
Introduction

EULOD: Living Organ Donation in Europe

Living organ donation is increasingly introduced by transplant centres as a valuable alternative to bridge the gap between demand and supply of organs. Living organ donation poses opportunities, but also involves ethical, legal and psychosocial implications. Moreover, there is large heterogeneity among European countries in terms of living donation rates, ethical concerns, legislation and protection systems for living organ donors.

The project on Living Organ Donation in Europe (EULOD), a Coordination Action funded by the Seventh Framework Programme of the European Commission, was a response to this European heterogeneity and to the urgent policy needs expressed by various EU institutions.

The project started in March 2010 and ended in September 2012. It aimed to establish an inventory of living donation practices in Europe, explore and promote living donation as a way to increase organ availability, and to present recommendations to improve the quality and safety of living organ donations in Europe. Eleven institutions from ten different European countries were involved. The partners collaborated closely with the European platform on Ethical, Legal and Psychosocial Aspects of Organ Transplantation (ELPAT) and the European Society for Organ Transplantation (ESOT).

This book presents the study results of this project. The results range from describing living organ donation practices across European countries, highlighting opinions and conceptions of individuals towards living donation, exploring ethical arguments for and against living donation, analyzing European transplant laws regarding living organ donation, to scrutinizing the current prohibition of organ trafficking and transplant commercialism in national and international law.

Discussions about expanding living organ donation in Europe do not occur without debate. The aim of this project hence was not to achieve consensus on ethical principles that accompany the expansion of live donation. The arguments presented in the six papers express the individual opinions of the authors and not of that of the consortium.

We are grateful for the commitment of all partners in this project, and would like to thank each of them for generating an output that is unique to this field of transplant medicine.

We trust that you will read our work with great interest. It is our hope that our results and recommendations will contribute to your every day practice, and that they will help you to consider ways in which living organ donation can be expanded safely and ethically in countries worldwide.

Rotterdam, February 2013

Frederike Ambagtsheer and Willem Weimar
Erasmus MC University Medical Center Rotterdam
Coordinators of the EULOD project

Living Organ Donation in Europe – Clinical Praxis*

Annette Lennerling¹, Charlotte Lovén¹, Frank JMF Dor²,
Frederike Ambagtsheer³, Nathalie Duerinckx⁴, Mihaela Frunza⁵,
Assya Pascalev⁶, Natalia Codreanu⁷, Willij Zuidema³, Willem Weimar³
and Fabienne Dobbels⁴

¹ Institute of Health and Care Sciences, University of Gothenburg, Gothenburg, Sweden (UGOT)

² Department of Surgery, Division of Transplant Surgery, Erasmus MC, University Medical Center, Rotterdam, The Netherlands (EMC) · ³ Department of Internal Medicine, Erasmus MC, University Medical Center, Rotterdam, The Netherlands (EMC) · ⁴ Centre for Health Services and Nursing Research; KU Leuven, Leuven, Belgium (KU) · ⁵ Babes-Bolyai University, Department of Philosophy, Cluj, Romania (SACRI) · ⁶ Bulgarian Center for Bioethics, Sofia, Bulgaria (BCB)

⁷ Renal Foundation, Chisinau, Moldova (FR)

Contents

Page

Introduction	10
Methods	11
Design and sample	11
Development of the survey	11
Procedure	11
Results	12
Living kidney donation	12
Living liver donation	12
Barriers to living kidney and liver donation programmes	15
Discussion	15
Donor selection and safety	15
Reimbursement	16
Follow-up	16
Barriers to living donation	17
Methodological limitations	17
Recommendations	18
Acknowledgement	18
Bibliography	19
Table 1	21
Table 2	22
Table 3	23
Table 4 a.	24
Table 4 b.	25
Figure 1, Figure 2	26

* This book chapter has been revised from its original published form, *Living Organ Donation Practices in Europe – results from an Online Survey* by Lennerling A, Lovén C, Dor FJ, Ambagtsheer F, Duerinckx N, Frunza M, Pascalev A, Zuidema W, Weimar W and Dobbels F, in *Transplant International* 2013; 26 (2): 145-53. doi: 10.1111/tri.12012. Epub 2012 Dec 1. Permission has been given by Verity Butler, Permissions Co-ordinator at Wiley.

Introduction

Since the early fifties, organ transplantation has been one of the most rapidly evolving areas in medical science, resulting in excellent survival and quality of life. This success is mainly due to the development of immunosuppressive drugs, better medical treatment including prevention of infections and rejection, improved organ preservation and surgical techniques. Transplantation, however, became the victim of its own success, resulting in far more patients being admitted to the transplant waiting lists than can be transplanted annually.

The organ shortage presents one of the major challenges in the field of organ transplantation today. In 2011, 49,477 persons were on waiting lists for kidney transplantation and 6,808 for liver transplantation in the 27 European Union (EU) countries (502 million inhabitants), while during the same year 18,712 kidney transplantations and 7,006 liver transplantations were performed [1]. The lack of organs for transplantation results in long waiting times for the patients in need and a high risk of dying before a suitable organ becomes available [2, 3]. Depending on blood type and other medical aspects, the average waiting time for a deceased donor kidney in Europe today is 3–5 years. Mortality rates among those waiting range from 15–30 % depending on organ, and approximately ten people die every day in the EU waiting for an organ transplant [4]. Despite strategies to enlarge the donor organ pool, such as adopting presumed consent systems and widening deceased donor criteria, the worldwide organ shortage persists.

