe coma (B). Brain death is characterized by an abolished end-diastolic blood velocity.

systolic reverse flow (RF) was determined (fig. 1). When present, the peak negative flow was measured by reference to the zero line.

Arterial blood gases were obtained by direct puncture of radial artery or sampled from a radial catheter. Jugular venous blood gases were sampled by direct puncture of the jugular bulb or by retrograde catheterization of the internal jugular vein under fluoroscopic control. Arterial and jugular blood oxygen contents were determined conventionally allowing computing of arteriovenous difference in O_2 (a-v D_{O_2} in ml $O_2/100$ ml).

STATISTICAL ANALYSIS

Comparison of the mean values for group 1 and group 2 of the two series was performed using Student's t test (for continuous criteria) and chi-square test (for categorical criteria). To obtain the discriminant parameters for the brain death diagnosis, we used logistic regression analysis.[20] The process of logistic regression analysis was carried out stepwise so that at each step in the process, the most discriminating variable was identified and included in the model. The process stopped when the remaining factors did not increase the discriminating power. The relative importance of each independent factor was indicated by its coefficient and the corresponding likelihood ratio test (chi-square test with 1 degree of freedom).

The results of this logistic discriminant process obtained from the first series yielded a discriminant function that was applied to the second series, allowing us to estimate the probability of misclassification. A cutoff point was thus deducted from the corresponding logistic equation and applied to the second series.[20]

Results

STUDY 1

Clinical characteristics are summarized in table 1. The mean age did not differ between the two groups of pa-

tients. The mean GCS value was significantly higher in group 2 (4.4 ± 0.3; range, 3–6) than in group 1 (3 for all patients) ($P < 0.001$). The mean arterial blood pressure was not different between the two groups (82.7 ± 4.8 *vs.* 85.5 ± 3.3 mmHg).

Table 2 shows the pulsed Doppler and metabolic parameters and their ranges for each group. The presence and the extent of RF velocity were not statistically different between the two groups. A trend toward a decrease in common carotid diameter was noted in brain dead patients, but it did not reach statistical significance. Except for these two parameters, all the variables differed significantly between the two groups. The highest significant levels were observed for V_{ed} and Q_{ed}, which are the two variables with no overlapping values between groups 1 and 2. Moreover, considering each variable separately as an independent variable in a logistic regression showed that these two variables had the highest discriminant power: the 1 degree of freedom chi-square likelihood ratio statistic was 38.8 ($P < 0.001$). The discriminant power of each of these two variables was not significantly improved by adding any other variable to the model.

The cutoff points obtained for the brain death diagnosis were as follows: 2.89 cm/s (95% confidence interval from 0.91 to 4.86) for V_{ed}, and 26.09 ml/min (95% confidence interval from 23.4 to 75.58) for Q_{ed}. Then the clinical decision-making rule was to diagnose a subject as brain dead if his V_{ed} or Q_{ed} values were lower than the cutoff points.

STUDY 2

Applying the decision rule described in study 1, we prospectively classified the 28 patients of study 2 as brain dead (group 1; 36 ± 5 yr) or not (group 2; 39 ± 4 yr). Their clinical characteristics are shown in table 3 and did not differ from those observed in study 1 with regard to mean arterial blood pressure and GCS values.

TABLE 1. Characteristics of the 28 Patients in Study 1

	Group 1 (brain death)	Group 2 (severe coma)
No. of patients	14	14
Age (yr)	35.2 ± 4	36.9 ± 4.2
Sex (M/F)	10/4	7/7
Cerebral disease		
Subdural hematoma	1	2
Epidural hematoma	0	2
Brain contusion	3	6
Gunshot head injury	3	0
Subarachnoid hemorrhage	4	1
Cerebral ischemia	3	3
Mean GCS value	3	4.4 ± 0.3
Survial (no.)/(%)	0/(0)	5/(35)

Values are mean ± SEM.

