Variability in hospital-based brain death guidelines in Canada

[Variabilité des directives sur le décès neurologique en milieu hospitalier au Canada]

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Purpose: Variability has been reported in the practices to determine death by neurological criteria for adults and children. The objective of this study was to determine if this variability exists in the Canadian context.

Methods: A cross-sectional survey of the Canadian intensive care units (ICUs) involved in the care of potential organ donors, and Canadian organ procurement organizations (OPOs) was undertaken. We contacted the medical directors of these units and asked them to provide their guidelines for the neurological determination of death (NDD). A framework, which identifies key diagnostic criteria for NDD, was used to assess the content of all study documents.

Results: With a response rate of 68%, we found that key diagnostic criteria for NDD were incorporated inconsistently in the guidelines from Canadian ICUs and OPOs. Areas of concern include omissions in: the testing of brainstem reflexes; components of the apnea test; indications for the use of supplementary testing; wait intervals prior to performing the first NDD examination; the definition of NDD; and potential confounding factors. In addition, inconsistencies were found pertaining to wait intervals required between examinations and the legal timing of death.

Conclusion: These findings reinforce the need to standardize the practice of the neurological determination of death in Canadian centres, which has the potential to reduce practice variation. Clear medical standards for NDD augment the quality, rigour and credibility of this determination.

***Objectif** : Une variabilité a été rapportée dans les pratiques de détermination de la mort par des critères neurologiques chez les adultes et les enfants. Notre objectif était de vérifier si cette variabilité existe dans le contexte canadien.*

***Méthode** : Une enquête transversale a été entreprise auprès d'unités de soins intensifs (USI) canadiennes, impliquées dans les soins à de potentiels donneurs d'organes, et de services canadiens d'approvisionnement en organes (SAO). Nous avons demandé aux directeurs de ces unités de fournir leurs directives pour le diagnostic du décès neurologique (DDN). Un cadre de travail, qui désigne les critères diagnostiques clés du DDN, a été utilisé pour évaluer le contenu de tous les documents de l'étude.*

***Résultats** : Nous avons appris, avec 68 % de répondants, que les critères diagnostiques pour le DDN étaient incorporés de façon irrégulière dans les directives des USI et des SAO canadiens. Les aspects préoccupants relevés étaient des omissions dans les tests de réflexes du tronc cérébral, des composantes du test d'apnée, des indications de l'usage de tests supplémentaires, les délais avant le premier examen du DDN, la définition du DDN et des facteurs de confusion possibles. De plus, il y avait des incohérences relatives aux délais requis entre les examens et la détermination légale de l'heure de la mort.*

***Conclusion** : Ces résultats renforcent la nécessité de normaliser la pratique de détermination neurologique de la mort dans les centres canadiens, ce qui pourrait réduire la variation de la pratique. Des normes médicales claires pour le DDN augmentent la qualité, la rigueur et la crédibilité de la constatation de la mort.*

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The neurological determination of death (NDD), also know as brain death, is a prerequisite to cadaveric organ donation in Canada. The clinical examination used for NDD should document the complete and irreversible loss of neurological function. Substantial international variability has been reported in the practices to determine death by neurological criteria for both adults[1–3] and children.[3–5] In all provincial and territorial statutes in Canada, death for the purposes of organ donation is legally defined as "according to accepted medical practice". Two documents: "Death and Brain Death: A New Formulation for Canadian Medicine"[6] and "Guidelines for the Diagnosis of Brain Death"[7] are the foundation for NDD guidelines in Canada. While these documents have provided clarification of diagnostic criteria, it is not clear if they are widely endorsed or applied uniformly. Hospitals and health regions have made adjustments to these criteria according to their individual context and requirements. In order to assess the variability of NDD guidelines in Canada, this study evaluated whether NDD guidelines from Canadian intensive care units (ICUs) and organ procurement organizations (OPOs) contained key diagnostic criteria to determine death.

