Renal Transplantation
A Guide to Clinical Practice

This book is an initiative of the EDTNA/ERCA President, Ms Jitka Pancirova & Ms Renata Mala, PharmaDr. EMEA Disease Area Lead, Immunology, Bristol-Myers Squibb.

A limited edition will be available in English
Acknowledgements
Renal Transplantation: A Guide to Clinical Practice

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Ray Trevitt
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A kidney transplant is the treatment of choice for most patients with end stage renal failure. A successful transplant gives a better quality of life and improved long-term health. It also costs substantially less than long-term dialysis. A successful transplant offers freedom from the restrictions of long-term dialysis, an improvement in sexual functioning and fertility with the possibility of parenthood, and a return to a more normal lifestyle. The imbalance between those waiting for a kidney transplant, and the number of deceased donor kidneys available, has led to various national initiatives to increase the number both of deceased and living donors. As transplantation is increasingly successful, largely due to improvements in drug therapy, the number of renal transplant recipients is growing and it is clear that transplant patients will soon become the largest group of RRT patients.¹

In addition to the increasing waiting lists for a kidney, the main challenges we face are to reduce the rate of graft loss and patient death, and to improve patient quality of life. The introduction of new immunosuppressants over recent years has seen an increase in graft survival and quality of life. For most health care professionals working in renal care, some knowledge of transplantation is essential, as they will be caring for patients who are waiting for a transplant, or are being prepared for transplantation, who are transplant recipients or who have a failing or failed transplant. Patients are faced with more possibilities than ever before – living or deceased donor, expanded criteria donors and immunosuppression regime, and will look to us for information and guidance in these matters.
This handbook is a guide to renal transplantation, and is divided into easy to follow sections designed for the reader to refer to whatever aspect of transplantation interests them.

References

Donation Issues
Learning Outcomes

• To better understand donation criteria
• To learn about the Spanish Model of organ donation

INTRODUCTION

The increasing success of kidney transplantation has, unfortunately, been accompanied by an inexorable rise in the prevalence of end stage renal disease and the demand for donor organs. In addition, the percentage of patients over 50 years on the waiting list has increased so that such patients now comprise > 50% of the total recipient candidate pool. It is well known that criteria for organ donation have changed over time.

From a theoretical point of view, if the preservation methods have been adequate and the surgical technique correct, any organ that functions in a donor should reproduce its function in the recipient.

All protocols of all transplant groups include a section indicating donor exclusion criteria. These only aim to assure as much as possible the viability of the organs that are going to be transplanted. Experience accumulated over the years in all transplant teams and the scarcity of organs needed for the continually growing waiting list have contributed to great flexibility of contraindications for the donation of all types of solid organs. Day by day clinical practice shows us the correct
functioning of transplanted organs that do not fulfill selection criteria. In this chapter we will analyze the viability criteria of the kidney and pancreas. Beginning with the conditions that the donors must fulfill, the microscopic and gross analysis of the organs, we will finish with the analysis of the experience accumulated by the different groups and donation under special circumstances.

“Spanish Model”

The demand is growing exponentially as a way to improve outcomes for survival. In the early nineties, Spain started an integrated approach to the shortage of organs for transplant, specifically designed to increase donation of organs from cadavers. The National Transplant Organization (ONT) was created in 1989; national coordinators were trained, highly motivated and with a specific profile. Since its inception, Spain has increased its donation rate (from 14 per million population (pmp) to 33-35 pmp). The essential mission of the ONT is to facilitate donation and transplantation of organs, tissues, and cells. It is then necessary to reach everyone and develop a whole multidisciplinary activity in which new technologies play an increasingly important role. The measures taken in
Spain to improve organ donation are known internationally as the “Spanish Model”. The success of this approach can be only understood from a multidisciplinary perspective that encompasses legal, financial, political and medical issues. The organization is structured into three levels: National, Autonomic (regional) and hospital (see figure 1 and 2).

The Hospital Coordinator usually is a physician partially dedicated to this task. The procurement of organs is the primary and principal task of the coordinator. The ONT made a great effort for the education coordinator and health care professionals through specific courses on each one of the procedural steps: donor detection, legal issues, interview with the family, organizational issues, management, communication.

Appropriate legislation, with a clear definition of brain death, organ extraction conditions, the lack of a financial motivation…, is essential to ensure the success of the model. Therefore, the “Spanish model” is very simple. Available in all hospitals are

![Figure 2: Organ donors in Spain. Annual rate per million population (pmp) (From National Transplant Organization).](image)
professionals specifically trained in the implementation of all steps to enhance the donation. The ONT displays in a web-friendly way all the steps necessary for the process be carried out with success (education, law, relationships with judges, with the press ...).²

KIDNEY VIABILITY CRITERIA

There are absolute kidney donor exclusion criteria that are shared by the donors of the other organs.³ These are: HIV infection, malignant neoplasms (included in the Central Nervous System), sepsis and disseminated infections uncontrolled with antimicrobial therapy (including bacteria, virus and fungi), multiorgan failure and uncommon diseases such as Creutzfeldt-Jakob and those caused by prions such as Kuru. Because of the danger of transmission of these diseases, it is also sensible to rule out as donors those individuals treated with cadaver derived pituitary hormones. In addition, as is logical, chronic renal failure is also an absolute renal donor exclusion criterion. We should stress that these donors may be valid for donation of the liver and other organs or tissues (Table I).

<table>
<thead>
<tr>
<th>Absolute exclusion criteria of kidney donor</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV (or risk group).</td>
</tr>
<tr>
<td>Sepsis or uncontrolled disseminated infection (bacteria, virus, fungi).</td>
</tr>
<tr>
<td>Multiorgan failure.</td>
</tr>
<tr>
<td>Malignant tumor disease with metastasizing capacity.</td>
</tr>
<tr>
<td>Patients treated with cadaver derived pituitary hormones.</td>
</tr>
<tr>
<td>Chronic Kidney Failure (structural damage).</td>
</tr>
</tbody>
</table>

Table I: Absolute exclusion criteria of kidney donor.

There are other renal donor exclusion criteria which, over time, now have so little importance that many of them should be eliminated (Table II). If we analyze the information offered
by the Organ Procurement Agency of Virginia (USA) on the causes for which transplant teams discarded kidneys from 1977 to 1982, we verify that most have been ruled out at present. They described that 1264 out of 6125 kidneys obtained (20%) were discarded. Many donors were excluded because they were younger than 15 or over 30, or because they had died from spontaneous brain hemorrhaging or had systolic blood pressure under 80 mmHg or serum creatinine greater than 2 mg/dl, or a diuresis rhythm less than 100 ml/h. If we were to apply these screening criteria nowadays, we would have to discard more than 50% of the kidneys that are implanted in our country.

Contraindications for kidney donation

<table>
<thead>
<tr>
<th>Age</th>
<th>Arterial hypertension</th>
<th>Diabetes</th>
<th>Acute renal failure</th>
<th>Prolonged warm ischemia</th>
<th>Glomerulonephritis and other nephropathies in normal renal function phase</th>
<th>Donors with positive serology for hepatitis B and C virus</th>
</tr>
</thead>
</table>

Table II: Contraindications for kidney donation.

In the evaluation of kidney transplant candidates, malignancy (pre-existing cancers) is very important. There is a great variation among the rates of recurrence of different tumors. The interval between the treatment of the patient and the transplantation played an important role. A waiting time of 2 years seems a reasonable compromise with most tumors.

1.1. Elderly kidney donors.

There is no doubt that kidney donor age is one of the many factors related to long-term function of the transplanted kidney. It is well known that the number of sclerotic glomeruli increases with age in the human being. In recent years, the
offer of cadaveric kidneys from elderly donors has increased. At the end of the eighties, some teams began to accept these kidneys for transplant and many more adhered to this policy that extended the age limit for kidney donation during the decade of the nineties. Although the results published by different groups have been different, in general, most consider that middle and long term survival of these grafts is less than that described in younger donors.7-14 Furthermore, the incidence of primary “non-function” is greater and the serum creatinine levels are higher.15 However, it can be extrapolated from the different studies that about 60% of the kidneys continue to have good function at approximately 5 years. These results have encouraged different groups to use these grafts, but establishing a series of use conditions to improve renal survival.

