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REVIEW

The European experience

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Summary

This mini-review on European experiences with tackling the problem of organ shortage for transplantation was based on a literature review of predominantly European publications dealing with the issue of organ donation from deceased donors. The authors tried to identify the most significant factors that have demonstrated to impact on donation rates from deceased donors and subsequent transplant successes. These factors include legislative measures (national laws and European Directives), optimization of the donation process, use of expanded criteria donors, innovative preservation and surgical techniques, organizational efforts, and improved allocation algorithms.

Introduction

Transplantation of organs from deceased or living donors has become the treatment of choice for many end-stage diseases thanks to continuously improving results. Data from the Council of Europe show that in 2008 a total of 27 809 transplants have been performed in the 27 countries of the EU (population: 493 million inhabitants) [1]. Unfortunately, transplantation has become the victim of its own successes as the number of available deceased or living donors seems to be insufficient to answer the growing demand for organs.

There are several possible approaches to address increasing gap between the number of patients in need for organ transplantation and the number of available donor organs:

1 Reduce the need for transplantation by either preventing the development of end-stage organ disease or at least slow down the progression of the underlying disease.
2 Make more donor organs available for transplantation either from deceased or living donors.
3 Prevent that reported suitable donor organs are not allocated and transplanted but discarded.
4 Apply special transplant techniques to make best use of available donor organs like split liver or domino transplantation.
5 Improve graft survival and reduce transplant loss to avoid the need for retransplantation.

There is a wide variety of donation and transplant rates between countries in Europe. We preferred to express countries' donation performance rates as *organs retrieved and transplanted* because from the point of view of a recipient waiting for a life-saving transplant, *organs* rather than *donors* seem to be relevant. Figure 1 depicts all deceased donor organs that were retrieved per country and

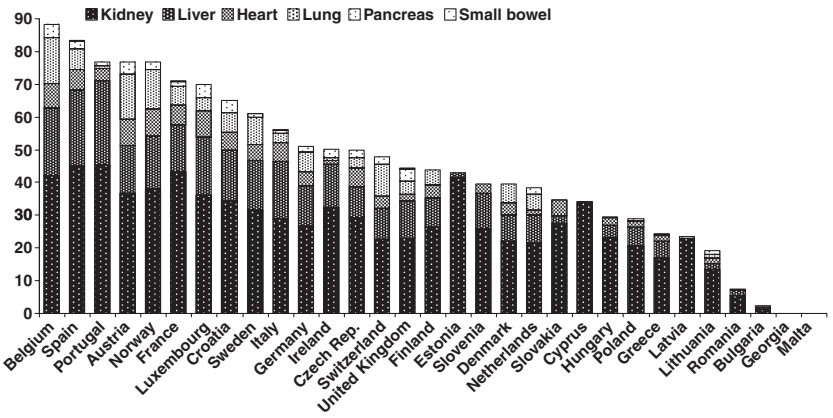

Figure 1 Deceased donor organs retrieved and transplanted, PMP – 2008 – Council of Europe, Eurotransplant data 2008.

subsequently transplanted either in the same country or abroad. In 2008, Belgium scored highest with nearly 90 organs per million population (PMP), closely followed by Spain, Portugal, Austria, and Norway with over 70 organs PMP [1,2]. Unfortunately, several countries were even unable to retrieve more than 20 organs PMP/year in 2008, which shows that there is definitely room for improvement and that it must be feasible to increase average donation rates in Europe substantially, based on best practice experience. But even in countries with currently already high organ-donation rates, there might be options to enhance organ transplantation further [3]. Therefore, this mini-review focuses on factors that have been demonstrated to impact on the availability of donor organs in Europe, such as legislative initiatives, optimization of the donation process, use of expanded criteria donors (ECD), innovative preservation, and surgical techniques as well as organizational efforts related to the allocation and transplantation process. It should be noted that this review does not cover the so-called ''Spanish Model'', which is subject of a separate article in this issue. Prevention and treatment of end-stage organ disease and the wide variety of steps taken to improve the long-term outcome of transplantation are beyond the scope of this review and will also not be described in detail in this article.

Legislative measures

In this chapter, we will focus primarily on the governing legal frameworks for organ donation from deceased donors in EU member states and some recent initiatives of the European Commission with regard to organ donation and transplantation.

Basically, two types of consent to donation from deceased donors can be distinguished today in national legislations: the principle of presumed consent or ''opting-out'' (contracting-out) and explicit consent or ''opting-in'' (contracting-in). In a presumed consent system, no explicit consent is required to become a potential donor.

Table 1. Legal systems regarding consent to organ donation in 25 EU Member States.

Country	Legal principle	Daily practice*	Date of Law
Austria	Opting out	?	1982
Belgium	Opting out	''Soft''	1986 (amended in 2007)
Bulgaria	Opting out	''Soft''	1996
Croatia	Opting out	''Soft''	2000
Czech Republic	Opting out	?	2002
Denmark	Opting out	''Soft''	1990 (amended in 2001)
Estonia	Opting out	''Soft''	2002
Finland	Opting out	''Soft''	2001
France	Opting out	''Soft''	1976 (amended several times)
Germany	Opting in	–	1997
Greece	Opting out	''Soft''	1999
Hungary	Opting out	?	1997
Ireland	Opting in	–	No law directly regulating organ donation
Italy	Opting out	''Soft''	1999
Latvia	Opting out	?	1995
Lithuania	Opting out	?	1999
Luxembourg	Opting out	''Soft''	1982
Poland	Opting out	''Soft''	1995 (amended in 2005)
Portugal	Opting out	''Soft''	1993
Slovakia	Opting out	?	2004
Slovenia	Opting out	''Soft''	2000
Spain	Opting out	''Soft''	1979 (amended in 1999)
Sweden	Opting out	''Soft''	1995
the Netherlands	Opting in	–	1996
UK	Opting in	–	2006

*Authors' survey, October 2010; ?, unknown.

The donation procedure can be initiated, unless the deceased person had objected during life. In an explicit consent system, the donor himself needs to consent to organ removal after death explicitly. In practice, and in the absence of such explicit consent, most laws require the deceased's next-of-kin to consent to post-mortem organ removal. A majority of European countries have transplant laws today based on the presumed consent

principle. Table 1 summarizes the current situation in 25 EU countries [4]. It should be noted that the practical application of national laws, particularly with regard to the role of next of kin in objecting or consenting to donation, varies substantially between countries, regions, hospitals, and even individual requestors and thus may impact on ultimate efficiency of national laws [4].

Several countries with a presumed consent law, such as Belgium, Croatia, France, Poland, and Sweden, have developed a national nondonor registry to collect citizens' objections during life. Interestingly, in almost all European countries with a presumed consent law, it is daily practice – especially in the absence of a registered will from the deceased – to approach donor families regardless of the legal situation. The families are, in this situation, not approached with a mostly confronting request to donate, but rather as an attempt to find out whether the deceased himself would have objected to donate. This subtle but fundamental difference in family-approach techniques between countries with an explicit consent law and those with a so-called ''soft'' presumed consent practice, by shifting the burden of a decision from the donor family to the donor himself, may be an important factor for explaining the significantly lower average refusal rates in the latter.

Some authors claim that given the multifactorial character of the donation process, national legislations alone are unlikely to explain variations in donation rates between countries [5,6]. Certainly, a combination of legislation, potential of medically suitable donors, investments in health care and infrastructure, underlying public attitudes, religion and, education may all play a role [3].

Donation figures within the Eurotransplant area, however, demonstrate a rather direct effect of legislative measures: organ donation rates in Belgium nearly doubled within 2 years after the implementation of a presumed consent law in 1987 [7]. When comparing four socioeconomically comparable countries within the Eurotransplant area, donation rates PMP are nearly twice as high in Austria and Belgium (presumed consent) compared to those in Germany and the Netherlands [8]. One cannot ignore the correlation between donation rates PMP in the above mentioned countries and the consent system they adhere, as demonstrated in Fig. 2 and based on Eurotransplant Annual Reports [9].

Two interesting studies based on a multi-variate analysis in 28 [10] and 22 [11] European countries have identified presumed consent laws as an independent factor that significantly impact on countries' donation rates.

A study based on representative data from the Eurobarometer survey 58.2 undertaken in 2002 confirmed that presumed consent organ donation policy positively affects

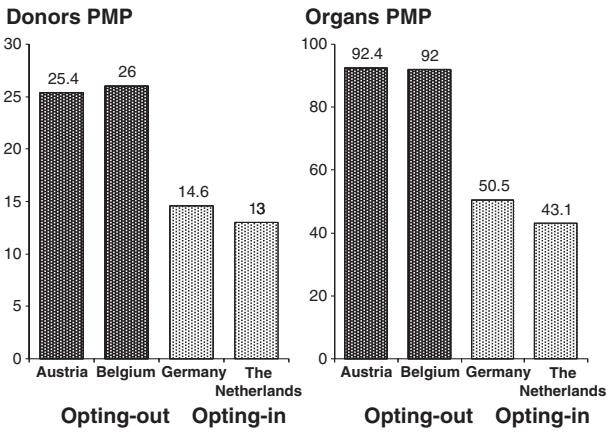

Figure 2 Eurotransplant: deceased donors and available organs PMP – 2009.

the willingness of individuals to donate their own organs and those of a relative [12].

Because of wide variations in quality and safety requirements between EU Member States (MS), the European Commission (EC) adopted in 2008 a proposal for a Directive on standards of quality and safety of human organs intended for transplantation [13]. This Directive also aims to facilitate the exchange of organs and expand the donor pool via several means:

- A competent authority in each MS will have to make sure that the quality and safety standards of the Directive are complied with;
- A system for the authorization of organ procurement and transplantation will be established;
- National quality programs will have to be introduced to ensure continuous monitoring of performance;
- MS will have to put in place organ traceability systems for the reporting of serious adverse events and reactions;
- Transplant teams in all MS will be assured to receive appropriate information required regardless of the country of origin of the organ.

After adoption by the EU Council and Parliament, and publication in the Official Journal in June 2010, member States now have 24 months to transpose the Directive into national law.

