Guidelines

The use of cerebral computed tomographic angiography as an ancillary investigation to support a clinical diagnosis of death using neurological criteria: a consensus guideline

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This is a consensus statement and has been endorsed by the following stakeholder professional organisations: British Society of Neuroradiologists; Clinical Radiology Faculty of the Royal College of Radiologists; Faculty of Intensive Care Medicine.; Intensive Care Society; Neuro Anaesthesia and Critical Care Society; Paediatric Critical Care Society; Society of British Neurological Surgeons; and Society of Radiographers.

Summary

This multidisciplinary consensus statement was produced following a recommendation by the Faculty of Intensive Care Medicine to develop a UK guideline for ancillary investigation, when one is required, to support the diagnosis of death using neurological criteria. A multidisciplinary panel reviewed the literature and UK practice in the diagnosis of death using neurological criteria and recommended cerebral CT angiography as the ancillary investigation of choice when death cannot be confirmed by clinical criteria alone. Cerebral CT angiography has been shown to have 100% specificity in supporting a diagnosis of death using neurological criteria and is an investigation available in all acute hospitals in the UK. A standardised technique for performing the investigation is described alongside a reporting template. The panel were unable to make recommendations for ancillary testing in children or patients receiving extracorporeal membrane oxygenation.

Recommendations

Where there is an intention to diagnose death using neurological criteria

1. Ancillary investigation is required in the following circumstances:
    a. a comprehensive neurological examination, including the apnoea test, is not possible;
    b. continuing effects of confounding conditions cannot be excluded.
2. Ancillary investigation should be considered in the following additional circumstances:
    a. uncertainty regarding the interpretation of possible spinally mediated movements;
    b. to promote understanding of the clinical confirmation of death using neurological criteria to families who are uncertain or unaccepting of such a diagnosis.
3. Cerebral CT angiography becomes the standard ancillary investigation of choice for supporting the diagnosis of death using neurological criteria in the UK.
4. Requests for cerebral CT angiography must be made by direct discussion between the treating intensive care consultant and radiology consultant. It should be made clear that the request is to support the clinical diagnosis of death using neurological criteria.
5. The cerebral CT angiogram should be reported by a consultant radiologist, after consultation with a regional neuroradiologist.
6. A clinical diagnosis of death using neurological criteria cannot be supported if the cerebral CT angiogram demonstrates contrast opacification of any of the vessels specified in the simplified four-point criteria [1].
7. There is insufficient evidence to make a consensus recommendation for the use of cerebral CT angiography as an ancillary investigation to support the clinical diagnosis of death using

neurological criteria in paediatrics. Where cerebral CT angiography is used it should be reported by a neuroradiologist experienced in paediatrics. Ancillary investigations should not be used in infants aged < 2 months.

8. There is insufficient evidence to make a consensus recommendation for the use of cerebral CT angiography as an ancillary investigation to support the clinical diagnosis of death using neurological criteria in patients receiving extracorporeal membrane oxygenation.
9. A system of auditing national practice on the use and outcomes of ancillary investigations to support a clinical diagnosis of diagnosis of death using neurological criteria should be established. We suggest that this is done by inclusion into the potential donor audit which already collects data on all patients in the UK in whom a diagnosis of death using neurological criteria is undertaken.
10. The process of diagnosing death using neurological criteria should be guided and documented using the forms for adults endorsed by the Faculty of Intensive Care Medicine and Intensive Care Society and the paediatric versions endorsed by the Royal College of Paediatrics and Child Health and Paediatric Critical Care Society.

What other guidelines are available on this topic?

Current national and international guidance on the diagnosis of death using neurological criteria address the issue of ancillary investigations to support the diagnosis [2-5]. Most discuss the investigations in terms of their sensitivity and specificity, availability, technical skills required to undertake the investigation and interpret the results, and costs. While some guidelines suggest that specific investigations are superior to others, clinical practice remains variable, with individual hospitals or regions using different investigations. Our guidance goes further by recommending the implementation of a standardised national ancillary investigation protocol, appropriate for current practice in the UK.

Why was this consensus guidance developed?

Following an incident in the UK where a patient who had undergone bilateral therapeutic decompressive craniectomies was inadvertently diagnosed as deceased, an expert group convened by the Faculty of Intensive Care Medicine and Intensive Care Society reviewed the case in detail. From that review, therapeutic decompressive craniectomy was added as a 'red flag' (Box 1) to the endorsed forms for the diagnosis of death using neurological criteria [6]. A further recommendation from the expert group was that the Faculty of Intensive Care Medicine, Intensive Care Society and other representative intensive care/critical care societies should, in collaboration with other relevant

professional groups, develop a UK consensus guidance on ancillary investigations to support the diagnosis of death using neurological criteria.

