Brazilian Journal of TRANSPLANTATION

https://doi.org/10.53855/bjt.v26i1.502_ENG

ORIGINAL PAPER

# Status of Brain Death Diagnosis in Brazil: The Role of Transcranial Doppler Ultrasonography

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Received: Feb. 14, 2023 | Accepted: Mar. 01, 2023

Section Editor: Ilka de Fátima Santana F Boin

How to cite: Barros MA, Kessler IM. Current Overview of Brain Death Diagnosis in Brazil: Role of Transcranial Doppler Ultrasonography. BJT. 2023.26 (01):e1323. https://doi.org/10.53855/bjt.v26i1.502_ENG

## ABSTRACT

Transcranial Doppler Ultrasonography (TCDU) comprises an indispensable tool for brain death (BD) protocol closure due to its practicality and low cost. In Brazil, it is used in most organ procurement organization (OPO) centers for this purpose. The evaluation of its importance in the diagnosis of BD in Brazil nowadays constitutes the main scope of this work. **Objectives:** analysis of the results of TCDU from a series of 100 consecutive patients with clinical diagnosis of BD, with calculation of sensitivity and time intervals for closure of protocols. Evaluation of the variables gender, age, diseases causing death and presence of decompressive cranial surgery in relation to time to death. **Methods:** evaluation of CT scans, TCDU and medical records of patients on BD protocol with statistical analysis of the sample. **Results:** 145 TCDU examinations in 100 patients (62% male) were evaluated. Systolic spicules were found in 40.1%, reduced flow velocity in 12.9%, diastolic reversal in 8.3%, no flow in 5.2% and normal flow in 3.5%. Sensitivity ranged from 69% to 90.5% when repeated serially. The mean time to complete the protocols was 35.4 hours (SD=±48.2h), with the majority (59.5%) within 24 hours. There was no statistically significant correlation between gender, age or diagnostic variables, presence of decompressive craniectomy and time to death. **Conclusion:** most TCDU confirmed the status of BD, but a small percentage (9.5%) did not complete the diagnosis, delaying the protocol in these cases.

Keywords : Transcranial Doppler Ultrasonography. Brain Death.

## *Panorama Atual do Diagnóstico de Morte Encefálica no Brasil: Papel da Ultrassonografia Doppler Transcraniana*

## RESUMO

A Ultrassonografia Doppler Transcraniana (UDTC) compreende uma ferramenta imprescindível para o fechamento de protocolo de morte encefálica (ME) devido à sua praticidade e baixo custo. No Brasil é utilizado na maioria dos centros de organização de procura de órgãos (OPO) para este fim. A avaliação da importância do mesmo no diagnóstico de ME no Brasil nos dias atuais constitui o principal escopo deste trabalho. **Objetivos:** análise de resultados de UDTC de uma série de 100 pacientes consecutivos com diagnóstico clínico de ME, com cálculo de sensibilidade e intervalos de tempo para fechamento de protocolos. Avaliação das variáveis sexo, idade, doenças causadoras do óbito e presença de cirurgias cranianas descompressivas em relação ao tempo até o óbito. **Métodos:** avaliação de tomografias computadorizadas, exames de UDTC e prontuários de pacientes em protocolo de ME com análise estatística da amostra. **Resultados:** foram avaliados 145 exames de UDTC em 100 pacientes (62% masculino). Espículas sistólicas foram encontradas em 40,1%, velocidade de fluxo reduzida em 12,9%, reversão diastólica em 8,3%, ausência de fluxo em 5,2% e fluxo normal em 3,5%. A sensibilidade variou de 69% a 90,5% quando repetido em série. O tempo médio para completar os protocolos foi de 35,4 h (DP=±48,2h), com a maioria (59,5%) em até 24h. Não houve correlação estatisticamente significativa entre o sexo, idade ou variáveis diagnósticas, presença de craniectomia descompressiva e o tempo até o óbito. **Conclusão:** a maioria das UDTC confirmou o *status* de ME, mas pequena porcentagem (9,5%) não concluiu o diagnóstico, atrasando o protocolo nesses casos.

Palavras-chave: Ultrassonografia Doppler Transcraniana. Morte cerebral.