Given the failure to meet the growing need for organs obtained from deceased donors, the use of living donors has increased, a fact also recognized by the European Commission in 2007 in its Communication on organ donation and transplantation [4]. In that paper, major policy challenges were identified, including organ availability. In 2008, the European Commission consequently adopted a proposal for a directive that defines quality and safety requirements for human organs intended for transplantation. This proposal was subsequently adopted by the European Parliament and on July 7, 2010 by the Council [5]. Paragraph 23 of this directive states that ‘living donations need to be performed in a manner that minimises the physical, psychological and social risk to the individual donor and the recipient’. It further mentions that ‘The potential living donor has to be able to take an independent decision on the basis of all the relevant information and should be informed in advance as to the purpose and nature of the donation, the consequences and risks. In this context, [...] the highest possible protection of living donors should be ensured’ [5, p 17]. In the light of recent cases of organ trafficking, the directive also stipulates that such unacceptable practices constitute serious violations of fundamental rights and, in particular, of human dignity and physical integrity.

Living organ donation (LOD) has long been an established practice in many European countries, and recent advances have been made regarding surgical methods, screening and selection of donors [6–11]. In 2011, 20.6 % (0–61 %) of all kidney transplants and 3.5 % (0–50 %) of all liver transplants performed in the European Union were using a live donor [1]. However, large differences across European countries in the rates of living donation can be observed (Figure 1). The Netherlands, Norway and Sweden are among countries with high rates of living kidney donations (LKD), whereas Poland, Finland and Belgium have low rates [1] and a few countries lack a LKD programme (e.g. Luxembourg & Montenegro). The barriers and incentives to conduct living donor, kidney or liver transplantations are not well understood. Differences between countries also exist regarding relations between donor and recipient that are acceptable, screening for potential donors and donor follow-up. Hence, it is currently unclear how European countries put the EU directive into practice to guarantee donor safety.

The aims of this study were to:

1. Survey the various practices of LOD in Europe
2. Identify possible legal, ethical and financial considerations that act as barriers towards LOD
3. Achieve full European geographical coverage

Methods

Design and sample

This is an exploratory survey and a descriptive cross-sectional design was used. Transplant professionals from kidney and liver transplant centres in all EU member states were invited to complete an online survey. Transplant units in non-EU member states were also invited when contact information was available. Only liver and kidney transplant centres were considered, as lung-, bowel- and pancreas transplantations from living donors are mainly in an experimental phase and are rarely being performed. To guarantee maximal response from as many transplant centres as possible no other specific inclusion or exclusion criteria were stated. Ethical approval to conduct the survey study was obtained from the ethical review board of the KU Leuven in Belgium February 24, 2011.

Development of the survey

Two separate, but similar questionnaires were constructed for living liver donation (LLD) and for LKD. A copy of both surveys is published on the EULOD website [12].

With permission of the authors, we used a survey on the selection of LKD in the US as the basis for our questionnaires [13]. The content was revised after extensive literature search, by iterative rounds of review and through pilot testing of the surveys by two transplant professionals. The questions focused on the prevalence and types of living donation performed, possible barriers towards living donation, the medical and psychosocial screening of donor candidates and follow-up.

In the literature, varying terminology for living organ donation can be found. In the survey various types of donor and recipient relations were listed, in all 17 alternatives (table 4 a), e.g. sibling, friend and stranger. However, we saw a need for a new classification to avoid confusion. Therefore we first assessed the existing terminology in the light of current living organ donation practices and thereafter suggested a more straightforward classification [14]. This was done in close collaboration with the Working Group on Living Organ Donation in the association *Ethical Legal and Psychosocial Aspects in organ Transplantation* (ELPAT a section of European Society on Organ Transplantation). We proposed to concentrate on the degree of specificity with which donors identify intended recipients and to subsequently verify whether the donation to these recipients occurs directly or indirectly. According to this approach, one could distinguish between “specified” and “unspecified” donation and within specified donation, a distinction can be made between “direct” and “indirect” donation (Table 1). This classification was used in the analysis.

The surveys were built in the online data collection software programme, called *examinare*® (www.examinare.com). The forms that *examinare*® creates are protected by Secure Socket Layer (SSL) and the information between server and browser is encrypted. The surveys were only created in the English language. This was decided for two main reasons: 1) the costs for producing surveys in several languages were not in the budget and 2) the international scientific language is English.

Procedure

The networks of the EULOD consortium, ELPAT, *European Society of Organ Transplantation* (ESOT) and some informal transplant networks were used to create a list with names and e-mail addresses of transplant professionals in liver and kidney transplant centres within Europe. This was done in order to get access to at least one centre within each EU member state, although maximal coverage was aimed for i.e. one reply from each existing transplant centre in each country. The same networks were used to reach out to non-member states in which transplant activities take place. From

March 2011 to December 2011, in total 331 letters of invitation to participate in the study were sent to kidney transplant professionals and liver transplant professionals in 45 countries. The letters included information on confidentiality and were sent together with a link to the online survey. A minimum of three reminders were sent to those who did not respond.

Nominal and ordinal results are presented as percentages. All responding centres were grouped into three geographical regions: North-Western, Mediterranean and Eastern. Responses between regions were compared (statistical analysis Chi-Square for nominal and Kruskal-Wallis testing for ordinal variables were used, statistical software SPSS version 19.0, statistical significance was set at $p < 0.05$).

Results

By January 2012, 113 kidney transplant centres from 40 countries and 39 liver transplant centres from 24 countries had completed the survey. In total, 25 out of the 27 EU-member countries were represented by kidney transplant centres and 18 by liver transplant centres. Out of the 18 non-member states contacted, we received replies from 15 countries regarding the kidney donation survey, and from six for the liver donation survey. The majority of the responders were transplant surgeons, nephrologists and transplant coordinators. Four of the replying centres did not have a living kidney donor programme and eleven did not have a living liver donor programme. Table 2 shows the numbers of responding centres from each country that were approached.

Living kidney donation

Living donor programmes for kidneys were practiced in all responding EU member states, and all but two responding non-member states. The majority of kidney centres (60 %) performed less than 25 LKD transplantations a year, 28 % between 26 and 50 while 12 % did more than 50 and of those, two centres did more than a hundred (The Netherlands and Turkey). When dividing Europe into three geographical regions, living kidney donation was performed in all responding centres in the North-West and in the Mediterranean region but not in all centres in the Eastern region (Table 2). Less than 25 LKD transplants per year were performed in 81 % of centres in the Eastern region, 73 % of Mediterranean centres as compared with 45 % in the North-Western region, while the volume of transplantations from deceased donors were about the same in all three regions.

