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**Rationale.** There have been only single studies conducted in the Russian Federation to characterize the posthumous donor population.

**Objective:** Identifying the main characteristics of the donor pool in N.V. Sklifosovsky Research Institute for Emergency Medicine of Moscow Healthcare Department and in the State Research Center - A.I. Burnasyan Federal Medical Biophysical Center, FMBA, for the period from 2008-2017.

**Material and methods.** The clinical records of 429 actual and effective posthumous donors were analyzed retrospectively. The following
characteristics were studied: gender, age, permanent place of residence, cause of death, the duration of mechanical lung ventilation, type of donation, total number of harvested organs, and number of organs recovered per donor.

**Results.** There were 281 male and 148 female donors. The increase in the mean age of donors from 37 to 48.5 years was noted.

Cerebrovascular disease and traumatic brain injury became the main causes of death. Since 2012, the rate of cerebrovascular diseases as the cause of donor death has increased from 30% to 70%.

Of 429 actual donors, the brain death was diagnosed in 366 (85.3%). Four hundred eight deceased became effective donors. A total of 1,247 donor organs (744 kidneys, 220 livers, 42 pancreas, 2 intestines, 180 hearts, 58 lungs, and 1 facial vascularized composite allograft) were obtained. The mean number of donor organs recovered per donor was 3.06.

**Conclusions.** The results obtained can be used to develop unified protocols and results of posthumous donors and to assess the possible volume of transplant care.

In the period 2008–2017 an increase in the average age of posthumous donors (from 38.1 to 48.7 years) due to the proportion of donors in the 18–29 age group (from 29 to 4%) and an increase in the proportion of donors in the age group over 60 (from 3 to 15%).

From 2012 to 2017 (from 68 to 29%) due to an increase in the number of donors who died as a result of cerebrovascular diseases (from 30 to 71%).

Among the posthumous donors delivered by ambulance teams directly to the intensive care units, 69% of the consciousness level was depressed to 5 and lower on the Glasgow coma scale.
Keywords: organ donation, brain death, mean number of organs recovered per effective donor

CVD, cerebrovascular disease
DBD (Donation after Brain Death), donor with ascertained brain death
DCD (Donation after Circulatory Death), donor after blood circulation arrest
ECD (Expanded Criteria Donor), donor with expanded selection criteria
GCS, Glasgow Coma Scale
MLV, mechanical lung ventilation
ORPD (organs recovered per donor), number of organs obtained from one donor
RTA, road traffic accident
SCD (Standard Criteria Donor), donor with standard selection criteria
TBI, traumatic brain injury
VCA (Vascular Composite Allograft), donor's body vascularized multiple structures designated for transplantation

Introduction
Since 1954 organ transplantation has moved from the field of daring experiments into clinical practice. After overcoming initial technical and immunological problems, organ transplantation has become an uncontested method for saving patients' lives in many diseases. One of the main results of such operations has been the increased world population of people living with transplanted organs. In the USA alone, the number of life years saved by transplantation between 1987 and 2012 accounted for 2.3 million [1].

However, the phrase "Transplantation can not do without donors" said by José Luis Escalante, the Doctor of Medicine, a leading specialist in the
field of Intensive Medicine and Coordination of Organ Donation in Spain [2], very accurately reflects the main problem in modern transplantation i.e. a shortage of donor organs. But the main reason is not a low number of potential donors in absolute terms, but the inability to identify them [3].

In Russia, unlike most countries with an advanced clinical transplantation system, there is no unified national system for postmortem organ donation management that would plan and regulate scientific research in this field, and also popularize organ donation among general population and medical care providers. The lack of reliable information about postmortem organ donation leads to the presentation of this process as "a by-product of unsuccessfully provided neurosurgical or neurological care" [4] both among lay people, and among doctors.

In the Russian medical literature, one can find only scarce reports on studying the characteristics of posthumous donor population, so we have conducted a study aimed at reviewing the pool of posthumous donors at N.V. Sklifosovsky Research Institute for Emergency Medicine, and A.I. Burnasyan Federal Medical Biophysical Center, FMBA, for the recent 9 years.

