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Original Article

Use of the apnea test and ancillary diagnostic methods in the brain death evaluation process: A retrospective intensive care unit analysis

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Abstract

Aim: Brain death (BD) determination is a standardized process primarily based on clinical evaluation, including the apnea test, with ancillary diagnostic methods used selectively when needed. In real-world practice, discordance between clinical assessment and ancillary imaging may complicate the evaluation process. To describe real-world use of the apnea test and ancillary diagnostic methods, particularly computed tomography angiography (CTA), during the brain death evaluation process in an adult intensive care unit (ICU).
Materials and Methods: This retrospective observational study included adult patients in whom the brain death evaluation process was initiated in a single ICU between January 2022 and September 2025. Clinical records were reviewed for apnea test performance, use of ancillary diagnostic methods, CTA findings, timing of diagnostic steps, and final clinical outcomes. The primary outcome was process-level concordance between apnea test results and CTA findings.
Results: The apnea test was completed in the majority of patients. CTA was used selectively as an ancillary diagnostic method and demonstrated heterogeneous findings. In a small subset of cases, CTA findings were discordant with the clinical evaluation, and definitive brain death was not confirmed in these patients. Early imaging and altered cranial integrity were common features among discordant cases.
Conclusion: In routine ICU practice, the apnea test is feasible in most patients undergoing brain death evaluation. Ancillary diagnostic methods, including CTA, should be interpreted within the broader clinical context, particularly when discordant findings arise. These results highlight the importance of a stepwise, context-sensitive approach to brain death determination.

Keywords: Brain death, death by neurologic criteria, apnea test, ancillary diagnostic tests, computed tomography angiography, intensive care unit

INTRODUCTION

Brain death (death by neurologic criteria, BD), is a highly standardized diagnostic process in intensive care practice with significant medical, ethical, and legal implications (1,2). International consensus guidelines emphasize that the determination of brain death is fundamentally based on a comprehensive clinical evaluation, which includes confirmation of coma, absence of brainstem reflexes, and completion of the apnea test under appropriate physiological prerequisites (1–5).

The apnea test is one of the core components of this process, as it directly assesses the absence of spontaneous respiration in response to hypercapnia, and when performed in accordance with established protocols, it is generally considered feasible in adult intensive care units (3,4). In selected situations where the clinical assessment cannot be reliably completed, the use of ancillary diagnostic methods may be required (1,2,5).

Computed tomography angiography (CTA) is increasingly used as an ancillary test because it allows assessment of cerebral

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circulatory arrest and is widely available (6,7). However, CTA is not universally accepted as a standalone confirmatory method, and its interpretation may be influenced by technical factors, imaging timing, and alterations in cranial integrity such as skull defects (7–10). These factors may lead to discordance between clinical assessment and CTA findings (7,10).

In routine clinical practice, ancillary diagnostic tests are generally applied selectively and in conjunction with bedside clinical evaluation rather than as independent determinants of diagnosis (1,5). Although the number of studies addressing the technical aspects of CTA and other ancillary methods has increased (9–12), data describing their practical use within intensive care workflows and their relationship with the clinical evaluation process remain limited.

This study aims to describe the use of ancillary diagnostic methods following the apnea test during the brain death evaluation process in an adult intensive care unit and their role in clinical decision-making. In addition, the impact of discordance between ancillary imaging findings and clinical assessment on the diagnostic process and final clinical outcomes in patients who completed the apnea test is described.

MATERIALS AND METHODS

Study Design and Ethical Approval

This retrospective observational study included patients in whom the brain death evaluation process was initiated in an adult intensive care unit. The study protocol was approved by the Karabük University Clinical Research Ethics Committee (Decision No: 2025/2521, Date: 03 November 2025), and the data were analyzed after anonymization.

Patient Selection

All patients aged ≥18 years in whom the brain death evaluation process was initiated in the adult intensive care unit between January 1, 2022, and September 30, 2025 were included in the study. For the purposes of this study, initiation of the brain death evaluation process was defined as the time of the first documented formal neurological examination performed for suspected brain death in the medical record. Patients with incomplete records related to the neurological examination or apnea test, as well as pediatric cases, were excluded.

