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ORGANIZATIONAL, MEDICAL AND EPIDEMIOLOGICAL PREREQUISITES FOR REVIEWING DONOR CRITERIA IN HEART TRANSPLANTATION

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Organ donation and transplantation in Moscow have witnessed changes in the last decade. These changes have led not only to quantitative growth in the number of effective donors but also to fundamentally new (for Russian medical practice) characteristics of the donor pool. As a result, the selection criteria for organ donors have undergone some radical revisions. **Objective:** to analyze the medical and epidemiological characteristics of the pool of effective heart donors and assess their impact on selection of heart transplants. **Materials and methods.** In our study, we used the medical and epidemiological data of 650 brain-dead donors whose organs were procured from January 1, 2012 to December 31, 2017. **Results.** During the study period, the number of effective heart donors in Moscow increased from 4.4 (2012) to 11.2 (2017) per million population per year. The medical and epidemiological characteristics of the total pool of donors and the pool of heart donors underwent major changes. Among effective heart donors, there was a dynamic increase in the average age from 38.4 to 47 years, predominance of a proportion of donors with stroke 38.2 (2012) vs 83.2 (2017) and, accordingly, an increase in the frequency of such comorbid conditions, as hypertension and diabetes. **Conclusion.** The results presented in the study indicate a growing practice of working with expanded criteria donors. This practice is most effectively developed in the field of heart transplantation than in transplantation of other extrarenal organs. Undoubtedly, the experience under study is unique and relevant not only for the Russian Federation, but also for the world of transplantology, as it allows to provide vital assistance to patients with end-stage heart failure within a reasonable timeframe.

Keywords: effective heart donors, donor pool characteristics, expanded criteria heart donors.

INTRODUCTION

The transplant community continues to look for ways to reduce the shortage of donor organs for transplantation [1]. The use of organs from high-risk donors, including the older age group, without compromising the results of transplantation, is the most obvious and affordable way to increase the number of donor organs.

MATERIALS AND METHODS

The present study used clinical data on 650 brain death donors who underwent organ explantation between January 1, 2012 and December 31, 2017. The general dynamics of donor activity in Moscow in 2012–2017 has been investigated providing the basis for development of donation and heart transplantation, as well as the comparative dynamics of the use of the donor heart and other extrarenal organs for transplantation. To perform a comparative analysis of the effectiveness of using donor hearts in Moscow, the number of heart ED per million population per year was used, which was compared with a similar indicator in several countries of Europe. To represent the population characteristics of ED, including heart ED, mean age and median age of donors, gender ratio, and the proportion of nosological forms, causes of donor deaths (%) were used.

All organ donors were divided into two main groups. The first group included 452 donors (69.5%) from whom the heart was taken for transplantation either in isolation or in the format of multi-organ removal. The second group consisted of 198 (30.5%) donors with organ extractions in various formats, while heart explantation was not performed for various reasons. To identify the factors causing the donor heart refusal, a number of donor characteristics were selected that, in our opinion, could influence the decision to refuse. Among the factors that cannot be changed by any influence, there are age, cause of death, gender, history of hypertension, and diabetes mellitus. As for the factors featuring donor homeostasis and open for medical correction, mean arterial pressure (MAP), pH, lactate, Na and blood glucose, and the dose of vasopressor support were chosen. All explanted donor hearts included in this study were transplanted at the

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Shumakov National Medical Research Center of Transplantology and Artificial Organs (Ministry of Health of the Russian Federation, Moscow). Statistical analysis was made with Statistica 12.0 for Windows software.

SOME CONDITIONS AND FACTORS DEFINING CRITERIA FOR SELECTION OF HEART DONORS

In Moscow, since 2012, there has been stable growth dynamics of effective donors whose death was ascertained on the basis of neurological criteria, e. g., diagnosed brain death (BD) [2]. Fig. 1 shows the absolute number of effective donors diagnosed with BD per million population per year [3].

The progressive growth of donor activity became possible due to a number of organizational measures, so-called the "Moscow model" of organ donation, among which it is necessary to point out the improvement of the regional regulatory framework, the new position of a transplant coordinator in the practice of medical institutions with the definition of functional responsibilities of this position, formulation and normative consolidation of the so-called triggers for identifying potential organ donors, monitoring the neurological and somatic status of probable and potential donors, etc. [4, 5]. The taken organizational measures resulted in annual increase in the number of ED per million population per year that reached 15.5 in 2017, while over the same period, the total donor activity in Eurotransplant countries was 13.9 [6].

