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EVOLUTION OF LIVER DONATION IN MOSCOW. MOVEMENT TOWARDS EXPANDED DONOR SELECTION CRITERIA

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The **objective** of the study was to investigate the evolution and trends in liver donation in the city of Moscow, with special focus on the expansion of liver donor selection criteria for transplantation. **Materials and methods.** The study included 1,548 effective donors (EDs) in the period from January 1, 2012 to December 31, 2020. Their basic characteristics – age and cause of death – are presented. The dynamics of changes in the age groups of donors and the dynamics of the number of ≥60-year-old liver donors were studied. The influence of expanded liver donor selection criteria over the dynamics of the number of transplant surgeries and patient flow on the waiting list was assessed. **Results.** During the study period, the number of effective liver donors (ELDs) in Moscow increased 4.7-fold. The average age of ELDs increased from 37.1 in 2012 to 48.8 in 2020. There was an absolute prevalence of donors who died from cerebrovascular accident compared with donors who died from traumatic causes, 83.4% vs 16.6%, respectively. Since 2016, there has been a progressive increase in ≥60-year-old liver donors; the number of such donors in 2020 reached 39, accounting for 13.6% of the total pool of EDs. The progressive growth in the number of liver transplants has significantly influenced patient movement on the waiting list. In 2012, there was a 25.2% increase in the number of liver transplants per 100 patients on the waiting list; by 2020, it had reached 86.6%. **Conclusion.** The results reasonably indicate an increase in liver donation and liver transplantation (LTx) in Moscow. Comparison of Russian data with those of leading foreign donor programs shows that the trends in the donor pool in the context of older age, including ≥60-year-old donors, and shifting causes of donor death towards cerebrovascular diseases are similar. An overall increase in donor activity and expansion of liver donor criteria contributed to an increase in the number of transplants performed per 100 patients on the waiting list, which, in turn, reduced the waiting time for a donor organ and increased the intensity of patient flow on the waiting list.

Keywords: effective liver donors, donor pool characteristics, expanded organ donation criteria.

INTRODUCTION

Today, LTx is considered the standard treatment for end-stage acute or chronic liver failure of all etiologies. More than 80,000 LTx procedures are performed worldwide every year. Survival rates are significantly better now than they were over the past 25 years, reaching 96% at 1 year and 71% at 10 years after transplantation, respectively. Among the most common nosologies in patients undergoing liver transplantation are cirrhosis (57.0%), primary and secondary (metastatic) liver cancers (15.0%), cholestatic liver diseases (10.0%), and acute liver failure (8.0%) [1, 2].

According to Eurotransplant, there were 1,481 people actively waiting for liver transplantation in 2020, and 2,446 new candidates were registered. During the same period, 1,323 deceased donor liver transplantations were performed [3]. The liver transplant waiting list in the Russian Federation in 2020 included 2,237 patients, and the number of transplants was 559 [4].

In Moscow in 2020, organ harvesting was performed in 263 EDs. Among the organs harvested were 187 livers used for transplantation (72.6%). Given the increase in the average age of effective organ donors, it is obvious that such a high proportion of donor liver explantation is associated with the expansion of liver donor selection criteria. The use of donors with extended criteria for liver transplantation is practically not studied in the publications of Russian authors. There are single publications, mainly devoted to the morphological assessment of the donor liver for the purpose of verifying its suitability for transplantation, without taking into account the donor's medical and epidemiological and clinical characteristics [5, 6]. The aim of this study is to investigate the evolution of liver donation in Moscow, the region with the highest donor activity in Russia, to analyze donors' medical and epidemiological characteristics and to identify donors that meet the expanded liver donation criteria as defined by leading world donor programs [1].

MATERIALS AND METHODS

The study included 1,548 EDs, of which 946 (61.1%) were ELDs in the period from January 1, 2012 to Decem-

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ber 31, 2020. We investigated the population characteristics of the ELDs – mean age, proportion (%) of nosological forms – causes of donor death, and the dynamics of donor age groups, taking into account the most common criterion for expanding the donor pool – ≥60-year-old donors. For the first time in population calculations, we used the number of transplants per 100 recipients of the waiting list and investigated its dynamics.