Most centres applied a donor age of 18 years as a minimum, but eight centres (7 %) also accepted minors as donors. An upper age limit was defined in half of the centres and then most often set at 70 or 80 years. A specific question about women in childbearing age as donors was asked. In 21 % of the centres they were excluded as donors and 3 % excluded women with young children.

Defined limitations for medical conditions precluding donation, e.g. body mass index (BMI), hypertension, diabetes or proteinuria, are shown in Table 3 (divided in the three European regions). The Eastern centres used less strict medical criteria for donors compared to the Mediterranean and North-Western regions. Diabetes type 1 was considered an absolute contraindication in 75 % of the centres in the Eastern region versus 97 % in North-Western. For diabetes type 2 the figures were 59 % for Eastern versus 77 % for the North-Western. A potential donor with a BMI over 40 was an absolute contraindication in 87 % of centres in the Mediterranean and 89 % in the North-Western regions compared to 75 % in the Eastern centres. For the 24 h urine protein of > 300 mg the greatest discrepancy was between the Eastern centres and the Mediterranean. This was an absolute contraindication for donation in 56 % of the centres in the Eastern region versus in 73 % of the centres the Mediterranean. Potential donors with well controlled treated hypertension were to a higher grade accepted in the North-Western centres, in 63 % of the centres versus 50 % in the Eastern.

A general method to evaluate kidney function is to measure the glomerular filtration rate (GFR). Normal results range from 90–120 mL/min/1.73 m², but GFR decreases with increasing age and therefore older people will have lower GFR levels. GFR was measured in the screening process of potential donors in all but four centres. A cut off limit was set at 80 mL/min per 1.73 m² body surface area in 42 % of the centres, at 75 mL/min in 18 %, at 70 mL/min in another 18 % and at 65 mL/min in 21 % of the centres.

Regarding specified direct donation (Table 1), i.e. donation from a person directly to an intended recipient, psychological screening performed by psychiatrists or psychologists, was included as a routine in the pre-donation evaluation in two thirds of the centres. In most other centres it was completed when problems were identified or suspected. Psychiatric disease or personality abnormalities were taken seriously and constituted absolute contraindications in the vast majority of centres. The results from the questions in this survey on psychosocial screening will be described and discussed in depth and submitted to a scientific journal for publication.

Specified direct donation was the predominant relation between donor and recipient in all centres. The vast majority of centres accepted parents, siblings, adult children, grandparents, other genetically related family, spouses and partners. Most centres also accepted in-laws and close friends (68 % and 69 % respectively). Specified indirect donation – i.e. when the donated kidney was used in an exchange programme, where the intended recipient received a kidney from another donor – was practised by almost half of the centres (43 %), (Table 4 a).

The type of specified LKD donations accepted varied in different parts of Europe: many Eastern countries did not accept donation to a genetically unrelated but emotionally related recipient other than spouses, while in the North-West friends and acquaintances were often accepted. Furthermore, centres in Mediterranean and Eastern countries less often accepted grown up children as donors than North-Western countries (Table 4 b).

During the last decade unspecified (anonymous) donation has become accepted in some European countries. Unspecified kidney donation was performed in one third (32 %) of the transplant centres responding (Table 4 a). In four centres, the anonymous donor was also allowed to define certain recipient characteristics, e.g. children (i.e. The Netherlands, Denmark and Sweden). Select a certain recipient was allowed only in one responding centre (The Netherlands).

Specified indirect LKD programmes (paired exchange programmes) and unspecified (“anonymous”) programmes had started during the last decade in 41 centres (36 %) in 13 countries (10 EU-member states, 3 non-members). In most centres, ten or less such donations had been performed since the start, but two centres – one in the Netherlands and one in Turkey – reported to have performed more than 50 cases each. The medical screening was the same as for specified direct donors in 18 of the 41 centres. Additional screening for the unspecified (“anonymous”) or specified indirect LKD (paired exchange programmes) was included in more than half of the centres and generally consisted of more extensive psychiatric or psychosocial evaluation.

While preparing the donor, information about the LKD was generally given both verbally and in writing. Audio-visual information techniques, such as DVD's or web sites, were used in 39 % of the centres. In most centres the information included legal conditions, the evaluation process, the surgical procedure, expected recovery period, possible short and long-term donor complications as well as risks involved for the recipient. Regulations on reimbursement for e.g. income loss were comprised in the information given in 65 % of the centres. Informed consent prior to donor nephrectomy was required in all transplant centres.

Several surgical techniques are used for the living donor nephrectomy. In this survey we defined four groups; 1) open surgery with flank incision and rib resection, 2) open surgery with an anterior approach, 3) laparoscopic technique and 4) robotic technique. More than one surgical technique was used in a number of centres. The laparoscopic technique was used in 66 % and the open flank incision with rib resection was in use in 29 %, (Figure 2). In respect to the different European regions the open flank incision with rib resection was more commonly used in the Eastern centres

than in the North-Western and Mediterranean centres, 57 % versus 12.5 % and 14.5 %. In contrast, laparoscopic techniques were used in 81 % of the North-Western and 50 % Mediterranean centres versus 37 % in the East (Table 3 and Figure 2).

Reimbursement for income loss during hospital stay and sick-leave period to kidney donors was not given at all in 54 % of the centres. Reimbursement to donors was clearly less given in the Eastern and Mediterranean regions (Table 3).

All but three centres (Croatia, Lithuania and the Russian Federation) offered postoperative follow-up and in 67 % it was reported to be life-long. The check-up included medical tests in all centres and psychosocial evaluation in 17 %. Follow-up was incomplete in 84 % of the Eastern centres, but was performed in all North-Western and Mediterranean centres. Donor data registers were kept by 92 % of kidney centres. Only 20.5 % also reported to European registries. The Eastern centres (81 %) tended to keep registers less often than the North-Western (97 %) and Mediterranean centres (93 %). The items most frequently reported in the registers, apart from identity and relation to the recipient, were pre-operative medical information and post-operative complications.

