
1187 Meeting, 11 December 2013

6 Social cohesion

6.1 European Directorate for the Quality of Medicines and Healthcare (EDQM) –

European Committee on Organ Transplantation (Partial Agreement) (CD-P-TO)

b. Resolution CM/Res(2013)56 on the development and optimisation of live kidney donation programmes –

Explanatory memorandum

Explanatory memorandum of the Resolution CM/Res(2013)56 on the development and optimisation of live kidney donation programmes

The rationale for this Resolution on the development and optimisation of live kidney donation programmes is to improve 'quality of life' and life-expectancy for patients with end-stage kidney disease by increased access to kidney transplantation.

Even though many countries with established transplant programmes have improved their deceased donation rates during recent years, none can cover the true need for kidneys from this source. One way of increasing the supply of kidneys for transplantation is to optimise the utilisation of live donors.

Shortage of kidneys for transplantation and its consequences

End-stage renal failure has been estimated to have increased at a rate of 3-9% each year for the last 5-10 years and it will probably continue to rise. This is mainly caused by the increasingly aged profile of the population and an increase in lifestyle-related diseases (such as obesity, diabetes, hypertension and cardiovascular disease). This represents a very serious challenge for patients, healthcare providers and national authorities (1, 2). Kidney transplantation is the best therapeutic alternative for patients with end-stage renal disease, both in terms of effectiveness and cost. Compared to dialysis, kidney transplantation provides longer survival and a better 'quality of life' (3, 4, 5). After the first year, kidney transplantation costs are up to 75% lower than those related to dialysis (6, 7).

For the year 2011, *Newsletter Transplant* registered 23,485 renal transplants in 36 Council of Europe member States (31.3 transplants per million population, *pmp*)¹ (8). At the end of the same year, there were 68,073 patients on the waiting list for a deceased donor kidney in those countries, indicating that only 34.5% were actually transplanted. Twenty-nine countries had registered 2,201 deaths on the kidney waiting lists that same year. There are substantial differences in kidney transplantation programmes between European countries. However, no country with an established transplant programme manages to cover the true need

¹ Countries included in the calculations: Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Georgia, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Republic of Moldova, Netherlands, Norway, Poland, Portugal, Romania, Russian Federation, Slovak Republic, Slovenia, Spain, Sweden, Switzerland, "the former Yugoslav Republic of Macedonia", Turkey and United Kingdom.

for kidneys. Most transplant centres within Europe have a waiting list that, by far, outnumbers available organs, typically by a factor of 2-3. Many patients deteriorate and die while waiting for an organ. In many countries, patients with limited survival expectancies (old age, concomitant diseases) will not even be considered for transplantation because of extensive organ shortages, thereby also masking the true need for organs (9).

Such discrepancies between the need for organs and lack of supply also results in desperate patients seeking alternative solutions outside their national healthcare systems. Such attempts include unrecognised listing on multiple organ waiting lists and engaging in transplant tourism and trafficking (10). The Joint Study of the Council of Europe and the United Nations on 'Trafficking in organs, tissues and cells and trafficking in human beings for the purpose of the removal of organs' addresses these problems (11).

Increasing organ availability from deceased donors

Deceased donation rates and derived transplantation activities differ between European countries. Countries continue to work on optimising deceased donation. This includes increased use of organs from expanded criteria donors; a concept which recognises that not all organs from deceased donors provide a similar outcome for the transplant recipient. However, the transplantation of these kidneys has been reported as beneficial, particularly when used in recipients with a limited life-expectancy (12, 13). The use of organs from donors whose death has been determined by circulatory and respiratory criteria is also being promoted in some European countries. Despite these aforementioned strategies, the availability of kidneys for transplantation remains limited, and even more so for young patients.

Kidney transplantation from live donors: present situation and regulations

According to the *Global Observatory on Organ Donation and Transplantation*, more than 40 per cent of the 73,179 kidney transplantations performed worldwide in 2010 were from live donors. The annual rate of live donor kidney transplantation in the member States of the Council of Europe in 2011 varied from 0 to 36.7 pmp (22 countries <5 pmp; 7 countries between 5-15 pmp; and 7 countries >15 pmp, including 3 countries >20 pmp).² This suggests that by engaging in and promoting the use of live kidney donation, rates can be substantially increased in many European countries. Many member States known for well-developed deceased donor programmes are realising that live donation must contribute to a greater extent if demands are to be met (14).

In many Council of Europe member States, well-established programmes that are approved by competent authorities regarding various live donor categories and strategies exist:

- the donor is genetically related to the recipient;
- the donor is emotionally, but not genetically related (spouse, in-law, long-term close friends);
- paired exchange of donors if multiple, blood group-incompatible donor-recipient combinations are present (15);
- use of blood group-incompatible live donors by absorption of blood group antibodies from the recipient;
- altruistic non-directed donations to patients on the waiting list without any economic or equivalent incentive.

