Chapter 6

Policies and Methods to Enhance the Donation Rates

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Additional information is available at the end of the chapter

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1. Introduction

The therapeutic promise of transplanting organs from cadaveric donors, as envisioned by the pioneers of transplantation, has never been kept because the demand for cadaveric organs has by far exceeded the supply.

Besides the fact that renal transplantation is the optimal treatment for patients with end stage renal disease, it provides benefits to the society as a whole as well as to the recipients. Yet, the donor shortage poses a significant challenge to the transplant community and bare unfavorable consequences: prolonged waiting time and compromise patient survival. Sustained efforts were done during times to increase both the deceased donor and living donor pool.

The expanded criteria donors also known as non-traditional donors has been credited to lessen the current shortage of grafts available for transplantation by providing more grafts. Any such attempt is a two-edged sword since it increases the outcome risk of the suboptimal grafts.

Criteria for living donation were more restrictive compared with cadaver donation but such reluctance to use living donor marginal grafts is declining since transplantation is a better option than dialysis.

Expansion criteria allows transplantation of grafts from deceased donors at the extreme age (above 60 and below 16), with history of hypertension, diabetes or malignancy, hemodynamically unstable, non-heartbeating, seropositive for hepatitis B or C, with systemic infections, at high-risk for HIV infection, reduced renal function, anatomic anomalies, or injuries [1].

The waiting list for transplant organs continues to grow and many patients continues to die while waiting or become unsuitable for organ transplantation. Consequently, many patients with end stage organ failure are no longer relaying on the waiting list for cadaver transplantation. There is a trend not only to reconsider the living donor but also to turn the attention toward spouses, friends or even strangers as possible donors. From medical point of view, all

these are acceptable alternatives due to advances in immunosuppression which have eliminated the requirement for a perfect genetic match for a successful organ transplantation. In many US transplant centers, the number of kidneys obtained from living donors has exceeded the number of kidneys obtained from cadaver [2].

Although organs from living donors can be transplanted safely, concerns about the protection of well-being of such donors has prompted the transplantation community to develop a consensus statement, emphasizing that a living donor should be competent, willing to donate an organ, and free of coercion.

Regardless of donor type and graft quality, one should keep in mind that never should be transplanted grafts with a heightened potential for the development of a progressive disease.

Since the rules are continuously evolving, the approach to use of each graft and recipient selection should be done with caution in order to obtain acceptable results.

2. The living donor

The use of living donors for renal transplantation was critical for the early development of the field, and in fact, preceded the use of cadaveric donors. At the moment, 20-22% of all kidney transplants performed in the world were done with grafts from living donors. Most donors are related genetically to the recipient, but there is an increasing percentage of cases, where donors are genetically unrelated and includes spouses, friends, or other emotionally related individuals. As it is known, ethical guidelines mandate that the living donors should not be coerced and there will be no evidence of financial profit for the donor. As a consequence, the donation should be considered "a gift of extraordinary value". It is known that the use of living donors has been associated with a higher success rate than that seen with cadaveric donation. Due to a higher demand for transplantation and the lack of a parallel increase in the number of available cadaveric organs, living donation is the only solution for some patients to avoid long times on waiting list, and occasionally, even the need of dialysis (1).

Better results (both long and short-term)
Consistent early function and easier management
Avoidance of long waiting time for transplantation
Less aggressive immunosuppressive regimens
Emotional gain to donor

Table 1. Advantages of living donation

There is a remote risk of catastrophic outcome of the living donor (1 in 3200 patients), but most transplant centers and surgeons accept this. Some centers accept only living related donors; others accept related as well as unrelated donors. These centers come to turns with the possibility of harming living donors by being highly selective in their acceptance of donors. While surgically

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pragmatic, there is a philosophic fallacy in this approach. The important issues regarding the donor, in addition to medical suitability, are whether the donor understands the risk of nephrectomy and whether the donor freely consents. The risk for the donor is the same regardless of the donor's relationship to the recipient and regardless of the recipient's outcome. The risk for the surgeon, that is the death of the donor, is no less devastating for the surgeon if the patient is a close relative to the recipient than if the donor is a stranger.

2.1. Evaluation of the living donor

Usually, the potential living donor is the one who initiates the discussion about donation, although the recipient or the physician can also rise the issue. The donor than meets with the nephrologist, transplant surgeon, social worker, and transplant coordinator. All donors are informed of the risks and benefits of the transplantation compared with the dialysis and the risks to themselves by donating a kidney, on both short and long term [3, 4]. 1995 data of US practices founded that reported mortality rate for living donors to be 0.03% and the morbidity rate to be 0.23%. It is important to screen any relative of a patient with familial renal disease (polycystic kidney disease, hereditary nephritis) for evidence of occult signs and symptoms, in order to exclude such donors [5]. On the other hand, kidneys with minor renal abnormalities can be used safely, once it is determined that function of the such kidneys could not be impaired after transplantation [6].

Initial evaluation of all potential donors consists of blood and tissue typing. Usually, those with ABO incompatibility are excluded; compatibility with the Rh factor is unnecessary. All blood group compatible donors are then tested with the T lymphocyte cross-match. A negative cross-match will allow further consideration for donation. In the case of multiple potential donors, the better the antigen match, the grater is the likelihood of being selected for donation, if all other testing are within normal limits. In general, as long as the donor and the recipient have a negative T cell cross-match, the operation can be cared out. This is true for both related and non-related donors who are ABO compatible. Many centers perform a mixed lymphocyte reaction (MLR) as part of the routine evaluation, but the importance of this test has decreased with the introduction of better immunosuppression.

Further evaluation for a potential donor consist of a complete medical history and a complete physical examination, routine laboratory, testing, and serologic evaluation for EBV, herpes virus, CMV, HIV, and hepatitis B and C viruses. Urinalysis and culture along with 24 hour urine collection for creatinine clearance and protein excretion, are included as part of the routine evaluation. If there is any concern regarding a borderline hypertensive pressure reading, the blood pressure should be measured on the least three and as many as ten separate occasions. Once all laboratory testing has been performed, the next step is renal arteriography with an excretion faze to visualize the collecting system. This eliminate the need for intravenous pyelography. Such testing can be performed on an outpatient basis. Nowadays spiral CT scan has been used routinely instead of conventional angiography in all centers. The use of magnetic resonance (MR) angiography is also growing in importance. Donors are judged unsuitably for a variety of reasons (2).

Absolute
Lack of discernment
Alcohol or drug addiction
Age less than 18 years
Hypertension: blood pressure over 140/90 mm Hg requiring medication
Diabetes: abnormal glucose tolerance test or HbA1c
Proteinuria: over 300 mg/24 hours
Abnormal glomerular filtration rate: creatinine clearance less than 75 mL/min.
Microscopic hematuria of unexplained cause
History of thrombosis or thrombembolism
Medical significant illness: chronic lung disease, recent malignant tumor, heart disease, vascular collagen disease,
History of bilateral kidney stones
Family history of autosomal dominant polycystic kidney disease (ADPKD), unless ultrasound or CT scan is normal and age is over 30 years
Familial history of renal cancer
Bilateral fibromuscular arterial dysplasia
Long-term use of nephrotoxic drugs
HIV positive
Hepatitis B antigen-positive to a negative recipient or unprotected
Other severe infections
Relative
Anatomic abnormalities of the donor's kidney: vascular or urological
Obesity: 30% or more above ideal weight
Young donor with a first degree relative with type I diabetes or renal disease
Significant previous abdominal surgery
Single history of unilateral renal stone disease
ABO incompatible
Positive cross-match
Smoking
Psychiatric disorders

Table 2. Exclusion criteria for living donors

Anyone at risk for the development of acquired renal disease should be excluded.This includes individuals with diastolic blood pressure constantly above 90 mm Hg, or who required hypertensive medication to control their blood pressure.