Because of age linked nephron loss and appearance of concomitant diseases such as arterial hypertension (AHT) and diabetes mellitus (DM), analysis of renal function based on serum creatinine, creatinine clearance and proteinuria does not have enough weight to accurately evaluate nephron loss grade. In the elderly donor who most often will have decreased nephron mass, it must be known that there is enough parenchyma to recover renal graft function after the transplant procedure.

In a first evaluation on the adequacy of kidneys from an elderly donor, we should check if the donor has normal serum creatinine when he/she is admitted to hospital or, even more exactly, creatinine clearance calculated in regards to weight and normal age (>60-70 ml/min) according to the Cockcroft-Gault formula. If the renal function is normal, the next step that must be done is to perform gross and microscopic evaluation of the renal grafts. If the gross appearance is normal, these kidneys should be considered valid for transplant. However, before they are implanted, a biopsy must be done to observe the number of sclerosed glomeruli and the condition of the
vessels and interstitium. In the Gaber et al. work in which renal biopsy was used as a marker of viability of the kidneys donated, it was seen that the greatest number of grafts that never functioned was accumulated in the kidney group with a percentage of glomerular sclerosis greater than 20% and that both transplant survival and function were considerably worse then those observed in the groups with a percentage of glomerular sclerosis less than 20%. Consequently, when it is being decided whether to use kidneys from an elderly donor, in addition to the renal function and gross appearance of these organs, the decisive point would be percentage of sclerotic glomeruli seen in the pre-implantation biopsy. In view of these data, those kidneys having a percentage of sclerotic glomeruli greater than 20% should not be used separately. A dual transplant should be done in a single recipient (see figure 3).

As the transplanted renal mass is doubled (theoretically, more functional units are transplanted than in a single graft from an ideal donor is implanted), the previously mentioned risks are offset with this option. A key point in the use of elderly donor kidneys is in what type of recipient they should be implanted. In general, following the dictates of common sense, many
groups have earmarked these kidneys for elderly recipients (“old for old”). This policy has been scientifically supported by the analysis of the UNOS registries made by Cecka et al.\textsuperscript{13} That dictated by common sense, such as placing kidneys from elderly donors in elderly recipients, has clear scientific support. Furthermore, considering that these transplants have shorter survival, it is logical to implant them in elderly recipients who have shorter life expectancy. Logically, mortality of elderly recipients is higher, as also occurs in dialysis or in the general population.

In 1996, our group adopted this policy of dual renal implant in a single recipient when the donor was over 75 years of age or in those between 60 and 74 years when the percentage of glomerulosclerosis exceeded 15% in the preimplant renal biopsy. When this biopsy showed percentages of glomerulosclerosis less than 15% in the donors between 60 and 74 years, a simple transplant was performed (that is, one kidney in each recipient).

Our results, which have been very satisfactory, have been published and distributed through different articles.\textsuperscript{18,20-22} In the first 80 dual implants conducted until October 2004, the mean donor age was 75±5 years (range 61-89) and that of the recipients 62±6 (range 49-73). Actuarial survival at 7 years of the recipient was 88% and of the graft 78%, with mean serum creatinine of the functioning kidneys 150,2 ± 53 mmol/l.

Furthermore, with this policy of dual or single implant using donors between 60-74 years of age with a glomerulosclerosis percentage below 15%, we have been able to reduce the number of kidney donors over 60 years who were discarded for transplant from 35% to 18%, thus increasing our transplanting activity from 7.5±3.4 transplants per month to 11±3 transplants per month.\textsuperscript{18} Our results are confirmed by the Remuzzi’s group where he demonstrated the excellent renal survival of graft recipients over 60 years after correct histological screening.\textsuperscript{25}
1.2. Kidneys from child donors

Kidneys from child donors may be successfully used in adults. The results are excellent when the donor age is greater than three years while survival is worse when the donors are under three years.26-27 Although the literature presents conflicting results; the success rate of renal transplantation in children younger than 3 years is lower than in older children. In children vascular thrombosis is an important cause of graft loss. Many centers prefer donors weighing more than 15 kg, although the ideal weight is around 20 kg. If a pediatric donor weighed lower than 15 kg, some groups transplanted the kidneys en bloc. We have set the minimal body-weight at 15 kg.

1.3. Kidneys from donors with diabetes and/or arterial hypertension

Nowadays, we have subtle renal injury markers caused by diabetes, such as microalbuminuria. However, this is practically impossible to measure in a brain dead patient. Thus, it is considered that a diabetic subject without proteinuria and with normal renal function can be an optimum kidney donor. 28 There are some clinical experiences that have raised questions, such as those in which renal transplants from donors with diabetes with normal renal function had histological lesions typical of diabetic nephropathy.29 The renal transplant functioned perfectly and the histological lesions returned to normal.30 The analysis of the outcome of the kidney transplants using kidneys from donors with arterial hypertension and diabetes from the US Renal Data System showed graft survival at three years of 71% versus 75% of the controls (p<0.001).31

These studies allow us to venture that those kidneys from diabetics, although the results are not ideal, have excellent survival. Thus, the analysis of renal function (serum creatinine on admission and/or calculated creatinine clearance) and glomerulosclerosis in the pre-transplant biopsy should be
maximized in these donors with a background of diabetes and/or arterial hypertension. According to the results obtained, it may be appropriate to select elderly recipients and/or make dual transplants in a single recipient, especially in cases when there is decreased functioning of the renal mass.

1.4. Kidneys of donors with Acute Renal Failure

Acute renal function deterioration in a donor does not contraindicate donation because it is generally reversible. If the donor has presumable acute renal failure at the time of the donation, renal extraction can be considered. Later, the gross appearance of the kidneys extracted and their histology will provide the final data in order to approve their implantation or not. It is uncommon for the donors to have acute renal failure due to hemodynamic disorders and certain treatments. However, if renal extraction is done and we verify that there is no cortical necrosis and that there is only tubular necrosis, these kidneys can be transplanted with good results. This is what our experience with 25 kidney transplants from donors who had acute deterioration of the renal function [mean serum creatinine: 2.5 mg/dL (2-7 mg/dl)] and the experience of the Philadelphia group have indicated.32-33

1.5 Kidneys from non-heart beating donors

One of the most attractive alternatives to increase donation rate is the use of non-heart beating donors. The Maastrich classification establishes four categories according to donation characteristics. Thus, types I and II are called “uncontrolled” donors because of where the cardiac arrest occurs in relation to the hospital scenario.34 In tables III and IV, we can observe the criteria of the possible non-heart beating donors. Age, times of cardiac arrest and warm ischemia are the principal factors to be considered before accepting these patients as potential donors.
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Table III: Criteria for possible non-heart beating donor.

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Death on arrival</td>
<td>Emergency</td>
</tr>
<tr>
<td>II</td>
<td>Unsuccessful resuscitation</td>
<td>Emergency</td>
</tr>
<tr>
<td>III</td>
<td>Waiting for cardiac arrest</td>
<td>ICU</td>
</tr>
<tr>
<td>IV</td>
<td>During or after the diagnosis of brain death</td>
<td>ICU</td>
</tr>
</tbody>
</table>

Table IV: Classification of non-heart beating donors (Maastricht criteria)

After irreversible cardiac arrest outside the hospital, the probable donation procedure is activated. Once the donor reaches the hospital site, the patient is connected to an extracorporeal circulation system while waiting for the family to consent to donation and subsequent organ extraction. The maximum time from when the patient has irrecoverable heart arrest until he/she is connected to the pump is 2 hours. This is
the most important and complex part of all the procedure (see figure 4).

Use of adequate sequential immunosuppression, very close monitoring of the times, use of extracorporeal preservation at normothermia and early and sequential renal biopsies every 7 days in case of persistent acute tubular necrosis have made it possible to use these donors with excellent survival results and very low rate of non-primary function. This has led to a considerable increase in the donation pool.

