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Brief Communication

Brain Death Determination in Israel: The First Two Years Experience Following Changes to the Brain Death Law—Opportunities and Challenges

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To increase support for the concept of brain death, changes accommodating requirements of the religious authorities were made to the Brain Death Act in Israel. These included (1) considering patient wishes regarding brain death determination (BDD); (2) mandatory performance of apnea and ancillary testing; (3) establishment of an accreditation committee and (4) requirement for physician training courses. We describe the first 2 years experience following implementation (2010–2011). During 2010, the number of BDD decreased from 21.9/million population (during the years 2007–2009) to 16.0 ($p < 0.001$). Reasons included family resistance to brain death testing (27 cases), inability to perform apnea testing (7) and logistic problems related to ancillary testing (26 cases). The number of physicians available to declare brain death also decreased (210 vs. 102). During 2011, BDDs increased to 20.5/million following the introduction of radionuclide angiography as an ancillary test; other reasons for nondetermination persisted (family resistance 26 cases, inability to perform apnea testing 10 cases). Instead of increasing opportunities, many obstacles were encountered following the changes to the Brain Death Act. Although some of these challenges have been met, longer term follow-up is required to assess their complete impact.

Key words: Brain death, religion; transplantation

Abbreviations: BDD, brain death; CTA, computed tomographic angiography; SPECT, single photon emission computed tomography; TCD, transcranial Doppler.

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Introduction

Since the first formalized definition of brain death in 1968 (1), the concept that patients with irreversible loss of brain function are in fact dead has become nearly universally accepted. In this regard, practice guidelines for brain death determination (BDD) exist in most Western countries (2). Since 1996, BDD in Israel was regulated as a clinical guideline for physicians by the Ministry of Health. The guideline, based on the American Academy of Neurology practice parameters (3), required the demonstration of a cause capable of resulting in neuronal death; the exclusion of reversible confounders and clinical findings, including the presence of coma and absence of brainstem reflexes and spontaneous breathing. Ancillary (or confirmatory) tests were not considered mandatory and required only in the presence of confounding factors.

The determination of brain death is the defining precondition in the process of organ donation. In Israel, which has an opting-in system, the consent rate for organ donation has remained low (between 45 and 50%) compared to that in many Western countries. A representative survey of the Israeli population performed in 2001 found that the commonest reason for refusal to donate organs (45% of respondents) was related to religious objections (4). In this regard, the Chief Rabbinate, a body made up of two Chief Rabbis who are selected by a body comprising members from both the secular (mainly politicians) as well as religious communities, issued a religious decree in 1986 accepting brain death as a valid determination of death. Despite this, religious parties opposed recognizing brain death in Israel and dissuaded the public from donating organs for transplantation until further requirements were met. However, despite intensive discussions over many years between representatives of both the medical community and the Rabbinate, consensus could not be reached regarding the validity of brain death criteria. In March 2008, an initiative of members of Parliament resulted in the passing into law of an Act which included most of the requirements of the religious authorities (5). An integral component of the new Act was related to the conviction of the Rabbinate that death may only be determined when spontaneous breathing function ceases irreversibly. For this reason, the Act, which came into effect in August 2009, was designated

the Brain-Respiratory Death Act and formally validated the concept of brain death in Israel for the first time.

In this paper, we will describe the changes made to the new Act, the challenges they imposed to BDD and the first 2 years experience following their implementation.

Patients and Methods

Study population

This retrospective, observational study included all cases during the years 2010 and 2011 in whom the clinical suspicion of brain-respiratory death was documented in the patient file but not formally determined (potentially brain-dead) as well as all cases where brain-respiratory death was formally declared (actual brain-dead). The clinical suspicion was based on an examination performed by the attending physician and required the demonstration of deep coma (Glasgow Coma Score of 3) and absence of all brain stem reflexes and spontaneous breathing. Actual brain-respiratory death demonstration required a clinical examination by two senior physicians, the performance of an ancillary test and the completion of a death certificate. Permission to perform the study was obtained from the Israel Ministry of Health, who waived the need for Helsinki approval as this was a retrospective, observational study using data entered into central databanks.

