



Clinical evaluation and ancillary testing for the diagnosis of death by neurologic criteria: a cross-sectional survey of Canadian intensivists

Évaluation clinique et tests auxiliaires pour le diagnostic de décès déterminé par des critères neurologiques : un sondage transversal auprès des intensivistes canadiens

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Abstract

Purpose Trust in the deceased organ donation process relies on the expectation that the diagnosis of death by neurologic criteria (DNC) is accurate and reliable. The

objective of this study was to assess the perceptions and approaches to DNC diagnosis among Canadian intensivists.

Methods We conducted a self-administered, online, cross-sectional survey of Canadian intensivists. Our sampling frame included all intensivists practicing in Canadian institutions. Results are reported using descriptive statistics.

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Results Among 550 identified intensivists, 249 (45%) completed the survey. Respondents indicated they would be comfortable diagnosing DNC based on clinical criteria alone in cases where there is movement in response to stimulation (119/248; 48%); inability to evaluate upper/lower extremity responses (84/249; 34%); spontaneous peripheral movement (76/249; 31%); inability to evaluate both oculocephalic and oculo-caloric reflexes (40/249; 16%); presence of high cervical spinal cord injury (40/249; 16%); and within 24 hr of hypoxemic-ischemic brain injury (38/247; 15%). Most respondents agreed that an ancillary test should always be conducted when a complete clinical evaluation is impossible (225/241; 93%); when there is possibility of a residual sedative effect (216/242; 89%); when the mechanism for brain injury is unclear (172/241; 71%); and if isolated brainstem injury is suspected (142/242; 59%). Sixty-six percent (158/241) believed that ancillary tests are sensitive and 55% (132/241) that they are specific for DNC. Respondents considered the following ancillary tests useful for DNC: four-vessel conventional angiography (211/241; 88%), nuclear imaging (179/240; 75%), computed tomography (CT) angiography (156/240; 65%), and CT perfusion (134/240; 56%).

Conclusion There is variability in perceptions and approaches to DNC diagnosis among Canadian intensivists, and some practices are inconsistent with national recommendations.

Résumé

Objectif La confiance dans le processus de don d'organes de donneurs décédés repose sur l'attente que le diagnostic de décès déterminé par des critères neurologiques (DDN)

soit précis et fiable. L'objectif de cette étude était d'évaluer les perceptions et les approches du diagnostic de DDN chez les intensivistes canadiens.

Méthode Nous avons mené un sondage transversal auto-administré et en ligne auprès des intensivistes canadiens. Notre base d'échantillonnage comprenait tous les intensivistes exerçant dans des établissements canadiens. Les résultats sont présentés à l'aide de statistiques descriptives.

Résultats Parmi les 550 intensivistes identifiés, 249 (45 %) ont répondu au sondage. Les répondants ont indiqué qu'ils seraient à l'aise de diagnostiquer un DDN en fonction de critères cliniques seulement dans les cas où il y a : un mouvement en réponse à une stimulation (119/248; 48 %); une incapacité à évaluer les réponses des membres supérieurs et inférieurs (84/249; 34 %); un mouvement périphérique spontané (76/249; 31 %); une incapacité à évaluer à la fois les réflexes oculo-céphaliques et vestibulo-oculaires (40/249; 16 %); la présence de lésions médullaires cervicales hautes (40/249; 16 %); et dans les 24 heures suivant une lésion cérébrale hypoxémique-ischémique (38/247; 15 %). La plupart des répondants étaient d'accord pour dire qu'un test auxiliaire devrait toujours être réalisé lorsqu'une évaluation clinique complète est impossible (225/241; 93 %); lorsqu'il y a possibilité d'un effet sédatif résiduel (216/242; 89 %); lorsque le mécanisme de la lésion cérébrale n'est pas clair (172/241; 71 %); et si une lésion isolée du tronc cérébral est suspectée (142/242; 59 %). Soixante-six pour cent (158/241) des répondants étaient d'avis que les tests auxiliaires étaient sensibles et 55 % (132/241) qu'ils étaient spécifiques pour le DDN. Les répondants ont jugé utiles les tests auxiliaires suivants pour le DDN : l'angiographie conventionnelle des quatre vaisseaux (211/241; 88 %),

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l'imagerie nucléaire (179/240; 75 %), l'angiographie par tomodensitométrie (TDM) (156/240; 65 %) et la perfusion en TDM (134/240; 56 %).

Conclusion *Les perceptions et les approches du diagnostic de DDN varient parmi les intensivistes canadiens, et certaines pratiques ne sont pas conformes aux recommandations nationales.*

Keywords death by neurologic criteria · brain death · neurologic determination of death · clinical evaluation · clinical examination · ancillary test · survey

Trust in the deceased organ donation process relies on the expectation that the diagnosis of death by neurologic criteria (DNC) is accurate and reliable. It is widely accepted worldwide that DNC can be diagnosed in patients with a catastrophic brain injury following a reliable clinical examination that shows irreversible cessation of consciousness, absence of response to stimulation, and brainstem areflexia.¹ Perfect specificity in DNC diagnosis (i.e., no false positives) is paramount to ensuring that the dead donor rule, which states that organs can only be recovered from a deceased individual, is respected.² In practice, clinical evaluation for DNC is not always reliable or feasible because of factors such as facial trauma, cervical myelopathy, severe metabolic disorders, drug intoxication, or cardiopulmonary instability. When a reliable clinical evaluation is not possible or the results are inconclusive, ancillary testing is required to confirm DNC.

