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Expanding donor pool

Deliverable 2.2: Position paper for expanding the donor pool

Work Package Leader: ONT. Spain

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Organizaçao Portuguesa de Transplantaçao	OPT	Portugal
UK Transplant	UKT	United Kingdom
Organización Nacional de Trasplantes	ONT	Spain

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I. INTRODUCTION

Since the first successful kidney transplant was performed in 1954 (1), organ transplantation has progressively become a health care practice of unequivocal importance. Kidney transplantation represents the best therapeutic option for patients with end stage renal disease, providing best outcomes in terms of survival (2), quality of life (3) and cost-effectiveness (4) than other renal replacement therapies. Liver, heart and lung transplantation represent an almost unique therapeutic alternative for patients with end stage liver, heart and lung failure, although liver transplantation has been also applied for the treatment of specific pathologies not causing end stage liver failure. Pancreas transplantation, in its different modalities, has become a solution to re-establish insulin secretion in selected diabetic patients aiming to improve patient survival and quality of life. Small bowel transplantation usually performed as a part of a multi-organ transplant is still a relatively rare procedure but aimed to solve life-limiting conditions.

Results with organ transplantation have also progressively improved over time, thank to the advance in surgical techniques, availability of new immunosuppressive drugs, and longer experience of the transplant surgical and medical teams. According to the OPTN/SDRD 2006 Annual report, in the USA, one, three and five-year unadjusted graft survival was 91%, 80%, and 70%, respectively, for kidney recipients of deceased non expanded criteria donors who received their grafts during the period 1999-2004. For the same follow-up periods, unadjusted graft survival for kidney recipients of expanded criteria donors was 82%, 68%, and 53% (5).

Improvement over time is apparent also regarding patient survival after liver transplantation. For instance, 3 year patient survival was 47.2% for patients transplanted in 1984-1987, increasing up to 76.6% for those patients receiving a liver during the period 2003-2005, according to the Spanish Liver Transplant Registry (6). Similar improved figures are drawn up by the European Liver Transplant Registry. While 10 year patient and graft survival were 36% and 31%, respectively for liver transplants performed during 1968 to 1988, the corresponding values were 60% and 51% for transplants performed after the year 1988 (7).

Half-life of adult heart transplanted patients during the years 1982 to 1988 was 8.2 years, reaching 10.2 years for those patients who received their grafts during the

period 1994 to 1998 and survival figures continue to improve, according to the International Registry of Heart and Lung Transplantation (8).

Many problems though ought to be solved in organ transplantation: grafts are mainly lost in the long-term due to the so called chronic rejection (chronic allograft nephropathy, chronic allograft vasculopathy, *obliterans bronchiolitis* syndrome) and death with a functioning graft, mainly due to cardiovascular pathology (9). Besides, short and long-term consequences of immunosuppression decrease longevity and quality of life of organ recipients.

Despite these problems, organ transplantation faces an even earliest barrier in the important gap existing between the number of patients waiting for a transplant and the number of patients who are indeed transplanted. This is due to the shortage of organs for transplantation in relation with organ demands. While the number of patients being included in the waiting list increases, the rate of donation and the number of organs available for transplantation does not increase or improves at a slower rate. Tables 1 and 2 show the evolution of the figures for patients admitted to the waiting list and grafted for both kidney and liver transplants, in some selected European countries from which there are data received by the Council of Europe since 1989 (10). It can be easily seen that the number of indications increased much more than the grafts performed.

Table 1. Kidney Transplants and Waiting List Patients

	1989		2005			
	WL	Tx	WL	Δ %	Tx	Δ %
France	4603	1957	5932	29	2572	31
Eurotransplant	9445	3172	11814	25	4242	34
Skandiatransplant	926	854	1333	44	954	12
U.K. /Ireland	3704	1960	7126	92	1984	1
Spain	5024	1039	4152	- 17	2200	112

Table 2. Liver Transplants and Waiting List Patients

	1989		2005			
	WL	Tx	WL	Δ %	Tx	Δ %
France	183	585	484	164	1024	75
Eurotransplant	180	499	2134	1085	1481	197
Skandiatransplant	21	65	120	252	257	295
U.K. /Ireland	51	298	390	664	661	122
Spain	90	170	605	572	1070	529

Data are presented as Waiting List Patients (absolute number on December 31st) and transplant patients (absolute annual number). Eurotransplant: Austria, Belgium, Germany, Luxembourg, Slovenia and The Netherlands. Population: 120 million inhabitants. France: Population: 61.8 million inhabitants. Skandiatransplant: Denmark, Finland, Norway and Sweden. Population: 24.2 million inhabitants. United of Kingdom + Ireland: Population: 63.0 million inhabitants. Spain: Population: 44.1 million inhabitants

A similar situation is drawn in the US. Table 3 represents the number of patients waiting for a solid organ transplant (11) and the number of organ transplants performed along the year 2006.

Table 3. Solid Organ Transplants performed during the year 2006 and Waiting List Patients (June 2007) in the US by type of organ. Number of transplants include those performed with living and deceased donors.

	Kidney	Liver	Pancreas	Kidney / Pancreas	Heart	Lung	Heart / Lung	Intestine
WL	72088	16865	1682	2344	2705	2721	118	230
Tx	17094	6650	463	924	2192	1405	31	175

The result of more patients joining the waiting list with a little increase in the number of patients transplanted is a longer time in the waiting list. Time waiting for a kidney transplant is expensive and has a negative impact on graft and patient survival (12). Besides, the number of patients who may die while waiting for a transplant may also increase.

This apparent shortage of organs for transplantation may be still underestimated, since the scarcity of organs precludes physicians from including more patients into the waiting lists.

The severe organ shortage for transplantation has several reasons. Demographic and socio-sanitary factors, as well as the legal and organizational background of a country may be related to the rate of donation. Any case, the majority of organ donors are patients who died in a hospital after a severe brain damage and can be diagnosed as having brain death. It has to be outlined that not more than 1% of death people and not more than 3% of the people who die in a hospital hits this situation. Therefore, the number of potential donors due to irreversible loss of brain functions is limited. Besides, the process of organ donation and procurement is a very delicate and complex one that implies the cooperation of many actors and can be broken at any time. Moreover it is subject to time pressure and should be done within few hours what enhances the weakness of the process itself. Two other origins of organs for transplantation have appeared as a real alternative to increase the donor pool: donors dead due to irreversible loss of cardio-respiratory functions, also referred as donors after cardiac death (DCDD) or non heart beating donors (NHBD) and living donors (LD).

The use of NHBD represents a potential way of significantly increasing the donor pool for specific organs, as kidney, liver and lung. However, the use of these organs is a more complex process than the use of organs from donors with brain death. It requires an adequate legal framework, as well as a careful examination of a country's ability and infrastructure and a continuous evaluation of results and research. In fact, the use of organs from NHBD is limited to some countries in the context of specifically designed programmes.

LD is an increasing alternative to face the scarcity of organs from deceased donors. Mostly kidney and liver, but also lung, pancreas and small bowel transplantation from living donors has been reported. Results with living kidney transplantation are even better than those achieved with kidneys from deceased donors (13) and with an apparent low risk of mortality for the donor, estimated on 0.03% (14). Results after living liver transplantation are not so good and risks for the donor are higher. This situation, along with the ethical implications of living donation, basically the violation of the traditional first rule in medicine, "*primum non nocere*" (above all, do not harm), has made that living donation is very variably implemented across the countries.

Since shortage of organs represents one of the most important problems in the field of organ transplantation, measures to increase the donor pool are imperative and should be developed in the three different origins of organs for transplantation:

donors with irreversible loss of brain functions, donors with irreversible loss of cardio-respiratory functions and living donors.

II. OBJECTIVES OF DELIVERABLE 2.2

The objective of deliverable 2.2. is to reflect a harmonized and common position of the consortium with regards to different types of initiatives to expand the donor pool and to maximize the potential of donation. Initiatives are discussed separately for the three different types of possible organ donors:

1. Deceased donors due to irreversible loss of encephalic functions or brain death donors or heart beating donors (HBD)
2. Deceased donors due to irreversible loss of cardio-respiratory function or non heart beating donors (NHBD)
3. Living donors (LD)

Initiatives may have the following nature:

1. Organizational initiatives
2. Human resources
3. Technical programmes
4. Training programmes
5. Financial initiatives

Legal and ethical initiatives targeted to increase the donor pool and to maximize the potential of donation are fully discussed within WP7.

III. METHODS

A specific questionnaire was designed in order to collect information on the different types of initiatives adopted or developed by the partners (Annex 1). A brief description if required was requested, since variations in the practical application of any of these initiatives were expected among the partners. Information on the usefulness of each specific initiative with regards to the expansion of the donor pool in each of the countries was also requested and graded as: not useful, little useful, useful or very useful. Also, information on the confirmation of the usefulness of the measure was requested. Unfortunately, the specific importance of an individual measure with regards to the expansion of the donor pool is difficult to evaluate and quantify from an evidence based approach.

After filling in this questionnaire an open discussion was developed in order to guarantee a detailed exchange of experiences and opinions among the partners.

IV. EXPANDING THE DONOR POOL: DONORS DEAD DUE TO IRREVERSIBLE LOSS OF ENCEPHALIC FUNCTIONS (BRAIN DEAD DONORS OR HEART BEATING DONORS)

1. THE PROCESS OF DONATION AFTER BRAIN DEATH

The donation process with donors, whose cause of death is the irreversible loss of brain functions, includes a series of sequential steps: donor identification, donor evaluation, donor maintenance, gathering consent and/or authorization to donation and organ retrieval, which are followed afterwards by allocation and transplantation of the removed organs (15). Some comments on the first steps of the process are displayed below in order to explain how potential donors or organs may be lost at every one of these steps.

1.1. Donor identification: All potential donors should be identified at the earliest stage as possible. This will facilitate donor evaluation and maintenance, but undoubtedly implies a proactive attitude at this first and crucial step.

1.2. Donor evaluation: The risk of transmission of a serious disease through organ transplantation (neoplasia or infection) from the donor to the recipient should be minimized. However, it must be ensured that only organs that should be discarded are so, avoiding an unjustified loss of organs. Guidance has been prepared by the Council of Europe and some member states on the serological and other screening methods that should be used to minimise the risk of transmission of infectious or malignant diseases to the recipient. Besides, a social history taken from the relatives must be enforced to exclude recent high risk behaviour, which might indicate a risk of a transmissible disease which is at too earlier stage to be detected by serological screening.

1.3. Donor maintenance: It is essential that organs are kept in adequate conditions before retrieval. The maintenance of the potential donor's physiological state while on intensive care and of the donor prior to and during retrieval can make a major difference to the condition of the organs. Poor donor maintenance can make organs unusable or increase the incidence of primary graft failure.

1.4. Consent/authorisation: Appropriate consent or authorisation has to be obtained before organs can be removed. Countries have different legal requirements with regards to consent to donate. While in some countries consent to donate is presumed, in others specific consent must be requested. However and from a practical point of view, in most of the European countries the family is always approached (ALLIANCE-O WP7), whether to find out what were the wishes of the deceased or to make a final decision in case those wishes were not known. Refusals to donate represent a very important barrier in the process of donation. Information on the rates of refusals to donate estimated over the number of families approached may be even well over 50% (10).

1.5. Organ retrieval: The surgical technique for removing organs from the body and the way those organs are subsequently handled and preserved prior to and during transportation are critical to the successful outcome of the transplant. Each year a number of organs are damaged during removal and/or transportation. Some can be repaired but a few will have to be discarded. Coordination of retrieval activities is needed to guarantee the success of the process.

1.6. Organ allocation: For some organs, particularly kidneys, hearts and paediatric organs, the successful long-term outcome of the transplant depends partly on appropriate matching between donor and recipient. A well-organised system for allocating and transporting donated organs in the most appropriate way is important. In some cases, optimum allocation will require exchange of organs between transplant organisations and countries. Co-operation between countries is increasingly important.

It is easy to understand that the process of donation and transplantation in the context of brain death is a delicate, complex and long one. The different steps are areas of potential losses of donors or organs for transplantation. Measures may be applied at every one of these areas in order to expand the donor pool and maximize the use of potential donors.

2. ORGANISATIONAL INITIATIVES TO EXPAND THE DONOR POOL AND TO MAXIMIZE THE POTENTIAL OF DONATION

Expanding the donor pool and maximizing the potential of donation should start by the development of an adequate organisational framework which supports,

monitors, and regulates the whole process of donation after brain death. The consortium agrees on the need of the following organizational initiatives as key issues:

- 2.1. Hospital transplant organization**
- 2.2. Network of transplant procurement hospitals**
- 2.3. Supra-hospital transplant organization¹**
- 2.4. Specific organisational programmes**

2.1. Hospital transplant organisation

The potential donors are to be found primarily in the intensive care units (ICU) of hospitals. Policies should be developed which encourage hospitals to engage actively in organ donation. With this aim, hospitals with an ICU should provide a team with the sufficient number of qualified professionals as well as the required structure. The first aim will be to develop a programme of proactive donor detection under the responsibility of a key individual ("Key donation person", see below), who should be in charge of:

- Development of a protocol for identifying potential donors, which includes events to be recorded and clarifies the roles and responsibilities of hospital professionals in donor identification
- Educational programmes for health staff about transplantation
- Auditing donor procurement and problems on a regular basis.

The profile and other responsibilities of the key donation person in the opinion of the consortium are described below (see Human resources).