TABLE 2. Results of CCBF Measurements and Metabolic Parameters from Study 1

	Group 1 (brain death) (n = 14)		Group 2 (severe coma) (n = 14)	
D (cm)	0.410 ± 0.025	(0.277–0.620)	0.460 ± 0.017	(0.381–0.589)
V_m (cm/s)	9.05 ± 0.93	(3–16.5)	22.1 ± 1.7*	(12–37)
CCBF (ml/min)	72 ± 10.7	(32.1–153)	217.7 ± 17.6*	(102.6–308.9)
a-v DO_2 (ml O_2/100 ml)	2.4 ± 0.4	(0.5–5.9)	4.5 ± 0.5†	(1.8–7.5)
V_s (cm/s)	38.6 ± 2.3	(22–51)	49.8 ± 4†	(34.8–87.3)
RF (cm/s)	−8.6 ± 2.8	(−31–0)	−4.7 ± 2	(−20.9–0)
V_{ed} (cm/s)	−1.4 ± 0.8	(−6.3–2.1)	12.7 ± 1.7*	(3.7–26.7)
Q_{ed} (ml/min)	−13.6 ± 7.3	(−69.8–12)	121.4 ± 12.9*	(42.6–182.4)

Values are mean ± SEM; ranges are given in parentheses.
* $P < 0.001$.
† $P < 0.01$.

None of the patients of this series was misclassified; EEG and angiography were used in 21 cases and in 6 cases, respectively, as a confirmatory test. In one case clinical evaluation was sufficient to eliminate brain death diagnosis.

Thereafter parameters were compared in the same manner as in study 1. The results, summarized in table 4, were similar to those obtained in study 1 except for peak systolic velocity, common carotid diameter, and carotid oxygen consumption. The presence and the amplitude ($P < 0.01$) of the RF velocity were significantly higher in the brain death group than in the severe coma group.

In study 2 there was no significant difference in peak systolic velocity between the two groups, and common carotid diameter was less in brain dead patients.

Finally, we considered the overall population to define the cutoff points, specificity and sensitivity more precisely (Table 5). V_{ed} and Q_{ed} were absolutely discriminating between brain death and severe coma groups and therefore had a sensitivity and specificity of 100% for the diagnosis of brain death (figs. 2 and 3). The cutoff points obtained for the diagnosis were as follows: 2.87 (confidence interval

TABLE 3. Characteristics of the 28 Patients in Study 2

	Group 1 (brain death)	Group 2 (severe coma)
No. of patients	14	14
Age (yr)	36.2 ± 5.3	38.9 ± 3.6
Sex (M/F)	11/3	9/5
Cerebral disease		
Subdural hematoma	4	3
Epidural hematoma	1	1
Brain contusion	3	3
Gunshot head injury	2	0
Brain abscess	1	0
Subarachnoid hemorrhage	1	4
Hydrocephalus	1	1
Cerebral ischemia	1	2
Mean GCS value	3	4.6 ± 0.4
Survival (no.)/(%)	0/(0)	7/(50)

Values are mean ± SEM.

from 1.25 to 4.49) for V_{ed} and 31.4 (confidence interval from 1.47 to 61.32) for Q_{ed}.

Figure 1 shows typical velocity tracings obtained from a severe coma and a brain dead patient.

Because of the key point of brain death diagnosis for patients with a GCS of 3, for whom brain stem function is difficult to evaluate, we focused on the analysis of the Doppler data for this particular group. In the overall population we found 32 patients with a GCS of 3: 28 of them were diagnosed as brain dead by EEG alone (n = 26) or by combination of EEG and angiography (n = 2). The four remaining patients were classified in severe coma group by EEG (n = 3) or angiography (n = 1). Table 6 summarizes the comparison between Doppler and reference diagnostic methods.

Discussion

This study demonstrates that CCBF measured by pulsed Doppler technique is an appropriate index of cerebral perfusion, allowing rapid and accurate assessment of brain circulatory arrest and subsequently brain death. Among the measured parameters, the end-diastolic blood flow is the most discriminating parameter, with a sensitivity and specificity of 100% for brain death diagnosis. This bedside technique could provide a noninvasive diagnosis of cerebral circulatory arrest, which might shorten the delay required for diagnosis of brain death and subsequent organ removal and/or for discontinuing active life support.