## INTRODUCTION

Brain death (BD) is characterized by irreversible damage to the brain, leading to death of the individual. The main causes are hypoxic-ischemic encephalopathies, traumatic brain injury, and stroke[1]. According to the CFM Resolution no. 2.173/2017, the attending physician is responsible for the initial diagnosis of BD, and this is obtained through a clinical history, physical examination, and complementary tests (required by Brazilian law)[2].

Some criteria must be present: total absence of brain activity, known cause, sufficient and irreversible, with imaging exams proving such an event, excluding alcohol or depressant drug intoxication.[3,4] The current protocol evaluates the following reflexes: pupillary control, ocular-cephalic, cornea-palpebral, vestibule-caloric, cough, apnea test, and motor reactions to painful stimuli. Two clinical examinations performed by two different physicians (with a minimum one-hour interval between them), an apnea test, and a complementary examination are required for this purpose in Brazil.[4]

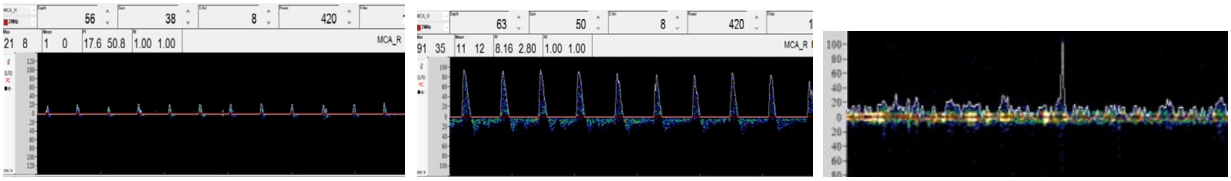
Transcranial Doppler ultrasound (TCDU) is one of the most widely performed complementary tests worldwide for the final diagnosis of BD because it is practical, relatively inexpensive, and easy to repeat.[5]

This article aims to analyze and describe the findings of TCD U in a series of consecutive patients with clinical diagnosis (suspected or confirmed) of BD, evaluating the sensitivity, the time intervals between the clinical and complementary exams performed and the description of the epidemiological profile, checking whether the variables gender, age, disease causing BD and presence of decompressive cranial surgery correlated with the longer time to close the protocols.

## METHODS

This is a prospective cross-sectional analytical study, including 109 consecutive patients seen in a tertiary hospital unit between May 2020 and April 2021 notified to the Organ Procurement Organization (OPO) with a clinic of BD, identified with first clinical examination and radiological investigation by cranial CT and TCD U. All patients were with systolic blood pressure above 90 mmHg, heart rate above 60 bpm, no hypoxemia (SpO2 >95%), and temperature above 35 °C. We excluded patients who did not have a CT scan of the cranial (image available), TCD U results not recorded in the device, patients with delayed clinical exams, apnea test or TCD U over 24h. The clinical examinations and the TCD U were performed by the OPO medical team (7 professionals) in the following sectors of the hospital: ICU, emergency rooms, hemodynamics, and post-anesthesia recovery. The TCD U exams followed the protocol standardized by The Brazilian Consensus on Neurosonology for BD diagnosis, 6 being performed in series (about 24, 72 or 96 hours after the first) when they did not show patterns of cerebral circulatory failure (CCF) in the first analysis. A Box X DWL Doppler device (ElektronischeSystemeGmbH, Germany, 2018) with a 2 MHz probe was used. The inconclusive cases of ME in the TCD U were subjected to other complementary diagnostic methods, such as angiography and electroencephalogram (EEG) by the same team.

The results of Doppler examinations, cranial CT and electronic medical records were collected by a single physician. The following variables were analyzed: age, gender, etiology of BD, time of protocol closure, TCD U results, CT scan results, and presence of decompressive surgery. As for the TCD U, the patterns of cerebral circulatory failure (CCF) compatible with BD were those of diastolic reversal, systolic spicules, or no flow, the latter only when a previous examination showed some residual flow as shown in Fig. 1. Such patterns had to be present in both middle cerebral arteries, vertebral arteries and eventually in the carotid siphons and basilar artery.