2.2. Network of transplant procurement hospitals

With variations regarding the number of deaths and specific characteristics, every acute hospital of a specific city/ region /country should be able to detect brain death and activate the process of donation. The higher the number of hospitals implicated in the process of organ procurement, the higher the possibilities of increasing the potential of donation, provided that a well coordinated hospital procurement network exists.

¹ The term supra-hospital organization is intended to be a descriptive one. The following types of organizations would be included under this term: Organ procurement organization (OPO), organ exchange organization (OEO) and organ sharing organization (OSO).

The potential contribution to organ donation of small hospitals, defined as hospitals with no transplantation facilities, is sometimes underestimated. For instance, 40% of deceased donors in Spain are detected and referred by these 112 small hospitals, representing a deceased donation activity as high as 14 donors pmp, rate which is similar to the one described for several European countries as a whole. On the other hand, large hospitals (defined as those with procurement and transplantation facilities), in a number of 44 in the year 2007, contributed with 60 % of the deceased donation activity, this meaning a rate of 20 donors pmp, approximately. Therefore, the implication of acute small hospitals, as previously defined, on the process of organ donation through their incorporation to the organ procurement network should be considered as an outstanding organizational initiative, which is in fact lacking in some of our countries.

2.3. Supra hospital transplant organization

The need for a supra-hospital transplant organization is considered by the consortium as one of the basic organizational issues to guarantee the success of donation and transplantation. Although there is consensus on the need of this organisation, there is no single formula for its structure to ensure good results. It has been argued that the ideal situation is an integrated organisation that can support the whole process of organ donation and allocation. There is, however, an apparent contradiction, which must be recognised because it has implications for the optimum size and type of organisation. As far as organ sharing is concerned, and with some limitations (time, cost), it has been accepted that "the larger the pool of patients, the better the match" (15). Suitable organs cannot easily be found for urgent patients and "difficult" recipients (children, highly sensitised renal patients, and rare HLA types) within the scope of a small organisation. Such considerations point to a large organisation as the optimum model.

However, when it comes to maximising organ donation, there are data, which indicate the opposite is true, i.e. that smaller organisations are more effective than the bigger ones (15). This is thought to be due to a better knowledge of local factors, knowing and being able to influence the professionals involved and more direct accountability for the whole process. Large centralised organisations whose staff do not fully participate in the decision making process are generally strongly de-motivating and so would not readily promote increased organ donation. Moreover, there are those who would argue strongly that organs from deceased donors procured within a community should be considered assets of the community

and that the community rather than just the medical profession should determine their allocation through agreed criteria.

The majority of the countries have a national transplant organisation in charge of different types of responsibilities within the process of donation. However, there are also supra-hospital organizations in support for the process of donation which are in charge of several countries. This is the case of Eurotransplant, supporting the process of donation/transplantation for Austria, Belgium, Germany, Luxembourg, Slovenia and The Netherlands. Independently of the type of organisational solution, this structure should offer the possibility of ensuring a common approach and standards with sufficient local autonomy to maintain enthusiasm and efficiency.

The existence of different levels of transplant coordination inside a specific country is not a common structure to the countries among the consortium. For instance, a three level transplant coordinator network (national, regional and hospital) is only present in Italy and Spain, but not in other countries. The existence of the intermediate structure, the regional organization, could possibly be considered in some countries on the basis of local and individual needs.

Ideally, the supra-hospital transplant organisation should fulfil two functions. It should be in direct charge for organ sharing, even at an international level. In fact, exchange of organs among European countries has proven to be effective in maximizing the use of otherwise surplus organs. Besides, this organisation should provide an overall support to the donation/transplantation process, maximizing the supply of donor organs. In order to accomplish with this objective, ideally this organization should develop different kind of activities:

- Evaluation and proposal of legal measures when needed in order to cover the needs generated by the scientific advance in the field of organ donation and transplantation. This organization would therefore act as a real interface between the hospital day to day practice and the political level.
- Development of specific programmes (see below) to detect, evaluate and correct eventual problems in the whole process of donation at a hospital and/or regional level
- Promotion of research, education and training.

With the global aim of supporting all the process of donation, the supra-hospital organization should be interpreted as a tool to increase donor supply and maximize

the potential of donation within a specific geographical area, but also as a way to ensure the quality of the whole process.

2.4. Specific organizational programmes

2.4.1. Programmes for Donor process's evaluation

Every one of the steps of the process of donation and transplantation may be potential weak areas where efforts should be made to ensure that donors and organs are not lost and that every potential donor may become an actual donor. To have the possibility of acting at any of these steps, a continuous and detailed evaluation of the whole process of donation should be performed in the context of a programme with the following objectives:

- To define the theoretical capacity of organ procurement, depending on the characteristics of a hospital
- To detect any obstacle in the process of organ donation and procurement contributing to potential donor losses, as a tool to identify the improvement areas
- To describe hospital factors which can influence the donation and transplantation process

This programme should be based on the retrospective review of the medical charts of patients dying at the ICUs. This has been recognized as the most adequate methodology to evaluate the potential of donation and the performance in the process (16-18).

Some local and international programmes aimed to analyse the donor process evaluation have been implemented in countries within the consortium. The method of evaluation is mostly based on internal and/or external audits performed over deaths occurring at the ICUs of transplant procurement hospitals (16). Final data obtained from this kind of programmes include the number of deaths, brain deaths and organ donors obtained at every ICU. Taking into account local-hospital factors affecting every one of these numbers (available beds, neurosurgery procedures and patients admitted at the ICU and emergency rooms), a calculation of specific indexes of efficiency of the process may be calculated and compared with standard or reference values. Some of these indexes have been provided in WP 4 and in D 2.5 of this WP. Because of its widespread use, the conversion rate, defined as the

number of actual donors over the number of potential donors (brain deaths with no medical contraindications to donate) is considered by ALLIANCE-O consortium as one of the most useful indexes to evaluate and compare the efficiency of the procurement systems. A diagnosis of weak steps in the process which may be susceptible of being improved is then available. This information is the clue to establish measures for correction.

With the obvious limitations to establish a cause-effect relationship between one action and the rate of donation, some authors have already published the positive impact of the application of these programmes in the rate of effective organ donation (19).

The consortium agrees that the implementation of programmes for the evaluation of the donor process is one important organisational initiative in order to maximize the potential of donation, by providing the knowledge about the weak areas where corrective measures should be applied. Strategies aimed to analyse the cost-effectiveness of these programmes should also be developed.

2.4.2. Quality management programmes

A quality management approach should also be considered as a tool to increase the donor pool. It would be defined as a group of measures aimed to monitor, detect and correct any weakness in the complex process of donation/transplantation. Although this programme should start and end at a hospital level, it should be understood as a regional and/or national strategy, with coordinated and planned actions.

There are several problems to detect and susceptible to be corrected in donation/transplantation: insufficient identification of potential donors, imprecise application of medical contraindications to donation, inappropriate management of the donor, high rate of refusals to donate, inadequate retrieval of the organs, problems in organ allocation, inadequate management of the recipient and others.

Protocols to standardize procedures, monitoring of the performance through audits and introduction of corrective measures should be established. A quality management approach of the donation/transplantation process may be considered as an ideal way of optimizing the potential of donation and something that should be progressively implemented in the future.

2.4.3. Other organizational initiatives: exchanging experiences and sharing best practices

From a different perspective, one organizational approach to face and solve organ shortage is represented by the exchange of experiences on the basis of sharing the best practices in organ donation and transplantation. This approach is very well represented by the different European programmes which have been developed in the last years in the field of organ donation and that have indeed contributed to better identify common problems in the field and to common initiatives to deal mainly with organ shortage.

A similar organizational and well known approach has been developed in the US by the Health Authorities: the Organ Donation Breakthrough Collaborative Collaboratives (20), which are based on the spreading of known best practices to the nation's largest hospitals to increase organ donation rates. They represent an intensive, full-court-press to facilitate breakthrough transformations in the performance of organizations, based on what already works. They are designed to define, document, and disseminate good ideas, accelerate improvement, achieve results and build clinical leaders of change. Initial results of this initiative are indeed promising.

2.5. Final recommendations on organizational initiatives to increase the donor pool

a) Every hospital with intensive care unit facilities should be available to detect brain death and activate the donation process. Policies should be developed which encourage hospitals to engage actively in organ donation

b) A sufficient number of qualified personal and an adequate structure should exist at any procurement hospital in order to effectively develop the activities of donation.

c) A key donation person should be appointed in every acute hospital. The key donation person should have as a main responsibility a proactive donor detection programme.

d) A network of transplant procurement hospitals should be developed, where small hospitals are progressively being incorporated.

e) To optimise organ donation, there is need for a supra hospital transplant organisation, appropriate in size and structure to the local

situation with specific responsibilities for the whole process of organ procurement.

f) The most effective organisational approach balances the requirements for effective organ procurement (small/local) with those for organ allocation (large, national/ multinational). The aim should be to optimise organ procurement whilst ensuring the most clinically effective allocation of organs and tissues.

g) A donor process evaluation programme should be developed in order to estimate the potential of donation within a hospital and to identify areas of improvement in the process of donation, providing the basis to introduce corrective measures. Strategies to evaluate the cost-effectiveness of these programmes should also be developed.

h) A quality management approach of the process of donation/transplantation should be developed which establishes standardized protocols, evaluates performance and introduces measures to improve. Participation of hospitals in the donation process should be considered a quality issue.

3. HUMAN RESOURCES TO EXPAND THE DONOR POOL AND TO MAXIMIZE THE POTENTIAL OF DONATION

The number of persons implicated in the process of donation should be **enough to efficiently cover all the steps of the process**. Different figures may exist at two different levels: hospital and supra-hospital organization.

3.1. Human Resources at the Hospital level

3.1.1. Key donation person

The presence of the key donation person at the hospital level, with the main responsibility of developing a proactive donor detection programme represents the most important human figure to optimize organ donation (15). The role of this key donation person is now considered by many to be fundamental to improve donor detection rates. It is he/she who will be responsible for integrating the actions noted above: the development of donor detection programmes and specific protocols and defining local benchmark figures and targets for improvement. The appointment of such a person will make the difference between a successful and a non-successful donation programme.

Secondary responsibilities to be developed by this key figure would include the progressive involvement in training, education, promotion and research.

Including all these responsibilities and according to the donation and transplantation activities within a specific hospital, it seems more reasonable to talk about a team of persons in charge of donation than only referring to a sole figure. This team should include the sufficient number of qualified personal in order to efficiently develop the activities of donation.

While there is a universal agreement across the ALLIANCE-O countries on the need of the figure of the key donation person, there is not a clear position with regards to the profile of this figure, widely variable among the partners. As described in recommendations set by the Council of Europe in terms of donation and transplantation issues (15, 21), ideally, this figure should belong to the hospital staff (in-house coordinator) and be closely related to the intensive care units. For instance, in some countries the key donation persona is in fact an intensive care unit specialist. He/She should work in close relation, but independent from any transplant team (s) and report directly to the medical director of the institution and/or the supra-hospital transplant organization.

3.1.2. Other human resources at the hospital level

Donation is progressively becoming a more complex process due to the increase in the use of the so-called expanded criteria donors, migration phenomena and other circumstances. In order to efficiently cover the process and maximizing the potential of donation, other human figures are being progressively needed. Although not available in each of our countries, we may consider them as ideal figures for the process. Some examples are provided bellow:

- The activities of detection, evaluation and management of the donor make imperative the implication of several specialists and techniques (ICU doctors, anatomopathologists, immunologists, others). In general terms, a multidisciplinary group of physicians and techniques should be available at each procurement hospital. Their support in the process of donation should enhance the possibilities of highly efficient performance in the process and therefore will increase the possibilities of donation.
- Although not a direct measure to increase the donor pool, the presence of a multidisciplinary and expert team in charge of retrieval of different types of organs at a specific area could be considered as an indirect way of

maximizing the potential of donation and the use of organs for transplantation. The existence of these groups may shorten the period of donation, decreasing the possibilities of problems during the delicate phase of the maintenance of the donor. Even more, it could decrease the possibility of damaging organs during retrieval. Pilot experiences with this approach are being developed in UK and France. Also, in Spain, for liver and pancreas retrieval specific teams within an area are in charge which indeed facilitate the process.

- Since immigration and tourism justify an increasing number of non-national donors with different ethnicity, customs, beliefs and languages, the figure of the cultural mediator in order to facilitate the family approach could be considered. This figure may help non citizens families at a moment of grief, may facilitate the understanding and may be crucial in order to obtain a consent to donation.

3.2. Human Resources at the Supra-Hospital level

In order to fulfil with its responsibilities (see organizational issues), the transplant supra-hospital organization should also be provided with the enough number of qualified figures. These figures should be in charge of the development of well planned and integrated activities to efficiently support the process of donation and transplantation.

3.3. Final recommendations on human resources

a) The number of persons implicated in the process of donation at every procurement hospital should be enough to efficiently cover all the steps of the process

b) The presence of the key donation person at every hospital with acute care facilities, with the main responsibility of developing a proactive donor detection programme represents the most important human figure to optimize organ donation.

c) Other figures to support specific activities in the process of donation should be taken into consideration.

d) A suprahospital, well organized team should exist, composed by the enough number of and sufficiently prepared figures to enforce and develop strategies to support all the process of organ donation.