The pulsed Doppler blood flowmeter technique has been previously widely validated[10-14] and used in clinical practice, especially for common carotid blood flow measurements[10,18,21,22] and measurement of other regional blood flows.[23]

Because low blood velocity measurements during diastole are crucial for brain death diagnosis, the resolution and the Doppler shift analysis system are extremely important. The resolution of our apparatus (1.9 cm/s) was

TABLE 4. Results of CCBF Measurements and Metabolic Parameters from Study 2

	Group 1 (brain death) (n = 14)		Group 2 (severe coma) (n = 14)	
D (cm)	0.448 ± 0.021	(0.346–0.660)	0.514 ± 0.018*	(0.416–0.690)
V_m (cm/s)	8 ± 1.2	(2–18)	21.5 ± 2.2†	(12–38)
CCBF (ml/min)	71.9 ± 9.8	(19.1–164.1)	260 ± 20.6†	(133–412)
a-v DO_2 (ml O_2/100 ml)	2 ± 0.3	(0.12–4.1)	4.3 ± 0.5†	(2.2–7.7)
V_s (cm/s)	43.9 ± 4.3	(24–73.3)	45.8 ± 2.6	(30.5–64.1)
RF (cm/s)	−13.2 ± 3.1	(−38.1–0)	−5 ± 2.7†	(−30–0)
V_{ed} (cm/s)	−0.3 ± 0.5	(−7–1)	16.2 ± 1.9†	(6–30.7)
Q_{ed} (ml/min)	−4.2 ± 5.9	(−77.6–9.5)	191.9 ± 16.9†	(90.5–338.7)

Values are mean ± SEM; ranges are given in parentheses.   † $P < 0.001$.
* $P < 0.01$.

appropriate for this study, and the lowest diastolic value in severe coma was 9.65 cm/s.[22] Doppler frequency shift was determined by a zero crossing detector, which has physical limitations because of electrical noise, which can result in false-positive velocity.[24] This problem was overcome by using an offset trigger level and a set/reset system. The advantages of this configuration can be summarized as follows: with signal plus noise the Doppler output is proportional to the signal frequency; with noise alone the output is zero; the output is constant over a range of Doppler input amplitude.[24] An error for end-diastolic velocity could be only an overestimation. However, although brain death seems to be diagnosed when end-diastolic velocity is lower than 2.87 cm/s, this suggests that these theoretical problems have no implications for this study.

The pulsed Doppler apparatus used with a double transducer probe permits an accurate internal arterial diameter measurement because of the precise knowledge of the ultrasonic incidence angle.[12,13,21] The accuracy is also improved by the absence of spatial ambiguity ensuring the measurement of flow for only the chosen vessel. The validation of pulsed Doppler diameter measurements has been carried out previously by Levenson et al. using the same apparatus.[12] The comparison between actual diameters and ultrasonic diameters of calibrated latex tubes showed an overestimation by the Doppler of approximately 0.35 mm. The smallest diameter measured in our study was 2.8 mm, resulting in a maximum error of 12.5% and a minimum error of 5%. In summary, the technique used in this study permits accurate vessel diameter, cross-sectional blood velocity, and blood flow measurements, due to a precise knowledge of the incidence angle, an electronic limitation of noise impact, and the absence of spacial ambiguity.

We have previously demonstrated that CCBF is related to hemispheric perfusion ($r = 0.73$, n = 21, $P < 0.001$),[10] the significantly lower CCBF values observed in patients with brain death compared with those with severe coma is not surprising. However, CCBF in brain death groups differed from zero because CCBF also concerns external carotid blood flow.[6]

In the case of brain death, it was demonstrated that the common carotid velocity patterns were strictly similar to those measured on the external carotid artery.[6] The average of mean CCBF in brain dead patients in this study was similar to external carotid blood flow value in humans. It can be concluded that almost all of the blood from the common carotid artery flowed into the external carotid in brain dead patients.[6,7]

TABLE 5. Results of CCBF Measurements and Metabolic Parameters from Overall Population

	Group 1 (brain death) (n = 14)		Group 2 (severe coma) (n = 14)	
D (cm)	0.43 ± 0.02	(0.28–0.66)	0.49 ± 0.01*	(0.38–0.69)
V_m (cm/s)	8.5 ± 0.7	(2–18)	21.8 ± 1.3†	(12–38)
CCBF (ml/min)	71.8 ± 7.1	(19.1–164.1)	238.9 ± 13.9†	(102.5–412)
a-v DO_2 (ml O_2/100 ml)	2.2 ± 0.3	(0.12–5.9)	4.4 ± 0.3†	(1.8–7.7)
V_s (cm/s)	41.2 ± 2.5	(22–73.3)	47.8 ± 2.4	(30.5–87.3)
RF (cm/s)	−10.9 ± 2.1	(−38.1–0)	−26 ± 1.1†	(−20.9–0)
V_{ed} (cm/s)	−0.9 ± 0.5	(−7–2.1)	14.5 ± 1.3†	3.7–30.7)
Q_{ed} (ml/min)	−8.9 ± 4.7	(−77.5–12)	156.6 ± 12.4†	(42.6–338.7)

