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Medical and legal significance of assessing the probability of brain death in patients after intraoperative cardiac arrest and successful cardiopulmonary resuscitation

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Abstract

Background. *After successful cardiopulmonary resuscitation for intraoperative cardiac arrest, most patients die in the Intensive Care Unit from multiple organ failure, cardiovascular complications that develop after hypoxic-ischemic damage to the central nervous system. In some patients whose heart is still beating in conditions of mechanical ventilation, a complete and irreversible cessation of all brain functions may occur, that is, brain death.*

Objective. *Based on clinical criteria, we made an attempt to assess the likelihood of developing a condition consistent with the diagnosis of brain death in those who sustained cardiac arrest during surgery or other*

medical manipulation and underwent successful cardiopulmonary resuscitation, but died later in the Intensive Care Unit.

Material and methods*. A retrospective analysis of medical records related to 45 clinical cases was performed to assess the likelihood of brain death according to the Quality Assurance Programme in the Deceased Donation Process (QAPDD) methodology, which has been used during an external audit in hospitals of Spain and specifically focused on the donation process after brain death.*

Results*. In 30 (66.7%) patients, based on the proposed criteria, a high probability of developing brain death was noted. At the same time, in 27 (90%) cases, clinical signs of brain death were noted within the first 6 days after cardiopulmonary resuscitation. Biological death in these patients was ascertained within 1 to 119 days from the moment of the development of clinical signs of brain death.*

Inference*. The concept of brain death has serious medical, economic, legal, and ethical implications. When clinical suspicion of brain death arises, it is important that all such undergo standard diagnostic procedures to objectively rule out or confirm the diagnosis of brain death.*

Conclusion. *The probability brain death occurrence in patients after intraoperative cardiac arrest and successful cardiopulmonary resuscitation is statistically siqnificant at 66.7% (p=0.0196).*

Keywords: perioperative cardiac arrest, cardiopulmonary resuscitation, brain death

Conflict of interest The authors declare no conflict of interest

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BD, brain death
CPR, cardiopulmonary resuscitation
FMEC, forensic medical examination commission
ICU, Intensive Care Unit

Introduction

Cardiac arrest in the operating room and procedure rooms (dressing rooms, manipulation rooms) can be associated with various causes and is a rare but potentially life-threatening event, and despite rapid recognition as the patients are usually under close observation, up to 70% of patients die in the Intensive Care Unit (ICU) within 30 days after cardiopulmonary resuscitation (CPR) [1–3]. Most patients die from multiple organ failure, cardiovascular complications developing after hypoxic-ischemic damage to the central nervous system [4–7]. In some heart-beating patients under conditions of artificial ventilation, a complete and irreversible cessation of all brain functions, i.e. brain death (BD), may occur [8].

However, the topic of the epidemiology of BD after CPR is poorly described in the literature and is rarely systematically reviewed.

Therefore, the aim of the study was to assess the probability of developing a condition corresponding to the diagnosis of BD, based on clinical criteria among those who died in the Intensive Care Unit after cardiac arrest during surgery or other medical manipulation and subsequent successful CPR.

Material and methods

In order to solve the task set, a retrospective analysis of the medical records of inpatients was made within the framework of medicollegal proceedings, as well as archival "Forensic Medical Expert Report" of commission forensic medical examinations (CFME) conducted at the

Federal State Institution "The Russian Center for Forensic Medical Examination" of the Health Ministry of the Russian Federation and the State Healthcare Institution of the City of Moscow "The Bureau of Forensic Medical Examination of the Health Department of the City of Moscow". All CFMEs were made with respect to those who died in an intensive care unit, in whom the cardiac arrest occurred during surgical operations and medical manipulations. The study included the deceased patients over 1 year of age, as per Order No. 908n from December 25, 2014 issued by the Health Ministry of the Russian Federation [9].

Since perioperative hypothermia, the effect of general anesthetics and muscle relaxants could distort the data of the clinical and neurological examination [9–11], the probability of BD development was assessed 24 hours after CPR and the spontaneous circulation had been restored [12]. The assessment of clinical signs of probable BD was not considered until the cessation of sedative therapy, either. We did not make an assessment of the CPR performance and the patient management in the ICU.

