

SHORT THESIS FOR THE DEGREE OF DOCTOR OF PHILOSOPHY (PHD)

**Study of the Factors Influencing the Success of the Kidney Transplant
Programme in the North-East Hungarian Region**

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**UNIVERSITY OF DEBRECEN
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Debrecen, 2022**

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Date of the defence: 20th of June, 1 p.m.

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Introduction

Along with the development of organ transplantation, the global demand for transplanted organs is continuously increasing. Unfortunately, there is a huge gap between the number of registered patients waiting for organs and that of transplantable organs. According to WHO data, the low number of potential donors eligible for organ harvesting and of donor referrals, combined with a continuously increasing number of patients on the waiting lists, is a huge problem around the world.

The Eurotransplant International Foundation (ET) was established in 1967, in part with the purpose of managing this problem. ET is a not-for-profit organisation that incorporates transplant centres, donor clinics and laboratories in 8 countries. They use a central donor referral system and a central waiting list to allocate each organ to the ideal recipient. Approximately 15,000 patients are registered on the central waiting list, allowing ET to find a patient for each organ, or even to find perfect matches, if necessary.

According to the most recent statistics, the number of cadaver organs per million population is 17.3 in Hungary, which means we lag far behind countries in the bottom-middle section of the ranking like Spain and Croatia.

In the last five years, the number of cadaver organs has been between 160 and 180 per year in Hungary, with a multiorgan donor ratio of 65-71%. The number of transplantations of kidneys from living donors is 40-45. Currently, 1154 registered patients are waiting for kidney, 94 for liver, 96 for heart, 15 for lung and 48 for pancreas transplant.

In 2020, the number of referring hospitals, donor referrals, and deceased donors fell by 14%, 37.30% and 38.33%, respectively, compared to the previous year. Out of 158 donor referrals 111 resulted in actual donation. In the same year 174 kidneys were retrieved from cadavers, and the numbers of deceased-donor and live-donor kidney transplants were 172 and 30, respectively. Compared to the previous year, the numbers of cadaver kidneys and kidney transplants dropped by 43.14%, and 24.06%, respectively.

On 1 July 2013, Hungary joined Eurotransplant as a full member, which resulted in a gradual increase in the number of organ donations. However, it was not sufficient to achieve a breakthrough.

Organisations, healthcare providers and transplant specialists make relentless efforts to promote and facilitate activities in the field of organ transplantation. To this end, one of the obvious options is to increase donation activity, in order to increase the number of organs available for transplantation. In Hungary this basically means cadaver organs; however, it should be noted that the number of live-donor organ transplants has also grown, although more slowly than desired. As for deceased donations, international data suggest that the number of NHB (non-heart beating or DCD, i.e., donor after cardiac death) donors is rising in certain countries but in Hungary, the establishment of the regulatory background of this option is happening now.

Several healthcare and non-profit organisations seek to change the negative attitude towards organ donation through dissemination of information and sensitization programs. They also make efforts to promote the acceptance of this treatment both among healthcare professionals and among members of society. In order to provide the target groups with adequate and relevant information, it seems necessary to conduct surveys to identify incomplete or false information that may hinder, and the educational activities that could contribute to a significant improvement of donation activity. In the first part of my work, I explored the factors that hinder progress.

The kidney transplant program was launched at the University of Debrecen in 1991. In this regard, in addition to making efforts to increase the number of live-donor transplants, one of the options to improve balance between the numbers of patients on the waiting list and of kidney donations is the use of marginal donor organs. Within the framework of the investigation explained in the second half of this study we reviewed the results achieved using expanded-criteria donor kidneys at our renal transplant centre.

Objectives

The present work includes two studies with the shared aim of finding ways to help patients on the kidney transplant waiting lists receive a donor organ.

In the first stage we wanted to identify the factors that affect donation activity in our region, with special regard to areas that we can influence.

- First, using a questionnaire, we wanted to find assess what detailed information healthcare professionals involved in any phase of the donation process and laypeople have about brain death determination and organ donation.
- In the second part of the questionnaire-based survey we tested the knowledge of the same groups about organ transplantation.

Our ultimate goal was to identify areas where education, further training and awareness –raising could be used to enhance donation activity.

In the second part of our examination we studied the proportion of ECD (extended-criteria donor) kidney transplants carried out at our transplant centre; whether it had changed during the studied period; the survival rate of ECD kidneys; and whether these numbers were in line with international trends. We also examined whether the proportion of ECD kidneys had changed after Hungary joined Eurotransplant.

Patients and Methods

Questionnaire survey on the knowledge of healthcare professionals and laypeople regarding brain death determination and organ donation

A team of anaesthesiologists, ICU health staff and transplant surgeons conducted a questionnaire survey among healthcare professionals and laypeople.

The questionnaire consisted of three parts. The first few questions related to the age, gender, educational level and religiosity of the participants. The second group of questions related to the knowledge of respondents about the regulatory background of brain death determination and organ transplantation in Hungary. The questions and the possible answers are shown in Table 1.

Table 1 – Questions and possible answers regarding the Hungarian regulatory background of brain death and organ transplantation

Question	Answer
To the best of your knowledge, what does organ transplant mean?	The transplantation of an organ from a dead body.
	The transplantation of an organ from a living person.
	Both of the above.
	I do not know.
Do you know anyone who has received or is waiting for a donor organ?	Yes, a family member.
	Yes, a person in my environment.
	I have only heard about such people in the media.
Are you familiar with the regulatory background of organ donation in Hungary?	Yes.
	No.
	I do not know.
To the best of your knowledge, which statement is true in the	The person registered for organ donation in their lifetime.

light if the Hungarian regulations regarding deceased organ donation? An organ can be transplanted only if:

The person submitted a consent statement in their lifetime.

The person did not submit a written opt-out statement regarding organ donation in their lifetime.

Family members consent to the donation of organs.

Family members do not submit an opt-out statement regarding organ donation.

I do not know.

Have you ever heard of the written opt-out statement regarding organ donation?

Yes.

No.

To the best of your knowledge, where can people make an opt-out statement?

At their GPs.

At a specialist in a hospital.

At the municipality.

All of the above.

None of the above.

I do not know.

What does brain death mean?

Coma.

Complete and irreversible loss of brain and brain-stem functions.

Making breathing and circulation stop.

All of the above.

None of the above.

I do not know.

According to the regulations, what is the main purpose of brain death determination in Hungary?

Organ retrieval for transplantation purposes.

To stop treatment.
 To determine the time of death.
 I do not know.

To the best of your knowledge, who is responsible for determining brain death in Hungary?	Nurse. Specialist. Head of hospital department. Brain death committee, which consists of 3 independent specialists.
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The next part of the questionnaire included questions related to organ transplant. We wanted to find out how much respondents knew about the efficiency of organ transplantation, and whether they were prepared to offer their organs for transplantation. The questions and the possible answers are listed in Table 2.