In Canada, national DNC recommendations endorse the use of four-vessel conventional angiography and nuclear imaging as ancillary tests,³ whereas other national guidelines also consider transcranial Doppler ultrasound, electroencephalography, or evoked potentials as valid ancillary tests.^{4,5} Despite their important contribution to DNC diagnosis in certain scenarios, ancillary test use remains heterogeneous, both in national guidelines and in local clinical practice.^{4,6} This variability may reflect uncertainty surrounding the diagnostic accuracy of ancillary tests, which is poorly documented.⁷ Ancillary tests assess different surrogates for cerebral function, such as cerebral blood flow, perfusion, or neurophysiologic function, and the results may conflict with the clinical evaluation or with themselves, complicating the diagnosis.⁸

Although clinical practice regarding DNC diagnosis has been extensively studied and contrasted to national guidelines in several countries, contemporary data are lacking in Canada. Hence, we sought to evaluate the perceptions and approaches to DNC diagnosis in Canada to identify areas that require further study, consensus, or clarification.

Methods

We conducted a cross-sectional, self-administered survey of Canadian adult and pediatric intensivists between 26 February and 26 March 2018. Questions exploring physician knowledge and perspectives regarding DNC, including clinical diagnostic criteria and the use of ancillary testing, were embedded into a larger survey on deceased donation practices in Canada. Results from the other domains of the survey have been previously reported.^{9,10} This study was approved by the Research Ethics Board of the Centre Hospitalier de l'Université de Montréal (CHUM) (approval number: 17.216/MP-02-2018-7521).

Population

Our sampling frame included Canadian intensivists practicing in institutions where physicians may provide care to patients who could be potential organ donors using a comprehensively validated list of practicing intensivists obtained from the Canadian Blood Services and the Canadian Critical Care Society to identify potential participants. To be included, intensivists were required to have an active licence for independent practice.

Survey development

The process of survey development followed recommendations for the development of clinician self-administered surveys.¹¹ A multidisciplinary steering committee comprising experts in critical care, epidemiology, survey methodology, organ donation, and social science, as well as a patient representative, identified pertinent domains of evaluating deceased organ donation eligibility, ancillary testing, obtaining consent, and clinician attitudes towards organ donation. The committee ranked items within each domain using a Delphi approach yielding a total of 26 final items for the survey (details in the Electronic Supplementary Material [ESM], eAppendices). The survey included a mix of open-ended and scenario-based closed questions (nominal responses or five-point Likert scale formats), as well as questions about the respondents' demographic characteristics. Respondents were presented with various scenarios in which DNC clinical evaluation may be challenging and asked whether they would be comfortable diagnosing DNC using only a clinical evaluation, i.e., without ancillary testing. For most of these scenarios, there are recommendations from Canadian national guidelines on DNC³ (Table 1). The study questionnaire is provided in the ESM (eAppendices).

Table 1 Summary of the Canadian recommendations on the diagnostic criteria for death by neurologic criteria (DNC)

Minimum clinical criteria for DNC

1. Established etiology capable of causing DNC in the absence of reversible conditions capable of mimicking neurologic death
2. Deep unresponsive coma with bilateral absence of motor responses, excluding spinal reflexes
3. Absent brainstem reflexes as defined by:
 - a. Absent gag and cough reflexes
 - b. Bilateral absence of corneal responses, pupillary responses to light (with pupils at mid-size or greater), and vestibulo-ocular responses (e.g., oculocephalic and oculovestibular reflexes)
4. Absent respiratory effort based on the apnea test
5. Absent confounding factors, including:
 - a. Unresuscitated shock
 - b. Hypothermia (core temperature < 34°C)
 - c. Severe metabolic disorders
 - d. Severe metabolic abnormalities
 - e. Peripheral nerve or muscle dysfunction or neuromuscular blockade potentially accounting for unresponsiveness
 - f. Clinically significant drug intoxications

Ancillary tests

Ancillary tests are recommended when it is impossible to complete the minimal clinical criteria (as above). Ancillary test results showing global absence of intracerebral blood flow are considered the standard for DNC determination by ancillary testing. Recommended tests are cerebral angiography and radionuclide imaging techniques.

Hypoxemic-ischemic brain injury

In cases of hypoxemic-ischemic brain injury, clinical evaluation should be delayed for 24 hr subsequent to the cardiorespiratory arrest or an ancillary test should be performed.

Pediatric minimum core temperature

The minimum core temperature to diagnose DNC for pediatric patients are:

- Term newborns (patients aged < 30 days): 36°C
- Children older than 30 days: 34°C

Based on Shemie *et al.*³

Survey validation and administration

The initial survey was evaluated for face validity by all steering committee members and then pilot-tested among trainees who were representative of the target population. The steering committee implemented changes following pilot testing and thereafter reassessed the survey for comprehensiveness, clarity, and face validity. Finally, the same trainees repeated the survey two weeks later to assess content validity and test-retest reliability. The survey was administered using an online platform (LimeSurvey™) and disseminated to a validated, comprehensive list of practicing intensivists obtained from the Canadian Blood Services and the Canadian Critical Care Society. A screening section at the beginning of the survey was used to confirm eligibility (including self-reported licence for independent practice) and consent. Two reminders were sent by e-mail to non-responders at 14-day intervals. Respondents did not receive compensation for participation in the survey.