Inclusion Criteria

- Initiation of the evaluation process based on clinical suspicion of BD,
- Completion of a standard neurological examination,
- Performance of the apnea test as part of the BD evaluation process,
- Availability of complete clinical records related to BD evaluation.

Exclusion Criteria

- Missing data related to the neurological examination or apnea test,
- Pediatric patients (<18 years),
- Presence of uncorrected hypothermia (core temperature <35°C) or severe metabolic/electrolyte disturbances during evaluation.

Patients with a history of craniectomy were not excluded, as the aim of the study was to reflect diagnostic challenges and sources of discordance encountered in real-world clinical practice during brain death evaluation.

Prerequisites for Brain Death Evaluation

Before initiating the brain death BD evaluation, exclusion of potential confounding factors was targeted in accordance with institutional intensive care unit protocols. In this context, clinical and laboratory records were retrospectively reviewed to confirm discontinuation of sedative and neuromuscular blocking agents, absence of residual drug effects, and achievement of normothermia and metabolic stability.

These data were obtained from patient medical charts, medication records, body temperature measurements, and laboratory results. Due to the retrospective nature of the study, not all prerequisites could be individually verified; however, documentation from routine clinical practice was used as the primary source of information.

Apnea Test Protocol

The apnea test was performed in accordance with the 2023 American Academy of Neurology (AAN) guidelines. Prior to testing, the following physiological conditions were documented as fulfilled:

- Core body temperature ≥36°C
- Systolic blood pressure ≥100 mmHg
- PaO_2≥200 mmHg

Patients were preoxygenated with 100% oxygen for 10 minutes while on mechanical ventilation. During the test, 100% oxygen at a flow rate of 6 L/min was administered via an external catheter. Arterial blood gas samples were obtained immediately before and at the end of the test.

The apnea test was considered positive in the absence of spontaneous respiratory effort and when $PaCO_2$ reached ≥60 mmHg or increased by ≥20 mmHg from baseline. The test was terminated if hypoxemia or hemodynamic instability developed. In the single case in which the apnea test was terminated early due to hypoxemia, CTA was subsequently performed as part of the evaluation process. This case was included in the descriptive concordance analysis, although the apnea test was not completed.

Computed Tomography Angiography (CTA)

CTA was performed after completion of the apnea test in cases where an ancillary diagnostic method was required during the clinical evaluation process. CTA was not routinely performed in all patients and was obtained based on clinical judgment

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rather than predefined institutional criteria. Indications for CTA were retrospectively determined through detailed chart review and categorized as clinical uncertainty, inability to complete the diagnostic process, or the need to support clinical decision-making. As this study reflects routine clinical practice, the selective use of CTA should be considered when interpreting concordance findings.

This study was not designed to reassess the diagnostic accuracy of CTA. Radiological evaluations were based solely on original reports generated during routine clinical practice, and imaging studies were not reinterpreted for the purposes of this analysis.

Classification of CTA Reports

CTA reports were classified as follows:

- Consistent with brain death: Absence of intracranial arterial and venous opacification
- Inconsistent with brain death: Preservation of intracranial vascular opacification
- Non-evaluable: Inadequate image quality or presence of significant artifacts

The timing of CTA acquisition was recorded relative to the initiation of the brain death evaluation process and analyzed descriptively. The terms “early” and “late” CTA were used descriptively without predefined temporal cutoffs. There was no standardized institutional protocol defining the exact timing of CTA acquisition during the evaluation process. CTA reports were interpreted according to the 4-point French scoring concept as reflected in routine radiology reports. This scoring system is based on the absence of contrast opacification in the cortical segments of the middle cerebral arteries (M4 segments) and in the internal cerebral veins.

Ancillary Diagnostic Tests

In cases where CTA could not be performed or was insufficient for evaluation, other ancillary tests such as electroencephalography (EEG) or cranial ultrasonography, if available, were recorded. These tests were performed based on clinical necessity and were not standardized within the scope of the study.