Table 2 – Questions and possible answers related to organ transplantation

Question	Answer
What is the main goal of transplantation? (You can select one or more answers.)	To save lives. To improve life quality. Organ trade. I do not know.
To the best of your knowledge, who can a living person voluntarily donate their organs to?	Relatives. Relatives and loved ones. Anyone, in exchange for money. I do not know.
	Kidney

Which organs can be transplanted from a living donor? (You can select one or more answers.)

- Heart
 - Liver
 - Liver segment
 - Lung segment
 - Pancreas
 - Cornea
 - Bone marrow
 - None of the above
 - I do not know
-

Which organs can be transplanted from a dead body? (You can select one or more answers.)

- Kidney
 - Heart
 - Liver
 - Liver segment
 - Lung segment
 - Pancreas
 - Cornea
 - Bone marrow
 - None of the above
 - I do not know
-

To the best of your knowledge, what are the most serious potential complications after organ transplant? (You can select one or more answers.)

- Infection
 - Organ rejection
 - Bleeding
 - None of the above
 - I do not know
-

What disease or condition makes a donor ineligible for organ donation?

- Malignant tumour
 - Benign tumour
 - Infection
 - None of the above
 - I do not know
-

25

100

How many patients do you think wait for kidney transplant a year in Hungary?	500 900-1,000
What percentage of patients on the kidney waiting list do you think receive a donor organ per year in Hungary?	100% 75% 50% 75% 25%
What kind of quality of life can a patient expect after a kidney transplant?	They will be confined to bed. Major damage, inability to work. Inability to do physical work. They can live a full life and engage in sports.
How long do you think can a transplanted kidney function?	For 1 year For 2-3 years More than 10 years
Would you allow your organs to be used for transplant purposes after your death?	Absolutely not. I would have no problem with it. I would give my consent. I would give my consent with conditions.

We distributed 1,000 questionnaires among the participants: we sent 56 to ICU specialists, 76 to healthcare professionals working at the Department of Anaesthesiology and Intensive Therapy, 188 to final-year medical students, and 320 to GPs practicing in the region of the Clinical Centre. In the letter sent to GPs we also asked them to distribute the questionnaire among their patients (360 questionnaires were sent), and collect them after completion.

The response ratio was 26/56 (45%) in the case of ICU specialists, 49/76 (64%) with ICU nurses, 50/188 (27%) with medical students, and 196/320 (61%) with GPs. The ratio was 166/360 (46%) in the case of laypeople. The responses were treated anonymously.

The answers were assessed by two independent evaluators, based on a list of predetermined correct answers. An analysis took place by calculating the percentages of correct answers compared to the number of individuals in each group. We used the χ^2 test to assess the differences between the groups regarding the percentage of correct answers.

In the second phase of our research, we performed a retrospective analysis of the data on cadaveric donors transported to our transplant centre between January 2011 and September 2014. We also examined the relative proportion of ECDs. The definition of ECD was: 1) donor age ≥ 60 ; 2) donor age 50-59; and 3) fulfilment of 2 out of the following criteria: hypertension, serum creatinine > 1.5 mg/dL, or death resulted from a cerebrovascular accident. Standard-criteria donors (SCDs) were those who did not meet the ECD criteria. Cold ischemic time (CIT) was defined as the time between two releases of the blood vessels during aortic cross clamping and kidney transplantation. Delayed graft function (DGF) was defined as the need for at least one dialysis during the first week after kidney transplantation.

We used induction therapy with ECD organ recipients, while SCD patients received standard tacrolimus, mycophenolate-mofetil and steroid triple therapy from the beginning. ECD organ recipients received 1.5 mg / kg bw antithymocyte globulin for 3 days in the form of induction therapy. We stopped induction therapy when serum creatinine dropped to half of its value after transplantation, or reached 2.83 mg/dL (250 μ mol/L). We compared the characteristics and post-operative complications in the ECD and the SCD groups.

Statistical analysis was conducted using SPSS version 22. Continuous variables were given in mean and standard deviations, while categories were given as frequency and percentage. For continuous variables independent-samples Student *t* test was used, and the Mann-Whitney *U* test was applied for non-normally distributed variables. The χ^2 test was used for the examination of categorical variables. Survival rates were estimated with the Kaplan-Meier method, and the statistical differences between groups were determined using the log-rank test. $P < 0.05$ was considered a statistically significant value.

Results

Questionnaire survey on the knowledge of healthcare professionals and laypeople regarding brain death determination and organ donation

A total of 487 respondents completed and submitted the questionnaire. The average age of the 304 women and 183 men was 41.7 ± 14.8 years. 22% of them were 18–25 years old, 25% between 26 and 40, 48% between 41 and 65, and 5% over 66 years of age. 0.2% completed elementary school (1 person), 30.4% had secondary education (148 persons), and 69.4% had higher-level education (338 persons).

Based on the answers provided in the first part of the questionnaire, the frequency of occurrence of religious beliefs was also determined. 59.3% of the respondents were Christian believers, and 40.7% were not religious. Table 3 shows the composition of each group by age, sex and religiosity.

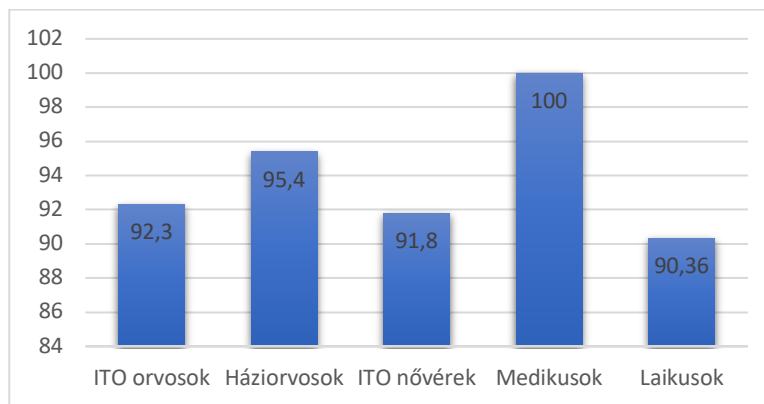
Table 3 – Demographic distribution of respondents

	ICU specialists (n=26)	GPs (n=196)	ICU nurses (n=49)	Final-year med. students (n=50)	Laypeople (n=166)
Age	38.1±8.9	51.7±11	38.3±10.4	24.3±1.1	37.6±14.8
Female/male	14/12	102/94	40/9	35/15	113/53
Religious Y/N	16/10	121/75	22/27	38/12	94/72