Sample size and analyses

Based on previous Canadian surveys conducted by the Canadian Critical Care Trials Group,^{12,13} we estimated our final sample to be between 300 and 400 respondents. To obtain a confidence level of 95% and a 5% margin of error, between 169 and 196 respondents were required, equivalent to a 49–56% response rate.

All survey responses are reported as descriptive statistics. We adjusted the denominator of respondents to account for those who did not respond to each specific question. We also conducted subgroup analyses by province of practice, as well as whether the respondents self-identified themselves as designated organ donation specialists and/or affiliated with organ donation organizations. Finally, we performed an additional post hoc subgroup analysis between adult and pediatric intensivists.

Results

Study population

The survey was sent to 550 Canadian intensivists. Of these, 21 did not meet our inclusion criteria. The response rate was 50% (263/529), of which 95% (249/263) completed the section of the survey on DNC. Participant characteristics are reported in Table 2. Most respondents (91%; 226/249) were affiliated with academic institutions and 13% (33/249) worked in pediatric intensive care units (ICUs). Twenty-one percent (53/249) of respondents reported being designated donation specialists within their institution.

Death by neurologic criteria based on clinical criteria only

For all presented clinical scenarios, there was heterogeneity in respondents' views as to whether it is acceptable to only complete a clinical DNC evaluation (without the need for an ancillary test) (Fig. 1).

Peripheral movement, incomplete brainstem examination, and spinal cord injury

In cases where the patient has peripheral movement in response to stimulation, 48% (119/248) of respondents indicated that they would be comfortable declaring DNC based on clinical criteria alone. The proportion of clinicians comfortable in making such a clinical diagnosis without ancillary testing decreased to 31% (76/249) if spontaneous peripheral movements were also present. Thirty-four percent (84/249) of respondents indicated they would be comfortable diagnosing DNC clinically despite inability to evaluate upper and lower limb responses to stimulation. In a situation where both oculocephalic and oculo-caloric reflexes could not be assessed, 16% (40/249) indicated they would be comfortable making a DNC diagnosis based on clinical criteria alone. This was also the case in the presence of high cervical spinal cord injury, where 16% (40/249) of respondents indicated they would be comfortable declaring DNC without ancillary testing. Overall, the proportions of respondents declaring being comfortable diagnosing DNC clinically (without ancillary testing) were as follows: 32% (80/249) for no scenario, 25% (63/249) for one scenario, 21% (53/249) for two scenarios, 12% (30/249) for three scenarios, 6% (14/249) for four scenarios, and 4% (9/249) for all five scenarios.

Table 2 Study sample demographic and professional characteristics

Surveyed population's characteristics <i>N</i> = 249*	<i>n</i> (respondents)	%
ICU population		
Adult	216	87%
Pediatric	33	13%
Type of ICU ^a		
Trauma ICU	119	48%
Neuro or neurosurgical ICU	144	58%
Cardiothoracic ICU	101	41%
Coronary care unit	32	13%
Medical unit	81	33%
Surgical unit	75	30%
Mixed unit (surgical/medical)	231	93%
Number of ICU beds		
0 to 10	25	10%
11 to 20	88	35%
21 to 30	79	32%
> 30	57	23%
Gender		
Male	173	70%
Female	66	27%
Prefer not to respond	10	4%
Age group		
31 to 40	86	35%
41 to 50	92	37%
51 to 60	54	22%
61 to 70	16	6%
≥ 71	0	0%
No response	1	0%
Province (territory) of practice ^{b,c}		
Alberta	23	9%
Atlantic Canada	20	8%
British Columbia	21	8%
Manitoba	13	5%
Ontario	86	35%
Quebec	78	31%
Saskatchewan	10	4%
Academic affiliation		
Yes	226	91%
No	21	8%
No response	2	1%
Years of independent practice		
0–5	61	25%
6–10	63	25%
11–15	44	18%
> 15	81	33%
Base specialty training		
Medicine ^d	131	53%
Pediatrics ^d	29	12%

Table 2 continued

Surveyed population's characteristics <i>N</i> = 249*	<i>n</i> (respondents)	%
Surgery ^d	22	9%
Anesthesia	46	19%
Emergency medicine	13	5%
Other	8	3%
Defined role as a donation specialist		
Yes	53	21%
No	196	79%
Practice in an institution with physician(s) with formal role as donation specialist(s)		
Yes	170	68%
No	79	32%

* Respondents are those who completed at least one of the survey-specific questions

^a This question allows multiple responses ("select all that apply"). The sum of the respondents per type of ICU can therefore be > 263

^b This question allows multiple responses (3 respondents answered they practiced in 2 different provinces and 1 respondent indicated 0 provinces)

^c Provinces of Atlantic Canada are New Brunswick, Nova Scotia, Prince Edward Island, and Newfoundland and Labrador. No responses were received from Northern Canada (Yukon, Northwest Territories, and Nunavut provinces)