RESULTS AND DISCUSSION

Between 2012 and 2020, there was a 4.7-fold increase in the number of ELDs in Moscow [4, 7]. Comparison of the absolute number of ELDs and the ELDs/Eds ratio, expressed in %, shows that, from 2012 to 2016, the total number of Eds increased by 124.7%, while the share of donor pool utilization for liver transplantation was less than 60.0%, almost unchanged since 2012. From 2017 through 2019, a similar level of donor pool utilization for liver transplantation persisted, not exceeding 63.26% in 2019, despite a 39.3% increase in the total number of EDs over that period. It is only in the 1-year period from 2019 to 2020 that we see a 9.72% increase in liver transplant donor pool utilization activity, with a comparable 10.49% increase in liver utilization activity over the preceding 7 years (2012 to 2019) (Fig. 1). These data indicate that LTx programs in Moscow are slow in adopting the criteria for expansion of the suitability of donor livers for transplantation and, as a consequence, incomplete use of the progressively increasing donor resource.

According to the Spanish National Transplant Organization (NTO), over a similar time period, among all donors offered, both brain-dead (BD) and asystolic (AS) donors, the proportion of liver explants was at 90.0%, with the proportion of livers transplanted not exceeding 70.0% in a context of active growth of AS use observed since 2015 [8]. As presented in Fig. 1, the efficiency of donor pool utilization for liver transplantation in 2020 in Moscow was comparable to 73.46%. It is important to note that this level of efficiency in the use of donor resource for liver transplantation has been achieved for the first time in Moscow. In our opinion, this is due to the stability and efficiency of the organizational system of organ donation for transplantation in Moscow and the accumulation of necessary experience in liver transplantation programs required to work with expanded criteria donors.

Donor age is one of the conventional factors considered in the evaluation of both standard liver donors and expanded criteria donors. Apart from age, conventional factors in liver donor evaluation also include elevated levels of liver enzymes in the blood, hemodynamic instability, including circulatory arrest in brain-dead donors, a history of alcohol abuse, hypernatremia, and liver steatosis [9]. From the position of expansion of donor criteria for liver transplantation, the age of the donor is certainly an important factor. According to the data presented by the world's largest donor organizations, the age of liver donors has been gradually but steadily increasing over the years. In the United States in 1994, only 20% of liver donors were over 50 years old; today this figure has doubled [10]. The annual number of liver donors older than 65 years, according to UNOS, increased 14-fold in the United States from 1991 to 2001. According to ELTR (European Liver Transplant Registry), the proportion of ≥60-year-old donors increased 10-fold, from 2% to 20% [11]. The average age of liver donors in our study is also increasing, from 37.1 years in 2012 to 48.8 years in 2020 (Fig. 2). Analysis of foreign data presented above, shows that the increase in the average age of donors is determined by the number of ELDs over 60 years old. According to the NTO, the age com-

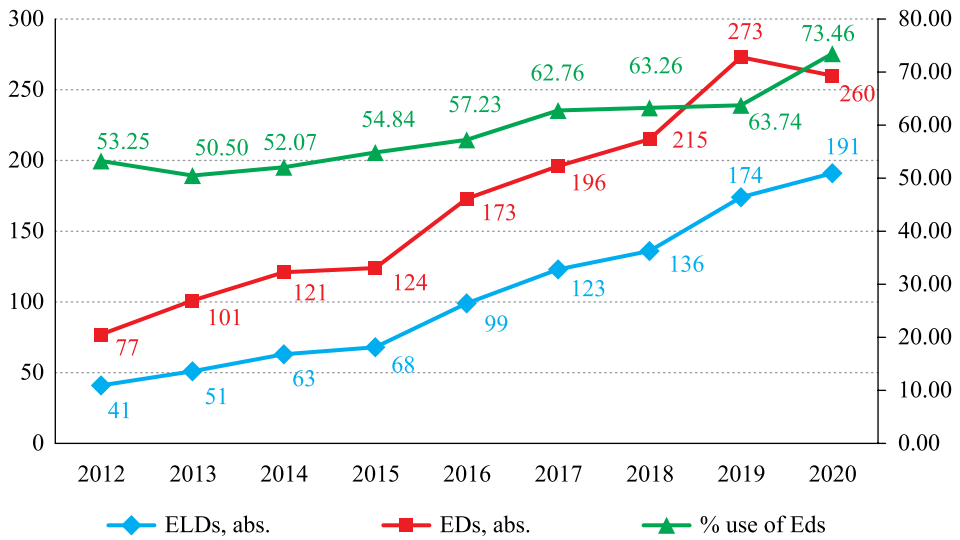

Fig. 1. Dynamics of the total number of effective donors (ED), total number of effective liver donors (ELD) and the ED/ELD ratio (%) in 2012–2020

position of the donor pool remained virtually unchanged from 2012 to 2020, with less than 10% of donors under 18 years and the 18–29 age range, 10–12% of donors aged 30–44 years, and quite equal shares of the so-called "older age" donors – 30.5% for age 45–59 years, 24.7% for age 60–69 years, 26.4% for donors ≥70 years [8].