Responses to the questions of the questionnaire:

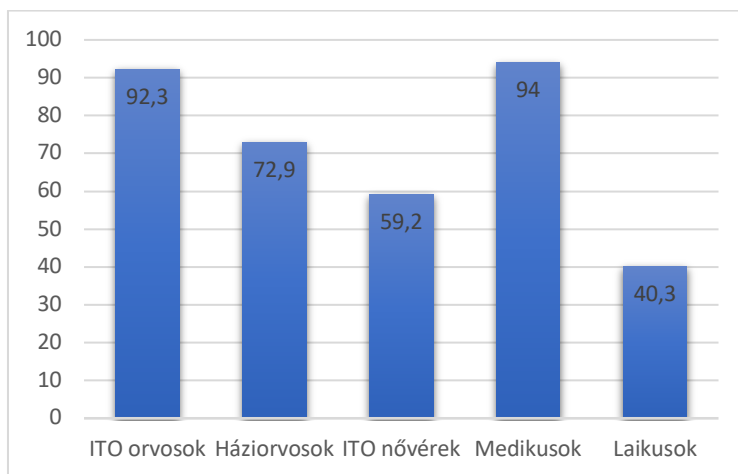
With the first question we wanted to find out what organ transplantation meant according to the respondent. As Table 1 shows, the percentage of correct answers exceeded 90% in each group, which means that the majority of healthcare professionals and laypeople were familiar with the concept.

Figure 1 – What do you think organ transplantation is? (Percentages of correct answers)



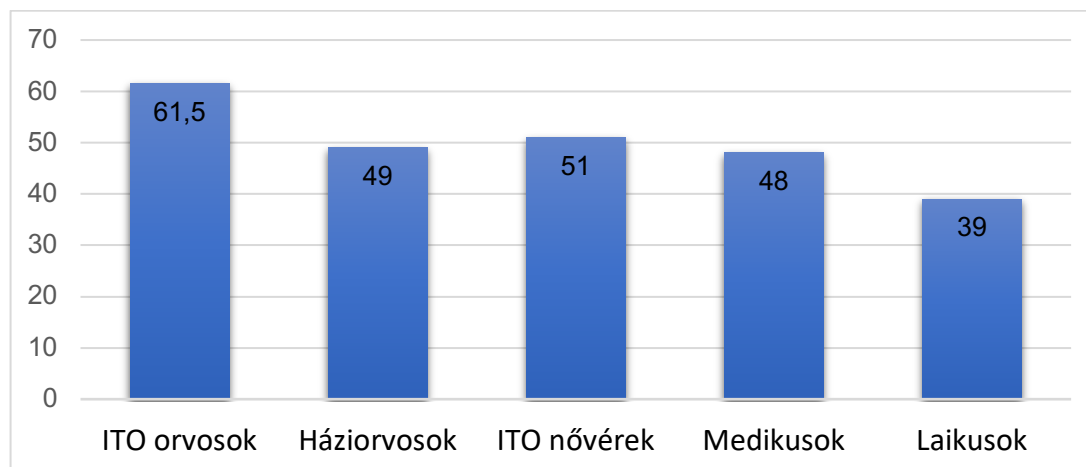
With the next question we wanted to find out how much respondents knew about the regulatory background of organ retrieval from dead bodies, and if they knew that in Hungary the principle of “presumed consent” is applied. Figure 2 shows that fewer than 50% of laypeople knew the correct answer, and more than 25% of their GPs did not have accurate information on the issue either. Of healthcare professionals, ICU nurses demonstrated a surprisingly high level of ignorance on the subject.

Figure 2 – To the best of your knowledge, how is the donation of organs retrieved from deceased people regulated? (Percentages of correct answers)



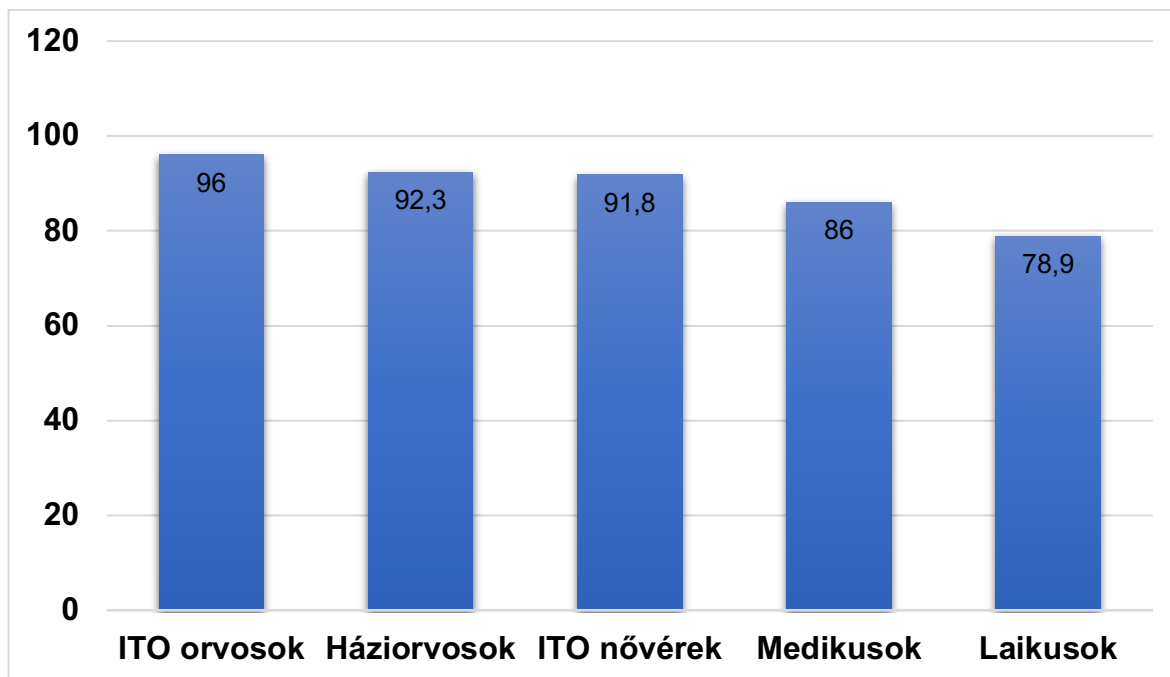
We wanted to find out if respondents knew where they had to submit an opt-out statement if they decided against offering their organs for transplantation after their death. 40% of laypeople proved to be well-informed on the subject. It was shocking to see that only 49% of GPs knew what to do with opt-out statements, despite the fact that they are legally responsible for collecting and forwarding such statements. It should be noted that none of the groups of healthcare professionals seemed to have accurate information on the issue in a satisfactory proportion. Figure 3 shows the percentages of correct answers.