4. TECHNICAL PROGRAMMES

4.1.Special Technical programmes

The shortage of organs has made the transplant groups and organizations to search for technical alternatives to maximize the potential of the already donated organs. Among the different special programmes or techniques, we should emphasize the following:

- Split liver transplantation
- Domino liver transplantation
- Double kidney transplantation
- Other: heart domino transplantation, en bloc double kidney transplantation from paediatric donors

4.1.1. Split liver transplantation

Splitting a liver allograft coming from an adult donor into two hemi-livers was initially applied to increase the possibilities of transplantation among paediatric patients. Pichlmayr reported the first clinical attempt of split liver transplantation in 1988 (22), but it was one year later when a split liver transplantation solved the situation of two patients with fulminant hepatic failure (23). After this first successful experience, the poor results obtained in a series of 30 split liver transplants performed in 21 children and 5 adults generated scepticism on this technique (24). Posterior efforts on the selection of the patients and the technical procedure gave as a result the transplantation of 98 patients out of 50 donated livers, represented in the *European Split Liver Registry*, which demonstrated no significant differences between split liver transplantation and conventional whole size liver transplantation (25). Since then, other multiple unicenter experiences have converted the split liver transplantation into a mature technique with comparable results to those obtained with conventional liver transplantation (26).

The initial aim of split liver transplantation as well as other reduced-size liver techniques was to benefit paediatric patients, who have a difficult access to transplantation due to the need of finding a size-matched liver graft. In

comparison with other reduced-size liver techniques, split liver transplantation deals with the problem of matching the size of the organ to the recipient, but also provides a solution to two recipients, usually an adult and a paediatric one.

However, the increasing disparity between the adult donor supply and demand has stimulated interest in extension of split liver to benefit two adults. A variation of the initial surgical technique, splitting the graft into a full left lobe and a full right lobe was reported to be suitable for two adult recipients (27, 28).

The results of split liver transplantation seem to be affected by the method used. Liver splitting was initially performed *ex situ*. With an increasing experience in living liver donation, splitting a liver turned to be an *in situ* procedure in the deceased donor (29). The *in situ* technique offers the advantage of diminishing the cold ischemia time and a lower incidence of bile leakage and haemorrhage from the cutting surface. However, it is a time-consuming technique that deserves coordination with other organ retrieval teams and provides an extra burden to the procuring hospital. These disadvantages of the *in situ* technique, as well as the need of a highly skilful surgeon in splitting a liver *in situ*, have led some groups to return to the *ex situ* or bench splitting technique.

Selection of the liver grafts suitable for splitting has been a matter of research. Demographic and clinical characteristics of the donor, besides a macroscopic observation and histological evaluation of the liver are considerations to keep in mind before accepting a liver graft to be splitted. The success of split liver transplantation is also based on an appropriate selection and management of the recipient (30).

Therefore and although the impressive results obtained with split liver transplantation in the last years, its success is based on a careful donor and recipient selection, a good knowledge of the liver anatomy, excellent surgical skills and meticulous postoperative management. On the other hand, it represents a real way of expanding the number of livers available for transplantation. For instance, some countries, as Germany, Italy and UK have been able to perform a large number of liver transplants with this technique (Table 4). In this context, the consortium thinks that split liver transplantation represents a real way to increase the donor pool in the sense that maximizes the use of the available donors and increases the opportunities of transplantation. This importantly applies specially to the paediatric population waiting for a liver transplant. In order to guarantee the

success of this type of programmes, **consensus documents and guidelines** could be helpful, based on the available evidence and describing the process of selecting the donor, adequating the recipient and the surgical technique. On the other hand, a continuous evaluation of results of split liver transplant programmes through **registries** is needed, providing the tool to analyze the results of split liver programmes.

4.1.2. Domino liver transplantation

One creative way to address the shortage of livers available for transplantation is the “domino” procedure. In a domino liver transplant, a liver that needs to be removed in one patient is transplanted into a second patient who also needs a liver. Although quantitatively limited, the domino technique has been also applied to heart transplantation. Domino liver transplantation has been mainly applied to familial amyloidotic polyneuropathy (FAP) (31), a rare disorder in which the liver produces an abnormal protein that damages the heart, the neurological system and the gastrointestinal tract. Apart from this abnormality, the rest of the liver functions are well preserved. The only effective treatment available for FAP is liver transplantation. The removed liver may be then successfully transplanted into a second patient in need for a liver transplant due to a different pathology. This second patient would not exhibit symptoms of FAP for 20 to 30 years, allowing him or her to live for at least two or three decades without experiencing problems from the disease. However, some reports have been published on an earlier development of symptomatology attributed to FAP in this second recipient (32).

Since FAP is prevalent in some geographic areas (Portugal, Sweden, Japan, Swiss-German, Swedish and others) (33) domino liver transplantation may not be considered as a whole a technical programme quantitatively important to expand the donor pool, but maybe important for specific countries or areas where the disease is prevalent or to other countries willing to use these livers. For instance, Portugal, where FAP is very prevalent, has obtained a high experience with domino liver transplantation, with even more than 40 domino liver transplants performed in a year basis in the country. France, Germany and Spain have been performing 8-18 domino liver transplants a year during the last two years and Spain has been using domino livers explanted in Portugal (Table 4). A continuous evaluation of the results is also much needed through properly designed registries.

Table 4: Split and Domino Liver Transplants performed in ALLIANCE-O countries. Absolute numbers (number, pmp).

	France	Germany	Italy	Portugal	Spain	UK
Split Liver Transplants						
2004	56 (0.9)	117 (1.42)	94 (1.6)	3 (0.3)	14 (0.3)	60 (1)
2005	61 (1)	84 (1)	127 (2.2)	10 (1)	22 (0.5)	85 (1.4)
Domino Liver Transplants						
2004	12 (0.2)	7 (0.08)	-	46 (4.6)	7 (0.2)	2 (0.03)
2005	18 (0.3)	10 (0.1)	2 (0.04)	40 (4)	10 (0.2)	-

4.1.3. Double kidney transplantation

Double kidney transplantation with kidneys obtained from specific types of expanded criteria donors (see definition below) in whom a reduced functional mass is expected has been successfully implemented in some units. This technique aims to supply an enough number of nephrons and metabolic capacity to cover the functional and metabolic requirements of the potential recipients. Double kidney transplantation with ECD may be considered a way of using kidneys that placed in a single fashion would not cover the metabolic demands of one recipient and therefore would not be considered for transplantation. This technique has been mainly applied to kidneys from aged donors, although "in block" double kidney transplantation from paediatrics donors has been also successfully attempted, a technique which deserves to be specifically addressed because of its special characteristics. The decision of using kidneys from ECD in a double fashion instead of in a single fashion has been based mostly on a histological evaluation of the kidneys once removed from the donor, whatever using a score combining several histological items (34, 35).

Based on this histological evaluation, results with kidneys from ECD implanted in a dual fashion have proven to be comparable to those obtained with more ideal kidneys implanted in a single fashion (34 - 37).

Although results with this technique seem to be promising it is still of variable use across the European countries. For instance, among ALLIANCE-O countries, the rates of double kidney transplantation range from 0.1 to 1.5 transplants pmp in years 2004 and 2005, with the highest number of cases having been performed in Italy (Table 5). Therefore, double kidney transplantation represents an area to increase the potential of donation which should be properly explored though

carefully evaluated pilot experiences. However, it should be outlined the importance that only those kidneys that would not be used in a separate fashion are the ones to be used as a double kidney transplantation. If not, this initiative, far from improving the availability of organs could imply a decrease of the kidney donor pool.

Table 4: Double kidney transplants performed in ALLIANCE-O countries. Absolute numbers (number pmp).

	France	Germany	Italy	Portugal	Spain	UK
2004	33 (0.5)	-	101 (1.8)	1 (0.1)	39 (0.9)	8 (0.1)
2005	50 (0.8)	9 (0.1)	83 (1.5)	2 (0.2)	20 (0.4)	11 (0.2)

4.2. Expanded Criteria Donors

To increase the supply of organs for transplantation, the medical contraindications to donate have been changing over time. In fact, there is an increasing use of organ donors who had not been classically accepted as such because of presenting specific pathologies or conditions. These donors have been named as ECD, sometimes referred as marginal or suboptimal donors.

Several definitions have been provided for ECD. UNOS define ECD as those with one or more of the following factors: age >55 years, history of hypertension longer than 10 years duration, history of diabetes mellitus longer than 10 years duration, NHBD and cold preservation time >36 (38). The consortium agrees on providing a general definition of ECD, as those potentially related to worse results in the recipients when compared to recipients receiving their organs from classical or more ideal donors. Under this concept we would include: extreme ages of life, transmissible diseases (infections and neoplasias) and other pathologies. The previously mentioned conditions and pathologies have been classically considered as formal contraindications for organ donation. However, we are acquiring increasing information on the fact that when organs coming from these donors are used in appropriate and specific conditions results may be very acceptable and even similar to those obtained with organs from more ideal donors. Therefore the use of organs from ECD has progressively become a real way to expand the donor pool.

Universally discarding organs from ECD may worsen the shortage of organs for transplantation, but universally accepting these organs for transplantation may

provide a burden of risk to the recipient outcome in terms of morbidity and mortality and a decrease in graft survival, unless used in very specific conditions. The decrease in graft survival due to the use of a marginal donor may on the other hand worsen the disbalance between organ supply and demand since loss of function of a previous graft is progressively representing a cause to return to the waiting list.

Therefore, the use of organs coming from ECD should always be performed under the scope of ensuring a quality of outcome. Pilot experiences should be carefully evaluated. Besides, national consensus documents and guidelines based on the available evidence should be properly designed. Finally, it seems mandatory to collect information on the outcome of recipients receiving grafts from these donors to evaluate the limits of safety.

4.2.1. Kidneys from old donors

Age of donors is progressively increasing over time. However, kidneys from old donors are frequently discarded. While more than 30% of the kidney or liver transplantation activity corresponds to aged donors (>60 years) (*ALLIANCE-O, D 2.4*) in Italy or Spain, this percentage is much lower in other countries. This decision is based in the worse results obtained with kidneys from old donors when compared with kidneys from young donors. The UNOS database (11) describes a 5 year graft survival much lower in recipients of a kidney from a donor over 65 years than for recipients of a donor under 65 years of age. These worse outcomes are based on the fact that kidneys coming from old donors present a decrease in nephron mass in relation to aging and/or subclinical pathologies related to aging. Besides, these organs are more susceptible to insults occurring during the process of transplantation, as ischemia-reperfusion injury. Although it is still a matter of debate, older kidneys may be more susceptible to suffer an acute rejection episode that may diminish the rate of success of the organ (39).

Despite all this, results with kidneys from old donors have been very acceptable and even excellent when using specific criteria for allocation. In this context, the old for old programmes, aiming to select recipients for old donors in the basis of age and not in the basis of HLA compatibility, as well as to minimize cold ischemia time, have been already applied in Europe. This is the case of Eurotransplant Senior Programme, successfully implemented in 1999 (40).

On the other hand, the application of **histological scores** in order to evaluate the acceptability of these organs and even their implantation in a **dual fashion** in case nephron mass is severely decreased has been performed and provided very good survival rates (34, 35).

Since results by using kidneys from old donors are very acceptable when used in the appropriate conditions and their use across Europe is widely variable, their use represents an area to really expand the potential of kidney transplantation in our countries. However, a continuous evaluation of results with these kidneys should be mandatory through the development of specific registries.

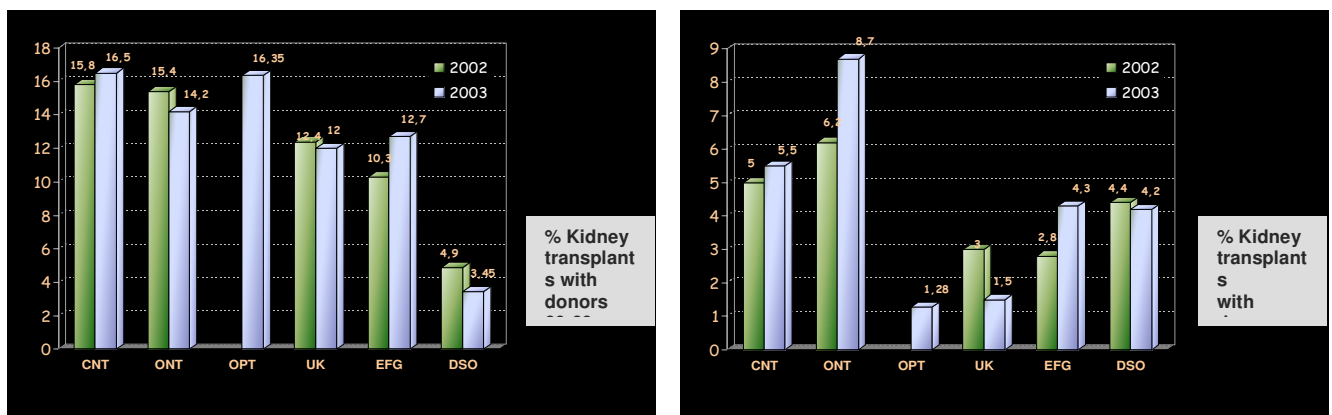


Figure 1: Kidney transplants performed with donors of 60 to 69 years of age and over or equal to 70 years of age in ALLIANCE-O countries. Years 2002 and 2003.

4.2.2. Non kidney Organs from old donors

In the past, most centres refused livers and hearts from donors who were 60 years of age or older, fearing that age-related changes in these organs might affect their performance in recipients. Registry studies have demonstrated that short and long-term survival of recipients of organs from older donors is encouraging (41).