1.6. Kidneys from donors with positive serology for hepatitis virus B and/or C

As explained in the introduction, another key point of the viability of an organ donor is to assure, as far as possible, non-transmission of infections or tumors. To do so, we must perform a series of serological tests in the donor to rule out hepatitis virus B and C and HIV infection. However, although all donors with HIV or suspected HIV should be discarded, hepatitis B and C virus carriers may be accepted, using their kidneys in recipients who are carriers of these same viruses.

Our group has followed the policy of performing transplants in AgHBs carrier recipients. AgHBs(+) carrier donors were used in a group of them. We found no differences in the
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development of hepatic disease when the evolution of the group who received a positive donor was compared with that of a negative donor, even in graft or patient survival. Thus, kidneys from AgHBs carrier donors may be used in AgHBs(+) recipients.³⁹

Although all renal transplant groups do not have a unanimous opinion, studies show that the use of renal grafts from donors with anti-C positive antibodies in anti-C positive recipients does not entail added morbidity or mortality.

Being able to measure the C virus antigen with a PCR analysis has made it possible to observe that the kidneys from a small number of donors with positive PCR transplanted to recipients with negative PCR produced its positivization and acute hepatitis, which, on the other hand, recovered perfectly. With this experience, the C virus antigen is measure with the PCR in all recipients on the waiting list who were positive for anti-VHC antibodies. Only those who had positive PCR for virus C could receive kidneys from donors with anti-VHC positive antibodies.⁴⁰ Although some groups, to avoid this policy, resort to genomic heterogeneity of virus C that could entail overinfection, others, considering the positive experiences published up to now, simply use donors with anti-VHC positive

![Figure 5: Management of donors with positive serology for virus C.](image-url)
antibodies in recipients with these same antibodies without previously testing PCR (see figure 5). 41

<table>
<thead>
<tr>
<th>Factors in the assessment of a living donor</th>
</tr>
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<tbody>
<tr>
<td>Good medical history</td>
</tr>
<tr>
<td>Physical examination</td>
</tr>
<tr>
<td>Laboratory tests (renal function, proteinuria, urinalysis, viral infections...)</td>
</tr>
<tr>
<td>Electrocardiogram and chest X ray</td>
</tr>
<tr>
<td>Spiral Computerized Tomography (High resolution)</td>
</tr>
<tr>
<td>Careful psychosocial evaluation</td>
</tr>
<tr>
<td>Financial inducement or through improvement in social status should be excluded</td>
</tr>
</tbody>
</table>

Table V: Principal factors in the assessment of a living donor.

1.7. Kidneys from living donors

The number of living-donor kidney transplants has increased over time. The use of kidneys from living donors for transplantation finds its most important justification in the existing shortage of organs from cadaveric donors. A second consideration is that graft survival and quality of recipient’s life are better when organs from living donors are used.

Current guidelines recommend a commitment to prospective, systematic long-term donor follow-up, and to treat individuals who develop hypertension, although the life expectancy of kidney donors appears to be similar to that of non-donors. However, at least two reports have described donors who needed a kidney transplant. Recently, Ibrahim et al. have studied 3698 living donors, showing a survival and risk of end-stage renal disease similar to the general population.42 Donor mortality after surgery is extremely low.

Laparoscopic donor nephrectomy has become the standard of care for live-donor nephrectomy. The use of laparoscopic removal of kidneys has shown a reduction in the number of hospitalization days and morbidity.

The donor should be healthy and free from complicating diseases. A definite age limit for donation cannot be given.
The clinical condition and renal function are the decisive criteria for acceptance as a kidney donor. The medical history and physical examination are key components of the donor evaluation. The principal factors in the assessment of a prospective donor are showed in Table V. Preoperative visualization of the renal arteries is obligatory in each living donor procedure, ideally, spiral computerized tomography with three-dimensional images.43,44

The results for survival of living donor kidney transplants are generally excellent and statistically better than those obtained with deceased donors. The principal factors influencing the survival are: HLA mismatches, cold ischemia time, delayed graft function, acute rejection, immunosuppressive therapy and the possibility of renal transplantation before starting dialysis.

The possibility of reducing the time on renal replacement therapy exerts a clear benefit on renal survival in the long term; probably this decreases the likelihood of developing cardiovascular complications.

Most centers using quadruple therapy with steroids, tacrolimus, basiliximab and mycophenolate mofetil.

In conclusion, living donor kidney transplantation is an excellent therapeutic option that should be offered routinely to patients with advanced renal insufficiency or dialysis program. For the donor short and long term morbidity is low, with a reasonably low risk of mortality.

2. PANCREAS VIABILITY CRITERIA

The pancreas shares the same donor selection criteria with the kidney, with the specific characteristic that pancreatic donors cannot have a personal background of alcoholism, personal or family background of diabetes or significant alterations in the serum amylase values or age over 45 years (Table VI).
Selection criteria of pancreas donor

- Donor age less than 45 years.
- No background of alcoholism.
- No personal or family background of diabetes.
- Normal biochemistry and serology.
- Stay in the ICU ≤ 3 days.
- Selection criteria of kidney donor.

Table VI: Selection criteria of pancreas donor.

SUMMARY

Donation criteria have been becoming more flexible over the years. Currently, the only absolute exclusion criteria are human immunodeficiency virus infection (HIV), uncontrolled tumor disease and bacterial or viral infections. Clinical conditions dictate organ viability criteria: biochemical, morphological and functional that must be fulfilled by the donors and their organs in order to orient the decision on which donor organs can be used. These criteria attempt to assure as far as possible that the transplanted organs function after the extraction, transformation, implantation and reperfusion process without transmitting any infectious or tumor disease. In recent years, the gross and microscopic appearance has become one of the fundamental criteria for selection of potentially viable organs. At present, there is no age limit for renal donation and the principal contraindication is chronic organ damage. However, the use of each organ must be decided individually after a profound analysis of all the viability criteria, weighing the advantages and disadvantages of the implant of a certain organ for the recipient.
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References


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Learning Outcomes

• To learn about the process of evaluating patients for transplantation
• To understand the rationale behind the evaluation process

Introduction

Pre-transplant education is an important contributing factor for improving outcomes of kidney transplantation. Information and education contributes to the patient’s decision to consent to kidney transplantation and has been shown to be beneficial both before transplantation and afterwards. One major benefit for a well educated patient is that the possibility of transplantation treatment is raised at the appropriate time, which gives the opportunity for assessment and inclusion on the waiting list before dialysis treatment begins and the possibility of pre-emptive transplantation. We should begin to prepare patients when e-GFR <20 mL/min/1.73 m², because they could be included on the waiting list or have potential living donors evaluated. Renal graft survival is higher in patients receiving a pre-emptive transplantation, and worsens with increasing time on dialysis, as illustrated in fig.1.

Access to good information and a thorough knowledge of renal replacement therapies enables patients to:

• become motivated and prepared as an active participant when choosing replacement therapy
• consider the issues around living donor and deceased donor kidney transplantation, including extended criteria kidneys
consider the positive and negative aspects of kidney transplantation as a renal replacement therapy

- actively cooperate during the evaluation procedures for the transplant waiting list and to maintain their health during waiting time while on the list,

- prepare themselves for the procedures immediately prior to the transplantation surgery,

- educate and prepare themselves for an active role in their treatment after kidney transplantation.

It is important to communicate to patients the most accurate and objective information on transplantation, as this will influence their expectations of kidney transplantation. This information must include an account of rejection, the side-effects of the immunosuppressive drugs such as cosmetic effects, increased risk of infection and malignancies, and basic outcome data on
graft survival. Adherence to medication, clinic visits and diet should be emphasized. Families and carers should be invited to education sessions as they play an important supportive role to the patient.

With the progress in immunosuppressive therapy and surgical methods kidney transplantation has become the most effective method of renal replacement therapy. Besides improved quality of life, the main gain of kidney transplantation is also improved survival in comparison to patients treated with dialysis. The benefits of kidney transplantation have led an increased number of candidates for whom a transplant is likely to offer a better outcome than dialysis. The success of transplantation depends on several variables and among the most important ones are those which lie with the recipient, which we determine after examinations and assessment of the patient before they are eligible for kidney transplantation.