Figure 3 – To the best of your knowledge, where can people make an opt-out statement? (Percentages of correct answers)



We also examined whether respondents had accurate information on the purpose of brain death determination. It was reassuring to find that in all groups of healthcare professionals over 90% of respondents knew that according to relevant regulations, the determination of brain death is a prerequisite for retrieving organs for transplantation purposes. The fact that only one fourth of laypeople knew the correct answer suggests that there is a need for awareness-raising in this matter. The percentages of correct answers are summarised in Figure 4.

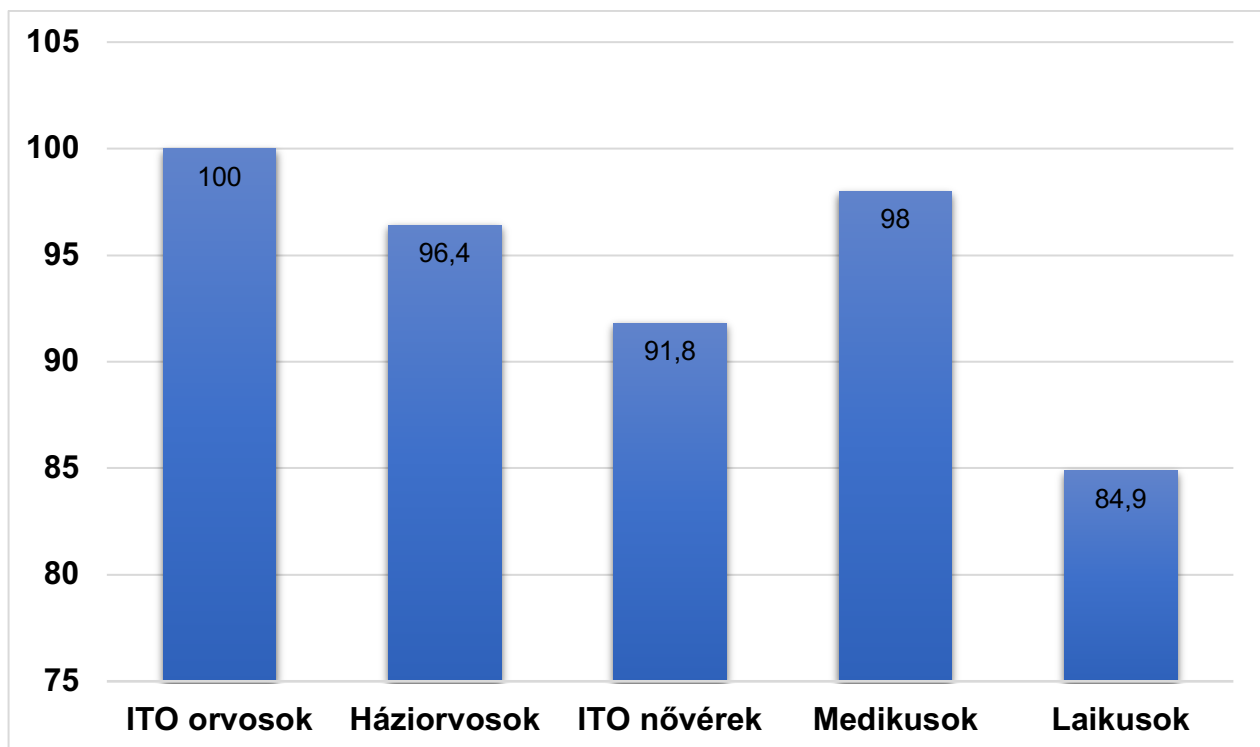
Figure 4 – According to regulations, what is the main purpose of brain death determination in Hungary? (Percentages of correct answers)



The question about responsibility for determining brain death primarily concerned healthcare professionals. More than 8% of ICU nurses did not know the correct answer, despite the fact that they are often present when a brain death committee is summoned. However, the majority of respondents had accurate information on the subject (Figure 5).

About 15% of laypeople did not know the correct answer, but this is irrelevant in practical terms.

Figure 5 – To the best of your knowledge, who is responsible for determining brain death in Hungary? (Percentages of correct answers)



Analysis of responses to the question about transplant procedure and respondents' willingness to donate their organs

The next part of the survey focused on organ transplant itself and related details. It should be highlighted that the primary goal and the significance of organ transplantation were well known among both healthcare professionals and laypeople. Unfortunately, healthcare

professionals and laypeople alike demonstrated a serious lack of information about live donation, including eligibility criteria and the organs (segments) that can be donated. Surprisingly, respondents were also rather ignorant regarding the organs that can be transplanted from a dead body. This suggests that further educational efforts should be made in these areas. However, both healthcare professionals and laypeople were quite well-informed on the potential complications after transplantation and the conditions that may render an individual ineligible for organ donation.

Apparently, all respondents were aware of the potential extent of life quality improvement following kidney transplantation. Most of them even had accurate information on the lifetime of transplanted kidneys.

Importantly, this part of the survey also revealed that a significant percentage of both healthcare professionals and laypeople were not aware of the gravity of the problem, namely the high number of patients waiting for a new kidney every year in Hungary. They hugely underestimated the figures. The results of the two groups were somewhat better regarding the number of patients on the waiting lists who receive a donor organ in a year in Hungary.

The absolute numbers and the percentages of correct answers are summed up in Table 3.

Table 3 – Number and percentage of correct answers to the questions related to organ transplantation