To assess the probability of BD, the QAPDD (Quality Assurance Programme in the Deceased Donation Process) methodology was used, as applied during an external audit in Spanish hospitals specifically focused on the donation process after BD [13, 14].

The following criteria were used to identify the number of cases with high probability of BD in the retrospective study.

I. Etiology.

A clinically, instrumentally and laboratory confirmed nosological entity that might be the cause of BD.

In our study, all deceased individuals had secondary brain damage as a result of hypoxemia of various origins, including the cessation or deterioration of systemic circulation.

II. Conditions.

- Coma III; Glasgow Coma Scale score 3 (no signs of spontaneous breathing or movement).

III. Results of examination (condition).

- Progressive mydriasis and the absence of pupillary light reflex that are not associated with the administration of drugs aimed at pupillary dilation.
- Absence of at least one of the following brainstem reflexes:
  - corneal;
  - oculocephalic;
  - oculovestibular;
  - pharyngeal;
  - tracheal.

IV. Clinical signs:

- severe hypotension requiring the administration of catecholamines or vasopressors in the absence of causes (hemorrhagic shock, sepsis, anaphylactic shock, etc.) other than possible BD;
- severe polyuria in the absence of other causes (administration of diuretics, hyperosmolar solutions, etc.).

A high probability of BD diagnosis was considered with a simultaneous combination of the following signs:

- •I + II + III (at least 1 sign) + IV (at least 1 sign);
- •I + II + III (2 signs).

To assess the probability of developing BD, the binomial distribution method was used; $p<0.05$ was considered a statistically significant result [15].

Results

Medical records and CFME were reviewed for 45 clinical cases, of which 13 were male and 32 were female; the mean age was 35.1±2.16 years. The preoperative physical status assessed by ASA Physical Status Classification System was as follows: ASA I in 28 patients; ASA II in 13 patients; ASA III in 4 patients. The causes of cardiac arrest are listed in the table.

Table. Causes of cardiac arrest

Cause	n	%
Respiratory disorders	29	64
High spinal block	6	13
Systemic toxicity of local anesthetics	5	11
Hemorrhagic shock	2	4
Anaphylactic shock	1	2
Undertaking cardioversion	1	2
Intraoperative acute cerebrovascular accident	1	2
Total	45	100

Based on the proposed criteria a high probability of developing BD was noted in 30 patients (66.7%). In 27 cases (90%), the BD clinical signs were noted during the first 6 days after CPR. In 3 cases (10%), the development of BD clinical signs could be assessed at analysis only on the 10^{th}, 14^{th}, 24^{th} day after the spontaneous circulation had been restored, which was associated with conflicting reports made by the doctors of various specialties (anesthesiologist-intensivists, neurologist, neurosurgeon) in the patients' medical records (Fig. 1).