At the same time, the Commission launched an Action Plan designed to promote the availability of deceased and living donors across the European Union, increase the supply of organs, enhance transplantation systems and ensure the quality and safety of procedures. The Action Plan [14] includes a number of priorities, which are grouped under three challenges:

- Increasing organ availability
- Enhancing the efficiency and accessibility of transplantation systems
- Improving quality and safety

Public campaigns to increase organ donation

Refusal to donate represents an obstacle for deceased donation, especially in countries with informed consent, but to a certain extent also in countries with presumed consent, as in everyday practice even in the countries with presumed consent the families are approached to understand what the wishes of the deceased were on donation [15]. In several European countries, family refusal rates are well above 40% [1]. Achieving a higher consent rate would therefore have a substantial impact on the number of available donor organs. In an effort to reach this goal, nationwide public campaigns to increase organ donation have been carried out in almost all European countries nationwide or are currently under way. They typically aim at informing the public, creating a positive attitude toward transplantation and make people formally declare their decision. Only a few of these public campaigns, however, have been systematically evaluated [16]. Available data show a (transient) effect on knowledge about donation and transplantation. The impact on consent rates and especially on the number of transplantations on the other hand is limited if at all detectable [17–19]. This might in part be due to the difficulty to quantify the effect of such campaigns [20]. Another aspect of general public campaigns is that they often do not address the cultural microdiversity in the population and therefore are not likely to be effective and efficient [21].

Tailored educational efforts for specific targets have turned out to be more effective: Recent reports show that with educational intervention programs especially designed for secondary school or university students, the knowledge about the brain death concept, organ donation and transplantation can be increased substantially, resulting in improved opinions about deceased organ donation and a higher intention to donate organs [22–25]. Almost 80% of the students discussed organ donation with their families multiplying the effect of this approach [24]. Nevertheless, the actual effect on organ donation is difficult to estimate and might only become evident over time.

Education and training of intensive care nurses and doctors have achieved the highest and most immediate impact on organ donation of all initiatives described so far [26]. These courses aim both at improving knowledge about donor identification and transplantation as well as changing attitudes toward transplantation [27]. This approach has been picked up in the multinational European Training Program on Organ Donation (ETPOD) project supported by the European Union [28]. The central role of the critical care unit personnel in the donation process will be further addressed in following section.

Optimizing the donation process: focus on Critical Care Units

A variety of organizational initiatives to increase deceased donation have been developed at international, national or local hospital level. Experience in Europe and the U.S. indicates that a consistent hospital donation protocol built on multidisciplinary consensus and team building can lead to a significant increase in donation [29]. This approach was picked up during the third WHO Global Consultation on Organ Donation and Transplantation organized by the World Health Organization, The Transplantation Society (TTS), and the Organización Nacional de Trasplantes (ONT) in Madrid in March 2010. A ''Critical Pathway for Organ Donation'' has been developed presenting an algorithm of progression from a possible deceased donor to a utilized organ donor that will aid global harmonization of practice in this area. Such a protocol supports teamwork toward common goals: to identify all potential donors and provide optimal care for families. As an added value, it also cultivates a sense of institutional ownership of the donation process among hospitals and their Critical Care Units (CCUs). Although reports of activities on a *local*, *regional* or *national* scale show fragmentary successes in achieving these goals [30–32], two long-standing *international* European initiatives deserve some closer attention.

The European Donor Hospital Education Program (EDHEP), a Eurotransplant initiative launched in 1991, was designed to meet the training needs of medical and nursing Critical Care (CC) staff in breaking bad news, caring for the bereaved and requesting donation [33]. EDHEP aims at improving the communication with donor relatives regarding death and donation by providing insight in the grieving process and relatives' emotional reactions related to the donation procedure [34]. The EDHEP Workshop ''The grief response and donation request'' has been organized hundreds of times and attended by several thousands of CC staff in Europe and beyond. It is available in over 15 languages and is part of post-graduation education today in over 35 countries all over the world [33].

Another initiative, and in fact a continuation of EDHEP but with a wider scope, is Donor Action® (DA), an international collaboration that brings together state-of-the-art expertise to help hospitals increase their donation performance through improved clinical practices [35,36]. Cornerstone of the DA program is its ''Diagnostic Review'' that takes a systematic approach toward achieving quality assurance in the whole donation process by helping CCUs to identify *when*, *where*, and *why* potential donors are missed along the donation pathway. DA's ''Diagnostic

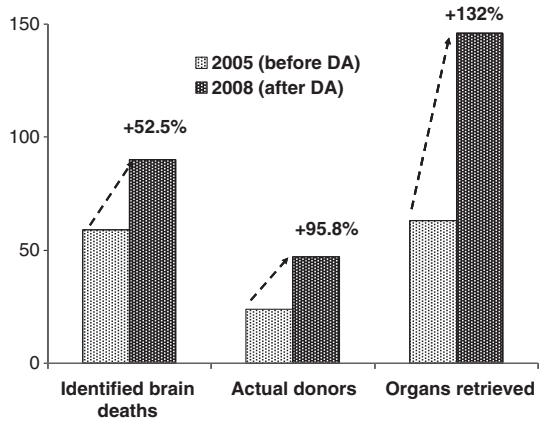

Figure 3 Impact of implementing Donor Action in France's EPACA/HC region.

Review'' has three components: a standardized Medical Record Review (MRR), a Hospital Attitude Survey (HAS), and a system database to analyze and report on collected findings. The program also provides improvement measures in modular format to fill gaps identified by the DA Diagnostic Review. A number of publications have reported on the feasibility of implementing this program locally and achieving donation increases between 70% and 160% in countries with sufficient follow-up [37–44]. A recent study from a French group reports an increase in donation rates from 13 to even 27.4 donors PMP (+95.8%), 2 years after implementing DA's methodology [45] (Fig. 3).

As mentioned already before, involving CC staff in the donation process is a key element to any successful program. Recent articles in this journal and elsewhere have identified a strong correlation between national donation rates and CC staff attitudes, confidence levels, and educational needs with regard to donation-related tasks [26,46].

Finally, and with regard to other educational initiatives on a European level, the European Society for Organ Transplantation (ESOT) has started offering a choice of courses and workshops aimed at enhancing professional skills of transplant coordinators and surgeons in the field of organ procurement:

- The annual Triple ''C'' course, which is an advanced course for deceased donor, living donor and recipient coordinators, aiming at providing insight and tools in addition to existing local, regional or national educational programs
- Regular hands-on TOP courses for young surgeons who are specializing in multiorgan procurement and transplant surgery

Expanded criteria donors, nonheart-beating donors

Kidneys

For reasons of a growing shortage of organs for kidney transplantation, the use of ECDs has increased significantly in recent years. The term ''expanded criteria donor'' (ECD) was introduced by Kauffman *et al.* in 1997 to describe transplantable organs that do not meet the standard criteria for organ donation (SCD), in preference to other descriptive terminologies in use, such as ''marginal'', ''suboptimal'', ''compromised'', ''inferior'' or ''nonstandard'' donor kidneys [47]. In 2002, the US Organ Procurement and Transplantation Network/United Network for Organ Sharing (OPTN/UNOS) established an ECD definition for kidneys based on donor age and three donor risk factors identified to be statistically significant in a previous Scientific Registry of Transplant Recipients (SRTR) analysis:

- History of arterial hypertension
- Terminal serum creatinine >1.5 mg/dl
- Cerebrovascular accident (CVA) as cause of death

Consequently, ECDs were defined as ''any donor 60 years or older, or older than 50 years with at least 2 of the cited risk factors'' [48].

Donor age in itself remains one of the most important risk factors impacting on renal transplant outcomes, as demonstrated in several multicenter studies. The number of patients, however, waiting for a kidney and aged 65 years and above is steadily increasing as well. Within the Eurotransplant area, there has been a significant increase in renal transplant recipients older than 65 years old from 3.6% in 1991 to 19.7% in 2007. During the same period, the proportion of deceased kidney donors in this age group increased from 2.3 to 18.1% [49]. These changing trends in donor and recipient profiles have encouraged Eurotransplant to launch in 1999 an old-for-old kidney allocation scheme named ''European Senior Program (ESP)'' with a twofold aim: to achieve a more efficient use of kidneys from older donors and to reduce the waiting time for elderly patients. The allocation scheme was solely based on the concept of matching between metabolic demand of the graft recipient and excretory capacity of the donor organ [50]. According to the ESP algorithm, kidneys from donors over 65 years were assigned with priority to registered ESP patients (inclusion criteria: recipient age >65 years, panel reactive antibodies <5%). Collaborating centers were required to keep the cold ischemia time as short as possible by circumventing HLA matching and transplanting kidneys into local recipients only [51]. Initial [51] and long-term [52,53] outcome evaluations have demonstrated that an old-for-old renal allocation algorithm can be successful

provided that risk factors such as cold ischemia time are reduced. Three-year data showed that there was no difference between patients who received grafts from elderly donors via ESP and those who received similar kidneys via the usual HLA-driven allocation procedure.

Hundreds of reports have been published meanwhile on the outcome of renal transplants from ECDs. A recent meta-analysis based on 1001 publications concludes that the use of ECDs for kidney transplantation increases the number of deceased donor kidneys available, results in shorter waiting times, and limits the morbidity and mortality associated with long-term dialysis therapy [54]. These kidneys are known to have worse long-term survival compared with SCD kidneys, and therefore adequate GFRs with acceptable histological characteristics remain to be required. Based on the available evidence, the authors conclude that patients under the age of 40 years or scheduled for kidney retransplantation should not receive an ECD kidney. Patients 40 years or older, especially with diabetic nephropathy or with longer waiting times, showed better survival receiving an ECD kidney than remaining on dialysis. An ECD kidney nephron-protecting strategy should be based on minimization of cold ischemia times, pulsatile perfusion preservation, and tailored immunosuppression.