Changes to the brain-respiratory death act

The changes made to the Brain-Respiratory Death Act and their rationales are shown in Table 1. These include (1) informing the next-of-kin when a patient is suspected of being brain-respiratory dead and inquiring whether the patient expressed an opinion, in writing, regarding the determination of brain death. The provision requires that these views be taken into consideration before performing formal brain death testing; (2) the mandatory performance of an apnea test according to established guidelines (6) including the use of a continuous positive airway pressure system (CPAP) where appropriate (7); (3) the mandatory performance of an ancillary test, using one of the following modalities: transcranial Doppler (TCD), computed tomographic angiography (CTA) or auditory brain stem evoked potentials. Radionuclide angiography, using hexamethylpropylene amine-oxime (HM-PAO) single photon emission CT (SPECT) was included as an option for ancillary testing in 2011; (4) the establishment of an accreditation committee, comprising 10 members, including three rabbis (one of them also a doctor), an ethicist, philosopher, lawyer and four physicians from various disciplines and (5) the requirement for all physicians determining brain-respiratory death to undergo a training course, whose content would be determined by the accreditation committee.

Data collection

Clinical data was extracted from the Israel Transplant Registry and Donor Action database (8) Donor Action, the national donor audit quality control program, captures patients with a Glasgow Coma Score of three in all intensive care departments and emergency rooms throughout Israel. Data within Israel Transplant was provided by the transplant coordinators who serve all major hospitals in Israel, whereas data within the Donor Action database was provided by one of the authors (J.C.). Data was collected over the period 2007–2011 and included (1) the number of formal BDDs; (2) the number of BDDs per million population; (3) the percent of actual/actual and potentially brain-dead patients and (4) the number of doctors available to perform BDD. In addition, reasons for nondetermination of brain-respiratory death were collected and categorized as (1) opposition of the next-of-kin to proceed with BDD; or (2) practical obstacles related either to an inability to perform an apnea test or to the requirement for an ancillary test.

Statistics

Results are expressed as mean ± standard deviation. The paired *t*-test was performed to compare the control period (2007–2009) with the study period (2010–2011).

Results

The effects of the changes in the Act are shown in Table 2. During the years 2007–2009, there was no statistically significant change in any of the parameters studied. During 2010, the number of actual BDDs decreased (160–122, $p < 0.001$ compared to 2009) as did the number of BDDs/million population (21.3–6.0, $p < 0.001$). This was associated with a decrease in the percent of actual/actual

Table 1: Changes introduced to the Brain-Respiratory Death Act and their rationalization

Component of the declaration	Previous protocol	New act	Rational for change
Family information before BD testing	Family informed of intention to perform BD testing	Seek information regarding patient's wishes, in writing, regarding concept of BD	Take into consideration strong religious views of ultra-orthodox community regarding BD
Apnea test	Performed wherever possible. Where not possible, ancillary testing required	Mandatory. Where not possible to perform, BD cannot be declared	Conviction of Rabbinate that death may only be determined when spontaneous breathing function ceases irreversibly
Ancillary testing	In the presence of confounding factors only	Mandatory	Requirement of Rabbinate for an objective test
Physicians required to undergo training course prior to receiving authorization to perform BD declaration	No such requirement	Mandatory. Course includes medical, religious and ethical components	To ensure all aspects of BD declaration fully understood
Authorization committee to oversee BD process in hospitals	No such requirement	Mandatory	To ensure BD declaration performed according to requirements of Rabbinate

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Table 2: Effects of changes in the Brain-Respiratory Death Act on BDD

Parameter	2007	2008	2009	2010	2011
BDDs, (n)	161	160	160	122*	160†
BDDs/million population, (n)	22.4	21.9	21.3	16.0*	20.5†
Actual/ actually + potentially brain dead (%)	93	90	91	67*	81†
Physicians available for BDD, (n)	210	210	210	102	102

*$p < 0.001$ for values 2009 versus 2010; †$p < 0.001$ for values 2010 versus 2011.

+ potentially brain-dead patients from 90.7% (9) to 67% ($p < 0.001$). The number of physicians available to perform BDD also decreased from 210 to 102.

Reasons for nondetermination of brain-respiratory death in 2010 and 2011 are shown in Table 3. In 2010, this was the result of family opposition in 27 cases; in no case was documentation of the patient's wishes requested or noted. All these patients continued to receive full mechanical ventilation and supportive therapy until cardiac arrest occurred. The apnea test could not be performed in seven cases due to the appearance of severe hypoxemia following disconnection from the mechanical ventilator. All these patients were immediately reconnected to mechanical ventilation and continued to receive supportive therapy until cardiac arrest occurred. In 26 cases, nondeclaration was related to the requirement for ancillary testing. In 13 cases, TCD or CTA demonstrated continued blood flow in patients who had undergone decompressive craniectomy. In a further seven cases, repeated CTA examinations revealed cerebral blood flow despite unequivocal clinical evidence of brain-respiratory death. Finally, in six cases, an ancillary test was not performed due to unavailability of appropriate equipment. In all these cases, cardiac arrest appeared before brain-respiratory death could be declared.