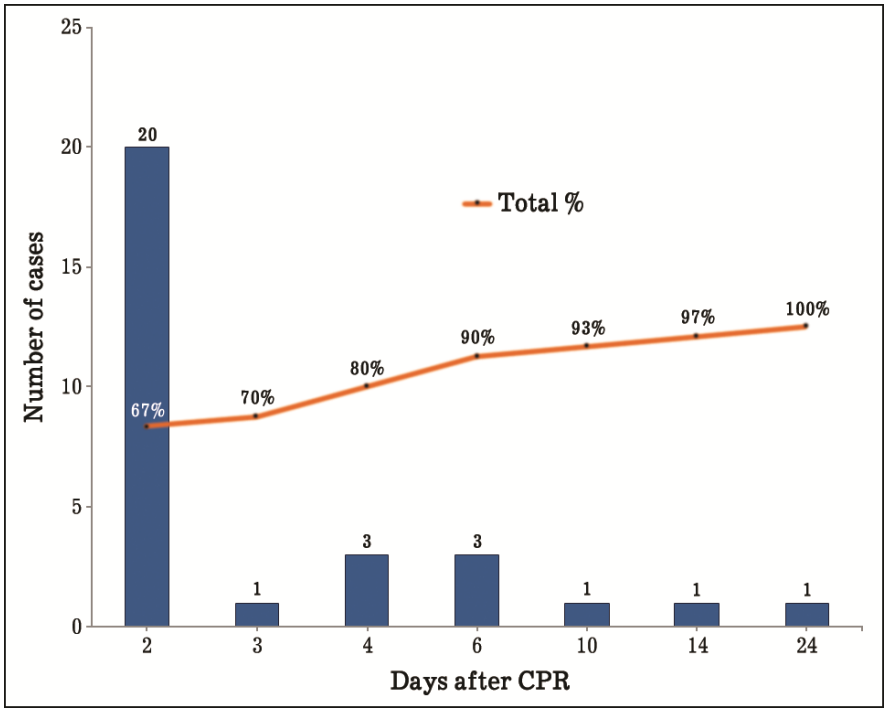

Fig. 1. The number of cases of the clinical brain death development by days after cardiopulmonary resuscitation

Biological death in these patients was confirmed within 1 to 119 days from the moment of developing BD clinical signs (Fig. 2).

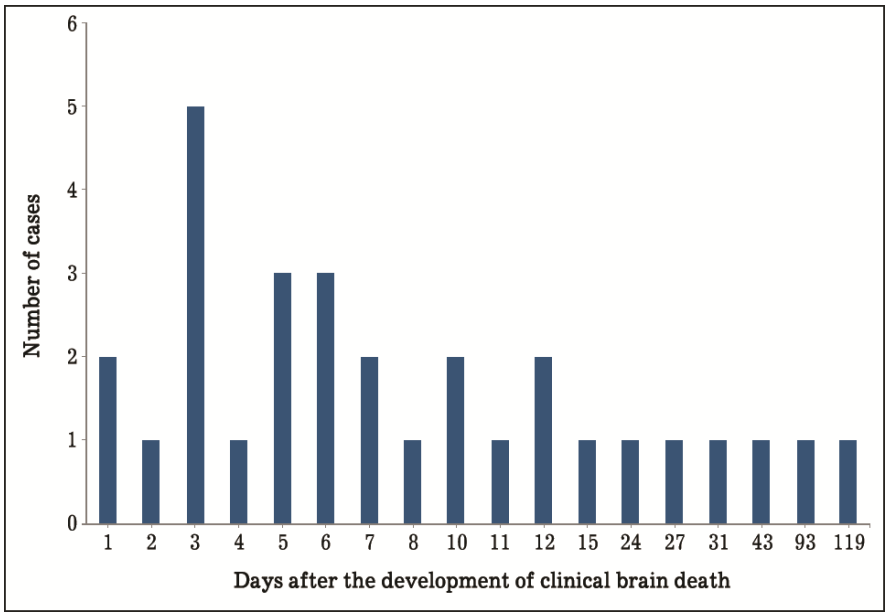

Fig. 2. Number of cases of declaring biological death by days after the development of clinical brain death

In none of the studied cases was the diagnosis of BD established or discussed. Only in 2 cases, at corpse examinations, the following statements were made and included in the forensic diagnosis: “intravital brain death” and “respiratory brain” (an outdated definition of brain death).

We do not claim that in all cases there was an objective possibility of diagnosing BD, since there was no information about the available equipment and specialists in accordance with Order No. 908n from December 25, 2014 of the Health Ministry of the Russian Federation [9].

Discussion

Currently, BD is legally recognized as equivalent to human death in most countries of the world, including the Russian Federation [9, 16], while the diagnosis and definition of BD are ambiguous and vary greatly depending on the legislation and compliance with the guidelines of scientific societies in individual countries. This is explained by the fact that the diagnosis of BD in many countries is inextricably linked with the assessment of donor potential, and it is implied that if a possible or potential donor has medical contraindications, then the procedure for diagnosing BD is not performed, although in 11% of cases this decision is incorrect [14].

Due to differences in terminology and definitions, it is sometimes difficult to compare BD incidence estimates. Only a small proportion of studies have been conducted at the national level, and most studies have been conducted at the base of one or a few hospitals. Therefore, BD incidence data from different studies are not always comparable with the data from national agencies [17, 18].