**Patient preparation for kidney transplantation**

At the beginning of the pre-dialysis period, or soon after end stage renal failure, absolute, relative or temporary contraindications for kidney transplantation should be evaluated. Children are referred to the more experienced Children’s Transplantation Centres.

The upper age limit for transplantation is not determined by chronological age; evaluation of the older patient is guided by biological age or the patient’s general health condition. With increasing age, the risk of surgery and immunosuppression increases however there is some evidence that the detrimental impact of age is diminishing.4

Some patients may decide not to be listed for a transplant, for example when the risk is felt to outweigh the potential benefit.
There is some variation between centres in evaluation of patients for transplantation but guidelines are widely available such as the European Best Practice Guidelines.5

**Cardiovascular system**

Cardiovascular disease is the leading cause of death in transplant recipients6 and before transplantation a thorough assessment of the cardiovascular system is needed, especially with diabetic patients, who often have a silent myocardial ischaemia. With some patients additional diagnostic measures are required beside ECG and echocardiogram, such as heart perfusion scintigraphy or coronary angiography. A successful transplant often results in improved cardiac function.7

Patients with signs or symptoms of peripheral vascular disease or atherosclerosis need vascular studies such as Doppler ultrasound. CT angiography may be required in patients with calcifications on abdominal x-ray or other suspected large vessel problems in the iliac area.

**Respiratory system**

Asthmatic patients, patients with chronic obstructive lung disease and smokers should have lung function testing (spirometry) performed in addition to chest x-ray. Patients with diseased lungs who are transplanted are at increased risk from general anaesthesia, pulmonary oedema and infections.

**Metabolic bone disease**

Patients with advanced and unstable secondary hyperparathyroidism need a parathyroidectomy before transplantation. With advanced secondary hyperparathyroidism, after transplantation the parathormone level is raised and tertiary hyperparathyroidism with hypercalcaemia develops. With only mild secondary hyperparathyroidism, after transplantation par-
Malignancy and screening for malignancy

Patients who have been treated for a malignancy should wait 2-5 years before being considered for transplantation. Women older than 40 years should have regular mammography while on the waiting list, or earlier if there is a positive family history of breast cancer. Cervical screening should also be carried out on women. Men older than 40 years should have prostate specific antigen (PSA) determined periodically according to local practice. Many centres will carry out faecal occult blood testing; and in those who are positive proceed to gastroduodenoscopy and colonoscopy.

Renal Disease

There is a risk of recurrence in the graft of certain renal diseases, most notably in Focal and Segmental Glomerular Sclerosis (FSGS), Membranoproliferative and membranous glomerulonephritis, which can lead to early graft loss. Patients should be aware of this risk and it may have a bearing on decisions to proceed with living donation. Patients with Alport’s syndrome are at a small risk of developing antibodies to the donor glomerular basement membrane causing anti-GBM disease following transplantation. Patients with clinically active systemic lupus erythematosus (SLE) are not candidates for transplantation; however positive serological tests are not a contraindication for kidney transplantation if lupus is not active. SLE patients with antiphospholipid syndrome have a significantly higher risk of morbidity and mortality after transplantation.

A pre-transplant history of immunosuppressive medications increases the likelihood of opportunistic infections and lymphomas after transplantation. If the patient has already
been treated with steroids, bone demineralisation may already be significant and early diagnosis beneficial.

Goodpasture’s Syndrome patients must wait until the disease is clinically stable, and blood examination reveals no antibodies against glomerular basement membrane for at least 6 months. ANCA positive vasculitis patients must be in remission, without or with minimal maintenance therapy. Patients with polycystic kidney disease have a higher risk of gastrointestinal complications after transplantation because of diverticulosis and magnetic resonance imaging (MRI) of the head may be indicated before transplantation because of the high risk of brain aneurysms. Patients on anticoagulant treatment need anticoagulant treatment scheme modification for transplantation prepared in advance, based on underlying kidney disease. Before transplantation the possibility of thrombophilia must be evaluated; SLE patients are particularly at risk of this, especially in the presence of anti-phospholipid antibodies; possible anti-thrombotic interventions include aspirin, heparin and warfarin.

**Vaccinations**

Response to vaccinations is decreased in patients with end-stage organ disease and in the first 6 months after transplantation. Before transplantation renal patients are generally vaccinated against hepatitis B and Pneumococcus. Annual immunisation against the influenza virus is generally recommended.

**Tissue typing and waiting list inclusion**

After examinations and testing for exclusion of any contraindications to transplantation, tissue typing and sensitivities of the patient need to be measured. Panel Reactive Antibody (PRA) is a measure of antibodies to foreign tissue types which is important for graft allocation. Sensitivities may
also be identified precisely as specific antibodies to a particular tissue type antigen. Then the patient can be enrolled on the waiting list. A blood test to measure antibody levels is required about every 3 months. Several years may pass from inclusion on the waiting list to the actual transplant. Some examinations may have to be repeated during this time and patients should be re-assessed periodically.

Gastrointestinal system

With asymptomatic cholecystolithiasis, cholecystectomy before transplantation should be considered and is necessary in patients with a history of cholecystitis as there is a high risk of serious complications after transplantation. With a past history of upper gastrointestinal ulcers, gastroduodenoscopy is necessary. An active ulcerative disease is a contraindication for kidney transplantation.

Liver disease

Hepatic cirrhosis, active hepatitis and some chronic liver diseases are contraindications for kidney transplantation. The side-effects of the immunosuppressants may aggravate liver disease.

Hepatitis B

Survival rates after transplantation are lower in patients infected with hepatitis B virus (HBV). The main cause of mortality is liver failure and infections. Suitability of the patient is determined on the basis of a liver biopsy and serological tests. Patients with severe chronic hepatitis or cirrhosis are not candidates for transplantation. Patients with positive HBsAg or HBV DNA before transplantation should be treated with antiviral medicines such as lamivudine, which prevents transcription of viral DNA. Successful treatment causes HBV
DNA to disappear from the blood and liver function tests normalise, however HBsAg positivity persists. Because of the possibility of resistance emerging treatment is usually long-term.15

**Hepatitis C**

Liver disease because of Hepatitis C virus (HCV) infection considerably shortens patients’ survival after kidney transplantation. The recipient candidate who is antibody positive for HCV needs to be assessed by measuring blood serum HCV RNA to evaluate viraemia. If RNA positive, or if an increased level of alanine aminotransferase (ALT) is found, a liver biopsy should be performed and all HCV positive patients should be considered for liver biopsy before transplantation.15 Patients with active hepatitis have treatment with interferon alpha. It is necessary for a patient with active HCV infection to be treated before transplantation as the treatment can cause allograft failure.

**Urinary tract**

Abnormalities of the urinary tract may require investigation, for example micturition cystogram to determine possible vesicourethral reflux and to evaluate the capacity of the bladder and urinary retention. Referral to a urologist may be warranted. Possible prostate hypertrophy should be evaluated and treated before transplantation. Neurogenic bladder is not a contraindication for transplantation, if the patient is well educated and versed in self-catheterization.

Nephrectomy may needed in vesicourethral reflux with repeated urinary tract infections or hydro-ureter. Nephrectomy is also warranted in patients with polycystic kidneys when these are infected, bleeding into the cysts or if their size prohibits implantation of a new kidney. When kidney stones are infected a nephrectomy may also be required.
Before kidney transplantation a battery of tests and exams is required (see Table 1), and additional exams and tests are performed based on co-morbidity, history or pathological findings.