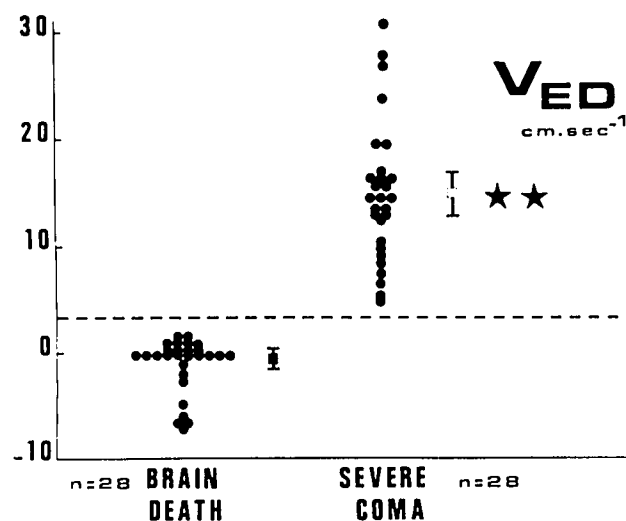Values are mean ± SEM; ranges are given in parentheses.   † $P < 0.001$.
* $P < 0.01$.

FIG. 2. Individual and mean ± SEM values of end-diastolic velocity values for the overall population. Dotted line corresponds to the cutoff point for brain death diagnosis. **$P < 0.001$.
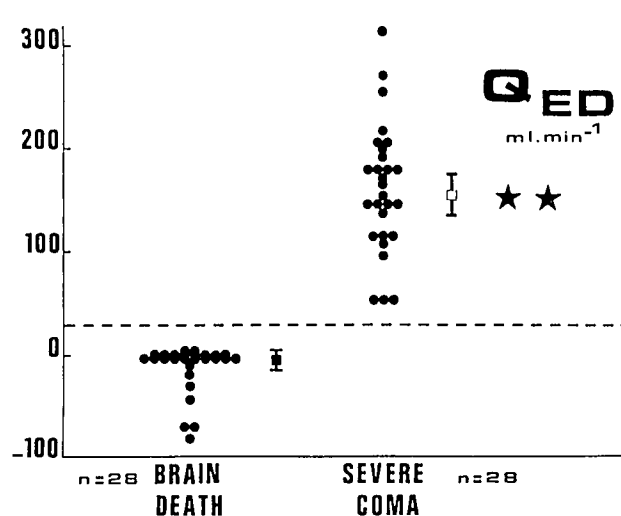

FIG. 3. Individual and mean ± SEM values of end-diastolic blood flow in the overall population. Dotted line corresponds to the cutoff point value for brain death diagnosis. **$P < 0.001$.

Few studies on common carotid blood flow velocity and not on flow in brain dead patients have been published.[6,9] All of them contained only information about the aspect of the velocity tracings, without any quantitative data. However, despite the methodologic limitations, these previous reports emphasized the possible usefulness of Doppler technique for brain death diagnosis. Based on the shape of the velocity tracings, Yoneda et al. concluded that brain death was characterized by "a single systolic peak and a marked reverse flow component."[6] The specificity of these patterns was questioned by Lewis et al.,[25] who reported a case of a patient having the criteria put forth by Yoneda et al.[6] but was discharged with no evident mental alteration. Kreutzer et al.[7] compared velocity patterns of brain dead patients with those from normal subjects, patients with arteriosclerotic internal carotid occlusion, and comatose patients. Using a multidimensional discriminant analysis, they found "pathognomonic" of brain death, the presence on common carotid velocity tracings of sharp systolic and diastolic peaks, and negligible end-diastolic velocity. However, the authors reported a false-positive diagnosis of brain death, which invalidated the use of the proposed criteria.[7]

