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E. Benedetti, R. Gruessner, J. Pirenne, G. Testa (eds.)

Living donor abdominal organ transplantation: state of the art

Sorrento, Italy, June 2008 – congress abstracts –

Contents

Abstracts

Expansion of the living donor pool for kidney transplantation: technical limits

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The steady growth of the cadaver waiting list for kidney transplantation in the US has not been matched by an adequate increase of the cadaver donor pool. To date, the most effective strategy to obviate this serious problem has been the remarkable increase in the number of living donor kidney transplants. Most of the US kidney transplant programs do currently use laparoscopic techniques for the donor nephrectomy. This strategy, introduced by Ratner et al (1), has contributed to the growing acceptance of kidney donation by potential living donors. The impressive growth in number of living donors has been sustained by a significant liberalization of the criteria for candidacy to donation, both from the medical and the surgical standpoints. The purpose of the present review is to assess if any purely technical limitations currently exist that would contraindicate laparoscopic donor nephrectomy in certain subgroups of candidates.
The use of obese donors, the laparoscopic procurement of the right kidney and the presence of multiple arteries in the donor kidney are the most hotly debated issues.

Obese donors
Obesity (BMI above 27- 30) has been traditionally considered a relative contraindication to living kidney donation. The present paragraph is not aimed to discuss the medical issues concerning the increased future risk of kidney disease in obese donors but simply to review the available literature concerning the technical impact of using such donors.
Pesavento et al. (2) have reported the Ohio State University experience with 107 obese compared to 116 non obese donors for kidney transplantation. In this series obesity was defined as BMI>27. The authors reported a slightly longer operative time in obese donors (151 min Vs 141 min). The overall complication rate was 16% in obese and 3.4 % in non-obese donors. However, the difference was due almost exclusively to higher incidence of superficial wound infections in the obese donors while the major complication rate and the length of stay were similar in the two groups.
Jacobs et al. (3) describe a series of 41 markedly obese donors (BMI>35) at the University of Maryland. In this report, no significant differences were found in operative time, length of stay and major operative complications. However a slightly increased warm ischemia time and wound complication rate was noted in comparison to non-obese donors.
Heimbach et al. (4) compared in a series from Mayo Clinic of 553 consecutive donors those with BMI >35 versus donors with BMI<25. The authors report the same rate of major complications, rate of conversion to open nephrectomy and length of stay. Once again, the only significant difference was an increased rate of superficial wound complications in the obese donors.
In our own series of robotic donor nephrectomies at the University of Illinois we reviewed 83 obese donors (BMI>30) in comparison to 131 non obese. We found no difference in operative time, warm ischemia time, length of stay, conversion to open, and complication rate; we did document a slighted increased intra-operative blood loss in obese donors (104 cc versus 78 cc), although no donor required blood transfusion.
In summary, in experienced centers, obese donors can be used with excellent results, although an increased risk of superficial wound infection has been observed. We believe that obese donors should be made aware of this increased wound complication risk during the informed consent process.

Laparoscopic procurement of the right kidney
Even in open surgery, the left kidney is preferentially procured because of the more favorable anatomy (wall quality and length) of the left renal vein. Concerns have been raised regarding the ability to procure adequate length of right renal vein during laparoscopic procurement of the right kidney.
Saad et al. (5) compared in a German community hospital 48 left versus 25 right laparoscopically procured kidney grafts. The

authors found no difference in operative time, warm ischemia time, rate of conversion to open, and length of stay. Although they stated that there was no statistical difference in technical complications, they do report a renal vein thrombosis occurring in a recipient of right kidney graft. Of course, although not statistically significant, the occurrence of one renal vein thrombosis out of 25 cases raises some concern in consideration of the gravity of the complication.

Borijian et al. (6) reported their experience with 40 right hand-assisted laparoscopic donor nephrectomies; in this series, no significant complication was reported either for the donors or for the recipients.

Finally, Minnee et al. (7) have published a randomized controlled trial comparing right versus left laparoscopic donor nephrectomies in 60 consecutive donors. The authors reported no difference in the rate of complication and noted a shorter operative time for the right donor nephrectomies.

In summary, the evidence available suggests that performing laparoscopic right donor nephrectomy does not increase the risk of complications compared to left nephrectomy.

Presence of multiple renal arteries

With increased experience in vascular reconstruction, the majority of transplant surgeons have been quite willing to use kidney graft with multiple arteries in the setting of living donor kidney transplant.

However, a report from Carter et al. (8) from the University of California at San Francisco has raised significant concerns specifically in relation to laparoscopic kidney procurement. In fact, in a series of 361 consecutive laparoscopic donor nephrectomies, the authors reported a 16% rate of urological complications in kidney graft with multiple arteries statistically increased in comparison to a rate of 3.2% in graft with a single artery. They also noted a significant increase in warm ischemia time in grafts with multiple arteries.

Hsu et al. (9) compared 277 grafts with single artery versus 76 with multiple arteries procured with laparoscopic technique. The presence of multiple renal arteries in this series did not have any impact on intra-operative blood loss, post-operative stay, and complication rate for the donors. On the recipient side, there were no differences in patient and graft survival, urological complications and creatinine clearance.

Desai et al. (10) found no difference in complication rates and long term outcome in a series comparing 58 kidney grafts with multiple arteries versus 245 with single artery procured with laparoscopic technique. The authors did find a longer operative time associated with the procurement of graft with multiple arteries.

Finally, in our own published series of 213 consecutive robotic donor nephrectomies (11), we compared 152 grafts with single artery to 61 with multiple arteries. We documented a slightly longer operative time (179 versus 166 minutes) and a minimal increased estimated blood loss (102 cc versus 54 cc) for kidney grafts with multiple arteries. However, we did not show any difference between the two groups in relation to length of stay, rate of conversion to open procedure, warm ischemia time in the donors. The rate of vascular and urological complications, the patient and graft survival, and the renal function were the same in the recipients regardless of the presence of multiple arteries.

In conclusion, there is only a single large series suggesting an increased risk of urological complications after laparoscopic procurement of kidney grafts with multiple arteries. All the other available studies have not documented any significant increased risk.

Conclusion

In experienced centers virtually any willing donor can be successfully used, regardless of the presence of obesity and multiple renal arteries in the graft. Obese donors should be informed however of an increased risk of superficial wound infections.

Right renal grafts have been successfully procured with laparoscopic techniques. However the number of published cases is relative small and some doubt regarding an increased risk of possible increased renal vein complications still linger. Additional studies will be needed to completely dispel the concern for this relatively rare but devastating complication.

Live donor liver transplantation: donor evaluation, exclusion and post-operative outcome

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Background and aims: Live donor liver transplantation is an important option for patients with end stage liver disease, surgical procedures are more complex than cadaveric liver transplantation subjecting healthy live donor to a potentially life-threatening operation. With reported donor deaths, more caution was taken in the evaluation and selection of live liver donors. Evaluation of living liver transplantation involves optimizing graft size in relation to donor and recipient safety. Donor post operative outcomes were reported in many studies, complications were ranging from 0% to 67%, and variability is due to lack of standardized system for classifying complications.

Aims: To study the exclusion criteria for donors evaluated for living liver transplantation, and to analyze post-operative outcomes in a single transplant center.

Patients and methods: From December 2005 through February 2008, 55 patients with end stage liver disease were presented to a multi-discipline committee for live liver transplantation, a total of 88 donors were evaluated according to an approved protocol. 19 donors underwent keratectomy (16 RT lobes, 3 LF lobes); post-operative complications were classified according to Clavier system classification of post-operative complications.