^d Including all relevant subspecialties

ICU = intensive care unit

Hypoxic-ischemic brain injury

Fifteen percent (38/247) of respondents indicated they would be comfortable determining DNC based on clinical criteria alone less than 24 hr after hypoxic-ischemic brain injury, 36% (90/247) after less than 48 hr, and 23% (57/247) after less than 72 hr. Seventeen percent (42/247) indicated that they would not be comfortable under any of the given timeframes and 8% (20/247) indicated that they did not know. Of those who indicated not being comfortable under any of the given timeframes, in an open-ended follow-up question, 67% (28/42) indicated a time frame longer than 72 hr, 7% (3/42) indicated a specific clinical criterion under which they would make the diagnosis, 7% (3/42) indicated that they would always use an ancillary test, 5% (2/42) indicated the time-window depends on cooling, and 2% (1/42) replied "after 48 hr", which could be interpreted as either within 72 hr or \geq 72 hr. The remaining 2% of respondents (5/42) did not provide further information.

Minimal body temperature

For adult patients, 4% (8/211) of adult intensivists indicated that a minimum temperature lower than 34°C or no minimum temperature should be required before making the clinical diagnosis of DNC (Fig. 2). For children, pediatric intensivists indicated a minimum temperature below 34°C. For newborn patients, 48% of pediatric intensivists (14/30) indicated a temperature below 36°C.

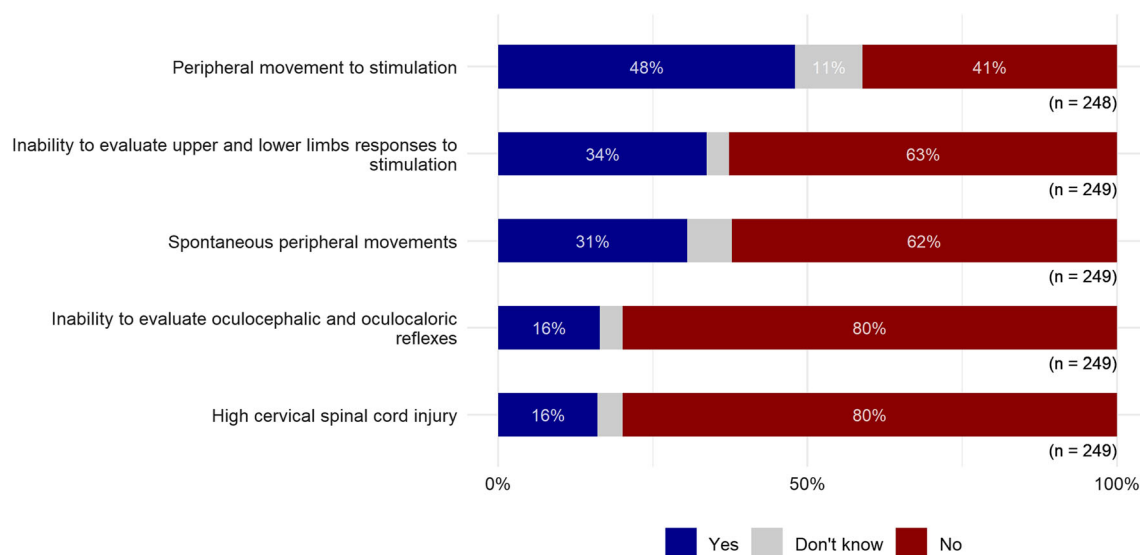


Fig. 1 Overall number of Canadian intensivists reporting being comfortable declaring death by neurologic criteria using clinical evaluation only (no ancillary tests) when faced with different situations.

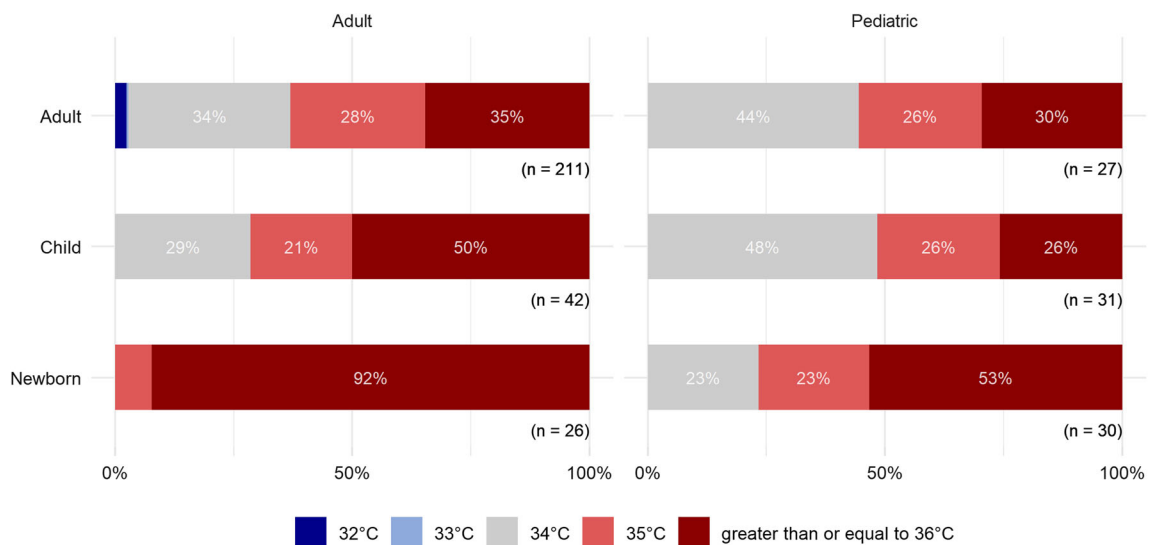


Fig. 2 Overall number of Canadian intensivists reporting the minimal temperature required to declare death by neurologic criteria using clinical evaluation only (no ancillary tests) according to patient population (adult, child, or newborn). Results are reported separately for adult (n = 216) and pediatric intensivists (n = 33).