Outcome Measures

The primary outcome measure was defined as process-level concordance between the apnea test and CTA findings. In this context, process-level concordance refers to the descriptive agreement between apnea testing and CTA findings within the clinical evaluation workflow, rather than a formal diagnostic accuracy comparison. Concordance analysis was performed among patients who underwent CTA, irrespective of apnea test completion status. CTA was not used as a confirmatory determinant, but rather as part of the overall clinical adjudication process. As CTA was not considered a reference standard, formal diagnostic accuracy analyses (e.g., sensitivity or specificity) were not performed.

Secondary outcome measures included:

- Frequency and characteristics of discordant cases
- Completion or early termination of the apnea test
- Descriptive analysis of the timing of diagnostic steps
- Final clinical outcome of the brain death evaluation process

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics version 29.0. The distribution of continuous variables was assessed using the Shapiro–Wilk test, and data were presented as mean±standard deviation or median [interquartile range], as appropriate. Categorical variables were expressed as numbers and percentages.

Concordance between the apnea test and CTA findings was evaluated descriptively in accordance with the observational study design. No multivariable analyses or diagnostic accuracy analyses were planned.

RESULTS

During the study period, medical records of patients in whom a BD evaluation process was initiated were reviewed retrospectively. A total of 22 patient records were identified. One patient was excluded due to incomplete documentation, leaving 21 patients included in the final analysis. The diagnostic workflow of the study population is summarized in Figure 1.

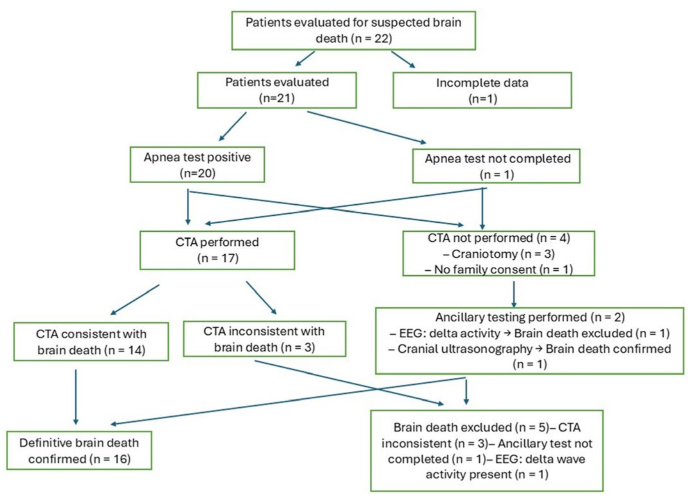

Figure 1. Flow diagram illustrating patient inclusion, exclusion, and diagnostic workflow of the brain death evaluation process

Baseline demographic and clinical characteristics of the study population are summarized in Table 1. The mean age of the cohort was 58.7±13.9 years (median 55 [44–69]), and 17 patients (81.0%) were male. The most frequent primary diagnoses leading to initiation of BD evaluation were intracerebral hemorrhage (52.4%) and post–cardiac arrest hypoxic injury (33.3%). A history of decompressive craniectomy was present in 3 patients (14.3%). Computed

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tomography angiography (CTA) was performed in 17 patients (81.0%), while ancillary diagnostic tests were used selectively, including electroencephalography in one patient and cranial ultrasonography in one patient. Overall, definitive clinical confirmation of BD was achieved in 16 patients (76.2%). No patient proceeded to organ donation during the study period.