Results: A total of 88 relatives were volunteered for liver donation, 62(70.5%) were males, mean age 32.1years, all were family members; 35% siblings, 28% parents, 16% brothers and sisters, 5% spouses, 16% cousins. 69/88(78.4%) donors were excluded because of different reasons; 17/69 (24.6%) were due to recipient reasons (advanced portal hypertension, co-morbid illness, advanced HCC), 52/69(75.4%) were excluded because of donor reasons; 8/52(15.4%) medical co-morbidity, 8/52 (15.4%) small left lobe, 7/52(13.5%) fatty liver, 7/52(13.5%) abnormal liver function tests, 7(13.46%) ABO mismatch, 6/52 (11.5%) HbcAb positive, 4/52(7.7%) small graft size, 3/52(5.7%) denied donation, 1(1.9%) was <18 years old, 1(1.9%) was pregnant. 19 donors underwent hepatectomy, their mean BMI was 24.8 (ranged from 18 to 31), postoperative hospital stay ranged from 6 to 35 days (mean 10.7 days), liver enzymes returned to normal levels within 7 to 60 days (mean 14.9 days). Two donors developed depression due to death of their recipients, one needed psychological support only, and the other started antidepressant therapy after failure of support. Other complications were classified according to Clavien system, overall complications occur in 12/19(63.2%), no death or sever complications were observed, 6 donors suffered Clavien grade 1 complications (pleural effusion, sub-diaphragmatic collection), 6 donors suffer Clavien grade 2 complications; 2 wound infection, 2 blood transfusion, 1 pneumonia, 1 acute hepatitis C infection (genotype 3) who were treated and cured.

Conclusion: Living liver donation is currently performed with a low risk of major morbidity, all efforts should be made to encourage live donation, and introduce deceased donor liver transplantation to increase overall liver donors.

Is living donor liver transplant necessary/indicated in the western world? Hepatologist Perspective

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In the United States the number of LDLT markedly increased from 1997 until 2002, but since then, it faced a reduction, as reported by Freeman (1).

According to the data collected by the European Liver Transplant Registry (ELTR) on behalf of the European Liver and Intestine Transplant Association (ELITA) it appears that the same trend is present in Europe. LDLT is performed in 55% of European liver transplant centers (1991-2006) (2).

We have observed in the more recent years that LDLT are performed more in adult then in pediatric recipients, with a significantly higher graft and patient survival

seen in children compared to adults (graft survival 76% versus 55% and patients survival 83% versus 63% at 5 years after transplant).

The outcome of HCV positive recipients – at the early stage of LDLT – was reported to be worse compared to DDLT, due to a faster and more severe fibrosis progression (3). However, in the most recent papers, this result, despite being still controversial, has not been confirmed and it is more likely that fibrosis due to HCV recurrence will progress after either LD and DDLT (4,5). Nevertheless, HCV positive recipients of living donor graft have a higher risk to develop cholestatic hepatitis C after transplant, as reported by a non randomized study (6).

The A2ALL study reported that survival is comparable in LDLT and DDLT recipients if the transplant center has performed at least 20 LDLT, the so called "learning curve effect". Other risk factors of graft loss in HCV positive LDLT recipients are the pre-transplant diagnosis of HCC and higher MELD at transplant (7).

Several concerns are related with the report that LDLT has been increasingly performed for HCC. We know that the waiting time for a deceased donor in the list, provides a natural selection for HCC positive patients and the drop out could select those patients who have a biologically more severe carcinoma. On the other side, there is no reason why we should offer a LDLT to stable patients with a small tumor who can benefit from surgery or downstaging procedures (8).

In the A2ALL study the probability of the freedom from HCC recurrence after transplant was higher for DDLT compared to LDLT, but the recurrence free patients survival was almost the same (9).

Finally, the LDLT has been performed in some centers for acute liver failure, with no difference on patient survival comparing LDLT with DDLT (10), similarly reported in Europe from ELTR database (2). But the prerequisite is donor safety, and a detailed full consent with repeated verification of the spontaneous willingness should be provided from all donors, specially in the urgent setting, while the donor may be overwhelmed by emotions.

Overall, donor complication rate accounts for 35-40% of cases, the most common being biliary stenosis (11) and donor selection has to be performed with caution, by performing liver biopsy in all patients with any doubt about liver function and morphology. This represents another crucial issue, since minor or major complications can develop after the procedure, in recent study 3.5% of donors developed some complications following liver biopsy requiring overnight admission (12, 13). In the US A2ALL study, living donor complications occurred in 38% of patients. The most common complications were infections, biliary leak, incisional hernia. Blood transfusions were the only significant predictors of overall complications (14). From ELTR data, donor morbidity ranged between 11% and 27%, donor mortality occurred in 4 out of 2043 (0.2%) of patients: two for sepsis, one for pulmonary embolism and the others for heart failure (2).

At the ATC in Montreal last May, a group from Toronto reported the data from a study they have conducted comparing the opinions of potential donors with transplant professional. It was clear from the results that potential donors are more prone to donate, taking higher risk, than a transplant professional (15).

In conclusion, there are still concerns on the need of LDLT in the western countries, due to both donor and recipient outcome. Donor biopsy would help in selecting the healthy donor but it might expose him/her to unnecessary risks. The donor psychological health is not always preserved as in the urgent setting of liver transplantation for acute liver failure. The HCV positive recipients of a living graft have at least no better outcome compared with deceased donor recipients, therefore no advantage is really offered to those patients with a LDLT. Finally, the right timing and criteria for living liver transplant in patients with HCC is still under debate.

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Anti-T cell monoclonal antibodies as privileged tools to promote immune tolerance in clinical organ transplantation

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Numerous anti-T cell monoclonal antibodies have been developed over the last two decades. Most of them, including those now routinely used for the prevention of acute allograft rejection, are essentially immunosuppressive. The aim of the presentation is to highlight the fact that a few anti-T cell antibodies targeting receptors involved in key signaling pathways such as anti-CD3 antibodies have the capacity to induce additional long lasting and non immunosuppressive effects leading to induction or restoration of immunological tolerance to antigens. First generation mitogenic anti-CD3 antibodies used in the clinic for their strong immunosuppressive properties were progressively abandoned due to intense antibody-induced T cell activation and cytokine release syndrome. Their remarkable tolerogenic capacity was nevertheless demonstrated in experimental models of allogenic transplantation and more impressively, in models of autoimmune diseases such as type 1 diabetes where it was shown that a short treatment could induce remission of established disease. The recent development of humanized non mitogenic anti-CD3 antibodies allowed the transfer of this promising immunointervention strategy to the clinic in a phase II placebo-controlled trial in patients recently diagnosed with type 1 diabetes. The trial demonstrated a preservation of residual beta-cell function as well as decreased daily insulin needs in anti-CD3-treated patients for at least 18 months following a one-week course therapy. The mechanisms of the tolerogenic effect of anti-CD3 antibodies in the experimental setting include transient effects acting only during antibody therapy (partial depletion of T cells, selective apoptosis of activated T cells and modulation of the CD3 molecule at the T cell surface) and most importantly, long lasting effects such as local expansion of TGF beta-dependent adaptive regulatory T cells. We propose a model in which anti-CD3 therapy creates a non-inflammatory and tolerogenic environment through TGF beta production that plays an orchestrating role through effects on T cells and antigen presenting cells in the presence of the relevant antigens. In the context of organ transplantation, a renewed use of anti-CD3 antibodies, in combination with conventional immunosuppressants preserving the regulatory capacities of the immune system or other tolerance promoting biological agents, could provide additional means towards the ultimate but still elusive goal of operational tolerance to alloantigens.

Management of the complex bile duct (Movie Presentation)

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Bile duct strictures and leaks remain the most common complications following right lobe living-donor liver transplantation (RL-LDLT), with a reported incidence ranging from 15 to 60%. Biliary strictures often require repeated therapeutic interventions, increase costs, decrease quality of life, and potentially compromise graft survival. In this presentation, we describe our experience with LDLT, and the principles we follow to minimize the risk of biliary complications. Since May 2000, 301 LDLT (262 adults; 39 children) have been performed at University Health Network. We analyzed 229 adult RL-LDLT performed between May 2000 and December 2007. Median patient follow-up was 33 months (range 3-110 month); 1-year actuarial patient and graft survival rates were 92% and 88%, respectively. A duct-to-duct (D-D) or roux-en-y (R-Y) anastomosis was performed in 121 and 109 patients, respectively. A ductoplasty was performed in 43 grafts with two ducts to create a "single" duct for anastomosis. A bile leak developed in 32 (14%) patients. The biliary stricture rate was 7% at 6 months and 22% at 5 years. Median time of biliary stricture diagnosis was 7 months. Biliary strictures were managed initially by percutaneous or endoscopic balloon dilation and stenting; 9 patients subsequently underwent conversion from D-D to R-Y drainage, and 1 patient progressed to graft failure and is listed for retransplantation.