TABLE I Key diagnostic criteria for the neurological determination of death

1. *Definition of neurological death*
   - Whole brain death: defined, in the United States Uniform Determination of Death Act,[14] as the irreversible cessation of all brain functions, OR
   - Brain stem death: defined by Pallis and Harley[15] and adopted in the United Kingdom[11] as the irreversible cessation of all brain stem functions.
2. *Minimum clinical criteria**
   - established etiology
   - deep unresponsive coma
   - minimum temperature
   - apnea
   - bilateral absence of brain stem reflexes: pupillary, corneal, oculocephalic, oculovestibular, gag, cough, suck/root (newborns).
3. *Potential confounders**
   - shock, severe hypothermia, treatable metabolic disorders, peripheral nerve or neuromuscular dysfunction or neuro muscular blockage, or drug intoxications.
4. *Supplementary tests**
   - radionuclide cerebral blood flow scan, cerebral angiography, electroencephalogram
5. *Number of examinations required & time intervals (before and between examinations)*
6. *Legal timing of death*
7. *Qualifications of practitioners*

*Should include explanations for what to do: (1) if unable to assess the minimum clinical criteria; (2) when there is suspicion of a potential confounder; (3) when supplementary tests should be used.

Methods

A cross-sectional survey of the Canadian ICUs involved in the care of potential organ donors, and Canadian OPOs was undertaken. Intensive care units within tertiary care or trauma centres handle the majority of potential organ donors. Therefore, we contacted the medical directors of these units and all the OPOs in Canada, inviting them to provide us with "the document used in your ICU for diagnosing brain death". If the first request did not receive a response within one month, a second contact was made, after which no further attempts were made to obtain information. The only documents assessed in this study were institutionally approved guidelines or checklists for NDD.

As no gold standard for NDD guidelines exists in Canada, we used a framework (Table I) developed by members of the planning committee for the Canadian Forum entitled "Severe Brain Injury to the Neurological Determination of Death".[8] This framework, based upon existing national[6,7] and international NDD guidelines,[9–11] identifies key diagnostic criteria for NDD. It was used to assess the content of all study documents to determine if they contained, at minimum, this information. According to the framework, the NDD examination should include the following information: (1) a definition of neurological death; (2) minimum clinical criteria to establish NDD; (3) a list of potential confounders which could preclude the clinical diagnosis; (4) a list of supplementary tests and their indications; (5) the number of examinations required and relevant time intervals (from brain injury to the first NDD and between examinations as required); (6) the legal timing of death and; (7) qualifications of practitioners to perform the examination. As the NDD clinical examination differs for adults and children, the adult and pediatric documents were assessed separately.

Results

Forty-two of the 62 contacted centres replied, resulting in a response rate of 68%. Of the centres which responded, seven did not provide any documents: three stated they used the "Guidelines for the Diagnosis of Brain Death"[7] from the Canadian Neurocritical Care Group; two stated they used their OPO guidelines; and the remaining two did not have any NDD guidelines or checklists. The remaining 35 respondents provided 51 documents. Of these documents, 14 were not included in this study: nine were duplicates; and five did not pertain to NDD. As

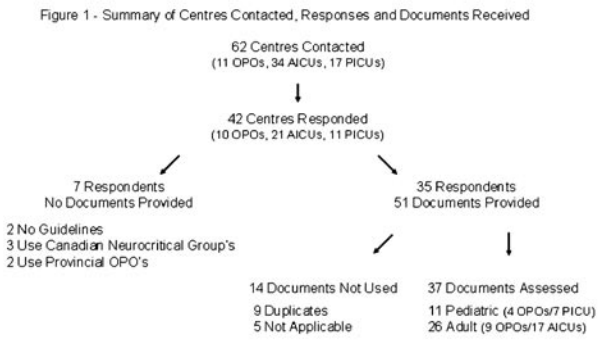

FIGURE 1 Centres contacted, responses and documents received. A summary of the number of Canadian intensive care units and organ procurement organizations contacted for information on their guidelines used for the neurological determination of death, the number that responded and a breakdown of information provided. AICUs = adult intensive care units; OPOs = organ procurement organizations; PICUs = pediatric intensive care units.

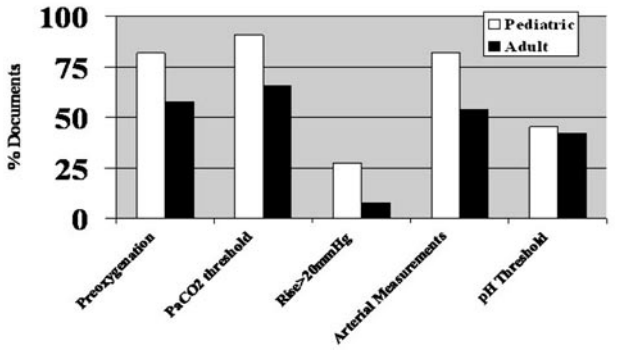

FIGURE 2 Apnea testing. The percentage of pediatric and adult documents which identified relevant components of the apnea test (Pediatric $n = 11$; Adult $n = 26$).

a result, 37 documents were entered into the study database (11 pediatric and 26 adult documents). A detailed breakdown of the numbers of centres contacted, respondents, documents received and assessed are presented in Figure 1.