The growing dynamics of donor activity has become a crucial drive for the development of extrarenal transplant programs. At the same time, the difference in the indicators of the use of the donor pool for each type of clinical transplantation is quite significant. Fig. 2 shows the relative share of the use of donors with BD for heart, lung, liver, and pancreas transplantation. In 2012–2014, there has been sharp variations in the use of ED in heart, liver and pancreas transplantation. In this period, transplant programs have been obviously adapting to new working conditions, a growing number of BD donors, an increase in vascular diseases as the predominant cause of donor deaths, etc. then in 2015–2017, the rate of donor organs used for heart transplantation remained at an average level of 72.8%, while only in the year of 2017 the corresponding figure for the liver transplants was 67.2%. There is seen a slight positive trend in the use of the donor pool for lung transplantation. The most ineffective was the use of the donor pool for pancreas transplantation, where a progressive decrease was recorded.

Due to the high efficiency of using the donor pool for heart transplantation, the number of heart donors per million population in Moscow in 2017 was 11.2, which is shown in Fig. 3. A similar indicator in Europe in 2017 was at the level of 4.8 [6].

As noted above, the intensity of the use of the heart for transplantation took place in the conditions of radical changes in the donor pool: increased age of donors, the prevalence of vascular diseases in the structure of donor deaths, increase in the rate of comorbid risk factors, including hypertension (HT), diabetes mellitus (DM), systemic atherosclerosis, etc.

In a relatively short period, the average age of all EDs in Moscow increased by 7 years, from 42.15 in 2012 to 49.02 in 2017 (Fig. 4).

Even more significant changes are seen in the average age of donors among the heart ED pool. In 2012, relatively young donors were engaged, with the average age of 38.4, while in 2017 the average age of EDs in-