Fig. 3 shows the percentage of the age groups of ELDs over the 2012–2020 period. Compared to the similar NTO data described above, the following age trends are evident in the Russian practice of liver donation – the youngest age group of donors (18–29 years) is progressively decreasing from 37.5% in 2012 to 6.3% in 2020; another group of young donors (30–39 years) for the entire study period remains fairly stable in the 20.0%–24.0% range; a similar stable situation is observed with the group of middle-aged donors 40–54 years, accounting for about 40.0%. The most significant changes are observed among the groups of older donors, contributing most significantly to the so-called "expanded donor criteria". The age 55–60-years-old group in our study went from 7.5% in 2012 to 24.1%. In 2012–2014, there were no ELDs in the 61–65 years age group; since 2015, their contribution to the ED pool has progressively increased, reaching 13.6% in 2020. The proportion of donors aged ≥65 years is still at a low level, up to 2.0% of the total ELD pool. Fig. 4 shows the evolution of the age of ELDs in Europe, according to the European Liver Transplant Registry. Noteworthy is the 30 years since the beginning of the work with donors in the ≥70 years age group, and more than 30 years of experience with donors in the 60–70 years age group. By 2019, the specific contributions of almost every age group except the youngest group 0–20 were comparable to each other, and the 60–70 and >70 age groups account for one-third of all ELDs. In other words, liver donors with expanded age criteria account for about 30.0% of the entire ELDs pool [12].