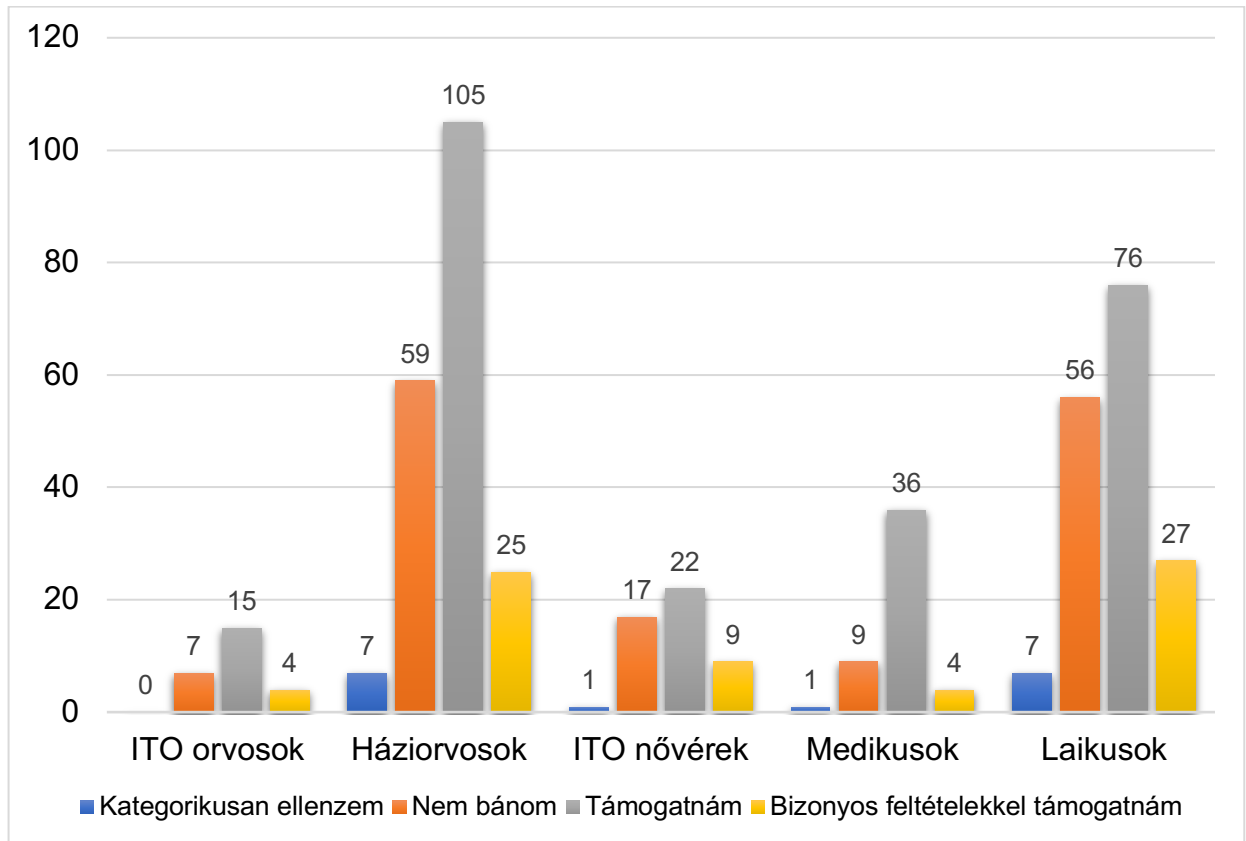
Question	ICU specialists (n=26)	GPs (n=196)	ICU nurses (n=49)	Med. students (n=50)	Laypeople (n=166)
What is the main goal of transplantation? (You can select one or more answers.)	26 (100%)	196 (100%)	49 (100%)	50 (100%)	163 (98%)
To the best of your knowledge, who can a living	15 (57.6%)	92 (46.9%)	20 (40.8%)	29 (58%)	67 (40.3%)

person donate their organs voluntarily?					
Which organs can be transplanted from a living donor? (You can select one or more answers.)	8 (30.8%)	142 (72.4%)	14 (28.6%)	22 (44%)	29 (17.5%)
Which organs can be transplanted from a dead body? (You can select one or more answers.)	7 (26.9%)	44 (22.4%)	14 (34.7%)	10 (20%)	10 (6%)
To the best of your knowledge, what are the most serious potential complications after organ transplant? (You can select one or more answers.)	26 (100%)	196 (100%)	49 (100%)	50 (100%)	164 (98.7%)
What disease or condition makes a donor ineligible for organ donation?	25 (96%)	181 (96.9%)	43 (87.7%)	47 (94%)	154 (94.6%)
How many patients do you think wait for kidney transplant a year in Hungary?	19 (73.8%)	87 (44.3%)	29 (59.1%)	12 (24%)	61 (36.7%)
What percentage of patients on the kidney waiting list do you think receive a donor organ per year in Hungary?	23 (88.4%)	171 (87.2%)	39 (79.6%)	37 (74%)	128 (77%)

What life quality can a patient expect after a kidney transplant?	26 (100%)	190 (96.9%)	42 (85.7%)	46 (92%)	166 (89%)
For how long do you think can a transplanted kidney function?	24 (92.3%)	191 (97.4%)	47 (95.9%)	44 (88.0%)	162 (97.6%)

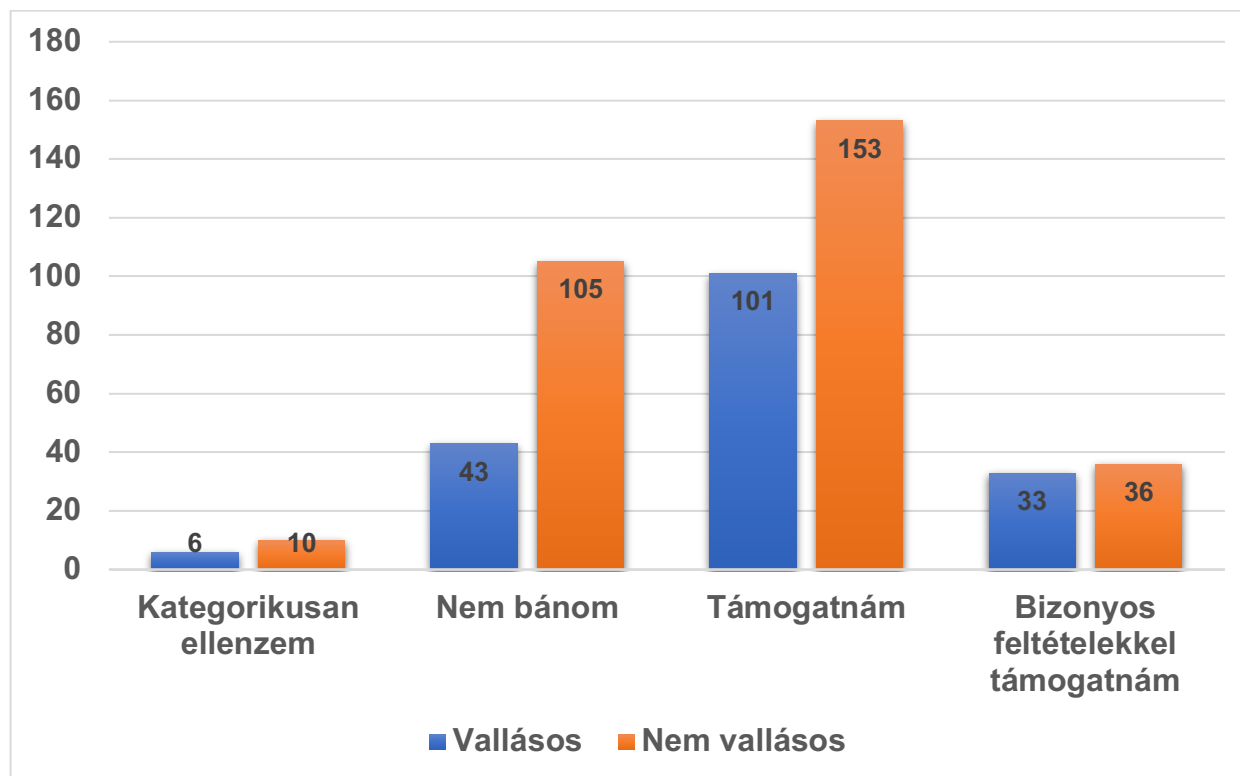
It was interesting to find out about the willingness of respondents to donate their organs. First, we compared the attitudes of healthcare professionals and laypeople. Interestingly, a high percentage of healthcare professionals, ICU specialists, GPs and ICU nurses alike, selected the “I would give my consent with conditions” option. It should be noted, however, that in each group most of the respondents took a neutral-supportive (“I would have no problem with it”) or a supportive stance. The percentage of total rejection was negligible in all groups, with laypeople and GPs on the top of the ranking. The percentages of the answers are shown in Figure 6.