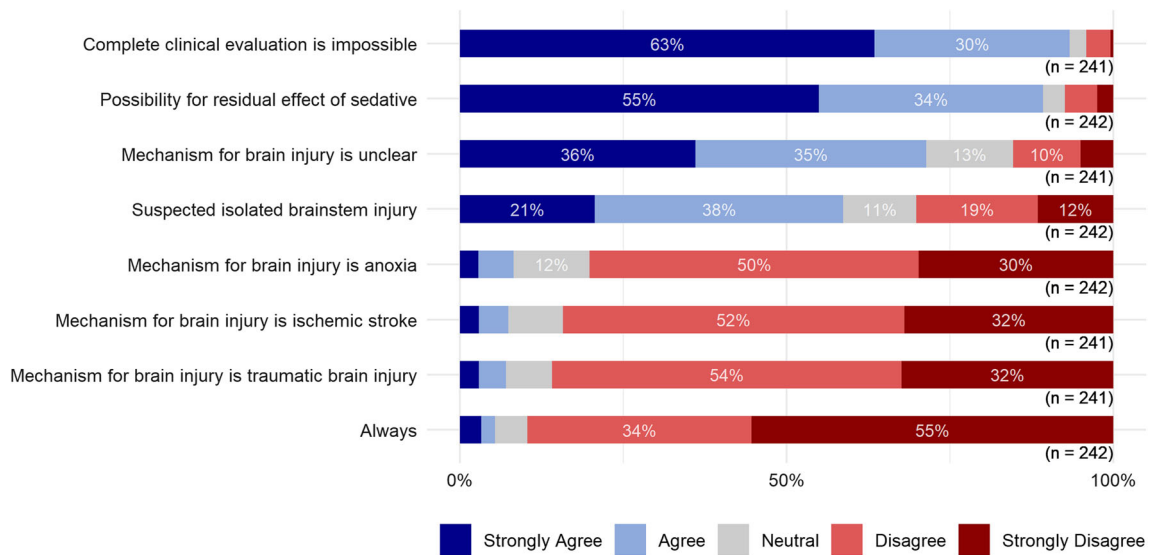


Fig. 3 Overall number of Canadian intensivists that strongly agree, agree, strongly disagree, disagree, or neither agree nor disagree that ancillary tests should always be conducted in the provided situations.

Use of ancillary tests

Respondents were asked whether an ancillary test was mandatory in a series of cases. Figure 3 provides details on the responses.

Ancillary test indications

Overall, 93% (225/241) of respondents agreed that ancillary tests should always be performed when a complete clinical evaluation is impossible. Most of the

respondents (89%, 216/242) agreed that ancillary tests should always be completed in the context of a possible residual effect of sedative, 71% (172/241) agreed with absolute indication of ancillary tests when the mechanism for brain injury is unclear, and 59% (142/242) of respondents agreed that ancillary tests are necessary if isolated brainstem injury is suspected. When asked if all cases of brain injury mechanisms required ancillary testing, 80% (194/242) disagreed for anoxia, 84% (203/241) disagreed for ischemic stroke, and 86% (207/241) disagreed for traumatic brain injury. When asked if

ancillary tests should always be performed for DNC diagnosis, 89% (216/242) disagreed, 5% (12/242) were neutral, and 6% (14/242) agreed.

Ancillary test diagnostic accuracy

Overall, 66% (158/241) and 55% (132/241) of respondents agreed that the ancillary tests currently available are sensitive and specific, respectively (Fig. 4). Respondents were generally skeptical of non-validated tests, with 70% (169/242) disagreeing that it is acceptable to use these tests to help determine DNC.

Ancillary test utility

Of the eleven ancillary tests listed in the survey, most respondents agreed that the following four tests were useful: four-vessel conventional angiography (88%; 211/241), nuclear imaging (75%; 179/240), computed tomography (CT) angiography (65%; 156/240), and CT perfusion (56%; 134/240) (Fig. 5). Some respondents believed that ancillary tests help families accept the diagnosis of DNC (46%; 111/242).

Subgroup analyses

Subgroup analyses according to province of practice and organ donation specialist status, as well as a post-hoc subgroup analysis stratifying adult from pediatric intensivists, are provided in the supplemental material. Visual inspection of these results suggested no meaningful differences between subgroups.