Material and methods

Terminology

Unfortunately, terminology and abbreviations concerning organ donation can not be called well-established in Russia. Therefore, in our report, we used the most common terminology regarding donation [5-8].

DBD (Donation after Brain Death) implies a donor with a confirmed brain death. These are the patients after the declared brain death on the basis of an established diagnosis of brain death, in whom mechanical lung
ventilation (MLV) is continued and the cardiac activity is managed by pharmacological support. The brain death occurs at a complete and irreversible cessation of all brain functions recorded with heart-beating and providing MLV.

_ECD_ (Expanded Criteria Donor) stands for a donor with expanded donor selection criteria in relation to the kidneys. The ECDs include the DBDs older 60 years or those aged 50-59 years who have at least two of the following criteria:

- hypertension disease;
- the serum creatinine level over 132 μmol/L (1.5 mg/dL);
- death as a result of cerebrovascular disease (CVD).

_SCD_ (Standard Criteria Donor) is a donor with standard selection criteria. These are DBD donors who do not meet any of the criteria for an ECD.

_DCD_ (Donation after Circulatory Death) implies a donor after blood circulation arrest. These are the patients with an irreversible arrest of blood circulation in the body for whom a biological death has been declared.

_An actual donor_ is a DCD or DBD donor for whom there are documented legal and medical grounds provided allowing the removal of donor organs from his/her body for the purpose of transplantation, and in whom an operative incision was made with the intent of organ recovery for the purpose of transplantation.

_An effective donor_ is a DCD or DBD donor from whom at least one organ was recovered for the purpose of transplantation.

_ORPD_ (organs recovered per donor) for all organs denotes the number of organs obtained from one donor, implies the mean of organs explanted
from one donor and is calculated by dividing the sum of all donor organs by the total number of all types of donors.

*ORPD* for individual organs denotes the mean of a specific organ amount (kidney, liver, heart, lung, pancreas, small intestine) explanted from one donor.

It is possible to get from 1 to 8 so-called solid organs from one donor: 2 kidneys, liver, pancreas, small intestine, heart, 2 lungs. Also in addition to solid organs, the donor vascular composite allograft (VCA) is now recognized as a donor organ, both in anatomical and functional terms (limbs, face, larynx, abdominal wall, tongue, and esophagus), transplanted from a donor to a recipient [9-11].

We analyzed retrospectively 429 donor records of actual and effective donors provided by the Sklifosovsky Research Institute for Emergency Medicine and by donor hospitals of FMBA of Russia for the period of 2008-2017. That number accounted for 10% of all posthumous donors in Russia for the period. The following donor characteristics were reviewed: gender, age, permanent place of residence, cause of death, time from the moment of patient placement on MLV till ascertaining the death, the donation type, total number of donor organs recovered, number of organs recovered per donor.

The results of the studies were mathematically processed using the standard method of variation statistics with Student's t-test calculations for pair-wise comparison. The difference was considered statistically significant at $p \leq 0.05$.

**Results and discussion**

There were 281 men (66%) and 148 women (34%) in the total pool of actual organ donors ($n=429$). The highest percentage of men (84%) was
among donors who died as a result of traumatic brain injury (TBI). Among donors with CVD, the number of men and women was almost equal making 50% for each gender (Fig. 1).

![Image]

**Fig. 1. The profile of the donor pool by gender**

The predominance of men over women among postmortem donors is noted in a number of studies by Russian and foreign authors. According to the OPTN/SRTR Annual Report (USA), a long-term tendency of male prevalence among donors persists at the level of 58-60% [7]. In the period from 1996-2009, the ratio of male and female donors in Hong Kong was 59% and 41%, respectively [12]. In St.Petersburg, according to O.N.Reznik, that ratio was 74% to 26% for the period from 2004-2007 [13]. The same ratio was reported by M.G.Minina in Moscow in 2009-2014 [14]. This predominance of men over women among postmortem donors is most likely due to the fact that the injury incidence among men is higher.