Liver

Exemplary for the growing trend of using organs from older donors is the evolution of the median deceased-donor age for different organs in Eurotransplant between 1990 and 2009, as depicted in Fig. 4 [9]. It demonstrates that not only for kidneys, but also for other organs, donor age and other criteria are changing dramatically to meet the organ shortage: since 1990, the median donor age for livers doubled from 26 to 53 years in 2009. In contrast to other organs, the liver may be more immune to senescence, particularly in the otherwise healthy donor, possibly because of the liver's large functional reserve, regenerative capacity, and dual blood supply, which exceeds its metabolic needs [55]. When controlling for other factors, older age may not adversely affect patient or graft survival, although recipients of older donor livers seem to experience more delayed function and a cholestatic pattern after transplantation [56]. Older donors have also an increased incidence of steatosis, which may potentiate preservation injury [57]. Therefore, and as grafts with more than 14 h of cold ischemia have been associated with a twofold increase in preservation damage [58,59], older donors need to be carefully selected, and each liver requires an assessment based on other risk factors, such as steatosis and cold ischemia time. In this context, two European review articles list following potential risk factors to be associated with liver graft dysfunction: donor age, gender, race weight, CVA as cause of death, lengthy stay in the ICU, high doses of inotropes, cold ischemia time >10–12 h, high serum sodium, elevated liver enzymes, and partial liver grafts [60,61]. Data analysis from the SRTR including 20 023 liver transplants from deceased donors identified several risk factors to have a significant impact on transplant outcomes: a donor age of >60 years, CVA as cause of death, nonheart-beating donor (NHBD) and split grafts, and cold ischemia time. Following analysis of this data, a donor risk index (DRI) was derived that correlated strongly with 1-year survival rates [62]. In March 2007, a Paris Consensus Meeting on Expanded Criteria Donors in Liver Transplantation was organized by the International Liver Transplantation Society (ILTS). Recommendations were formulated to define better which ECDs should be considered for transplantation, how they have to be managed, and in which candidates they should be transplanted to optimize scarce resource utilization [63].

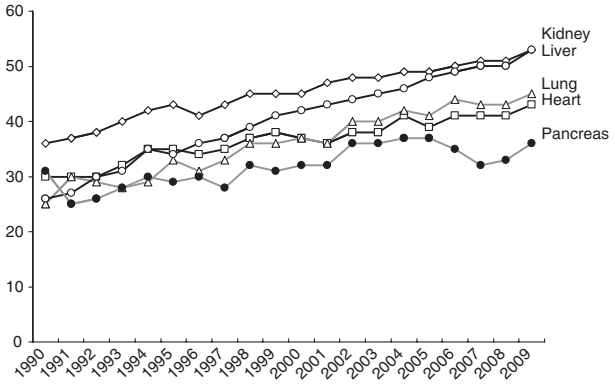

Figure 4 Median age of deceased donors in Eurotransplant, 1990–2009.

Heart

''Certainly it makes little sense to replace one diseased heart with another'' is a well-known quote by DePasquale [64]. Forty years later, Wittwer *et al.* from the Cologne Heart Center (Germany) published an excellent review in this journal on the use of ''marginal'' heart donor grafts based on 25 years of experience [65]. The authors suggest a series of acceptance criteria for heart transplantation using marginal donors (Table 2), but emphasize that the decision making on whether a certain donor heart can be suitable for transplantation should be based on an individualized and recipient-oriented assessment, which is the responsibility of the transplanting physician, and which has to be based on a specific profile of risk factors and critical conditions of the particular recipient.

Table 2. Acceptance criteria for heart transplantation using expanded donors, according to Wittwer *et al.* [65].

Age up to 65 years
Undersizing/oversizing by >20% body weight
Prolonged hospitalization
History of chest trauma
Open cardiac massage
Elevation of myocardial enzyme levels
Prolonged cardiopulmonary resuscitation (>5 min)
Transient hypotension (>30 min)
High-dose vasopressor requirement
Wall motion abnormalities by echocardiography
Long-distance procurement (>1000 miles)
Persistent conduction disturbances
Cold ischemia time up to 4–5 h
Bypassable one- or two-vessel disease
Correctable valvular dysfunction by echocardiography

Lung

Lung donor shortages, too, have resulted in the critical appraisal of deceased donor criteria in Europe and the gradual relaxation of once-strict guidelines. By necessity, most centers now routinely accept donors older than the original cut-off of 55 years, although concerns about reduced graft longevity have been raised. Recipients of lungs from older donors (up to 77 years of age), for example, show a higher incidence of the bronchiolitis obliterans syndrome (BOS) [66]. Nevertheless, an increasing number of centers will accept the lungs from donors in their seventies, as long as there are no other adverse features. In case of a younger donor, they will accept prolonged ischemia times and less optimal gas exchange, expecting the greater physiological reserve to allow recovery from ischemia–reperfusion injury [67]. In Europe, Belgium and Austria are currently taking the lead in offering deceased donor lungs for transplantation with respectively 14.0 and 13.9 lungs PMP, more than twice as high compared to US figures (see Fig. 1) [1]. The Leuven (Belgium) and Vienna (Austria) groups have published extensively on their experience with ECD lungs [68,69]. Meers *et al.* recently demonstrated in this journal that they could increase utilization rates of lung donors to 34.1% of all donors in their network of donor hospitals [68], which is significantly more than the average 25.3% in the Eurotransplant area or a 23% rate in North America [70]), and which resulted in doubling the number of transplants in their center. Successful techniques such as segmental resection, lobe transplantation, and pulmonary bipartitioning have been developed to transplant grafts from larger donors into smaller recipients [71]. The number of teams reporting successful transplantation of lungs from NHBDs, both controlled and uncontrolled, has increased over the past few years. Ex vivo perfusion for reconditioning of initially rejected donor lungs appears to be a promising development to increase the lung donor yield [69,72–74].

Table 3. Maastricht categories of nonheart-beating donors [78].

Maastricht category	Description
I	Dead on arrival (uncontrolled)
II	Unsuccessful resuscitation (uncontrolled)
III	Awaiting cardiac arrest (controlled)
IV	Cardiac arrest while brain death (uncontrolled)

Nonheart-beating donation (NHBD), donation after euthanasia

Historically, Europe has been playing a pioneering role since the mid-1990s in elaborating the concept of ''nonheart-beating donation (NHBD)'' or ''donation after cardiac death (DCD)'' [75–77]. At the first international workshop on NHBD organized by Kootstra and his group in Maastricht in 1995, four NHBD types were categorized (Table 3) [78].

Liberal use of kidneys from NHB donors may increase the number of organ donors by 2.5 to 4 times, which could be sufficient to reduce or even eliminate the waiting list for kidney transplantation [77]. Compared with brain-dead donors, organs from NHB donors inevitably sustain a period of warm ischemia from circulatory arrest until start of preservation, resulting in ischemic injury and a subsequent incidence of primary nonfunction (PNF) and delayed graft function (DGF). A number of studies have described good medium-term graft survival rates for NHBD kidney transplants, despite poorer initial function [79]. In a review by Kootstra *et al.*, the authors conclude that, despite a significantly higher incidence of DGF in NHBD kidneys (20–80%) compared to the 20–30% in HBD kidneys, medium-term survival rates are similar in both groups [80]. Barlow *et al.*, in a report on long-term results of 112 NHBD renal transplants, mostly from uncontrolled donor cases, compared with a matched group of 162 HBD transplants, conclude that, despite increased DGF and creatinine levels, survival rates between the two groups remain comparable after 15 years [81].

Figure 5 shows the number of NHBD in Europe PMP and as a percentage of total deceased donors in 2008, demonstrating a leading position of the Netherlands and the UK. But every coin has two sides: optimism over NHBD might give the false impression that this process could compensate for the dwindling supply of HB donor organs. This, however, is not the case, at least not in the Netherlands and the UK. Published NHS statistics show that the huge rise of NHBDs, from 73 in 2004–2005 to

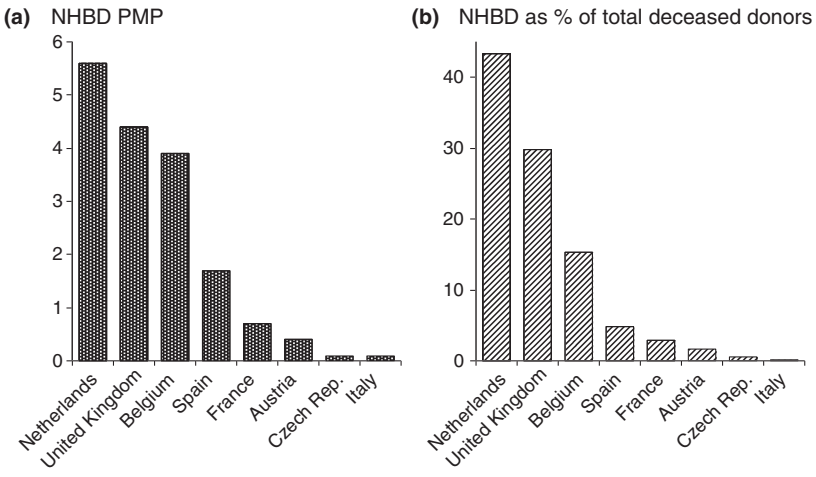

Figure 5 Nonheart-beating donors in different European countries – 2008.

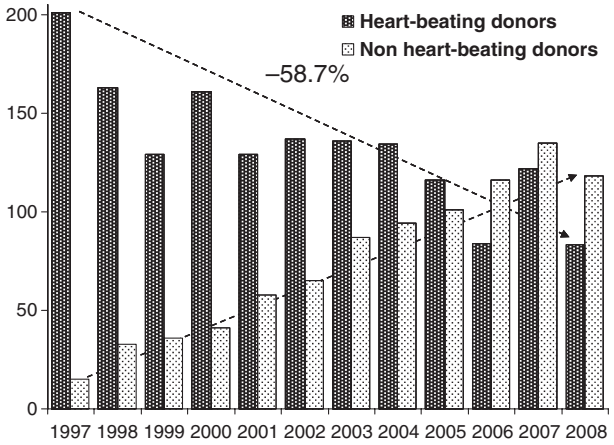

Figure 6 The Netherlands: evolution of heart-beating versus non-heart-beating donation.

200 in 2008–2009, has coincided with a marked fall in HBD (from 697 to 609). Moreover, the average HB donor provides some 3.4 organs, whereas on average, only 2.1 organs are transplanted from a NHBD. As a consequence, NHBD is more resource intensive than HBD as more retrievals will be required to produce the same number of organs [82]. Figure 6 illustrates an even more dramatic evolution in the Netherlands, with a 58.7% decrease in HB donation after starting a NHBD program. Interestingly, at least one study reports on significantly lower family refusal rates among NHBD families (4%) compared to 24% ($P < 0.01$) among HBD families [83].