Systolic spikes | Diastolic reversal | Absence of signal

Source: Author's own

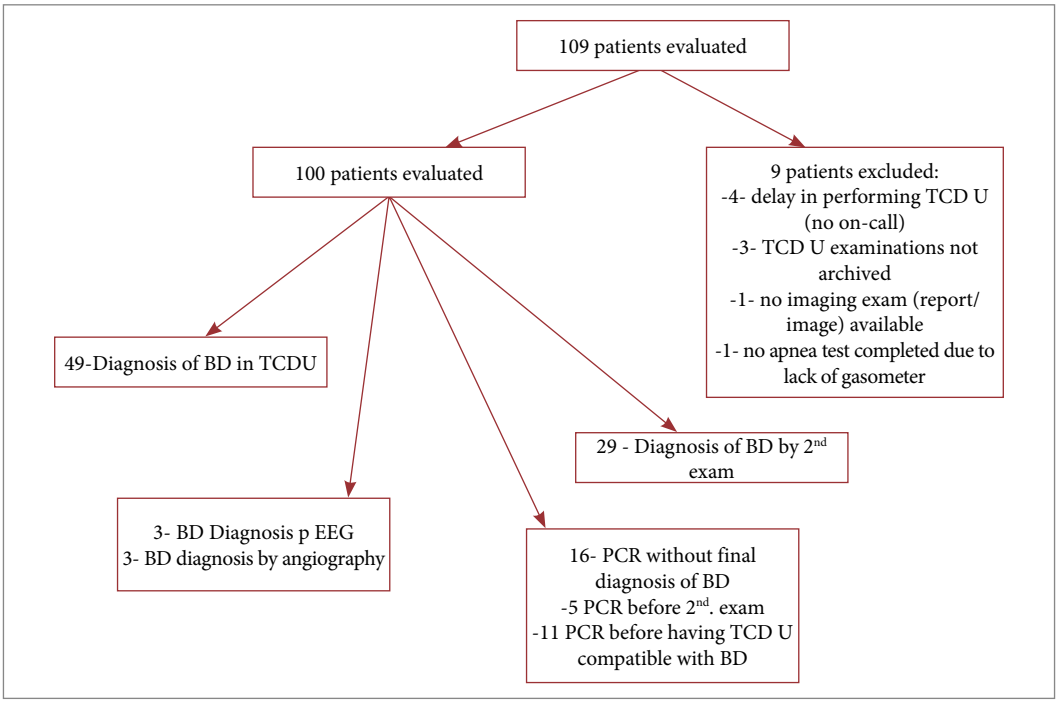
**Figure 1.** Brain death patterns on transcranial Doppler ultrasound.

Statistical analysis used IBM SPSS (Statistical Package for the Social Sciences) 23, 2015 software. The significance level used in all studies was 5%. The study was divided into agreement and association/correlation analysis. The result of the first clinical examination for BD was considered the gold standard and used as the reference in the concordance analysis. To determine the normality of data distribution and considering time as a quantitative variable, the Kolmogorov-Smirnov test was applied. For all times, non-parametric tests were applied, rejecting the null hypothesis. The 16 patients who had cardiac arrest before the final diagnosis of brain death (Fig. 2) were not used in the agreement analysis, therefore, they did not enter the sensitivity calculation.

The Project was submitted to the CEP (Conselho de Ética em Pesquisa "Research Ethics Board") of the tertiary hospital unit in September 2019, approved, according to REC/IGES-DF Opinion no. 3,955,101 of 05/04/2020 and followed all ethical aspects described in CNS/MS Resolution 466/2012.

## RESULTS

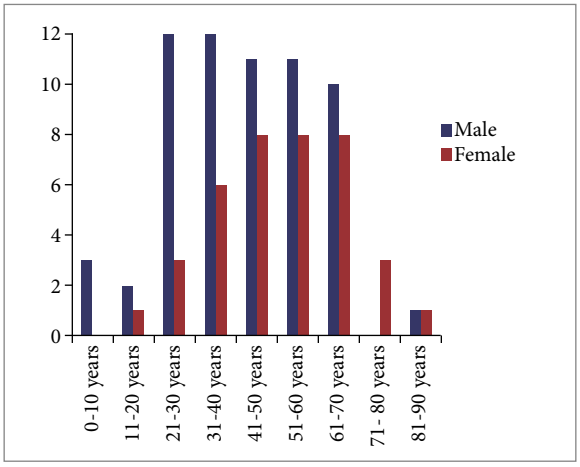
From May 2020 to April 2021, the electronic medical records and cranial CT scans of 109 consecutive patients with brain death clinic notified to OPO, who performed at least one TCD U as a complementary diagnostic exam, were evaluated. Three patients were excluded due to lack of recording of the TCD U exams in the device, 1 due to loss of the CT exam, 4 due to delay in performing the TCD U exams (more than 24h) and 1 due to unavailability of the device gasometer to perform the apnea test according to Fig. 2.