History of hypertension is not by itself a reason for exclusion if the donor is normotensive and off medication, but the donor should be carefully examined for preexisting renal disease or for the risk of development of renal disease later in life.

Potential donors for siblings with diabetes routinely undergo a five hours glucose tolerance test, and 24 hour urine specimen must be free of proteinuria. Some centers require that the

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donor be at least 10 years older than the age of the recipient at the time of diagnosis of the diabetes. The measurement of the haemoglobin A1c and anti-islet antibodies also can be included in the evaluation of any potential related living donor for a recipient with diabetes. Unexplained microscopic hematuria may be an indication of an underlying renal disease such as glomerulonephritis, but it may not be detected before donation. Finding as few as three red cells per high power field may appear unimportant at first but may be an indicator of potential future problems.

History of thrombembolism or thromboflebitis places the potential donor at increased risk of pulmonary embolism and therefore it precludes donation. This is also true for patients with heart disease, or history of malignant neoplasia. Obesity may be a relative contraindication for any potential donor, if it is more than 30% above ideal body weight. These individuals should be advised to loose the excess body weight before the transplant is scheduled, to decrease the risk of pulmonary embolism or cardiac complications.

Patients with clinically significant psychiatric disorders should be fully evaluated by a psychiatrist to established that the donor understands and agrees to the proposed procedure.

Once a full evaluation has been performed, if examination of the donor's kidney vascular supply and drainage system reveals an abnormality, it must be decided whether the risk imposed on the donor or the recipient are too great. With regard to vascular abnormalities we tend to use donor kidneys with three or more arteries if there is a good immunological correspondence and a strong determination for donation and if dialysis tolerance of the recipient is bad [7,8]. Abnormalities such as aneurisms, renal artery stenosis, fibro-muscular dysplasia, if limited in sized and area, can often be resected, repaired, or excised on the back table. Such pathological addition should bee limited to one kidney, living as a rule, the normal kidney in place. Given this caveats, it may be possible to use such donors [9].

Excision and reconstruction of such abnormalities is, in a sense, a of form of treatment of this donors, although care must be taken to avoid living either the donor or the recipient with less than a perfect outcome.

2.2. Preoperative management

Once the evaluation has demonstrated that there are no abnormalities serious enough to exclude donation, the donor can be admitted to the hospital after a spiral CT scan was performed. Many insurance companies are now restricting admissions to the day of the operation. In such cases intravenous hydration can be given overnight on an outpatient basis, or started on arrival at the hospital. Such hydration is important to help ensure adequate diuresis during the donor operation. Preoperative assessment by the anesthesiologist and the pain management team can make for a more comfortable postoperative recovery.

The donor is instructed preoperatively on the use of spirometer, and on the use of leg support stockings and the sequential compression device system to prevent venous stasis. After entering the operating room and before the incision, the patient should receive a dose of intravenous antibiotic. Although preoperative skin cleaning is recommended; hair clipping is avoid until just before incision.

2.3. Surgical alternatives in life donor nephrectomy

Regarding the surgical habits and the existing experience, there are several ways of harvesting kidneys from living donors [10-12].

- Classic transperitoneal approach, either throw midline, or throw a left or right subcostal incision.
- Subcostal extraperitoneal approach (left or wright).
- Dorsal lumbotomy approach. The incision can be performed either underneath the XIIth rib, resecting the XIIth rib, or above the XIIth rib (extraperitoneal, extrapleural).
- Laparoscopic approach either transperitoneal or retroperitoneoscopic.

2.4. Laparoscopic approach for living donor nephrectomy

The introduction of laparoscopic living kidney donation has been a major advance in organ donation. First introduced with some reticence only in selected centers, this procedures are now the preferred surgical approach in almost all transplant programs in United States and Europe. Usually, the program that offers this kind of procedure have a high rates of living kidney donation. The major benefit of laparoscopic technique includes significant reduction of surgical pain, postoperative convalescence, and recovery time. As a result, the laparoscopic donor nephrectomy has been responsible for expanding the pool of living donors and may account for the increased popularity and frequency of living donation. Long term renal function is not different between open nephrectomy and laparoscopic nephrectomy. About 75% of living donor transplant nephrectomies world wide employ laparoscopic technique, either transperitoneal or retroperitoneal.

2.5. Open living donor nephrectomy

The traditional method for removing kidney from a living donor has been open surgical technique, in majority of cases using a flank incision. In selected cases in which the donor has motivation which precluded laparoscopic access (e.g. significant prior abdominal surgery), or in some cases of complex vascular anatomy, an open surgical approach is preferred. Some centers advocate the use of open surgery for pediatric patients, although the age of recipient is not universally considered an indication for open renal procurement. Most donor surgeon use a donor flank incision, extra pleural and extra peritoneal above or below the XIIth rib.

As it is in any surgical approach, the kidney must be very carefully dissected to preserve renal veins and periureteral blood supply. Excessive pressure on the renal artery is avoided to prevent a vasospasm. After the renal vessels are securely ligated and divided the kidney is removed and placed in a basin of frozen saline slush to decrease the renal metabolism and after that the vessels are un-ligated and flushed with heparinized solution for both procedures, either laparoscopic harvesting or classic surgery.

2.6. Postoperative care

Postoperative care of a living donor is fairly standard. Adequate postoperative analgesia is a key factor including postoperative complications such atelectasia and pneumonia [15]. Infections should not occur with appropriate antibiotic prophylaxis. The continuous use of leg stoching and sequential compression devices are essential to prevent deep venous thrombosis of the lower limb. Most patients are often ambulatory by postoperative day 1 or 2 and tolerating oral feedings by postoperative day 2 or 3. The donor can be discharged by postoperative day 2 to 6. The renal function of the donor should be assessed periodically after the operation, as some patients experience a 25% increase in serum creatinine level; this should return near baseline by 3 months after the operation. In fact there are no convincing data to suggest that living donors are at any increased long term risk as a result as having donating the kidney.

2.7. Long term complications

The immediate operative risk to the donor can be stated with some certainty but the long terms effects are not completely understood. Follow-up, in general, is reassuringly but incomplete. Most folow-up studies of living kidney donors find no decrease in long term survival. All existing follow-up found an at least 85% survival up to 31 year after donation, compared to a predicted 66% in general population of similar age. The survival advantage at the living donors was attributed to the selection bias of only healthy individual as renal donors and at better follow up for them. Concerns regarding the possibility that donors will develop end stage renal disease (ESRD) is:

- hyper filtration in the remaining kidney will lead to focal segmental glomerulosclerosis and renal failure, that is donation per se will cause renal failure,
- the second concern is that donor will develop primary renal disease. The donors who develop primary renal disease will progress to renal failure more quickly because they have a lower than normal renal mass at onset of a primary renal disease. The later concern applies to a family with a history that put them for a risk of renal disease, for example: patient with type II diabetes.