Finally, a new category of NHBDs was recently introduced in Belgium: ''NHBD after euthanasia'' [84]. Since 2005 till 2007, at least four patients expressed their will to donate their organs after euthanasia (legalized in Belgium since 2002). After clinical diagnosis of cardiac arrest by a separate medical team, organ procurement resulted in eight kidneys, four livers, two pairs of lungs, and one pancreas (islets) available for transplantation, or an organ/donor yield of 4.25, which is superior to the average yield of 3.44 organs in this country (Fig. 7).

Optimizing organ yield and quality by better clinical management and better organ preservation

Donor management

Innovations in the field of donor management and organ preservation may offer a realistic hope to improve both the quality and size of the currently insufficient organ supply. As shown in Fig. 7, the average number of organs recovered and transplanted per deceased donor in 28 European countries, based on 2008 Eurotransplant and Council of Europe data, varies between 4.06 in Switzerland and only 1.8 in Latvia [1,2]. These data show that a substantial increase in overall transplant rates could be achieved by just retrieving and transplanting all suitable organs from available donors. One of the suggested strategies involves maximizing the number of organs from the available pool of deceased donors by using donor management protocols that treat the profound physiological disturbances associated with brain death.

Although the basic science dissecting the complex processes of brain death and subsequent ischemia/reperfusion injury is marked by exciting discoveries, the clinical science investigating donor management and organ preservation has been rather sparse [85].

Brain death can be considered a physiologic, cellular, and molecular catastrophe, associated with ischemia/reperfusion injury [86] and known to evoke an inflammatory response leading to endothelial dysfunction and release of cytokines in the circulation [87]. Biological modulation of renal ischemia/reperfusion injury holds the potential to reduce the incidence of early graft dysfunction and to

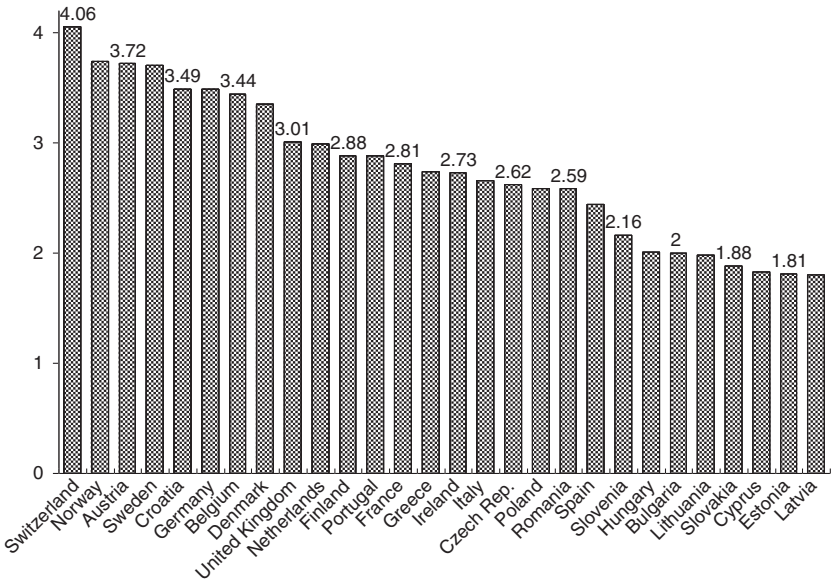

Figure 7 Transplanted organs/deceased donor in different European countries – 2008.

Table 4. Deceased donor management goals, according to Dictus *et al.* [90].

MAP ≥60 mmHg
CVP 6–10 mmHg
LVEF ≥45%
Urinary output 1.0 ml/kg/h
Core body temperature ≥35 °C
Blood glucose 80–150 mg/dl
Sodium <150 mM
Hemoglobin ≥10 g/dl
Platelet count 50 000/mm^3
INR ≤1.5

expand safely the donor pool with kidneys that may have suffered prolonged ischemic injury before organ recovery [88].

A landmark article published already in 1995 by the Papworth, UK group proves that optimizing donor cardiovascular performance has a tremendous impact on the viability of all transplantable organs [89]. Clinical donor management today focuses on achieving and maintaining normal hemodynamics, cardiac output, volume status, oxygenation, ventilation, electrolyte balance, acid base status, coagulation parameters, and normothermia. Table 4 summarizes these goals [90].

Keeping a balance between an adequate fluid resuscitation for optimal organ perfusion versus minimizing the extravascular lung water from overzealous fluid resuscitation is challenging and requires vigilance with invasive monitoring. Because of a disparity between right- and left-sided filling pressures after brain death, central venous pressure monitoring alone to guide fluid loading may be misleading and the use of a pulmonary artery catheter may be helpful in selected cases to monitor pressures and cardiac performance correctly [74,91]. Vasopressors and inotropes may help stabilize fluctuations in blood pressure to optimize organ perfusion with the lowest myocardial oxygen demand. In a randomized, open-label, multicenter controlled trial, Schnüelle *et al.* could demonstrate that pretreatment of brain-dead donors with a low-dose regimen of dopamine (4 μg/kg/min) significantly improved early graft function in kidney transplant recipients [92]. Damage of the hypothalamus and the pituitary gland during brain death results in decreased circulating levels of adrenocorticotrophic hormone, vasopressin, triiodothyronine, and thyroxine in animal models and brain-dead donors [93]. Attempts to reverse these brain death sequels by hormonal substitution therapy have been reported to be successful, both in animal studies and humans [94,95]. Since these initial observations, several other groups, ours included, have confirmed the beneficial effect of hormonal resuscitation [96–98]. Hormonal substitution therapies are now widely used as an essential component of successful donor management strategies.

Organ preservation

Maintaining organ viability after donation and until transplantation is key to optimal graft function and survival after transplantation. To date, static cold (ice) storage (CS) is the most widely used technique of preservation in daily clinical practice. The principle of CS preservation is based on suppression of cell metabolism and catabolic enzymes by hypothermia (4 °C). Cell metabolic rates are halved with each 10 °C drop in temperature

Table 5. Anticipated/emerging benefits of hypothermic machine perfusion, according to Taylor *et al.* [102].

1. Maintaining the patency of the vascular bed
2. Providing nutrients and low-demand oxygen to support reduced energy demands
3. Removal of metabolic by-products and toxins
4. Provision of access for administration of cytoprotective agents and/or immunomodulatory drugs
5. Better access for viability assessment and tissue matching
6. Facilitation of a change from emergency to elective scheduled surgery with reduced costs and improved outcomes
7. Improved clinical outcomes as demonstrated by reduced PNF and DGF parameters
8. Improved stabilization or rescue of ECD kidneys or organs from NHBD that increase the size of the donor pool
9. Significant economic benefit for transplant centers and reduced health care expenditures

DGF, delayed graft function; ECD, expanded criteria donor; NHBD, nonheart-beating donor; PNF, primary nonfunction.

[99]. In an excellent overview of principles, pathophysiological mechanisms and current techniques in abdominal organ preservation, Maathuis *et al.* question whether this method is able to prevent deterioration of organ quality in the present era of organ retrieval from older, more marginal and even NHBDs [100]. To improve organ viability further, a more dynamic preservation method is needed therefore the possibilities of machine perfusion (MP) are currently revisited. Since its clinical application by Belzer *et al.* in the late 1960s, retrospective studies have suggested that MP may result in better short-term outcome, with lower rates of DGF after transplantation of kidneys from standard and ECDs [101]. In an excellent state-of-the art overview, Taylor *et al.* list several benefits of MP over CS (Table 5) [102].

Only recently, an international, randomized, controlled trial was organized by Eurotransplant to compare CS with MP in 672 kidneys from 336 consecutive donors [103]. This Machine Perfusion Trial (MPT) demonstrated that MP reduced the incidence and duration of DGF and that machine-perfused renal allografts had an improved 1-year graft survival as compared with CS kidneys. Groen *et al.* could demonstrate that MP results in more life-years and quality adjusted life-years, reduced costs, and more favorable cost-effectiveness and cost-utility compared with CS [104]. Outcome data from this same MPT have been used also to conduct a comparative cost-effectiveness analysis based on preservation method for both standard criteria and ECD kidney transplants in the United States [105]. At 1-year post-transplant, machine perfusion was a more cost-effective option than cold storage for organ preservation in transplants involving either standard or ECD kidneys. Moreover, the cost-effectiveness ratios for transplants involving MP ECD kidneys were similar to those for transplants using CS standard criteria kidneys.

Since the mid-1990s, the Maastricht group and others have suggested intravascular resistance measurement and glutathione s-transferase release in the MP perfusate as kidney-viability testing tools [77,106], yet their use is limited, and their role in predicting kidney *in vivo* function and transplant outcome remains controversial.

True resuscitation, viability testing, and active biological modulation of an ischemically compromised graft may require not just oxygen and substrates offered by MP but also normothermia. Several European teams are actively exploring this technically challenging but potentially more effective new approach for kidney [107], liver [108,109], and lung [72,110,111] preservation. Normothermic MP is definitely much more than an alternative preservation method. It may be the storage method of choice in the future, not only because it is a superior method of preservation, but also because of its potential of resuscitation and prediction of post-transplant function.

Transplantation techniques to maximize use of available organs

Split liver transplantation

To expand the donor pool, the surgical technique of reduced liver transplantation first performed in 1984 [112] was modified to allow the transplantation of two recipients with one donor organ. For this purpose, the liver was divided into a left lateral lobe graft (segment II, III) typically for a pediatric and a remnant extended right lobe graft (segment I, IV–VIII) suitable for the transplantation of an adult recipient [113,114]. Besides this classical asymmetric split in later years, techniques for separating the liver into a full left lobe [segment (II–IV or I–IV)] and a full right lobe (segment I, VI–VIII or IV–VIII) were developed to serve two adult recipients with one donor liver (symmetric, true or full split technique) [115,116].

Two approaches are available to generate split-liver allografts: the *ex vivo* technique, in which the organ is removed from the donor and divided on the back table after the organ has been flushed and cooled, and the *in situ* technique, in which the dissection and parenchymal division is performed in the donor while the organs are still being perfused. *In situ* splitting has the advantage of avoiding prolonged cold ischemia time and rewarming during the bench procedure typical for ex vivo splitting [117].

Complications after split-liver transplantation (SLT) are in general similar to those of whole-organ liver transplantation with a slightly elevated rate of bile leaks [117,118].