The use of live donors as a source of kidneys for transplantation has been debated and is still controversial in some countries; although, in a few States, only live donors are used.

The Additional Protocol to the Convention on Human Rights and Biomedicine on Transplantation of Organs and Tissues of Human Origin (ETS No. 186), January 2002 states under Chapter III, Article 9 – General rule that: "Removal of organs or tissue from a living person may be carried out solely for the therapeutic benefit of the recipient and where there is no suitable organ or tissue available from a deceased person and no other alternative therapeutic method of comparable effectiveness."

² Countries included in the calculations: Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Georgia, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Republic of Moldova, Netherlands, Norway, Poland, Portugal, Romania, Russian Federation, Slovak Republic, Slovenia, Spain, Sweden, Switzerland, "the former Yugoslav Republic of Macedonia", Turkey and United Kingdom.

An explanatory report to this Convention has been produced by the Council of Europe. Under Chapter III "Organ and tissue removal from living persons," Article 9 - General rule, the following are stated:

"59. This implies that organs and tissues from living persons should not be used where an appropriate organ or tissue from a deceased person is available."

"60. The transplant must therefore be necessary in the sense that there is no other treatment that would produce similar results. In this respect dialysis treatment is not considered to provide results in terms of the patient's quality of life comparable with those obtained by a kidney transplant."

"61. However, if the results of a living donor transplantation is expected to be significantly better than those expected utilising a graft removed from a deceased person, live donation may be the preferred therapeutic option for a particular recipient."

Under Article 11 - Evaluation of risks for the donor, it is stated:

"In judging the risks involved, the donor's interest must take precedence, although in some circumstances the balance of risk to the donor compared to potential benefit to the recipient may be taken into consideration."

The European Commission's Action plan on organ donation and transplantation (2009-2015): strengthened cooperation between member States (2009/2104 (INI)) recognises live donation as a real alternative to improve the availability of organs for transplantation. It calls on member States to promote the exchange of best practices on live donation programmes, considering these as complementary to deceased donation. The development of live organ donation under such a framework has to be linked to the provisions of Directive 2010/53/EU of the European Parliament and of the Council on quality and safety aspects of human organs intended for transplantation, which sets out measures dedicated to the protection of live organ donors.

These aforementioned international standards demonstrate an evolution in the perception of live kidney transplantation; from an activity that should be restricted to specific cases, to an option regarded as appropriate for patients with end-stage renal disease, as long as the protection of live organ donors is ensured.

Advantages of using live donor kidneys for renal transplantation

Live kidney transplantation provides better graft and patient survival compared to kidney transplantation from a deceased person. There are several reasons for this improved outcome:

- a suitable live donor can be sought well ahead of actual surgery, and the operation can be performed as an elective procedure during normal working hours, offering the best capacity and most competent hospital staff;
- the transplantation can be well planned and, ideally, be performed before the patient has to start dialysis (pre-emptive transplantation), at which stage the operative procedure will be better tolerated. This is particularly important in paediatric or diabetic recipients. It is noteworthy that time on dialysis is an important indicator of reduced patient and graft survival. Pre-emptive transplantation also decreases the total costs;
- planned surgery also allows pre-operative treatment with removal of antibodies, allowing transplantations that otherwise would not be possible (ABO blood group-incompatible transplantation or patients with donor-incompatible HLA antibodies);
- live donor kidneys come from healthy people; usually both younger and with less co-morbidity than deceased donors, and with completely normal kidney function. The superior physiological state of the organ compared with a deceased donor kidney is due to the fact that hours/days of intensive care before organ procurement are not present. Morbidity linked to brain death is absent;

- the kidney is transplanted immediately, with a time out of circulation (cold ischemia time) usually less than 3 hours, which does not have any significant effect on the kidney;
- most live donors are genetically related to the recipient and, in most cases, share tissue (HLA) antigens with them. This reduces the likelihood for rejection episodes, thereby prolonging graft survival.

Risk-benefit evaluation using live kidney donors

Unilateral nephrectomy is usually safe for a healthy individual but, as for all surgical procedures, it does entail a certain risk. Studies have indicated 3.1 surgical mortalities per 10,000 living donor operations during the last 15 years, despite varying criteria and operative methods (16). Minor and major complications related to the donation procedure have been reported at a rate of 18% and 3%, respectively. By applying modern laparoscopic techniques, both major and minor complication rates may be further reduced, which can also facilitate a more rapid medical, social and work-related rehabilitation. Long-term follow-up of live donors has shown life-expectancy to be superior or comparable to that of the general population (17, 18).

In contrast, the risk that a patient with renal failure will die while undergoing dialysis treatment is estimated at 5-20% per year. If a patient is successfully transplanted, the risk of dying will be less than half of that per year (3, 4). In other words, the benefit to the recipient is huge, while the danger to the live donor is minimal.

Safety measures for live donors

Kidney transplantation from live donors should only be promoted when a rigorous legal, ethical and medical framework of donor care exists. This general principle is consistently reflected in all available international standards.