Discussion

In this contemporary, cross-sectional survey, we found significant heterogeneity in Canadian intensivists' perceptions and beliefs on DNC diagnosis. Views differed on the necessity to apply ancillary tests in different clinical scenarios, the minimum core temperature required to diagnose DNC, the minimum delay to diagnose DNC following the onset of hypoxic-ischemic brain injury, and the utility and diagnostic accuracy of ancillary tests. Some intensivists also held views that differed from national recommendations.³ These findings are consistent with those of prior studies showing variability in DNC perceptions and clinical practice on both individual^{14,15} and institutional levels^{6,16} abroad.

Several self-reported practices documented in this study diverge from national recommendations.³ These recommendations state that “an ancillary test be performed when it is impossible to complete the minimum clinical criteria”. In contrast, our survey found that an important proportion of intensivists were comfortable diagnosing DNC in situations where the clinical exam may have been unreliable or incomplete. For example, roughly a third or more would diagnose DNC based on clinical examination alone despite the presence of peripheral movement to stimulation or spontaneous movements, and roughly one third would do so even if they were unable to evaluate upper and lower limb responses. This is even though stimulation-evoked peripheral movements caused by spinal reflexes can be difficult to distinguish from organized motor responses, which would be inconsistent with DNC. More importantly, one in six respondents also mentioned being

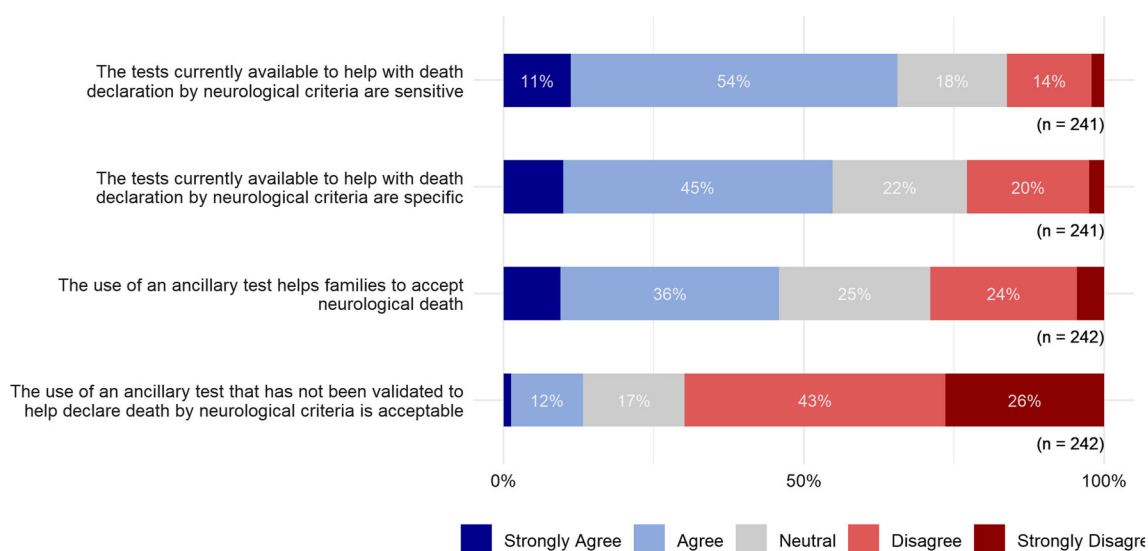


Fig. 4 Overall number of Canadian intensivists reporting, based on their personal experience, to strongly agree, agree, strongly disagree, disagree, or neither agree nor disagree with the provided statements.

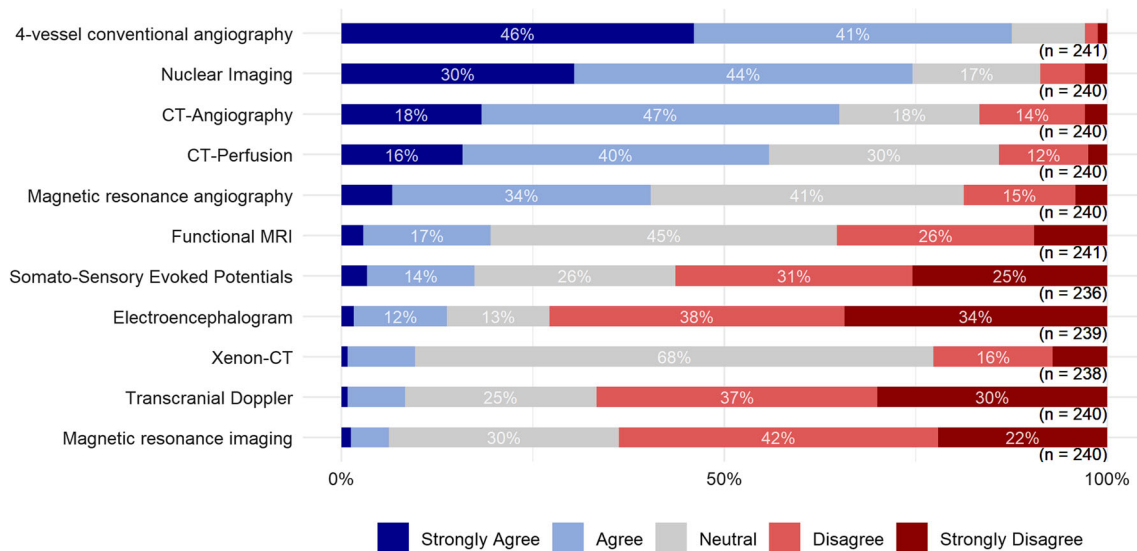


Fig. 5 Overall number of Canadian intensivists that strongly agree, agree, strongly disagree, disagree, or neither agree nor disagree that the mentioned ancillary tests are useful to confirm the diagnosis of death by neurologic criteria.