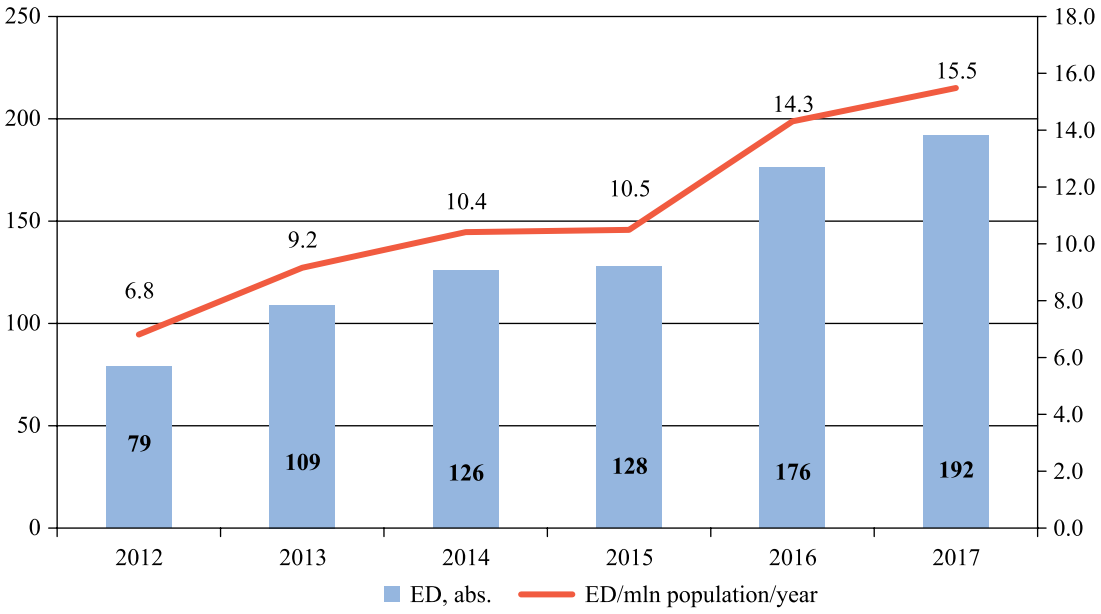

Fig. 1. Donor activity in Moscow in dynamics, 2012–2017

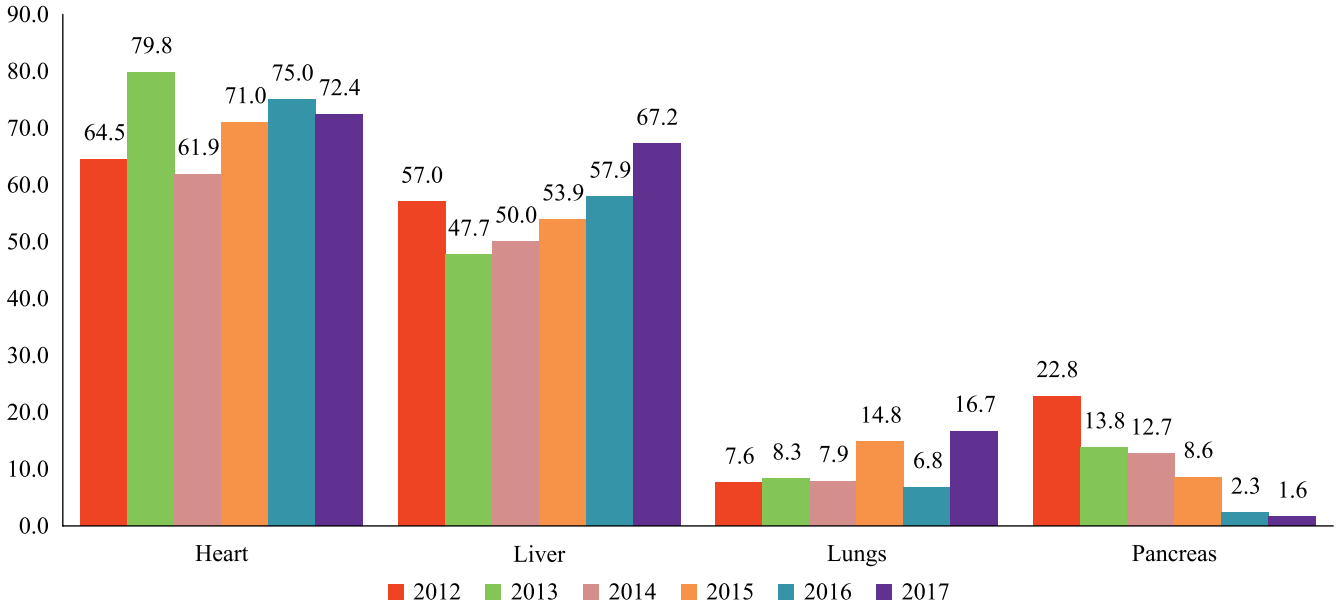

Fig. 2. Dynamics of the donor pool use for transplantation of extrarenal organs, 2012–2017

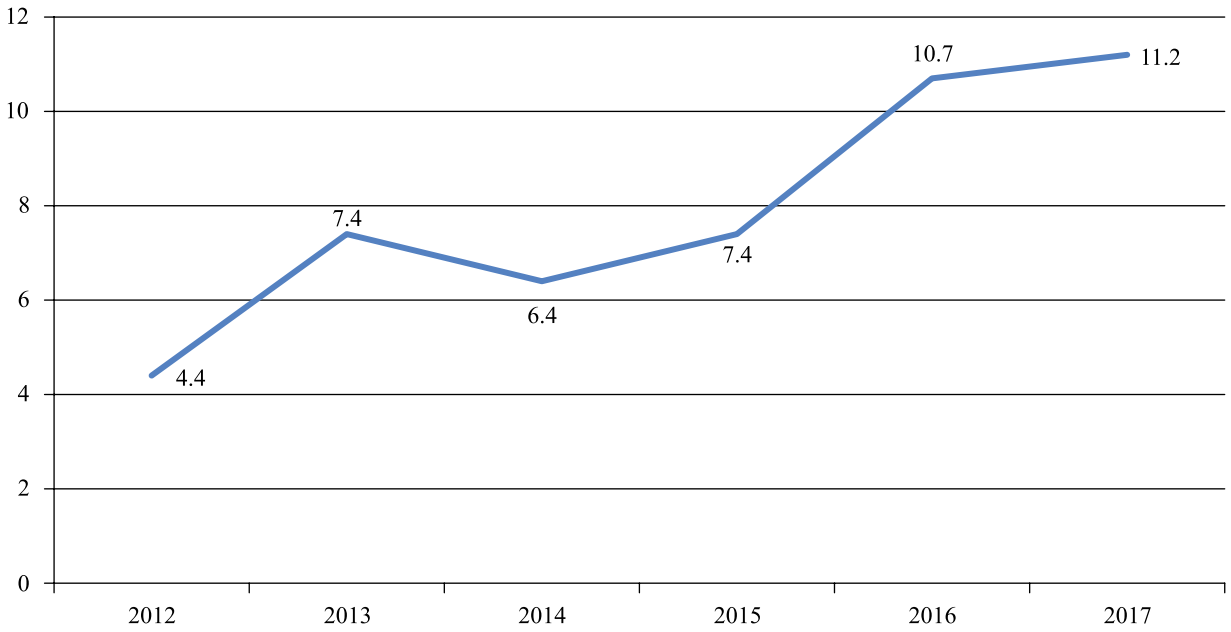

Fig. 3. The number of effective heart donors per million population per year, 2012–2017

creased to 47.0 (Fig. 5). For comparison, the average age of heart donors in Europe in 2017 was 43; in North America, for 30 years the median age of the donors has remained in the range of 25–27 [6, 7]. Accordingly, the greatest progress in engaging donors over 40 years of age has been achieved by European countries, including Russia, the experience of its city of Moscow is presented in this study.