Specific requirements for the selection, use and follow-up of live donors are set out in the Additional Protocol to the Convention on Human Rights and Biomedicine concerning Transplantation of Organs and Tissues of Human Origin (ETS No. 186) from 2002.

“The Consensus Statement of the Amsterdam Forum on the care of the Live Kidney Donor”, from 2004 defines criteria both for donor selection and post-donation, long-term follow-up to minimise the risk for donors.

This consensus statement has the support of the European Committee on Organ Transplantation (Partial Agreement) (CD-P-TO) of the Council of Europe.

Directive 2010/53/EU of the European Parliament and of the Council on quality and safety standards of human organs intended for transplantation also sets out requirements for the evaluation, selection and care of live organ donors. Moreover, the aforementioned Directive establishes the obligation for EU member States to develop registries where information on live organ donors and on their outcomes after donation is recorded.

The CD-P-TO considers this requirement essential for countries where live organ transplantation is to be carried out.

References

1. Wolfe RA, Roys EC and Merion RM. Trends in organ donation and transplantation in the United States, 1999-2008. *Am. J. Transplant.* 2010; 10:961-972.
2. Donovan K, Ford D, van Schalkwyk D and Ansell D. Nephron. UK Renal Registry 12th annual report (December 2009): Chapter 16, International comparison with the UK RRT programme. *Clin. Pract.* 2010; 115 Suppl. 1:309-320.
3. Wolfe R, Ashby V, Edgar MA *et al.* Comparison of mortality in all patients on dialysis, patients on dialysis awaiting transplantation, and recipients of a first cadaveric transplant. *N. Engl. J. Med.* 1999; 341:1725-1730.
4. Navarro JM, Ortega M, Gutierrez MJ *et al.* Survival of patients older than 60 years with kidneys transplanted from Spanish expanded criteria donors versus patients continued on hemodialysis. *Transpl. Proc.* 2009; 41:2376-2378.

5. Heldal K, Hartman A, Grootendorst DC *et al.* Benefit of kidney transplantation beyond 70 years of age. *Nephrol. Dial. Transplantation.* 2010; 25:1680-1687.
6. Blotière P.O, Tuppin P, Weill A, Ricordeau P, Allemand H. The cost of dialysis and kidney transplantation in France in 2007, impact of an increase of peritoneal dialysis and transplantation. *Nephrol. Ther.* 2010 July; 6(4):240-7 (Epub: 31 May 2010).
7. Wong G, Howard K, Chapman JR *et al.* Comparative survival and economic benefits of deceased donor kidney transplantation and dialysis in people with varying ages and co-morbidities. 2012; *PLoS ONE* 7(1):e29591.doi :10.1371/journal.pone.0029591.
8. Council of Europe. *Newsletter Transplant.* 2010 September; Vol. 15.
9. Oniscu GC, Schalkwijk AH, Johnson RJ *et al.* Equity of access to renal transplant waiting list and renal transplantation in Scotland: cohort study. *Br. Med. J.* 2003; 327:1261-1263.
10. Yosuke S. The state of the international organ trade. A provisional picture based on integration of available information. *Bull. World Health Organization.* 2007; 85:955-962.
11. Joint Council of Europe/ United Nations study on trafficking in organs, tissues and cells and trafficking in human beings for the purpose of removal of organs. Council of Europe website. http://www.coe.int/t/dghl/monitoring/trafficking/default_en.asp.
12. Veroux M, Grosso G, Corona D *et al.* Age is an important predictor of kidney transplant outcome. *Nephrol. Dial. Transplant.* 2011 (16 September); doi:10.1093/ndt/gfr524.
13. Foss A, Helldal K, Scott H *et al.* Kidneys from deceased donors more than 75 years perform acceptably well after transplantation. *Transplantation* 2009; 87:1437-1441.
14. Dominguez-Gil B, De La Oliva Valentin M, Escobar EM *et al.* Present situation of living- donor kidney transplantation in Spain and other countries: past, present and future of an excellent therapeutic option. *Nefrologia.* 2010; 30 Suppl. 2:3-13.
15. Roodnat JI, Kal-van Gestel JA, Zuidema W, van Noord MA, van de Wetering J, IJzermans JN, Weimar W. Successful expansion of the living donor pool by alternative living donation programs. *Am. J. Transplant.* 2009 Sep;9(9):2150-6.
16. Dorry LS, Abimereki DM, Brian SC *et al.* Perioperative mortality and long-term survival following live kidney donation. *J. Am. Med. Assoc.* 2010; 303(10):959-66.
17. Ibrahim HN, Foley R, Tan L *et al.* Long-term consequences of kidney donation. *N. Engl. J. Med.* 2009; 360(5):459-469.
18. Mjoen G, Reisaeter A, Hallan S *et al.* Overall and cardiovascular mortality in Norwegian kidney donors compared to the background population. *Nephrol. Dial. Transplant.* 2011; 0:1-4, doi: 10.1093/ndt/gfr303.