Independent risk factors for bile duct stricture were biliary leak and donor age >50 years. Other factors including recipient

age, etiology of liver disease, type of biliary anastomosis, and era were insignificant.

During the movie presentation, key principles in the donor and recipient that we believe reduce the risk of biliary comlications were discussed. First, donors with complex biliary anatomy (e.g. multiple small diameter right bile ducts) should be identified by preoperative imaging (magnetic resonance cholangiography or CT cholangiography) and avoided. The biliary anatomy should be confirmed by intraoperative cholangiogram before proceeding with the hepatectomy. Second, direct dissection of the bile duct should be minimized to reduce the risk of devascularization. We delay duct division until >80% of the parenchyma has been divided, which can help visualize the biliary duct confluence without the need for direct dissection. We also make an effort to leave liver parenchyma around the bile duct by veering slightly into the base of segment IV. Third, the duct is divided sharply and perpendicular to its long axis, giving particular attention to avoid duct skeletonization. A repeat cholangiogram with a metallic clip placed at the proposed site of transection can help guide division when the right duct is short.

We prefer D-D anastomosis in the recipient because it is easier and faster to perform, eliminates enteric contamination, is more physiologic, and provides easier access for imaging and treatment of biliary strictures. However, D-D is clearly not advisable if there are concerns with blood supply, excessive tension, or size mismatch, or when then there are multiple donor ducts.

We reported earlier (Am J Tx 2007;7:161) that all biliary strictures presented de novo before 24 months. With longer follow-up, however, 9 patients were diagnosed beyond 24 months, indicating that close follow-up is required long-term. Fortunately, graft failure resulting from biliary strictures remains uncommon.

Living donor renal transplants: long-term outcomes, challenges and coming attractions

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Although success rates for living donor kidney transplants are superior to those for deceased donor transplants, actuarial survival analyses of data from the OPTN/UNOS renal transplant registry suggest that only 25% of living donor kidney transplants continue to function for 20 years. Nearly half of graft losses that occurred more than 10 years after transplantation were due to the constellation of immunologies, pathologies and toxicities reported as “chronic rejection” (43%) or to recurrent disease (5%). These patients return to dialysis and to the waitlist for retransplantation. Many become broadly sensitized as a result of their graft loss and are difficult to retransplant with a crossmatch compatible donor. One third of graft losses were attributed to patient death either with a functioning graft (19%) or in conjunction with graft failure (14%). Twenty-year graft survival censored for death with a functioning graft was 45% among recipients of HLA-identical sibling transplants and 35% for transplants from HLA-mismatched siblings, both considerably better than the 20% for deceased donor kidney recipients. These estimates must be regarded as minimum projections due to the high percentage of patients lost to follow-up over the period, who may not be representative of those whose follow-up is more complete.

Despite good early success rates for unrelated living donor transplants, strategies for desensitization, ABO incompatible transplantation and living donor paired exchanges, the growth of living donor transplants in the US has slowed in recent years. During 2004, 6,647 living donor kidney transplants were reported to UNOS compared with only 6,039 in 2007. Transplants between spouses increased from 127 in 1994 to 721 in 2002, but only 759 were reported in 2006, suggesting that most medically suitable spouse donors are now being accepted. The number of non-spouse unrelated living donor transplants increased 10-fold between 1995-2004, but leveled off at about 1,450 each year. The increase in deceased donors resulting from concerted efforts to increase donor conversion rates may be partly responsible for this fall off, but the slowing growth of living donor

transplants also may reflect limitations at some centers for processing potential living donors.

More than half (55%) of newly waitlisted patients in 2006 were over age 50 and with increased waiting times and pressures to make the best use of deceased donor kidneys, older patients may have more limited options for transplantation. One option may be older living donor transplants. Transplants from living donors aged 60 or over doubled from 105 in 1995 to 210 in 2004. We recently analyzed the results of 1,135 older (>55 years) living donor transplants in patients aged 60 or older (Gill, et al. AJKD 2008, in press) and found similar 3-year patient survival rates (88%) among recipients of older and younger (<55 years) living donor kidneys. While 3-year graft survival rates were slightly higher for recipients of younger kidneys (85.7%) than older donor kidneys (83.4%), both were superior to those for recipients of deceased donor kidneys, whether from standard or expanded criteria donors. Complications of the donor surgery were not different for older and younger living donors, although data were limited.

Medication adherence in living related donation

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Non-adherence with immunosuppressive drugs (NA) in renal transplant recipients (RTx) is a prevalent problem with 35.6 per 100 persons per year not taking their immunosuppressants correctly (Dew et al., Transplantation 2007) and is associated with a higher incidence of acute rejection episodes and graft loss. Understanding risk factors for NA and developing profiles of patients at risk is an important step in targeting patients with adherence enhancing interventions. The literature is not conclusive if NA differs among RTx different graft source (cadaveric, living related and living non related donation). We therefore examined if differences in NA can be observed between RTx with different graft sources using a secondary data analysis of the SMART study.

Methods: The SMART study is a prospective cohort study including 249 adult RTx (155 cadaveric, 75 living related, 19 living unrelated) more than 1 year post-Tx. NA was assessed using electronic monitoring (EM) during a 3 months period. Selected risk factors for NA were measured at inclusion in the study, such as demographic variables, medication, transplant-related variables, health behavior (e.g., smoking), medication beliefs, depression, …). Variables that significantly differed between the graft source types were added in an ordinal logistic regression model predicting NA. Factors that explained differences in NA among the graft source groups were retained in a multiple model.

Results: Simple logistic modeling showed that patients with a living related donor were significantly more non-adherent than patients with a cadaveric donor (0.0008). NA between RTx with cadaveric donor and living unrelated donor were comparable. Factors explaining the NA differences between cadaveric and living-related donors were: a lower number medications, the belief of being protected because of the relationship, lower self-efficacy for medication taking, a higher proportion of pre-emptive transplantation, a busier life style, and younger age.

Discussion and conclusion: Our analysis suggests that the higher level of NA in RTx with living related donation needs to be seen as a 'proxy' for a higher risk profile in view of selected demographic (younger age), behavioural (previous NA) cognitive (health beliefs, self-efficacy, treatment (complexity of regimen), life style (busyness) and clinical (pre-emptive transplantation) factors. These results show similarities with another EM study in RTx (Butler et al., Nephrol. Dial. Transplant. 2004; 19: 3144). Future research should focus on scrutinizing if there is a differential impact of NA on graft survival for recipients of cadaveric, living related and living unrelated grafts controlling for other factors impacting clinical outcome as part of cohort studies assessing NA as a time dependent variable.