The use of livers from otherwise selected donors over 60, 70 and even 80 years of age has demonstrated similar results to those obtained with younger donors in some unicenter and multicenter experiences (42-45).

Hearts from donors over the age of 46 years provided a 1 year survival only 8.4% lower than the one described for recipients of hearts coming from younger donors, difference explained by the poor survival of patients over 50 years candidates to heart transplantation (46). Also, survival figures of recipients of hearts coming from

donors over 48 years of age are similar to those described for recipients of younger donors (47). In selected cases, if hemodynamic values are in the normal range during mild to moderate inotropic support, hearts from donors older than 60 years have been shown to be acceptable for transplantation (48).

As previously mentioned for kidney, the collection of information within this project has reflected the lack of uniformity among our countries with regards to the use of livers from old donors (Figure 2). Room for improvement is detected again. The possibility of expanding the use of livers and even hearts from older donors should be explored. Again, a continuous evaluation of results should be ensured through properly designed registries.

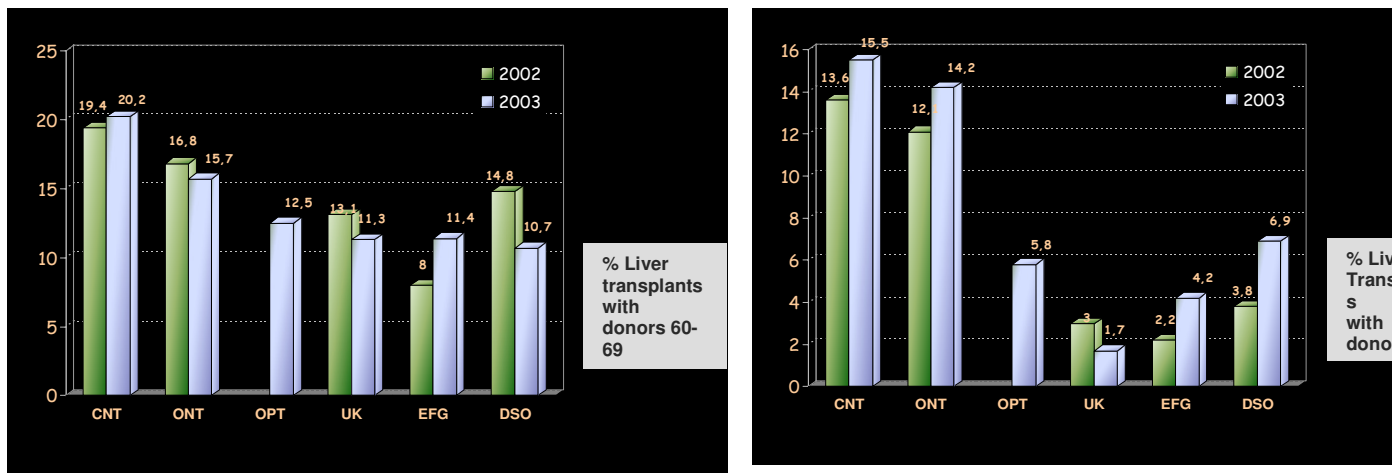


Figure 2: Liver transplants performed with donors of 60 to 69 years of age and over or equal to 70 years of age in ALLIANCE-O countries. Years 2002 and 2003.

4.2.3. Donors with transmissible diseases

Infections and neoplasias are diseases susceptible of being transmitted through transplantation and, in general terms, have been considered as classic contraindications to donate. However, and also in the context of donor and organ shortage, knowledge has been accumulated on the circumstances in which these donors could be safely used. While the knowledge is limited on some of these conditions, there is wide experience on the use of organs coming from donors affected by some of these diseases. Despite this, the use of these donors is still limited in some of our countries. General consensus documents and guidelines have been created in different countries which could serve as a basis to guide the use of

these organs. For instance, France, Germany, Spain and UK have already available documents for the evaluation of neoplastic and infectious diseases in the donor and the subsequent use of organs for transplantation. Any case, the evolution of recipients of these organs should be properly collected in specific registries. Since some of these conditions, as neoplastic diseases, are of limited prevalence among potential donors, the creation of international registries that could accumulate the experiences of different countries could be considered.

Information on the experience acquired so far with the different types of donors with infectious and neoplastic diseases is probably out of the scope of this report. However, in order to provide an example of the possibilities of using these donors, the example of the use of donors with HCV positive serology is provided bellow.

Donors with HCV positive serology

Transmission of HCV infection through organ transplantation was described by several groups along the nineties, although the frequency of the transmission and its clinical characteristics vary depending on the group describing this transmission (49). These observations prompted the majority of transplant groups and organizations to recommend avoiding the use of anti-HCV positive donors into anti-HCV negative recipients. However, it is still a matter of debate whether the use of Anti-HCV positive donors is acceptable for Anti-HCV positive recipients. Experiences are mainly limited to kidney and liver transplantation.

In the field of kidney transplantation, several unicenter experiences have reported a similar outcome in HCV positive recipients transplanted from an anti-HCV positive donor than in HCV positive recipients transplanted from an HCV negative donor (50-54). Limiting the use of these organs to HCV RNA positive recipients would more precisely avoid the transmission of the infection (50). Matching donors and recipients in terms of HCV genotype would improve even more the consequences of this policy, since superinfection *phenomena* with very negative consequences for the recipients have been reported in the literature (55). An apparent advantage of the use of HCV positive donors for HCV positive recipients seemed to be a shorter time in the waiting list when compared to HCV positive recipients transplanted from HCV negative donors (52-54). Some limitations of these unicenter experiences are the low number of patients evaluated, as well as the short time of follow-up, although at least the Spanish experience has reported the outcome of more than 100 HCV positive recipients of a kidney from an HCV positive donor with a mean

follow-up of almost 5 years. Despite their limitations, these experiences have been the basis for the development of international guidelines supporting the use of HCV positive kidneys into HCV positive recipients (56).

On the other hand, the UNOS database recently offered negative results in terms of patient survival among recipients transplanted from HCV positive donors, independently of the HCV status of the recipient (57). The worse survival was apparent from the second year of transplantation on, leading the authors to suggest that co morbidity such as postransplant diabetes mellitus could be the responsible for this difference (58). The debate on the use of HCV positive donors has therefore risen again, although obvious limitations of this study were also evident: first, it was based in the retrospective and uncompleted nature of data included in a registry and second, a lack of an specific policy in the use of HCV positive kidneys was apparent. In fact, these kidneys had been allocated into the recipients with the worse clinical and immunological conditions. Besides, the UNOS database also demonstrated that receiving a kidney from an HCV positive donor provided a survival benefit versus remaining in the waiting list (59).

Until more information is available, we could conclude that offering kidneys from HCV positive donors to be transplanted into HCV positive recipients seems to be safe according to the results of limited unicenter experiences. It seems that the possibility of transmission is decreased by limiting these organs to recipients with a positive RNA before transplantation and that matching donor and recipients in terms of HCV genotype would be a more advantageous approach. However, the negative impact of survival described in an important national registry should not be forgotten with the previous outlined limitations. The beneficial impact of a decreased time in the waiting list should be taken into consideration, and the possibility of offering these kidneys in a pre-emptive fashion could be approached.

The use of HCV positive kidneys represents a way of expanding the donor pool, avoiding the loss of organs that may be of excellent characteristics apart from its HCV positive condition. However, the research performed within ALLIANCE-O has pointed out the fact that, while the use of kidneys and livers from HCV positive donors is common in some countries, HCV positive serology represents an absolute contraindication to donate in some other countries. Therefore, the use of these organs may be enlarged in the future, providing a way to increase the donor pool, in several of the European countries. Any case, the use of anti-HCV positive kidneys should be a matter of national consensus and guidelines, also reviewing allocating

considerations. A continuous evaluation of results is again imperative. Research in this field should be promoted.

4.2.4. Donors with other conditions

No accurate figures on the presence of conditions such as arterial hypertension or diabetes mellitus in organ donors can be provided. These two conditions may generate renal disease and therefore may preclude the use of organs for kidney transplantation. Some limited experiences exist with the use of these donors (60). Provided an adequate functional and/or histological evaluation is performed, those conditions themselves may not be considered as formal medical contraindications to donate. Once more, experience should be properly and continuously collected in the future to ensure that only those kidneys that should be discarded on the basis of functional and/or histological impact of arterial hypertension and diabetes mellitus are so.

Other conditions such as rare diseases in the donor, acute intoxications and poisoning as a direct or indirect cause of death and others (e.g. acute renal failure at the moment of donation) are progressively being evaluated trying to identify the limits in safety with their use. As previously said, the development of Consensus Documents and Guidelines, already available in some countries, is needed. Even more, for these infrequent conditions the creation of international registries that guarantee the collection of information on the outcome of a sufficiently large number of recipients is also a necessary tool.

4.3. Final Recommendations for Technical Programmes

a) The use of special techniques as split and domino liver transplantation or double kidney transplantation with kidneys from expanded criteria donors may be considered areas to expand the donor pool, provided an adequate registry of results by using these organs is ensured.

b) The consortium agrees on providing a general definition of expanded criteria donors, as those potentially related to worse results in the recipients when compared to recipients receiving their organs from classical or more ideal donors. Under this concept we would include:

extreme ages of life, transmissible diseases (infections and neoplasias) and other pathologies. When allocated in specific conditions, the use of organs from expanded criteria donors may be related to very acceptable results. Pilot experiences should be carefully and properly evaluated.

c) The safety limits in the use of organs obtained from expanded criteria donors should be properly evaluated through the development of registries collecting information on the outcome of the corresponding recipients. Consensus Documents and Guidelines on the adequate use of organs from expanded criteria donors should be created if not available and properly updated with an evidence based approach.

5. TRAINING PROGRAMMES TO EXPAND THE DONOR POOL AND TO MAXIMIZE THE POTENTIAL OF DONATION

As already described, the process of donation and transplantation after brain death is a long and complex one, including a number of steps. Each of the steps of the process is vulnerable and mistakes at every one of them have a direct impact in the number of potential, effective and utilised donors. On the other hand, the knowledge on donation and transplantation evolves with time and research. Therefore, to avoid donors and organ losses as much as possible and increasing the donor pool the need for continuous and actualized training should be considered a key issue.

Differences among partners within ALLIANCE-O have been noticed with regards to the implementation of specific training programmes. For instance, programmes aimed to cover all the process of organ donation (e.g. Transplant Procurement Management courses) have not been universally implemented within the group. The same applies to those courses targeted to the family approach, this specific step of the donation process not being covered by all the countries (examples of this type of courses are EDHEP seminars, modified in its content and development in some countries, as France and Spain). Training programmes covering other steps, as brain death diagnosis, maintenance of the donor or communication with the mass media are also developed in some of the countries within the consortium, but not in others. Apparently, the previously described training programmes seem to be organized without pre-existing specific plans in most countries.

The usefulness of training activities in organ donation rates has not been fully demonstrated and it has even been a matter of discussion whether it may or it may not have an impact on the donation rates.

The consortium understands that a properly designed training programme should allow increase detection of potential donors and ensure brain death referral for organ donation. Training should also improve the correct comprehension of absolute and relative medical contraindications to donate, so only those donors who should not be accepted are so. Besides, problems with the maintenance of the donor should be decreased through a proper training on the physiopathological phenomena related to brain death and their medical approach. Refusals to donate, one of the most important obstacles in the process of donation could be diminished through training programmes covering the moment of the family approach. Finally, organ retrieval could be considered a matter of training; with the proper approach, the loss of organs at this delicate moment could be avoided in many cases.

Training should be targeted to all professionals involved in the process of donation in a direct or indirect way and should cover all the steps of the donation process after brain death. With regards to the dimension of the training programmes, a local approach dealing with local problems should not be incompatible with a **Harmonized National Training Programme**. The advantage of this global approach would be a better use of national resources and efforts. Ideally, this national programme **should be accredited** by representative institutions and/or scientific societies.

A continuous/dynamic evaluation of the efficacy of this national training approach on the rates of donation, as well as in the quality of the process should also be taken into consideration.

5.1. Final recommendations on training initiatives

a) All professionals direct or indirectly involved in the process of donation should be the target for training activities in the donation process.

b) Training should properly cover all the steps of the donation process: brain death diagnosis, brain death referral, evaluation of the donor, maintenance of the donor, family approach and organ retrieval.

c) Training in the context of a properly planned, Harmonized and Accredited National Programme would be the ideal approach.

d) A system to continuously evaluate the efficacy of the training programme should be developed.

6. FINANTIAL INITIATIVES TO EXPAND THE DONOR POOL AND TO MAXIMIZE THE POTENTIAL OF DONATION

Organ transplantation may be considered a **cost-effective procedure**. It has been calculated that 10,000 renal patients living with a functioning kidney graft are saving to the health systems over 200 million € annually (in terms of differences of the economical costs of the different replacement therapies for the end stage kidney patients, when comparing the cost of transplantation versus the costs of dialysis treatment). This is just taking into account daily dialysis costs and not including structural costs. Cost-saving and cost benefits referred to Qualy's gains can be increased with a transplant. It has been defined that an increase of 6 donors p.m.p. in a country like Germany will lead to 29 Qualy's gains of patients with end-stage renal disease (calculation was made over a 20 years period) (61). In this context, financial initiatives aimed to expand the donor pool are clearly justified.