Source: Author's.

**Figure 2.** Flowchart of analyzed patients.

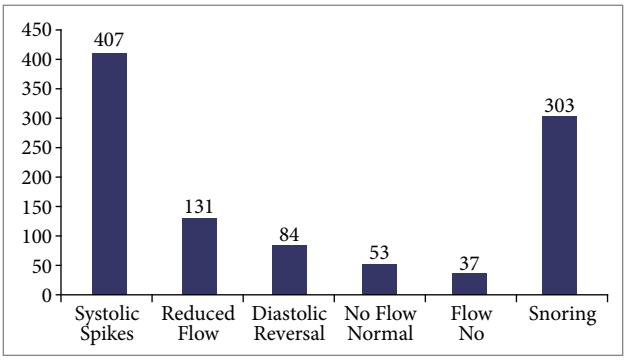
One hundred and forty-five TCD U examinations in 100 patients were analyzed, 62% male and 38% female. One TCD U examination was performed in 73 patients, two in 12 patients, three in 12 patients, and four in 3 patients. The age range and sex, as well as the prevalence of diseases associated with BD, are summarized in Fig. 3.




Source: Author's.

**Figure 3.** Epidemiological profile of the sample by age and sex.

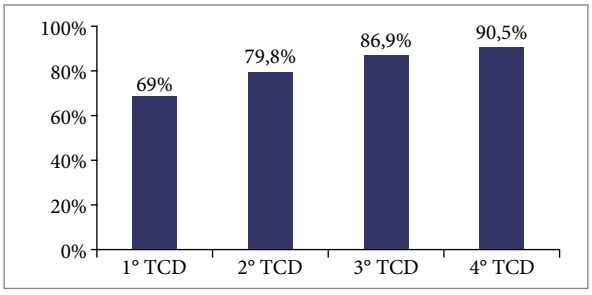
Systolic spicule patterns were described in 40.1%, reduced flow velocity in 12.9%, diastolic reversal in 8.3%, no flow in 5.2% and normal flow velocity in 3.5% as shown in Fig. 4.




Source: Author's.

**Figure 4.** Main findings of transcranial Doppler ultrasound examinations.

The sensitivity of the test ranged from 69 to 90.1% when performed serially (Fig. 5). The mean time between the two clinical examinations was estimated to be 12.9h (SD=±12.4h) and the mean time between the first clinical examination and the first TCDU was 12.5h (SD=±12.6h).




Source: Author's.

**Figure 5.** Sensitivity of transcranial Doppler ultrasound in sequential examinations.

The mean time to complete the protocol was estimated at 35.4h (SD=±48.2h). The range ranged from 1.6h to 291.2h (12 days and 13h) with the majority (59.3%) being completed within 24 hours of initiation (48% between 6 and 12h). Only 16.6% were completed within 6 hours and 9.5% were completed within 96 hours.

Table 1 shows the statistical correlation between sex and time to death in hours, with no statistical difference between the two sexes using the Mann-Whitney U-test.

**Table 1.** Association between the time until death (brain death confirmation) and the variable gender.

| Gender | Time until death (hours) | | *P** |
|---|---|---|---|
| | Median | Interquartile range | |
| Male | 25.44 | 41.04 | 0.752 |
| Female | 22.56 | 53.28 | |

* Mann-Whitney's U-test. Source: Author's.

The correlation between the diagnostic variables correlated with the etiology of BD and the time until the end of the protocol did not show statistical significance according to the Kruskal-Wallis's test, as presented in Table 2.

**Table 2.** Association between the time until death (brain death confirmation) and the diagnosis variables in notified patients.

| Diagnosis | Time until death (hours) | | *P** |
|---|---|---|---|
| | Median | Interquartile range | |
| Hemorrhagic Stroke | 25.22 | 55.33 | 0.055 |
| Ischemic stroke | 20.13 | 17.89 | |
| Anoxic Encephalopathy | 9.00 | 29.08 | |
| Spontaneous subarachnoid hemorrhage | 36.93 | 101.36 | |
| Brain Infection | 71.87 | 90.98 | |
| Firearm projectile | 84.42 | 85.21 | |
| Traumatic brain injury | 21.24 | 25.45 | |
| Brain tumor | 18.58 | 110.80 | |

* Kruskal-Wallis's test. Source: Author's.