The role of a transplant coordinator in a living donation transplantation program in Europe. A literature search and an European survey

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Introduction: In Europe the numbers of living and deceased donor organ transplantation vary between the different countries. The aim of this study was to determine the role and the benefit of a dedicated clinical transplant coordinator (CTC) in a living donation transplantation (LDTx) program in this European heterogeneous setting.
Methods: A search in international *literature* (via Medline/Pub Med) provided a view on the role and benefit of a dedicated CTC in a LDTx program. A *survey* was sent to 218 transplantation centres, who have a kidney and/or liver transplantation program, in 29 European countries. Questions involved availibility, number and type of LDTx programs, members of the multidisciplinary team and their role in evaluation, surgery and follow-up of (potential) living donors (LD), the specific role and characteristics of the CTC.
Results: A *search* in international literature (via Medline/Pub Med) provided a view on the role and benefit of a dedicated CTC in a LDTx program. The CTC plays a crucial role in the coordination of evaluation, hospitalisation, surgery and follow-up of LD and is a factor of continuity of care, safeguarding stepwise protocols throughout the whole procedure and thus ensuring that nothing is left to the hazard. To increase the efficiency of the potential LD work-up, the employment of a dedicated CTC guarantees a rapid and efficient assessment. The CTC is the key contact person for LD, recipients, health care professionals and general public and links donor and recipient teams. The CTC can be responsible for education, database management and registries.
Survey: From 19 European countries, 59 transplantation centres (27%) responded (75.3% LD kidney Tx, 21.1% LD kidney and liver Tx, 1.8% LD liver Tx, 1.8% LD kidney, liver and small bowel Tx). 2 centres declared to have no LDTx program. 57 centres provided a convential LDTx program, 21 centres provided also a ABO-incompatible LDTx program, 20 centres a Paired Exchange LD-Tx-program, 28 centres considered altruistic LD. The transplant surgeon (in 61% centres) and the CTC (43.8% centres) are the factor of continuity of care throughout the whole procedure. The CTC is a nurse (81%) or has a paramedical (10%) or medical (9%) background. 66% of the CTC had no specific training; 24.56% CTC received a local training; 17.54% national and 10.52% international training. CTC is involved in medical (71.2%), psychosocial (70.6%) and surgical (61.5%) evaluation and follow-up (75%). Other tasks for the CTC are: administration (67.3%), education (79.2%), information (84.9%), attendance out patient clinic (67.9%), attendance dialysis unit (25%), communication (83%), database management (71.7%), registries (66%), clinical studies and audits (64.2%), other Tx programs (47.2%), procurement (26.4%).
Conclusions: The profile of the European CTC for a LDTx program is heterogeneous in background, training and responsabilities. There is a need for more and specific training of the CTC. A dedicated CTC LDTx program ensures an efficient management of the LDTx procedure, with early triage of suitable donors, efficient use of resources (reduction workload and costs), ensuring a continuity of care using stepwise protocols and clinical pathways.

Induction of tolerance to living donor liver transplantation using peritransplant donor hematopoietic stem cells infusion after mild myeloconditioning

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Side effects of chronic immunosuppression (IS) represent now the principal cause of long-term morbidity and mortality after solid organ transplantation. For this reason, the definition of new therapeutic approaches allowing to minimize or to withdrawn posttransplant IS would represent a major progress. Induction of so-called central tolerance using donor hematopoietic cells (DHC) infusion, leading to at least transient macrochimerism, has been proven as the

most reliable method to promote graft acceptance, both in animal and clinical studies. The mechanisms involved in this phenomenon are not fully elucidated, relying on central negative selection but also on peripheral regulation, suppression or anergy of anti-donor reactive cells. As a proof-of-concept, it was observed that patients receiving a bone marrow transplant may develop a full tolerance to a subsequent solid allograft from the same donor. A step forward, it has been shown in several pilot studies, essentially in renal transplantation, that DHC infusion, after recipient's myeloconditioning, may promote long term transplantation tolerance while establishment of macrochimerism remains inconstant. On these bases, we designed a pilot study in liver transplantation (LT). As compared with others transplants, liver grafts have indeed unique characteristics that might be critical to develop such experimental approaches in ethically acceptable conditions: 1) LT are globally well-accepted, even with minimal or, in rare cases, without IS and 2) episode of acute rejection (AR) are fully reversible when diagnosed and treated promptly, making the tolerance hypothesis possible to test in safe conditions. Our protocol was designed in living donor LT (LDLT), using donor CD34+ stem cells (SC) as tolerogenic cells. Five patients have been included in 2 different versions of this protocol. In the first (2 patients), donor SC were given prior to LT after recipient's conditioning with high-doses ATG and cyclophosphamide. In the second (3 patients), donor SC were given on day 7 after LT, after posttransplant conditioning using high-doses ATG only. In the 2 versions, posttransplant early IS consisted in sirolimus monotherapy which was withdrawn as soon as the clinical situation was normalized. A transient macrochimerism was observed in 1 out of the 2 first patients but in none of the 3 patients who received donor SC after LT. In the 2 first patients, receiving pre-LT donor SC infusion, IS was successfully withdrawn, respectively on days 90 and 28 post-LT, without subsequent episode of AR. Among the 3 other patients receiving post-LT SC infusion, IS could be withdrawn in 2, on days 18 and 23 respectively, followed by 1 episode of reversible AR in the 2 cases. In the patients who accepted their liver graft without IS for a prolonged period, a donor-specific hyporesponsiveness was demonstrated in mixed lymphocytes reactions in vitro (low proliferation indexes and decreased production of interleukin-2 as compared with stimulation with third party antigens). These first results demonstrated the potential of this approach in LT using donor SC as tolerogenic cells and mild conditioning regimen. At this stage however, longer follow-up and namely, the verification of the absence of chronic rejection phenomenon, remains needed.

Best treatment for HCC: living donor liver transplantation

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Hepatocellular Carcinoma is the 5th most common cancer and the 3rd cause of cancer related death. The incidence is rising all over the world, including Europe and more than 80% of the cases occur in the context of cirrhosis. However while in Asia it is mostly hepatitis B virus related, in Europe and most of the western world, it is hepatitis C virus related. Taking this into account, treatment should be considered in relation to tumor growth (size, number of nodules, vascular invasion etc…) as well as the extent of the underlying cirrhosis and patient's general condition. The "Barcelona Clinic Liver Cancer" (BCLC) staging and treatment strategy algorithm has recently been endorsed by the European as well as the American Association for the Study of the liver (EASL, AASL), as it considers both the tumor growth as well as the underlying disease. This staging system identifies a group of patients suitable for curative treatments with an expected survival at five years of 50-75% (1). The best treatment for those with the so called early cancer (5 cm tumors or 3 nodules of less than 3 cm, Milan Criteria) is liver transplantation since it eliminates both the tumor and the cirrhosis. In this context results are very good with a low tumor recurrence, between 7-15%, and a good five year survival, up to 75%. However the limited number of donors may jeopardize the overall results, since many patients may not reach the transplant mainly due to tumor progression, this is why living donor liver transplantation offers an added advantage limiting the risk of dropping out from the waiting list. However the theoretical survival benefit of LDLT for

early hepatocellular carcinoma depends on two important aspects. First, there is live donor for every recipient and second, the outcome is basically the same.
The applicability rate differs from the east to the western countries, our group (2) as well as the group of Essen (3) , has shown that the applicability rate is very low, performing between 17-20% of the total possible number. Besides, although some groups have suggested that the results may not be the same, the Asian groups with the worlds biggest experience have shown that the results are similar to those of deceased donor liver transplantation (DDLT) being tumor progression at the time of transplantation the most important prognostic factor (4). Those within the Milan Criteria achieved a five year survival similar to the results of DDLT in the western world. Recently major concern has arisen in relation to avoiding the waiting time on the list, suggesting a natural selection of those with more aggressive biological behaviour and drop out. However this does not seem to be the case in the Asian experience and it seems to be early for the western experience. Nevertheless two other factors may affect the overall results of LDLT in HCC, such as the regeneration process of the partial graft that may affect and accelerate tumor recurrence since in the process of regeneration an intense acute-phase injury as well as angiogenesis associated phenomenon take place. In summary, LDLT is the best option to prevent drop-outs, however it is limited by the fact that not every patient has a potential donor. There is a lack of control studies comparing LDLT to DDLT, but it seems that the results are similar in cohort analyses. Extending the criteria seems to be feasible, but there is an urgent need for new means of classifying HCC based on specific tumor biology.