Many follow-up studies have noted an increase in hypertension and proteinuria as well as a statistically but not clinically significant increase in serum creatinine. There are studies which found an increase in 20% of patients with blood pressure (15%-48%) [16] but it is not clear if hypertension is more common to this group than in general population.

Another study is finding that 35% of patients are taking anti-hypertensive medications and 23% are having proteinuria compared with 44% and 22% respectively for controls [17]. On the other side, even if the donor has a normal renal function, the glomerular filtration rate is in fact maintained by hyper filtration.

One thing is for sure, that in all follow-up studies, majority of the donors which are altruistic donors, drive a tremendous degree of satisfaction and an increased of self esteem for their donation. As a consequence, donors interviewed considered their donation as an act of heroism and generosity with which nothing else in their life can be compared [18]. More than 90% said

that they would donate if they have it to do over again, and fewer than 10% expressed any regret about donating [19].

2.8. Policies to enhance living donation

The therapeutic promise of transplanting organs from cadaveric donors has never been kept because the demand for transplantation has by far exceeded the possibilities. The waiting list for transplants continues to grow and in 2005 nearly 5000 patients were removed from the waiting list because of the death. Consequently many patients with end stage organ failure are no longer relaying on waiting list. Than the attention was turning toward living donors others than they have been classically admitted i.e. toward spouses, friends, or even strangers, as possible donors. From medical point of view, these are acceptable alternatives, due to the fact that immunosuppression has eliminated the requirement for a perfect genetic match in order to have a successful transplantation [20]. In many centers world wide, specially US transplantation centers and scandinavian transplant centers, the number of kidneys transplanted from living donors has exceeded the number of kidneys obtained from cadaver donors (over 35%) [21].

Although donors from living donors can be transplanted safely, concerns about the protection of well being of donors has prompted the transplantation community to develop a consensus statement emphasizing that a living donor should be competent, willing to donate an organ, and free of any kind of coercion [22]. More than that, the new reliance on organs from living donor has increased the risk of donation for financial reasons, especially in the case of unrelated donor. It is world-wide admitted that organ donation has to rely on the voluntarism and altruism, and uncompensated family members of the donor.

Donor type	1990	2000	2010	relative ratio
Cadaveric	4306	5489	7241	+ 1,68
Biologically related living donors	1831	4030	3046	+ 1,66
Emotionally related living donors	59	667	715	+ 12,11
Unrelated living donors	204	804	2516	+ 12,33
Total transplants	6400	10990	13518	+ 2,11

Table 3. Reported kidney transplants performed in USA [OPTN data]

The purchase of organs is explicitly unlawful in Europe, US, as virtually all other countries but the shortage of cadaveric organs has led to a world-wide black market for organs from living donors. That's why patients with sufficient means can travel to distant locations in order to purchase kidneys for transplantation [23, 24].

This is a dramatic situation which is generated by continuous shortage of organs for transplantation and by the increasingly donation rate from unrelated living donors. Such a situation require significant changes in the transplantation laws which should permit the increase of living donors and in the same time to stop the organ trade. Very difficult task.

The rate of living donation can be increased by two methods:

- organizing and ethic alternatives,
- medical methods are represented by: laparoscopic harvesting, paired kidney exchange, transplantation of grafts with anatomic abnormalities (vascular, urinary tract or fusion), acceptance of patients with low compatibility after a treatment with plasmapheresis and iv Ig.

2.8.1. Organizing and ethic alternatives to increase the rate of living donation

The motives of living donors and the motives of families of deceased donors, are complex and not necessarily always pure altruistic [25]. Spouses and siblings, who act as a living donor, experience a personal reward seeing that the recipient well being is restored. Because the organ donation is a voluntary and valuable act it should be considered as a charitable gift. Society could explicitly thank the organ donors for their gift, as it is done with other charitable contributions, without jeopardizing its altruistic basis. New legislations should embrace ethically acceptable ways to encourage such charitable donation of organs.

2.8.1.1. Incentives for organ donation

The issue of public incentives to enhance donation is more than just complex but mainly sensitive. From a philosophical point of view, the body is a part of our personality, thus in respect with human dignity it would be wrong to use parts of our body as means only [26]. On the other hand, one may assert that everyone is the rightful owner of his person supporting the idea that the self can decide over its body like any kind of property [27].

Most frequently, the background attitude of general population is to reject incentives for donation but there might be circumstances under which attitudes may change [28]. For instance, when the process became transparent: the amount of compensations are specified or there might be some ethical reasons to do so. The main risk is exploitation of those severe impoverished on a black market [29].

The valuable exchange of organs is prohibited worldwide, yet there exists national law or regulations which allows incentives for deceased or living donation [30]. Such incentives including financial reimbursement, health care-related reimbursement or other recognition for living donors or deceased donors' families have been widely debated [31].

Donor medal of honor. Organ procurement organizations must have ceremonies which recognize and appreciate organ donation. A donor medal of honor enacted by a top official of the country expresses the appreciation and gratitude on behalf of the whole community to the living donors and even to the families of the deceased donor [32, 33].

Medical leave for organ donation. Currently organ donors risk loss of wages or even loss of employment because the time away from the work that is required for donation [34,35]. In many countries there are legislations that provide a 30 day medical leave for all employees who donate an organ for transplantation [36]. However, no one should have to incur a personal expense for donating an organ. Many national organizations are doing an effort to encourage hospitals with transplantation services to provide paid medical leave for employees who become organ donors. Even if legislation emphasizing that enrichment should not be the reason for the donation, paid medical leave has to be available to a larger number of would-be donors [37].

Ensuring access to organs for previous donors. As you have seen up to now, the majority of living donors are doing well after donation. However, it has been established that at 10 years after donation, under 5% of those who donated the kidney developed ESRD; this donors are being placed on waiting list for cadaver organs [38]. Despite the additional allocation priority points, these donors have to wait for a cadaveric kidney, some of them for a long period of time. The health and well being of living donor should be monitored in a follow-up register in order to document medical problems associated with donation that occur over ensuing years [22]. The need for a transplant in a previous kidney donor should be considered a high priority in the allocation of the organs.

Donor insurance. The fact that there are being cases in which a kidney donor died immediately after donation or needed a kidney transplant at a later date, serves as a reminder that a nephrectomy (any kind of nephrectomy) is not a risk free procedure. A survey at some centers of transplantation show that at least two kidney donors had died from perioperative complications after a kidney donation and some of them had a persistent complication [39].

As a consequence, it should be enacted national plans to provide life and disability ensures for all living donors including a mechanism to ensure that they do not incur catastrophic medical expenses as a result of a donation.

2.8.1.2. Organ exchanges

Since the report of Rapaport which introduced the concept of paired kidney exchange as a method to enhance the number of living donors, these techniques have been applied in several countries with lower cadaver donation rates like Mexico, South Korea, Japan, and Europe (Holland and Romania).

Many persons who wished to donate an organ to a spouse or another family member where unable to help them due to incompatible blood type or other immunological barriers (positive cross-match). A program of paired kidney exchange addresses this problem by permitting an exchange of organs from two living donors [34] or from one living donor to one deceased donor. In the later approach, recently introduced in New England and Holland, a living donor incompatible with his intending recipient, donates an organ to a compatible patient on the waiting list for cadaveric organs in exchange for a priority allocation of a cadaveric organ to the donor's intended recipient. Thus, two transplantations are performed in circumstances that otherwise had permitted neither. Because such exchange could open the door to a paid

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donorship, the same prohibition against the payment donor should be applied to organ exchanges.