Living liver donation

We received in total 28 responses from living liver donor programmes in 18 member states and in five non-members states (Table 2). Living liver donations were more frequent in the North-Western region than in the Eastern and Mediterranean.

Two-thirds of the 28 reporting liver centres performed five or less living liver transplantations a year and the remaining centres never performed more than 25.

Specified direct donation was predominant in all centres, the vast majority accepting parents, siblings, adult children, grandparents, other genetically related family, spouses and partners. Most centres also accepted in-laws and close friends as liver donors, 50 % and 61 % respectively. Specified indirect donation – in an exchange programme – was an accepted practice in six of the 28 centres and unspecified (anonymous) donation in seven. However, only eight such donations had actually been performed, in seven centres representing four countries. Any anonymous donor was permitted to define certain recipient characteristics in four centres and to select a certain recipient in three centres (Table 4 a).

All centres had a lower donor acceptance age of 18 years, while an upper age limit was set in 57 % of the centres, most often at 60 years. Women in childbearing age were accepted as LLD in 83 % of the centres, while 17 % excluded them. Few medical conditions would preclude LLD and most often they were considered to be only relative contraindications. Liver steatosis in the donor was accepted in a range varying from none in three centres to more than 10 % in seven centres.

Psychological screening, performed by a psychiatrist or psychologist, was included as a routine in the pre-donation evaluation in 82 % of the centres and otherwise when problems were identified. In analogy with kidney donation, psychiatric disease or personality abnormalities were taken seriously and seen as absolute contraindications in almost all centres.

As for the kidney donors, information on the LLD was given both verbally and in writing, and the contents were similar. Regulations about reimbursement for e.g. income loss were included in 70 %. The majority of the liver donors, 68 %, did not get any reimbursement for income loss and other expenses.

Informed consent was obtained prior to surgery in all centres. All but one centre had a medical follow up for the liver donors postoperatively. In nine centres this was intended to be life-long. LLD registers were kept by all 28 centres, but only five of them reported to European registries.

Barriers to living donation programmes

Four (3.5 %) of the responding 113 kidney transplant units and eleven (28 %) of 39 liver transplant units lacked a living donor programme. Thus, the number of replies to the question about possible barriers to living donation was small. The four centres which did not have a LKD programme were all about to start programmes and no barriers were identified. Regarding the eleven transplant centres lacking LLD programme the reasons mentioned were:

- a) financial barriers
- b) no need due to sufficient supply of livers from deceased donors
- c) it had never been discussed in the transplant centre
- d) a negative attitude among health care professionals to such programme
- e) a lack of surgical expertise

For specified indirect donation – in an exchange programme – and unspecified (anonymous) donation for both kidney and liver donation the barriers stated from the few responses were:

- a) these donations are illegal in the country
- b) these donations were thought to be unethical and could not be justified
- c) a negative attitude among transplant professionals, other health care professionals and within the society
- d) financial reasons and lack of resources

Discussion

As far as we know, practices in living organ donation in European countries have not been studied previously making this an unique study. In total, responses were obtained from 40 European countries (89 %) out of the 45 countries contacted with kidney transplant programmes and from 25 countries with liver transplant programmes. Responding transplant professionals represent centres from both from EU member states and non EU members. For the EU member states close to full coverage was achieved with responses from 25 out of 27 countries. Although most EU member countries are performing LKD, the rate per million people (pmp) shows a great discrepancy (Figure 1). For instance in 2011 Finland had 2.4 LKD transplants pmp and Italy had 3.5 LKD pmp respectively, The Netherlands had 26.3 LKD pmp and Sweden had 19.6 LKD transplants pmp [1]. This shows that there is a large potential for increasing the number of LKD in many EU countries.

Donor selection and safety

The study showed that some aspects related to donor selection and safety, were not always guaranteed. Selection criteria are not uniform and sometimes not sufficiently restricted. The World Health Organisation states in their guiding principles on Human cell, tissue and organ transplantation from 2010 that, “Live donations are acceptable when the donor’s informed and voluntary consent is obtained, when professional care of donors is ensured and follow-up is well organized, and when selection criteria for donors are scrupulously applied and monitored. Live donors should be informed of the probable risks, benefits and consequences of donation in a complete and understandable fashion; they should be legally competent and capable of weighing the information; and they should be acting willingly, free of any undue influence or coercion” [15, p. 3]. Further, in the EU directive for quality and safety for human organs intended for transplantation requirements are stated to ensure protection of the live donor [5].

Our results showed that one fourth of the centres in the Eastern European region did not consider diabetes type 1 as an absolute contraindication for kidney donation (Table 3). This is clearly not

in accordance with the above mentioned directives on safety and quality since diabetes mellitus is a common diagnosis leading to end stage renal failure. Another risk factor for the donor is obesity. Potential donors with a BMI above 40 were accepted in 25 % of the kidney transplant centres in the Eastern region. Due to most international guidelines this is considered to be a contraindication for kidney donation. Additionally GFR at 65 ml/min was an accepted level for LKD in as many as 21 % of all responding centres. It has been recommended for a potential donor to have a GFR of 80 ml/min as the lowest level, though the potential donor's age has to be taken into consideration as well [16].

Several randomized studies have demonstrated that laparoscopic techniques are safe for live donor nephrectomy and are to be preferred over the open approaches [17-19]. Laparoscopic techniques have several advantages for the donor; less pain, shorter hospital stay and a shorter recuperation time [20]. The results of this survey clearly demonstrate that in many centres especially in the Eastern countries, the laparoscopic donor nephrectomy still needs to be implemented (Figure 2). Training programmes for laparoscopic donor nephrectomy have been developed for this purpose.