Table 3: Reasons for nondetermination of brain-respiratory death

Reason	Number 2010 (total = 60)	Number 2011 (total = 37)
(1) Opposition of next-of-kin to performing BD testing	27	26
(2) Related to logistic problems	33	11
(i) inability to perform apnea test	7	10
(ii) related to ancillary testing	26	1
-following decompressive craniectomy	13	0
-CTA interpretation	7	0
-unavailability of appropriate ancillary test	6	1
-unavailability of interpretation	1	0

CTA = computed tomographic angiography.

During 2011, the number of BDDs increased to 160 ($p < 0.001$ compared to 2010) as did the number BDDs/million population ($p < 0.001$) and the percent of actual/actual + potentially brain-dead patients ($p < 0.001$). The number of physicians available for determination remained unchanged.

In 2011, the main reason for nondetermination (26 cases) was the result of family opposition The number of apnea tests which could not be performed increased to 10 cases. Finally, nondetermination related to ancillary testing decreased to one case.

Discussion

Changes to the Brain-Respiratory Death Act were anticipated to provide an opportunity to increase the number of BDDs as a result of consensus between the medical profession and the Chief Rabbinate. In practice, under appreciation of their consequences had an immediate result, that is, a decrease in the number of formal BDD in the first year following implementation. This presented significant challenges to the medical community who maintains a high level of motivation in ensuring that all potentially brain-dead cases are declared actually dead.

The main reason for nondetermination was related to the requirement for obtaining information regarding a patient's views on brain death. This was introduced to take into consideration the strong negative views held by the ultra-orthodox Jewish community regarding brain death. In these circumstances, it was accepted that death would be declared and the time of death fixed solely on the basis of cardio-respiratory criteria. This special consideration regarding an individual's personal religious beliefs is not limited to the Israeli Act. Thus, the New York State Task Force on Life and the Law, while recommending the adoption of the brain-death standard, also provided an exception directed primarily toward the religious beliefs of Orthodox Jews (10). Although the requirement appears to increase patient autonomy by allowing an individual to express his/her wishes regarding the determination of death, it also states that the attending physician need only take the patient's wishes into consideration, that is, they are not binding. This dichotomy has posed difficulties with interpretation of the requirement and in practice, most attending physicians have not proceeded with the determination in the presence of any opposition expressed by the

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next-of-kin, irrespective of whether this is based on religious or other grounds and whether expressed in writing by the patient or not. Although the reasons for this require further analysis, we speculate that they could include an uncertainty with the intent of the requirement, a reluctance to confront a family in times of extreme stress and the possibility of legal action when denying the apparent wish of a patient. The number of such cases has not changed over the 2-year period of study and this requirement remains a challenge to those declaring brain death. The intention of the law may well have been to decrease the number of BDDs among a sector of the population, that is, ultra-orthodox, whose values do not support it and who would refuse organ donation if approached. However, as mentioned above, the letter of the law is not being adhered to and there are other distinct negative consequences to this requirement: patients who should have been declared dead continue to receive full medical treatment in the intensive care unit and the concept that brain death is actual death is severely challenged.

