ABSTRACT
The Islamic Republic of Iran has a long history of medicine. The principles derived from core Islamic teachings provide a comprehensive moral, ethical, and legal framework for the practice of medicine. The issue of brain death has significant impact on the procurement of organs from cadavers. It is a major subject of debate and interest to bioscientists, legal experts, religious scholars, and the general public. Laws related to the ethical and legal aspects of cadaver organ donation from the brain dead have not been defined in many Muslim countries. This report presents recent advances in Iranian law with regard to the ethics of organ transplantation and the definition of brain death.

ORGAN transplantation (OT) has been advanced for end-stage failure of vital organs because of the developments in surgical and immunosuppressive techniques and public awareness. This applied medical knowledge has shown a high impact to save life and improve the quality of a patient's life. Success in the implementation of OT programs in a country depends on different factors including economic situation, religious permission, public views, medical expertise, and existing laws. There are some Islamic countries that have a positive Fatwa (religious opinion) for OT, but have not adapted it as law, such as Pakistan, Egypt, and Syria.1 Iranian laws, with majority of its population as Muslims, are derived from the teachings of the Quran and the sayings of Prophet Muhammad. With regard to contemporary problems related to bioethics, such as brain death and organ donation, Iranian laws during the last 20 years have been amended to be in accordance with Islamic teachings with general public approval via the parliament.

Availability of organs for transplantation is a global problem. Brain dead cadavers are one of the prime sources of donated organs. However, public acceptability of brain death and attitudes toward the brain dead are deeply influenced by literacy level, prevalent social customs, and religious backgrounds. Keeping in view these limitations to cadaver donation, the Iranian Parliament recently passed an act that has facilitated the procurement of organs from brain dead patients. In this report, we describe the history and background of the relevant aspects of brain death and OT in Iran. We hope that other countries worldwide, especially Islamic countries, can adopt similar legal measures to raise public awareness and acceptability with regard to brain death and cadaveric organ donation.

BRAIN DEATH DEFINITION
The concept of brain death has been historically modified several times.2 The earlier “heart-lung” death definition was not satisfactory for all conditions. Therefore, it was first improved by the Harvard criteria in 1968.3 A summary statement on “Practice Parameters for Determining Brain Death in Adults” was issued by the American Academy of Neurology (AAN) in 1995.4 In 1999, a review by Jenkins et al presented a protocol for rapidly determining brain death.5 A significant reduction in the time to declare brain death was obtained by the brain death determination protocol, which is currently accepted worldwide.6

Brain death is defined as complete and irreversible cessation of all brain and brain stem functions synchronously. It is characterized by complete apnea, absent brain stem reflexes, and cerebral unresponsiveness.4,7 Usually the brain dead patient is in a coma requiring a ventilator with a known cause of serious brain damage, such as traumatic injury.

RELIGIOUS AND HISTORIC BACKGROUND
There are more than 1.3 billion Muslims worldwide. The majority live in Asia or Africa. Iran has land spread over 1.6 million sq km with 99% of its 68 million population being

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Muslim. Islam has introduced its own moral, ethical, and social framework for human life. Islam has granted a certain privilege for saving a human’s life. The Quran explicitly mentions “who so ever gives life to a soul, it shall be as if he had given life to mankind altogether” (5:32).

Therefore, any medication, treatment, and prevention considered as a vital step to maintain normal health of mankind is not only accepted but also recommended. OT is not exempted from this rule. There is no ruling against organ donation in Islam as long as it is done with respect to the deceased and for the benefit of the recipient.

OT has been similarly accepted by different religions such as Christianity, Judaism, Hinduism, and Islam. Generally, Christianity accepts the rule “Give it and it will be given to you” in this matter. Transplantation is believed to be a life-saving procedure by Judaism, and, according to Hinduism, donation after death alleviates suffering.

Ayatollah Khomeini, a prominent Shia scholar, pointed out in response to an istifta (religious question) regarding OT from the brain dead with irreversible life, “It is authorized to use organs such as heart, liver, etc. of a definite brain dead with permission of organ owner for transplantation if someone else’s life is depended on it”. In response to a similar istifta, Ayatollah Khamene’i responded “In such situation, there wouldn’t be any problem using organs if someone’s life is depended on the organ”.