Many European centres perform few live organ donations annually. For LLD our results show that 63 % of all centres performed five or less donor hepatic lobectomies per year. This activity requires high level of surgical skills and great understanding of the vascular and biliary anatomy of the liver [21].

We also found large disparities regarding LKD between European regions, with a low volume of LKD transplantations in most Eastern and Mediterranean centres. It appears to be a highly prestigious activity in many ways for hospitals to have a transplant programme. To ensure a high enough surgical volume a centralisation of programmes using living organ donors for transplantation could be beneficial. This would also enable the transplant team to develop the highest level of skills in all phases of the donation process and most probably improve donor safety.

Reimbursement

A remarkably high number of the responding centres did not offer the donors reimbursement for income loss or other costs. Kidney donors were not reimbursed in 54 % of the centres and the liver donors not in 68 %. This finding reflects the reluctance of governments in Europe to implement compensation and reimbursement policies for the living donors. The World Health Organization guiding principles permits reimbursement for "reasonable and verifiable expenses incurred by the donor, including loss of income" [15, p. 5]. The European Convention on Human Rights and Biomedicine also states that the prohibition of financial gain "shall not prevent payments which do not constitute a financial gain or a comparable advantage" [22]. We believe that many countries may not be aware that offering compensation and reimbursement of costs is legally acceptable. The lack of reimbursement and compensation should not be a reason to discourage persons to become live organ donors. All donors should be offered the possibility of compensation and reimbursement of costs made that were a (direct or indirect) consequence of their donation. The Competent Authorities in EU Member States and other European countries should be made aware that the above mentioned compensations are legitimate and in line with international rules and guidelines. Furthermore, they should be encouraged to put in place appropriate reimbursements for living donors.

Follow-up

Most centres in this study indicated that they had follow-up programmes and generally registers on living donor follow-up were kept, though one third of the kidney transplant centres did only keep the register in the centre and did not report on a national level. As for any surgical procedure living

organ donation involves risk for morbidity and mortality [21, 23–25]. We argue that medical and psychosocial follow-up programmes and registers of living organ donors should be mandatory. This is also fortified by the WHO Guiding Principles, the Declaration of Istanbul and the EU Directive on standards of quality and safety of human organs [5, 15, 26]. To increase the knowledge about the long term consequences of living organ donation and to guarantee safety for future donors, lifelong follow up is required. Registries on living organ donors should be implemented and regularly monitored on a national level. These registries should, at a minimum, include information concerning serious adverse events and reactions after donation [5].

Barriers to living donation

The few responses given in this study regarding possible barriers for increasing living donation were e.g. financial barriers, a negative attitude among health care professionals towards such programmes and lack of surgical expertise. Today the financial barrier seems challenging to overcome due to the economic crisis in many European countries. However, living kidney transplantation is by far more cost-effective than dialysis treatment [27]. It has been shown that kidney transplantation leads to a cost benefit in the second and subsequent years [28]. Although renal transplantation is not the main treatment for end stage renal failure, it is the treatment of choice, with lower costs and better outcomes [29]. Liver transplantation is a life-saving therapy, since there is no medical procedure designed to prolong or substitute the liver function, comparable with dialysis for end stage renal failure. The benefits for the liver recipient with transplantation cannot be disregarded.

According to the sixty-third World Health Assembly 2010, “donation from deceased persons should be developed to its maximum therapeutic potential, but adult living persons may donate organs as permitted by domestic regulations” [15, p. 3]. We argue that it is necessary that nephrologists and hepatologists develop a positive attitude towards living organ donation, as they play a crucial role for transplantation to become reality for even more patients in need of a new organ. To use live organ donors for transplantation is a prerequisite in addition to deceased donation to overcome the organ shortage.

In this study, acceptance of relation between donor and recipient throughout Europe has been explored for the first time. The most common relations accepted were parents, siblings, other genetically related and spouses. Although not shown in our results as barriers, various legal and societal hurdles towards several types of donation, for instance, unspecified donation or specified direct donation to a stranger, exist in many countries. There are opinions recommending the removal of these barriers and focus on “safety by procedures” [30]. This process depends to a great extent by the willingness to modify restrictions within every country. To partake in cooperative activities such as the EULOD project, may possibly open the discussions in these states and encourage them to give up these restrictions. This might result in a change of attitudes.

Methodological limitations

We attempted to reach a complete coverage of the EU member states. Of the 27 member states 25 responded to the LKD survey, but the responses were not equally distributed over the area. Quantitative analyses comparing conditions in different states could therefore not be made.

Another limitation might have been that centres without a living donor programme were less likely to reply. Furthermore, the fact that the survey language was English seems to have been an obstacle in parts of Europe. Despite our efforts in contacting numerous transplant centres ($n = 331$), there were few responses especially from the Mediterranean region and also from some states in Eastern region.

Recommendations

The European Commission puts organ donation and transplantation high on their policy agenda and strongly supports the use of living donors to increase the organ availability for transplantation. A prerequisite is that a legal framework is in place and that safety can be guaranteed for both the donor and recipient [5].

In line with the EU directives [5] and as a result of this study the following is suggested to improve the quality and safety of living organ donation as well as an increase in the general organ supply in Europe:

- There is a need to **utilise the existing potential** of living organ donation as one resource to decrease the imbalance between the demand and the supply of available organs for transplantation.
- A **harmonisation of practices** in Europe built on scientific research and evidence based guidelines is necessary. Medical contraindications to donation should be agreed on, e.g. diabetes type 1 should disqualify for living donation.
- Living donor programmes should be focused to lesser number of units in each country to enable sufficient volumes. This enables a **high level of surgical skills** as well as development of expertise in all phases of the donation process. Surgeons performing live donor nephrectomies should be adequately trained in laparoscopic techniques, through hands-on courses or fellowships/proctorships, to be able to deliver **state-of-the-art care** for the live kidney donors. Obviously, surgical training should be obtained to permit live donor liver transplantation at all.
- **Reimbursement** should be offered to all living organ donors for loss of income during hospital stay and sick leave, preferably also for expenses during work-up and recovery. Non-reimbursement may form a major obstacle to many potential donors. Governments should be made aware of what is legally acceptable and they should be encouraged by the EU to implement these policies.
- **Follow-up** of living organ donor morbidity (and mortality) should be mandatory. The follow-up results should be documented in National and/or European registries. These registries should publish the results on a regular basis e.g. every other year. The minimum threshold should be the reporting of serious events.