The time to death confirmation and age were analyzed by the non-parametric Spearman correlation, considering that time did not present a normal distribution. Table 3 shows that there was no correlation between the time to death and the patient's age.

**Table 3.** Correlation analysis between the time until death (brain death confirmation) and the age of the notified patients.

| | | Age |
|---|---|---|
| Time until death | Spearman's Correlation Coefficient* | 0.012 |
| | *P* | 0.905 |
| | n | 100 |

Non-parametric Spearman's correlation*. Source: Author's.

The performance of decompressive surgery (craniectomies, EVD, ICP monitor) and the association with increased time to diagnosis of BD were related by calculating the Odds-Ratio between the variables' surgery versus no diagnostic confirmation at the first TCD. This relationship was weakly positive, with a value of 1.942, and the application of Pearson's chi-square test with continuity correction showed no statistically significant correlation between these variables in this study (P=047.3, CI=95%) as shown in Table 4.

**Table 4.** Association between the performance of surgery and non-confirmation of brain death in the 1st transcranial Doppler ultrasound examination in notified patients.

| | | | Confirmation at the 1st TCD U | | Total | OR | C.I.95% | *P** |
|---|---|---|---|---|---|---|---|---|
| | | | Yes | No | | | | |
| Surgery | No | n | 55 | 34 | 89 | 1.942 | 0.550 – 6.849 | 0.473 |
| | | % | 61.8 | 38.2 | 100 | | | |
| | Yes | n | 5 | 6 | 11 | | | |
| | | % | 45.45 | 54.55 | 100 | | | |
| Total | | n | 60 | 40 | 100 | | | |
| | | % | 60 | 40 | 100 | | | |

TCD U = Transcranial Doppler Ultrasound; OR= Odds Ratio; CI= Confidence Interval * Pearson's chi-square test with continuity correction. Source: Author's.

## DISCUSSION

The Brazilian legislation related to the diagnosis process of BD is still very strict, requiring four minimum steps (two clinical exams, apnea test and complementary exam) for its completion and a team of at least two physicians trained to perform it, as well as minimum parameters for its development.[2]

The need for confirmation of possible organ donors, the growing demand for intensive care beds, and cost reduction make the diagnosis of BD an essential service in large hospitals.[7-8] We think that this series, which, we believe, is the first study on the subject in Brazil after the new CFM Resolution - no. 2,173/2017, is of great relevance, considering the number of patients and the uniformity of having been performed in a single service, with the same protocol and data collection by a single researcher. Most studies involving TCD U and BD, according to the most recent meta-analysis,[6] evaluated less than 100 patients[9-11].

The flow velocity parameters in the vessels studied showed systolic spikes patterns in 40.1%, reduced flow velocity in 12.9%, diastolic reversal in 8.3%, no flow in 5.2%, and normal flow velocity in 3.5%. The sensitivity of the test ranged from 69 to 90.1% when performed serially. DOMINGUEZ-ROLDAN [12] found systolic spicule patterns in 11 patients evaluated (45.8%) and diastolic reversal in 9 (37.5%). HASSLER, STEINMETZ, and PIRCHEL[9] showed 26.9% systolic spikes, 20% diastolic reversal, and 53% no detected flow in their series. DUCROCQ et al.13 showed diastolic reversal in 73% and systolic spikes in 24%, with only 3.8% absence of flow in their series.

These findings reflect different levels of an ascending curve of a continuous phenomenon that is cerebral circulatory failure (CCF). Some authors have had more patients in a situation of frank failure, characterized by the absence of cerebral blood flow. All of them show that most of the patients present results compatible with one of the patterns described above, except a small portion that has not yet entered the CCF curve. It is noteworthy that in relation to the patterns of flow velocity described in this series, there is probably a sampling bias, considering that 29.85% of the windows (303/1015) were not evaluated, due to not performing completely some tests (at the examiner's discretion) because viable flow was evidenced in one of the main diagnostic arteries at the beginning of the procedure.