Figure 6 – Would you allow your organs to be used for transplant purposes after your death? Number of respondents by answers in each group.



We wanted to know how religiosity, or the lack thereof, affects the willingness of respondents to donate their organs for transplantation. While religious and non-religious respondents were represented in equal proportions among those who firmly rejected donation, non-religious individuals were in majority both among passive and active supporters. Figure 7 reflects the attitudes of religious and non-religious respondents regarding the donation of their organs.

Figure 7 – Would you allow your organs to be used for transplant purposes after your death? Distribution of responses by religious belief.



Analysis of kidney transplantation data based on expanded donor criteria in our centre

In the period between January 2011 and September 2014, 215 cadaver donors were reported in our region and a further 14 kidneys were offered to our centre by Eurotransplant. We rejected 81 (35%) donor kidneys. The most frequent reasons for the rejection of the organs were proteinuria (5.8%), the family's objection (5.3%), or severe atherosclerosis (4.1%). Of the reported donors 91 (40%) were ECD, and 123 (54%) SCD. In 15 cases (6%) ECD-criteria data were insufficient. These donors were excluded from further analyses. 47 (52%) of the rejected kidneys came from ECD and 32 (26%) from SCD ($P < 0,001$). These donations enabled us to perform 84 kidney transplants in our institute. The proportion of transplanted ECD kidneys increased after 2011 (from 3.7% per annum in 2011 to 48.1% in 2014, $P .006$), while that of SCD kidneys showed a gradual decrease. After joining Eurotransplant the proportion of ECD-grafts distributed to our centre increased, too, (40.7% before, and 59.3% after joining ET, $P .003$).

Table 5. summarises the characteristics of the SCD and ECD groups and the postoperative complications. In terms of total donations, the body mass index (BMI) of ECD kidneys was higher. Diabetes was more frequent compared to SCD (P .002, and P .004, respectively). A tendency could be observed that older diabetic patients were more likely to receive ECD graft. More recipients received induction treatment using an ECD kidney compared to SCD kidneys (P. 036). The proportion of DGF during ECD graft transplantation was identical to that compared to SC kidneys.

Table 5. Characteristics of donors and recipients as well as postoperative complications in the ECD and SCD groups

	ECD	SCD	P
Total donations	(n = 91)	(n = 123)	
Donor BMI	28.1 ± 5.8	25.1 ± 5.9	.002
Donor diabetes	16.4%	3.9%	.004
Donor proteinuria	46%	35%	.111
Transplanted kidneys, Debrecen	(n = 27)	(n = 58)	
Recipients age(years)	52.4 ± 10	46.1 ± 14.8	.074
Recipients diabetes	36.4%	17.4%	.084
CIT (hours)	14.1 ± 4.2	12.87 ± 4.7	.367
Induction therapy	59%	28%	.036
DGF	17.4%	20%	.853

The transplant survival rates at 1 and 3 years and patients' survival rates in the SCD group was 90.7%, and 76%, and 98%, and 90%, respectively (Figure 8). In the ECD group there was no graft loss or patient loss during the examined period.