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Moving beyond altruism: why incentives are the best approach

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In her presentation, Professor Goodwin argues that the best way to promote organ donation and to save lives is to allow incentives, including payments for organs. Goodwin maintains that organ purchasing currently occurs on black markets and that such transactions will continue to occur so long as altruistic procurement is the exclusive supply mechanism. National organ transplantation waitlists are overwhelmed with thousands of individuals who will die before the possibility of transplantation. In direct response to indefinite delays on the national transplantation waitlists and an inadequate supply of organs, a growing number of terminally ill Americans are turning to international underground markets for organs. Chinese inmates on death-row and the economically disadvantaged in India, Russia, and Brazil are the often compromised co-participants in the private negotiation process, which occurs outside of the legal process – or in the *shadows of law*.
Unfortunately, the American altruistic procurement model has been unsuccessful in meeting the growing demand for organs needed by the critically ill. As a result, seven thousand Americans on organ transplantation waitlists die each year from treatable diseases. This figure, however does not include those who were never placed on the waitlists, died while on dialysis, or had limited access to medical treatments (the undetected vulnerable). The shortage particularly disadvantages minorities. In a recent article, Professor Stephen Ceccoli noted that people of color comprise over forty percent of those on the list and account for more than half of the deaths. African Americans are the most disproportionately affected among racial and ethnic groups in the United States awaiting kidneys. Altruism, many commentators suggest, is a losing battle.
In Professor Goodwin's lecture, she contends that *exclusive* reliance on the present

altruistic organ procurement process in the United States is not only rife with problems, but also improvident. Such reliance, in light of alternatives, undermines the very purpose of volunteerism and non-coercion by fueling *living-donor* markets in developing countries. Other options that deserve research and scrutiny include directed donations and commoditization.

Goodwin argues that the veneer of altruism ignores preexisting commercial relationships that dominate human biological material transactions, including *private* or *black market* negotiations for body parts. It also overlooks race and status in both the procurement and allocation processes. Among other considerations, African Americans demonstrate a diminished or guarded willingness to participate in the present altruistic system. Their concerns are well-documented in the literature: mistrust of the medical profession and doubts that their organs will be used to benefit other African Americans. Racial profiling and social valuing in the physician referral process, which arguably blocks access for many African Americans who ultimately are channeled to dialysis treatment, are considerable concerns. Exclusive reliance on the *over* capacitated altruistic system does not answer this dilemma.

Goodwin concludes by suggesting that incentive based programs, which might include a broad spectrum of possibilities could easily coincide with altruistic organ donation.

Living donor kidney exchange program in the Netherlands

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Introduction

In order to meet the increasing donor shortage, diverse strategies have been developed to expand the donor pool. One of the options for kidney transplantation is using living kidney donors. Since direct donation between a donor recipient pair is not always possible due to ABO incompatibility or a positive cross-match, a living donor kidney exchange program was started in January 2004.

National program

All kidney transplantation programs collaborate within one kidney exchange program following a national protocol. In addition there is an independent organization to supervise the exchange procedures to ensure that allocation and matching take place in a fair, transparent and objective way. The Dutch Transplant Foundation (NTS) was asked to perform this task.

The national program includes the following:

The medical evaluation of the donor- recipient pair takes place in their own centre. After acceptance the pair will be registered on a national waiting list, maintained by the NTS. All relevant donor and recipient data are stored in a centralized database. Four times a year a match run will be performed, in which the computer program identifies all suitable donor-recipient combinations for an exchange. The matching algorithm is based on 6 conditions; first aim is to identify the maximum number of matched couples. Since there is the possibility that one donor-recipient pair can be matched to several other pairs, a further selection is required based on blood type (first identical than compatible), match probability, shortest chains (maximum of 4), the distribution of donor-recipient couples over the centres and waiting time, calculated from the first day of dialysis.

After the match has been performed all transplant centres are informed on the match results. The report is also sent to the National Reference Laboratory for Histocompatibility in Leiden to verify whether the selected combinations are compatible and to perform the cross-matches. In the Netherlands it has been agreed upon that the donor travels to the centre where the selected recipient is treated. If the donors are accepted as suitable candidates, in all centres the surgical procedures – which have to take place simultaneously within one exchange chain – are to be scheduled in two months. After transplantation strict anonymity will be maintained between the donor and recipient. The follow-up will be collected in the recipient centre.

Results of the program

In the period January 2004 until June 2008 18 match procedures were performed in which 276 donor-recipient pairs participat-

ed; 143 pairs because of blood type incompatibility and 133 because of a positive cross match. Out of these 276 pairs, for 159 pairs (58%) a suitable match was found: 99 pairs in the immunized patients group (74%) and 60 blood type incompatible pairs (42%). Even for the blood type O recipient the program was able to find a suitable combination in 27 % of the cases.

Management of patients with high MELD score by living donor liver transplantation

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High model for end-stage liver disease (MELD) score usually means that greater than 25 or 30, showing as acute liver failure (ALF) or acute-on-chronic liver failure (ACLF). Such conditions usually require urgent liver transplantation (LT). If deceased donor organ is not available, living donor LT (LDLT) should be considered.

The most common cause of patient death from ALF is either cerebral edema or sepsis. Major advantages of LDLT over deceased donor LT (DDLT) for ALF are known as timely implantation of liver graft before serious deterioration of hepatic encephalopathy and use of non-fatty and shortly preserved liver graft. However, application of LDLT for ACLF is still controversial since poor patient survival rate does not justify the potential risk for the living donors.

The potential rationales of LDLT for high-MELD patients should be verified from 3 different aspects such as outcome comparable to that of DDLT, timely performance of LDLT before further worsening, and no increase of donor risk from rapid assessment.

First, the outcome of LDLT for high-MELD patients was assessed. In our 2-year series of consecutive 578 LT cases from January 2006 to December 2007, 111 adult patients (19.2%) underwent LDLT (n=90) and DDLT (n=21) due to ALF (n=40) and ACLF (n=71). Mean MELD score was 34.9±3.9. Graft types for LDLT were 77 right lobes, 2 left lobes and 11 dual grafts. Graft-recipient weight ratio was 1.04±0.2. One-year patient and graft survival rates were 80.0% and 81.2% after LDLT and 79.4% and 79.4% after DDLT respectively, showing no statistical difference. Multivariate analysis showed that significant risk factors for patient survival are hepatorenal syndrome, pretransplant existence of infection and pretransplant use of inotropics. From these results, LDLT is proven as an effective life-saving procedure comparable to DDLT.

Second, optimal timing to decide performing LDLT should be defined in patients waiting for DDLT. According to data from Korean Network for Organ Sharing, mean waiting period was 2 days for ALF and 4 days for ACLF. After these periods, the possibility of DDLT was rapidly decreased. Early decision for performing LDLT in ALF patients seems to be important to prevent irreversible brain damage. Peritransplant continuous consciousness monitoring using Bispectral index appears beneficial. In ACLF patients, it seems to be beneficial to perform aggressive pretransplant intervention such as correction of renal function and pulmonary edema by early start of continuous renal replacement therapy.

Third, the influence of rapid donor assessment on donor safety should be investigated. In our series of 1711 living donors for 10 years, major donor complications occurred in only around 2 % after learning curve. Urgent donation did not increase donor complication rate, but smokers should be avoided due to increased risk of pulmonary complications.

In conclusion, LDLT for high-MELD patients showed the same outcome comparing with DDLT, implicating applicability of the same patient selection criteria. Urgent LDLT strategy includes early timely transplantation for ALF and vigorous correction of risk factors for ACLF. High MELD score contributed to 10% increase of early patient mortality despite intensive peritransplant care.

Is a living donor liver transplantation necessary/ indicated in the western world? What kind of question is this? Or, do you need to ask?

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"Primum Non Nocere" – First Do No Harm, is a mantra established by Galen of Pergamum (129AD – 216AD). Galen grew up in Pergamum in Musia, now Western Turkey, and studied to become a physician. He became the personal physician of Emperor Marcus Aurelius, as well as, to Commodus and Severus. Galen was known to have written approximately two-hundred books. Unfortunately most of them were lost in the destruction of the library in Alexandria. Much of his legacy that we have today comes from the twenty books that survived through Arab translations that were made of his publications. His importance and impact on medicine antiquity was substantial and extends into current times. His statement to not harm the patient is as relevant today as it was 1900 years ago.