Methods

Representatives from the Faculty of Intensive Care Medicine, Intensive Care Society, Neuro Anaesthesia and Critical Care Society and Paediatric Critical Care Society worked collaboratively with the British Society of Neuroradiologists, Clinical Radiology Faculty of the Royal College of Radiology, Society of Radiographers and Society of British Neurological Surgeons to consider the development of a standard ancillary investigation to support the diagnosis of death using neurological criteria. The objective was to propose a pragmatic guideline that would be workable in all UK hospitals where the diagnosis and confirmation of death using neurological criteria is undertaken.

Where in the UK is the diagnosis and confirmation of death using neurological criteria performed?

In the UK the diagnosis of death using neurological criteria is almost exclusively undertaken on critical care by intensive care doctors. Data from the potential donor audit conducted by NHS Blood and Transplant shows that testing for death using neurological criteria is undertaken in approximately 1500 patients per year in the UK [7]. Further analysis by NHS Blood and Transplant reveals that over the last four years, 45% of tests for death using neurological criteria were conducted in hospitals with a neuroscience ICU. The proportion of tests undertaken in NHS hospitals without a neuroscience ICU has increased from 53% in 2018 to 58% in 2021 (Fig. 1).

Current UK practice

The Academy of Medical Royal Colleges Code of Practice for the Diagnosis and Confirmation of Death was published in 2008 [2]. This provides guidance on how doctors in the UK should diagnose and confirm death using neurological criteria. The confirmation of death using neurological criteria is primarily a clinical diagnosis made by at least two doctors. Both doctors should have been fully registered with the General Medical Council (or equivalent international professional body) for more than five years and be competent in the conduct and interpretation of the clinical tests. At least one of the doctors must be a consultant. Testing should be undertaken by the nominated doctors acting together and must always be performed on two occasions, including two apnoea tests. The guidance does not recommend the routine use of ancillary investigation to support the clinical diagnosis of death using neurological criteria. In most cases this diagnosis is made clinically by establishing the cause of the irreversible coma and apnoea, excluding confounders and by demonstrating the loss of brainstem reflexes and apnoea. Courts in the UK continue to uphold the confirmation of death using

neurological criteria when the recommendations of the Academy of Medical Royal Colleges code of practice are followed [8].

Since 2012, the Faculty of Intensive Care Medicine and Intensive Care Society have endorsed the use of standardised testing forms as an aid in making this diagnosis [9,10], with the Royal College of Paediatrics and Child Health and Paediatric Critical Care Society endorsing similar forms for children in 2019 [11]. These forms are designed as clinical aide memoires and audit tools. The forms are entirely consistent with, and should always be used in conjunction with, the Academy of Medical Royal Colleges code of practice. One innovation in the forms is the addition of 'red flag' patient groups. Red flags are specific conditions or circumstances that have been identified in the literature or from clinical experience as requiring additional clinical caution (Box 1). When faced with a red flag situation, clinicians should consider the need to delay testing and/or perform ancillary investigations.

In certain situations, it may not be possible to perform or complete all the clinical tests necessary to diagnose death using neurological criteria. The Academy of Medical Royal Colleges code of practice advises that in such circumstances, ancillary investigations may be necessary to support clinical testing [2]. Most ancillary investigations are designed to either confirm the absence of cerebral blood flow or neurophysiological activity. The ancillary investigation undertaken depends on local availability and access to expertise to interpret the result. No single ancillary investigation has worldwide consensus, though there has been a shift toward ancillary investigations that confirm the absence of cerebral blood flow [3].

The Academy of Medical Royal Colleges code of practice does not make recommendations as to which ancillary investigation should be used [2]. The choice of investigation is decided by the individual ICU, radiology and/or neurophysiology departments. There is no accurate information available for how often ancillary investigation is undertaken in the UK to support a clinical diagnosis of death using neurological criteria.

Recommended indications for ancillary investigation

Ancillary investigation is indicated only when there is strong clinical suspicion that death has occurred. The ancillary investigation should be additional to the fullest examination and clinical testing, carried out to the best of the capabilities of the two doctors performing the tests in the given circumstances.

