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Opinion

"Let's Live Life - Let's Give Life": Donor Program Improvement as the Key to Transplantation Success in 21st Century - A Croatian Experience

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Abstract

Transplantation is a widely accepted and successful life-saving treatment for hundreds of thousands of patients. However, transplant medicine still faces a number of obstacles. One of the most significant is the large disparity between the number of donors and recipients and the growing need for re-transplantation. In the last two decades, the improvement and organization of the national transplantation program in Croatia have resulted in a steadily increasing donor rate and therefore the transplantation numbers. As the key points of the donor program's success, I would single out the appointment of hospital and national transplant coordinators, the financial reimbursement model for additional medical staff engaged with the donors, the adoption of new legislation, public awareness campaigns and international cooperation with Eurotransplant.

Keywords

Donor organization network; organ allocation; solid organ transplantation

Transplantation is a widely accepted and successful life-saving treatment for hundreds of thousands of patients. However, many people die while waiting for an organ transplant [1]. Organ

shortage is the greatest challenge facing the organ transplantation field today. A variety of approaches have been implemented to expand the organ donor pool, including live donation, a national effort to expand deceased donors, split organ transplantations, paired donor exchanges, national sharing models and greater utilization of expanded criteria donors. Increased public awareness, expansion of the living donor pool and the development of standardized donor management protocols have led to unprecedented rates of organ procurement and transplantation [2].

In the last two decades, Croatia has experienced an enviable growth in organ donation and transplantation. From a very low donation rate (2.6 donors per million population [p.m.p.] in 2000), the transplant program has steadily improved and reached the highest level of donation rate among European countries in 2015, with a donor p.m.p of 40.2 [3] (Figure 1). Just for comparison, last year Spain, with 45.30 million inhabitants had a donor rate of 40.79 p.m.p., while the United States, with a population of 332.90 million, had a donor rate of 41.64 p.m.p. [2, 3]. Moreover, it is important to note that these two countries have a long tradition and well-developed donor and transplant programs compared to Croatia. The factors that contributed the most to the success of the Croatian donor program are presented in Figure 2.

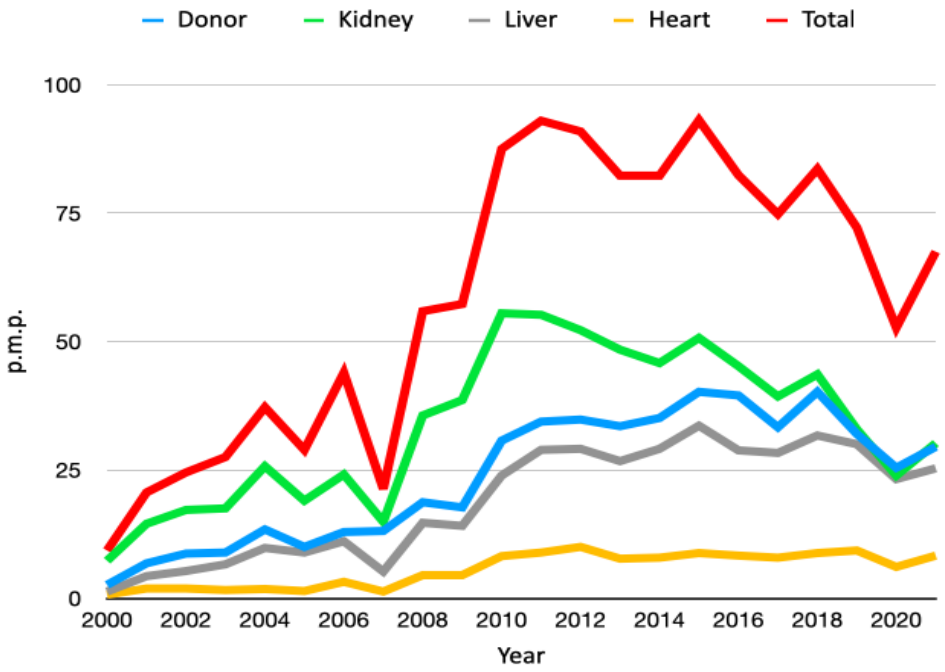

Figure 1 The number of deceased organ donors (both donors after brain death and donors after circulatory death), the number of solid organ transplants (kidney, liver, heart) and the total number of transplanted patients; the annual rate is expressed as per million population (p.m.p) [1].