### Laboratory tests
- Full Blood Count
- CRP
- Electrolytes
- Liver function tests
- Ca, PO4, ALP, PTH
- Lipid profile
- Haemostasis screen
- Serological testing for HBV, HCV, HIV, EBV, CMV, VZV, syphilis, Mantoux
- Urine protein and culture
- ECG, echocardiogram; referral to cardiologist if indicated
- Chest and abdominal x-ray
- Abdominal ultrasound
- Parathyroid series (hands, cranial, thoracic vertebrae and pelvis x-rays)
- Micturition cystourethrogram
- Ophthalmological examination
- Ear/Nose/Throat examination
- Dental examination
- Gynaecological examination for women
- Urological examination for men
- Anaesthesiologist assessment
- HLA tissue typing and antibody screening

Table 1. Tests and examinations before transplantation

### Lifestyle factors
**Obesity**: this presents a higher risk for peri and post operative complications, notably wound infections and burdens the
transplanted kidney. The upper limit of body mass index for standard risk transplantation is 30 kg/m². Overweight patients should be seen by a dietitian. Because of high motivation for a successful transplant, patients are often successful with their weight loss.

**Smoking:** is not an absolute contraindication for transplantation, however we do wish for patients to give up smoking before transplantation, since it has an important detrimental effect on the cardiovascular complications rate, cancer and shortens allograft survival.

**Adherence:** patients who do not comply with advice regarding dialysis, fluid intake, medications and diet may continue this behavior after transplantation. Regardless of the circumstances or aetiology of patient non-cooperation at the time of preparation and evaluation, it is usually associated with non-adherence after transplantation. Ongoing education and support of these patients and their carers can help, and a partnership approach may be most productive. Cooperation of the patient depends to a large extent on the aspirations of the health team, who educate, inform and assist the patient.

In some cases it is better to wait for a few months and re-assess the patient, and they may need referral to a counselor or clinical psychologist. Non-adherence is most commonly encountered in teenage years and among young adults and non-adherence to medication is a major cause of graft loss.

**HLA tissue typing and antibody screening**

Patients may develop antibodies to HLA tissue types and so regular screening samples of serum should be obtained at least 3 monthly. Antibodies can develop as a result of blood transfusions, pregnancy or previous transplants. These samples are kept frozen and may be used for a pre-transplant crossmatch against the donor cells to assess compatibility.
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Previous transplants

The reason for loss of earlier grafts is important. Immunological causes of graft loss mean that there is a less good outcome expected with a subsequent graft than if the previous graft loss was due to non-immunological reasons. Patients who received a previous transplant will also have accumulated a greater immunosuppressive load with its consequent side-effects. Other causes of past failure such as technical problems, disease recurrence or non-adherence may also have a bearing on re-listing and on outcome if transplanted. Patients with multiple previous grafts may need imaging of the iliac vessels to ascertain where a further graft could be placed.

The waiting list

Patients on the waiting list for a transplant should be monitored for the development of any conditions which may require temporary or permanent removal from the waiting list. Periodic re-evaluation may be necessary for both patients who remain active on the list and for those temporarily removed. National allocation schemes have formal algorithms for deciding which patient is offered a deceased donor kidney.

Pancreas Transplant

A pancreas transplant can improve or stabilize some of the consequences of diabetes such as diabetic nephropathy, retinopathy and neuropathy and should be offered to suitable patients with Type 1 diabetes.\(^{21, 22, 23}\)

Contraindications for transplantation

Some infections can present temporary contraindications for some time after healing. Patients with sepsis or active serious infection such as tuberculosis should be excluded until the condition has been effectively treated.\(^{9}\) Repeated infections of
the urinary tract demand a nephrectomy. Peritoneal dialysis patients with peritonitis may be suspended from the waiting list for up to 6 weeks after completed treatment, depending on severity. HIV infection should no longer be an absolute contraindication to transplantation.24

Chronic diseases of other organs are contraindications for kidney transplantation when they cause the patient to be unfit for the surgery itself, or immunosuppressive treatment following the transplantation would aggravate the disease, such as severe liver, heart or lung disease. Such patients, however, may be candidates for a combined organ transplant. Patients are not included on a waiting list if expected survival in their particular case is short, for example less than 2 years. Severe chronic lung disease can present an obstacle for safe general anaesthesia, advanced peripheral vascular disease can prevent successful vascular anastomosis and seriously endanger leg blood supply.

Patients with psychiatric illness need to be psychiatrically evaluated, for the possible detrimental effect of immunosuppressive medication on mental illness, to ensure consent can be properly obtained, and to make a judgment on future adherence to medication. Counseling may be needed for patients with a history of suicide attempt, psychosis and alcoholism. Alcoholism and drug abuse are absolute contraindications for kidney transplantation.

Malignancy: patients should wait for 2 to 5 years after treatment to be included on a waiting list based on the risk of recurrence.8 Immunosuppressive drugs after transplantation can reignite an uncured malignancy. Even these precautions do not guarantee that there will not be a relapse. Patients should be assessed again before being included on a waiting list for kidney transplantation.

Relative contraindications include non-adherence, elderly patients, and the severely obese.
References


Renal Transplantation: A Guide to Clinical Practice


Bibliography


The Kidney Transplant: nursing management of the patient
Learning Outcomes

- To gain knowledge of the management of a patient having a renal transplant
- To understand the rationale underpinning the management of the patient

This chapter takes an overview of the process of renal transplantation and then describes the pre and postoperative care that is essential for nurses to understand so that the recipient can have a positive outcome and hopefully a fully functioning transplanted kidney when they are discharged from hospital.

The kidney transplant operation itself involves the surgeon placing a healthy kidney from a donor into a recipient whose own kidneys are not functioning. The operation involves a diagonal cut to the abdomen to one side below the navel (iliac fossa). The transplanted kidney has an artery connected to the kidney so blood flows to the kidney, and a vein to take the blood away. The ureter is attached to the recipient’s bladder so that urine can exit the body.

Broadly speaking we can describe three levels of graft function: excellent graft function, moderate graft dysfunction and delayed graft function. The patient with delayed graft function will often require dialysis and this form of dysfunction usually occurs from deceased donors and only in extraordinary circumstances does this occur from a living donor. Unfortunately transplants do not always immediately work yet the earlier they work, usually the longer they survive. On occasion they do not
produce urine for days or even weeks, but this does not mean that they will never work.\textsuperscript{2}

**Diabetic patients:**

Diabetic Nephropathy is a growing cause of End Stage Renal Failure (ESRF) and The Renal Association Guideline\textsuperscript{3} states that Simultaneous Kidney Pancreas (SKP) transplantation or living donor transplantation is the treatment of choice for patients with type one diabetes mellitus. The European Best Practice Guidelines for Transplantation\textsuperscript{4} state SKP should be offered to juvenile diabetics as it helps prolong survival and for all diabetic patients pre-emptively or soon after commencing RRT to avoid diabetic sequelae. Once a recipient has a fully functioning SKP this means they no longer need insulin, but this double operation may require additional surgery in the following three months post transplantation. The transplanted pancreas secretes insulin and HbA1c normalizes within three months of transplantation.\textsuperscript{5, 6} SKP transplantation does carry a slightly increased mortality and morbidity risk due to the increased immunosuppression, but the long-term benefits outweigh these risks and can increase the 10-year survival of diabetics compared to diabetics with renal transplantation alone.\textsuperscript{7} Although data collected by the US registry suggest diabetic recipients of deceased donor SKP transplantation and living donor kidney alone (KA) transplants have similar 5 year mortality risks, they are appreciably better than that of diabetic recipients of deceased donor KA transplants.

**Potential Problems after transplantation**

Several complications can occur after transplant. The most common complications will be explained further. Acute rejection is short term with rapid onset and requires immediate action. A biopsy will confirm that a kidney is either being rejected, or that it is still recovering from the surgery and is suffering
from Acute Tubular Necrosis (ATN) or shows drug toxicity. Rejection usually occurs between 4 days and 3 months after transplantation. It occurs due to the immune system rejecting the new kidney as a foreign body, it is usually asymptomatic and is often suspected if the blood creatinine does not come down after a transplant, or has started to fall, but then remains stable or increases again. Some symptoms that might occur include pyrexia, weight gain and decreased urine output, rising or elevated serum creatinine, swelling and pain of the transplant, ankle oedema, and flu like symptoms.