Practical obstacles accounted for most of the challenges related to changes in the Act. The first was related to the mandatory requirement for an ancillary test. Numerous articles have stressed the potential pitfalls associated with their use (11–13). Thus, for example, in the presence of skull defects, such as occur following traumatic skull fractures, ventricular drainage or decompressive craniotomy, the increase in intracranial pressure following severe brain injury may be compensated for (14,15). In this instance, clinical findings may be compatible with brain death while angiographic studies or TCD may reveal persistence of some cerebral blood flow, giving a false negative result. This was the case in 13 patients in 2010 in whom brain-respiratory death could not be declared. Another situation relates to the nature of the test itself. In this regard, the authors of a recent paper caution against the use of CTA as a standard ancillary test (16). This is due to the presence of both false negative (persistence of cerebral blood flow despite clinical evidence of brain death, as was the case in seven of our patients in 2010) and false positive results with CTA (17). In our study, brain-respiratory death could not be declared in these cases as the other available tests were not appropriate (absence of bone window for TCD and absence of wave 1 for BERA). To meet this challenge, pressure from the medical community resulted in the inclusion of radionuclide angiography (SPECT) as an option for ancillary testing. Studies have shown this test to be reliable in the diagnosis of brain death (18) and unaffected by the presence of skull defects (19). SPECT is now widely used in Israel as the ancillary test of choice, in particular where TCD is technically not possible (absent bone window) or inappropriate (decompressive craniectomy). However, this test, too, has limitations: uptake of radioisotope may be affected by hypothermia and barbiturates, studies may be negative early on in the setting of brain death, thus possibly delaying diagnosis (12) and the radioisotope is not always readily available. Finally, performance of this and other ancillary tests (e.g. CTA) requires the patient to be transported from the ICU to the radiology suite. This poses an additional hazard and in fact, during 2011, two cases developed severe hemodynamic compromise during transport with subsequent cardiac arrest before brain-respiratory death could be determined.

The second practical obstacle was related to the mandatory requirement for an apnea test, despite the fact that the absence of intracranial blood flow, which characterizes brain death, is always associated with the loss of spontaneous breathing and thus is a scientifically sound surrogate for the absence of breathing. Typically, the period of apnea required to maximally stimulate the medullary respiratory center (the result of an increase in the partial pressure of carbon dioxide >60 mmHg) is between 7–10 min (20). However, significant hypoxemia and severe respiratory acidosis may develop during this period, resulting in hypotension, cardiac arrhythmias and even cardiac arrest. Indeed, a recent study found that the apnea test was aborted in 3% of cases due to such complications, whereas the test was deemed unsafe to perform in a further 7% (21). In this situation, it is accepted practice to perform an ancillary examination, an option which is not available in the new Act. In our study, the apnea test was aborted in 7 cases in 2010 so that brain death could not be declared. In 2011, this figure increased to 10 cases. This challenge has prompted the very recent introduction (January 2012) of an alternative apnea test, as described by Sharpe et al., during which the patient remains connected to the mechanical ventilator which is connected to a gas mixture comprising 97% oxygen and 3% carbon dioxide (22). Apnea time is thus decreased and the consequences of disconnection avoided.

The final obstacle was related to the requirement that physicians performing BDD undergo a training course, which includes medical, ethical and religious aspects and under the auspices of both the Medical Council and the Rabbinate. Many physicians have refused to participate in these courses, both because they reject elements of the new Act and because the Rabbinate is seen to have influence over a purely medical decision, that is, the declaration of death. For this reason, the number of physicians available to perform BDD has decreased, resulting in delays in determination and possible deterioration in the condition of potential organ donors.

Guidelines for BDD are usually given by national medical societies (2,23), as disclosed in the Uniform Determination of Death Act in the United States which stated that "the determination of death must be made in accordance with accepted standards" (24). In some countries, however, such as Finland (25), and now in Israel, detailed instructions for BDD have been written into law. Although brain death was defined more than 30 years ago, in some cultural and religious environments it is still not accepted (2,26). The law

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in Israel was thus changed to accommodate the views of a part of the religious population. Jews comprise 75.3% of the Israeli population whereas 20.5% are Arabs. As of 2009, only 8% of Israeli Jews defined themselves as ultra-orthodox whereas an additional 12% defined themselves as "religious" and 13% as "religious–traditionalists". On the other hand, 25% defined themselves as "nonreligious–traditionalists" (not strictly adhering to Jewish law) and 42% as "secular." Changes in BDD were neither a requirement of the Muslim nor secular population. Rather the formulation of the new Act was the result of a public discussion including the ultra-orthodox minority with an attempt to include all the criteria required by the Jewish minority groups. This compromise was intended to unify these minorities regarding the definition of death. The law is supposed to reflect negotiation between the different parties and once approved with a majority vote, should apply to all citizens.

In conclusion, changes made to the BDD required by the religious authorities in Israel were introduced with under appreciation of their consequences. Thus, instead of providing increased opportunities, practical obstacles negatively affected the ability to perform BDD. This presented significant challenges to the medical community and some of these obstacles have been overcome. The long-term effects of the changes, however, including any effect on organ donation, remain to be determined.

Disclosure

The authors of this manuscript have no conflicts of interest to disclose as described by the *American Journal of Transplantation*.

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