Legal issues. Initially, most countries limited traditional transplantation to genetically of strong emotionally related pairs. With extend of paired kidney donation, such limitations were removed to allow both altruistic non-directed donation and paired donation. Although, any exchange in paired donation represent in fact a transaction between parts, it do not involve financial values. It is advisable that such a issue should be explicitly addressed by the legal framework of every country.

Allocation algorithm. Grafts allocation in paired kidney donation is one of the domain who largely benefits from theories derived from economics regarding stable allocation and the practice of market design [40]. The main goal is to maximize the number of matched pairs. Any such program should overcome the disadvantage of O recipients by increasing the likelihood to receive a compatible graft. The risk of a positive cross-match with a from the donor pool might be assessed by considering the HLA antibody profile of the recipients and the HLA profile of the donors [41, 42]. When done on a national scale, such a matching should include distance between transplant centers, matching the virusologic profile of the recipient and donor, donor's age and size. Recipients from such pairs will be suspended from the waiting list until either they will be transplanted or a incompatibility test will reveal that the exchange is not possible. List paired donation may increase the rate of transplants by expanding the donor pool. In such an exchange, an incompatible donor who will donate to a recipient from the waiting list while his recipient will receive a high priority for the allocation for a deceased donor kidney [43, 44]. There are several concerns regarding ethical and legal issues. Such a transplant is designed to give an alternative to O blood type recipients with a non-O incompatible donor. The immediate consequence is the transplantation of a non-O blood group recipient from the waiting list and the addition of a O blood group recipient. This way, there will be an increased pressure over the O blood group recipients [43, 44].

Matching algorithms. Different matching algorithms were designed to maximize the number of recipients with an incompatible living donor will undergo renal transplantation. After an initial experience with two pairs, the number of pairs involved in a paired kidney transplantation increases to three, four and even more and the procedure gain worldwide acceptance. Involving of more than two pairs increases the chances to get a renal transplant but in order to avoid the withdrawal risk requires six or more operations to be done at the same time. Designed for O blood group recipients, exchanging of an incompatible kidney for a preferential position on the waiting list increases the recipient's chances for a renal transplantation but decreases the chances of other O blood group recipients from the waiting list [45-48]. This situation creates ethic dilemmas. Generalizing such list exchanges to any blood group recipient with a living donor available but incompatible, may overcome this issue.

Altruistic donation or non-directed donation is more ethical and legal challenging. It is difficult to believe and understand that a good Samaritan really exists and even when exists, national law framework should allow transplantation from unrelated living donor. Altruistic donors may be allocated to a waiting list or to initiate an open chain of paired transplantations [46,49].

Utilizing living donors may decrease the pressure for renal transplantation. Moreover, implementing of different types of kidney exchange could give further solutions to increase the transplantation rates. Combining different approaches to kidney exchange may create complex and versatile solutions to the incompatibility issue, even finding a better match for compatible pairs.

2.8.2. Medical methods to increase the number of living donation

2.8.2.1. Acceptance of grafts with anatomic anomalies

The number of donations can be increased by accepting donors with anatomic anomalies (multiples arteries, multiple veins, moderate dysfunction of the UPJ, renal cyst, complete duplicate ureteral system, solitary stone) which can be corrected in bench surgery.

Anatomical anomalies of the kidney have been considered for a long time as an absolute contraindication for living donation. Even now, many nephrological centers are including in their exclusion criteria for live related or unrelated donation items like urological abnormalities in donors or history or presence of any kidney stones.

But in our days, the majority of transplant centers with experience in the field, due to the shortage of the living donors pool, are considering the contraindication for using grafts with anatomical anomalies just a relative contraindication. Occasionally, the donor has minor unilateral abnormalities such as a renal cyst, ureteropelvic junction obstruction, solitary stones, duplex ureteral system, etc. If the related donor with a good immunological correspondence with the recipient has an abnormal kidney and is the only one available and the evolution of the recipient on hemodialysis is unacceptable, it is advisable to transplant the abnormal kidney, living the donor with the best one.

2.8.2.2. Acceptance of donors with multiple arteries and veins

The management of multiple renal arteries (MRA) are considered technically demanding in renal transplantation programs with kidneys from related or unrelated living donors. Some programs consider the use of multiple arteries and veins as a relative contraindication, because of increased risk of vascular and urological complications.

In addition, the rapidly increasing laparoscopic kidney donation has been accompanied by a significant shift in surgical practice [50,51]. Many centers which are performing laparoscopic harvesting restrict it to the left kidney [52-54]. The limitation to the left kidney leads to a higher utilization rate of kidneys with multiple arteries; in the literature, incidence of unilateral multiple renal arteries is between 18% and 30%, unless one limits laparoscopic nephrectomy only to the kidney with normal anatomy which is precluding 30% of all donors.

By accepting grafts with multiple renal arteries, one may theoretically accept an adverse effect on the outcome of those grafts. Previous authors [55,56], stated that MRA in their reconstruction were associated with several post-transplant complications. This is the motivation why such anatomy was considered to be a transplant contraindication. The most frequent vascular

complications which were encountered in reconstruction of multiple arteries were graft thrombosis, stenosis of the renal artery, and an increased risk of reno-vascular hypertension [55-57]. The most frequently ureteral complication encountered [58] were ureteral necrosis and pelvi-caliceal fistulas.

Smaller arteries are more prone to develop premature atherosclerotic occlusion. If that happens with a small accessory lower pole artery it would lead to ischemic distal ureteral stricture.

Any way, recent data collected from the centers and program of renal transplantation with experience in the field, display above any doubt that procurement of kidneys with multiple renal arteries can be accomplished safely and not impose additional medical, social, economical or postoperative clinical evolution burden, on the donor and the recipient.

Overall intraoperative and early postoperative complications of the recipients are not significantly different from the evolution of the recipients who received grafts with single arteries. A low rate of vascular complications is achieved using standard microvascular reconstruction technique with or without autologous vein patches [59-61] or extension graft. More than that, early graft function assessed by urine output and serum creatinine measurements were not significantly different among grafts with single arteries or grafts with multiple reconstructed arteries. In addition, long term quality of function, rejection, graft loss rates and graft survival were also similar. More than that, overall graft survival rates of this patients is exceeding 90% at 3 years.

In summary, the introduction of laparoscopic donor nephrectomy has significantly increased the number of grafts with multiple renal artery. Utilization of this donors, increase the rate of donation with 30% in specific centers. Modern techniques based on microsurgery have reduced dramatically incidence of above mentioned complications. From a patient outcome based perspective, this change in practice showed to be safe for both donors and recipients.

2.8.2.3. Laparoscopic donor nephrectomy - alternative to increase the rate of living donation

One great potential means for obtaining more kidneys is throw live donation. When compared with cadaveric renal transplantation, living donor transplantation has several advantages, in fact well known, which includes better graft survival, more rapid renal function after transplantation, shorter hospitalization and finally lower cost. However, several barriers exists for potential living donors. Significant time is involved when one donates a kidney. Many individuals do not have adequate financial and social support available that would allow them to make a personal sacrifice and a time commitment necessary for kidney donation. Moreover, the relatively prolonged convalescence can have significant financial impact on donor. Finally, fear of pain as well cosmetic concerns, associated with flank incision, can militate against kidney donation.