Another typical complication that occurs more frequently with split grafts is the small-for-size syndrome (SFSS) [119].

In the early reports, results of split liver transplantation were poor [120], but meanwhile several reports of larger series of classical split liver transplants [121–124] including matched pair analyses [125] show comparable results of classical split and whole liver transplantation. Prerequisite for achieving these good results is careful donor and recipient selection and sufficient experience in split liver transplantation. Data on the short- and long-term results of true split transplants are sparse, but show that with highly selected donors acceptable short- and long-term results can be achieved [126].

Although split liver transplantation remains infrequent in the adult population, with only about 7.2% of all deceased donor liver transplants in 2009 in the Eurotransplant countries [9], it has become an increasingly frequent procedure in the young pediatric population, accounting for almost a third of all transplants in this recipient group [123]. If all suitable donor organs were split, waiting time for pediatric patients would substantially decrease [127] and thereby the need for performing living related liver transplants would be reduced significantly.

Single lung versus bilateral lung transplantation

Since the late 1980s, single lung transplantations (SLT) were successfully performed as an alternative procedure to bilateral lung transplantation (BLT) [128]. Typically, SLT is performed in patients with a diagnosis of either chronic obstructive pulmonary disease (COPD) or idiopathic pulmonary fibrosis (IPF). An argument in favor of single-lung transplantation are some reports showing perioperative and early postoperative survival advantage of single versus double lung transplantation [129,130]. More recent data indicate that with increased experience in the management of recipient in the early phase after lung transplantation, the perioperative risk is similar for SLT and BLT. Today, long-term survival is substantially better in double lung transplant recipients and BOS develops less frequently in these patients [131–133]. This has resulted in an ethical dilemma of either using one donor for a BLT transplanting only one patient or performing two SLT helping two patients with on the other hand reduced long-term outcome. In view of the current donor shortage, some authors still advocate SLT, especially for patients with IPF [134], others are more reserved and either rather recommend BLT (especially for patients with COPD) [131] or suggest to conduct a randomized trial to identify the optimal treatment strategy for these patient groups [133]. In clinical reality a continuous shift toward BLT has already taken place over the last years [135]. Nevertheless, SLT can still be considered a valuable option for selected recipients and in situations where only one lung of a donor is suitable for transplantation.

Domino transplantation

The use of explanted livers for transplantation from patients who themselves underwent liver transplantation was first performed in Portugal in 1995 [136]. This technique has been named ''domino liver transplantation (DLT)'' and can be considered in patients with selected genetic or biochemical disorders. The liver must be fully functional and the genetic defect should recur in the recipient with a sufficient latency period [137]. The classical indication fulfilling these criteria is familial amyloidotic polyneuropathy (FAP) [138].

Domino liver transplantation is justified for patients who have a live expectancy that is shorter than the time needed to develop disease symptoms, either due to their age or the underlying disease. Therefore, the procedure is typically performed in recipients older than 60 years or with malignancies such as hepatocellular carcinoma [139]. The Familial Amyloidotic World Transplant Register (FAPWTR) and the Domino Liver World Transplant Register (DLTR) are two registers containing data on transplanted FAP patients and on domino liver transplant recipients. As of 31.12.2009, a total of 790 DLT have been registered, the largest number (371) of this type of transplants has been performed in Portugal. DLTR data on survival and cause of death of domino liver transplant recipients show results comparable with other deceased donor liver transplants, especially when taking into account the recipient age and the underlying diseases of the recipients [139]. The procedure does not add any additional risk to the donor as compared with the risk of a conventionally performed transplantation.

In summary, the domino liver procedure has become a useful tool to increase the supply of livers available for transplantation especially in areas where FAP is endemic like Portugal.

Organ-allocation-related options to reduce organ discard rates and to improve transplant outcomes

As described in chapter 4, the disparity between organ availability and the growing demand for transplantation has motivated most organ procurement organizations to broaden the strict criteria for organ reporting to the transplant programs. Older donors and other extended criteria donors are therefore offered more often to the transplant centers now. In fact, the most rapid numerical increase in donation during the last decade has been in

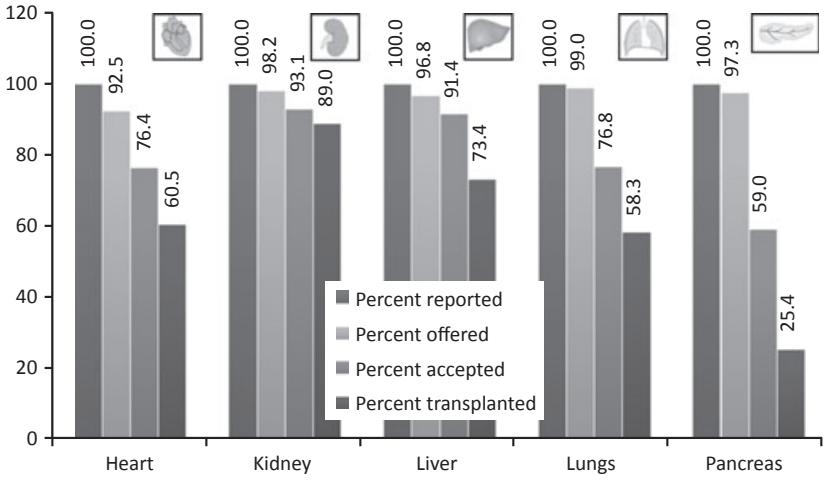

Figure 8 Organ transplant realization rate: Organs offered, accepted and transplanted as fraction of all reported deceased donor organs – Eurotransplant 2006.

ECD, both in the Eurotransplant countries and in the US [140]. This worsening of the donor profile raises the pressure on organ allocation organizations to minimize the organ discard rates. Unfortunately, reliable data on the organ discard rates in the different European countries are not available. Figure 8 depicts the transplant realization rate for all organs reported to Eurotransplant in 2006, showing the fraction of all reported organs that were offered and accepted as well as those that were finally transplanted. Discard rates vary substantially from organ to organ and are the highest for pancreas. Experiences in the US suggest that with the increased reporting of organs form ECD, discard rates tend to increase [141]. Several modified allocation protocols established by the different European organ exchange organizations (EOEO) aim at reducing this discard rate:

By introducing and documenting detailed donor-specific recipient profiles, it is possible to offer donor organs from ECD only to those recipients who are suitable for these donor organs and have previously indicated to be willing to accept these organs. This approach will be the more successful, the larger the potential recipient pool. Therefore, structured regional and national organ sharing has been established that aims at allocating organs that would otherwise be discarded, because no suitable recipient could be found in the donor center or region. The SITF Project (Innovative strategies to expand cadaveric donor pool for liver transplantation), a network between Italian transplantation centers to improve the use of split livers is an example of such cooperation [142]. In fact, the previously described Eurotransplant Senior Program for the allocation of kidneys of donors older than 65 years to recipients older than 65 years can be regarded as a large-scale approach to match ECD organs to suitable recipients better.

Another option to prevent discarding suitable donor organs is the establishment of a rescue allocation policy. In the Eurotransplant countries, allocation can be switched from the classical patient-oriented scheme to rescue allocation in case of impending organ loss due to either donor instability or difficulty to allocate the donor organ based on medical reasons related to the donor. In practice, rescue allocation is started if an organ offer has been turned down three times (five times for kidneys) from different transplant centers for donor or organ quality reasons. The major feature of this rescue allocation policy is that the offers are no longer made to individual patients but to the transplant center, where any listed recipient can be selected from the local waiting list [143,144]. Obviously, such a rescue allocation policy is of special relevance for organizations with otherwise patient-oriented organ allocation. This rescue allocation policy turned out to be quite effective, more than 50% of the ECD organs that had been turned down several times by different transplant centers could ultimately be allocated successfully and were used for transplantation [144].

The exchange of organs is often not limited to organs that would otherwise be discarded. In most countries, rules for mandatory exchange between centers or regions are established to help special vulnerable patients groups like children, highly urgent or highly immunized patients. In addition, mandatory exchange targets at achieving optimal donor and recipient matching to improve long-term outcome of organ transplantation. HLA-matching, has a significant influence on kidney graft survival [145–150], therefore the achievement of an optimal HLA-compatibility between donor and recipient has traditionally been an aim of organ exchange organizations.

These benefits of cooperation (Table 6) within a country can be further enhanced if the exchange of organs is extended beyond country borders. The most prevalent type of international cooperation between the different countries and their organ exchange organizations is based on the principles of the above described rescue allocation

Table 6. Benefits of international cooperation in organ transplantation.

Preventing organ loss
Addressing the needs of special patient groups
Improving the outcome of organ transplantation
International harmonization of activities in organ donation and transplantation
Scientific cooperation in the area of transplantation

Table 7. Levels of international cooperation in organ transplantation.

No cooperation – isolation
Exchange of organs in case there is no suitable recipient in the donor country
Cooperation for special patient groups
Optional organ exchange
Mandatory organ exchange
Common waiting list with harmonized allocation rules
With national balancing rules
Without national balancing rules

policy. Most EOEOs have agreed upon a loose form of cooperation to facilitate exchange of otherwise lost organs even across borders. In case an organ can not be allocated within the area of an EOEO, the donor organ is offered to other neighboring organizations. Allocation follows the first come first serve principle, the OEO transplant center that accepts the donor organ first, receives first the organ for transplantation.

In some European areas, a more structured international cooperation has been developed with the establishment of multinational EOEOs: England, Scotland, Wales, and Northern Ireland cooperate in what was formally known as ''UK-Transplant'' [now part of National Health Service Blood and Transplant (NHSBT)]. Denmark, Finland, Iceland, Norway, and Sweden participate in Scandiatransplant [151], an organization established in 1969, and Austria, Belgium, Croatia, Germany, Luxemburg, the Netherlands, and Slovenia are linked together via Eurotransplant, an organization founded in 1967. Within each of these different multinational EOEOs, rules for mandatory organ exchange have been developed to address the needs of special patient groups and to improve transplant outcome [152]. The Eurotransplant kidney allocation system (ETKAS) goes even a step further with the establishment of a common multinational waiting list for patients from all participating countries [153]. Due to this international cooperation, the median waiting time of highly urgent liver transplant recipients can be kept as low as 2 days in the Eurotransplant area and full HLA-A,B,DR-matching can be achieved in more than 20% of the kidney recipients receiving their organ via standard allocation. To prevent an unacceptable mismatch in organ exchange between the countries of such a multinational organ exchange organization that could easily result in case of different organ donation rates per country, specific balancing rules between the countries are typically established.