comfortable diagnosing DNC clinically even if they were unable to evaluate both oculocephalic and oculo-caloric reflexes, or if the patient had a high cervical spinal cord injury. In the prior case, the requirement for documented brainstem areflexia is not fulfilled, whereas in the latter, motor response to stimulation and apnea testing cannot be assessed because of cervical myelopathy-related disruption of ascending and descending tracts. Similarly, almost one in five intensivists was comfortable diagnosing DNC based on a clinical evaluation alone less than 24 hr after the onset of hypoxic-ischemic brain injury. In the early hours following the initial hypoxemic injury, a patient with hypoxic-ischemic encephalopathy may exhibit spontaneous improvement in consciousness, which informs the current recommendation to observe the patient for at least 24 hr before the DNC clinical evaluation.¹⁷ Despite these findings, most but not all respondents (93%) agreed that ancillary tests were indicated when a complete clinical evaluation was not possible.

Ancillary tests may be over requested in some circumstances; for example, 72% of respondents agreed that tests are mandatory when the mechanism of brain injury is unclear. It is possible that some respondents confused diagnostic paraclinical tests, which serve to identify the etiology of the causal brain injury (aiming to answer the question: “What caused this patient’s condition?”) with ancillary tests, which serve as adjuncts to clinical evaluation (“Does this test support the determination of DNC?”). A particular test modality may be useful for both questions, but the information yielded by the test, as well as test accuracy, are different depending on the objective.

The indication for ancillary testing in patients who fulfill all clinical criteria for DNC following an isolated brainstem injury remains subject of international debate, with some claiming DNC requires death of the entire brain and others believing isolated brainstem death is sufficient.¹⁸ In Canadian recommendations, there is no firm indication for ancillary testing in this condition—but in cases where a patient with an isolated brainstem injury undergoes an ancillary test, only results compatible with whole-brain death are considered acceptable for DNC diagnosis.³ Since 58% of survey respondents considered ancillary tests mandatory in patients with isolated brainstem injury, there may be divergent views on the role of ancillary testing in this clinical scenario and on the acceptability of isolated brainstem death for DNC.

Another topic of variability in DNC guidelines between jurisdictions is the acceptability of respective ancillary tests. In Canadian recommendations, only four-vessel angiography and nuclear imaging are endorsed ancillary tests, but survey respondents reported that CT angiography (64%) and CT perfusion (56%) are useful ancillary tests for DNC. Although these imaging modalities were not as commonly available or used when Canadian recommendations were initially formulated in 2006, recent guidance from the World Brain Death Project published in 2020 stated that these tests are currently not sufficiently validated.¹

We suspect the variability in perceptions and approaches to DNC may be attributable to different factors. First, these results could indicate a knowledge gap on what constitutes a complete and reliable DNC clinical evaluation. Second, respondents may have interpreted the questions or the proposed clinical

scenarios differently. For instance, some respondents may have declared being comfortable diagnosing DNC clinically (without ancillary testing) in the presence of peripheral movement because they assumed that the question included clear spinal reflexes. This possibility of diverging interpretation is less likely in other scenarios, such as the inability to evaluate both the oculocephalic and oculovestibular reflexes. Third, there may be some disagreement on what constitutes a complete and reliable clinical examination. Fourth, some intensivists may deliberately proceed with DNC determination without ancillary testing despite an incomplete or unreliable clinical examination. Finally, heterogeneity in DNC national guideline recommendations abroad may influence clinical practice in Canada.

This study contributes to our understanding of Canadian intensivists' perspectives and approaches to DNC determination. While the reason for variability in perspectives is unknown, this study nonetheless highlights specific topics that may require further clarification or discussion to improve consensus and practice uniformity. Contrary to expectations, survey results did not meaningfully differ between donation specialists and those with no formal donation responsibilities. Therefore, efforts to improve DNC diagnosis perceptions and practices must involve all physicians who may be called upon to identify a potentially neurologically deceased individual, regardless of expertise. Studies to validate appropriate ancillary tests for DNC and to implement knowledge translation initiatives involving organ donation researchers, policy makers, and physicians can improve alignment of physician perceptions on DNC and promote more standard clinical practice in the field.

Our study has several strengths. The survey was rigorously developed following standardized guidelines, our sampling frame included a comprehensively validated list of practicing ICU physicians obtained from the Canadian Blood Services and the Canadian Critical Care Society, and we obtained a reasonable response rate. Furthermore, we conducted subgroup analyses to explore whether response patterns would differ according to donation specialist status, province of practice, and patient age group. Our study also has limitations. Although our survey included a significant number of Canadian intensivists, there may have been selection bias if non-respondents had very different perspectives and beliefs regarding the subject of interest than respondents did. The relatively small subsample of non-academic intensivists (9% of the total sample) makes it difficult to estimate differences between academic and non-academic intensivists—although, *a priori*, we might expect frequent referrals of severe neurologic injuries from non-academic

to academic centres to result in different experiences and thus different perspectives and beliefs between these two groups. Nevertheless, given the sizable number of academic intensivists and organ donation specialists in our sample, their perspectives are still reflected in our aggregate results. Moreover, since structured questions included in the survey often did not allow respondents to give detailed responses, our capacity to capture any nuance in their answers may have affected the internal validity of our findings. Finally, as the study focused on Canadian intensivists, results may not be generalizable to all physicians involved in DNC determination (e.g., neurologists, neurosurgeons, or community-based ICU generalists) or to other countries.