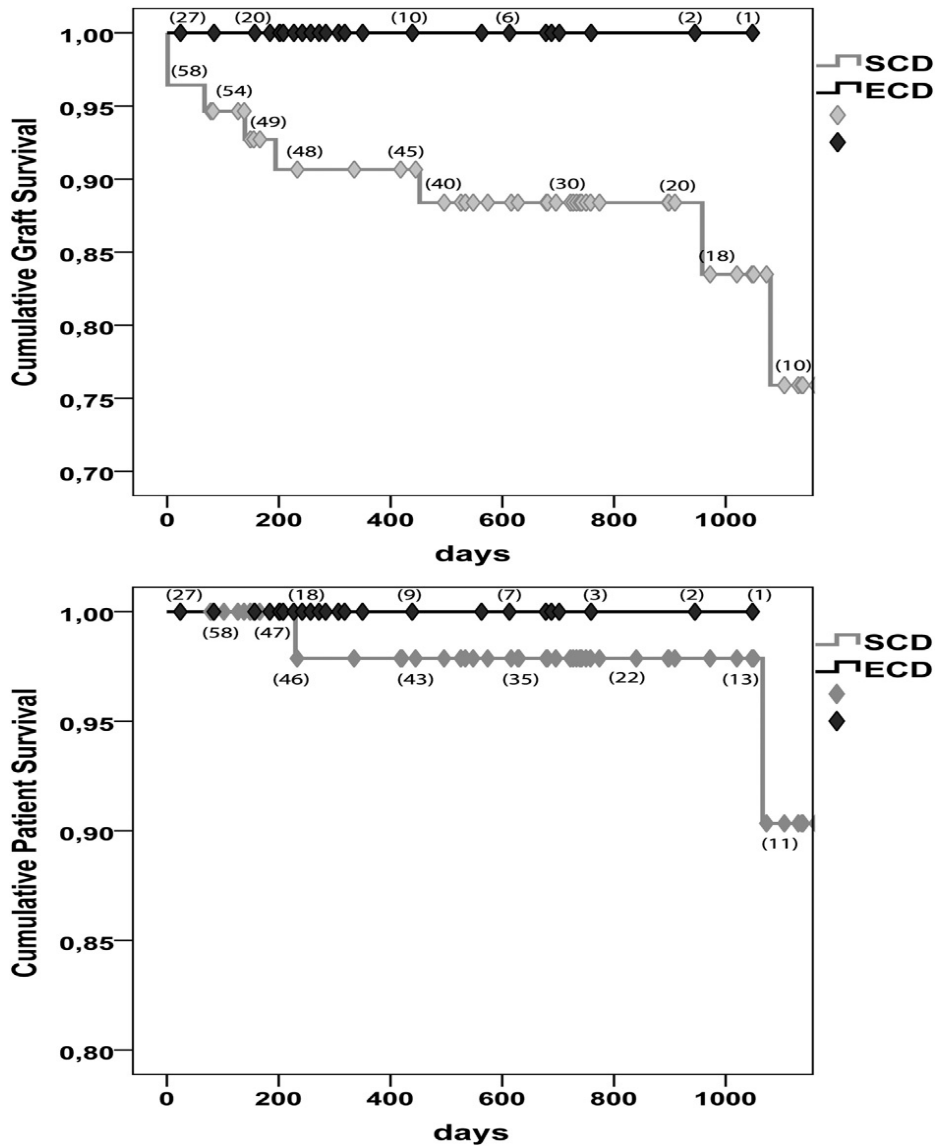


Figure 8. Cumulative graft and patient survival in the standard (SCD) and the expanded donor (ECD) groups. The numbers in brackets indicate case numbers in the relevant periods.

DISCUSSION

In our questionnaire-based study we showed that knowledge about domestic legislation governing donor donation among both health specialists and laypeople is sorely lacking. In addition, accurate knowledge of transplantable organs of deceased and living persons is rather limited, and all groups have underestimated demand for organs.

In Hungary, a law governing organ donation and transplantation has existed since 1997. This regulation prescribes an opt-out system for organ donation, which means that all citizens need to dissent to their organs being harvested after death. This written statement can be left with the general practitioner or the specialist responsible for regular care (nephrologist, cardiologist, pulmonologist, hepatologist, etc.) The regulation stipulates that the written statement needs to be forwarded to a central registry. This registry system provides information for registered users only if they count as organ donors, i.e., after brain death is declared; the intensivist needs to access the system on a case by case basis, so that they can report the donor. If there is no registered dissenting statement, organ donation can be considered even in spite of the family's objection. Thus the fact that two thirds of family doctors were not aware of this regulation should be considered a serious issue which can be changed only through a programme of training and refresher courses for general practitioners and residents, and refresher courses for specialists, through consistent education. The fact that close to half of the laypeople interviewed believed that it takes either positive consent (in other words, an active support statement that the patient has made during his life time) or a consent gained from the family to regard the deceased as a potential donor should be considered a further problem. The opt-out (presumed consent) system is effective in 24 countries, and a similar albeit stronger form of presumed consent is used in countries like Austria, Denmark, and France. Unfortunately, during our review of the literature we were unable to find data on how knowledgeable general practitioners are in other countries regarding regulations governing organ donation, hence we are unable to compare our data with other countries' experience.

Our investigations have made it clear that healthcare staff play an important role in informing patients about organ donation. In a Danish study only 42% of intensivists had the necessary knowledge to explain the importance of organ donation to bereaved families. Earlier studies have revealed that the education and attitude of healthcare providers are related to the proportion of organ donation in different countries. Earlier studies have also proved that educational programmes are necessary to expand health care professionals' knowledge, and that the execution of educational trainings can be effective. In Hungary the duty of communicating with the deceased patient's relatives lies primarily with the intensivist. Our study has shown that the overwhelming majority of intensivists in the region were well-informed about the regulatory environment governing organ donation. This was the result of a consistent, decades-long training programme during which every qualified resident in the region is obliged to attend a training program on the legal and technical conditions of determining brain death. An important part of this training programme is for prospective specialists to familiarize themselves with communication with relatives within the framework of psychology situational exercises. As revealed by this study, it is vital to expand knowledge about the determination of brain death, regulation governing organ donation, and the efficacy of transplantation among members of the population. In our literature review we showed that about one-third of harvested organs fail in Hungary, and the majority do so as a result of intense objection by family members. Although we can say that the regulations provide protection for the medical team even in the face of family objection, in a given psychological situation the intense objection of relatives from certain social and ethnic backgrounds can create situations where the doctors eventually rescind donation. Recent international studies have also indicated that family objection can impede organ donation even in countries with an opt-out (presumed consent) system but it particularly does so in countries with opt-in (donor card, active consent) systems. This situation can be improved only through long, detailed, and extensive awareness-raising among the population. A more active use of modern media, e.g. social media, TV and different internet based devices, could be beneficial for the dissemination of information among the general population regarding donation and transplantation. Publications have appeared about the efficiency of family interviews in connection with the transplant procedure in countries with opt-in systems

which have proved to be rather successful. In Hungary the National Blood Bank operates a homepage for the general population, where laypeople can find information about brain death and donation, familiarize themselves with the position of the churches on organ donation and try to improve the acceptance of organ donation by relating personal stories. Regular campaigns in the electronic and other media, threads that show positive examples incorporated in the popular series of commercial TV channels as well as the regular sensitizing programs held by transplant recipients' organizations can all increase the social acceptance of donation. The Gerundium Contemporary Education Program as created at our University with this aim in mind. During our investigation we had an interesting observation: the willingness to donate organs among people who regarded themselves as religious was considerably lower despite the fact that all Hungarian churches are, in fact, supportive of organ transplantation.

In this study, willingness to support donation of their own organs among the physicians and nurses of the intensive care unit was not high. This can be seen as an important issue because the attitude as well as verbal and non-verbal communication of the staff of the ICU can affect the family's attitude, i.e., their support of, or aversion to donation and the transplantation procedure. Similar to our observations, Bogh et al. found in their study that only 49% of health workers of an intensive care unit were willing to donate organs themselves in a given situation. 54% of the care workers in the ICU were willing to offer their own organs for donation despite the fact that 76% of them supported organ and tissue donation after death. A similar proportion of surgeons and surgery residents (64%) of the care workers in an Iranian intensive care unit were willing to donate their own organs. These data show that training programs are indispensable.

Based on our results we can conclude that cooperation between numerous professional and non-professional (including churches) organizations as well as long-term awareness-raising and training programs are necessary to familiarize the population with donation-related knowledge, reduce uncertainty and aversion and highlight the positive sides of organ donation. Long-term and persistent programs are needed to implement this awareness-raising, in which all traditional and novel forms of information dissemination need to be employed over an extended period of time, and sometimes even using campaign-like elements.

In addition to factors affecting availability of a sufficient number of donated organs our study also performed a critical analysis of our expanded criteria kidney donation activity. In recent years most Hungarian transplant centres have been forced to perform ECD kidney transplants due to a shortage of organs. In their retrospective analysis conducted on Hungarian patients over several periods Végső et al. concluded that in the three periods (1994-1998; 1999-2000; and 2000-2002) primary function disorder was observed in 8.5% and 2.8% of grafts and acute rejection rate was 35-36 and 32%, respectively. 1-year graft survival rate was 71.2-91 and 92 %, respectively, in the above periods.