Ayatollah Fazel Lankarani responded to brain death istifta that taking organs of a person with no hope of life due to brain infarction or accident but with heart beating is difficult. However, it is permissible for organs other than the heart if someone’s life is dependent on it.

Ayatollah Noori Hamedani answered that OT of a brain dead patient is permissible but should be authorized by a Faqih (religious scholar) in the case of not having a will from the patient.

Ayatollah Makarem Shirazi permitted OT from a brain dead patient if it is completely and definitely diagnosed to be irreversible.

**OT HISTORY IN IRAN**

During the last two decades, Iran has developed facilities and education for OT. Most facilities are located in Shiraz and Tehran university hospitals. In recent years, developments in OT have resulted in a large number of Iranian expert staff working on cornea, bone marrow, skin, heart, kidney, liver, cardiac valves, bone, ligament, cartilage, and lung transplantations. There are 22 hospital wards for kidney transplantation, 2 for liver, 2 for heart and heart-lung transplantation, and 2 for bone marrow transplantation in Iran.

Iran is a pioneer in kidney transplantation among Middle Eastern countries with approximately 24 transplantation per million population per year. The first kidney transplantation was done in 1967 in Shiraz (south Iran) and the first hospital ward for kidney transplantation was established in 1985 in Tehran. More than 10,000 renal transplantation procedures were performed between 1980 and 2000. The expense of renal transplantation is much less in Iran (approximately $5000 [United States; US]) compared with European countries.

In Iran, commercial OT is not a serious issue and donors and recipients know each other in almost all cases. There is no unknown origin kidney transplantation. Although approximately 80% of living donors belong to the low economic class, it is the same for more than 50% of the recipients. A rewarded gift (approximately $1000 US) is paid by the government to the kidney donors via the Charity Foundation for Specific Disorders (CFFSD), which is a nongovernmental organization (NGO). This was established according a law approved by the government in 1997. There are other reasons to overcome this issue, such as the Islamic culture that looks to organ donation as a charitable act, the performance of OTs only in governmental university hospitals, and the payment for all hospital expenses by the government.

In a study of 8409 renal transplantations in Iran, 63.4% of recipients were men and 36.6% were women, whereas the majority of donors were men (64.7%) without familial relations (67.8%) with the recipients.

Heart transplantation was first performed in 1993. By the end of 2002, more than 45 procedures were reported in Tehran university hospitals. The first liver transplantation was performed in 1993 in Shiraz. By the end of 2002, there were approximately 72 liver transplantation cases in both Tehran and Shiraz. For pancreatic β-cell transplantation, initial work has started.

**NEED FOR LEGISLATION**

Despite the permission of religious scholars, the lack of legislation was the main problem for the practical implementation of cadaveric OT all in Iran. In this regard, the issue of brain death was first discussed in the Iranian Parliament in 1995, but was not approved at that time. It was again discussed in 1999 in the Parliament. At last the act of “Deceased or Brain Dead Patients Organ Transplan-
tation” was passed on April 6, 2000 by the Parliament27 (Table 1). Executive bylaw of this act was then passed by the Cabinet Council on May 15, 200228 on a proposal made by the Ministry of Health and Medical Education (MHME)29 (Table 2) in compliance with note 3 of above act.

In this regard, a protocol was approved by the MHME to define criteria for the determination of brain death. According to this protocol, the clinical diagnosis of brain death involves a neurologist, neurosurgeon, anesthesiologist or internist, and a doctor from the forensic department. If necessary (and in doubtful situations), the next stages of approval of brain death are done by paraclinical standard tests. In addition, all the necessary conditions for OT and the patient’s will or approval by first-degree relatives are mandatory for organ donation. The brain death form is filled and signed by all 4 professional experts mentioned above according to article 2 of the executive bylaw (Table 2) and part 6 of the following protocol.