The largest numbers of documents originated from the provinces of Ontario (32%, 12/37) and Quebec (24%, 9/37). The OPOs provided four of the 11 pediatric documents and eight of the 26 adult documents assessed by the study. Sixty-four percent (7/11) of the pediatric documents and 62% (16/26) of the adult documents came from ICUs in tertiary care university-affiliated hospitals. A majority of the documents, 55% (6/11) pediatric and 69% (18/26) adult, were based on a specific reference document. The most commonly cited (13/24 citations) reference document was the Canadian Neurocritical Care Group's 1999 *Guidelines for the Diagnosis of Brain Death*.[7]

With respect to minimum clinical criteria and apnea testing, the majority of documents contained the basic components of the minimum clinical criteria to establish NDD: (1) an established etiology capable of causing NDD (100%, 11/11 pediatric, 88%, 23/26 adult); (2) deep unresponsive coma (100%, 11/11 pediatric, 92%, 24/26 adult); (3) a minimum core temperature (91%, 10/11 pediatric, 77%, 20/26 adult); (4) absent respiratory effort based on an apnea test (100%, 11/11 pediatric, 85%, 22/26 adult); (5) and a list of absent brainstem reflexes for NDD (100%, 11/11 pediatric, 96%, 25/26 adult). Although these documents contained the basic minimum clinical criteria required in the framework, several omissions were identified. Ninety-one percent (10/11) of the pediatric and 65% (17/26) of the adult documents included tests for all brainstem reflexes. Even though 91% (10/11) of the pediatric and 73% (19/26) of the adult documents provided descriptions of apnea testing, they did not include all the required components of the test to document acute hypercarbic stimulation of the medullary respiratory centre (Figure 2). For example, very few documents (27%, 3/11, pediatric and 12%, 3/26, adult) indicated the need for a $PaCO_2$ rise of 20 mmHg above baseline. As well, less than half the documents (5/11 pediatric and 11/26 adult) specified a pH threshold to be attained during apnea testing.

With respect to supplementary testing, all (11/11) of the pediatric and 88% (23/26) of the adult documents included information on supplementary tests for NDD. Sixty-four percent (7/11) of the pediatric and 42% (11/26) of the adult documents indicated that supplementary testing was recommended to confirm a diagnosis when all the minimum clinical criteria could not be completed. The percentage of documents recommending supplementary testing, specifically: radionuclide cerebral blood flow scan, cerebral angiography and electroencephalogram (EEG) are presented in Figure 3. Of note, an EEG was recommended almost three times more often in pediatric

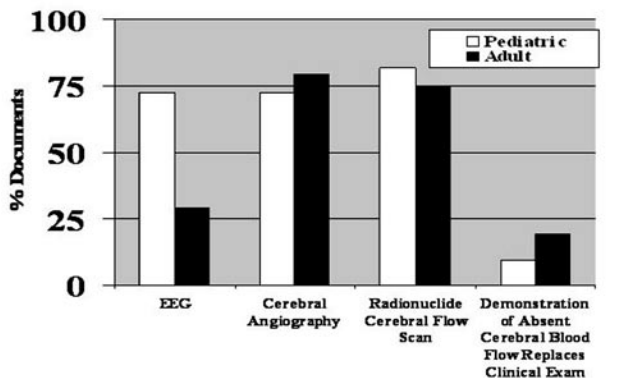

FIGURE 3 Supplementary tests. The percentage of pediatric and adult documents which identified the use of each of these supplementary tests for the neurological determination of death (NDD). The fourth column represents the percentage that indicated that the demonstration of absent cerebral blood flow could be used to replace a clinical exam for NDD (Pediatric n = 11; Adult n = 26). EEG = electroencephalogram.

compared to adult documents. For two adult documents, if the radiographic scan demonstrated absent intracranial perfusion, no clinical exams were required. One pediatric and one adult document indicated that in this situation only one other physician's assessment was necessary to complete a declaration of NDD for the purpose of organ donation. Two adult documents accepted cerebral blood flow scanning as an alternative to a second examination only in the case of a very unstable potential donor.