Acknowledgements

We would like to wholeheartedly thank the following persons:

All transplant professionals in Europe taking part in this study,
James Rodrigues, for letting us use the survey performed in the US on medical screening of living kidney donors as an inspiration when constructing our survey,
The ELPAT working group on Living Organ Donation, for identifying the living organ donation classification and helpful comments when constructing the surveys,
All ELPAT members, for assisting in finding key transplant professionals within Europe,
A special thanks to Consultant Nurse Lisa Burnapp in London UK, for assisting in sending surveys in the UK,
Dr Leonie Lopp (EULOD Work Package 3 part 1), for helpful comments and suggestions on the manuscript drafts,
Mrs Marian van Noord, secretary of ELPAT, for support and for assisting in finding key transplant professionals within Europe,

Bibliography

- [1] Council of Europe Newsletter Transplant. *International figures on donation and transplantation 2011*. Rafael Matesanz (Ed), vol 17, No 1, September; 2012.
- [2] Wolfe RA, Ashby VB, Milford EL, Ojo AO, Ettenger RE, Agodoa LYC, Held PJ, Port FK. Comparison of Mortality in All Patients on Dialysis, Patients on Dialysis Awaiting Transplantation, and Recipients of a First Cadaveric Transplant. *New England Journal of Medicine* 1999; 341 (23): 1725-1730.
- [3] Kim RW, Biggins SW, Kremers WK, Wiesner RH, Kamath PS, Benson JT, Edwards E, Therneau TM. Hyponatremia and Mortality among Patients on the Liver-Transplant Waiting List, *New England Journal of Medicine* 2008; 359 (10): 1018-1026.
- [4] Commission of the European Communities. *Communication from the Commission to the European Parliament and the Council Organ Transplantation: Policy Action at EU level*; COM(2007) 275 final, Brussels: Commission of the European Communities; 2007. http://ec.europa.eu/health/ph_threats/human_substance/documents/organs_com_en.pdf
- [5] Directive 2010/45/EU of the European Parliament and of the council of 7 July 2010 on standards of quality and safety of human organs intended for transplantation. EURLEX 32010L0045(01).Official Journal L 207 , 06/08/2010 P. 0014 – 0029; 2010
- [6] Agishi T, Takahashi K, Yagisawa T, Ota K. Immunoabsorption of anti-A or anti-B antibody for successful kidney transplantation between ABO incompatible pairs and its limitation. Japanese Biosyn-sorb Research Group. *ASAI/O transactions/American Society for Artificial Internal Organs* 1991; 37: 3: M496-498.
- [7] Ross LF, Woodle ES. Ethical Issues in Increasing Living Kidney Donations by Expanding Kidney Paired Exchange Programs, *Transplantation* 2000; 69 (8): 1539-1543.
- [8] Matas AJ, Garvey CA, Jacobs CL, Kahn JP. Nondirected donation of kidneys from living donors. *New England Journal of Medicine* 2000; 343 (6): 433-436.
- [9] Adams PL, Cohen DJ, Danovitch GM, Edington RM, Gaston RS, Jacobs CL, Luskin RS, Metzger RA, Peters TG, Siminoff LA, Veatch RM, Rothberg-Wegman L, Bartlett ST, Brigham L, Burdick J, Gunderson S, Harmon W, Matas AJ, Thistlethwaite JR, Delmonico FL. The nondirected live-kidney donor: ethical considerations and practice guidelines: A National Conference Report. *Transplantation* 2002; 74 (4): 582-589.
- [10] Trotter JF, Wachs M, Everson GT, Kam I. Adult-to-Adult Transplantation of the Right Hepatic Lobe from a Living Donor. *New England Journal of Medicine* 2002; 346 (14): 1074-1082.
- [11] Tydén G, Kumlien G, Fehrman I. Successful ABO-incompatible kidney transplantations without splenectomy using antigen-specific immunoabsorption and rituximab. *Transplantation* 2003; 76 (4): 730-731.
- [12] Living organ donation in Europe. The EULOD project. *Results work package 2. Living Unrelated Organ Donation Practices in Europe, Work Package 2 descriptive part*. <http://www.eulod.org/?section=ExpectedResults&item=32> (accessed August 2012)
- [13] Mandelbrot DA, Paklavis M, Danovitch GM, Johnson SR, Karp SJ, Khwaja K, Hanto DW, Rodrigue JR. The medical evaluation of living kidney donors: a survey of US transplant centers. *American Journal of Transplantation* 2007; 7 (10): 2333-2343.
- [14] Dor FJ, Massey EK, Frunza M, Johnson R, Lennerling A, Lovén C, Mamode N, Pascalev A, Sterckx S, Van Assche K, Zuidema WC, Weimar W. New classification of ELPAT for living organ donation. *Transplantation* 2011; 91 (9): 935-938.
- [15] World Health Organisation (WHO). GUIDING PRINCIPLES ON HUMAN CELL, TISSUE AND ORGAN TRANSPLANTATION <http://www.who.int/transplantation/publications/en/index.html> (accessed March 2012) WHO Guiding Principles on Human Cell, Tissue and Organ Transplantation 1. *Transplantation* 2010; 90 (3): 229-233. doi: 10.1097/TP.0b013e3181ec29f0