Differences among countries with regards to financial initiatives to expand the donor pool and maximize the potential of donation are outstanding. It is to be outlined that hospital reimbursement for the donation process is not available in all ALLIANCE-O countries. Specifically reimbursement is missing in UK and Germany. The consortium agrees that donation activities should not be disincentive activities for the hospitals. Therefore, human and material resources set by the hospitals in order to effectively cover all the donation process should be properly funded.

The programmes and initiatives of different nature that have been proposed by the consortium as valuable to increase the donor pool and maximize the potential of donation should also be adequately resourced after and appropriate analysis and in the context of a national strategic plan.

6.1.Final recommendations on financial initiatives

a) Hospitals should be sufficiently resourced to efficiently develop all the activities related to donation and transplantation. Donation should never be a disincentive activity for procurement hospitals.

b) To develop their specific functions related to increase the donor pool, the suprahospital transplant organizations should also be sufficiently resourced.

c) European / National programmes/activities aimed to expand the donor pool while ensuring quality should be properly funded: donor process evaluation, quality management, training, organ registries, among others.

V. EXPANDING THE DONOR POOL: DONORS DEAD DUE TO IRREVERSIBLE LOSS OF CARDIO-RESPIRATORY FUNCTIONS

1. NON HEART BEATING DONATION: DEFINITION AND CLASSIFICATION

There is a basic distinction between heart-beating and non heart beating donation (NHBD) or donation after cardiac death (DCD). Heart beating donors die because of an intracranial injury that results on the irreversible loss of encephalic functions while the person is on a life support machine. In NHBD the first damage is a fatal cardio-respiratory arrest, which derives in the irreversible cessation of cardio-respiratory functions and finally the irreversible cessation of the cerebral flow.

In the early days of organ transplantation, the source of transplantable kidneys was either living donors or deceased donors who have died from a cardio respiratory arrest. However, the wide acceptance of the definition and criteria for the diagnosis of brain death made that the use of organs from brain death donors almost fully replaced the use of the former. At present, due to the shortage of organs for transplantation, together with promising results with transplants from these donors, a renewed interest in obtaining organs from NHBD has been observed. This interest has lead to several consensus conferences and meetings that tried to face the inherent technical, ethical and legal issues that did arise (62-64). While activity with NHBD has increased in the USA, activity in this field is almost anecdotic in Europe, with some exceptions. The research performed within ALLIANCE-O provided information on the fact that only 10 out of the 35 analyzed countries did register any activity with NHBD, although this activity was very low in every single case. For instance, during the year 2005, only 3 European countries did register a significant number of NHBD, in particular the Netherlands, with 120 (7.3 pmp), UK with 121 (2.1 pmp) and Spain with 71 donors (1.6 pmp) (10). This limited activity probably reflects the difficulties and dilemmas that this activity deserves from the ethical, technical and organizational point of view.

The First International Workshop on NHBD, held in Maastricht (62), identified four categories of NHBD, depending on the context in which cardiac arrest takes place:

- Maastricht Category type 1 (dead on arrival) refers to persons who suffer a cardio-respiratory arrest outside the hospital. Resuscitation manoeuvres are unsuccessful and the subjects are transported into the hospital specifically for the purposes of organ donation.

- Maastricht Category type 2 donors (unsuccessful resuscitation) are derived from patients who die inside the hospital after an unsuccessful attempt of cardiopulmonary resuscitation.
- Maastricht Category type 3 donors (awaiting cardiac arrest) derive from patients who are receiving life support inside an ICU and in whom life support measures are withdrawn, which leads to cardiac arrest. This category usually derives from patients with severe and irreversible brain damage that has not led to brain death.
- Maastricht Category type 4 donors (Cardiac arrest while brain death) include brain death potential donors who suffer from a cardio-respiratory arrest before organ retrieval takes place.

There has been considered by some groups the existence of a fifth category of NHBD, which refers to people suffering from cardiac arrest inside the hospital but, specifically, inside the ICU (65). This differentiation in what it has been previously described as Maastricht Category type 2 is based on the observation that outcome of organs from these donors are diminished compared to that observed with organs from people suffering from cardiac arrest inside the hospital, but outside the ICU.

While type 3 category has been also referred as controlled or expected death, in the sense that cardiac arrest is anticipated, the rest of the categories include uncontrolled or unexpected death, since cardiac arrest is not anticipated. This differentiation distinguishes between specific circumstances that may affect the donation process: time until initiation of preservation manoeuvres, psychological preparation of the family and ascertainment by the health-care team for the potential of donation.

Type 3 category is the most frequently type of NHBD used not only in Europe, but also in the USA. However, some large experiences are being accumulated with Maastricht categories 1 and 2 donors, which bring promising results and offer a realistic approach to enlarge the donor pool and increase the opportunities of transplantation (66, 67).

2. ETHICAL ISSUES IN NON HEART BEATING DONATION

Several ethical issues arise in the context of NHBD, some specific aspects varying from one Maastricht category to the other. Some of these aspects have been properly discussed in WP 7, but it should be outlined the vital importance of

ensuring complete transparency on the process of NHBD, since loss of public trust in the system could have a very deleterious impact not only on NHBD, but also in the context of donation after brain death.

3. TECHNICAL ISSUES IN NON HEART BEATING DONATION

One of the most important differences between NHBD and heart-beating donation refers to the existence of a warm ischemic time, variably long, depending on the type of Maastricht category (68). Warm ischemic time is considered to be very deleterious for the organs, which explains that NHBD is subjected to more strict time constraints than those already described for HBD. Therefore, the possibilities of delayed graft function or primary non function of the grafts are potentially increased when comparing heart beating and non heart beating donation. In this context, the need to base donor selection on the duration of the warm ischemic period is needed, and most programmes exclude potential donors or organs from NHBD with long warm ischemia times. Even more, because of the negative impact of warm ischemic in the outcome of the grafts, most programmes select also the potential donors according to other strict medical criteria. For instance, there is usually a limit of 60 years of age to accept NHBD in most of the running programmes, since the decline of kidney function as a result of aging along with warm ischemic time may lead to poor graft function and survival rates .

There is another important consequence of the warm ischemic time in the context of non heart beating donation, which is the need to apply preservation procedures to reduce ischemia-reperfusion injury of the organs (68). Several types of *in situ* organ cooling have been described, as the intravascular method, the intra peritoneal method for abdominal organs or the intrathoracic technique for lungs (69) and the extracorporeal whole body cooling. Although each of the different methods has proven their effectiveness in the clinical setting, there is paucity of work comparing the efficacy of the different techniques.

Once removed, preservation of organs has been also a matter of different procedures, mainly cold storage of the organs in ice is being confronted with pulsatile machine perfusion. Pulsatile perfusion machine is more expensive and complex, but could potentially lead to some advantages in the outcome of kidneys obtained from NHBD, not only with regards to diminish ischemic-reperfusion injury, but also in order to evaluate the conditions of the kidneys on the basis of their perfusion characteristics (70). Some comparisons have been performed with no

overall differences in the rate of delayed graft function. On the contrary, another study has observed a higher incidence of initial graft function with pulsatile machine perfusion, but this study had a very limited number of cases (71). Besides, it is still to be proven what the results are in the long-run.

Finally, for cold storage, there is also controversy with regards to the most appropriate preservation solution, yet to be established (72).

4. ORGANIZATIONAL ISSUES IN NON HEART BEATING DONATION

Organizational issues in the context of NHBD are possibly one of the most important limitations that have precluded this kind of programmes from a more generalized implementation. The need for a highly trained, properly coordinated team inside the hospital is a requisite in order to establish a programme of NHBD, whatever the type of Maastricht category being used. This team should be highly trained in *in situ* organ cooling and preservation manoeuvres. Availability should be of 24 hours a day, since even in controlled circumstances the moment in which cardiac arrest takes place may not be anticipated in an accurate way.

In the case of Maastricht category type 1, another more complex organizational issues must be faced, which refers to a close coordination with extrahospital emergency facilities, which would ensure that patients who suddenly die outside the hospitals are transported into the hospital for the only purpose of donation and in the most adequate conditions. This implies that specific protocols must be put in place in order to select the potential donor already outside the hospital, protocols that ensure the extra hospital emergency team should continue providing cardiac massage mechanical ventilation and intravenous fluid perfusion to maintain adequate hemodynamic conditions during the transportation. These protocols, very well developed in the city of Madrid in Spain, raise awareness of the complex process of NHBD with Maastricht type 1 category donors. It is obvious also from the description above, that these programmes may be considered for large cities with excellent extra hospital emergency care facilities.

One issue that arises from the organizational difficulties of NHBD programmes is whether NHBD may have a negative impact on HBD, since concentrating efforts in such a complex programme may undermine those efforts targeted to detect, refer and maintain potential brain death donors. For instance, the Netherlands experienced a 21% decrease in HBD during a 5-year period, during which there was

a 129% increase in NHBD (73). It is important to underline that although NHBD is a real way of expanding the donor pool, it should always be understood as a complementary activity of heart beating donation, not in competency.

5. RESULTS OF ORGAN TRANSPLANTATION FROM NHBD

Experience with kidneys obtained from NHBD type 1 and 2 categories is scarce, with the exception of the one acquired by the group of San Carlos Clinico Hospital in Madrid, Spain. This group recently demonstrated through a large retrospective cohort study that although the incidence of delayed graft function was significantly higher in recipients of kidneys NHBD when compared to recipients of kidneys from HBD, graft and patient survival, even in the mid-term was similar (66).

Experiences with non kidney transplantation from NHBD are more limited. For instance, among ALLIANCE-O partners, some countries are not allowed to retrieve specific types of organs from NHBD for the purpose of transplantation (e.g. in France, lung transplantation from NHBD is not allowed).

The enthusiasm on NHBD in the field of kidney transplantation has not been equal for liver transplantation, since results with livers from these sources were clearly worse than the ones obtained with HBD, with higher incidence of primary non function and of biliary complications. These poor results have improved through a judicious donor selection, but results are still worse than those obtained with HBD. For instance, a recent analysis from the United Network of Organ Sharing showed a three year survival of 63% compared with 72% for HBD. Although these results have improved when compared to the first experiences, they are still limited and research is underway in order to improve these results and decrease the incidence of biliary complications.

Very promising results are also being offered with lung transplantation from DCD donors in controlled or uncontrolled conditions (67).

6. POSITION OF THE GROUP ON NON HEART BEATING DONATION

- a) NHBD may be considered a real alternative source of organs to face donor shortage, so provisions should exist in the countries in order to allow this kind of programmes to be drawn up. NHBD should always be considered as a complementary activity to HBD.**

- Maastricht category type 1 NHBD offers with no doubt a large potential to increase deceased donation activity, although experiences with this type of donors is still very limited.**
- b) Non kidney transplants from NHBD should be properly explored and evaluated. Research should be promoted to ensure that results with specific types of organs (e.g livers) are susceptible of improvement.**
 - c) NHBD should be approached under the scope of pilot experiences arisen from highly motivated teams and ensuring that a continuous interchange of experiences takes place.**
 - d) NHBD programmes should take into consideration the need for a highly trained hospital team, 24 hours a day available. Specifically, a high qualification with regards to preservation techniques to guarantee the quality of the organs retrieved should be mandatory. It would be highly advisable that this team is led by or well coordinated with the so-called key donation person, ensuring a close link between NHBD and HBD programmes. Hospital facilities (eg emergency room) should be available to ensure that preservation maneuvers start at the right time.**
 - e) Extraordinary and highly trained extra-hospital emergency care teams are a necessary human resource in order to implement any programme with type 1 Maastricht category NHBD.**
 - f) Development of specific protocols, guidelines and consensus documents should be encouraged, up-dated on an evidence based approach, to ensure the quality of the organs obtained from this source and results being improved over time. Registration and continuous evaluation of results obtained with organs from NHBD seem mandatory through local, national or international registries.**
 - g) Research should be promoted to ensure that quality of organs obtained from these donors progressively increases and provides increasingly better results. Preservation techniques represent an area where research should be highly supported.**
 - h) Continuous training of teams with ongoing activity and teams developing new programmes should be ensured. Specific attention should be paid to the continuous training of extra-hospital emergency care teams in the case of Maastricht type 1 NHBD, to ensure a proper detection and maintenance of the potential donor.**

- i) Specific budget to hospitals developing NHBD programmes should be ensured, covering human and material resources, as well as training and research. Cost-effectiveness evaluation of NHBD is needed.**

VI. EXPANDING THE DONOR POOL: LIVING DONATION

1. INTRODUCTION

The first successful kidney transplant dates from the year 1954 (74). Joseph Murray, from the Brigham Hospital in Boston, subsequently a Nobel Price winner, performed this surgery between identical twins, so the immunological obstacle that precluded transplant from becoming a successful procedure was avoided. Therefore, in the first days of successful kidney transplantation, the origin of the organs was the living related donor. It was in 1955 when the first kidney transplant from a not genetically related donor took place in the Foch Hospital, in Paris. Living donation was the only available source of organs for transplantation until some experiences with NHBD were initiated and the subsequent description and wide acceptance of brain death. Over the years, many patients have been transplanted from genetically or not genetically related living donors and, among the latest, from donors with an emotional or even with no emotional relationship at all. Even more, while initially living donors were used for kidney transplantation, over the last years living donation has also become a real source of organs for liver, but even for lung, pancreas and intestine transplantation, although the three last types of organs are not quantitatively so important yet.