With the implementation of the EU Directive on standards of quality and safety of human organs intended for transplantation, it is expected that the different forms of international organ exchange (Table 7) will be further facilitated with increasing donor quality and safety resulting from clearly defined standards for organ characterization on the one hand and an international cooperation for organ vigilance on the other hand.

Summary

Professionalization of donor identification and management including the establishment of in-house transplant coordinators is currently considered in most European countries the most promising approach for further fostering organ donation and transplantation. The careful evaluation and broader use of extended criteria donors like older donors and nonheart beating donors together with tailored allocation mechanisms including international cooperation have in the past years resulted in a substantial increase in the donor pool and will contribute also in the future to address the organ need. The most controversial and emotionally discussed approach at least for countries with an informed consent system is a change in legislation with the move towards a presumed consent system. Available evidence shows that such a change has a positive albeit limited effect on organ availability. Perhaps the biggest risk associated with this approach is that it could distract discussion and efforts from the other well defined measures to improve organ donation. Therefore, it is important to keep in mind that any legal environment – whether based on presumed, informed or explicit consent – that shifts the burden of a decision on donation from grieving relatives to the deceased himself will most probably be an efficient one.

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References

1. Matesanz R, ed. *International Figures on Organ Donation and Transplantation – 2008*. Madrid, Spain: Aula Medica Ediciones, 2009: 60 pp.
2. Eurotransplant International Foundation Annual Report 2008. Eds. Oosterlee A, Rahmel A. Leiden, the Netherlands: 76 pp.
3. Roels L, Spaight C, Smits J, Cohen B. Donation patterns in four European countries: data from the donor action database. *Transplantation* 2008; **86**: 1738.
4. Nys H. Removal of organs in the EU. *European Ethical-Legal Papers* 2007; **4**: 50.
5. Rithalia A, McDaid C, Suekarran S, Myers L, Sowden A. Impact of presumed consent for organ donation on donation rates: a systematic review. *BMJ* 2009; **338**: a3162.
6. Gevers S, Janssen A, Friele R. Consent systems for post mortem organ donation in Europe. *Eur J Health Law* 2004; **11**: 175.
7. Roels L, Vanrenterghem Y, Waer M. Three years of experience with ''presumed consent'' legislation in Belgium: its impact on multi-organ donation in comparison with other European countries. *Transplant Proc* 1991; **23**: 903.
8. Roels L, de Meester J. The relative impact of presumed-consent legislation on thoracic organ donation in the Eurotransplant area. *J Transpl Coord* 1996; **6**: 174.
9. Eurotransplant International Foundation Annual Report 2009. Eds. Oosterlee A, Rahmel A. Leiden, the Netherlands: 96 pp.
10. Gimbel RW, Strosberg MA, Lehrman SE, Gefenas E, Taft F. Presumed consent and other predictors of cadaveric organ donation in Europe. *Prog Transplant* 2003; **13**: 17.
11. Abadie A, Gay S. The impact of presumed consent legislation on cadaveric organ donation: a cross-country study. *J Health Econ* 2006; **25**: 599.
12. Mossialos E, Costa-Font J, Rudisill C. Does organ donation legislation affect individuals' willingness to donate their own or their relative's organs? Evidence from European Union survey data. *BMC Health Serv Res* 2008; **8**: 48.
13. Directive 2010/53/EU of the European Parliament and of the Council on standards of quality and safety of human organs intended for transplantation. http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:32010L0045(01):EN:HTML (accessed January 14, 2011).
14. Action Plan on Organ Donation and Transplantation (2009–2015): Strengthened Cooperation between Member States. {COM(2008) 818 final} {SEC(2008)2956} {SEC(2008)2957}, online accessible: http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=COM:2008:0819:FIN:EN:HTM (accessed January 14, 2011).
15. Dominguez-Gil B, Martin MJ, Valentin MO, *et al.* Decrease in refusal to donate in Spain despite no substantial change in the population's attitude towards donation. *Organs, Tissues & Cells* 2010; **13**: 17.
16. Morgan SE. The intersection of conversation, cognitions, and campaigns: the social representation of organ donation. *Communication Theory* 2009; **19**: 29.
17. Matesanz R, Miranda B. Organ donation – the role of the media and of public opinion. *Nephrol Dial Transplant* 1996; **11**: 2127.
18. Matesanz R. Organ donation, transplantation, and mass media. *Transplant Proc* 2002; **35**: 987.
19. Krekula LG, Malenicka S, Tibell A. From word to action – influence of two organ donation campaigns on knowledge and formal decision making. *Clin Transpl* 2009; **23**: 343.
20. Coppen R, Friele RD, Gevers SKM, van der Zee J. Donor education campaigns since the introduction of the Dutch organ donation act: increased cohesion between campaigns has paid off. *Transpl Int* 2010; **23**: 1239.
21. Schulz PJ, Nakamoto K, Brinberg D, Haes J. More than nation and knowledge: cultural micro-diversity and organ donation in Switzerland. *Patient Educ Couns* 2006; **64**: 294.
22. Piccoli GB, Soragna G, Putaggio S, *et al.* Efficacy of an educational programme for secondary school students on opinions on renal transplantation and organ donation: a randomized controlled trial. *Nephrol Dial Transplant* 2006; **21**: 499.
23. Canova D, de Bona M, Rumiati R, *et al.* Understanding of and attitude to xenotransplantation among Italian university students: impact of a 3-yr university course. *Xenotransplantation* 2006; **13**: 264.
24. Alarcón R, Blanca MJ, Frutos MA. Assessment of an educational program for adolescents about organ donation and transplantation. *Transplant Proc* 2008; **40**: 2877.
25. Manyalich M, Paredes D, Ballesté C, Menjívar A. The PIERDUB project: International Project on Education and Research in Donation at University of Barcelona: training university students about donation and transplantation. *Transpl Proc* 2010; **42**: 117.
26. Pelleriaux B, Roels L, van Deynse D, Smits J, Cornu O, Delloye C. An analysis of critical care staff's attitudes to donation in a country with presumed-consent legislation. *Prog Transplant* 2008; **18**: 173.
27. Siminoff LA, Arnold RM, Caplan AL. Health care professional attitudes toward donation: effect on practice and procurement. *J Trauma* 1995; **39**: 553.

28. Paez G, Valero R, Manyalich M. Training of health care students and professionals: a pivotal element in the process of optimal organ donation awareness and professionalization. *Transplant Proc* 2009; **41**: 2025.
29. Shafer TJ, Wagner D, Chessare J, *et al.* US organ donation breakthrough collaborative increases organ donation. *Crit Care Nurs Q* 2008; **31**: 190.
30. Polak W, Chudoba P, Patrzalek D, Szyper P. How local transplant coordinators might increase the number of potential donors: our experience in Lower Silesia. *Transplant Proc* 2000; **32**: 68.
31. Pokorna E, Vitko S, Ekberg H. Medical-record review of potential donor pool in the Czech Republic suggests a possible increase to more than double the number of donors. *Transpl Int* 2003; **16**: 633.
32. Bozzi G, Matesanz R, Saviozzi A, RossiFerrini P. Summary: the quality improvement program in organ donation of the Tuscany region. *Transplant Proc* 2004; **36**: 424.
33. Blok GA, van Dalen J, Jager KJ, *et al.* The European Donor Hospital Education Programme (EDHEP): addressing the training needs of doctors and nurses who break bad news, care for the bereaved, and request donation. *Transpl Int* 1999; **12**: 161.
34. Blok GA, Morton J, Morley M, Kerckhoffs CCJM, Kootstra G, van der Vleuten CPM. Requesting organ donation: the case of self-efficacy – effects of the European Donor Hospital Education Programme (EDHEP). *Adv Health Sci Educ Theory Pract* 2004; **9**: 261.
35. Wight C, Cohen B, Roels L, Miranda B. Donor Action: a quality assurance program for intensive care units that increases organ donation. *J Intensive Care Med* 2000; **15**: 104.
36. Roels L, Cohen B, Gachet C, Miranda BS. Joining efforts in tackling the organ shortage: the Donor Action experience. *Clin Transpl* 2002: 111.
37. Alonso M, Fernández M, Mataix R, *et al.* Donor action in Spain: a program to increase organ donation. *Transplant Proc* 1999; **31**: 1084.
38. Patrzalek D, Plaksej R, Zaleska P, *et al.* Donor Action Program in Poland – first results. *Polski Przeglad Chirurgiczny* 2002; **74**: 324.
39. Roels L, Patrzalek D, Cohen B, Gachet C, Wight C. Non-exploited potential for organ donation: donor action pre intervention data and the Polish case. *Transplant Proc* 2003; **35**: 1159.
40. Höckerstedt K, Heikkiläl M, Holmberg C. Substantial increase in cadaveric organ donors in hospitals implementing the donor action program in Finland. *Transplant Proc* 2005; **37**: 3253.
41. Nowikowska AM, Milecka A, Sledzinski Z, Rudkowski B. The influence of Donor Action program on increasing organ and tissue donation in Pomerania region. *Transpl Int* 2005; **18**: 262.
42. Tuppin P, Maroudy D, Gachet C, Roels L. Boosting donation rates by implementing Donor Action in France. *Transplantation* 2006; **82**: 663.
43. Falaschini A, Bonnano MC, Delvecchio C, Ridolfi L. Activity results after 10 years of a Donor Action program in the Emilia-Romagna region. *Organs, Tissues & Cells* 2009; **12**: 125.
44. Matesanz R. *International Figures on Organ Donation and Transplantation – 2007*. Madrid, Spain: Aula Medica Ediciones, 2008: 56 pp.
45. Jambou P, Demont F, Henceler J, *et al.* Substantial increase in cadaveric organ donors in hospitals implementing the Donor Action (DA) program. *Organs, Tissues & Cells* 2009; **12**: 125.
46. Roels L, Spaight C, Smits J, Cohen B. Critical Care staffs' attitudes, confidence levels and educational needs correlate with countries' donation rates: data from the Donor Action database. *Transpl Int* 2010; **23**: 842.
47. Kauffman HM, Bennet LE, McBride MA, Ellison MD. The expanded donor. *Transplant Rev* 1997; **11**: 165.
48. Port FK, Bragg-Gresham JL, Metzger RA, *et al.* Donor characteristics associated with reduced graft survival: an approach to expanding the pool of kidney donors. *Transplantation* 2002; **74**: 1281.
49. de Fijter JW. An old virtue to improve senior programs. *Transpl Int* 2009; **22**: 259.
50. Chapman J, O'Connell P, Nankivell B. Chronic renal allograft dysfunction. *J Am Soc Nephrol* 1996; **7**: 1106.
51. Smits JMA, Persijn GG, van Houwelingen HC, Claas FHJ, Frei U. Evaluation of the Eurotransplant Senior Program. The results of the first year. *Am J Transplant* 2002; **2**: 664.
52. Cohen B, Smits JM, Haase B, Persijn G, Vanrenterghem Y, Frei U. Expanding the donor pool to increase renal transplantation. *Nephrol Dial Transplant* 2005; **20**: 34.
53. Frei U, Noeldeke J, Machold-Fabrizii V, *et al.* Prospective age-matching in elderly kidney transplant recipients – a 5-year analysis of the Eurotransplant Senior Program. *Am J Transplant* 2008; **8**: 50.
54. Pascual J, Zamora J, Pirsch JD. A systematic review of kidney transplantation from expanded criteria donors. *Am J Kidney Dis* 2008; **52**: 553.
55. Popper H. Aging and the liver. *Prog Liver Dis* 1986; **8**: 659.
56. Yersiz H, Shaked A, Olthoff K, *et al.* Correlation between donor age and the pattern of liver graft recovery after transplantation. *Transplantation* 1995; **60**: 790.
57. Adam R, Sanchez C, Astarcioglu I, Bismuth H. Deleterious effect of extended cold ischemia time on the posttransplant outcome of aged livers. *Transplant Proc* 1995; **27**: 1181.
58. Ploeg RJ, D'Alessandro AM, Knechtle SJ, *et al.* Risk factors for primary dysfunction after liver transplantation – a multivariate analysis. *Transplantation* 1993; **55**: 807.
59. Briceño J, Marchal T, Padillo J, Solórzano G, Pera C. Influence of marginal donors on liver preservation injury. *Transplantation* 2002; **74**: 522.