- [16] Delmonico F. Council of the Transplantation Society. A Report of the Amsterdam Forum On the Care of the Live Kidney Donor: Data and Medical Guidelines. *Transplantation* 2005; 79 (6 Suppl): S53-S66.
- [17] Kok NF, Lind MY, Hansson BM, Pilzecker D, Mertens zur Borg IR, Knipscheer BC, Hazebroek EJ, Dooper IM, Weimar W, Hop WC, Adang EM, van der Wilt GJ, Bonjer HJ, van der Vliet JA, IJzermans JN. Comparison of laparoscopic and mini incision open donor nephrectomy: single blind, randomised controlled clinical trial. *British Medical Journal* 2006; 333 (7561): 221.
- [18] Nicholson ML, Kaushik M, Lewis GR, Brook NR, Bagul A, Kay MD, Harper SJ, Elwell R, Veitch PS. Randomized clinical trial of laparoscopic versus open donor nephrectomy. *British Journal of Surgery* 2010; 97 (1): 21-28.
- [19] Øyen O, Andersen M, Mathisen L, Kvarstein G, Edwin B, Line PD, Scholz T, Pfeffer PF. Laparoscopic versus open living-donor nephrectomy: experiences from a prospective, randomized, single-center study focusing on donor safety. *Transplantation* 2005; 79 (9): 1236-1240.
- [20] Wilson CH, Sanni A, Rix DA, Soomro NA. Laparoscopic versus open nephrectomy for live kidney donors. *Cochrane Database of Systematic Reviews* 2011; 11: CD006124.
- [21] Russo M W, Brown Jr R S. Adult Living Donor Liver Transplantation. *American Journal of Transplantation* 2004; (4) 4: 458-465
- [22] Council of Europe. *Additional Protocol to the Convention on Human Rights and Biomedicine concerning Transplantation of Organs and Tissues of Human Origin*. <http://conventions.coe.int/Treaty/en/Treaties/Html/186.htm> Strasbourg, 24.1.2002; 2009 (Accessed March 2012)
- [23] Muzaale AD, Dagher NN, Montgomery RA, Taranto SE, McBride MA, Segev DL. Estimates of Early Death, Acute Liver Failure, and Long-term Mortality Among Live Liver Donors. *Gastroenterology* 2012; 142 (2): 273-280.
- [24] Ibrahim HN, Foley R, Tan L, Rogers T, Bailey RF, Guo H, Gross CR, Matas AJ. Long-term consequences of kidney donation. *New England Journal of Medicine* 2009; 360 (5): 459-469.
- [25] Mjøen G, Øyen O, Holdaas H, Midtvedt K, Line PD. Morbidity and mortality in 1022 consecutive living donor nephrectomies: benefits of a living donor registry. *Transplantation* 2009; 88 (11): 1273-1279.
- [26] The Declaration of Istanbul on Organ Trafficking and Transplant Tourism. International Summit on Transplant Tourism and Organ Trafficking. *Clinical Journal of American Society of Nephrology* 2008; 3 (5): 1227-1231.
- [27] De Charro F, Oppe M, Bos MA, Busschbach J, Weimar W. A Regulated Organ Market? In: Weimar W, Bos MA, Busschbach J (Eds). *Organ Transplantation: Ethical, Legal and Psychosocial Aspects Towards a Common European Policy*. Lengerich: Pabst; 2008. pp. 43-48.
- [28] National Health Services (NHS), *Blood and Transplant, Organ Donation Newsroom, Cost effectiveness of transplantation*. http://www.organdonation.nhs.uk/ukt/newsroom/fact_sheets/cost_effectiveness_of_transplantation.asp (accessed March 2012)
- [29] Garcia GG, Harden P, Chapman J. The Global Role of Kidney Transplantation. *Transplantation* 2012; 93 (4): 337-341.
- [30] Land W and Gutmann T. Breaking Barriers in Living Donor Organ Transplantation: A European Perspective. *Transplantation Proceedings* 2003; 35 (3): 926-929.

Table 1. Classification for living organ donation defined by the working group Living Organ Donation in the association Ethical Legal and Psychosocial Aspects in Organ Transplantation [14].

Specified donation:
<i>Direct donation:</i> when a person donates directly to his or her intended recipient. - donation to a genetically and emotionally related recipient (e.g. mother to child) - donation to a genetically unrelated but emotionally related recipient (e.g. spouse) - donation to a genetically related but emotionally unrelated recipient (e.g. estranged father) - donation to a genetically and emotionally unrelated recipient, but the recipient (or the group to which he/she should belong) is specified (e.g. a child) <i>Indirect donation:</i> when a person donates indirectly to his or her intended recipient i.e. donation to a specified recipient through an exchange programme
Unspecified donation:
Donation to an anonymous and unspecified recipient (donating to the waiting list)

Table 2. In total, 331 surveys were sent to transplant professionals in 45 European countries. 113 kidney transplant units from 40 countries and 39 liver transplant units from 24 countries completed the survey. 4 replying centres did not have a living kidney donor programme and 11 replying centres did not have a living liver donor programme, these are marked **[bold –]**. The replies are grouped into 3 geographical regions i.e. the North-Western, the Mediterranean countries and the Eastern. **Bold country** = EU-member.

Country	Surveys sent	Replies [kidney/liver]	Country	Surveys sent	Replies [kidney/liver]
North-Western			Eastern		
Austria	(5)	[1/1]	Albania	(1)	[1/0]
Belgium	(14)	[7/4, 1–]	Armenia	(1)	[1/0]
Denmark	(6)	[3/1]	Belarus	(3)	[1/0]
Finland	(1)	[1/0]	Bosnia Herzegovina	(3)	[1/0]
Germany	(50)	[16/3, 1–]	Bulgaria	(5)	[1/0]
Iceland	(1)	[1/0]	Croatia	(6)	[2/1]
Luxembourg	(1)	[0/0]	Czech Republic	(11)	[3/0]
Netherlands	(11)	[7/2]	Estonia	(1)	[1/0]
Norway	(2)	[1/ 1–]	Georgia	(1)	[1/0]
Republic of Ireland	(1)	[1/0]	Hungary	(6)	[2/ 1–]
Sweden	(7)	[4/2]	Kazakhstan	(1)	[0/0]
Switzerland	(10)	[3/0]	Kosovo	(4)	[0/0]
UK	(35)	[17/5]	Latvia	(2)	[1/1]
			Lithuania	(2)	[1/1]
Mediterranean countries			Moldova	(1)	[1– /0]
Cyprus	(2)	[0/0]	Montenegro	(1)	[1– /0]
France	(20)	[2/ 1–]	Poland	(21)	[5/1, 1–]
Greece	(7)	[2, 1– / 1–]	Romania	(8)	[1/1]
Italy	(7)	[4/1, 1–]	Russian Federation	(10)	[2/ 1–]
Malta	(2)	[1/0]	Serbia	(7)	[4/0]
Portugal	(9)	[1/ 1–]	Slovakia	(2)	[2/0]
Spain	(32)	[5/1]	Slovenia	(2)	[1– /1]
			Former Yugoslavian Republic of Macedonia	(1)	[1/ 1–]
			Turkey	(2)	[1/1]
			Ukraine	(6)	[0/0]