At the Vancouver Forum of the Living Organ Donation in September 2007 the morbidity after a right lobe donation was reported about 35% and the mortality from the right lobe donation at 0.3%. The morbidity reported for left liver, which is probably by far left lateral segments, was 9% and a mortality of 0.07%. From the A2ALL study in the United States, which is a prospective multi-center study supported by the NIH and ASTS not quite two-thirds were complication free; 21% of the patients had one complication and 17% had two complications; most of the complications were minor, but biliary leaks were seen in 9% of the donors; portal vein thrombosis in two patients and then IVC thrombosis in one patient; one re-admission in 10% and 2-5 re-admissions in 4% of the patients. The severity of the complications were primarily Grade-1 in 27%; Grade-2 meaning, potential life threatening, but no residual in 26% of the patients and Grade-3 life threatening with residual in 2%. There was actually one death post-op day 21 from multi-organ failure and one later from suicide.

Summary: Living donation from liver donors is an activity that carries with it significant mortality and morbidity and these risks must be weighed against the risk for death and chance of success for the recipient. It has been shown by Merion et al using the SRTR Registry that the risk of death for the recipient with a transplant is higher than without a transplant for patients with a MELD score of 14 or less. Thus, it is difficult to conceive that to perform liver transplantation in patients whose chance of survival would not be enhanced by liver transplantation and even more difficult to subject the donor to the risk of donation if there is not a substantial survival benefit from a transplant. Thus, the patient must be sick enough to justify the risk to the donor.

In summary the risk for donor morbidity for mortality is statistically constant. The benefit to the recipient changes with time. The first question must be how can we justify the risk to a living donor for a patient with a MELD score of less than 15? And the second question that may not have an answer at this time is how can we ever justify using a living donor for a high risk operation since first and foremost we must Do No Harm.

Has the number of arteries in the remnant kidney any influence on donor outcome?

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Introduction: A kidney with a single artery is preferred for donation. How often is the donor left with double or treble arteries in the remnant kidney, and does this have any implications in the long-term?

Methods: All consecutive donors from 1984–1989, who underwent surgery at Sahlgrenska University Hospital, were re-evaluated in 2007 for kidney function, microalbuminuria and hypertension.

Results: In total, 154 donor nephrectomies were performed with an open anterior extra peritoneal technique. The right kidney was removed in 117 cases. Ninety-eight patients were left with one single artery in the remnant kidney and 56 (36%) with more than one. Six individuals were left with three arteries. The mean age at donation was 48 (SD12) years and mean age at re-evaluation was 68 (SD 12) years.

In the group with remnant single artery the mean preoperative S-creatinine level was 86 (SD 12) µmol/L, at 6 months post donation it was 127 (SD 20) µmol/L, and in 2007 it was 89 (SD 22) µmol/L. Estimated GFR was 67 (SD 18) mL/min. Thirty-three per cent of the donors had developed hypertension. Urine albumin/creatinine ratio was increased in 15% (above 5 mg/mmol). In the group with multiple remnant arteries, the mean preoperative S-creatinine level was 87 (SD 11) µmol/L, at six months post donation it was 131 (SD 20) µmol/L, and in 2007 it was 100 (SD 45) µmol/L. Estimated GFR was 64 (SD 16) mL/min. Twenty-eight per cent of the donors had developed hypertension and 40% had increased urine albumin/creatinine ratio. The higher frequency of microalbuminuria was a significant difference ($p<0,05$) compared with the single artery group.

Conclusions: One-third of the kidney donors had been left with double or treble arteries to the remnant kidney. The 20-year follow-up showed no significant difference in renal function between the two groups. However, there was a difference in albuminuria frequency indicating further study.

Training donor advocates

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Adrian McNeil's presentation, entitled *Training Donor Advocates* focused on the system of Independent Assessors (IAs) created in the UK. IAs are trained and accredited by the Human Tissue Authority (HTA) to act on behalf of the putative donor and also on behalf of the HTA. The HTA is a public body required by law to regulate, through a system of approval, all living organ donations.

The purpose of IAs is fourfold: to ensure that the donor understands fully the risks and implications of donating an organ; where appropriate, to obtain evidence that the donor and recipient have a genetic or emotional relationship; to ascertain that consent has been freely given; and to ensure that no payment or reward has been made to the donor. These criteria, which are required under UK laws, must be satisfied before approval for the donation to proceed can be given by the HTA.

The IA must be independent of the transplant programme to avoid any conflict of interest. They must be a member of a professional group – a proxy for recruiting people who are capable of receiving and analysing information and making judgements based on that information. Typically, IAs are physicians, psychologists, psychiatrists or nurses.

Training of the first 140 IAs was completed by means of a one day intensive training workshop that consisted of two elements: the first was to understand the theory – the law, what consent means, the IA's role and logistics. The second element concentrates on practical work involving casework scenarios. The faculty consisted of two members of the senior policy team from the HTA and three practitioners – a transplant surgeon, a renal physician and a consultant nurse responsible for co-ordinating a transplant programme in a large hospital. IAs are reaccredited on an annual basis depending on an assessment of the quality of the reports submitted to the HTA. Partial or full refresher training is given through a new interactive e-learning programme that follows the pattern of the face to face workshops.

Wider training needs are met through codes of practice on consent and donation of organs, specific guidance for IAs and transplant teams, a bi-monthly IA newsletter and an annual conference. Most cases submitted to the HTA are the subject of discussion between the IA and the HTA. This iteration itself provides another means of helping IAs to improve the quality of their reports. Experience has shown that IAs need practical support and guidance if they are to perform to a high standard.

Future directions in transplant immunosuppression

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Four generations of immunosuppressants have been developed for solid organ transplantation: 1) Pre-cyclosporine, 2) Cyclosporine, 3) Post-cyclosporine and 4) Current drugs in trials. With each generation, immunosuppressive efficacy and safety have improved causing progressively lower incidences of acute rejection and im-

proved one year graft and patient survival rates.

The discovery, development and regulatory approval of substantially improved immunosuppressants, however, remains a very high unmet need. Five year mortality rates for recipients of all types of organ grafts are the same or higher than mortality rates from common malignancies five years after diagnosis. In addition, improvements in long term graft survival times have improved little in the last 10 years. Clearly, both safety and immunosuppressive efficacy still need to be improved.

The pre-cyclosporine generation using whole body X-radiation advanced to using dual drug therapy with steroids and azathioprine but was insufficiently safe or effective for transplantation to be the therapy of choice for end-stage organ failure. Cyclosporine, with its improved efficacy and lack of myelotoxicity led to transplantation becoming a far more acceptable therapeutic option.

A series of third generation drugs (tacrolimus, mycophenolate mofetil, sirolimus, anti-IL2 receptor monoclonal antibodies as well as second-in-class agents [everolimus and enteric coated mycophenolic acid sodium with different profiles]) has further reduced acute rejection rates and severities as well as mitigated adverse events from calcineurin inhibitors. The vast majority of the second and third generations of immunosuppressants are natural microbial products. All of the first three generations of immunosuppressants suffered from the disadvantages of their heritage, since none was specifically discovered and developed from the outset as an immunosuppressant for transplantation. Steroids and azathioprine were borrowed from other indications (rheumatoid arthritis and oncology, respectively). Cyclosporine and tacrolimus were discovered to be immunosuppressive without knowing their mechanisms of action. Sirolimus and mycophenolic acid were drugs that had failed for their intended indications (candida and rheumatoid arthritis, respectively). None of these classes of immunosuppressants is ideal, since their drug targets were either pre-ordained or unknown, thus limiting the efficacy and safety of these drugs. The exception was the development of anti-IL2 receptor antibodies. The selection of this immune cell-specific target was rewarded with a high margin of safety, but redundant pathways of immune cell activation limit the efficacy of these antibodies.

None of the fourth generation immunosuppressants in trials is a natural product; each is either a synthetic organic or biologic molecule, and all were designed to block pre-selected targets to produce safe and effective immunosuppression. Since none of the fourth generation agents has been approved, it is impossible to predict their utility. Nevertheless, these new classes of immunosuppressants created by rational drug design have diverse mechanisms of action: 1) Inhibition of signal 1 and co-stimulation by blocking protein kinase C (AEB071, sotrastaurin), 2) Inhibition of signal 1 and adhesion by blocking CD11a (efalizumab), 3) Inhibition of co-stimulation by blocking CD80/CD86, and CD40 (belatacept, alefacept and anti-CD40 mAb 4D11, respectively), and 4) Inhibition of signal 3 by blocking JAK3 (CP-690-550).