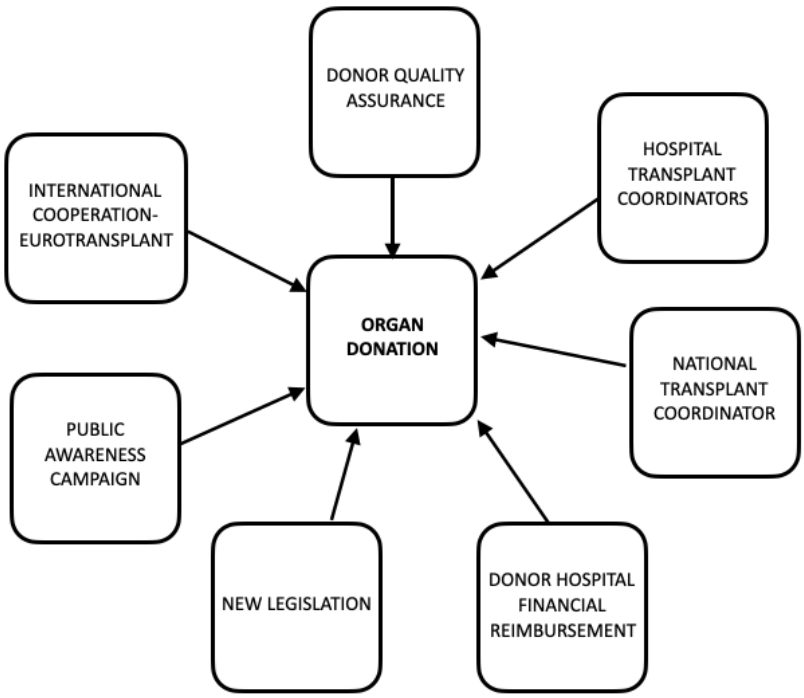

Figure 2 Factors associated with increased organ donation and solid organ transplantation.

Croatia has 4.04 million inhabitants and there are 5 major transplant centers and 32 hospitals participating in organ procurement. A crucial step in the Croatian transplant program was the reorganization of our healthcare system, which meant the appointment of hospital transplant coordinators in 1999 and the national transplant coordinator in 2000 (located in the Ministry of Health). The national coordinator formed a coordination team at the Ministry of Health to attend the 24-hour shifts to support the hospital coordinators and procurement teams. Hospital transplant coordinators are well-experienced and highly skilled ICU specialists, who work part-time on the organ donation process. Most of them have received additional training in organ donation management in internationally recognized and licensed training courses for transplant coordinators (i.e., Transplant Procurement Management Course). Also, the implementation of standardized protocols for optimal donor management and early identification of potential donors has led to an increase in organ donation and transplantation [4]. Furthermore, the reimbursement of donor hospitals, implemented in 2006, partially compensated for the lack of financial resources, inadequate salaries, and shortage of health personnel in Croatia [5]. Until then, the transplant program had been kept alive, mainly by the enthusiasm of the transplant team in each transplant center.

After confirmation of the patient's death, the treating ICU specialist and the transplant coordinator engage with the family in a professional and compassionate manner to offer psychological support, which has been shown to be crucial in lowering the refusal rate for organ

donation [6]. If the deceased did not object to the donation, the procedure is performed by respecting the highest standards, including the protection of the body and dignity of the deceased. However, if the family objects to organ donation, this will be always respected in accordance with bioethical principles.