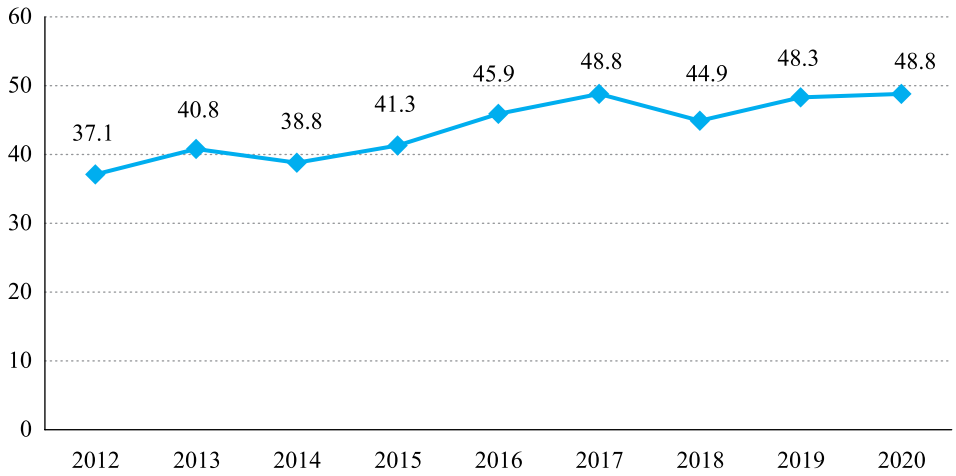

Fig. 2. Dynamics of the average ELD age in 2012–2020

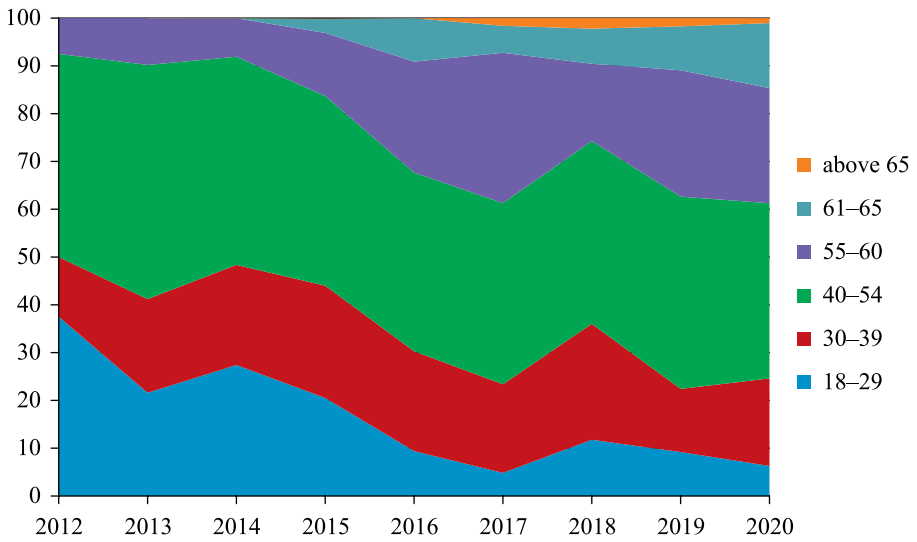

Fig. 3. Dynamics of the ELD age in 2012–2020

ELD age ≥60 years, according to the current selection criteria in Europe and the world, is classified as expanded [3]. In Moscow, there has been a progressive increase in the number of ELDs ≥60 years since 2016 (Fig. 5). The ratio of ELDs with expanded age criteria to the total number of ELDs shows that the proportion of expanded criteria donors is quite comparable with the foreign data given above, 20.4% in 2020. However, it is important to note that the number of liver donors in European countries also includes children, the 0–20-years-old age range, and people ≥70 years old.

Examination of the frequency of age distribution of ELDs in our study shows that 75.7% of expanded criteria donors are slightly older than 60 years, while there are single cases of liver donations from donors older than 65 years, and one case of liver donation was from a donor over 70 years old (Fig. 6). Of course, with the overall growth of donor activity and the accumulation of experience in liver transplantation programs, there is an obvious shift towards working with expanded criteria donors, but the age range of donors is practically not increasing, remaining within the 60–63-year range.

Along with the donor's age, the cause of death is of paramount medical and epidemiological importance. A number of papers presented by authors from the Moscow Organ Donation Coordination Center, Botkin City Clinical Hospital, and published in research journals have demonstrated serious changes observed in the structure of mortality in brain-dead donors in Moscow [7]. Obviously, these changes are also fully valid for ELDs. For instance, since 2015, there has been a progressive increase in the number of donors who died from acute stroke and there is an almost mirror-like decrease in the