The sensitivity curve of the TCD U for confirming BD has been the subject of several studies with ranges ranging from 53% 14 to 100%.[14-15] The present study showed a sensitivity range of 69 to 90.1%, like several studies.[7,13,16.17] It is also believed

that the differences are due to the different samples as well as the methodologies applied to perform the test, which is not standardized worldwide.

The protocol was completed within 6 hours in 16.6% of cases, 48% between 6–12 hours, and 59.3% within 24 hours. Only 9.5% in more than 96 h, which is compatible with other listed studies, even with differences in the methodology of performing the TCD Us as well as the clinical diagnostic tests. In one study,[8] of 28 patients out of 84 (33.33%) completed the protocol in 24 hours, 18 patients in 48 hours, and 9 patients in 72 hours. In another study,18 only 5% of patients completed the protocol within 12 hours, 16% within 24 hours, and 47% within 48 hours. While another study[19] showed a distribution curve of 44% in 12 hours, 25.5% in 24 hours and 22% in more than 24 hours.

Although it is recommended that the time to perform a TCD U for the first examination be as short as possible,[2] the estimated mean time to perform the first TCD U after the first clinical examination was 12.5h (SD=±12.5h) in this series. Several factors accounted for this delay: hypotension after the initial clinical examination (6 patients), hypothermia (one patient), delay in communication from the assisting team (10 patients), and delay by the team to perform the examination (6 patients). The mean time between the two clinical examinations was 12.9h (SD±12.4h).

The correlation sex versus protocol completion time showed values of 25.4 hours for men and 22.5 hours for women. Using the Mann-Whitney U test, no statistical correlation was found for the difference in protocol completion time between them. One study[19] described a series of 270 patients, with a statistical difference, that the time to loss of flow signal was higher for women (Odds ratio of 3.7; P=0.03), but the same authors in another series of 100 patients did not find this difference[20]. In no other work this relationship is studied, with little basis to be stated.

The causes of BD were also correlated with the time of protocol termination through the Kruskal-Wallis's test. One study[21] mentioned that the confirmation of BD by TCD U is influenced by the causative mechanism and, in some cases, the theory of a classical mechanism of a supratentorial injury causing mass effect and subsequently increasing ICP, causing a trans tentorial herniation, would lead to a faster CCF, differing from the mechanism of diffuse edema, as in anoxic encephalopathy, diffuse subarachnoid hemorrhage, or diffuse cerebral edema post TBI. These would, in theory, have more time to maintain a viable intracranial flow. However, one study[19] showed no significant difference in time between the different mechanisms of BD. Our results also showed no difference in this respect (P=0.055).

One research[21] suggests that decompression surgeries may slow down the process of CCF by reducing the ICP caused by the bony decompression itself. He also mentions that children with open fontanelles may also present the same problem of flow persistence in examinations due to compensatory mechanisms of ICP. Two cases of operated patients with flow persistence, however, do not conclude that this relationship is true, considering that other five patients evaluated persisted with flow even without having been operated.[22]

One study[20] found no difference in their series regarding this aspect. While another study[13] described only one patient with flow maintenance in the TCD when evaluated for BD, and this patient had been submitted to craniectomy. In the same series, 13 patients were children and none of them had delayed diagnosis of BD. The present study found Odds Ratio of 1.942 for the variable decompressive surgery *versus* negativity in the first TCD U, suggesting that such a relationship exists, but it was low and not statistically significant.

In the present study, of the three patients under the age of 10 years, only one patient (male, 6 years old, TBI victim, submitted to craniectomy) showed flow maintenance in the first TCD, performed 14 hours after the first clinical examination, and was compatible in the second TCD performed 42 hours later. The other two patients (TBI and stroke victims, respectively) had their first DTC already compatible. However, neither of them was less than one year old.

Finally, in general, the TCD is examiner-dependent [22,24] with possible biases, but the error rate for using the probe with an angle close to 90° in almost all evaluations is close to zero. Some studies[13,19] describe a single examiner for their entire series, but most do not report it[9,15] and others mention "specialized team "[12]. "*O Consenso Brasileiro de Neurossonologia*" (The Brazilian Consensus on Neurosonology) for the diagnosis of BD does not specify the need for the examiner to be the same in cases of serial diagnoses of TCDU to BD.[6]

For calculation purposes, only the first TCD U performed was considered for comparison with imaging exams. Since the mean time to perform the first TCD was 12.5 hours (SD= ±12.5 hours), it is believed that this time interval may have influenced the results found.