Laparoscopic living donor nephrectomy (LLDN) with all its alternatives (transperitoneal approach, retroperitoneal approach, hand assisted laparoscopic nephrectomy) was introduced in 1995 by Ratner and Kavoussi [62].

Laparoscopic nephrectomy is more technically demanding than other standard abdominal laparoscopic procedures. The surgeon experience is crucial for minimizing potential morbidity. Significant operative differences are between open and laparoscopic donor nephrectomy. The later approach requires a different set of technical skills than that associated with traditional open surgery. The endoscopic video image is only two dimensional and much narrower when compared with direct vision afforded by open surgery. The types of instrumentation available for working throw the small incision afford only restricted degrees of freedom when compared to the human hand. Moreover, the tactile sensation, currently can not be transmitted through the instrument. The differences are giving a longer operative time with one or even two hours when compared with open donation. All these drawbacks are only partially eliminated by robotic surgery, even if now there is a three dimensional vision of operative field and the mobility of the working instruments is better than that of human hand.

Even so, laparosccopic renal donation and robotic laparoscopic harvesting offers both introperatively and postoperatively great benefits to the donor.

Due to magnification provided by the optical system and the video camera, in experienced hands, the dissection of the renal pedicle is more accurate and if it is realized through retroperitoneal approach it is much more direct and quicker than classical approach.

The decreased size of the incision for extracting kidney and placement of that incision in the lower abdomen, significantly reduce postoperative pain when compared with traditional opened surgery; it also reduce traumatism of the abdominal wall, which is followed by a quicker and better healing and mobilization postoperatively and quicker reintegration of the patient in society.

Usually, these patients resume their oral intake in the first postoperative day and normal alimentation in maximum two days after surgery.

All retrospective comparations between open and laparoscopic kidney donation show that analgesic requirements for LLDN and robotic LDN, were 30% lower than those for open procedures. Need for oral pain medication is also reduced.

Return to physical demanding work also occurs, on average, 17th days sooner for the laparoscopic group compared with classic operation.

Recipient and graft survival. All retrospective review of the recipient who received a kidney through laparoscopic or robotic laparoscopic donation compared with those who received kidney via standard open nephrectomy shows no statistical differences if the groups are matched in regard with the number of HLA mismatches, donor relationship, diabetes, previous transplant, gender, or race.

Allograft function. The majority experience in the field attest that all grafts functioned intraoperatively and no clinical significant injury occurred to the graft.

	Laparoscopic	Open	P value
Estimated blood loss (mL)	266+/-174	393+/-335	0.027
Operative time (min.)	232+/-33	183+/-27	<0.001
Hospital stay (days)	3.0+/-0.9	5.7+/-1.7	<0.001
Analgesia (days of use)			
Oral narcotics	4	12	<0.001
Acetaminophen	3	17	<0.001
Resumed oral intake (days)	0.8+/-0.5	2.6+/-1.0	<0.001
Returned to work (weeks)	4.0+/-2.3	6.4+/-3.1	0.003

Table 4. Open versus laparoscopic donor nephrectomy

Allograft rejection. The pneumoperitoneum and retropneumoperitoneum reduces renal blood flow and urine output. The potential for ischemia can make the donor kidney more allogenic by inducing MHC class II expression. This problem could be avoided giving donors intraoperatively a 6-8 liters of crystalloid to promote brisk diuresis, and having an accurate dissection of the renal pedicle and harvesting the kidney only in full diuresis. Biopsy proved rejection in laparoscopically obtained kidney occurred in 30% of cases compared with 35.4% of cases of kidneys harvested by open procedure. At 12 months, creatinine clearance in recipient of kidney from laparoscopic and open procedure were both 66 mL/min. (p = not significant).

Laparoscopic nephrectomy gives less postoperative pain, quicker convalescence, better cosmetic results when compared with traditional open operation. In experienced hands, this procedure is accomplished without increasing the risks to donor safety and allograft function. Complications are comparable to those reported in historic series using open surgery. Longer operative time and the need of disposable equipment result in greater hospital costs. However, quicker convalescence permit patients to resume activities sooner and produce market cost savings both for patients and employer.

2.8.2.4. HLA sensitized and ABO incompatible donor and recipient

During the past decade, several innovative protocols have been adopted to overcome transplantation across a positive cross-match or an ABO blood group barrier. Protein A immunoadsorbtion, high dose intravenous immunoglobuline (IVIG), low dose iv Ig in combination with plasmapheresis, rituximab, splenectomy, all of them alone or in combination, can abrogate a positive cross-match and enhance the chance of a highly sensitized patients to receive a cross-match negative organ. Similar strategies can be used for ABO incompatible donors and are particularly effective when the titter of blood group antigen is low.

Plasmapheresis and intravenous immunoglobuline as a rescue therapy for a positive cross-match live donor kidney transplants. The positive cross-match can present a virtually an insurmountable barrier to kidney transplantation. Anti HLA antibodies have been identified as the predominant cause of early graft failure from hyperacute rejection and acute humoral rejection.

Once the consequence of performing a transplant, in the face of a circulating donor specific alloantibody were fully appreciated and routine pre-transplant cross-matching emerged as a standard, hyperacute rejection became rare, but a large population of a highly sensitized patients who have a little hope of receiving transplant has been subsequently identified.

Some of the longest waiting times for a kidney transplant are observed in patients who are allo-sensitized because of a prior transplant, blood transfusions or pregnancy. Some of these recipients have live donor, meet standards criteria for living donor transplantation, but have a positive cross-match with their donor. A combination of plasmapheresis and IVIG under the cover of standard doses of calcineurin inhibitors or rituximab, together with mycophenolate mofetil and steroids, can effectively and durably remove donor specific anti-HLA antibody, preemptively desensitize the recipient who had positive cross-matches with a potential live donor, allowing the transplantation of this patients using a live donor without cases of hyperacute rejection [63].

This preemptive therapy is initiated several weeks before a planned live donor transplant. Our standard protocol was designed to include oral immunosuppressants before first plasmapheresis treatment followed by a maximum six plasmapheresis on alternate days. The recipients, also received seven days of IVIG (100 mg/kg/day).

Cross-over transplantation and paired kidney exchange as a method to fill the gap of positive cross-match and ABO incompatibility. The gap between the number of donors and number of patients waiting for a kidney transplant continues to widen. Fewer patients get transplants every year because of the organ shortage. This patients can receive a donor from a living donor such a family member, a friend, or even a foreign individual.

The pool of such kidneys has not been fully utilized because not all living donors are compatible with their recipient. Patients with available living donor continue dialysis and many of them die because of ABO incompatibility, cross-match positive, low HLA-matching. Since the report made by Rapaport, when was set the bases of kidney exchange between two donor-recipient pairs in order to obtain a better compatibility, things have changed [64-66]. A spouse donor would give her kidney to an unrelated recipient who matched her blood type. That recipient's mate would provide a kidney for the donor's ill spouse. This swap would imply more than two pairs in order to obtain best compatibility. A cross-over renal transplantation or a paired kidney exchange transplantation is defined by a living kidney donation or a living kidney cadaver pool donation and exchange between two or more such couples who are hindered by ABO incompatibility or positive cross-match to give the kidneys not to the own recipients but solve the problem by cross-exchange the kidney between the pairs to make more matches.