The first living liver transplant was first performed in 1989, when Raia transplanted a small child in Brazil (75). For instance, living liver transplantation programmes were firstly developed in countries with no legislation and organizational background for deceased donation, as Japan, Korea, Brazil or Turkey. The first living liver transplantation programme in an occidental country was developed by the University of Chicago (76). The successful results obtained with paediatric patients made the surgeons offer this alternative to adults (77-80).

The evolution of living donation along the years should be described under two different situations. On one hand, there are countries in the world without a well developed system that allows an important activity with deceased organ donation; therefore, living donation may be the only possible source of organs for transplantation and it has represented the main or even the unique source for many years.

The situation in countries with a more or less well developed system on deceased organ donation is different. For instance, living donation is seen in many of these

countries as another possibility to increase the availability of organs for transplantation, at a moment of shortage of deceased organ donors. In this context, living donation activity has progressively increased during the last years in many occidental countries. According to data from the year 2006, living kidney transplant activity in Europe ranges from 1 to 16.6 procedures pmp and the percentage of living kidney transplant procedures over the total of kidney transplants performed ranges from 0 to 80.9% (10). The activity of living liver donation is still limited, since the complexity of partial hepatectomy and the risks for the living donor are clearly higher than those derived from a nephrectomy (see below). For instance, while 2617 living kidney transplants (5.4 pmp) were performed in the European Union in the year 2006, only 238 (0.5 pmp) living liver transplants were performed (10).

Living donation offers, in general terms, undeniable advantages to the recipient and the system. First, contrary to deceased donation, living donation is an elective procedure. Second, and due to the deep evaluation and selection of the donor, the kidney or the liver to be transplanted are supposed to be of high quality. Third, the damage of the graft in the context of the physiopathological changes of brain death and ischemia-reperfusion injury is minimized. Third, living kidney transplantation may be performed in a pre-emptive fashion, avoiding dialysis therapy, with the corresponding savings to the health-care system. Finally, kidney living transplantation is related to better results than those obtained with kidneys from deceased donors.

However, living donation deals with the main inconvenience of violating the traditional first rule in medicine, "*primum non nocere*" (above all, do not harm), since no single surgical procedure, including a nephrectomy or a hepatectomy is completely out of risk. For instance, a set of ethical considerations derive from living donation, which have been evaluated under the scope of international consensus conferences aimed to ensure the protection of the donor, as the Amsterdam Forum (81), focused on the living kidney donor and the Vancouver Forum (82), focused on the living non kidney donor. Other international recommendations have been produced with the same approach and as a basis to guide the development of international and national legislations (83). The legal and ethical issues that arise in living donation have been fully described and discussed in WP 7 within ALLIANCE-O. In the present section of WP2, we intend to review the results of living donation, as well as some technical and organizational aspects,

reflecting a common position of the ALLIANCE-O consortium regarding these previously mentioned issues.

2. RESULTS OF LIVING DONATION

2.1. Results of living kidney transplantation and donation

Living kidney transplantation has been classically related to better outcome results in the recipients than deceased kidney transplantation, independently of the HLA compatibility and the existence or not of a genetic relationship between the donor and the recipient. According to the OPTN national data, 1 year graft survival is 89% and 95.1% for kidney recipients from deceased *versus* living donors, with a more important difference in the long term, since 5 year graft survival is 66.5% *versus* 79.7%, respectively (11). Similar figures have been provided by the Collaborative Transplant Study (84). When analyzing first kidney transplants performed in Europe during the years 1985-2005, estimated death censored graft survival at 20 years was 65% when donor and recipient were HLA identical siblings, 45% for 1 haplotype related donor and recipients and 34% for recipients of deceased donors.

Better results obtained with living than with deceased kidney transplantation have been related to a shorter ischemic time and the absence of the lesions derived from the physiopathological changes suffered by the organ during brain death. Besides, in the context of a genetic relationship between the donor and the recipient, there is a better HLA compatibility and less amount of immunosuppression is required. Finally, one important advantage of living kidney transplantation is the fact that it may be performed in a pre-emptive fashion, this means, before the recipient is treated with long term dialysis techniques. Since time in dialysis has been described to negatively impact graft and patient survival (85), the fact that living kidney transplantation may be performed in a pre-emptive fashion may also explain the better results observed in recipients of kidneys from living *versus* deceased donors.

Besides, living kidney donation is considered as a relatively low risk procedure for the donor. Mortality risk has been estimated to be of 0.03%, according to several studies (86). Besides, the risk of short-term complications (as bleeding or infection) is low, although variable according to the surgical technique used to perform the nephrectomy in the donor, whether open nephrectomy, hand assisted or non hand assisted laparoscopy (86). Long term follow up of living kidney donors has not generally revealed a higher incidence of chronic renal failure or other medical

complications than those observed in the general population. However, it should be outlined the fact that most of these reports are retrospective experiences, with an important number of losses to follow-up and that the outcome comparisons with the general population may not be the more appropriate, since living kidney donors should be considered healthier than the general population (87). There are also reports from living donors developing a progressive decline in renal function and some of them becoming kidney transplants candidates in the long-run (88).

2.2.Results of living liver transplantation and donation

Survival of living liver transplanted patients is similar to that described for recipients of livers from deceased donors. According to the OPTN registry, for liver transplants performed during the years 1997 to 2004, 1 year patient survival was 86.3% and 90.2% and 1 year graft survival was 82% and 82.6% for recipients of deceased *versus* living donors, respectively. Corresponding 5 year patient survival figures were 72.1% and 77.8%, respectively, with no differences either in graft survival (65.2% *versus* 65.9%) (11). However, living liver recipients have been described to develop higher postransplantation morbidity, especially regarding biliary complications. In addition, the so-called small-for-size syndrome has been virtually described in cases of adult to adult living liver transplantations, a syndrome resulting from not receiving enough functional liver mass. Some series has also questioned whether living liver transplantation may facilitate HCV and tumour recurrence in patients who have been transplanted due to these conditions (89).

The outcome of living liver donors is not at all similar to that described for living kidney donors, due to the risks related to the performance of a partial hepatectomy, even in a healthy person. The incidence of complications associated with living liver donation is variable, according to the series. However, a list of these complications has proven to be as high as 21 to 28% (90, 91), with right lobe liver donation being associated with a more increased morbidity than left lobectomy or left lateral segmentectomy. The rate of catastrophic complications, defined as the death of the donor, the need for a liver transplant or the development of a vegetative state has been described to be not negligible, with rates of 0.4 to 0.6% (82).

2.3. Non medical complications of living donation

Besides the medical complications that have been described among living organ donors, some reports have observed the possibility of non medical complications (90). For instance, psychological and/or social repercussions of living donation, as financial and occupational disadvantages, have been described in the literature and they represent a matter of concern for the international transplantation community (92).

3. TECHNICAL AND ORGANIZATIONAL ISSUES OF LIVING DONATION

3.1. Evaluation of the donor

One of the technical features of living donation relies on the need of a thorough evaluation of the potential living donor. A good health state, with minimal anaesthetic risks should be ensured, as well as the absence of potentially transmissible diseases and normal function of the organ to be removed. ABO and HLA compatibility with the recipient must be evaluated. However, while ABO incompatibility was initially an obstacle to proceed with living kidney donation, cross over donation (see below) and protocols to dilute anti-ABO antibodies have provided a solution to face this barrier (93). Finally, an evaluation of any special morphologic peculiarity of the donor should be evaluated.

As special medical features in the context of the evaluation of the potential living liver donor, an evaluation of the size of the graft in relation to the recipient's weight should be considered to test the feasibility and avoiding the "small for size" syndrome (89).

Besides the need for a physical evaluation of the potential donor, a psychological assessment is also needed. Transplantation teams generally include a psychologist who interviews potential donors to assess their motivation, who examines with them the psychosocial issues involved, and who supports them as they decide whether in fact to donate. A very important feature of the living donor evaluation is the informed consent, where the risks of the procedure in the short and long run should be described as well as the therapeutic alternatives that the potential recipient has. The issue of the informed consent to the potential living donor has been deeply analyzed in international ethics statements and in WP 7 of ALLIANCE-O project.

Finally, the evaluation of the procedure by a third independent party (independent of the donor, the patient and the medical and surgical team) has been established in most of the countries as a way to protect the donor and to avoid organ commercialization (see WP 7).

3.2. Surgical issues.

Surgical issues of living donation are out of the scope of this review. However, there is a surgical issue that should be mentioned in the context of living kidney donation since it has arisen from the interest of ensuring an early physical and social recovery of the donor: the surgical boarding for nephrectomy in the donor.

Open lumbothomy was the initial surgical procedure applied for nephrectomy in the donor. Laparoscopic living donor nephrectomy was first described in 1995 (94). Since then, laparoscopy has progressively become the standard approach for living kidney nephrectomy in many centres (95), although the *pros* and *cons* of this new approach and its variations are still a matter of debate. While laparoscopy seems to be related to an earlier recovery of the donor, with clear psychological and social advantages, the need for a reintervention and a delay in the kidney function once grafted are a matter of concern (96). Besides, it should be outlined the need for specific highly trained professionals to undergo laparoscopy.

3.3. Cross over kidney donation

Kidney living donation and transplantation between one specific donor and recipient may be sometimes difficult to perform by the presence of a positive cross match or ABO incompatibility between the recipient and the selected living donor. This circumstance led to the suggestion and subsequent development of specific programmes allowing what it has been called cross-over donation or kidney pair donation/exchange (97, 98). In cross-over kidney donation, the kidney from the donor of the donor-recipient pair X is transplanted into the recipient of the donor-recipient pair Y and *vice versa*. This exchange allows solving the problem of ABO incompatibility or positive cross-match. In this context, paired kidney donation has been considered a way of expanding the kidney donor pool and increasing the possibilities of transplantation.

Kidney paired donation deals with many ethical considerations, including confidentiality, conditionality of donation, synchronicity of operations and the possibility of disadvantaging blood group O recipients, some of them addressed in WP 7. Besides, logistical barriers hampering kidney paired donation programmes involve the location of donor surgery and organ transport (99).

4. POSITION OF THE GROUP ON LIVING DONATION

a) Living transplantation activity is progressively increasing, but it is still widely variable in European countries: while very frequent in some countries, it still remains anecdotic in others. Living donation is a real alternative to improve the availability of organs for transplantation. However, there is a need for drawing up living programmes in a complementary way to the deceased donation ones, never in competition. There should not exist a negative correlation between the living and the deceased transplantation activity.

b) Morbidity and mortality related to living donation differs according to the type of donated organ. While referring to the most frequent living donation procedures, this means kidney and liver donation, a explicit differentiation should be outlined, because of the different risks related to nephrectomy and partial hepatectomy, even in a healthy person.

c) Adequate tools (as local, national or international registries, as well as periodic surveys and others) should be developed in order to ensure that information on the medical, psychological, financial and social complications related to living donation in the short and the long run is properly collected. This information should help to develop evidence based guidelines and consensus documents, addressing the selection, evaluation and follow-up of the living donor.

d) The development of new surgical alternatives and any other type of initiative in living donation and transplantation, aiming to increase the donor's safety, facilitate the recovery and incorporation of the donor to an active and normal life and to improve recipient's outcome should be highly encouraged and research should be promoted in this field.

f) The possibility of living donation should be offered to any patient accessing the waiting lists, always on the basis of individual circumstances. Adequate and complete information should be provided to the patients and relatives. The appointment of specific professionals in charge of providing this kind of information could be considered in hospitals with an important living transplantation activity. In the case of living kidney transplantation, this figure could even be evaluated for large dialysis units or for a set of small ones.

g) Living donation should be properly resourced, especially keeping in mind the benefit not only for the recipient, but also for the community, since it allows one person being removed from the waiting list at a moment in which deceased organ donation is insufficient to fulfil the demand of organs for transplantation. Living donation should never be a disincentive activity for hospitals.

e) Authorities should ensure the health-care coverage of the living donor before, during and after the procedure, ensuring the long-term access of the living donor to the health care system. Social benefits for living donors should be explored, as well as ensuring that health/life insurances do not penalize the living donor.

f) Continuous training of professionals in charge of an ongoing or new living donation programme should be guaranteed. Interchange of experiences among medical and surgical teams should be encouraged.

g) While many ethical and technical aspects remain to be solved, paired kidney donation (cross over kidney donation) represents a valuable approach to increase the kidney donor pool and the possibilities of transplantation. Provisions may exist so this kind of specific programmes may be drawn up on the basis of local circumstances.