## CONCLUSION

The present study evaluated the findings of TCD U in a series of patients with a clinical diagnosis of BD (confirmed or not), analyzing the sensitivity of the exam, the time intervals between the clinical and complementary exams performed, and the epidemiological profile of the population studied.

Systolic spicule patterns were the most described (40.1%) and the sensitivity of the test ranged from 69% to 90.5%, increasing as the tests were repeated serially.

There was no evident statistical correlation between gender, causative disease or age with the time to end of protocol, considering that CCF is a dynamic and individual process. There was no evidence that cranial decompression procedures increased the time to diagnosis of BD completion.

Although the TCD U is an important tool for the final confirmation of the diagnosis of BD, in some cases the test did not demonstrate this response (9.5%), delaying the final confirmation of BD.

The current Brazilian BD protocol, although designed to be completed within one hour of its opening, has extended in this casuistry mostly 12 hours or more, with another minority going beyond this interval.

## CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

## FINANCING

This research did not receive a specific grant from any funding agency in the public, commercial, or non-profit sectors.

## AUTHORS' CONTRIBUTION

**Substantive scientific and intellectual contributions to the study:** Barros MA; **Conception and design:** Barros MA; **Data analysis and interpretation:** Barros MA; **Article writing:** Barros MA; **Critical revision:** Kessler I; **Final approval:** Barros MA.

## AVAILABILITY OF RESEARCH DATA

All dataset were generated or analyzed in the current study.

## ACKNOWLEDGMENTS

We thank the whole NOPO-DF team, composed of doctors, nurses, and nursing technicians, who contributed to the basis of this work.

## REFERENCES

1. André C. O Guia Prático da Neurologia. Rio de Janeiro: Guanabara Koogan; 1999. p.70-3.
2. Conselho Federal de Medicina (CFM – Brasil). Resolução CFM nº 2.173 de 23 de novembro de 2017. Define os critérios do diagnóstico de morte encefálica. Brasília: Diário Oficial da União, 15 de dezembro de 2017, Ed: 240. Seção 1, p. 250-75. Retrieved from: https://portal.cfm.org.br/noticias/cfm-atualiza-resolucao-com-criterios-de-diagnostico-da-morte-encefalica/. Accessed on:
3. Dominguez-Roldan JM, Garcia-Alfaro C, Jimenez-Gonzalez PI, Rivera-Fernandez V, Hernandez-Hasanas F, Perez-Bernal J. Brain death due to supratentorial masses: diagnosis using transcranial Doppler sonography. Transplant Proc. 2004 Dec;36(10):2898-900. https://doi.org/10.1016/j.transproceed.2004.11.017.
4. Westphal GA, Veiga VC, Franke CA. Determinação da morte encefálica no Brasil. Rev. bras. ter. intensiva. 2019;31(3):403-9. Retrieved from: https://doi.org/10.5935/0103-507X.20190050.
5. Aaslid R, Newell DW. Transcranial Doppler. New York: Raven Press; 1986. p. 1-8.
6. Lange MC, Zétola VF, Miranda-Alves M, Moro CHC, Silvado C E, Rodrigues DLG, et al. Brazilian guidelines for the application of transcranial ultrasound as a diagnostic test for the confirmation of brain death. Arq. Neuro-Psiquiatr. 2012 May;70(5):373-80. https://doi.org/10.1590/S0004-282X2012000500012.

7. Dosemeci L, Dora B, Yilmaz M, Cengiz M, Balkan S, Ramazanoglu A. Utility of transcranial Doppler ultrasonography for confirmatory diagnosis of brain death: two sides of the coin. Transplantation. 2004 Jan; 77(1):71-5. https://doi.org/10.1097/01.TP.0000092305.00155.72.

8. Hadani M, Bruk B, Ram Z, Knoller N, Spiegelmann R, Segal E. Application of transcranial Doppler ultrasonography for the diagnosis of brain death. Intensive Care Med. 1999 Aug;25:822–8. https://doi.org/10.1007/s001340050958.

9. Hassler W, Steinmetz H, Pirchel J. Transcranial Doppler study of intracranial circulatory arrest. J Neurosurg. 1989 Aug;71(2):195-201. https://doi.org/10.3171/jns.1989.71.2.0195.