Rejection

Rejection of the transplanted kidney occurs when the body recognizes it as not belonging, and tries to destroy it. Rejection can occur at anytime, but the greatest risk is the first three months post transplantation and about 10-20% of patients will have an episode of rejection during this time. Even when the transplant is ‘well matched’ (few or no HLA tissue type differences), some level of acute rejection can occur. Increasing the immunosuppressant medication can control rejection, but the more immunocompromised the patient becomes, the greater risk they have of getting a life threatening infection or sepsis due to the immunosuppressant drugs required to decrease the rejection risk. During the first three months when often higher doses of immunosuppressive medications will be given to prevent rejection, frequent clinic visits will be required to monitor the recipient closely.

Rejection is a major cause of graft damage; if the injury to the tubules and glomeruli is severe, the kidney may not recover. Acute rejection needs to be diagnosed as soon as possible so that prompt anti-rejection therapy can be commenced. The success with which rejection can be reversed by immunosuppressive agents will determine the long-term success of the transplanted organ. The most common type of rejection is acute cellular rejection were the kidney is infiltrated.
with white cells from the immune system. This is treated with an infusion of methyl prednisolone once daily for 3 days. More severe rejection will have vascular involvement and is generally treated with anti-thymocyte globulin, a polyclonal antibody which has a much greater effect on the immune system. A transplant recipient is more at risk of developing cancer due to the dosages of immunosuppressants, the most common type being skin cancer.

Acute rejection, fortunately, is often mild, and a severe rejection is rare, but can result in complete loss of graft function. Furthermore, graft function following living donation is usually instantaneous compared with deceased kidneys and fewer problems are experienced with ATN. This is related to the shorter cold ischaemic time in which the kidney, after removal, is perfused to enhance preservation. In living kidney transplantation the organ is transplanted almost immediately, versus the possible 12-48 hour delay that can occur with a deceased organ. This lengthened cold ischaemic time can result in delayed function of the kidney. If acute rejection has not occurred within one year of transplantation it is unlikely to occur as long as the patient continues to take regular anti-rejection drugs.

Hyperacute rejection, on the other hand, occurs within minutes or hours of transplantation and is caused by ABO incompatibility between the donor and the recipient or by preformed cytotoxic antibodies in the recipient's blood. Damage caused by hyperacute rejection is almost always irreversible and the graft is lost. Rejection can occur at any time, but the greatest risk of rejection occurs within the first three months after transplant. Immunosuppression is discussed fully in another chapter.

Chronic rejection can also occur many years after transplantation, so it is very important that recipients still attend clinic appointments as requested. It can be distressing for a transplant recipient to realise that the average lifetime for a donor kidney is ten to fifteen years, at which time they
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would need to return to dialysis for a length of time, until another transplant became available. Hypertension post transplantation occurs frequently and can lead to the kidney gradually becoming scarred. Most patients’ blood pressures can be controlled with changes in medications and a blood pressure of 130/80 or below is the ideal. Controlling weight, limiting salt in the diet and exercising will also help.

Pre operative education:
When an ESRF patient is being given advice about kidney transplantation, they and their family / carer need to be fully informed of the benefits as well as the risks/disadvantages of renal transplantation. They need to be given education

<table>
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<th>Information: discussion</th>
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<td>3. Previous surgery</td>
<td>● Graft survival rates – cadaveric &amp; living donor</td>
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<td>● Patient undecided – does not want a transplant</td>
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<td>● Unsuitable for transplant due to?</td>
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regarding medication and its effects on physical appearance. If patients are willing to look at renal transplantation as an option, then particular tests will be undertaken. Education on how to cease smoking needs to be given and obese patients need to be screened for cardiovascular disease and each case considered on an individual basis.

**Final cross matching:**

When a recipient is advised that there is a possible kidney available for them, they usually need to have a confirmation cross match done. The result takes approximately six hours and transplantation is confirmed once this result is available, unless the patient is known to have no antibodies from a recent serum screening. With a living donor, most of this preparation is done prior to admission and the recipient cross match will have previously been confirmed. The tissue type match is not always good, for example between spouses there is no reason to expect any match at all. There is a slightly increased risk of rejection and consequent antibody formation, but overall results are still better for living donors whatever the match. With deceased donors, the cross match is not confirmed until after they are called in for a possible transplant. At this point a sample of the recipient’s blood is mixed with cells from the
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donor and if a reaction occurs the transplant is cancelled, this is known as a positive cross match. A negative match means that no reaction occurred when the donor cells were mixed with the recipient's blood, therefore the transplant can go ahead as the recipient should not reject the kidney when immunosuppression medication is given.13

Pre-operatively:

Pre-operative medications need to be given to the recipient which include immunosuppressant medication, this is usually done once the cross match is confirmed as this is when you the operation is confirmed as going ahead. You need to confirm the patient is well enough for the surgery: undertake a physical exam to ensure they are not pyrexial and are physically well enough to be given a general anaesthetic. This is where your nursing assessment skills are important and you need to liaise regarding your findings with the multi disciplinary team, as all will be involved in the recipient's hospital admission.

Fluid overload and electrolyte imbalance needs to be resolved pre-operatively, so haemodialysis or rapid exchange peritoneal dialysis may be required. If the patient is normokalaemic when they have surgery then early postoperative dialysis is usually not required. A peritoneal dialysis patient needs their exit site examined for infection, the catheter fluid drained, fluid sample collected and the catheter capped. A physiotherapist might commence chest physiotherapy and advise the recipient regarding early postoperative mobility.

Clinical observations are needed such as patient weight, blood pressure, pulse, respirations, temperature, blood glucose level, urinalysis, MRSA swabs taken and all exit wounds swabbed. A urinary indwelling catheter is placed in the bladder pre or intra-operatively. It is crucial though that you do not forget the importance of education and so you need to explain pre and postoperative care to the recipient and family.
There are other tests that may need to be taken such as a pregnancy test for female patients of childbearing age. A chest X-ray, ECG, numerous blood tests as per hospital policy and the patient’s notes need to be taken to theatre with them. 4.5% Albumin is required for theatre as albumin helps maintain oncotic pull, so that fluid is kept within the vascular system. Most importantly the recipient needs to sign the consent form to give their informed consent to the procedure. There is some evidence that using low dose peri-operative aspirin may reduce the risk of transplant renal vein thrombosis. The use of preoperative beta-blockers can be used with high risk cardiovascular patients, but the evidence of its efficacy from randomized clinical trials is limited. At the time of surgery a double J stent may be inserted into the ureter to prevent it from becoming blocked. This is usually removed 6-12 weeks later as a day surgery procedure.

Post-operatively:

Surgical issues tend to predominate the first postoperative days and medical and immunological issues thereafter. Potential postoperative complications can include shock, haemorrhage, fluid and electrolyte imbalance, infection, respiratory problems and deep vein thrombosis. Imbalances in electrolytes including calcium and phosphate can lead to bone problems and so regular blood tests are required. If a combined SKP transplant has occurred, the incidence of urinary tract infection is common and they are also susceptible to metabolic acidosis and dehydration.

Post operatively the goal is to support primary transplant function and for the recipient to have a favourable recovery. Infection control procedures are paramount throughout their recovery. Postoperative surgical management is to optimize graft function, to assess the significance of urine output and to undertake prompt therapeutic intervention. On return from theatre they will have numerous tubes and lines in situ, good
preoperative education should have prepared them and their family appropriately for this. Fluid assessment is exceedingly important, so the indwelling urinary catheter will remain for five or more days to allow accurate fluid measurement and protect bladder-ureter anastamosis from any urinary retention. Urine may be blood stained due to the surgery and blood clots may occur which require gentle sterile bladder washouts. Urine output is measured hourly, strict fluid balance charts maintained, daily urinalysis and specimens taken for microbiology as per policy.