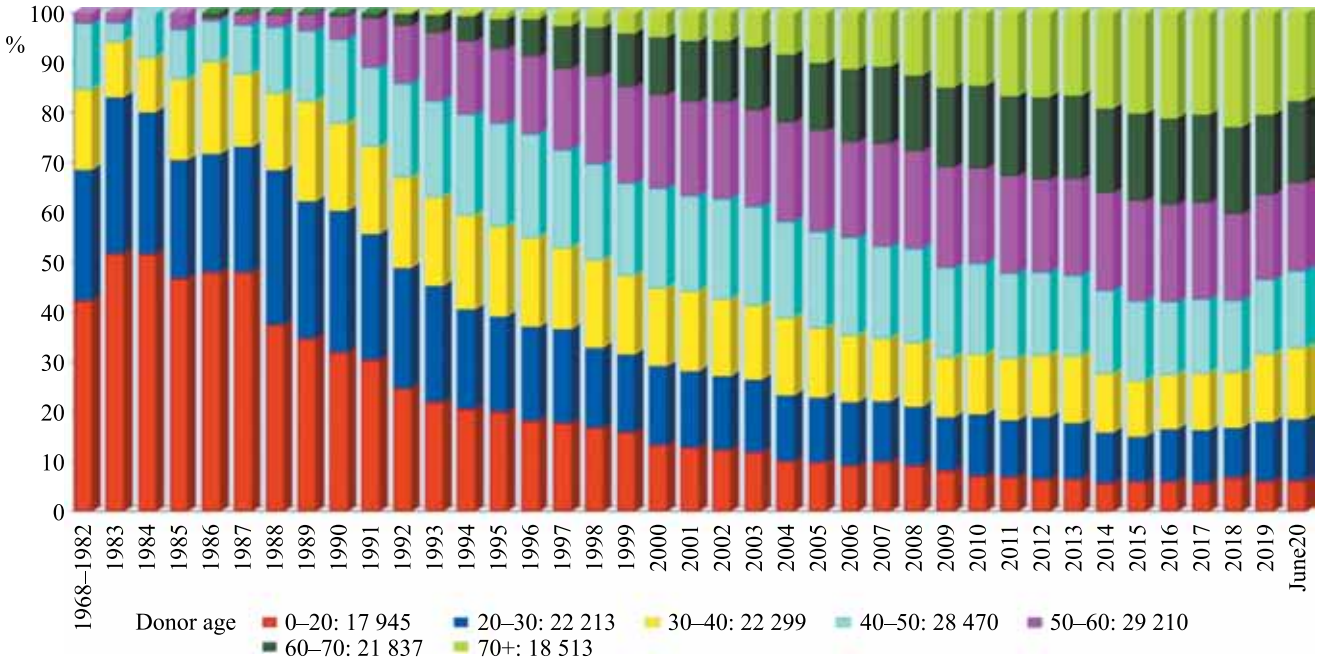

Fig. 4. Evolution of the ELD age in Europe according to the European Liver Transplant Registry (http://www.eltr.org)

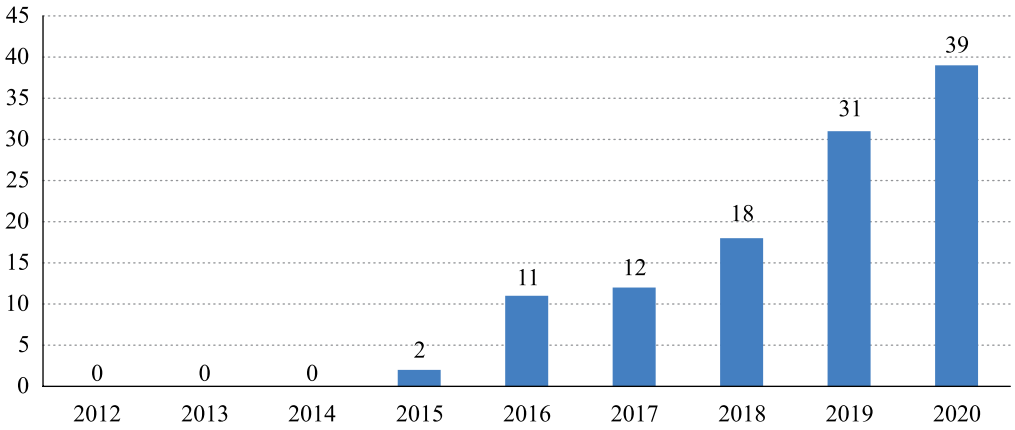

Fig. 5. The number of ≥60-year-old ELDs in 2012–2020

number of donors who died from traumatic brain injury (TBI). (Fig. 7).

Such significant changes in donor activity and donor mortality patterns could not but affect the evolution of liver donation in general and the development of donation according to expanded criteria. This is confirmed by the analysis of liver donors rejected for transplantation according to the age of the donor (Fig. 8). Against the background of some predominance of donors with TBI in the 2012–2014 period, we see a rather high proportion of liver rejections in the youngest age group of donors 18–29 years, accounting for 16.7% in 2012, and steadily decreasing to 4.1–6.4% only from 2016, when the number of TBI donors was sharply decreasing.

The most important social indicator of the effectiveness of organ transplantation is the movement of patients on the waiting list. Fig. 9 shows the dynamics of the indicator reflecting the number of liver transplantations per 100 patients on the waiting list per year. We can see that since 2016, after the expansion of liver donor selection criteria, this indicator begins to grow, indicating, on one hand, the effectiveness of the approach to the issue of selection in the context of increasing the number of transplants and the intensity of waitlist traffic. On the other hand, guided by the experience of foreign countries, where the same indicator reaches a maximum of 65, it indicates the need for further improvement of the waiting list with the formation of optimal routing of patients for inclusion in the waiting list (Fig. 9) [16].