Analysis of the main death causes of all EDs in Moscow revealed a significant predominance of donors who died of cerebrovascular diseases, in comparison with the number of donors who received traumatic injuries (Fig. 6). In the Eurotransplant countries, already in 2012, EDs with CVA dominated (78.3% of the total pool of all donors) [6]. Comparing foreign data with those obtained in this study, it is important to note that the appearance of similar donor tendencies in Russia testifies to the identical principles of organizing the donor process [5].

In the context of changes in Moscow donor pool, an extremely uneven transplantation activity of medical institutions performing heart transplantation was observed (Fig. 7). Only cases of heart donation sent for transplantation to Shumakov National Medical Research Center of Transplantology and Artificial Organs were included in the study, since heart transplantation is most

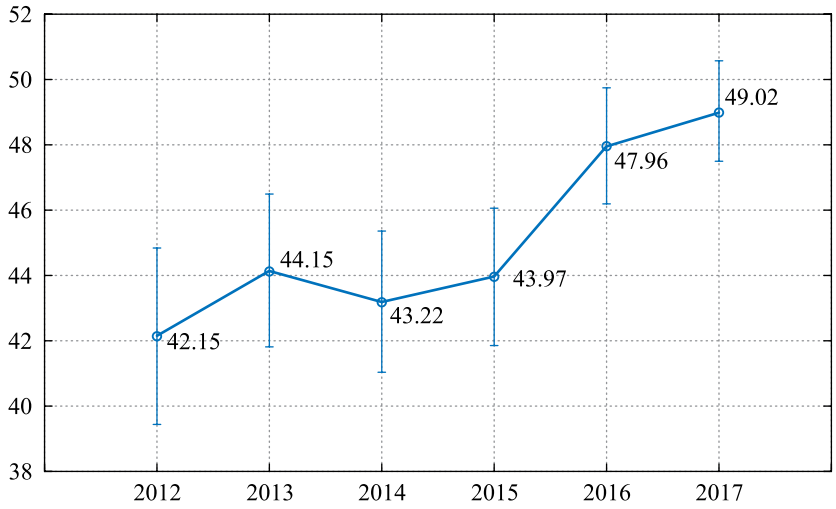

Fig. 4. Comparative dynamics of the average age of effective donors, 2012–2017. X axis, years; Y axis, age

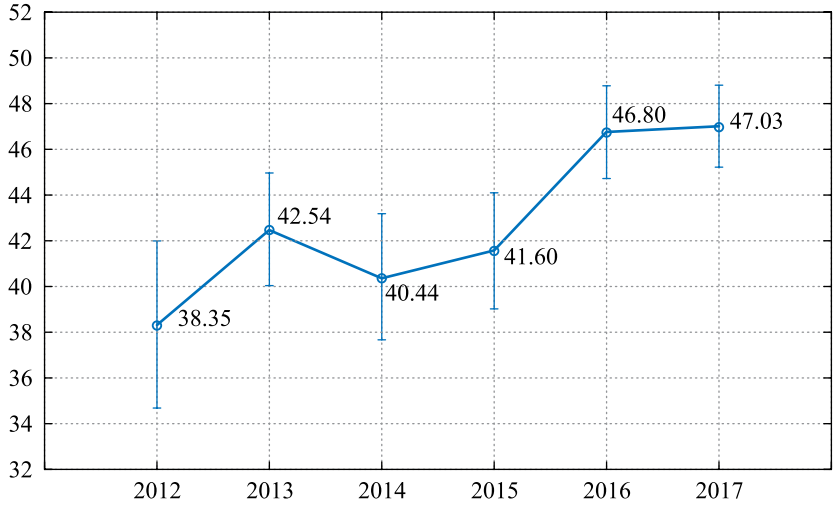

Fig. 5. Comparative dynamics of the average age of effective heart donors, 2012–2017. X axis, years; Y axis, age