Table 1. Deceased or Brain Dead Patients Organ Transplantation Act

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<td>OT-equipped hospitals with written permission of MHME can use the healthy organs of dead patients or brain dead patients granted by specialists. This is based on the patient’s will or his/her guardian’s agreement to be used in patients whose lives depend on OT.</td>
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<tr>
<td>1. Diagnosis of brain death shall be established by professional experts in a governmental university equipped hospital. Those experts are appointed by the health minister for 4 years.</td>
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<td>2. A member in the brain death diagnosis team should not be the members of the transplantation team.</td>
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<td>3. Members of teams would not be entitled to pay diyyah (a fine to harm the body) in compensation for dismembering (or removal of organ[s]) from the dead body.</td>
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<td>Executive bylaw of this act should be prepared by MHME, judicial representative, in correlation with medical council and CFFSD during 3 months and approved by cabinet.</td>
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Table 2. Executive Bylaw of Deceased or Brain Dead Patients Organ Transplantation Act

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<td>1. Brain death consists of irreversible termination of cortical, subcortical, and brain stem functions. Brain death protocol should be determined and notified by MHME within this regulation.</td>
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<td>2. With this regulation, brain death diagnostic confirmation should be certified by 4 clinicians: a neurologist, a neurosurgeon, an internalist, and an anesthesiologist.</td>
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<td>2-1. Mentioned experts would be chosen and qualified by the minister of MHME for 4 years in any university equipped hospitals.</td>
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<td>2-2. Each of the aforementioned clinicians should examine the patient, and complete and sign the special form individually. In the case of complete agreement of 4 clinicians, brain death would be established.</td>
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<td>2-3. It is necessary that the specific form should be confirmed by forensic consultants regarding their related responsibilities.</td>
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<td>2-4. The brain death ascertainment and confirmation specific form should be designed by MHME and be accessible to brain death diagnosis centers.</td>
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<td>2-5. Confirmed diagnosis of brain death must be done in governmental university hospitals.</td>
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<td>3. Team members of brain death diagnosis and confirmation must not be of the transplantation team.</td>
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<td>4. All country hospitals are bound to report brain deaths to the TSDMC, so they can be confirmed by diagnosis team.</td>
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<td>5. After confirmed brain death, the next steps will be followed if there is a patient’s will and guardian’s permission.</td>
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<td>6. According to the law, the patient’s will with respect to OT could be either oral or in written form and can be approved by written notice of an heir apparent. If the original will was not available, a special form designed by the MHME would be signed by informed heirs.</td>
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<td>7. The dead’s guardians are heirs apparent who are authorized to consent to OT. Heir’s permission is mandatory.</td>
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<td>7-1. The dead’s guardian permission should be written and recorded.</td>
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<td>7-2. The dead’s guardian written permission is the basis of evidence.</td>
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<td>8. To conduct this code, necessary co-ordination would be done by TSDMC.</td>
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<tr>
<td>9. MHME will inform the MPO for providing expenses for OT (expenses of intensive care unit, cadaver transport, preparation and organ transport, and organ operation) and educational matters. MPO will also provide necessary funds every year specifically from the budget of the country.</td>
</tr>
<tr>
<td>10. According to the law and this code, other necessary orders would be issued and be communicated to relevant centers.</td>
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Abbreviations: MPO, Management and Planning Organization; TGDNC, Transplant and Specific Diseases Management Center.
C. The cause of the coma has been defined as far as possible.

3. Essential clinical evaluations are as follows: absence of spontaneous movement and no responsiveness to the hardest painful stimuli. Absence of brain stem reflexes (Fixed pupils with no response to different levels of light stimuli, absence of oculovestibular reflex [caloric test], and absence of response in Gag test).

4. If necessary, clinical findings can be confirmed using complementary paraclinical tests. First, positive apnea test: giving 100% oxygen to the patient before separating from a ventilator then giving 6 L/min \(O_2\) and letting the \(PCO_2\) increase to 60 mm Hg. No signs of respiration means a positive apnea test and confirms brain death. Second, electroencephalograph (EEG) for 20 minutes on 2 occasions at least 6 hours apart. Two occasions of iso-electric EEG confirm brain death.