CONCLUSION

The number of liver transplants in Moscow is increasing annually. At the beginning when the organizational structure of organ donation for transplantation was

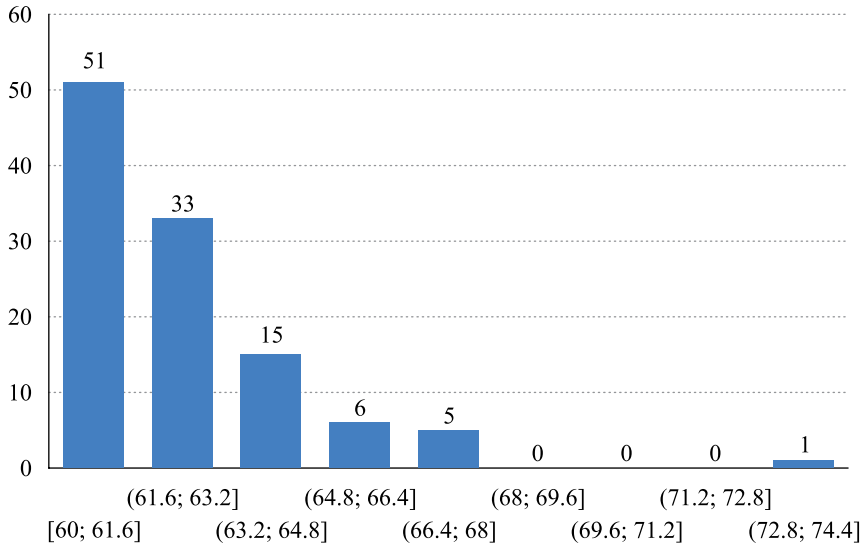

Fig. 6. Histogram of distribution of the frequency of liver donation from donors ≥60 years old in 2012–2020

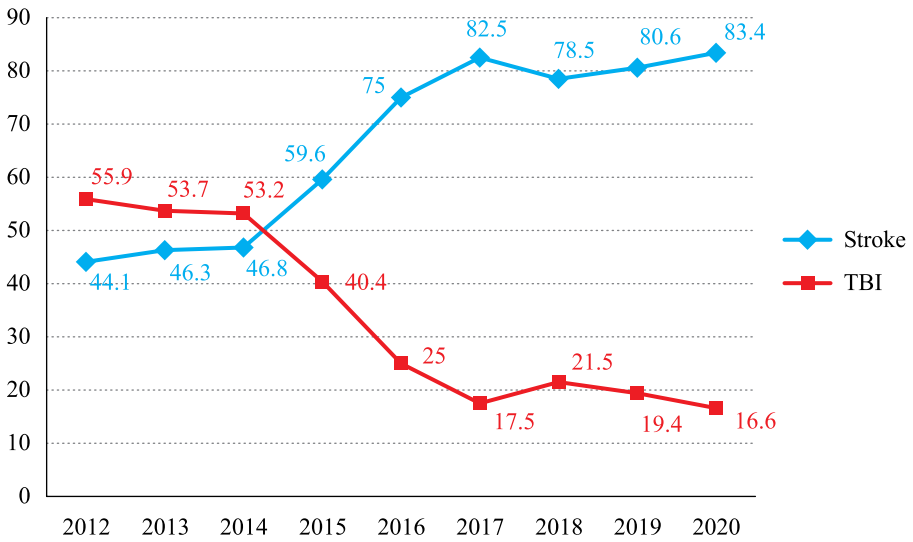

Fig. 7. Dynamics of ELDs depending on cause of death in 2012–2020 (%)

being formed in Moscow in 2012, there were 41 liver transplant surgeries per year, which was less than 20% of the need for this type of transplant care. In 2020, 191 liver transplants were performed in Moscow. Such a progressive increase in the number of transplants in a relatively short period of time was facilitated by a general increase in donor activity in Moscow as a result of implementation of the transplant coordination system, positive initial experience with expanded criteria donors, including donors ≥65 old, accumulated experience by transplant centers including with older donors, and increased number of liver transplant programs in the Moscow healthcare system.

To date, it is impossible to provide full-fledged transplantation care without working with expanded criteria donors. On one hand, the donor pool has significantly changed – the age of donors has increased and, accordingly, the incidence of comorbid diseases has increased; the main cause of donor death has become acute cerebral haemorrhage. On the other hand, the number of patients with end-stage chronic liver diseases is increasing and, accordingly, the number of donor organs suitable for transplantation needs to increase. Over the past 2 decades, the global transplant community has accepted the concept of expanded criteria donation. There is no universal definition of an expanded criteria organ donor; in general, it is a set of certain donor characteristics that can potentially increase the risk of organ transplantation for the recipient. For the liver, there are several lists of such donor characteristics, formulated by different authors in different years, with differences mainly affecting the "cut-off points", i.e. borderline values of certain indicators that allow the use of a liver for transplantation [17]. The most available indicator to estimate the volume of donation according to expanded criteria in the overall pool of effective donors is the age of the donor. For the