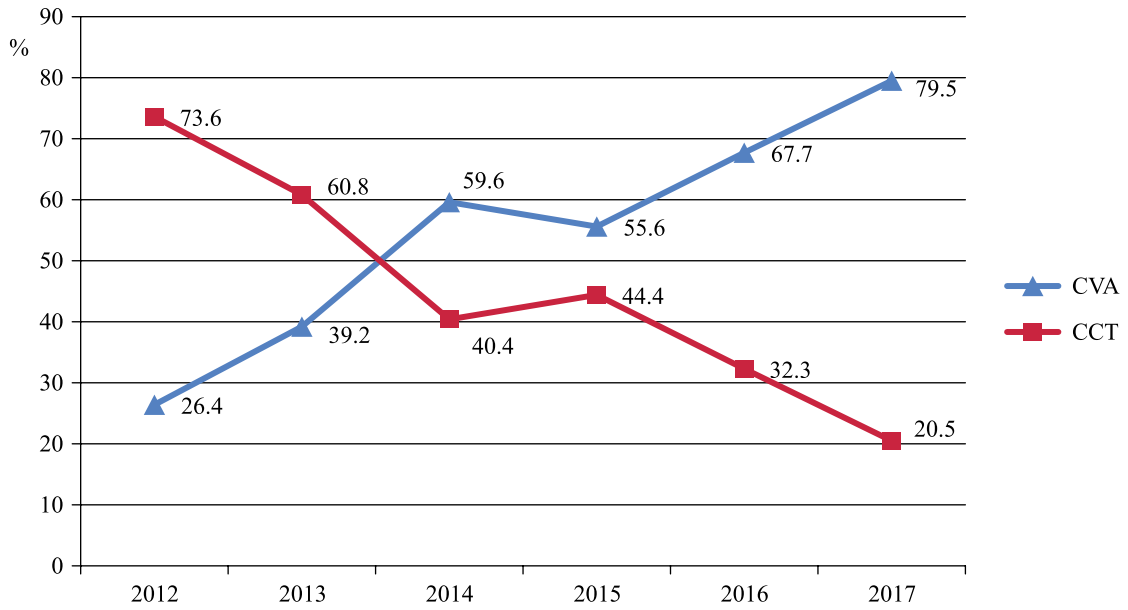

Fig. 6. The percentage of the major death causes in ED, 2012–2017

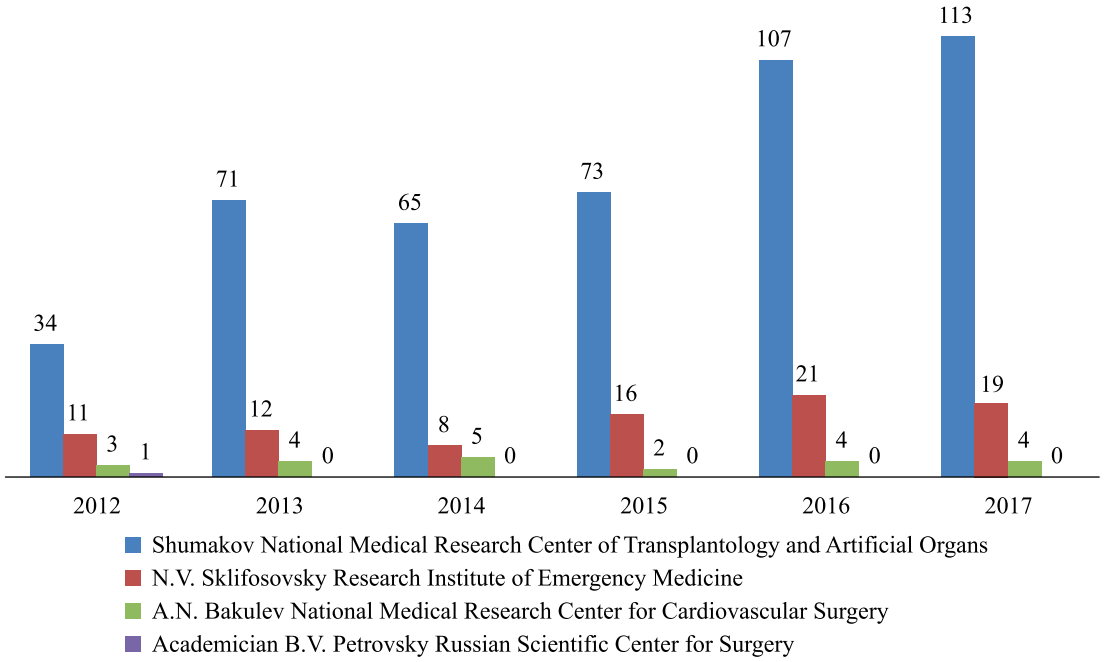

Fig. 7. Activity of heart transplant centers, 2012–2017

developed in this institution. By scientific publications of the Center, effective use of the changed donor pool in the city of Moscow seem to become possible primarily due to the timely revision of the donor selection criteria for heart transplantation [8, 9].

Organizational approaches in working with high-risk donors used in the joint work of the Moscow City Coordination Center for Organ Donation (MGKTsOD) and Shumakov National Medical Research Center of Transplantology and Artificial Organs have radically changed heart transplantation in the Russian Federation, making it more accessible in conditions when the number of "ideal" donors will only decrease.