Any change in urine output needs to be immediately reported as it may signify dehydration, a problem with the transplanted kidney or simply that the indwelling catheter has a blockage. If there is no blockage evident, then the patient may require a diuretic in the form of intravenous frusemide and if no response occurs then dialysis may be required to remove the excess fluid. A blockage in the renal artery can cause hypertension or lead to failure of the new organ, so a renal angiogram may be necessary to determine if there is a blockage. Some living donor recipients can become polyuric, so regular blood tests are required to ensure that they do not become hypocalcaemic or hypokalaemic.

A Central Venous Pressure line will have been placed under the collarbone or in the side of the neck, to measure the pressure of blood in the heart. You need to ensure that an X-ray has confirmed it is appropriately positioned before it is used. Inadequate hydration can adversely affect graft function, so the aim is to keep the recipient mildly hypervolaemic, with hourly CVP measurements and urinary output used as a guide to appropriate fluid intake. Fluid intake is usually the previous hour’s output plus 40-50mls with the aim of achieving a CVP of 10-15cm. This fluid intake will be via intravenous fluids immediately postoperatively until oral fluids are reintroduced. Intravenous access will be maintained throughout their hospital stay for the giving of medications. Urine output can vary in
range postoperatively so it is important to know if the patient had any preoperative native urine output. Cardiovascular observations and physical examination are necessary, this includes daily weight.

All clinical observations should be taken as per post operative policy; usually quarter hourly, then half hourly, decreasing to hourly and less, and patient stability dependent. These should include 24 hour ECG monitoring, pain relief and early chest physiotherapy. As with all the observations the nurse makes, it is essential that any abnormalities are immediately reported to a senior nurse and the medical team. Oxygen is given postoperatively with respirations and oxygen saturations monitored closely to ensure they are within acceptable limits. Intravenous pain relief is given which can decrease respiratory drive, so needs careful monitoring.

Oral fluids are usually recommenced on day one, recommencing food is as per medical staff orders, once bowel sounds have been confirmed; still constipation may be a problem. To encourage mobility patients are encouraged to sit out of bed on day one and to start mobilizing soon after. They will be required to wear anti-embolism stockings until they are fully mobilizing. The CVP line can be removed after 48 hours once nutrition has been recommenced. As the postoperative week progresses such close observation of urine output and fluid replacement is no longer required and can become 4 – 8 hourly. Incisional pain may persist, but is usually mild. Prophylactic antibiotics decrease the risk of infections and staples or sutures are usually removed at 14 - 21 days.

**Post operative Patient Education:**

Patient education regarding immunosuppressants needs to commence early so they are clear on these prior to discharge. Self medication is encouraged as soon as possible as the recipient or carer will be responsible for these and needs
to understand the importance of dosage levels, side effects and how to take the medication. Post operatively it is also important to check dialysis arterio venous fistula (AVF) access for function four hourly. The recipient should be reminded that if they have an arm AVF, they should not allow blood pressure measurement or venepuncture on that arm.

The patient will be subject to many blood tests to determine graft function and also may have abdominal drains in situ to drain excess fluid from around the kidney. Document all care and note down oozing, increase in pain or swelling. Record all drainage on the fluid balance chart and report abnormalities. Aseptic dressing technique is required to review or change a dressing, being aware that diabetes and immunosuppressive therapy might impede the healing process.

Discharge, if uncomplicated, can occur 4 – 10 days post operatively, so it is imperative that all education is timed to be completed prior to discharge and at a pace and format that the recipient and their family understand.1,10 One prime example of the importance of education is that graft tenderness is usual immediately postoperatively, but if this occurs at a later date it can be a sign of graft rejection and so the recipient needs to know to contact the hospital.15 Fever is not uncommon and is usually a drug reaction or atelectasis, but a persistent fever, with no obvious infective source may signal graft rejection.

Education that anti rejection medication is needed for as long as they have the kidney, and not just for the post operative period, is essential for them to understand. Patients also need to be familiar with medication names, doses, purposes, side effects and possible drug interactions. Diet, exercise, skin protection and wound care all need to be discussed. They must be able to recognize signs and symptoms of infection and rejection and know who to contact if they suspect either of these. Educative involvement is important for recipients, as they require sufficient knowledge to manage their health. Once discharged the patient will have regular clinic appointments,
usually several times a week to monitor for early signs of infection and rejection. Once stable kidney function has been established this decreases as per local hospital policy.

**Psychological care:**

Post operatively, recipients often feel elated but can then become anxious that the graft may reject. Sadness may also be linked to thoughts of the donor family if they have received a deceased organ. Anxiety is linked to fear of complications such as rejection, infection and graft loss of the precious gift they have been given. A successful transplant is the closest an ESRF patient will have to normality, but is not a cure for ESRF. It is important they are well prepared both physically and psychologically for the procedure so that they can make fully informed choices about how to manage their new kidney in both the immediate and the longer term.

Holistic care is essential in addressing physical and psychosocial needs, and nurses also need to empower the patient to achieve optimal rehabilitation. Unfortunately no matter how good the recipient is with the care that they give to their kidney, approximately 10% of transplants will not be functioning at the 12-month mark and recipients must be informed of this right from the outset.¹
References:


Immunology and Immunosuppression
Learning Outcomes

- To gain knowledge and understanding of immunosuppressant therapies in Renal Transplant
- Be up-to-date on immunosuppressant availability

Introduction

Over the recent years we have witnessed an important change regarding the objectives and priorities in renal transplants, and for this reason, immunosuppressant standards have also undergone a profound change. This change is largely due to the introduction of new generations of immunosuppressants, for example the incorporation of cyclosporine (Cyclosporine A) in 1983. Since 1995 new immunosuppressants have been introduced, such as Tacrolimus, Mycophenolate and more recently Sirolimus and Everolimus. These have expanded the possibilities of immunosuppressant treatment, allowing for multiple combinations either with or without polyclonal anti-T-cell antibodies, more recent humanized antibodies or anti-IL-2Rα receptor antibodies. All of them all been shown to be effective in obtaining an extreme drop in the incidence of acute rejection. They have also led to a significant improvement in graft and patient survival.
Current Immunosuppressant Agents

- Corticosteroids
- Calcineurin inhibitors: Cyclosporine A, Tacrolimus and Tacrolimus prolonged release
- Anti-proliferative: Azathioprine, Mycophenolate sodium, and Mycophenolate Mofetil (MMF)
- mTOR inhibitors: Sirolimus and Everolimus
- Polyclonal antibodies: anti-thymocyte, anti-lymphocytic, and cytokine globulin
- Monoclonal anti-IL-2Rα receptor antibodies: Basiliximab and Daclizumab
- Co stimulation Inhibitors: Belatacept

The standards for immunosuppressant treatment should always be individualized according to the clinical profile of the patient. The current immunosuppressant therapy that is most frequently used is based on three agents: a calcineurin inhibitor (CNI), an anti-proliferative and corticosteroids with or without the induction of polyclonal or monoclonal antibodies.

There is an increasing tendency to avoid or eliminate administration of corticosteroids from immunosuppressant treatment, to a more generalized use of Tacrolimus as a calcineurin inhibitor and to a gradual increase in use of Mycophenolate as an anti-proliferative.

The use of poly and monoclonal antibodies has increased recently. The anti-IL-2Rα receptor antibodies Basiliximab and Daclizumab and anti-thymocyte rabbit globulin are the most frequently used. The incorporation of the mTOR inhibitor Sirolimus and more recently Everolimus have without a doubt increased the therapeutic options in renal transplantation because they can be used for initial immunosuppression as well as for maintenance.
Also the use of new medicines in primary immunosuppression like co-stimulation inhibitors opens new doors to the prevention of chronic graft dysfunction.

**Facts about the different Immunosuppressants**

**Corticosteroids**

*Mechanism of action*

Corticosteroids have a potent anti-inflammatory action due to their effect on different cellular chains involved in the inflammation process; they block the chemo attractant and vasoactive release factors, inhibiting cellular growth and generation. They also have a powerful anti-inflammatory effect as a result of inhibiting prostaglandin synthesis. Their immunosuppressive action blocks T cells and interleukin 2 synthesis.