Living donor laparoscopic anterior retroperitoneal nephrectomy: preliminary results

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Introduction: During the past decade, the advantages of laparoscopic solid organ surgery have been well established. Laparoscopic donor nephrectomy is the standard of care for living donor (1). However, there has been much controversy over minimally invasive surgery with transperitoneal or retroperitoneal approach for nephrectomy (2). Our institution has seen a dramatic transformation in practice patterns and patient outcomes in the 1 year following the introduction of the laparoscopic anterior retroperitoneal nephrectomy (LARN). In this non-randomized retrospective study, the authors review their 3-year experience with LARN.

Patients and Methods: From January 2004 to December 2007, 21 laparoscopic anterior retroperitoneal nephrectomies were performed in our centre. All donors were examined preoperatively by helical computed tomography (CT), arteriography

with three-dimensional reconstruction, and isotope nephrography. Of them, 12 were male (57.15%) and 9 females (42.85%) with average age of 42.2 years (range: 30-63). Our donors patients were studied for: sex, age, BMI, number of renal vessels, operation time, blood loss, cold and warm ischemic time, complications, hospital stay, timing of the pain-control therapy. We recorded the recipient recovery renal function and postoperative graft lost.

Surgical techniques: Retroperitoneoscopic donor right nephrectomy is similar to the left. Briefly, the donor was placed in a lateral decubitus position. Four retroperitoneoscopic ports were inserted in a retroperitoneal space made by a self-made dilation balloon. The ureter with adequate periureteral tissue was clipped and cut at the level of the iliac vessels. The renal artery and vein were controlled and ligated by endo-GIA stapler. After the isolation of the kidney, a 7 cm skin incision was made along the axillary line. Then the kidney was swiftly removed from the incision.

Results: A total of 17 patients (80.9%) underwent left-sided nephrectomy, whereas 4 patients (19.1%) underwent right-sided nephrectomy. 1 patient has two renal arteries. 8 (38%) of our patients had BMI >25. The success rate of this approach was 100% and no intra-operative complications were reported. The mean operative time (min) was 150±50. The mean graft removal time was 4.29 min (range: 40sec-10min). There were no reported post-operative complications and mortality. The mean blood lost was 115 ml and no patients required blood transfusion. All patients passed to the oral pain-control therapy after the first post-operative day. The mean hospital stay was of 2.3±0.8 days. No dialysis treatment after the transplantation was reported and there was no graft loss or delayed graft function.

Conclusion: Laparoscopic nephrectomy is not a novel technique; however, we have seen that the method used to develop and promote a particular technique within an institution can substantially affect its acceptance and success. The laparoscopy anterior retroperitoneal nephrectomy represents a valid alternative to the "conventional" trans-peritoneal laparoscopic living donor approach. In fact, it is a safe, feasible and effective procedure. LARN offers a shorter operative time and a warm ischemic time compared with the "conventional" retroperitoneal operations. Furthermore, in our experience no peri-operative complications were reported and the donor compliance was excellent.

Table: Donor/recipients details

Donor	
Age (yrs)	39.5 (20-58)
Gender (male)	9 (42.9%)
BMI>25% (n° patients)	8 (38%)
Left kidney procured	17 (81%)
Right kidney procured	4 (19%)
> 1 renal artery	1 (4.7%)
Recipient	
Age (yrs)	25.3 (4-41)
Gender (male)	10 (52.3%)
Operative details	
Operative time (min)	150 ±50
Warm ischemia time (min)	4.29 ± 3
Blood loss (ml)	115±245
Blood tranfusions	0
Conversion to open	0
Postoperative course	
Morbidity rate	0
Needs of i.v. analgesia (days)	1±0.5
Graft function recovery (days)	1
Hospital stay (days)	2.3 ±0.8

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Living donor kidney transplantation using a mini invasive open retroperitoneal nephrectomy

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Living donation kidney transplantation (KTx) is popular worldwide to increase the donor pool. In Belgium, the rate of living donation is low *versus* other countries. This is partly due to the high cadaveric organ offer (~ 25 donors per million inhabitants), compared to other countries. However, increasing waiting times on cadaveric waiting list and the better results of live donation *versus* cadaveric KTx led to a reappraisal of this strategy. In our center living donation KTx was started in 1997. Since then, 55 cases were performed. There are classically 2 approaches for a nephrectomy in a living donor: i) the traditional surgery through a large lombectomy, and ii) the more recent laparoscopic approach. Laparoscopic intraperitoneal nephrectomy at least in its initial development was associated with longer period of surgery, the possibility for intraperitoneal complications {bleeding, splenic rupture, adhesions etc… published and unpublished severe complications}. In addition, vessels procured *via* laparoscopic technique are shorter and right kidneys are more difficult to procure. Urethral complications were also described. Cosmetically the length of the cumulated port incisions and the incision required for kidney extraction exceeds 10 cm. All this led us to design the *open mini-invasive retroperitoneal nephrectomy*. This procedure requires a 10 cm length flank incision and is entirely retroperitoneal. This procedure is extremely safe for the donor because the peritoneal cavity is avoided at all times and control over the major vessels is permanent excluding the possibility of major bleeding. This technique is extremely safe for the graft allowing to procure long vascular pedicules. Right and left kidneys are procured indifferently. Kidney manipulation is minimal. Abundant diuresis is maintained throughout the whole procedure, something essential to achieve good results in the recipient. Another advantage of the mini-invasive open retroperitoneal nephrectomy is that the warm ischemia time is negligible. Cosmetically, the patient ends up with a short flank incision and no abdominal scar.

Living kidney donor results. There was no perioperative complication except for 1 bleeding from a left renal artery that was easily controlled and required no transfusion. Obstipation and tachycardia was noticed in 10.5%, urinary infections in 10.5%, arterial hypertension in 7.9%, wound infection in 5.2%, and a chyle leak in 2.6%. The majority of patients experienced no complications post donation. 2 patients had chronic pain at the wound site. Unlike in the US there is no pressure for living donors to be discharged early and the hospital stay was ~ 1 week. The mean systolic and diastolic blood pressure has remained within normal range. A slight increase in the serum creatinine and a decrease in glomerular filtration rate were documented. A minority of patients has experienced some very mild degree of proteinuria post donation.

Results in recipients. Of 55 consecutive cases, there was no case of primary graft non function. There was 1 case of combined delayed graft function and biopsy-proven humoral rejection. Graft survival at 1 month is 100%, at 1 year 98%. 1 graft was lost to non-compliance. Recipient survival at 1 year is 100%.

TACKERS: Young transplant patients spread their wings

L. Schick

TACKERS, Anzere, Switzerland

Background: TACKERS (Transplant Adventure Camps for Kids, Education, Recreation & Sport) is an International camp for children who have received an organ or bone marrow transplant. It is a non profit organisation that runs a camp for a week in the ski resort of Anzère in Valais, Switzerland. About 50 children stay in a communal chalet which also houses staff and volunteers.

The **aim** is to offer these special children the adventure of a lifetime. The camps give them the chance to develop and test their independence, as well as to meet other children from quite different backgrounds who have also had a transplant. TACKERS was founded in 2002 by Liz Schick, who is a liver transplant recipient. Since then hundreds of children from over thirty countries have attended its winter adventure camps.

Taking part in outdoor activities improves the physical health of the young organ recipients and increases the likelihood of long-term graft survival. TACKERS adventure camps provide a fun-filled, friendly environment away from hospital where the children are able to develop support networks and build their self-esteem.

Funding & Costs: The camps are funded by pharmaceutical companies, fund raising events, private donations and various associations and foundations mostly transplant associated. There is a participation fee of 300 € to help with, but which does not cover, the running costs. TACKERS organises and supplies airport transfers, ski equipment (clothes, skis/snowboard, boots, helmets) ski pass, ski lessons, food, lodgings, accident insurance, 24 hours medical care and surveillance and all other activities. Non ski activities have included paragliding, flying lessons (light aircraft), diving initiation, dog sledding, motivational workshops, snow shoeing, karaoke, arts and crafts, games, dance and theme evenings. For most children this is the first encounter with snow.