10. Paolin A, Manuali A, Di Paola F, Boccaletto F, Caputo P, Zanata G, et al. Reliability in diagnosis of brain death. Intensive Care Med. 1995;21:657-62. https://doi.org/10.1007/BF01711544

11. Powers AD, Graeber MC, Smith RR. Transcranial Doppler ultrasonography in the determination of brain death. Neurosurgery. 1989 Jun;24(6):884-9. https://doi.org/10.1227/00006123-198906000-00015.

12. Dominguez-Roldan JM, Garcia-Alfaro C, Jimenez-Gonzalez PI, Rivera-Fernandez V, Hernandez-Hasanas F, Perez-Bernal J. Diagnosis of brain death by transcranial Doppler sonography: solutions for cases of difficult sonic windows. Transplant Proc. 2004; 36(10):2896-7. https://doi.org/10.1016/j.transproceed.2004.10.052

13. Ducrocq X, Braun M, Debouverie M, Junges C, Hummer M, Vespignani H. Brain death and transcranial Doppler: Experience in 130 cases of brain dead patients. J Neurol Sci.1998 Sep;160(1):41–6. https://doi.org/10.1016/S0022-510X(98)00188-9

14. Abadal JM, Llompart-Pou JA, Homar J, Velasco J, Ibáñez J, Pérez-Bárcena, J. Ultrasonographic cerebral perfusion in assessment of brain death: a preliminary study. J Ultrasound Med. 2008 May;27(5):791–4. https://doi.org/10.7863/jum.2008.27.5.791

15. Newell DW, Grady MS, Sirotta AP, Winn HR. Evaluation of brain death using transcranial Doppler. Neurosurgery. 1989 Apr;24(4):509-13. https://doi.org/10.1227/00006123-198904000-00004.

16. Azevedo E, Teixeira J, Neves JC, Vaz R. Transcranial Doppler and brain death. Transplant Proc. 2000 Dec;32(8):2579–81. https://doi.org/10.1016/S0041-1345(00)01794-2

17. Van Velthoven V, Calliauw L; Diagnosis of brain death: transcranial Doppler sonography as an additional method. Acta Neurochir (Wien). 1998.;95(1-2):57–60. https://doi.org/10.1007/BF01793084.

18. Pimenta FP, Amorim BRV, Silva LJ. Morte encefálica: diagnostico possível sem utilização de exames complementares; Arq Bras Neurocir. 2012;31(1):22-7. Retrieved from: http://files.bvs.br/upload/S/0103-5355/2012/v31n1/a2833.pdf. Accessed on:

19. De Freitas GR, André C. Sensitivity of transcranial Doppler for confirming brain death: a prospective study of 270 cases. Acta Neurol Scand. 2006 Jun;113(6):426–32. https://doi.org/10.1111/j.1600-0404.2006.00645.x

20. De Freitas GR, André C, Bezerra M, Nunes RG, Vicent M. Persistence of isolated flow in the internal carotid artery in brain death. J Neurol Sci. 2003 Jun;210(1-2):31–4. https://doi.org/10.1016/S0022-510X(03)00065-0.

21. Chang JJ, Tsivgoulis G, Katsanos AH, Malkoff MD, Alexandrov V. Diagnostic accuracy of transcranial Doppler for brain death confirmation: systematic review and meta-analysis. AJNR Am J Neuroradiol. 2016 Mar;37(3):408-14. https://doi.org/10.3174/ajnr.A4548.

22. Cabrer C, Dominguez-Roldan JM, Manyalich M, Trias E, Paredes D, Navarro A. et al. Persistence of intracranial diastolic flow in transcranial Doppler sonography exploration of patients in brain death. Transplant Proc. 2003 Aug;35(5):1642-3. https://doi.org/10.1016/S0041-1345(03)00692-4.

23. Dominguez-Roldan JM, Garc8a-Alfaro C, Jimenez-Gonzalez PI, Rivera-Fernandez V, Hernandez-Hasanas F, Perez-Bernal J. Brain death due to supratentorial masses: diagnosis using transcranial Doppler sonography. Transplant Proc. 2004 Dec;36(10):2898-900. https://doi.org/10.1016/j.transproceed.2004.11.017.