REFERENCES

1. Murray JE, Merrill JP, Hartwell Harrison J. Renal Homotransplantation in identical twins. *Surg Forum* 1955; VI: 432-436.
2. Wolfe RA, Ashby VB, Milford EL, Ojo AO, Ettenger RE, Agodoa LY et al. Comparison of mortality in all patients on dialysis, patients on dialysis awaiting transplantation, and recipients of a first deceased transplant. *N Engl J Med* 1999; 341: 1725-1730.
3. Keown P. Improving the quality of life. The New Target for Transplantation. 2001; 72:567-574.
4. Winkelmayr WC, Weinstein MC, Mittleman MA, Glynn RJ, Pliskin JS. Health economic evaluations: the special case of end-stage renal disease treatment. *Med Decis Making* 2002; 22:417-430.
5. 2006 OPTN / SRTR Annual Report: Transplant Data 1996-2005. Organ Procurement Transplant Network Web site. Available at: <http://www.optn.org/AR2006/default.htm>. Accessed September 1, 2007.
6. 2005 Spanish Liver Transplant Registry Annual Report. Spanish National Transplant Organization Web site. Available at: http://www.ont.es/RETHMemGeneral?id_nodo=276&accion=0&&keyword=&auditoria=F. Accessed September 1, 2007.
7. Evolution of liver transplantation in Europe. European Liver Transplant Registry Web site. Available at: http://www.eltr.org/publi/results.php3?id_rubrique=44. Accessed September 1, 2007.
8. Taylor DO, Edwards LB, Boucek MM, Trulock EP, Waltz DA, Keck BM, Hertz MI; International Society for Heart and Lung Transplantation. Registry of the International Society for Heart and Lung Transplantation: Twenty-third Official Adult Heart Transplantation Report—2006. *J Heart Lung Transplant* 2006; 25: 869-879.
9. Kreis HA, Ponticelli C. Causes of late renal allograft loss: chronic allograft dysfunction, death, and other factors. *Transplantation* 2001; 71 (11 Suppl):SS5-9.
10. International figures on organ donation and transplantation-2005. *Transplant Newsletter – Council of Europe* 2006; 11 (1). Spanish National Transplant Organization Web site. Available at: <http://www.ont.es>. Accessed September 1, 2007.

11. Data on organ donation and transplantation. Organ Procurement Transplant Network Web site. Available at: <http://www.optn.org/AR2006/default.htm>. Accessed September 1, 2007.
12. Goldfarb-Rumyantzev A, Hurdle JF, Scandling J, Wang Z, Baird B, Barenbaum L, Cheung AK.. Duration of end-stage renal disease and kidney transplant outcome. *Nephrol Dial Transplant* 2005; 20: 167-175.
13. Gjertson DW. Look-up survival tables for living-donor renal transplants: OPTN/UNOS data 1995-2002. *Clin Transpl.* 2003;:337-386.
14. Johnson EM, Remucal MJ, Gillingham KJ, Dahms RA, Najarian JS, Matas AJ. Complications and risks of living donor nephrectomy. *Transplantation* 1997; 64: 1124-1128.
15. Meeting the organ shortage: current status and strategies for improvement of organ donation. A European consensus document. Council of Europe Web site. Available at: http://www.coe.int/t/e/social_cohesion/health/Activities/Organ_transplantation. Accessed September 1, 2007
16. Cuende N, Cañón JF, Alonso M, Martín C, Sagredo E, Miranda B. Programa de garantía de calidad de la Organización Nacional de Trasplantes para la evaluación del proceso de donación. *Nefrología* 2003; 23 (5): 28-31.
17. Luskin RS, Buckley CA, Bradley JW, O'Connor KJ, Delmonico FL. An alternative approach to evaluating organ procurement organization performance. *Transplant Proc* 1999; 31: 353-355.
18. Gortmaker SL, Beasley CL, Brigham LE, Franz HG, Garrison RN, Lucas BA y cols. Organ donor potential and performance: size and nature of the organ donor shortfall. *Crit Care Med* 1996; 24: 432-439.
19. Hockerstedt K et al. Substantial increase in deceased organ donors in hospitals implementing the donor action programme in Finland. *Transplant Proc.* 2005 Oct;37(8):3253-3255.
20. Organ donation breakthrough collaborative: from best practice to common practice. Available at: <http://www.organdonationnow.org/>. Accessed September 1, 2007.
21. Recommendation Rec (2005) 11 of the Committee of Ministers to member states on the role and training of professionals responsible for organ donation (transplant "donor co-ordinators"). Accessible at: http://www.coe.int/t/e/social_cohesion/health/activities/organ_transplantation/. Accessed September 1, 2007.

22. Pichlmayr et al. Transplantation of a donor liver to 2 recipients- a new method in the further development of segmental liver transplantation. *Langenbecks Arch Chir* 1988; 373: 127-130.
23. Bismuth H et al. Emergency orthotopic liver transplantation in two patients using one donor. *Br J Surg* 1989; 76: 722-724.
24. Broelsch CE et al. Application of reduced size liver transplants as split grafts, auxiliary orthotopic grafts and living related segmental transplants. *Ann Surg* 1990; 212: 368-377.
25. De Ville de Goyet J. Split liver transplantation in Europe- 1988 to 1993. *Transplantation* 1995; 59: 1371-1376.
26. Wilms C et al. Long-term Outcome of Split Liver Transplantation Using Right Extended Grafts in Adulthood: A Matched Pair Analysis. *Ann Surg* 2006; 244:865-873.
27. Yersiz H 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: 1077-1080.
28. Yersiz 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: 78-81.
29. Rogiers X et al. In situ splitting of deceased livers. The ultimate expansion of a limited donor pool. *Ann Surg* 1996;224: 331-339.
30. Yan et al. Split liver transplantation: a reliable approach to expand the donor pool. *Hepatobiliary Pancreat Dis Int* 2005; 4: 339-344.
31. Ericzon BG, Larsson M, Herlenius G, Wilczek HE, Familial Amyloidotic Polyneuropathy World Transplant Registry. Report from the Familial Amyloidotic Polyneuropathy World Transplant Registry and the Domino Liver Transplant Registry. *Amyloid* 2003; 10 Suppl 1: 67-76.
32. Stangou AJ, Heaton ND, Hawkins PN. Transmission of systemic transthyretin amyloidosis by means of domino liver transplantation. *N Engl J Med* 2005; 352: 2356.
33. Ando Y, Araki S, Ando M. Transthyretin and familial amyloidotic polyneuropathy. *Intern Med* 1993; 32: 920-922.
34. Remuzzi G et al. Long-term outcome of renal transplantation from older donors. *N Engl J Med* 2006; 354:343-352.
35. Andrés A et al. Double versus single renal allografts from aged donors. *Transplantation* 2000; 69: 2060-2066.
36. Moore PS et al. Experience with dual kidney transplants from donors at the extremes of age. *Surgery* 2006; 140: 597-605.

37. Nardo B et al. Double kidney transplantation: initial experience of the Bologna Transplant Center. *Int J Artif Organs* 2006;29: 701-702.
38. Ojo A et al. Survival in recipients of marginal cadaveric donor kidneys compared with other recipients and wait-listed transplant candidates. *J Am Soc Nephrol* 2001; 12:589-597.
39. De Fitjer et al. Increased immunogenicity and cause of graft loss of old donor kidneys. *J Am Soc Nephrol* 2001; 12: 1538-1546.
40. Smits JM et al. Evaluation of the Eurotransplant Senior Programme. The results of the first year. *Am J Transplant.* 2002; 2: 664-670.
41. Alexander JW et al. The use of marginal donors for organ transplantation: the influence of donor age on outcome. *Transplantation* 1991; 51: 135-141.
42. Hoofnagle JH. Donor age and outcome of liver transplantation. *Hepatology* 1996;24:89-96.
43. Gastaca M et al. Donors older than 70 years in liver transplantation. *Transplant Proc* 2005; 37:3851-3854.
44. Zapletal Ch et al. Does the liver ever age? Results of liver transplantation with donors above 80 years of age. *Transplant Proc* 2005;37:1182-1185.
45. Cuende N et al. Liver transplant with organs from elderly donors. Spanish experience with more than 300 liver donors over 70. *Transplantation* 2002; 73: 1360.
46. Alexander JW et al. The use of marginal donors for organ transplantation: the influence of donor age on outcome. *Transplantation* 1991; 51: 135-141.
47. Mercer P et al. Evaluating the donor pool: impact of using hearts from donors over the age of 49 years. *Transplant Int* 1998; 11: Suppl 1: S424-S429.
48. Tenderich G et al. Extended donor criteria: hemodynamic follow-up of heart transplant recipients receiving a cardiac allograft from donors \geq 60 years of age. *Transplantation* 1998; 66: 1109-1113.
49. Morales JM, Campistol JM ; Andrés A, Domínguez-Gil B et al. Policies concerning the use of kidneys from donors infected with hepatitis C virus. *Nephrol Dial Transplant.* 2000;15 Suppl 8:71-73.
50. Morales JM, Campistol JM, Castellano G, Andres A, Colina F, Fuertes A, Ercilla G, Bruguera M, Andreu J, Carretero P, Rodicio JL, Levey AS, Pereira BJG. Transplantation of kidneys from donors with hepatitis C antibody into recipients with pre-transplantation anti-HCV. *Kidney Int* 1995; 47: 236-240.
51. Ali MK, Light JA, Barhyte DY, Sasaki TM, Currier CB, Grandas O, Fowlkes D. Donor hepatitis C virus status does not adversely affect short-term outcomes in HCV+ recipients in renal transplantation. *Transplantation* 1998; 66: 1694-1697.

52. Mandal AK, Kraus ES, Samaniego M, Rai R, Humphreys SL, Ratner LE, Maley WR, Burdick JF. Shorter waiting times for hepatitis C virus seropositive recipients of deceased renal allografts from hepatitis C virus seropositive donors. *Clin Transplant* 2000;14: 391-396.
53. Woodside KJ, Ishihara K, Theisen JE, Early MG, Covert LG, Hunter GC, Gugliuzza KK, Daller JA. Use of kidneys from hepatitis C seropositive donors shortens waitlist time but does not alter one-yr outcome. *Clin Transplant* 2003;17: 433-437.
54. Veroux P, Veroux M, Puliatti C, Cappello D, Macarone M, Gagliano M, Flamingo P, Di Mare M, Spataro M, Ginevra N. Kidney Transplantation From Hepatitis C Virus-Positive Donors Into Hepatitis C Virus-Positive Recipients: A Safe Way to Expand the Donor Pool?. *Transplant Proc* 2005; 37: 2571-2573.
55. Schussler T, Sttafeld-Coit C, Eason J, Nair S. Severe hepatitis C infection in a renal transplant recipient following hepatitis c genotype mismatch transplant. *Am J Transplant* 2004; 4: 1375-1378.
56. Viral hepatitis guidelines in hemodialysis and transplantation. *Am J Transplant* 2004; 4 (Suppl 10): 72-82.
57. Abbott KC, Bucci JR, Matsumoto CS, Swanson SJ, Agodoa LY, Holtzmuller KC, Cruess DF, Peters TG. Hepatitis C and renal transplantation in the era of modern immunosuppression. *J Am Soc Nephrol* 2003; 14: 2908-2918.
58. Abbott K et al. Impact of diabetes and hepatitis after kidney transplantation on patients who are affected by hepatitis C virus. *J Am Soc Nephrol* 2004; 15: 3166-3174.
59. Abbott KC, Lentine KL, Bucci JR, Agodoa LY, Peters TG, Schnitzler MA. The impact of transplantation with deceased donor hepatitis c-positive kidneys on survival in wait-listed long-term dialysis patients. *Am J Transplant* 2004; 4: 2032-2037.
60. Wolters HH et al. Kidney transplantation using donors with history of diabetes and hypertension. *Transplant Proc* 2006; 38: 664-665.
61. Leo Roels, Bernard Cohen, Caroline Gachet and Blanca Miranda. Joining Efforts in Tackling the Organ Shortage: The Donor Action Experience. *Clinical Transplants* 2002;Chap. 8:111-120.
62. Kootstra G. The asystolic, or non-heartbeating, donor. *Transplantation* 1997; 63: 917-921.
63. Donation after cardio circulatory death. A Canadian Forum. Report and Recommendations. Canadian Critical Care Society. Canadian Society of Transplantation. Feb. 17-20-2005 Vancouver British Columbia ISBN O-9738718-06 July 2005.

64. Bernat JL, D'Alessandro AM, Port FK et al. Report of a National Conference on Donation after Cardiac death. *Am J Transplant* 2006; 6: 281-291.
65. Sánchez-Fructuoso AI, Prats D, Torrente J et al. Renal transplantation from non heart beating donors. A promising alternative to enlarge the donor pool. *J Am Soc Nephrol* 2000; 11: 350-358.
66. Sánchez-Fructuoso AI, Marques M, Prats D, Conesa J, Calvo N, Pérez-Contín MJ, Blazquez J, Fernández C, Corral E, Del Río F, Núñez JR, Barrientos A. Victims of cardiac arrest occurring outside the hospital: a source of transplantable kidneys. *Ann Intern Med* 2006; 145: 157-164.
67. De Antonio DG, Marcos R, Laporta R, Mora G, Garcia-Gallo C, Gamez P, Cordoba M, Moradiellos J, Ussetti P, Carreno MC, Nunez JR, Calatayud J, Del Rio F, Varela A. Results of clinical lung transplant from uncontrolled non-heart-beating donors. *J Heart Lung Transplant* 2007; 26: 529-534.
68. Brook NR, Nicholson ML. Kidney transplantation from non heart beating donors. *Surgeon* 2003; 1: 311-322.
69. Gámez P, Córdoba M, Ussetti P, Carreño MC, Alfageme F, Madrigal L, Nuñez JR, Calatayud J, Ramos M, Salas C, Varela A. Lung transplantation from out-of-hospital non-heart-beating lung donors. one-year experience and results. *J Heart Lung Transplant* 2005; 24:1098-1102.
70. Maathuis MH, Leuvenink HG, Ploeg RJ. Perspectives in organ preservation. *Transplantation* 2007; 83: 1289-1298.
71. Moustafellos P, Hadjianastassiou V, Roy D, Muktadir A, Contractor H, Vaidya A, Friend PJ. The influence of pulsatile preservation in kidney transplantation from non-heart-beating donors. *Transplant Proc* 2007; 39:1323-1325.
72. Bernat JL et al. Report of a National Conference on Donation after Cardiac Death. *Am J Transplant* 2006; 6: 281-291.
73. Cohen B, Smts JM, Haase B, Persijn G, Vanrenterghem Y, Frei U. Expanding the donor pool to increase renal transplantation. *Nephrol Dial Transplant* 2005; 20: 34-41.
74. Murray JE, Merrill JP, Hartwell Harrison J. Renal Homotransplantation in identical twins. *Surg Forum* 1955; VI: 432-436.
75. Raia S, Nery JR, Mies S. Liver transplantation from live donors. *Lancet* 1989; 2:497.
76. Broelsch CH, Whittington PF, Edmond JC. Liver transplantation in children from living related donors. *Ann Surg* 1991; 214:418-439.
77. Marcos A, Fisher RA, Ham JM, Shiffman ML, Sanyal AJ, Luketic VA et al. Right lobe living donor liver transplantation. *Transplantation* 1999; 68:798-803.