The mean donor age was 42.1 ± 0.62 years old (min=18 years, max=77 years).
The maximum age of posthumous donors for individual organs was:
- 77 years old for kidneys;
- 71 years old for the liver;
- 58 years old for lungs;
- 61 years old for the heart;
- 55 years old for the pancreas.

In 2008, the mean age of posthumous donors was 38.1 ± 2.2 years old. From 2010, there was a progressive increase in the mean age of posthumous donors, and from 2014, that increase acquired a statistically significant difference; and in 2017, the mean donor age was 48.7 ± 1.5 years (Fig. 2). That trend was consistent with a change in the distribution of donors by age group. So, in 2008 the most representative age group comprised those who died at the age of 18-29 (29%), and the age group over 60 years comprised only 3% of the deceased, but in 2017, the age group of 18-29 years decreased to 4% with a simultaneous increase to 15% in the number of donors in the age group over 60 years, and the donors aged 50-59 years were the most representative age group (36%) (Fig. 3).
Fig. 2. Changes in the mean age of posthumous donors over time from 2008–2017

Fig. 3. The contribution of different age groups to the total donor pool in 2008–2017
A progressive increase in the number of patients on waiting lists due to expanding the indications for transplantation, has considerably accentuated the problem of donor organ shortage that has entailed the expansion of the criteria for organ donation, including those by age. Thus, from 2000 to 2016, the proportion of posthumous donors in the age group over 60 years in Spain increased from 31.5 to 54.8 %. Moreover, 9.8% of the total pool was made up of donors over the age of 80 years. The maximum age of posthumous donors was:

- 90 years old for the liver;
- 89 years old for kidneys;
- 74 years old for lungs;
- 79 years old for the heart;
- 55 years old for the pancreas [15].

In the period from 1996-2005, the mean age of donors in Hong Kong increased from 38.8 to 50.2 years old, and the age group of donors over 60 increased to 17% [12]. In 20002009, the same trend was also observed in South Korea where the mean age of donors increased from 32.9 to 41 years old [16]. According to Eurotransplant International Foundation, over the recent 15 years the number of donors in the age group over 65 years has increased from 20.7 to 26% [17].

However, over the recent 10 years, in the USA, unlike most other countries, the number of donors in the age group over 65 years has decreased from 9.1 to 6.55%, and the number of donors in the age group of 18-34 years has increased from 26.1 to 30.8% [7].

In studies by Russian investigators, we have not found the results similar to ours. So, I.V. Loginov noted only a statistically insignificant
increase in the mean age of donors from 39 to 44 years [18]. M.G.Minina in her study of donor age for the period of 2009-2014 revealed only a small fluctuation of 0.8-1.3% in the share of the age group over 60 years in the total pool of posthumous donors [14].

All donors from the FMBA donor hospitals were residents of the cities where those hospitals were located. Of interest was the distribution of donors from the Sklifosovsky Research Institute for Emergency Medicine by their place of residence: 58% donors were Moscow residents, 11% were the residents of the Moscow Region, 12% of donors were from other Russian cities, and 10% of donors were foreign citizens; in 9% of donations the donor personality was not identified at the time of organ withdrawal procedure (Fig. 4).