The incidence of reported BD cases in the United States is relatively low and, according to the results of a cross-sectional study of data from the Healthcare Cost and Utilization Project (HCUP), which was conducted in the United States from 2012 to 2016, BD accounted for 2.06% of all deaths in US hospitals [19].

In 2015–2016, a prospective multinational observational study "Eticus" was conducted in 199 ICUs in 36 countries. The study focused on global differences in end-of-life care practices in patients over 13 years of age. BD included in a separate pre-defined category, averaged 5.1% [20].

In Australia, during an audit of the DonateLife program in 2012–2014, the incidence of confirmed and probable cases of BD among deceased patients in intensive care units was 14.8% [21].

Implemented in the period from 2000–2009 *Improving the Knowledge and Practices in Organ Donation* (DOPKI) *Project* revealed that in the countries participating in the project, 15% of all deceased patients in intensive care and critical care units had a clinical presentation of BD [13].

According to the review by L. Roels et al., among 17,903 patients aged up to 76 years who died in 605 hospitals in six European countries, 4,855 cases (27%) met the diagnostic criteria for BD [22].

The likelihood of developing clinical BD abruptly increases among the patients with primary and secondary brain damage.

According to a retrospective analysis from 2001 to 2010, among all the patients registered in the north-eastern regional office of Deutsche Foundation Organtransplantation (DSO) (*Eng.* the German Foundation for Organ Transplantation), who died in the acute phase after severe traumatic brain injury, BD was diagnosed in 45.3% [23]. In Italy, 41.8% of patients in this group were in a condition that met the criteria for BD [24].

In Spain, the incidence of BD diagnosis remained stable over the period from 2009–2018, averaging 17.8% of deaths from primary and secondary brain injuries. In hospitals without neurosurgical departments, the proportion of BD-diagnosed deaths made 13%, while in hospitals with neurosurgical departments and neurosurgical intensive care, the incidence of BD diagnosis increased to 33% [14, 25, 26].

In a retrospective review of all patients registered in the Tuscan Donor Quality Program between 2003 and 2007 who died from primary or secondary brain damage, the incidence of BD was 48.1% [27].

The incidence of BD secondary to CNS injury following cardiac arrest and subsequent CPR is rarely reported and has not been systematically reviewed.

According to a systematic review and meta-analysis conducted by S. Sandroni et al. [28], the overall prevalence of BD in adult patients who died before hospital discharge after CPR for cardiac arrest was 13% and varied by the CPR type. The incidence of BD was significantly higher in patients receiving the CPR with the use of extracorporeal membrane oxygenation compared to patients after traditional CPR and made 28% versus 8.3%, respectively. The diagnosis of BD was made on average on the 3rd–6th day after restoring the spontaneous circulation.

A similar pattern was observed in our study. In 90% of cases, the development of BD clinical symptoms occurred on the 2nd–6th day after CPR. This is consistent with the fact that massive cerebral edema that occurs after global ischemia and leads to BD is usually delayed and develops within 48–72 hours [12, 29–31]. According to R. Cloutier et al., a later detection of BD clinical signs is explained by frequent incomplete and incorrect recordings of the consciousness level and other neurological signs, since not all doctors have a clear understanding of the thanatogenesis of BD [32], which is what we observed in our study.

In the Russian Federation, there are no data on the epidemiology of BD, which can be explained by at least two reasons:

- diagnosis of BD is made exclusively in hospitals participating in donor programs. According to the XV report of the Russian Transplant Society Registry, in 2022, donor programs were implemented in 34 constituent entities of the Russian Federation and the number of effective donors with a diagnosis of "brain death" was 725 [33].
- In hospitals not included in the donor program, BD diagnosis is not performed (with the exception of individual cases) and the statistics on the number of BD cases are not kept, since the Russian-language version of ICD-10, unlike the English-language version (ICD-10), does not have a coding for brain death (G93.82).