Table 1. Baseline demographic and clinical characteristics (n=21)

Variable	Value
Age, years	58.7±13.9; median 55 [44–69]
Sex, n (%)	Male 17 (81.0); female 4 (19.0)
Primary diagnosis leading to BD evaluation, n (%)	Intracerebral hemorrhage 11 (52.4)
	Post–cardiac arrest 7 (33.3)
	Intracranial tumor 2 (9.5)
	Methanol intoxication 1 (4.8)
Decompressive craniectomy history, n (%)	Yes 3 (14.3); no 18 (85.7)
CTA performed, n (%)	17 (81.0)
Ancillary tests performed, n	EEG 1; cranial ultrasonography 1
Final clinical determination outcome, n (%)	BD confirmed 16 (76.2); BD not confirmed 5 (23.8)
Organ donation, n (%)	0 (0.0)

Values are presented as mean±SD, median [IQR], number of patients, or number (%), as appropriate. CTA: computed tomography angiography; EEG: electroencephalography, USG: ultrasonography

The apnea test was attempted in all 21 patients as part of the brain death evaluation process. The test was successfully completed in 20 patients (95.2%) and was terminated early in one patient due to hypoxemia. Transient hypoxemia (SpO_2 <90%) occurred in two patients during testing. Detailed characteristics of apnea testing are summarized in Table 2. The mean duration of the apnea test was 8.5±1.47 minutes. Mean arterial carbon dioxide levels increased from 42.0±4.5 mmHg at baseline to 72.0±8.3 mmHg at test termination. All tests were performed using external oxygen supplementation.

Table 2. Apnea test characteristics (n=21)

Variable	Value
Apnea test attempted, n (%)	21 (100)
Apnea test completed, n (%)	20 (95.2)
Test terminated early, n (%)	1 (4.8)
Hypoxemia during testing (SpO_2 <90%), n (%)	2 (9.5)
Apnea test duration, min	8.5±1.47
Baseline $PaCO_2$, mmHg	42.0±4.5
Final $PaCO_2$, mmHg	72.0±8.3
Oxygen delivery during test	External O_2, 6 L/min

Values are presented as mean±SD or n (%), as appropriate. $PaCO_2$: arterial partial pressure of carbon dioxide

Computed tomography angiography was performed in 17 of 21 patients (81.0%) following completion of the apnea test, based on clinical judgment. CTA findings were reported as consistent with cerebral circulatory arrest in 14 patients (82.3%), while three patients (17.7%) demonstrated preserved intracranial vascular opacification and were therefore considered discordant with the clinical evaluation. Detailed CTA findings are summarized in Table 3. In discordant cases, CTA was performed within a median of 3 hours [IQR 2.5–9.5] after initiation of the brain death evaluation process.

Table 3. Computed tomography angiography (CTA) findings (n=17)

Variable	Value
Patients undergoing CTA, n (%)	17 (81.0)
CTA findings consistent with BD, n (%)	14 (82.3)
CTA findings inconsistent with BD, n (%)	3 (17.7)
CTA performed early in the evaluation process*, n	9
CTA performed later in the evaluation process*, n	8

Values are presented as n (%), as appropriate. BD: brain death; CTA: computed tomography angiography. *CTA timing is reported descriptively relative to the initiation of the BD evaluation process; no standardized imaging delay protocol was applied

CTA was performed at variable time points during the BD evaluation process. Nine examinations were obtained relatively early, whereas eight were performed later in the course of evaluation. No standardized timing protocol was applied.

Three patients demonstrated discordance between apnea test completion and CTA findings. The clinical and imaging characteristics of these cases are summarized in Table 4. In all discordant cases, definitive brain death was not clinically confirmed during the evaluation process.

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Table 4. Characteristics of cases with discordant CTA findings (n=3)

Case	Age/Sex	Primary diagnosis	Decompressive craniectomy	Timing of CTA*	CTA finding	Ancillary test	Final clinical determination
1	62/M	Intracerebral hemorrhage	Yes	Early	Preserved vascular opacification	Not performed	BD not confirmed
2	54/M	Post–cardiac arrest hypoxic injury	Yes	Early	Preserved vascular opacification	Not performed	BD not confirmed
3	67/F	Intracranial tumor	No	Early	Preserved vascular opacification	EEG (delta activity present)	BD not confirmed

CTA timing is reported descriptively relative to initiation of the brain death evaluation process. BD: brain death; CTA: computed tomography angiography; EEG: electroencephalography

DISCUSSION

This retrospective observational study describes real-world experience with the use of the apnea test and ancillary diagnostic methods during the brain death (BD) evaluation process in an adult intensive care unit. The study characterizes process-level concordance and observed discordance between clinical assessment and ancillary imaging.