Fig. 4. Distribution of donors in the Sklifosovsky Research Institute for Emergency Medicine by the place of their permanent residence
Many countries stipulate that donors are to be registered, indentifying their place of birth, place of residence, religion, nationality, and even profession. In most cases, this is due to possible problems with getting the family's consent to organ donation, with the allocation procedure for scarce donor organs, the risk of transmission of tropical and geographically restricted infections. P.Mart'n-Da'vila et al. wrote, "We are living in an increasingly globalized world in which ... massive tourist movements, international migration, and increases in world commercial exchanges act as important underlying factors for the emergence and reemergence of specific infectious diseases." On this basis, the authors recommended that the donor selection protocols should be updated to include the latest microbiological diagnostic screening techniques to be used for the detection of potentially transmissible infections from areas of endemicity. It is necessary to identify the potential donor's risk factors, to make special emphasis on the donor's travel and sexual history, exposure to animal or insect bites, history of prior blood transfusions, as well as the country of birth and residence of both the donor and his or her parents [19]. In our opinion, given the fact that 22% of posthumous donors are not residents of Moscow, but came from various regions of the Russian Federation and CIS countries (mainly from the Asian republics), and the donor selection protocols include no diagnostic techniques for identifying potentially transmissible infections from areas of endemicity, this issue should be discussed with infectious control specialists and epidemiologists.

The draft of the Federal Law On donation of human organs, parts of organs, and their transplantation [20] provides for a ban on the retrieval of donor organs from unidentified persons, which may lead to a 9% decrease in the number of posthumous donors.
The main causes of death among all patients who became posthumous donors included various CVDs in 49.8%, and TBI in 45.3%. In 4.9% of cases, death occurred due to other causes: brain anoxia, acute occlusive hydrocephalus, and primary brain tumors (Fig. 5).

![Fig. 5. The profile of the donor pool considering the cause of death](image)

When considering the changing ratio of the causes of death over time, we noted that from 2008 to 2012, the TBI prevalence as the cause of death increased from 44% to 68%; and further it continuously decreased to 29% in 2017. There was no regularity in the frequency variation for other causes of mortality (from 0% to 9%) (Fig. 6).
Fig. 6. Changes in the profile of the donor pool considering the cause of death for the period from 2008–2017

In all countries with a well-developed transplantation service, there is a tendency to a reduction in the incidence of TBI-related deaths among donors. First of all, this can be explained by the results of systematic work aimed at reducing the number of road traffic accidents (RTAs) and increasing the active and passive motor vehicle safety, as well as by undeniable progress in the treatment of TBI patients. Simultaneously, the increased number of CVDs in donor mortality profile was resulted from the increase in the upper age limit in postmortem donors.

In Spain, the proportion of donors killed as a result of RTA decreased from 43% in 1992 to 4.4% in 2016, while the share of CVD increased from 39 to 61.2% [15]; CVD accounts for 58% in Switzerland, [22], and for 68.5% in Hong Kong [12]. As can be seen, despite some variability among
the data published in different countries, the overall pattern of proportions is similar.

However, there is a slightly different trend in the United States. The prevailing nosological causes of death among donors have been brain anoxia, CVD, and TBI. From 2008 to 2017, there was a decrease in the share of TBI (from 37% to 28%) as the cause of donor death in the donor pool against the background of a decreased number of RTAs as the circumstances of the injury (from 15 to 13%). But at the same time, there was a decrease from 40 to 27% in the CVD prevalence. And the share of anoxic brain damage increased significantly (from 22 to 42%), which can be explained by a considerable increase in the non-medical use of opiate-containing drugs among young people in the United States and Canada, which have recently become epidemic [7, 23, 24].

According to I.V. Loginov and O.N. Reznik, there was a significant decrease in mortality from TBI with a stable high mortality from cerebrovascular diseases in St. Petersburg in 2006-2009. That led to a 3.8-fold increase in CVD donors (up to 67%) [13, 18]. In Moscow, according to M.G. Minina, the incidence of CVD increased from 27.4% to 40.4% from 2009 to 2014 [14]. In 86% of the actual DBD donors delivered by ambulance teams directly to the Intensive Care Unit (ICU), the level of consciousness was depressed to coma, as assessed by Glasgow Coma Scale (GCS ≤ 8). At the same time, 69% of them were in deep and atonic (grade IV coma) (GCS ≤ 5) (Fig. 7).
Fig. 7. Donor level of consciousness assessed by Glasgow Coma Scale on admission to the Intensive Care Unit

Similar results and the assessment by GCS as an excellent measure of neurological status in terms of brain death prediction, especially in deep coma assessed as GCS score ≤ 5, were presented by J.S.Ibanes et al. in their observation (2007) [25].