With respect to examination intervals: all (11/11) of the pediatric and 96% (25/26) of the adult documents indicated the need to perform two examinations for NDD. Few included information on wait intervals before performing the first NDD examination. Only one pediatric document indicated a wait interval (two hours) prior to performing the first NDD. Four adult documents contained information about this interval, with one mandating a two-hour wait and three mandating a 24-hr wait. Intervals between examinations were based on type of brain injury (hypoxic-ischemic encephalopathy or not) and additionally, in pediatric documents, the age of the patient. These intervals ranged from two to 48 hr in pediatric documents, and from two to 24 hr in adult documents (Table II).

With respect to professional qualifications, 73% (8/11) of the pediatric and 65% (17/26) of the adult documents indicated that the examiners must be independent of any transplant procedures if the patient is being considered for organ donation. Only 36% (4/11) of pediatric and 42% (11/26) of adult documents indicated that they should be physicians. Forty-six percent (5/11) of the pediatric and 42% (11/26) of the adult documents indicated that the practitioners should be specialists who treat patients with severe brain injury, for example: neurologists neurosurgeons, and intensive care physicians.

Finally, with respect to definition, confounders and timing of death, few documents contained information regarding the final three framework components: definition of neurological death, potential confounders, and the legal timing of death. Thirty-six percent (4/11) of the pediatric and 35% (9/26) of the adult documents included definitions of neurological death. Of these, all four pediatric and seven of the nine adult documents used the "whole brain death" definition. Only 18% (2/11) of pediatric and 31% (8/26) of adult documents contained all of the potential confounders listed in the framework. Figure 4 provides a breakdown of this information. Fifty-five percent (6/11) of the pediatric and 46% (12/26) of the adult documents provided information on the legal timing

TABLE II Wait intervals between neurological determination of death (NDD) examinations suggested by adult and pediatric documents

Interval between NDD exams	*# Adult documents*		*# Pediatric documents*				
	HIE	*Non-HIE*	*HIE*	*Non-HIE*			
				< 7 days	7 days to < 2 months	2 months to < 1 yr	1 to < 18 yr
2 hr		15		1	3	4	4
6 hr			2				
12 hr	2			1	1	1	7
24 hr	8		6	5	4	6	
48 hr					2		
Cannot be done				4	1		
Not clearly defined	16	11	3				

NDD = neurological determination of death; HIE = hypoxic ischemic encephalopathy.

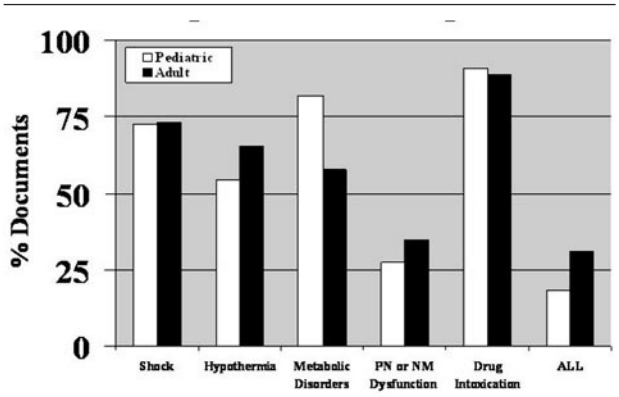

FIGURE 4 Confounding factors. The percentage of pediatric and adult documents which indicated each of the factors (identified in the graph) as possibly precluding a clinical diagnosis of the neurological determination of death (Pediatric $n = 11$; Adult $n = 26$). NM = neuromuscular; PN = peripheral nerve.

of death. Fifty percent (3/6 pediatric and 6/12 adult) of these documents indicated that the legal time of death was that of the first clinical examination, whereas the remaining 50% of documents indicated the time of the second clinical examination.

Discussion

In view of the variability in hospital-based brain death guidelines described in other countries, we sought to examine areas of consistency and variation in a cross sectional survey of Canadian guidelines. This study found that key diagnostic criteria for NDD were not consistently contained in the guidelines from Canadian ICUs and OPOs. Areas of concern include omissions in: the testing of brainstem reflexes; components of the apnea test; indications for the use of supplementary testing; wait intervals prior to performing the first NDD examination; the definition of NDD; and potential confounding factors. In addition, inconsistencies were found pertaining to wait intervals required between examinations and the legal timing of death. Our findings support the variability found by other researchers[1–5] for the process of NDD.