60. Busuttil RW, Tanaka K. The utility of marginal donors in liver transplantation. *Liver Transpl* 2003; **9**: 651.
61. Attia M, Silva MA, Mirza DF. The marginal liver donor – an update. *Transpl Int* 2008; **21**: 713.
62. Feng S, Goodrich NP, Bragg-Gresham JL, *et al.* Characteristics associated with liver graft failure: the concept of a donor risk index. *Am J Transplant* 2006; **6**: 783.
63. Durand F, Renz JF, Alkofer B, *et al.* Report of the Paris consensus meeting on expanded criteria donors in liver transplantation. *Liver Transpl* 2008; **14**: 1694.
64. DePasquale NP, Burch GE. How normal is the donor heart? *Am Heart J* 1969; **77**: 719.
65. Wittwer T, Wahlers T. Marginal donor grafts in heart transplantation: lessons learned from 25 years of experience. *Transpl Int* 2008; **21**: 113.
66. de Perrot M, Waddell TK, Shargall Y, *et al.* Impact of donors aged 60 years or more on outcome after lung transplantation: results of an 11-year single-center experience. *J Thorac Cardiovasc Surg* 2007; **133**: 525.
67. Botha P. Extended donor criteria in lung transplantation. *Curr Opin Organ Transplant* 2009; **14**: 206.
68. Meers C, van Raemdonck D, Verleden GM, *et al.* The number of lung transplants can be safely doubled using extended criteria donors; a single-center review. *Transpl Int* 2010; **23**: 628.
69. van Raemdonck DEM, Verleden GM, Coosemans W, *et al.* How to increase the donor pool? *Eur Respir Mon* 2009; **45**: 1.
70. Hornby K, Ross H, Keshavjee S, Rao V, Shemie SD. Non-utilization of hearts and lungs after consent for donation: a Canadian multicentre study. *Can J Anaesth* 2006; **53**: 831.
71. Aigner C, Winkler G, Jaksch P, *et al.* Extended donor criteria for lung transplantation – a clinical reality. *Eur J Cardiothorac Surg* 2005; **27**: 757.
72. Neyrinck A, Rega F, Jannis N. *Ex vivo* reperfusion of human lungs declined for transplantation: a novel approach to alleviate donor organ shortage? *J Heart Lung Transplant* 2004; **23**: S173.
73. Steen S, Ingemansson R, Eriksson L, *et al.* First human transplantation of a nonacceptable donor lung after reconditioning *ex vivo*. *Ann Thorac Surg* 2007; **83**: 2191.
74. van Raemdonck D, Neyrinck A, Verleden GM, *et al.* Lung donor selection and management. *Proc Am Thorac Soc* 2009; **6**: 28.
75. Booster MH, Wijnen RM, Ming Y, Vroemen JP, Kootstra G. *In situ* perfusion of kidneys from non-heart-beating donors: the Maastricht protocol. *Transplant Proc* 1993; **25**: 1503.
76. Wijnen RM, Booster MH, Stubenitsky BM, de Boer J, Heineman E, Kootstra G. Outcome of transplantation of non-heart-beating donor kidneys. *Lancet* 1995; **345**: 1067.
77. Daemen JW, Oomen AP, Janssen MA, *et al.* Glutathione S-transferase as predictor of functional outcome in transplantation of machine-preserved non-heart-beating donor kidneys. *Transplantation* 1997; **63**: 89.
78. Kootstra G, Daemen JH, Oomen AP. Categories of non-heart-beating donors. *Transplant Proc* 1995; **27**: 2893.
79. Brook NR, Waller JR, Nicholson ML. Nonheart-beating kidney donation: current practice and future developments. *Kidney Int* 2003; **63**: 1516.
80. Kootstra G, van Heurn E. Non-heartbeating donation of kidneys for transplantation, Nature clinical practice. *Nephrology* 2007; **3**: 154.
81. Barlow AD, Metcalfe MS, Johari Y, Elwell R, Veitch PS, Nicholson ML. Case-matched comparison of long-term results of non-heart beating and heart-beating donor renal transplants. *Br J Surg* 2009; **96**: 685.
82. Devey L, Wigmore SJ. Non-heart-beating organ donation. *Br J Surg* 2009; **96**: 833.
83. Andrés A, Morales E, Vázquez S, *et al.* Lower rate of family refusal for organ donation in non-heart-beating versus brain-dead donors. *Transplant Proc* 2009; **41**: 2304.
84. Ysebaert D, van Beeumen G, de Greef K, *et al.* Organ procurement after euthanasia: Belgian experience. *Transplant Proc* 2009; **41**: 585.
85. Feng S. Donor intervention and organ preservation: where is the science and what are the obstacles? *Am J Transplant* 2010; **10**: 1155.
86. Pratschke J, Tullius SG, Neuhaus P. Brain death associated ischemia/reperfusion injury. *Ann Transplant* 2004; **9**: 78.
87. Bouma HR, Ploeg RJ, Schuurs TA. Signal transduction pathways involved in brain death-induced renal injury. *Am J Transplant* 2009; **9**: 989.
88. Snoeijs MGJ, van Heurn LWE, Buurman WA. Biological modulation of renal ischemia-reperfusion injury. *Curr Opin Organ Transplant* 2010; **15**: 190.
89. Wheeldon DR, Potter CD, Oduro A, Wallwork J, Large SR. Transforming the ''unacceptable'' donor: outcomes from the adoption of a standardized donor management technique. *J Heart Lung Transplant* 1995; **14**: 734.
90. Dictus C, Vienenkoetter B, Esmaeilzadeh M, Unterberg A, Ahmadi R. Critical care management of potential organ donors: our current standard. *Clin Transplant* 2009; **23**(Suppl. 21): 2.
91. Pennefather SH, Bullock RE, Mantle D, Dark JH. Use of low dose arginine vasopressin to support brain-dead organ donors. *Transplantation* 1995; **59**: 58.
92. Schnuelle P, Gottmann U, Hoeger S, *et al.* Effects of donor pretreatment with dopamine on graft function after kidney transplantation: a randomized controlled trial. *JAMA* 2009; **302**: 1067.
93. Novitzky D, Cooper DK, Wicomb WN. Endocrine changes and metabolic responses. *Transplant Proc* 1988; **20**: 33.
94. Novitzky D, Cooper DK. Results of hormonal therapy in human brain-dead potential organ donors. *Transplant Proc* 1988; **20**: 59.
95. Cooper DKC. Hormonal resuscitation therapy in the management of the brain-dead potential organ donor. *Int J Surgery (London, England)* 2008; **6**: 3.