Compared to other European countries, Croatia is a very small country with an ethnically and religiously largely homogenous, mainly Roman Catholic population. It is worth mentioning that all religious communities in Croatia (Roman Catholic, Orthodox Church, Protestants, Judaism and Islam) generally support organ donation and regard it as an altruistic and generous act. Religious views have been identified as a factor influencing the willingness to donate, with religion tending to be cited as a barrier to donation. Those who are described as being more religious may be less likely to support donation, believing that their religions oppose donation. The conservativeness of religious beliefs, rather than religiosity itself, may be the underlying factor against donation [7]. Christian-dominated European and American countries have higher organ donation rates [8]. However, organ donation rates vary between countries and ethnic groups within a religion. For example, in 2019, three homogenous Catholic countries, Spain, Italy and Poland, had significantly different donor rates of 49.61, 25.25 and 13.26 p.m.p., respectively. Countries with larger and non-Roman Catholic populations than Croatia, with a long-standing transplantation program and a more developed and organized healthcare system, have a lower rate of organ donation, e.g., the UK and Sweden with 24.67 and 19.6 p.m.p. in 2019, respectively [1]. Likewise, in the United States within the Catholic religion, African Americans showed the lowest rate of willingness to organ donation. These findings are related to several factors: lack of transplantation awareness, distrust of the medical community, fear of premature declaration of death after signing a donor card, fear of racism, and religious beliefs and misperceptions [9].

Based on these findings, we can confirm that religion is only one of the factors that can influence the organ donation rate. However, it is important to raise public awareness about transplantation and organ donation and upgrade confidence in the healthcare system.

One of the key factors for a successful transplant program is a positive public attitude towards organ donation, solidarity, and willingness to help others. Croatia has a long tradition in transplant medicine, ever since the first kidney transplantation in 1971 at the Clinical Hospital Centre Rijeka, the leading kidney transplant center in the former Yugoslavia [10]. During the last two decades, public awareness of organ donation has been improved through continuous education, donor card promotion, and national public campaigns organized by the Ministry of Health and non-governmental organizations, one of the slogans of which is “Let's live life - let's give life”. Also, better information availability provided by the professionals experienced in transplantation medicine and recipients who presented their life stories in the mass media improved organ donation.

In Croatia, cadaveric organ donation is mainly based on donation after brain death. Determination of brain death is determined by well-defined and objective criteria and is assessed by strict protocol. The first legislation on the determination of brain death was adopted in 1982, and since 1988 the legal regulation for cadaveric donation in Croatia has been based on presumed consent. Likewise, all ethical principles defined in the Declaration of Istanbul and the Convention on Human Rights and Biomedicine have been implemented in the Croatian Transplant Act 2004 [11]. Transplantation clinical practice was harmonized with the state of the art of bioethical principles defined in the Code of Ethics of the Croatian Medical Chamber [12] and the Additional Protocol to

the Convention on Human Rights and Biomedicine, on Transplantation of Organs, and Tissues of Human Origin, which was adopted by the Croatian Parliament in 2003 [13].

Continuous improvement of the organ donation rate was one of the preconditions for Croatian membership in Eurotransplant (ET). After intensive preparations and negotiations led by the Ministry of Health, Croatia became a full member of ET in 2007, and the only one outside European Union (at that time). Croatian transplant program benefits from ET membership as it provides a larger donor pool and thus better accessibility of organs, especially for patients in need of urgent transplantation [14]. Furthermore, the ET membership contributed to the strengthening of public trust in the Croatian transplant program and fair organ allocation criteria.

Given the success of the "Croatian model", ET appointed Croatia as the Regional Health Development Centre for organ donation and transplantation medicine in Southeastern Europe.