Organisation: TACKERS works with Viamonde, a company that organises school trips for international schools. Their highly qualified counsellors are an international team, teaching ski and snowboard. They all have an affinity with children and also supply 24 hour surveillance and organise varied afternoon and evening activities. The ratio of counsellors is 1:5.

The camp also offers a specialist team of paediatric transplant experts and other volunteers such as teachers and linguists who play an important role at TACKERS and offer a broad range of key skills. Often camp volunteers are themselves transplant recipients.

Benefits of sport and being independent: For many children this is their first time away from home, they discover their limits and goals and how to be realistic about achieving them. The camp gives children a sense of well being – promoting a positive attitude by learning to do new things and to spread their wings.

Practising sport is good for their health necessary to stay as healthy as possible.

Conclusion: Children definitely benefit from the camp. Parents realise that they can live, in many cases, like other children. They gain confidence at TACKERS. One mother said, "I sent my little boy to TACKERS and a lovely young man came home." Children are the best ambassador for organ donation and material, footage, photographs and interviews post camp, are invaluable to promote organ donation in each child's respective country. Our film "To Give is to Love" is used around the world and available online in 6 languages to promote organ donation. TACKERS is a project of the FSOD (Swiss Foundation for Organ Donation). For more information contact Liz Schick, liz.schick@tackers.org or visit the TACKERS website www.tackers.org. Next camp 14-21 March 2009.

Is living donor liver transplant necessary/indicated in the western world

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Since liver transplantation was established as the only effective treatment for end stage liver disease, the discrepancy between demand for liver grafts and available grafts has steadily increased. Every year about 2,000 patients are dying on the waiting list before liver transplantation. The mortalities on waiting lists are 22%, 45% and 10% for patients on status 1, MELD of higher than 30, and MELD between 21-30 respectively. The median waiting time for liver transplantation in the US although longer, 402 days, in 2004, was still about 1 year, 306 days, in 2006. At the present time liver transplantation with extended criteria liver graft (ECD) or living donor graft (LDT) are the only practical and real options to expand the donor pool. In the USA ECD donors have been used in increasing numbers while LDT has seen a continuous decline. Both practices aim at solving or easing the donor shortage but there are definite differences in recipient outcome that must be considered when addressing the need for living donor in the western world. Although we lack a precise definition of an ECD, there are criteria both in the European and American literature that refer to age, clinical conditions, clinical history and liver pathologies to describe it. Moreover there are no doubts that nowadays a DCD donor is considered an ECD. A review of the outcome of recipients of DCD liver grafts in all procurement organizations in USA showed a 1 graft year survival of 68%

a retransplant rate of 13% and a re-listing rate of 20%. Needless to say that these data are much worse than the 1 year survival the transplant community and the patients expect. The first LDT for an adult patient in the United States was performed in 1997 and was followed by an enthusiastic increase in the number of programs performing LDT until 2001 when the death of a donor completely reversed the trend. In the past 6 years annual number of LDT has stabilized around 250. However, there seem to be still valid reasons to pursue living donor liver transplantation in the Western world. Recent report from the A2ALL study group shows that LDT provides a magnitude of mortality reduction among the largest observed with any form of transplant intervention and most importantly LDT graft and patient survivals is better or equal under all aspects and parameters. This is particularly important when comparing outcomes in recipients with MELD between 14 and 20 who in many USA regions have practically no access to good liver grafts and are often offered only ECD grafts. There are no doubts that especially in USA the transplant community should have been more careful and demanding stricter rules when a sharp increase in the number of LDT occurred. The colleagues from the Asan Medical Center in Seoul have clearly shown that even in programs with decades of expertise in liver surgery and liver transplantation the learning curve for LDT is counted in dozens of cases. Still today the UNOS requirement for performing adult LDT is to have first assisted 7 LDT procedures. In summary LDT is the only solution with proven good outcome readily available to decrease mortality on the waiting list. The western world embraced LDT with too much enthusiasm and little scrutiny and dismissed it too fast. The transplant community must work harder to achieve the safety for the donors and the results in the recipients that are innate to LDT. A new framework based on real expertise, real need for the transplant and correct reporting should be the starting point. “Primum non nocere” remains a basic ethical principle in the practice of medicine that must be valid for the recipient as much as for a donor of a liver transplant, especially when the outcome is determined by the quality of the graft. It is clear that in this context the ethics of LDT should be part of a broader discussion involving the ethics of transplantation in general.

Medical limits: The mildly hypertensive, the mildly obese and the mildly diabetic renal donor

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The lack of organ donors has raised the temptation to use living kidney donors despite somatic handicaps. We have analyzed the long-term outcome of living kidney donors with mild hypertension, mild obesity or mild diabetes before donation (bD).
The analysis is based on 1036 living kidney donors followed prospectively by the Swiss Organ Living Donor Health Registry (SOL-DHR) since 1993.
171 donors had mild hypertension (MHD) bD defined as systolic blood pressure (BP) >140 and or diastolic BP >90 mmHg or treated with 1 antihypertensive drug (AHD). They were compared to 798 normotensive donors bD (NTD). At 10 years after donation 50% of MHD required more than 1 AHD as compared to 9% NTD. MHD developed microalbuminuria (m-Alb-U) in 14% despite taking ACEI or ARA in 46% (lowering albuminuria) as compared to 8% in NTD taking ACEI or ARA in 19% only.
79 mildly obese donors (MOD) defined as a BMI >30.0 - 35.0 were compared to 521 donors with normal BMI (18.5 – 25.0) (NBMID). At 10 years after donation 86% of MOD were hypertensive and 57% required more than 1 AHD, whereas 39% of NBMID became hypertensive and 12% only required more than 1 AHD. At 10 years 14% of MOD had microalbuminuria despite taking ACEI or ARA in 43% as compared to 8% with m-Alb-U in NBMID (21% treated with ACEI or ARA). The results seen in MHD and MOD show similar patterns, although being two separate cohorts overlapping only partially (19 donors were both mildly hypertensive and mildly obese bD).
GFR (estimated by the MDRD formula) was followed in the MHD and MOD bD and compared to 437 donors, which were neither hypertensive nor obese bD (NHNOD). At 10 years after donation GFR was highest in the MOD (66±9 ml/min/1.73m^2) and lowest in the MHD (54±12). GFR in the NHNOD at 10 years was 62±12 ml/min. GFR is not a problem in MOD.
Among all 1036 living kidney donors only one had insulin dependent Typ 2 diabetes bD. He was accepted for donation because

the diabetes was judged to be mild (GFR 110 ml/min/1.73m^2, no microalbuminuria, no hypertension, no retinopathy). At 1 year after donation GFR fell to 63 ml/min and hypertension developed. He refused treatment. At 3 years after donation GFR fell further to 47 ml/min and massive microalbuminuria appeared. He now accepted treatment with an ARA and since then albuminuria and blood pressure improved, but GFR fell to 41 ml/min at 7 years after donation (GFR is normally rising slowly after the initial fall seen at year 1 after nephrectomy). Although the experience is fortunately limited to one donor it became evident, that accepting an insulin dependent person as kidney donor is a mistake and all arguments claiming little risk because of a "mild form" of diabetes are misleading.

11 other kidney donors developed typ 2 diabetes after donation. If potential donors with a BMI >30 or hypertension bD would have been strictly excluded, only 5 out of these 11 donors (developing diabetes later on) would not have been taken as kidney donors.

Conclusions: Individuals with mild hypertension or mild obesity before donation run a high risk for glomerular damage (microalbuminuria) and for hypertension requiring multidrug treatment. Thus they should be informed about and not be taken as kidney donors if no medical follow-up is provided and if they can't afford antihypertensive drugs (no health insurance). Diabetic individuals should never be taken as kidney donors.

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