96. Roels L, Pirenne J, Delooz H, Lauwers P, Vandermeersch E. Effect of triiodothyronine replacement therapy on maintenance characteristics and organ availability in hemodynamically unstable donors. *Transplant Proc* 2000; **32**: 1564.
97. Rosengard BR, Feng S, Alfrey EJ, *et al.* Report of the Crystal City meeting to maximize the use of organs recovered from the cadaver donor. *Am J Transplant* 2002; **2**: 701.
98. Rosendale JD, Kauffman HM, McBride MA, *et al.* Hormonal resuscitation yields more transplanted hearts, with improved early function. *Transplantation* 2003; **75**: 1336.
99. Southard JH, Belzer FO. Organ preservation. *Ann Rev Med* 1995; **46**: 235.
100. Maathuis MJ, Leuvenink HGD, Ploeg RJ. Perspectives in organ preservation. *Transplantation* 2007; **83**: 1289.
101. Wight JP, Chilcott JB, Holmes MW, Brewer N. Pulsatile machine perfusion vs. cold storage of kidneys for transplantation: a rapid and systematic review. *Clin Transplant* 2003; **17**: 293.
102. Taylor MJ, Baicu SC. Current state of hypothermic machine perfusion preservation of organs: the clinical perspective. *Cryobiology* 2009; **60**(3 Suppl.): S20.
103. Moers C, Smits JM, Maathuis MJ, *et al.* Machine perfusion or cold storage in deceased-donor kidney transplantation. *N Engl J Med* 2009; **360**: 7.
104. Groen H, Smits J, Treckmann J. Long term cost-effectiveness of hypothermic machine perfusion versus static cold storage in kidney transplantation. *Am J Transplant* 2009; **9**: 227.
105. Garfield SS, Poret AW, Evans RW. The cost-effectiveness of organ preservation methods in renal transplantation: US projections based on the machine preservation trial. *Transplant Proc* 2009; **41**: 3531.
106. Daemen JH, Heineman E, Kootstra G. Viability assessment of non-heart-beating donor kidneys during machine preservation. *Transplant Proc* 1995; **27**: 2906; discussion 2907.
107. Brasile L, Stubenitsky BM, Haisch CE, Kon M, Kootstra G. Repair of damaged organs *in vitro*. *Am J Transplant* 2005; **5**: 300.
108. Monbaliu D, Brassil J. Machine perfusion of the liver: past, present and future. *Curr Opin Organ Transplant* 2010; **15**: 160.
109. Vogel T, Brockmann JG, Friend PJ. *Ex-vivo* normothermic liver perfusion: an update. *Curr Opin Organ Transplant* 2010; **15**: 167.
110. Steen S, Liao Q, Wierup PN, Bolys R, Pierre L, Sjöberg T. Transplantation of lungs from non-heart-beating donors after functional assessment *ex vivo*. *Ann Thorac Surg* 2003; **76**: 244; discussion 252.
111. Rega FR, Jannis NC, Verleden GM, Lerut TE, van Raemdonck DEM. Long-term preservation with interim evaluation of lungs from a non-heart-beating donor after a warm ischemic interval of 90 minutes. *Ann Surg* 2003; **238**: 782; discussion 792.
112. Bismuth H, Houssin D. Reduced-size orthotopic liver graft in hepatic transplantation in children. *Surgery* 1984; **95**: 519.
113. Bismuth H, Morino M, Castaing D. Emergency orthotopic liver transplantation in two patients using one donor liver. *Br J Surg* 1989; **76**: 722.
114. Pichlmayr R, Ringe B, Gubernatis G. Transplantation of a donor liver to 2 recipients (splitting transplantation) – a new method in the further development of segmental liver transplantation. *Langenbecks Arch Surg* 1989; **373**: 127.
115. Yersiz H, Renz JF, Hisatake G, *et al.* Technical and logistical considerations of *in situ* split-liver transplantation for two adults: part I. Creation of left segment II, III, IV and right segment I, V-VIII grafts. *Liver Transpl* 2001; **7**: 1077.
116. Yersiz H, Renz JF, Hisatake G, *et al.* Technical and logistical considerations of *in situ* split-liver transplantation for two adults: part II. Creation of left segment I-IV and right segment V-VIII grafts. *Liver Transpl* 2002; **8**: 78.
117. Renz JF, Yersiz H, Reichert PR, *et al.* Split-liver transplantation: a review. *Am J Transplant* 2003; **3**: 1323.
118. Muiesan P, Vergani D, Mieli-Vergani G. Liver transplantation in children. *J Hepatol* 2007; **46**: 340.
119. Dahm F, Georgiev P, Clavien P. Small-for-size syndrome after partial liver transplantation: definition, mechanisms of disease and clinical implications. *Am J Transplant* 2005; **5**: 2605.
120. Broelsch CE, Emond JC, Whitington PF, Thistlethwaite JR, Baker AL, Lichtor JL. Application of reduced-size liver transplants as split grafts, auxiliary orthotopic grafts, and living related segmental transplants. *Ann Surg* 1990; **212**: 368; discussion 375.
121. de Ville Goyet J. Split liver transplantation in Europe – 1988 to 1993. *Transplantation* 1995; **59**: 1371.
122. Oswari H, Lynch SV, Fawcett J, Strong RW, Ee LC. Outcomes of split versus reduced-size grafts in pediatric liver transplantation. *J Gastroenterol Hepatol* 2005; **20**: 1850.
123. Yan J, Becker T, Peng C, Li H, Klempnauer J. Split liver transplantation: a reliable approach to expand donor pool. *HBPD Int* 2005; **4**: 339.
124. Decoster EL, Troisi R, Sainz-Barriga M, *et al.* Improved results for adult split liver transplantation with extended right lobe grafts: could we enhance its application? *Transplant Proc* 2009; **41**: 3403.
125. Wilms C, Walter J, Kaptein M, *et al.* Long-term outcome of split liver transplantation using right extended grafts in adulthood: a matched pair analysis. *Ann Surg* 2006; **244**: 865; discussion 872.
126. Azoulay D, Castaing D, Adam R, *et al.* Split-liver transplantation for two adult recipients: feasibility and long-term outcomes. *Ann Surg* 2001; **233**: 565.
127. Porta E, Cardillo M, Pizzi C, Poli F, Scalamogna M, Sirchia G. Split liver is an effective tool to transplant paediatric patients. *Transpl Int* 2000; **13**(Suppl. 1): S144.

128. The Toronto Lung Transplant Group. Unilateral lung transplantation for pulmonary fibrosis. *N Engl J Med* 1986; **314**: 1140.
129. Meyer DM, Edwards LB, Torres F, Jessen ME, Novick RJ. Impact of recipient age and procedure type on survival after lung transplantation for pulmonary fibrosis. *Ann Thorac Surg* 2005; **79**: 950; discussion 957.
130. Whelan TPM, Dunitz JM, Kelly RF, *et al.* Effect of preoperative pulmonary artery pressure on early survival after lung transplantation for idiopathic pulmonary fibrosis. *J Heart Lung Transplant* 2005; **24**: 1269.
131. Hadjiliadis D, Angel LF. Controversies in lung transplantation: are two lungs better than one? *Semin Respir Crit Care Med* 2006; **27**: 561.
132. Mason DP, Brizzio ME, Alster JM, *et al.* Lung transplantation for idiopathic pulmonary fibrosis. *Ann Thorac Surg* 2007; **84**: 1121.
133. Neurohr C, Huppmann P, Thum D, *et al.* Potential functional and survival benefit of double over single lung transplantation for selected patients with idiopathic pulmonary fibrosis. *Transpl Int* 2010; **23**: 887.
134. Rinaldi M, Sansone F, Boffini M, *et al.* Single versus double lung transplantation in pulmonary fibrosis: a debated topic. *Transplant Proc* 2008; **40**: 2010.
135. Christie JD, Edwards LB, Aurora P, *et al.* Registry of the International Society for Heart and Lung Transplantation: twenty-fifth official adult lung and heart/lung transplantation report – 2008. *J Heart Lung Transplant* 2008; **27**: 957.
136. Furtado A, Tomé L, Oliveira FJ, Furtado E, Viana J, Perdigoto R. Sequential liver transplantation. *Transplant Proc* 1997; **29**: 467.
137. Golling M, Singer R, Weiss G, *et al.* Sequential (domino) transplantation of the liver in a transthyretin-50 familial amyloid polyneuropathy. Special reference to cardiological diagnosis and complications. *Langenbecks Arch Surg* 2000; **385**: 21.
138. Azoulay D, Samuel D, Castaing D, *et al.* Domino liver transplants for metabolic disorders: experience with familial amyloidotic polyneuropathy. *J Am Coll Surg* 1999; **189**: 584.
139. Wilczek HE, Larsson M, Yamamoto S, Ericzon B. Domino liver transplantation. *J Hepatobiliary Pancreat Surg* 2008; **15**: 139.
140. Sung RS, Galloway J, Tuttle-Newhall JE, *et al.* Organ donation and utilization in the United States, 1997–2006. *Am J Transplant* 2008; **8**: 922.
141. Cecka JM, Cohen B, Rosendale J, Smith M. Could more effective use of kidneys recovered from older deceased donors result in more kidney transplants for older patients? *Transplantation* 2006; **81**: 966.
142. Santori G, Andorno E, Valente R, *et al.* Innovative strategies to expand cadaveric donor pool for liver transplantation (SITF project): a network between Italian transplantation centers supported by the Ministry of Health. *Transplant Proc* 2005; **37**: 2415.
143. Schemmer P, Nickkholgh A, Gerling T, Weitz J, Büchler MW, Schmidt J. Rescue allocation for liver transplantation within Eurotransplant: the Heidelberg experience. *Clin Transplant* 2009; **23**(Suppl. 21): 42.
144. Vinkers MT, Smits JM, Tieken IC, de Boer J, Ysebaert D, Rahmel AO. Kidney donation and transplantation in Eurotransplant 2006–2007: minimizing discard rates by using a rescue allocation policy. *Prog Transplant* 2009; **19**: 365.
145. Smits JM, de Meester J, Persijn GG, Claas FH, Vanrenterghem Y. Long-term results of solid organ transplantation. Report from the Eurotransplant International Foundation. *Clin Transpl* 1996: 109.
146. Smits JM, de Meester J, Persijn GG, Claas FH, van Houwelingen HC. The outcome of kidney grafts from multiorgan donors and kidney only donors. *Transplantation* 1996; **62**: 767.
147. Hata Y, Ozawa M, Takemoto SK, Cecka JM. HLA matching. *Clin Transpl* 1996: 381.
148. Morris PJ, Johnson RJ, Fuggle SV, Belger MA, Briggs JD. Analysis of factors that affect outcome of primary cadaveric renal transplantation in the UK. HLA Task Force of the Kidney Advisory Group of the United Kingdom Transplant Support Service Authority (UKTSSA). *Lancet* 1999; **354**: 1147.
149. Opelz G, Wujciak T, Döhler B, Scherer S, Mytilineos J. HLA compatibility and organ transplant survival. Collaborative Transplant Study. *Lancet* 1999; **1**: 334.
150. Opelz G, Döhler B. Effect of human leukocyte antigen compatibility on kidney graft survival: comparative analysis of two decades. *Transplantation* 2007; **84**: 137.
151. Madsen M, Asmundsson P, Brekke IB, *et al.* Scandiatransplant: thirty years of cooperation in organ transplantation in the Nordic countries. *Clin Transpl* 1998: 121.
152. Persijn GG. Allocation of organs, particularly kidneys, within Eurotransplant. *Hum Immunol* 2006; **67**: 419.
153. Mayer G, Persijn GG. Eurotransplant kidney allocation system (ETKAS): rationale and implementation. *Nephrol Dial Transplant* 2006; **21**: 2.