The most frequent reason for ABO incompatibility, preventing living donors from donating is a blood group A or B donor and a blood group O recipient. There are many vice-versa pairs

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but the problem is that the blood group O donors are universal donors for all blood groups. They can give the kidney directly to their recipients than rather to a stranger. When the cross-match is positive with own one's recipient, but this recipient has a negative cross-match with blood group A or B donor from another couple, the problem is solved by exchanging the kidneys between these pairs. Another reason for kidney exchange is when the O to A or B pair get a better HLA matching from 6 miss-matches to 0-3 miss-matches by swapping the kidney with a A or B to O pair.

The pairs involved in a paired exchange program are interviewed to exclude any coercion of the donor, they are informed about the advantage and the risk of the living donation and the informed consent is obtained. Beside that, all donors undergo psychological evaluation.

The inclusion criteria pursued the goal of exchanging equivalent kidneys with equivalent size, anatomy, similar renal function and similar age. The donor are assessed preoperatively by high resolution iv pyelograms, quantitative renal scan and spiral CT scan or MRI. As a general rule, the donors accept to join this program as this is the only way to help their relatives or friends. The transplants involving two or three pairs can be performed simultaneously excepting the session with more than three pairs when the transplants are performed successively. All the transplants are performed by the same surgical team in respect to the principle to equivalent quality of the surgical act.

The basic principle of kidney exchange is the equivalent exchange. To accomplished this, high resolution preoperative work-ups required and unpredicted situation which can hinder harvesting are avoided. This way, simultaneously harvesting is not mandatory.

By using kidney exchange, the recipient benefit from the better matching as well as the known advantages of living donation. Paired kidney exchange reduce the duration of dialysis before transplantation and expand the pool of living donors.

In the countries where the living donation is the main source of organs, cross-over transplantation may become more popular as it increase the number of transplants. The kidney exchange program has to be promoted as it offers solutions where apparently there is none.

Transplantation of ABO incompatible pairs. Developed initially in countries with predominant living donation, transplantation of a ABO incompatible kidney is a demanding task but it was possible mainly due to development of more potent immunosuppressive drugs which reduces the risk of hyperacute rejection [67]. In japan, transplantation of a ABO incompatible kidney from a living donor is preferred to a deceased donor graft but the experience already acquired was extended in many other countries for recipients having only a ABO incompatible donor willing to donate [68].

The procedure involves a pretransplant treatment in order to remove the ABO antibody and to prevent furture production. Thus, Rrituximab is administred one month before transplantation followed by plasmapheresis 7 to 14 days before transplantation. With Rituximab there is no need for splenectomy and plasmapheresis is done in alternate days or even daily in order to reduce the ABO antibody titer under 8. The plasma removed is replaced with albumin solution and a combination of albumin and fresh frozen solution just immediately before

transplantation to correct the coagulation. A key point is the administration of IVIG immediately after each plasmapheresis. The plasmapheresis is continued in the first two weeks after transplantation if ABO antibody titer was over 256 before Rituximab, if there is an increase of ABO antibody more than three times after transplantation, and if the serum creatinine increases more than 15% in two weeks after transplantation. The immunosuppression includes Tacrolimus, mycophenolate mofetil and steroids. In the first three weeks, the patient is at high risk of developing hyperacute humoral rejection, thus a graft biopsy is warranted whenever the serum creatinine increase over 15% in two weeks [69].

The use of specific immunoadsorbtion instead of plasmapheresis is not only less aggressive but also more effective since it allows more than two plasma exchange equivalent per one session [70].

Even if renal transplantation agains ABO blood group is expensive and, due to the increased immunosuppression, increases the infectious and malignancy risk, graft function at five years is slightly similar to transplantation of ABO compatible grafts [68].

2.9. Commercial renal transplantation

World Health Organization condemned the sales of organs since 1989. Sales of organs and tissues has been made illegal in the majority civilized states of the world. The difference between altruistic donation of a kidney and selling off a kidney is viewed as similar to the difference between marriage and prostitution. The first is a sacrament, the second a sin.

Reimbursement for expenses related to the donation process, such as for traveling and lodging is not prohibited, although a formal mechanism to make such reimbursements is not available everywhere, a factor that could act as a decentive to donation for some potential donors.

Iran is currently the only country in which payed donation is officially sanctioned, almost all the donors are pour and uneducated and follow-up studies have shown that their lives are not improved.

Despite the legal constraints on organ sales, commercial kidney transplantation is a common phenomena in many parts of the world, and in some cases has been linked to criminal activity. The donors are typical pour or under great financial stress, the recipients are often wealthy or come from other wealthier countries, and middleman or brokers are often involved.

Arguments against payed donation shows:

- The donor's choice is not voluntary because he is compelled by circumstances of poverty to donate a kidney. Poverty-stricken donors choose what they see as the best of a group of bed options. Compared to some other possibilities such working under unsafe conditions, kidney donation might carry less risk to the donor than other choices and at the same time might accomplish more good for society and for the donor.
- Paid donors are usually pour and uneducated, so making them understand the risks is all but impossible.

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- Commercial donation will result in the rich having access to organs for transplantation while the pour do not.
- Donors will be exploited by unscrupulous middleman and sometimes, even by the surgeons. The medical care of both donor and recipient will suffer generally.
- The pour don't know how to handle the money that comes to them and will make no permanent difference in their poverty. This perception may be based on experience with lottery winners and other recipients of a sudden winfall. Donors will have widely differing abilities to plan for the future and would be difficult to predict what they will do with the payment for their donation. The possibility off misuse of money does not justify the overriding the donors wish to give up a kidney.
- During its entire history, transplantation has relayed on the altruism of donors and their families. Commercial donation would change the fundamental character of organ donation and likely would lead to the disappearance of altruistic donor. If any transplants are payed for, all will have to be. Most of payed donors are giving an organ to a specific individual. Payed donors would not have a choice about recipient. Thus, altruistic donation should continue.
- The initial enthusiastic support of organ transplantation has been replaced by suspicion. Although no evidence has proved the charges that are widely accepted urban myths regarding transplantation. This includes stories of people, particularly south-american children being kidnapped and killed for their organs, and people being drugged and kidnaped only to awaken in an alley with a flank incision and no kidney on that side. The myths can only be dispelled by the education, nothing else. Moreover, the possibility exists that skillful paper editors and television producers will exploit current practices for purposes of sensationalism.

Available data on the outcome of organ vending for the donors, indicates that the most of them have a pour outcome. On the other side, recipient of vended organ are subject to an increased risk for complications, particularly infections, likely as a result of a break-down of trust and honesty that is a byproduct of commercialization of organ donation. Evidence from several countries has shown that commercialization of organ donation comes at the expense of program for the related and unpaid living unrelated donation.

3. Cadaveric donation

The modest increase in cadaveric renal transplant in USA has been achieved in principally by extending use of older and younger donors [71]. Fortunately, the death from motor vehicle accidents has decreased over the passed 20 years mainly due to laws meant to increase the safety on the road: the seat belt laws, passive restraints, child safety seats, and stricter drunk driving laws. The greatest number of lives saved by improved highway safety has been specially at the 15 to 40 years old age group. On the other hand, another concern is related to the estimation that 10% of potential donors might be ineligible because of HIV infection [72].