In this cohort, the apnea test was successfully completed in the majority of patients, which is consistent with previous studies reporting high feasibility of the test in adult intensive care populations (13,14). Transient hypoxemic episodes observed during testing were infrequent and did not prevent test completion in most cases. These findings align with the literature indicating that, when standard physiological prerequisites are met, the apnea test is a safe and feasible procedure in clinical practice (13,15).

CTA was used as an ancillary diagnostic method in selected cases and demonstrated heterogeneous results (14,16,17). Although findings suggestive of cerebral circulatory arrest were reported in most examinations, preservation of intracranial vascular opacification was observed in some patients despite completion of the apnea test (16,18-20). Notably, definitive BD was not clinically confirmed in any of these discordant cases. This observation suggests that CTA results, when discordant with clinical assessment, may influence clinical decision-making during the evaluation process (15,21).

Common features among discordant cases included early application of CTA during the evaluation process and, in some patients, altered cranial integrity due to decompressive craniectomy. Previous studies have reported that early imaging and skull defects may permit residual intracranial blood flow, potentially leading to discordant or inconclusive CTA findings (21–23). Although the present study does not establish causality, these factors may plausibly contribute to discordance observed in real-world clinical practice (24,25).

Ancillary diagnostic tests other than CTA were used in a limited number of cases, typically when CTA could not be performed or yielded inconclusive results. While the small number of such cases precludes definitive conclusions, this approach is consistent with current guidelines recommending selective, context-dependent use of ancillary tests in brain death evaluation (1,2,5,21).

This study has several limitations. Its retrospective, single-center design and small sample size limit generalizability and preclude advanced statistical analyses. Imaging assessments were based on original clinical reports without blinded re-evaluation, and CTA timing was not standardized. Additionally, although physiological prerequisites were documented according to institutional protocols, the retrospective nature of the study limited complete verification of all potential confounders. Additionally, CTA was not performed in all patients. This selective application may introduce potential selection bias and limits the generalizability of CTA-related findings. Additionally, the absence of a standardized timing protocol for CTA acquisition may have influenced the interpretation of radiological findings and contributed to heterogeneity in imaging results. Furthermore, although no patients proceeded to organ donation during the study period, evaluation of organ donation processes was beyond the scope of this study.

Despite these limitations, the study provides a concise depiction of the BD evaluation process in routine intensive care practice and emphasizes the importance of integrating clinical examination, apnea testing, and ancillary diagnostic methods within a stepwise and context-sensitive framework. Ancillary tests should not be interpreted as independent determinants but rather as components of the overall clinical context, particularly when discordant findings arise. In daily ICU practice, these findings support a cautious and structured approach to ancillary imaging, particularly when early CTA findings appear discordant with clinical assessment. Awareness of potential timing-related and anatomical factors may assist clinicians in avoiding premature diagnostic conclusions.

CONCLUSION

In this retrospective single-center study, the apnea test was shown to be feasible in the majority of patients undergoing brain death evaluation in an adult intensive care unit. Ancillary diagnostic methods, particularly computed tomography angiography (CTA), were used in selected cases and demonstrated heterogeneous

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findings when integrated into the clinical assessment process. Discordance between CTA findings and clinical evaluation was observed in a small number of patients, and definitive brain death was not confirmed in these cases. These findings highlight the importance of interpreting ancillary test results within the overall clinical context and underscore the need for context-sensitive integration of imaging into the brain death determination process.

Conflict of Interests

The authors declare that there is no conflict of interest in the study.

Financial Disclosure

The authors declare that there is no financial support.

Ethical Approval

The study protocol received approval from the Karabük University Clinical Research Ethics Committee (Decision No: 2025/2521, Date: 03 November 2025).

Patient Consent

Not necessary for this manuscript

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