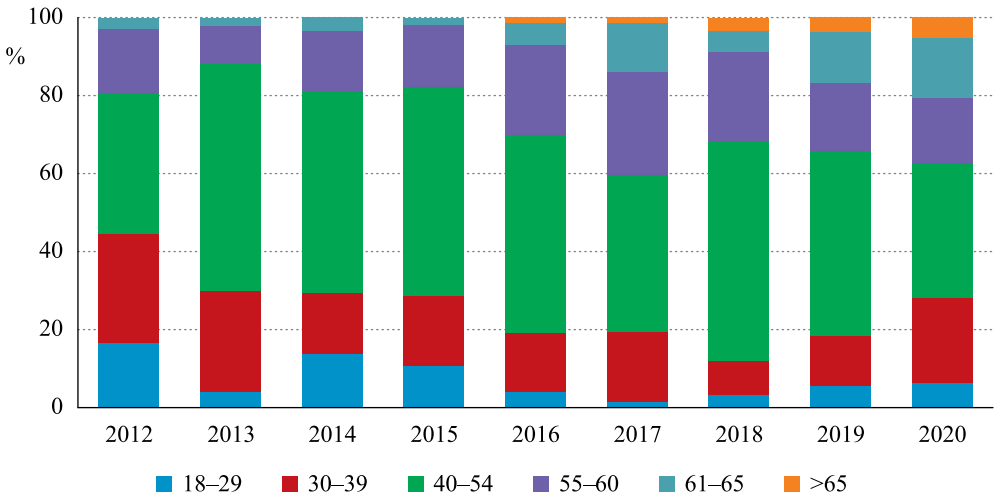

Fig. 8. Dynamics of the number of livers rejected for transplantation in different age groups of donors in 2012–2020 (%)

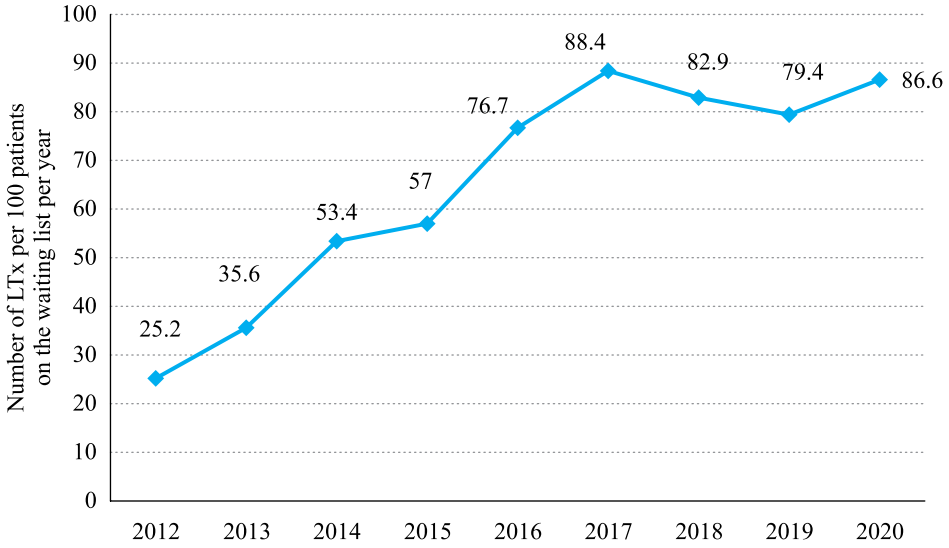

Fig. 9. Indicator reflecting the number of liver transplants per 100 patients on the waiting list per year

liver, the donor age defining a person as a standard or expanded criteria donor starts at 60 years of age, with no upper age limit defined; a number of authors indicate an age of up to 80 years [17].

Analysis presented in this study shows that there were liver donors over 60 years old in the donor pool in 2015; they are very few, 2 people, 2.9% of the total ED pool. Then the number of such donors increases every year, reaching 39 (13.6%) in 2020. At the same time, the proportion of organs rejected for transplantation increased; in 2020, 15.4% of livers were rejected for transplantation in this age group. In the vast majority of cases, the main reason for rejection was hepatic steatosis, detected both visually and by a "null" biopsy performed during the explantation procedure.

According to the largest foreign donor and transplant agencies, the 5-year survival rate of patients who received livers from donors 65 years and older is 74%, while the survival rate of recipients who received livers from younger donors was 75% [16].