Although the common carotid artery is an extracranial vessel, its velocity wave forms might differ from those of the intracranial vessels, especially in brain death. Recently, McMenamin and Volpe[9] reported velocity patterns of common carotid and middle cerebral arteries during brain death in newborns. They showed similar blood velocity modifications in both arteries, such as a loss of diastolic flow and an appearance of retrograde flow during diastole. The aspects of cross-sectional velocity tracings in our study

were comparable to those obtained by McMenamin and Volpe.[9]

Because of the technical advantages of our system and the limitation of the previous reports to qualitative criteria, we attempted to provide quantitative values and to define a threshold below which brain death diagnosis would be certain. Before the discussion of the results, we should note that carotid measurements were performed on only one side. This was decided after the first eight measurements performed in both carotids. The mean difference between both sides was less than 10%, a value that included the small inequality between carotid arteries and errors due to the machine and the investigators. Moreover, it was shown that in head-injured comatose patients focal changes in cerebral blood flow were of smaller magnitude than the global perfusion and the difference between the two hemispheres was small.[26] This practice could be incorrect in the presence of carotid artery lesions, such as stenosis or thrombosis. However, it was demonstrated that velocity patterns were completely different in patients with atherosclerotic carotid lesions and in brain death.[7,11] Furthermore, organ procurement

TABLE 6. Pulsed Doppler *Versus* Conventional Methods for the Diagnosis of Brain Death in 32 Patients (studies 1 and 2) with a GCS of 3

	EEG	Angiography	Doppler
Severe coma (n = 4)	3	1	4
Brain death (n = 28)	28	2	28

Note that two patients with brain death diagnosis received both EEG and angiography.

essentially concerns young people (younger than 35 yr), which considerably reduces the potential impact of atherosclerosis. This problem would probably be reconsidered in the future as age criteria for organ removal change.

The first part of this prospective study allowed us to define discriminant parameters for brain death diagnosis. This study covered a population of patients with an established diagnosis based on clinical and electroencephalographic or angiographic examination. The use of logistic regression analysis showed that end-diastolic velocity (V_{ed}) and blood flow (Q_{ed}) classified 100% of the brain dead patients without any false-positive diagnosis in the severe coma group. The second part of the study blind tested the validity of these diagnostic parameters on a second study of patients with severe coma (GCS < 7). The Doppler classification was then compared with the results of the conventional methods used for brain death diagnosis. Once again, no misclassification was noted between severe coma and brain dead patients. Because V_{ed} and Q_{ed} are dependent variables, they have the same discriminant power using the likelihood ratio test, i.e., 38.7. However, using Student's t test, Q_{ed} can be considered the most powerful variable and can be used alone for classification (table 5). For the clinician this result permits avoiding jugular blood gas analysis, offering a strictly noninvasive assessment of brain death. Data from both studies were pooled to define a cutoff value for brain death diagnosis on a larger population. The Q_{ed} value confirming a diagnosis was 31.4 ml/min. For an individual patient the clinical diagnostic rule indicates a diagnosis of brain death if Q_{ed} is less than 31.4 ml/min and an absence of brain death if Q_{ed} is above this value. Because Q_{ed} depends on carotid diameter and end-diastolic blood velocity, these data should be discussed.

Although end-systolic back flow has previously been proposed as a brain death criterion, it appeared in our study to be nonspecific, as suggested by Lewis et al.[25] Even though it was more frequently observed in brain dead patients, it was also present in patients with severe coma. In addition, quantitative measurements of negative peak velocity of the back flow were not significantly different between the two groups. This retrograde movement of the blood results from the increased downstream resistance associated with carotid systolic blood loading.[27]

An arteriojugular difference in oxygen less than 2 ml O_2/100 ml has also been proposed for brain death diagnosis.[4] Although a-v D_{O_2} was statistically less in patients with brain death, the discriminant power was low. The large overlapping of the values between the two groups and the power of Q_{ed} renders measurement of a-v D_{O_2} of little interest with respect to diagnosing brain death.

In conclusion, although these results need to be confirmed for a larger population, this study demonstrates that pulsed Doppler for CCBF measurements in combination with accepted clinical criteria provide a rapid, accurate, and noninvasive assessment of cerebral circulatory arrest in young brain dead patients that can be performed at the patient's bedside. However, before legal acceptance of these criteria, this inexpensive method could be helpful, especially in small institutions, to prompt performance of legally accepted diagnostic procedures. A beneficial impact on reducing the delay for organ removal and on improving availability of organs for transplants could be expected.

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