Conclusion

In our survey, we observed variability in the perceptions and approaches to DNC diagnosis among Canadian intensivists. A significant proportion of respondents reported practices that diverge from national recommendations. These findings may reflect knowledge gaps that will require additional investigation.

Author contributions All authors participated in conceiving this study, provided input into the protocol, gave critical feedback on the manuscript, and approved the final manuscript. *Michaël Chassé* and *Matthew J. Weiss* contributed to all aspects of this study, including study conception and design; acquisition, data analysis, interpretation of data; and drafting the article. *Shane W. English*, *Frédéric D'Aragon*, *François Lauzier*, *Alexis F. Turgeon*, *Sonny Dhanani*, *Lauralyn McIntyre*, *Sam D. Shemie*, *Gregory Knoll*, *Dean A. Fergusson*, and *Samantha J. Anthony* contributed to the study conception and design, data interpretation, and reviewing the final draft. *Joel Neves Briard*, *Michael Yu* and *Livia P. Carvalho* contributed to data analysis, data interpretation, and drafting the article.

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References

1. Greer DM, Shemie SD, Lewis A, et al. Determination of brain death/death by neurologic criteria: the World Brain Death Project. *JAMA* 2020; 324: 1078-97.
2. Truog RD, Robinson WM. Role of brain death and the dead-donor rule in the ethics of organ transplantation. *Crit Care Med* 2003; 31: 2391-6.
3. Shemie SD, Doig C, Dickens B, et al. Severe brain injury to neurological determination of death: Canadian forum recommendations. *CMAJ* 2006; 174: S1-13.
4. Lewis A, Bakkar A, Kreiger-Benson E, et al. Determination of death by neurologic criteria around the world. *Neurology* 2020; 95: e299-309.
5. Wijdicks EF, Varelas PN, Gronseth GS, Greer DM; American Academy of Neurology. Evidence-based guideline update: determining brain death in adults: report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology* 2010; 74: 1911-8.
6. Greer DM, Wang HH, Robinson JD, Varelas PN, Henderson GV, Wijdicks EF. Variability of brain death policies in the United States. *JAMA Neurol* 2016; 73: 213-8.
7. Chassé M, Glen P, Doyle MA, et al. Ancillary testing for diagnosis of brain death: a protocol for a systematic review and meta-analysis. *Syst Rev* 2013; DOI: <https://doi.org/10.1186/2046-4053-2-100>.
8. Plourde G, Neves Briard J, Shemie SD, Shankar J, Chassé M. Flow is not perfusion, and perfusion is not function: ancillary testing for the diagnosis of brain death. *Can J Anesth* 2021; 68: 953-61.
9. Weiss MJ, English SW, D'Aragon F, et al. Survey of Canadian critical care physicians' knowledge and attitudes towards legislative aspects of the deceased organ donation system. *Can J Anesth* 2020; 67: 1349-58.
10. Weiss MJ, English SW, D'Aragon F, et al. Survey of Canadian intensivists on physician non-referral and family override of deceased organ donation. *Can J Anesth* 2020; 67: 313-23.
11. Burns KE, Duffett M, Kho ME, et al. A guide for the design and conduct of self-administered surveys of clinicians. *CMAJ* 2008; 179: 245-52.
12. Lamontagne F, Cook DJ, Adhikari NK, et al. Vasopressor administration and sepsis: a survey of Canadian intensivists. *J Crit Care* 2011; 26: 532.e1-7.
13. McIntyre LA, Hebert PC, Fergusson D, Cook DJ, Aziz A; Canadian Critical Care Trials Group. A survey of Canadian intensivists' resuscitation practices in early septic shock. *Crit Care* 2007; DOI: <https://doi.org/10.1186/cc5962>.
14. Braksick SA, Robinson CP, Gronseth GS, Hocker S, Wijdicks EF, Rabinstein AA. Variability in reported physician practices for brain death determination. *Neurology* 2019; 92: e888-94.
15. Shappell CN, Frank JI, Husari K, Sanchez M, Goldenberg F, Ardeli A. Practice variability in brain death determination: a call to action. *Neurology* 2013; 81: 2009-14.
16. Hornby K, Shemie SD, Teitelbaum J, Doig C. Variability in hospital-based brain death guidelines in Canada. *Can J Anesth* 2006; 53: 613-9.
17. Cronberg T, Greer DM, Lilja G, Moulaert V, Swindell P, Rossetti AO. Brain injury after cardiac arrest: from prognostication of comatose patients to rehabilitation. *Lancet Neurol* 2020; 19: 611-22.
18. Manara A, Varelas P, Wijdicks EF. Brain death in patients with "isolated" brainstem lesions: a case against controversy. *J Neurosurg Anesthesiol* 2019; 31: 171-3.

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