78. Kiuchi T, Tanaka K. Living donor adult liver transplantation: status quo in Kioto and perspectives in the new millennium. *Acta Chir Belg* 2000; 100:279-83.
79. Miller CM, Gondolesi GE, Florman S, Matsumoto C, Muñoz L, Yoshizumi T et al. One hundred nine living donor liver transplants in adults and children: a single-center experience. *Ann Surg* 2001; 234:301-311.
80. Brown RS Jr., Russo MW, Lai M, Shiffman ML, Richardson MC, Everhart JE et al. A survey of liver transplantation from living adult donors in the United States. *N Engl J Med* 2003; 348: 818-825.
81. The Ethics Committee of the Transplantation Society. The Consensus Statement of the Amsterdam Forum on the Care of the Live Kidney Donor. *Transplantation* 2004; 78 (4): 491-492.
82. Pruett TL et al. The ethics statement of the Vancouver Forum on the live lung, liver, pancreas, and intestine donor. *Transplantation* 2006; 81: 1386-1387.
83. Recommendation No R(97)16 of the Committee of Ministers to member states on liver transplantation from living related donors (adopted by the Committee of Ministers on 30 September 1997, at the 602nd meeting of the Ministers' Deputies). Council of Europe web site. Available at [http://www.coe.int/t/e/social_cohesion/health/Recommendations/Rec\(1997\)16.asp#TopOfPage](http://www.coe.int/t/e/social_cohesion/health/Recommendations/Rec(1997)16.asp#TopOfPage). Accessed September 1, 2007.
84. Collaborative transplant study website. Accessible at: <http://www.ctstransplant.org/>. Accessed September 1, 2007.
85. Cecka JM The OPTN/UNOS Renal Transplant Registry 2003. *Clin Transpl* 2003;:1-12.
86. Matas AJ, Bartlett ST, Leichtman AB, Delmonico FL. Morbidity and mortality after living kidney donation 1999-2001: survey of United States transplant centers *Am J Transplant* 2003; 3 (7) 830-834.
87. Ommen ES, Winston JA, Murphy B. Medical risks in living kidney donors: absence of proof is not proof of absence. *Clin J Am Soc Nephrol*. 2006;1: 885-895.
88. Delmonico F. A report of the Amsterdam Forum on the Care of the Live Kidney Donor: data and medical guidelines. *Transplantation* 2005;79: Suppl 6: S53-S66.
89. Florman S, Miller CM. Liver donor liver transplantation. *Liver Transpl* 2006; 12; 499-510.
90. Brown RS Jr, Russo MW, Lai M, Shiffman ML, Richardson MC, Everhart JE, Hoofnagle JH. A survey of liver transplantation from living adult donors in the United States. *N Engl J Med* 2003; 348: 818-825.

91. Lo CM. Complications and long-term outcome of living liver donors: a survey of 1,508 cases in five Asian centers. *Transplantation* 2003; 75 (Supp 3): S12-S15.
92. Reimer J, Rensing A, Haasen C, Philipp T, Pietruck F, Franke GH. The impact of living-related kidney transplantation on the donor's life. *Transplantation* 2006; 81:1268-1273.
93. Ratner LE, Ciseck LJ, Moore RG, Cigarroa FG, Kaufman HS, Kavoussi LR. Laparoscopic live donor nephrectomy. *Transplantation* 1995; 60:1047-1049.
94. Tyden G et al. Implementation of a Protocol for ABO-incompatible kidney transplantation: a three-center experience with 60 consecutive transplantations. *Transplantation* 2007; 83: 1153-1155.
95. Buell JF, Lee L, Martin JE, Dake NA, Cavanaugh TM, Hanaway MJ et al. Laparoscopic donor nephrectomy vs. open live donor nephrectomy: a quality of life and functional study. *Clin Transpl* 2005; 19:102-109.
96. ...
97. Delmonico FL. Exchanging kidneys-advances in living donor transplantation. *N Engl J Med* 2004; 350: 1812-1814.
98. Thiel G et al. Crossover renal transplantation: hurdles to be cleared!. *Transplant Proc* 2001; 33: 811-816.
99. Mahendran AO, Veitch PS. Paired exchange programmes can expand the live kidney donor pool. *Br J Surg* 2007; 94: 657-664.

ANNEX 1: SET OF RECOMMENDATIONS OF ALLIANCE-O CONSORTIUM ON INITIATIVES TO EXPAND THE DONOR POOL

1. Donors dead due to irreversible loss of encephalic functions (encephalic dead donors or heart beating donors)

Organizational initiatives

a) Every hospital with intensive care unit facilities should be available to detect brain death and activate the donation process. Policies should be developed which encourage hospitals to engage actively in organ donation

b) A sufficient number of qualified personal and an adequate structure should exist at any procurement hospital in order to effectively develop the activities of donation.

c) A key donation person should be appointed in every acute hospital. The key donation person should have as a main responsibility a proactive donor detection programme.

d) A network of transplant procurement hospitals should be developed, where small hospitals are progressively being incorporated.

e) To optimise organ donation, there is need for a supra hospital transplant organisation, appropriate in size and structure to the local situation with specific responsibilities for the whole process of organ procurement.

f) The most effective organisational approach balances the requirements for effective organ procurement (small/local) with those for organ allocation (large, national/ multinational). The aim should be to optimise organ procurement whilst ensuring the most clinically effective allocation of organs and tissues.

g) A donor process evaluation programme should be developed in order to estimate the potential of donation within a hospital and to identify areas of improvement in the process of donation, providing the basis to introduce corrective measures. Strategies to evaluate the cost-effectiveness of these programmes should also be developed.

h) A quality management approach of the process of donation/transplantation should be developed which establishes standardized protocols, evaluates performance and introduces measures to improve. Participation of hospitals in the donation process should be considered a quality issue.

Human resources

a) The number of persons implicated in the process of donation at every procurement hospital should be enough to efficiently cover all the steps of the process

b) The presence of the key donation person at every hospital with acute care facilities, with the main responsibility of developing a proactive donor detection programme represents the most important human figure to optimize organ donation.

c) Other figures to support specific activities in the process of donation should be taken into consideration.

d) A suprahospital, well organized team should exist, composed by the enough number of and sufficiently prepared figures to enforce and develop strategies to support all the process of organ donation.

Technical Programmes

a) The use of special techniques as split and domino liver transplantation or double kidney transplantation with kidneys from expanded criteria donors may be considered areas to expand the donor pool, provided an adequate registry of results by using these organs is ensured.

b) The consortium agrees on providing a general definition of expanded criteria donors, as those potentially related to worse results in the recipients when compared to recipients receiving their organs from classical or more ideal donors. Under this concept we would include: extreme ages of life, transmissible diseases (infections and neoplasias) and other pathologies. When allocated in specific conditions, the use of organs from expanded criteria donors may be related to very acceptable results. Pilot experiences should be carefully and properly evaluated.

c) The safety limits in the use of organs obtained from expanded criteria donors should be properly evaluated through the development of registries collecting information on the outcome of the corresponding recipients. Consensus Documents and Guidelines on the adequate use of organs from expanded criteria

donors should be created if not available and properly updated with an evidence based approach.

Training initiatives

a) All professionals direct or indirectly involved in the process of donation should be the target for training activities in the donation process.

b) Training should properly cover all the steps of the donation process: brain death diagnosis, brain death referral, evaluation of the donor, maintenance of the donor, family approach and organ retrieval.

c) Training in the context of a properly planned, Harmonized and Accredited National Programme would be the ideal approach.

d) A system to continuously evaluate the efficacy of the training programme should be developed.

Financial initiatives

a) Hospitals should be sufficiently resourced to efficiently develop all the activities related to donation and transplantation. Donation should never be a disincentive activity for procurement hospitals.

b) To develop their specific functions related to increase the donor pool, the suprahospital transplant organizations should also be sufficiently resourced.

c) European / National programmes/activities aimed to expand the donor pool while ensuring quality should be properly funded: donor process evaluation, quality management, training, organ registries, among others.

2. Donors dead due to irreversible loss of cardio-respiratory functions (non heart beating donors)

a) NHBD may be considered a real alternative source of organs to face donor shortage, so provisions should exist in the countries in order to allow this kind of programmes to be drawn up. NHBD should always be considered as a

complementary activity to HBD. Maastricht category type 1 NHBD offers with no doubt a large potential to increase deceased donation activity, although experiences with this type of donors is still very limited.

b) Non kidney transplants from NHBD should be properly explored and evaluated. Research should be promoted to ensure that results with specific types of organs (e.g livers) are susceptible of improvement.

c) NHBD should be approached under the scope of pilot experiences arisen from highly motivated teams and ensuring that a continuous interchange of experiences takes place.

d) NHBD programmes should take into consideration the need for a highly trained hospital team, 24 hours a day available. Specifically, a high qualification with regards to preservation techniques to guarantee the quality of the organs retrieved should be mandatory. It would be highly advisable that this team is led by or well coordinated with the so-called key donation person, ensuring a close link between NHBD and HBD programmes. Hospital facilities (eg emergency room) should be available to ensure that preservation maneuvers start at the right time.

e) Extraordinary and highly trained extra-hospital emergency care teams are a necessary human resource in order to implement any programme with type 1 Maastricht category NHBD.

f) Development of specific protocols, guidelines and consensus documents should be encouraged, up-dated on an evidence based approach, to ensure the quality of the organs obtained from this source and results being improved over time. Registration and continuous evaluation of results obtained with organs from NHBD seem mandatory through local, national or international registries.

g) Research should be promoted to ensure that quality of organs obtained from these donors progressively increases and provides increasingly better results. Preservation techniques represent an area where research should be highly supported.

h) Continuous training of teams with ongoing activity and teams developing new programmes should be ensured. Specific attention should be paid to the continuous training of extra-hospital emergency care teams in the case of Maastricht type 1 NHBD, to ensure a proper detection and maintenance of the potential donor.

i) Specific budget to hospitals developing NHBD programmes should be ensured, covering human and material resources, as well as training and research. Cost-effectiveness evaluation of NHBD is needed.

3. Living donors

a) Living transplantation activity is progressively increasing, but it is still widely variable in European countries: while very frequent in some countries, it still remains anecdotic in others. Living donation is a real alternative to improve the availability of organs for transplantation. However, there is a need for drawing up living programmes in a complementary way to the deceased donation ones, never in competition. There should not exist a negative correlation between the living and the deceased transplantation activity.

b) Morbidity and mortality related to living donation differs according to the type of donated organ. While referring to the most frequent living donation procedures, this means kidney and liver donation, a explicit differentiation should be outlined, because of the different risks related to nephrectomy and partial hepatectomy, even in a healthy person. Living liver donation (especially right lobe) should be cautiously considered.

c) Adequate tools (as local, national or international registries, as well as periodic surveys and others) should be developed in order to ensure that information on the medical, psychological, financial and social complications related to living donation in the short and the long run is properly collected. This information should help to develop evidence based guidelines and consensus documents, addressing the selection, evaluation and follow-up of the living donor.

d) The development of new surgical alternatives and any other type of initiative in living donation and transplantation, aiming to increase the donor's safety, facilitate the recovery and incorporation of the donor to an active and normal life and to improve recipient's outcome should be highly encouraged and research should be promoted in this field.

f) The possibility of living donation should be offered to any patient accessing the waiting lists, always on the basis of individual circumstances. Adequate and complete information should be provided to the patients and relatives. The appointment of specific professionals in charge of providing this kind of information could be considered in hospitals with an important living transplantation activity. In the case of living kidney transplantation, this figure could even be evaluated for large dialysis units or for a set of small ones.

g) Living donation should be properly resourced, especially keeping in mind the benefit not only for the recipient, but also for the community, since it allows one person being removed from the waiting list at a moment in which deceased organ donation is insufficient to fulfil the demand of organs for transplantation. Living donation should never be a disincentive activity for hospitals.

e) Authorities should ensure the health-care coverage of the living donor before, during and after the procedure, ensuring the long-term access of the living donor to the health care system. Social benefits for living donors should be explored, as well as ensuring that health/life insurances do not penalize the living donor.

f) Continuous training of professionals in charge of an ongoing or new living donation programme should be guaranteed. Interchange of experiences among medical and surgical teams should be encouraged.

g) While many ethical and technical aspects remain to be solved, paired kidney donation (cross over kidney donation) represents a valuable approach to increase the kidney donor pool and the possibilities of transplantation. Provisions may exist so this kind of specific programmes may be drawn up on the basis of local circumstances.