The mean duration of mechanical ventilation from the moment of intubation to the diagnosis of brain death in DBD donors was $78.6 \pm 4.15$ hours (min = 9 h, max = 816 h) (Fig. 8).
However, there was no statistically significant difference in the duration of mechanical ventilation between DBD donors died as a result of TBI or CVD. In 83% of DBD donors, organ harvesting had been undertaken by their 5th day (120 hours) on ventilation.

Biological death was stated in 44% of DCD donors in the first 6 hours after admission to the ICU (2.2 ± 0.29 hours). In 6% of DCD donors, a cardiac arrest occurred after the brain death diagnosis had been established; in 50% of DCD donors, the biological death was stated in the period between 2 and 10 days (115.2 ± 28.99 hours) of being on MLV in the ICU.
Different studies by foreign authors present the data on DBD donors being on mechanical ventilation for 24 to 72 hours and more. The mean duration of mechanical ventilation was 42.8 hours in Australia in 2016, 25.9 hours in New Zealand [26]; in Hong Kong, 64.2% of DBD were on the ventilator within 48 hours [12]. We did not find any data on this parameter in the Russian medical literature on the topic.

Until recently, there was a general consensus that the earlier the donor organs are removed from the "hostile" environment of the host's body (acute impairments of homeostasis, water-electrolyte balance, the arterial hypotension, etc.), the more acceptable they would be for transplantation. However, an alternative opinion has recently taken shape. W.N. Nijboer et al. in their studies noted that the increased duration of the so-called Aggressive Organ Donor Management (ADM), which, in our understanding, means a more intensive and prolonged conditioning of the donor, reduces the incidence of delayed kidney transplant function and graft failure in the first 3 years [27]. A.B. Christmas et al. demonstrated in their study, that the conditioning of the donor for more than 20 hours led to an increase in the number of harvested organs, especially the heart and lung [28].

Of 429 actual posthumous donors, 366 (85.3%) had brain death (DBD donors), 63 (14.7%) had biological death (DCD donors).

At surgery, we refused from organ harvesting in 21 donors for various reasons, so only 408 deceased became effective donors. Of those, there were 357 DBD donors (87.5%), and 51 DCD donors (12.5%). Among DBD donors, 310 were SCDs (76% of the effective donors), 47 were ECDs (11.5% of the effective donors) (Fig. 9).

There were 1,247 organs obtained from 408 effective donors (Table 1).
<table>
<thead>
<tr>
<th>Donor organ</th>
<th>Number</th>
<th>ORPD by organ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kidney</td>
<td>744</td>
<td>1.82</td>
</tr>
<tr>
<td>Liver</td>
<td>220</td>
<td>0.54</td>
</tr>
<tr>
<td>Pancreas</td>
<td>42</td>
<td>0.1</td>
</tr>
<tr>
<td>Intestines</td>
<td>2</td>
<td>-</td>
</tr>
<tr>
<td>Heart</td>
<td>180</td>
<td>0.44</td>
</tr>
<tr>
<td>Lung</td>
<td>58</td>
<td>0.14</td>
</tr>
<tr>
<td>Facial VCA</td>
<td>1</td>
<td>-</td>
</tr>
</tbody>
</table>

Total ORPD for all organs: 1247, 3.06

Fig. 9. The posthumous donor pool profile.
In 63.7% of cases, 3 organs or more were obtained from one donor (Fig. 10). The mean ORPD for all organs was 3.06.

When ORPD for all organs was compared in different age groups, it was noted that the highest ORPD was in the group of 18-29 years of age, which was statistically significantly different from the ORPD of the age groups of 50-59 years old and over 60 years of age having a statistically significant difference between each other as well, and in relation to other groups. However, there was no statistically significant difference between the age groups of 18-29 and 30-49 years old (Fig. 11).
There was also a statistically significant difference in ORPD for all organs between the Sklifosovsky Research Institute for Emergency Medicine (3.34 ± 0.089) and FMBA donor hospitals (2.52 ± 0.088).