In the same time, the number of older cadaver donors doubled between 1990 and 2000 especially due to a 10 fold increase in donors older than 60 years.

The percentage of donors dying in motor vehicle accidents decreased from 34.4% to 24.00% while the percentage of donors dying from stroke increased from 27% to 42% [71]. Despite the decrease in motor vehicle accidents, enough deaths still occur under circumstances that allow transplantation and could reduce the gap between the need for and the supply of kidneys in all civilized states in the world. The failure to make use of these organs has been attributed to the failure of the intensive care unit staff to recognize potential donors as well as the high refusal rate by families of potential cadaveric donors. Multiple new mechanisms for preventing potential donor from being missed in ICU appear to have been successful. Hospital staff are recognizing over two thirds of potential donors, are asking their families about donation but only half of them agree to donate.

Much attention has been focused on disparity among different ethnic groups as organ donors. A study of 1772 requested donation in come important cities from USA reported a family refusal rate of 17% in whites, 43% in Hispanics, and 45% in blacks [73], but the situation has changed in last period due to intensive efforts done to encourage minority families to donate. As a consequence the rate of cadaver kidney donation became similar for whites, blacks and Hispanics but remained low for Asians. Estimate of the overall refusal rate in the USA is between 38% to 50%. The refusal to donate lead to a 4755 kidneys lost for donation but the true potential in higher since we can't determine the real number of potential donors. This number would have enclosed 81% of the gap between the yearly increase in need and the available kidneys. Even so, the shortage of kidneys can not be closed by eligible donors lost by families refusal to donate and the difference would have to be provided by new cadaveric sources and by living donation.

3.1. Disparity among attitudes regarding cadaver donation

Even it might be only a believing, there is a dichotomy between the public and the medical community regarding cadaveric organ donation. The medical community is preferring cadaver organ donation since there are less concerns on the quality and risks associated with the donor's organs. Physicians don't share the cultural and religious believes of families opposed to organ donation. The doctors are relieved of concerns regarding doing harm to the donor because they often see the main problem as one that may be corrected by education and right information.

Even though over 90% of the public supports allowing living donation [74], many people do have reservations about cadaveric organ donation due to cultural and religious beliefs or beliefs that the dead can still suffer. The concept of brain death remains only a concept when it is about a loved one who has died unexpectedly. Families also express concern that the deceased's own wishes cannot be known or carried out. People might fear that being identified ahead of time as an organ donor would lead the medical team to make less than the maximal effort to save them [75].

3.2. Legislation means

An array of various laws have been passed to maximize the number of cadaveric donor transplants. In USA, the Uniform Anatomical Gift Act, have been passed for over 30 years by american Congress and authorize individuals to give their organs and specified who could give consent if the donor were unable to do so [76]. By now, many states have such a law in place and many of them use the driver license as a donor card.

"Routine inquiry" is active in many hospitals in Europe and USA. Majority of the hospitals who are doing or not transplantation, have routine inquiry policies which qualifies for social reimbursement. Hospitals are required to notify families of potential donors about the possibility of donation and to notify organ procurement agency approved by health care finance administration. In the first years after the passage of required request laws, donation increased slightly but then reached a new plateau.

Another way to approach organ donation, especially in European countries is that of presumed consent. Unless the potential donor has previously expressed a wish not to donate, he is presumed to have agreed to donate. The role of the family is to confirm that the deceased has not expressed an unwillingness to be a donor. The application of the law is variable and approximatively one half of the nations continues to depend on family consent in practice. The effect of donation have been variable; the refusal rate in Austria and Belgium, where the law is strictly applied dropped under 10%. In USA, public opinion shows little support for presumed consent law with only 7% supporting this approach.

An alternative to presumed consent has been proposed in the USA which is mandated choice [77]. When getting or renewing a driving license, a person would have to decide whether to become a potential donor, and the person's choice would take precedence over the family's wishes.

Another law which is active in some states in USA and some countries in Europe, is to provide a compensation for the donor's family. The fund for such thing is obtained by voluntary donations. One thing which is important here that the law makes the distinction between purchasing organs and bestowing a gift to the family in appreciation of its generosity.

3.3. Expanding donation criteria

When efforts that increase the consent rate for cadaver donors, another approach expanding the criteria for an acceptable cadaver donors, also has attempted to increase the number of kidneys available for transplantation. Less than 25% of the increase in cadaveric donors has come from traditional pool age 16 to 50 year age donors. The criteria have been expanded further in some instances by use of donors with encephalitis and core antibody positivity for hepatitis B [78]. Recent data have confirmed that safety of even using kidney from infected donors with blood cultures with pseudomonas and candida, provide appropriate antibiotic treatment is given [79]. There are studies which determined that bacteriemia accounted for 30% of medically unsuitable kidneys in brain death potential donor. There are also transplantation of horse shoe kidney [80] or kidneys from non renal organ transplant recipient which have to be mentioned. From any point you are going to look at this problem, the greatest

potential to increase the potential donor pool comprises non-hard beating cadaver kidneys and kidneys from older donor.

Situations requiring edge biopsy
All people with normal renal function regardless of age (graft biopsy in donors over 60 years)
Diabetic donors with normal renal function and without severe proteinuria
All hypertensive donors with normal renal function
All hypotensive donors
Infected donors excluding viral hepatitis, HIV, Jakob-Creutzfeldt disease, viral encephalitis, malaria, disseminated TB
CMV + RPR
Positive urine cultures without pyelonephritis
Bacteremic donors
Donors with abnormal renal function
Donors at high risk for infection (but negative on high sensitive tests)
Donors with a history of malignancy disease-free for two years
Skin tumors without metastases, excluding melanoma
Primary CNS tumors without VP shunt

Adapted from [65]

Table 5. Expanded criteria for cadaveric donors

Non heart beating donors where widely used before the definition of brain death was accepted. They remain the major source of cadaver donors in countries such as Japan and Mexico, where brain death was recognized officially only recently and where social acceptance it is still limited [82]. Non heart beating donors yield about 5% of all cadaveric kidneys transplanted in USA. Use of non-heart beating cadaver donor kidneys has increased in last years. The one year survival of graft from non-heart beating donors was 83% and for brain death donors was 86%. Early function was not as good: 48% of recipient of non-heart beating donor kidneys required dialysis in the first week after transplantation compared to 22% of the recipients of kidneys from brain death donors. Primary non-function was slightly increased also (4% versus 1%). The serum creatinine level at discharge from hospital was higher in the first group. At one year follow-up, the serum creatinine levels for the two groups was, in fact, similar (1.9 mg/dL versus 1.8 mg/dL). When traumatic death were analyzed separately, the one year survival of non heart beating donors kidneys was 89% compared with 70% one year survival for non-traumatic death. Not all programs have found the same results from non-heart beating donors, but the finding of more frequent delayed function and need for dialysis has been universal. The potential for increasing the donor supply from non-heart beating donors has been estimated to be as high as 40% [83].