MEDICAL AND EPIDEMIOLOGICAL CHARACTERISTICS OF EFFECTIVE HEART DONORS

Heart donors in 2012–2017, in line with the stated above trend of changes in the entire donor pool, also underwent changes. Fig. 8 shows the percentage of the main death causes of heart donors included in the study. In 2012, heart donors with CCTs predominated (61.8% versus 38.2% of donors who died from stroke). By 2015, the numbers of donors with both nosologies equaled, and in 2017 the number of donors who died of CCT has become 3.7 times less than in 2012, and the proportion of donors with CVA has increased to 83.2%.

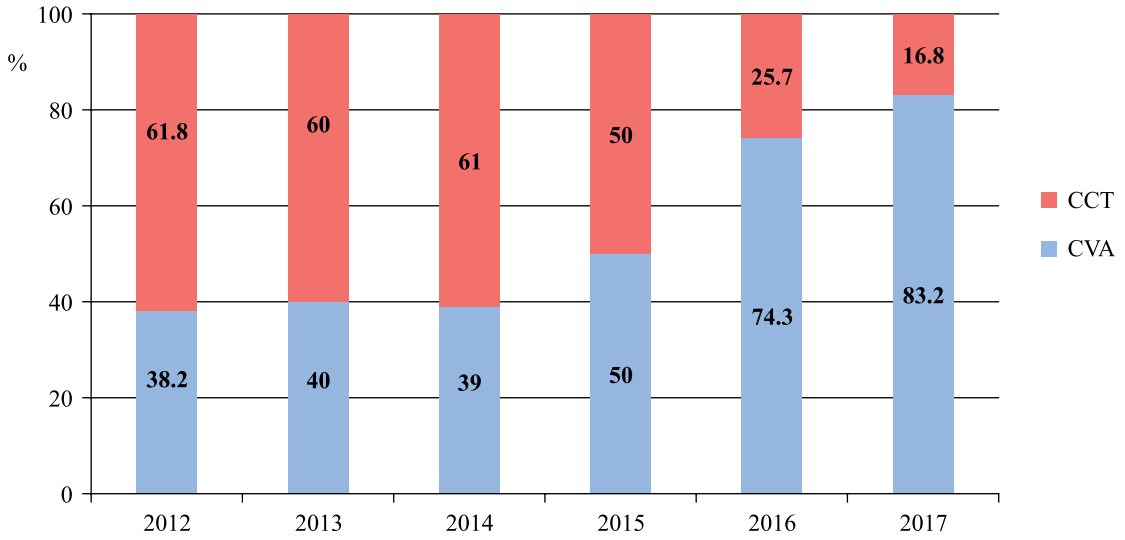

Fig. 8. Percentage of major death causes of heart donors, 2012–2017

According to the registry of the International Society for Heart and Lung Transplantation (ISLHT), in 2010–2018 there was a global decrease in the number of heart donors who died from CVA from 48.8 to 40.5%, and an increase in heart donors who died due to anoxic brain injuries from 7.7 to 21.5% [7].

The age of the heart EDs included in the present study corresponds to the aging trend of the entire pool of donors. If in 2012 85.3% of the total number of heart EDs were donors under 50, then in 2017, their share was 50.4%, along with an increase in the number of donors in the older age group (51–60) to 41.6 % vs 14.7% in 2012. In 2017, for the first time in the Russian Federation, heart donors whose age was in the range of 61–69 accounted for 7.1% of the total heart ED pool. Besides, in 2017, there was one case of heart explantation from a donor of the age group 70+. Over six years, the median age of heart EDs has increased from 41 to 50 years (Fig. 9.) In global practice, over the same period, there is also an increase in the number of donors in the older age group, but still a larger number, about 70% of the total number of heart EDs, were donors under 40. The median age of heart EDs in the world remained at the level of 32 in 2012–2017 [7].

If to speak of the gender distribution of effective heart donors, there is a persistent predominance of male donors. In 2017, there were 2.9 times more male donors than female donors; the proportion of male donors was 75.2% (Fig. 10). According to ISLHT, in 2009–2016 the male donors in Europe were 62.4%, 70.1% in North