It is recommended that ancillary investigation is required in the following circumstances: where a comprehensive neurological examination, including the apnoea test, is not possible (e.g. extensive maxillofacial injuries, high spinal cord injury); and/or where continuing effects of confounding conditions cannot be excluded (e.g. residual sedation, metabolic or pharmacological derangement, decompressive craniectomy or another unresolvable red flag scenario).

It is recommended that ancillary investigation should be considered in the following additional circumstances: where there is uncertainty regarding the interpretation of possible spinally mediated movements; and/or to promote understanding of the clinical confirmation of death using neurological criteria to families who are uncertain or unaccepting of such a diagnosis.

Recommended ancillary investigation

In the UK the ancillary investigation that is available most widely in hospitals (not just neuroscience centres) is cerebral CT angiography (CTA). This investigation is performed commonly for other indications at most acute hospitals and the acquisition can be highly protocolised to reduce variation in technique.

We acknowledge that the World Brain Death Project [3] does not currently recommend cerebral CTA for this purpose, but it is a well-established ancillary investigation in Europe [1,5,12-14]. Many of the other techniques recommended by the World Brain Death Project are less widely available in the UK context, as is the expertise in acquisition and interpretation. The World Brain Death Project rightly notes that clinicians should first follow national guidelines that take account of any necessary variation in national practice [3].

We recommend that cerebral CTA becomes the standard ancillary investigation of choice for supporting the clinical diagnosis of death using neurological criteria the UK. Specifically, we recommend that the four-point cerebral CTA criteria should be adopted [1]. These criteria have a considerable evidence base and fit best with current UK practice [4-5,12-16]. The four-point cerebral CTA criteria have been shown to have a 100% specificity in confirming of death using neurological criteria [1,15]. The false negative rate of 15% (85% sensitivity) for the four-point cerebral CTA criteria is acceptable as it represents a safe standard which prioritises specificity over sensitivity [16].

Other methods for assessing the images in the future may improve the sensitivity of cerebral CTA in confirming the diagnosis of death using neurological criteria and may prove useful when further evidence is available to support their adoption [5,13].

Recommended cerebral CTA process

Requests must be made by direct discussion between the treating intensive care consultant and radiology consultant. The request should be made specifically as an ancillary investigation to support the clinical diagnosis of death using neurological criteria to ensure the correct cerebral CTA technique is protocolled.

The scan should be performed by a suitably trained radiographer using a defined protocol (Box 2). The scan should then be reported by a consultant radiologist. In centres that do not have an available in-house neuroradiologist, a consultant neuroradiology review of the images should be sought from the regional neurosciences centre, and the opinion (along with the name of the neuroradiologist) should be documented in the formal cerebral CTA report. The reporting radiologist is advised to review the images using multiplanar reformats of the axial datasets as appropriate. Sagittal and coronal reformats may either be pre-specified reformats on the scan protocol that are generated automatically or produced by the reviewing radiologist in the image viewing software, according to local preference.

The cerebral CTA criteria for supporting a clinical diagnosis of death using neurological criteria are shown in Box 3. Suggested wording for the consultant radiologist report of the cerebral CTA is provided in online supporting information Appendix S1. The radiologist should adapt these according to the specific situation, adding other relevant findings as per normal practice.

Recommendations for special circumstances

Paediatrics

Use of ancillary investigations to support a clinical diagnosis of death using neurological criteria is not recommended in neonates aged < than 2 months of corrected gestational age [17]. There is a paucity of evidence addressing the use of cerebral CTA in the paediatric population (aged < 16 y), which is also reflected in the scant practical experience in the UK. Until further evidence is available, we are not able to make consensus recommendations for the use of ancillary investigations in the paediatric population. In clinical situations where ancillary investigations are considered necessary, there should be a local case-by-case discussion. Magnetic resonance angiography may have a role in

UK paediatric populations given its accessibility and use in this population and increasing recognition for its role in supporting the clinical diagnosis of death using neurological criteria worldwide [18].

Extracorporeal membrane oxygenation (ECMO)

Until further evidence is available, we are unable to make consensus recommendations for the use of ancillary investigations in patients receiving ECMO. In clinical situations where ancillary investigations are considered necessary there should be a local case-by-case discussion.

Auditing these recommendations

We recommend that a system of auditing national practice on the use and outcomes of ancillary investigations to support a clinical diagnosis of death using neurological criteria is established. We suggest that this is done by inclusion into the potential donor audit which already collects data on all diagnoses of death using neurological criteria undertaken in the UK.