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3.3.1. Older donors

Already, older donors are a major source of cadaveric donation. Some doctors found out an inferior outcome from transplants from cadaveric donors over 55 years of age. Not only did a higher percentage of recipients of such kidneys required dialysis but one year serum creatinine level was higher than that from recipient of transplants from cadaveric donors aged 5 to 55 years and the estimated halve life of the kidney was 5.8 +/- 0.3 years compared to 11+/- 0.3 years. Other analysis have found similar results but suggests that the adverse effects of the donor ages affect only certain subgroups particularly black recipients.

3.3.2. Hypertension

Recipients of kidneys from donors with hypertension were more likely to have anuria and to require dialysis immediately after transplantation. Their serum creatinine level was significant higher at one year than that of recipients of kidneys from donors who were not hypertensive and the predictive graft survival was shorter (halve life of 7.7 +/- 0.5 years versus 10.7 +/- 0.3 years). Graft survival was better with 1 to 5 years of hypertension compared to 6 or more years of hypertension. The difference in serum creatinine and predicted graft survival between kidneys from diabetic and non-diabetic donors was of borderline statistical significance. Serum creatinine at one year was 1.8 +/- 0.8 mg/dL in recipient of kidneys from diabetic donors compared with 1.6 +/- 0.8 mg/dL in recipients of kidney from non-diabetic donors. Predicted halve life in this graft was 8.4 +/- 1.5 years compared with 10.1 +/- 0.3 years.

3.4. Strategies for increasing organ donation

In developing new strategies for increasing kidney available for transplantation we would do well to remember that from its beginning organ transplantation has relied on public good will and support. When public opposition exists, we sometimes avoid using approaches that we find ethically acceptable. Because we really don't know what ideas or practices will strengthen public support for all organ donation the introduction of new practices should be undertaken as pilot projects.

The public already accept living donors who were not considered 50 years ago such unrelated living donors and spouses, which are now widely excepted. Once we accept the donors autonomy and remind ourselves that the risk to the donor is not related to his relationship to the recipient, we will be able to accept the wide arrange and greater number of emotionally related donors. We need to understand that the altruistic donor, although unusual, is not pathologic. The altruistic donor can be considered an emotionally related donor who is emotionally related to all mankind. Thus, this approach to this type of donor is not to keep a registry of willing donors and their HLA types. The altruistic donor is not waiting for the right HLA type but for the right story. The acceptance of donor autonomy would allow for accepting donors with increased risk, but will require careful follow-up thus an increased risk of complications can be recognized.

3.5. Conclusions

During the last period of time, there was a spite of papers from individual countries and registries, which examined the ways in which the number of kidney donors could be increased.

Most studies examined single initiatives, such as changing the transplant law, rather than the development of integrated donor programs. The act of donation is a complex phenomenon depending on many factors and interactions, few of which individually have been proven useful or generally applicable throw the out the european community. Well designed studies are needed urgently. A donation is the result of a chain of events, the final result of which will depend upon its weakest link.

Even when the individual links have been strengthened, each element of the process of donation must be integrated into the operational policies developed in toon with national moral and cultural values. It is easy to set a minimum standard to which countries should aspire. But it is another matter to recommend specific, donor promoting activities for which individual countries and profesional organizational should aim.

Although, living donor rate are no increasing in Europe, rates could be further improved at different stages in the referral process:

- Nephrologist at non transplanting as well as transplanting centers, should be encouraged to discuss openly the subject of living donation with family of patients suffering ESRD, preferably before the patient begins dialysis. This will results in predialysis transplantation, increased transplant rates, and is more efficient in case of reduced dialysis resources.
- Canceling facilities (e.g. by a senior nurse or living donor coordinators) should be available to discuss screening tests, provide information, and arrange eventually reimbursement of donor expenses allowed in law.
- Each transplant center should work to an approved screening protocol, such that the predicted mortality risk of living donation does not exceed 1 in 3000 cases.
- If legally permitted, living unrelated donors should be encouraged. In many countries in Europe, altruistic non related kidney donation is allowed legally, provided that checks are made for altruistic motivation and exclusion as far as possible of the possibility of organ sale.
- Non-directed living donor transplantation between altruistic donor and recipient unknown to the donor is possible and have been developed in few centers. Although controversial, there seem no moral or social reason to exclude such donors. However, there are ethical and legal concerns about this type of donation, which at the moment make it difficult to include in a recommendation list.

Increase supply and use of cadaveric kidneys:

Donor cards. In many countries publicity schemes encourage the population to carry donor cards, or to register their wish to donate (opting-in) on a computerized donor register. Even if in UK 8 mil. of individuals are now registered in the opting-in computer, only 10% of the

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population is currently caring donor cards. No more than 50 donor per year results from this initiative. For the success of such schemes, continuous publicity is essential to increase opted-in donors and transplant centers. Intensive care physicians and transplant coordinators should be mandated to access registry routinely, to identify the wishes of potential cadaveric donors.

Improved organization and resources. Services must be more organized and better resourced to increase cadaver donation. In several countries, the number of intensive care beds is probably too low to achieve more than 20 donors per million from intensive care patients. In high donating countries, with better resourced intensive care units, the staff responsible for donation (transplant coordinators), have been expanded and given proper financial support. Transplant coordinators are also to be given the responsibility of public relations, with the aim of avoiding adverse media publicity, and liaising with the coroners.

Opting-out legislation. The introduction of opting-out legislation appears on first site of the data available to be associated with the increased rates of cadaveric donation. In Europe, four countries which exceeded 20 kidneys donor per million population per annum, all have opting-out legislation. In France however, opting-out legislation has not achieved such a successful donation rates. This may be because France choose initially, hard line opting-out, in which donation takes place if the donor has not opted-out irrespective of families wishes. Adverse publicity led to a softening of the practice, which consequently increases the donation rates. Other countries which presumed consent law practices soft presumed consent, in which the families are taking into account in all situations. In general, countries with informed consent do not perform as well, main exception being USA, where kidney donation rates exceed 25 donors per million population.

Criteria for donor suitability. Non-heart beating donors (NHBD) are well known to produce a high rate of primary non-function and their acceptability was low. Recently introduced in situ perfusion of the dead bodies, which has been successfully developed in UK and Holland, are bringing in encouraging results. After harvesting, kidneys may be put into continuous perfusion machine, and their viability assessed using flow measurements and urinary and enzyme excretion. As a matter of fact, presumed consent legislation will allow more NHBD. Rapid intraarterial cold perfusion over recently deceased persons should be allowed before family consent low operate but perfusion without relatives permission is technically unwarranted assault. Agreement by a coroner should allow perfusion without permission and that could expand significantly NHBD.

Elderly donors. Even if long term survival for kidneys from elderly donors (over 60 years old) is 10-15% less than those taken from younger donors, better results may be obtained with carefully selected older donors and shortening of the cold ischemic time.

A good quality organ must be guaranteed to the recipient and every transplant center must established its own guidelines on organ acceptability. If the transplant center uses a less than optimum organs from old subjects to expand the pool of donors, the donors must be evaluated according to age, vascular condition and renal function. The inferior limit for a single kidney transplant is considered creatinine clearance more than 60 mL/min. If the calculated creatinine clearance is between 60 and 50 mL/min. the donor may be considered marginal. If the calcu-

lated creatinine clearance is less than 50 mL/min. than the kidney should not be used for a single transplantation, however, as they are organs that nobody wants they can be used for dual transplantation. When this policy is established, it is necessary to inform the patient on the waiting list.

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