When ORPD was compared with respect to mechanical ventilation duration (≤ 5 days vs. > 5 days), no statistically significant difference was found between those periods (3.27 ± 0.08 vs. 3.16 ± 0.139, respectively).

There were no statistically significant differences in ORPD with regard to the cause of death or gender.

The mean number of organs recovered per donor is considered to be an integrative measure to assess the work of the donor coordination service and the donor conditioning in the ICU, and also the overall level of transplantation system development (the need, and the readiness of using the expanded criteria donors). In 2016, the mean ORPD, including all donors, in
the USA was 3.50 (2.76-4.20, depending on the region) [7]. At the same time, ORPD for individual organs was:

- 2.00 for kidney;
- 0.32 for pancreas;
- 0.43 for heart;
- 0.77 for lung.

Y.F. Tong et al. noted that ORPD is influenced by the factors such as the cause of death, donor's age, concomitant diseases, and the quality of the conditioning performed [12]. According to the authors' observations, the highest ORPD (3.32) was observed in donors aged 20-29 years. In donors who died as a result of TBI, ORPD was higher than in those who deceased as a result of CVD: 3.18 vs. 2.59 organs per donor, respectively. Similar results have also been found in other authors [12, 29].

In 2016, the mean number of ORPD in Russia was 2.7 (3.1-1.9 depending on the region). This parameter showed best values in the regions where transplantation of extrarenal organs was performed and/or interregional coordination was carried out [21]. In our opinion, this parameter is also affected by the ability to solve logistical problems. So, only 2 of 28 donor hospitals of FMBA of Russia have been involved in the Transplantation Program. The remote location of transplantation hospitals, the lack of direct flights, and the absence of interdisciplinary interactions lead to the situation where organs such as the heart, or lungs are not even considered as donor organs. Quite opposite situation in the arrangement of the donor process can be seen in Spain where the sources of 40% of posthumous donors are small hospitals that do not have their own transplantation departments. [3].
Summary

The data from literature and the results of the analyzed characteristics of postmortem organ donor population suggest their overall changes both in countries with an advanced transplantation system, and in the Russian Federation.

1. An increase in the number of transplants is impossible without an effective system of postmortem organ donation. It is impossible to maintain this process at the level appropriate to the needs of clinical transplantation without studying the donor process: from identifying and examining a potential donor, diagnosing brain death, conditioning, explanting and preserving organs to distributing and creating transport logistics, investigating and analyzing the epidemiology of postmortem organ donation. The lack of a federal service for organ donation, whose task would have been the development of standardized protocols for the donor selection and management, impedes organizing the donor process as a single technological chain. At the same time, the obtained results could be used to develop standardized protocols for identifying and examining posthumous donors and assessing the possible amount of the transplant care.

Conclusions

1. Donors with the diagnosed brain death constitute the major part (85.3%) in the structure of posthumous donor pool. Most of them are men (66%).

2. In the period from 2008-2017, an increase in the mean age of posthumous donors from 38.1 years to 48.7 years old was observed due to a decreased number of donors in the age group of 18-29 years old from 29%
to 4% and an increased number of donors in the age group over 60 from 3% to 15%.

3. From 2012 to 2017, the number of donors who died as a result of traumatic brain injury decreased (from 68 to 29%) alongside with an increased number of donors who died as a result of cerebrovascular diseases (from 30 to 71%). Among the posthumous donors delivered by ambulance teams directly to the ICUs, 69% showed a depressed consciousness level to score 5 by Glasgow Coma Scale. The mean MLV duration in the donors with the diagnosed brain death made 78.6 hours.

4. The mean number of organs recovered per patient was 3.06.

**Conflict of interests.** Authors declare no conflict of interest.

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