We also recommend that the process of diagnosing death using neurological criteria is guided and documented using the forms endorsed by the Faculty of Intensive Care Medicine and Intensive Care Society [9,10] and the paediatric version available from the Paediatric Critical Care Society. This will help standardise the process and increase the opportunities for useful audit.

Conclusion

The diagnosis of death using neurological criteria in the UK is primarily a clinical diagnosis, carried out almost exclusively by intensive care doctors. Any ancillary investigation for the clinical diagnosis of death using neurological criteria should always be considered as an addition to the full clinical testing and examination carried out to the best of the two doctors' capabilities in the given circumstances. However, where there is an intention to diagnose death using neurological criteria, but a comprehensive neurological examination is not possible or confounding conditions cannot be excluded, ancillary investigation will be required to make the diagnosis. We recommend that the protocol outlined above for cerebral CTA becomes the standard ancillary investigation of choice for supporting the clinical diagnosis of diagnosis of death using neurological criteria in the UK. This should be adopted into local and regional guidelines and any future national update of the Academy of Medical Royal Colleges code of practice.

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Box 1. Red-flag conditions for the diagnosis of death using neurological criteria (adapted from [9]).

- Testing < 6 h after the loss of the last brain-stem reflex or < 24 h after loss of the last brain-stem reflex if primarily anoxic damage
- Hypothermia (24-h observation period following rewarming recommended)
- Patients with any neuromuscular disorders
- Steroid administration for space occupying lesion (e.g. abscess)
- Prolonged fentanyl infusions
- Aetiology primarily located in the brainstem or posterior fossa
- Therapeutic decompressive craniectomy

Box 2. Recommended cerebral CT angiogram technique to support a clinical diagnosis of death using neurological criteria.

- The patient should have an 18-g (or larger) cannula sited in a large vein.
- Immediately prior to scanning, a mean arterial pressure > 60 mmHg (or age-appropriate parameters in paediatrics) should be confirmed and documented.
- Three similar acquisitions are performed starting at the C2 level to the convexity.
- The first scan is acquired before the injection of contrast.
- Non-ionic contrast medium (120 ml (1-2 $ml.kg^{-1}$ in paediatrics); minimum iodine concentration of 340 $mg.ml^{-1}$) is injected at a rate of 3 $ml.s^{-1}$ using a power injector.
- The second scan is acquired 20 s after commencing the contrast injection.
- The third scan is acquired 60 s after commencing the contrast injection.
- Images are acquired with a section thickness of ≤ 1.25 mm at 120 kV, 250 mm field of view and 512 x 512 matrix.
- Images must be clearly labelled as to whether they are the pre-injection, 20 s or 60 s runs.
- The localisation images (including the scanned range) should be saved and included in the image set sent to the picture archiving and communication system.

Box 3. Criteria to be met for a cerebral CT angiogram (CTA) to support a clinical diagnosis of death using neurological criteria

- The pre-injection acquisition is inspected for any pre-existing vascular density which could confound interpretation, such as intravenous contrast from a recent previous contrast-enhanced imaging study, hyperdense intravascular thrombus or vascular calcifications.
- Opacification of superficial temporal arteries is assessed on the second acquisition at 20 s to confirm the correct injection of contrast medium.
- The third acquisition at 60 s is used to evaluate opacification of intracranial vessels at four anatomical locations:
    1. cortical segments (M4) of the left middle cerebral artery;
    2. cortical segments (M4) of the right middle cerebral artery;
    3. left internal cerebral vein; and
    4. right internal cerebral vein
- A clinical diagnosis of death using neurological criteria cannot be supported if the cerebral CTA demonstrates contrast opacification in any one of the four vessels specified above. Absence of contrast in these four vessels has a specificity of 100% and a sensitivity of 85% [1,15-16].
- Provisional reports should not be issued. The final typed and verified report should be issued by the consultant radiologist at the earliest opportunity, and the intensive care consultant made aware of the availability of the report on the computer system.

Figure legend

Figure 1. Proportion of deaths diagnosed using neurological criteria in UK hospitals with a neuroscience ICU (black) vs. those without a neuroscience ICU (white). These data exclude stand-alone paediatric hospitals. Data provided by NHS Blood and Transplant

Online Supporting Information

Appendix S1. Suggested wording for consultant radiologists report of CT angiography when used to support the clinical diagnosis of death using neurological criteria.