The only study on assessing the epidemiology of BD is an external audit in 26 donor databases of the Federal Medical and Biological Agency of Russia to assess the effectiveness of identifying potential organ donors with developed clinical manifestations of BD. A retrospective analysis showed that among patients aged 18 to 65 years with severe primary and secondary brain damage who died in intensive care units, the BD probability was assessed as high in 20.3% of cases [34].

There is a generally accepted opinion in medical literature that patients diagnosed with BD are able to “live” for several days or even for a week in some cases until irreversible cardiac arrest [35]. In some situations, doctors consciously continue somatic support of the mother to ensure the viability of the fetus and maximize the perinatal outcome for the sake of preserving the fetus viability. In a systematic review of the literature, M.G. Dorado et al. described 35 cases of somatic support of the pregnant women diagnosed with BD [36]. BD was diagnosed at mean of 20 weeks of pregnancy, and the somatic support of the mother aimed at maximizing the perinatal outcome lasted for about 7 weeks, with 77% of

newborns being born alive and 85% of these infants had a normal outcome at 20 months of life.

No such studies have been described in medical literature in the Russian Federation.

Undoubted interest has arisen to the study by A. Shewmon who, thanks to his personal observations and analysis of articles from various sources and a systematic database, identified 175 BD cases in patients with a survival time (with stable heartbeat and circulation functions) of at least 1 week. In 56 cases, there was sufficient information for a meta-analysis of factors influencing survival. Of these 56 cases, stable hemodynamics were maintained in 27 patients for more than 1 month, in 17 patients for more than 2 months, in 7 for more than 6 months, and in 4 patients for more than 1 year. One 18-year-old patient, named "TK", at the time of the study had maintained stable hemodynamics for 14 years after diagnosing BD at the age of 4 years [37]. The cardiac arrest was noted only 20 years later. The results of this patient's monitoring and brain autopsy data were described in 2006 by S. Repertinger et al. [38].

Thus, the use of the QAPDD methodology in intensive care units allows identifying the patients with developed BD clinical signs with a high degree of reliability. In general, it can be noted that our results correlate with the data of the world scientific literature.

Conclusion

The concept of brain death has serious medical, economic, legal and ethical implications. When clinical suspicions of brain death arise, it is important that all such patients undergo investigation procedures for the diagnosis of brain death to objectively exclude or confirm this diagnosis. From the point of view of relatives and family, unambiguous criteria for brain death are necessary to prevent the physician from

treating the patient as if he or she were dead. From the point of view of medicine, the diagnosis of brain death is necessary first of all to stop senseless expensive "treatment" and to care for a dead patient ("terror of humanity") as if he were alive.

The moment of the human brain death is defined as both the biological death (irreversible death of a human), and also as the death of the human brain. This has an important legal significance, consisting in the loss of the birthrights and freedoms of a person (patient) who is in a hospital with a diagnosis of brain death.

A brain-dead patient loses the right not only to health care and medical assistance (resuscitation and supportive therapy are discontinued), but also to inheritance, disposal of property, etc. Obviously, the time of death will be decisive in the event of inheritance disputes.

Meanwhile, the moment of death is usually considered to be the moment of biological death of a human being, rather than the death of his/her brain. In the medical records of a hospital patient, this is the date and time recorded, while the moment of brain death could have occurred much earlier. This, in our opinion, contradicts the definition of the moment of death established by law.

The experts in the course of conducting forensic medical examinations are asked the question: "When did death occur?" In expert practice, it has become established that when answering this question, the expert commission uses the data entered in the medical record of the inpatient, namely, the time of biological death. Meantime, when conducting examinations, a possible brain death, which has independent legal significance, is not analyzed. This will be of particular importance in cases where the brain death could have been diagnosed several days (and not several hours) before the occurrence (and recording) of biological death.

It is obvious that neither the legislator nor the medical community has any doubts about brain death as an irreversible process, however, neither clinical doctors, nor forensic experts, nor lawyers have paid due attention to the moment of brain death as a legal fact.

Based on the above, the following conclusion can be made:

The probability of developing brain death in patients after intraoperative cardiac arrest and successful cardiopulmonary resuscitation is statistically significant at 66.7% (p=0.0196).

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