5. All clinical findings and tests should not change for 24 hours.

6. Clinicians determining brain death include 2 neurologists and/or 1 neurologist and 1 neurosurgeon who fill out the form for brain death. They examine the patient individually, then sign and stamp the brain death form. This form should also be signed and stamped by an anesthesiologist and a doctor from the forensic department after examining and assessing the patient.

Notes: (1) Children younger than 5 years should be kept for at least 72 hours on the ventilator. (2) The responsible clinician would start investigating brain death and ask for medical consultation. (3) The special brain death form should be completed for every brain death case and sent to the Transplant and Specific Diseases Management Center (TSDMC). The TSDMC affiliated with MHME established the Iranian Network for Organ Procurement to overcome the absence of a registry. This central registry facilitates the communication between referral hospitals, donors and recipients, and transplantation units, as well as handling the training and research in this matter. A unique organ donation informed consent was introduced by this network. This form represents the written or verbal will or consent of legal heirs of the heart or brain dead patients.

DISCUSSION

The practice of medical ethics is influenced by religion, social and cultural background, or affiliation. The relevant aspects of Islamic biomedical ethics can be reviewed in different reports. Generally, the aim of Islamic medical ethics is to seek a compromise between Islamic custom and the achievements of modern medicine, as long as basic Islamic doctrine is not dishonored. Shia school of thought, whose followers comprise about 15% of the world Muslims, has historically developed its own jurisprudence and methodology of interpretations in many Islamic issues. However, on the whole, its bioethical rulings do not differ fundamentally and overlap with different Sunni schools of thought.

In the ethics of OT, lack of legislation was the main problem in Iran. However, with the approval of the brain death act, decree, and MHME protocol, the rate of OT has increased significantly. OT from brain dead patients has increased more compared with (“heart-lung”) cadavers.

This legislation has been drafted with consideration of ethical issues in Iran and worldwide standards. The advantages of this legislation can be highlighted by the exact definition of brain death, necessity of confirmation by 4 professional experts who are not from the transplantation team, and emphasis on a consent form. It can contribute to improving many ethical issues of OT. This legislation facilitates signing organ donation cards and seeking approval from relatives of brain dead patients.

A minimum level of cultural awareness is a necessary prerequisite for the delivery of care that is culturally sensitive. Appreciation of the beliefs, perspectives, and conceptual frameworks used by people are essential parameters when discussing medical ethics concerns. In this regard, public awareness has increased recently and more people have completed organ donation cards and agreed to donate their organs in cases of brain death. This is also reflected by an increased rate of OT from brain dead patients in Iran. Because of their impact, the cultural beliefs and knowledge of different population groups in Iran regarding OT and brain death need further investigation.

A few additional points require clarification and necessary revision of the current MHME protocol, including the limitations of diagnosis and the definition of brain death at university hospitals based on the precise definition of an iso-electric EEG. For example, there are some patients with defined clinical brain death for whom it is not always possible to have 2 iso-electric EEGs. Clarification of this point may define the legal status and the timely supply of organs from a potential cadaver donor, which may not be otherwise possible.

Renal transplantation first began in Iran with living related donors (LRD) and later in 1988 as a controlled program to procure kidneys from living unrelated donors (LURD). The number of kidney donations from LURD has steadily increased because of this program. Although precise data in the country are unavailable, a large recent renal transplantation study in Iran showed the fraction of LURD versus LRD to be 84%. However, the rate of cadaveric kidney transplantation has remained low due to our respect for the corpse and the illegality of corpse mutilation in Islamic culture. In the year 2002, although 1520 kidneys were transplanted from live donors, only 90 donations came from cadavers.

We conclude that public understanding of brain death and cadaver organ donation needs further attention and participation of media, scholars, physicians, nursing staff, and leaders of society. We hope that the current legislation
will contribute to increasing public awareness and the rate of OT from cadaveric donors in Iran.

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