Brain death is sound in concept and the general consistency of the basic clinical criteria across Canadian guidelines is reassuring. However, the credibility of the determination may suffer if existing guidelines are not clear and consistent. This process should begin with a clear definition of death determined by neurological criteria because the clinical criteria document the absence of brainstem function, they do not discriminate whole brain definitions (adopted in the United States)[12] from brainstem definitions (adopted in the United Kingdom)[11] of death. In addition, NDD testing must include all of the minimum clinical criteria required to ensure the complete and irreversible loss of neurological function. Similar to the findings of Powner *et al.*[2] and Wang and Wallace,[3] we found examples of incomplete testing of brainstem reflexes. This was particularly apparent in adult documents where only 65% (17/26) included tests for all brainstem reflexes. We also identified variations in targets for apnea testing, a finding consistent with several other studies.[1,2,4]

Further variation was found pertaining to potential confounders and supplementary testing. All potential confounders must be taken into consideration prior to commencing NDD. Identification of all potential confounders and their impact on the clinical examination was absent in a majority of the guidelines. Only 18% (2/11) of pediatric and 31% (8/26) of adult documents contained all of the confounders considered to potentially preclude a determination. Both Mejia *et al.*,[4] in the pediatric setting, and Powner *et al.*,[2] in the adult setting, found similar results. One solution to the identification of a possible confounder is to use a supplementary test. However, practitioners must understand which test to use, when to use such a test, and whether it can be used to replace one or both clinical examinations. Based upon the findings of our study, the indications are not entirely clear in the Canadian context. Confusion over the use of supplementary tests (sometimes called confirmatory tests) has also been shown to exist internationally for both adult[1,2] and pediatric[4] populations.

How many of these examinations should be performed, and when? Current provincial and territorial legislation mandates that at least two physicians determine death for the purposes of organ donation without reference to an interval between examinations. From such legislation, it is not surprising that most guidelines assessed in our study require two examinations. Of concern is the lack of information on when to perform the first examination, and inconsistencies pertaining to wait intervals between examinations. Variations in the timing between examinations are a common finding in other studies.[1,3]

A disconcerting finding in our study was that pertaining to the legal timing of death. For the 55% (6/11) of pediatric and 46% (12/26) of adult documents that provide information on the timing of death, half consider the potential donor to be dead after the first clinical assessment. In these cases, if organ donation is not to proceed, it is unclear whether a second clinical examination is required for diagnostic

purposes. Considerable confusion would be generated if it were widely known that some institutions in Canada determine death after the first examination, while others wait until the second. This uncertainty has potential family, legal and insurance ramifications, particularly if the examinations are made on two separate days.

Limitations of current investigation

A principle limitation of our study was that we assessed guidelines for NDD instead of observing actual clinical practice. We were unable to show that the variability found in NDD guidelines is also occurring at the bedside, as guidelines do not necessarily reflect clinical practice.[13] It is possible that practitioners could compensate for this variability, however we speculate that actual practice has greater variation. Of note, other investigators have shown substantial variability in the documentation of the clinical examination in the medical chart.[3] Given the consistent findings of variation of practice in the determination of death using neurological criteria found elsewhere,[1–5] it is likely that actual practice in Canadian centres varies at least to the extent found in these guidelines.

With a response rate of 68%, another limitation of our study is that of potential non-response bias. All surveys encounter and attempt to minimize non-response bias.[14] The proportion of non-responders to our study was reduced by making a follow-up contact for missing information. However, it is unknown if the 20 non-responders had NDD guidelines that were systematically different from the ones assessed in this study. One possible explanation is that these centres did not have any NDD guidelines. Another possibility is that the non-responders used their provincial OPO guidelines or another NDD guideline reference, such as the *Guidelines for the Diagnosis of Brain Death*.[7] Including such documents may have reduced the variability observed in this study.

Conclusion

This is the first study to assess the variability of NDD guidelines in Canada. Given that the sampling frame included nearly the entire population of potential users of these guidelines and achieved a response rate of 68%, this study broadly represents the Canadian experience. Even taking into consideration the study limitations, the level of variability found is concerning, given the fundamental nature of NDD, the consequences of an erroneous determination, and its implications for organ donation. These findings reinforce the need to standardize the practice of the NDD in Canadian centres, which has the potential to reduce practice variation. Public and professional confidence in the practice of determining death by neurological criteria is essential. Clear medical standards for NDD augment the quality, rigour and credibility of this determination.

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