Similarly to international trends, the number of transplanted ECD kidneys in our centre has increased considerably in the past 4 years. Older recipients were more likely to receive ECD grafts (Table 6.). This is the result of the ET Senior Program, which allocates older donors' kidneys to older recipients. The program disregards HLA matching and only non-immunized (panel reactive antigen below 5%) recipients are selected who are first kidney transplants.

Earlier observations suggest that ECD kidneys present a 70% higher risk for graft damage than do SCD kidneys. ECD kidney transplants are accompanied by an increased risk of protracted cold ischemia time (CIT) and DGF, which results in lower graft survival. Hence the ET Senior Program tries to minimize CIT to prevent DGF and kidney loss. The best way to reduce CIT is to allocate older kidneys (> 65 years) to older recipients (> 65 years) in the donation region. As a result of these efforts there was no difference in patients' death-censored graft survival at 3 years between the ET Senior Program and HLA governed allocation systems.

Worldwide, one of the key characteristics of expanded kidney donation is the fact that organs come from older donors; a trend pioneered by Spain, with a traditionally exceptionally active role. Follow-up studies have clearly demonstrated that advanced donor age is associated with the worsening of donor graft function and graft survival time. At the same time it should be noted that, for patients in the dialysis program even transplantation of a kidney from an older donor offers a better option long term than staying on the waiting list. Comparison of ECD kidney transplants with that of patients in the chronic dialysis program reveals a rather characteristic difference in 1-year mortality

rate and long-term mortality rates: while in the former there is no difference in mortality at 1 year between transplant patients and those in the dialysis program, metaanalyses find a significant survival advantage for transplants in survival rates at year 5. At the same time it should also be noted that although there is sufficiently strong evidence for the former statement, this advantage is not so significant for the transplantation of higher risk recipients. This statement has particular relevance to re-transplants. Our results are in accordance with international reports and the Hungarian ones mentioned earlier, which come from other centres. In our material no difference was found in CIT and DGF rate, or in cumulative survival in patients and grafts between the ECD and SCD groups. The decision to allocate ECD grafts to suitable recipients is controversial not only in the case of kidney but also other organ transplants. Results of multicenter studies suggest that ECD kidneys should be allocated to patients over 60, patients with diabetes over 40, patients with a risk of vascular event, and to patients whose waiting time on the waiting list exceeds their life expectancy without transplantation. Some studies have confirmed that, compared with SCD transplants, in patients aged 60 and over ECD kidney transplant is associated with an increase in patients' mortality rate at 1 year. However, other studies have shown survival advantage for patients over 70 and 75 in the case of ECD kidney transplants compared with patients receiving dialysis. Overall, however, both international and domestic data confirm that kidney transplants from ECD donors play an important role in reducing the number of patients on the waiting list. After the application of appropriate donor and recipient selection criteria as well as diagnostic and therapeutic interventions this program will be able to function successfully, offering patients a health advantage.

Finally, another piece of data that provides a connection between our two studies and that is in need of further analysis. Since the region belonging to the University of Debrecen is the most active donor-reporting region in Hungary, 40% of the kidneys offered here were ECD kidneys, our results can be regarded as being representative for the entire country. The underlying reason for the relatively high ECD proportion is not known to us, either, at this point, but it could be caused by the more severe comorbidity condition of our region's population revealed by epidemiological studies.

Own results:

1. We were the first both internationally and domestically to conduct an extensive, questionnaire-based survey among different actors of the health care staff and non-health related, laypeople to examine their knowledge about brain death, organ donation, and organ transplantation.
2. We have concluded that, within the health care staff, knowledge about brain death determination and organ donation is extremely scarce among general practitioners and members of the general public.
3. Willingness of the (theoretical) voluntary donation of one's own organs among the health care and general populations was roughly the same, with a higher proportion of refusal among religious people.
4. Our study draws attention to the necessity of professional training courses in the topic as well as information dissemination and sensitization programs for the public.
5. We have concluded that organs from ECD donors are taking up an increasingly larger proportion in our population of regional transplant patients.

Analysis of our kidney transplants performed in accordance with expanded donor criteria has shown that in the SCD group transplant (kidney) rates at 1 and 3 years were 90.7% and 76%, and patient survival rates at 1 and 3 years were 98% and 90%, respectively. The results are in line with international literature data.

Summary

The main goal of the thesis was to analyze the possible factors influencing the success of our regional kidney transplantation program and thereby to shed light on actions that are needed to improve efficacy. There were two main fields of the investigations: First, we assessed the knowledge and the attitudes of healthcare workers as well as laypeople regarding brain death, organ donation and organ transplantation using a questionnaire. Second, we aimed to analyze the results of ECD kidney transplantations within our regional transplant centre and find out whether transplantation of kidneys based on ECD criteria could effectively contribute to the reduction of waiting lists.

The results suggest that the knowledge about brain death determination and organ donation of general practitioners and laypeople is sorely lacking. Respondents' willingness to donate their organs was roughly the same among healthcare workers and laypeople, but religious behaviour was associated with lower willingness. Our results underline the importance of training and education programs both for healthcare professionals and for laypeople in order to improve donation activity and to decrease family-initiated refusals. We have concluded that organs from ECD donors are taking up an increasingly larger proportion in our population of regional transplant patients. We have concluded that in the SCD group transplant (kidney) rates at 1 and 3 years were 90.7% and 76%, and patient survival rates at 1 and 3 years were 98% and 90%, respectively. The results are in line with international literature data.



Registry number: DEENK/189/2022.PL
Subject: PhD Publication List

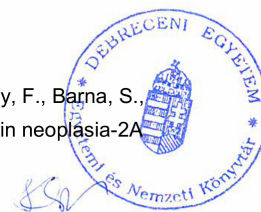
Candidate: Zsolt Kanyári
Doctoral School: Doctoral School of Neurosciences

List of publications related to the dissertation

1. **Kanyári, Z.**, Cservényák, D., Tankó, B., Nemes, B. Á., Fülesdi, B., Molnár, C.: Knowledge and Attitudes of Health Care Professionals and Laypeople in Relation to Brain Death Diagnosis and Organ Donation in Hungary: a Questionnaire Study.
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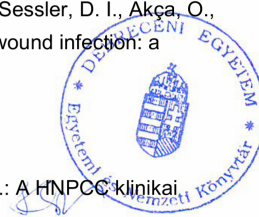


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Total IF of journals (all publications): 12,952

Total IF of journals (publications related to the dissertation): 1,933

The Candidate's publication data submitted to the iDEa Tudóstér have been validated by DEENK on the basis of the Journal Citation Report (Impact Factor) database.

13 April, 2022