Obviously, with comparable survival rates of recipients, the "60+" and "65+" donor categories can reasonably be used for transplantation, within the limits of acceptable safety for patients. It is important to note that a weighted and acceptable (for recipients) expansion of liver donation criteria is an effective organizational tool, allowing to reduce the waiting time for a transplant and to provide a more dynamic movement of patients on the waiting list.

In Moscow, the practice of using donors of the "60+" category has positive stable dynamics. Taking into consideration foreign and already available national experience, we consider it appropriate to develop and improve the engagement of expanded criteria donors in addition to the general development of organ donation for transplantation so that more effective transplant assistance could be provided to the Russian population.

The authors declare no conflict of interest.

REFERENCES

1. EASL Clinical Guidelines liver transplantation. European Association for the Study of the Liver (EASL). *Journal of Hepatology.* 2016; 64: 433–485.
2. *Adam R, Karam V, Delvart V, O'Grady J, Mirza D, Klempnauer J et al.* Evolution of indications and results of liver transplantation in Europe. A report from the European Liver Transplant Registry (ELTR). *J Hepatol* 2012; 57: 675–688.
3. https://www.eurotransplant.org/wp-content/uploads/2021/09/ETP_AR2020_opmaak_LR2.pdf.
4. *Gautier SV, Khomyakov SM*. Organ donation and transplantation in the Russian Federation in 2020 13th Report from the Registry of the Russian Transplant Society. *Russian Journal of Transplantology and Artificial Organs*. 2021; 23 (3): 8–34.
5. *Khubutiya MS, Zimina LN, Galankina IE, Gulyaev VA, Novruzbekov MS, Olisov OD, Magomedov KM*. Morphofunctional evaluation of liver grafts obtained from standard donors and expanded criteria donors. Transplantologiya. *The Russian Journal of Transplantation*. 2018; 10 (2): 87–97.
6. *Nuriakhmetov RR, Musin IR, Kornilov MN, Salimgareev IZ, Zagitov AR, Pogadaev VV, Ivanov II.* Donors with expanded criteria in the regional liver transplantation program. *Bulletin of Transplantology and Artificial Organs*. 2021; 23: 74.
7. *Minina MG.* Development and implementation of an innovative model of organ donation in healthcare practice. [Dissertation]. Moscow., 2016.
8. Actividad de donación y trasplante hepático españa 2021, a document from the site Organización Nacional de Trasplantes, http://www.ont.es.
9. *Nemes B, Gámán G, Polak WG, Gelley F, Hara T, Ono S et al.* Extended criteria donors in liver transplantation Part I: reviewing the impact of determining factors. *Expert Rev Gastroenterol Hepatol*. 2016 Jul; 10 (7): 827–839.
10. *Mullhaupt B, Dimitroulis D, Gerlach JT, Clavien PA.* Hot topics in liver transplantation: organ allocation – extended criteria donor – living donor liver transplantation. *J Hepatol.* 2008; 48 (1): 58–67.
11. *Nickkholgh A, Weitz J, Encke J et al*. Utilization of extended donor criteria in liver transplantation: a comprehensive review of the literature. *Nephrol Dial Transplant*. 2007; 22 (8): 29–36.
12. http://www.eltr.org., European Liver Transplant Registry.
13. *Tenchurina EA, Minina MG.* Organizational, medical and epidemiological prerequisites for reviewing donor criteria in heart transplantation. *Russian Journal of Transplantology and Artificial Organs*. 2020; 22 (3): 43–52.
14. *Tenchurina EA, Minina MG.* A donor heart scoring model to predict transplant outcomes. *Russian Journal of Transplantology and Artificial Organs.* 2020; 22 (4): 27–31.
15. *Tenchurina E.A.* A model of score evaluation of heart donors. [Dissertation]. Moscow, 2021.
16. *Kwong AJ, Ebel NH, Kim WR, Lake JR, Smith JM, Schladt DP et al*. OPTN/SRTR 2020 Annual Data Report: Liver. *Am J Transplant*. 2022 Mar; 22 Suppl 2: 204–309.
17. *Bruzzone P, Giannarelli D, Adam R.* Preliminary European Liver and Intestine Transplant Association – European Liver Transplant Registry Study on Informed Recipient Consent and Extended Criteria Liver Donation. *Transplantation Proceedings.* 2013; 45 (7): 2613–2615.

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