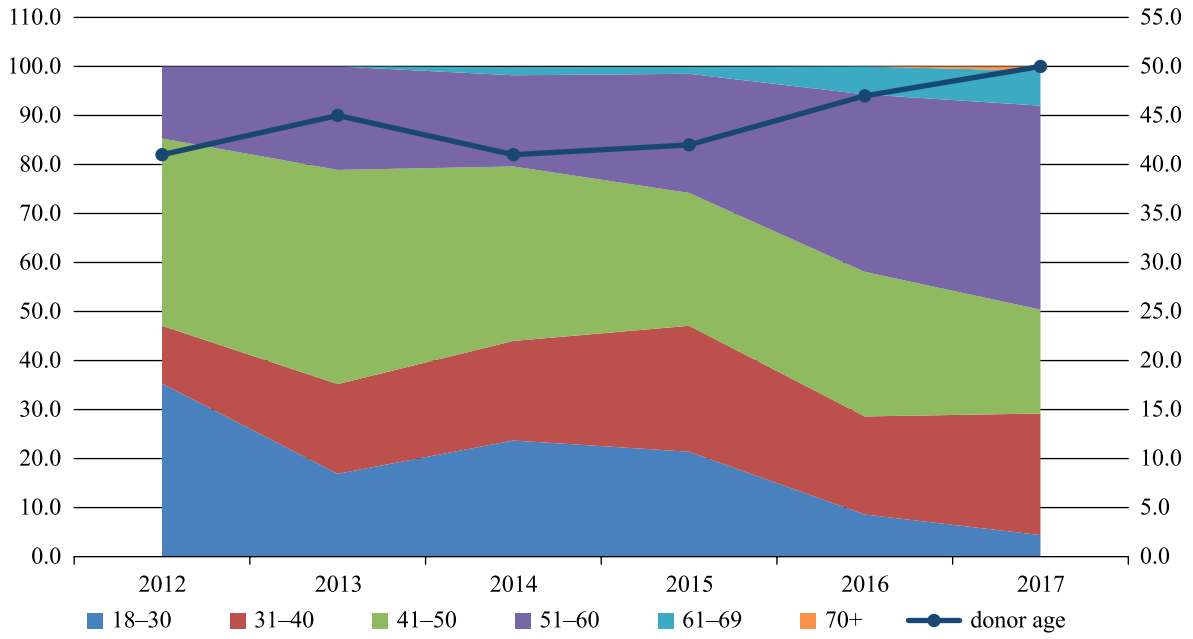

Fig. 9. Dynamics of the specific weight (%) of age groups of heart ED; median age (years) of heart ED in Moscow, 2012–2017

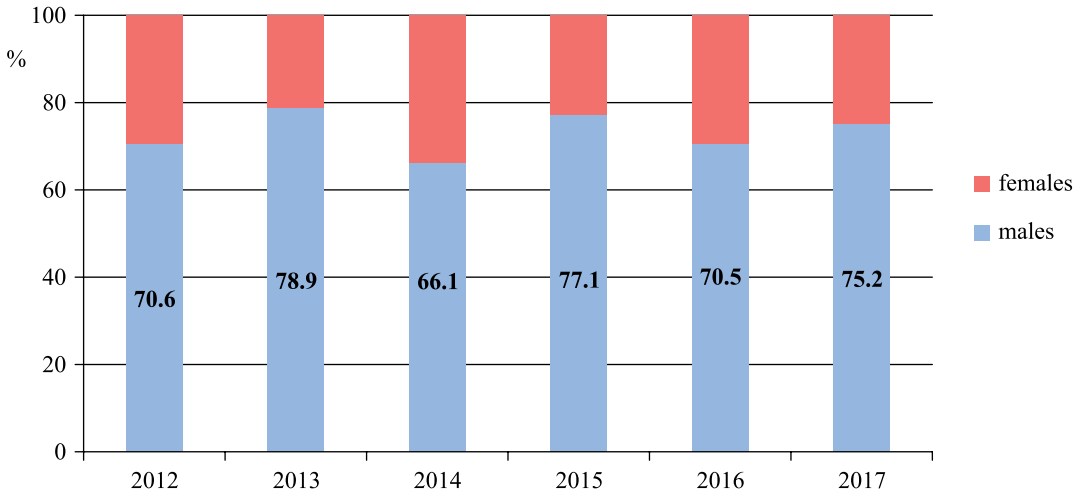

Fig. 10. Percentage of male and female heart donors, 2012–2017

America, 78.3% in other countries [7]. The predominance of male donors can be considered as a positive factor influencing the survival rate of male recipients, since, according to E.S. Weiss (2009), men who received hearts from male donors had the highest cumulative survival in 5 years [10].

In general, the given characteristics of heart donors in Moscow follow the trend of changes in the donor pool on a global scale, and even surpass it in a number of characteristics, in particular, in terms of the age of effective heart donors. Considering the data obtained, the development of a special tool (mathematical model) is becoming extremely urgent, as at the stage of organ donation it would allow to objectively assess the donor heart, considering the maximum number of donor factors available for research. Following the goal of developing such a model, we selected a number of donor risk factors that could cause the donor heart refusal.