Table 3. Results from LKD survey divided in three geographical regions in Europe.

	Living kidney donor programs (N = 109)			p-value
	North-West N = 62 (%)	Mediterranean N = 15 (%)	East N = 32 (%)	
Living kidney donor transplantations				
< 25 LKD/year	28 (45)	11 (73)	26 (81)	0.023
Absolute contraindication for LKD				
Diabetes type 1	60 (97)	12 (80)	24 (75)	0.045
Diabetes type 2	48 (77)	11 (73)	19 (59)	0.142
BMI > 40	55 (89)	13 (87)	24 (75)	0.340
BMI > 35	39 (63)	9 (60)	14 (44)	0.388
BP > 140/90 mmHg	12 (19)	2 (13)	7 (22)	0.555
Well treated hypertension	2 (3)	0 (0)	3 (9)	0.428
Urine protein > 300mg/24 h	40 (65)	11 (73)	18 (56)	0.527
Surgical techniques				
Open flank incision, rib resection	9 (15)	2 (13)	18 (57)	< 0.001
Laparoscopic techniques	50 (81)	8 (50)	12 (37)	< 0.001
Reimbursement	41 (66)	3 (20)	6 (19)	< 0.001
Donor follow-up	62 (100)	15 (100)	12 (40)	< 0.001
Donor registries, national level	60 (97)	14 (93)	26 (81)	0.034

Table 4 a. Various types of relations accepted between donor and recipient in Europe in centres with living donor programmes, categorised with ELPAT's classification for living organ donation [14].

Who of the following potential donor can donate at your transplant centre?	Kidney donation N = 109 (%)	Liver donation N = 28 (%)
Specified donation, direct <i>Person who donates directly to his or her intended recipient.</i>		
Parent	109 (100)	28 (100)
Sibling	102 (94)	21 (75)
Child (adult)	65 (71)	15 (54)
Grandparent	96 (88)	18 (64)
Other genetically related family/relative	96 (88)	21 (75)
Spouse	97 (89)	25 (89)
Partner	91 (84)	21 (75)
Other NON genetically related family/relative	74 (68)	14 (50)
Friend with close emotional relationship to recipient	75 (69)	17 (61)
An employer or supervisor of recipient	18 (17)	4 (14)
An employee or supervisee of recipient	18 (17)	3 (11)
Co-worker	29 (27)	4 (14)
Acquaintance without close emotional relationship to recipient	23 (21)	4 (14)
A stranger donating anonymously to a specific recipient e.g. a famous person	1 (1)	3 (11)
A stranger anonymous to a recipient with defined characteristics e.g. a child	4 (4)	4 (14)
Specified donation, indirect <i>Person who donates indirectly to his or her intended recipient</i>		
Paired exchange "organ swapping"	47 (43)	6 (21)
Unspecified donation <i>Donation to an anonymous and unspecified recipient</i>		
A stranger anonymous to any recipient	35 (32)	7 (25)

Table 4 b. Types of relations accepted between donor and recipient for kidney transplantation divided by geographical region and categorised based on ELPAT's classification for living organ donation [14].

Type of relationship accepted	Living kidney donor programs (N = 109)			p-value
	North-West N = 62 (%)	Mediterranean N = 15 (%)	East N = 32 (%)	
Specified donation, direct <i>Person who donates directly to his or her intended recipient</i>				
Parent	62 (100)	15 (100)	32 (100)	0.07
Sibling	62 (100)	10 (67)	30 (94)	< 0.001
Child (Adult)	51 (82)	3 (19)	17 (49)	< 0.001
Grandparent	58 (94)	11 (73)	27 (84)	0.014
Other genetically related	58 (94)	12 (80)	26 (81)	0.019
Spouse	61 (98)	13 (8)	23 (72)	< 0.001
Partner	61 (98)	14 (93)	16 (50)	< 0.001
Other NON genetically related family/ relative	55 (89)	8 (53)	11 (34)	< 0.001
Friend with close emotional relationship to recipient	57 (92)	8 (53)	10 (31)	< 0.001
An employer or supervisor of recipient	27 (44)	0 (0)	1 (3)	0.001
An employee or supervisee of recipient	16 (26)	1 (7)	1 (3)	0.006
Co-worker	26 (42)	1 (7)	2 (6)	< 0.001
Acquaintance without close emotional relationship to recipient	21 (34)	1 (7)	1 (3)	< 0.001
A stranger donating anonymously to a specific recipient e.g. a famous person	1 (2)	0 (0)	0 (0)	0.66
A stranger anonymous to a recipient with defined characteristics e.g. a child	4 (7)	0 (0)	0 (0)	0.18
Specified donation, indirect <i>Person who donates indirectly to his or her intended recipient</i>				
Pared exchange “organ swapping”	35 (57)	7 (47)	5 (16)	< 0.001
Unspecified donation <i>Donation to an anonymous and unspecified recipient</i>				
A stranger anonymous to any recipient	31 (50)	3 (20)	1 (3)	< 0.001