As previously stated, transplantation centers worldwide are under increasing pressure to increase the overall donor pool, including the use of extended criteria donors, donors of extreme ages and donors with prolonged intensive care admission [15]. Prevention of infection and malignancy transmission from donors to recipients is one of the main goals of donor assessment. Transplant clinicians are often reluctant to accept organs from donors with a cancer history, except for those with low-grade tumors. For living donation, comprehensive cancer screening among live donors is now in place, particularly for common cancer types such as breast, colorectal, prostate and cervical cancers [16]. However, routine cancer screening in deceased donors is not always feasible. Current guidelines for screening donor organs and tissues in transplantation have been inconsistent, particularly among donors with borderline transmission risk. Croatia has embraced donor evaluation according to ET principles, which are also in force in other European countries. The Italian national transplantation center has successfully elaborated those multidiscipline principles consistent with clinical, radiological, and laboratory tests, as well as the intraoperative pathological assessment of suspicious lesions [17]. Certainly, transplant clinicians should be aware of the potential donor's medical history and, if in doubt, should exclude organs from donors with any history of high-risk cancers. Each state member of ET must comply with quality and safety standards for organ transplantation and ensure that a reporting system is in place so that vital information can flow if serious adverse events after organ transplantation.

Nowadays, Croatia has achieved a relatively sufficient number of donors. Maybe it is time to take an additional step in organ assessment to attempt to reduce graft rejection or its' early dysfunction. The crucial point is graft perfusion during organ retrieval. The standard preservation technique today is static cold storage with the University of Wisconsin solution. However, cold and warm ischaemic times are independent risk factors for the development of delayed graft function. That is why new perfusion technologies are being considered. Developments in hypothermic (HMP) and normothermic machine perfusion (NMP) technologies have shown potential in clinical kidney transplantation [18]. HMP involves the use of a mechanical pump to circulate cold preservation fluid in the graft, while during NMP, the graft is perfused at near-physiological temperatures and pressures, allowing cellular metabolism and function to be restored. The Netherlands is the first country to introduce HMP for all deceased donor kidneys as standard practice, as the use of HMP enhances 1-year graft survival [19]. Also, NMP shows great promise in the delivery of therapeutics that modify the graft during perfusion or target specific immune processes. Likewise, innovative solutions for improving the biochemical functions of the stored organ have been developed. Antioxidants represent a promising group of compounds with which to modify the compositions of

organ perfusion and preservation fluids to increase their quality and efficacy. A full range of compounds (selenium, zinc, vitamins C and E, carnitine, flavonoids, resveratrol, tanshinone IIA, lecithinized superoxide dismutase, mitoquinon, edaravone, nicaraven, propofol, deferoxamine, PrC-210 aminothiol) is currently being studied in the animal models, but have not been followed up with clinical trials in humans [20]. We can only hope that the progress of technology will lead to the enhancement of graft quality and survival.

Last year we celebrated the 50th anniversary of the first kidney transplant in Croatia. However, the transplant program nowadays is faced with a great challenge, not only in our region, but globally. The COVID-19 pandemic has become an everyday occurrence that has tested the endurance of our health system to its limits and briefly stopped this branch of medicine. In the pandemic 2021, the total donor rate dropped to 29.5 per million inhabitants and the total solid organ transplant rate to 65.4 per million inhabitants. However, compared to 2020, the number of total transplants in 2021 increased by 26.5%, kidney transplants by 26%, liver by 9.5%, and heart by 36% [1] (Figure 1). We all hope that the pandemic will soon be put under control to unburden the healthcare system and with continuous public promotion, we hope to see an increase in organ donation, allocation, and transplantation as it once was.

In the near future, the basis of the Croatian transplant program will remain cadaveric donations as long as the number of donors is sufficient. Organ transplantation from living donors will be performed in individual cases, after approval by the institutional ethical committee, while respecting professional and bioethical principles. Thanks to the highly developed awareness of donation and solidarity of our citizens, excellent transplant teams and an efficient organizational model, Croatia is one of the leading countries in the world in the field of organ donation and transplantation.

With an excellent donor program, significant improvements in waiting list management and pre-transplant evaluation for solid organ transplantation can be achieved. The effectiveness of organ allocation and transplantation can be improved by updating waiting lists with well-established algorithms and carefully evaluating potential recipients. This also strengthens the enthusiasm and motivation of all medical staff involved in donor procurement and organ transplantation.

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Author Contributions

Katarina Tomulic Brusich was the sole author.

Competing Interests

The author has declared that no competing interests exist.

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