ANALYSIS OF CAUSES OF DONOR HEART REFUSAL

For the study, donor factors were selected that were not amenable to correction, e. g., age, death cause, gender, HT, diabetes mellitus, and factors that determine the state of donor homeostasis: SBP, pH, lactate, blood Na and glucose, and dose of vasopressor support.

The Table shows the number of donor heart refusals (%) depending on the presence/absence of a donor factor. The analysis revealed a linear increase in the number of donor heart refusals with increasing age of the donor. In the 41–50 age group, the refusal rate is 27.5, in the 51–60 group 41.4, and in the 60+ age group it increases to 57.9%. The expansion of the selection criteria for heart donors contributed to a decrease in the number of refusals from donors who died of CVA, which made the difference in refusals from donors who died from CCT

Table

Studied donor factors and percentage of refusals from the donor heart

Donor factors	Total donors with BD	Group 1 (explanted heart)	Group 2 (not explanted heart)	Donor heart refusal, %
Donor age, years				
18–30	78	67	11	14.1
31–40	113	96	17	15.9
41–50	193	139	54	27.5
51–60	227	133	94	41.4
61–69	38	16	22	57.9
70+	1	1	0	0.0
Death cause				
CCT	239	179	60	25.1
CVA	411	273	138	33.6
Gender				
Male	464	329	135	29.1
Female	186	123	63	33.9
Hypertension				
Yes	364	231	133	36.5
No	286	221	65	22.7
Diabetes mellitus				
Yes	155	124	31	15.7
No	495	328	167	33.7
Mean arterial pressure (MAP), mm Hg				
≤60	46	31	15	32.6
≥61	604	421	183	30.3
pH, mmol/L				
≤7.0–7.2	31	21	10	32.3
≥7.3	582	414	168	28.9
n/a	37	17	20	
Lactate, mmol/L				
0.1–2.2	229	165	64	27.9
2.3–5.9	179	132	47	26.3
6.0–13.0	40	25	15	37.5
>13.0	5	3	2	40.0
n/a	197	127	70	

End of table 1

Donor factors	Total donors with BD	Group 1 (explanted heart)	Group 2 (not explanted heart)	Donor heart refusal, %
Na, mmol/L				
120–135	66	47	19	28.8
136–145	293	204	89	30.4
146–155	133	94	39	29.3
≥156	122	90	32	26.2
n/a	36	17	19	
Glucose, mmol/L				
≤8.3	213	153	60	28.2
8.4–10.9	161	118	43	26.7
>10.9	221	149	72	32.6
n/a	55	32	23	
Norepinephrine (NA), ng/kg/min				
<100	44	35	9	20.6
100–400	182	129	53	29.1
401–800	166	119	47	28.3
>800	111	72	39	35.2
n/a	11	7	4	

comparable (33.6 vs 25.1, respectively). The SBP parameter did not significantly affect the percentage of donor heart refusals, while the growth of the most important indicator of homeostasis, blood lactate, was associated with an increase in the number of donor heart refusals. In donors with blood lactate in the range of 6–13 mmol/L (3–6 times higher than the reference), heart failure was 37.5%. There was no significant difference in the rate of donor heart refusals depending on the pH The proportion of failures at low pH values is slightly higher (32.3%) than when it is normalized (28.9%). There was no significant difference in the number of donor heart refusals depending on the blood Na value, both with its normal and increased values, the proportion of refusals averaged 28.7%. Diabetes history of donors did not significantly affect the number of refusals. At the same time, in isolation, blood glucose values above 10.9 mmol/L were the reason for 32.6% of donor heart refusals. An increased number of donor heart refusals was revealed, associated with an increase in the dose of vasopressor support (NA), at its minimum values up to 100 ng/kg/min, a decision was made to refuse in 20.6% of cases, with an increase in the injection rate over 800 ng/min. kg/min the failure rate was 35.2%.

CONCLUSION

As the donor activity in the city of Moscow rises, there is an increase in the number of heart transplants. The most significant increase is seen in Shumakov National Medical Research Center of Transplantology and Artificial Organs. The results of the present study of the medical and epidemiological characteristics of donors show that without a balanced revision of the donor selection criteria, the effectiveness of the provision of transplant care not only for heart transplantation, but also for other types of transplantation, will be at a minimum level, and the number of recipients on the waiting list and the waiting time for donor organs will grow. To improve the provision of transplant care, a thorough analysis of donor characteristics and their impact on the suitability of the donor heart for transplantation is required. The article presents the initial results of such an analysis, which showed the identity of Russian and foreign practices and trends in heart transplantation, and the need to continue scientific research of donor criteria in order to create an objective tool for assessing donor heart.

The authors declare no conflict of interest.

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