*Side effects*

In spite of their widespread use for decades in organ transplantation, their negative side effects are widely recognized:

- In metabolism, they increase total and LDL cholesterol, change the distribution of body fat with the appearance of Cushing’s syndrome, and may induce hyperglycaemia and the development of diabetes mellitus.
- They produce a negative calcium balance with the consequent appearance of osteoporosis.
- They are responsible for osteonecrosis and steroid myopathy.
- They provoke or worsen hypertension and can be involved in the development of cataracts.
Corticosteroids are gradually eliminated during maintenance therapy in patients with favourable clinical course and without immunological risk factors in order to avoid the secondary effects of long-term corticosteroid use.2-6

Azathioprine

Mechanism of action
Azathioprine, a purine analogue, impedes the synthesis of nucleic acids and hinders the proliferative activity of the T and B lymphocytes once activated by the IL-2. The azathioprine-steroid combination (classic immunosuppression) was the standard for immunosuppression from the early 1970s until the end of the 1980s. Its immunosuppressive power was modest, as was shown by studies, with an acute rejection rate of between 70-80% and a rate of loss of the graft between 12-60%, primarily during the first year after transplantation. With Cyclosporine A the incidence of acute rejection dropped, and the survival of the implant was 6% to 21% better in patients treated with it. Since the era of Cyclosporine A, its combination with azathioprine and steroids, called the triple therapy, was the most common.

Side effects
Haematological toxicity with development of leucopenia, thrombocytopenia and anaemia

Mycophenolate Mofetil (MMF)

Mechanism of action
This immunosuppressant agent is the pro-drug of active metabolite Mycophenolic Acid. This is also available as Mycophenolate sodium. It has an anti-proliferative effect directed toward the population of T and B lymphocytes by
inhibiting purine synthesis and consequently interfering with DNA replication.

At the beginning of the 1990s many renal transplant clinical trials were started using MMF, which was added to Cyclosporine A and corticosteroids, substituting the classical triple therapy agent azathioprine.

Enteric coated Mycophenolate sodium (ECMPS) is an advanced formula of Mycophenolate, developed with the aim of reducing the negative side effects of MMF on the gastrointestinal tract, in order to avoid dose reduction or the withdrawal of the medicine.

Side effects
The main adverse events of Mycophenolate are gastrointestinal symptoms such as diarrhoea, nausea, vomiting and abdominal distension, haematological toxicity with development of leucopenia, thrombocytopenia and anaemia. There are indicators of an increase in infections such as cytomegalovirus infection.7-12

Calcineurin Inhibitors: Cyclosporine A and Tacrolimus

Mechanism of action
Cyclosporine A and Tacrolimus are the only calcineurin inhibitors (CNIs) available in the market; their mechanisms of action are alike with a similar safety profile. Their fundamental mechanism of action inhibits the CD4+ T cell activation in response to antigenic stimulation. They are used in primary immunosuppression and in maintenance, adjusting the plasma levels by dose changes in order to obtain the desired immunosuppressant effect in each stage, and avoid the toxicity associated with the medicine. In general, Cyclosporine A and Tacrolimus have been used in renal transplantation as part of a therapy in association with other immunosuppressants.
In this way the CNIs have been combined with steroids, with or without an anti-proliferative medicine and with or without the use of induction therapy with depleting antibodies or non-depleting lymphocytes.

The choice of whether to use Cyclosporine A or Tacrolimus during induction and maintenance therapy has been the object of debate in recent years. When speaking about the efficiency of both immunosuppressant agents, we generally refer to their ability to prevent acute rejection and corticosteroid-resistant acute rejection. The long-term efficiency of both medicines can also be evaluated by other parameters such as the incidence of chronic nephropathy and graft and patient survival. Studies show the greater immunosuppressive ability of Tacrolimus, demonstrating its efficiency in controlling the corticosteroid-resistant acute rejection in comparison to other anti-rejection therapies in chronic therapy with Cyclosporine A. 13-19

Tacrolimus is currently available as a standard, twice daily formulation Prograf and also in the form of once daily Advagraf, a slow-release formulation that produces a profile of continuous oval absorption.

Side Effects

Safety Profile of Calcineurin Inhibitors:
Cyclosporine A and Tacrolimus share many of the same negative side effects, although with relevant differences, which is striking considering their mechanisms of action are similar. It is important to point out that the majority of these negative side effects are dependent on the dose and are reversible when the dose is reduced, or the medicine is eliminated in extreme and serious cases. It must be noted that specific side effects can be controlled with the conversion of Cyclosporine A to Tacrolimus and vice versa. 20,21
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Nephrotoxicity

Although CNIs can induce nephrotoxicity, there is more and more evidence showing that Tacrolimus is not as nephrotoxic as Cyclosporine A. Some comparative studies of Tacrolimus and Cyclosporine in renal transplantation have shown better long-term renal function in patients treated with Tacrolimus, as well as the existence of fewer fibrotic changes and a diminished expression of TGF-β. However, the differences in histology and renal function among transplant patients treated with Tacrolimus and Cyclosporine A could be a consequence of the differences in degree of immunological protection, rather than a difference in the nephrotoxic effect of both medicines.22, 23

Neurotoxicity

From a clinical point of view there are numerous signs of neurotoxicity induced by CNIs. The most frequent symptoms include trembling, insomnia, agitation, headache and paresthesia; the first two being more common with Tacrolimus. There are other symptoms that point to illnesses, however they are very infrequent and usually depend on the existence of elevated concentration of calcineurin inhibitors: convulsions, aphasia, coma and delirium. In fact, the presence of convulsions is due to toxic encephalopathy which is very infrequent and is completely reversed when calcineurin inhibitors are suspended.

Cardiovascular Risk Factors

Treatment with CNIs is negatively associated with many different cardiovascular risk factors, which contribute to the morbidity and mortality of the transplant population.

a) Hypertension (HT)

Hypertension following renal transplantation is present among 70-90% of patients that receive Cyclosporine A
therapy as apposed to 45-55% of transplant patients from the pre-Cyclosporine era. HT associated with the use of Cyclosporine A is based on its ability to induce systemic and renal vasoconstriction, mechanisms possibly shared with Tacrolimus.

\textbf{b) Hyperlipidaemia}

Cyclosporine A induces hyperlipidaemia, which is the elevation of LDL (low density lipoprotein) cholesterol levels caused by a decrease in the catabolism of the LDL particles by the hepatic cells. Different comparative studies have shown that hyperlipidemia, especially hypercholesterolemia, seems to be less frequent with Tacrolimus.\textsuperscript{24}

\textbf{c) Post-Transplantation Diabetes Mellitus (PTDM)}

Tacrolimus and Cyclosporine A are toxic to pancreatic B-cells, which contributes to the risk of developing post-transplantation diabetes mellitus. This effect is dose dependent and in general it is accepted that Tacrolimus is more diabetogenic than Cyclosporine A.

Many of the cases of PTDM induced by Tacrolimus and Cyclosporine A are reversible after reducing the dose and exposure to calcineurin inhibitors and by reducing or eliminating steroids.\textsuperscript{25-27}

\textbf{Cosmetic Side Effects}

Chronic treatment with CNIs is associated with a frequency of cosmetic side effects, with special relevance in the paediatric and adolescent population, leading to failure to complete treatment. While Cyclosporine A treatment induces gingival hyperplasia and hirsutism, the most common cosmetic effect is alopecia. Different conversion studies have shown that these problems can be reversed with the elimination of the corresponding calcineurin inhibitor.
To summarize, in light of the existing evidence, it can be affirmed that tacrolimus presents a lower hypertensive effect and a better lipid profile control; however, it is associated with a great risk of developing diabetes mellitus. See Table 1, adapted from Webster et al.

### What we know

- Cyclosporine and Tacrolimus increase survival of the graft, but Tacrolimus has a significantly lower rate of acute rejection.
- Tacrolimus is associated more with diabetes mellitus and neurotoxicity but provokes less hypertension, dyslipidaemia and fewer cosmetic side effects than Cyclosporine A.

### New Findings

- Tacrolimus increases the survival of the graft compared with Cyclosporine A, with 44% decrease in loss during the first 6 months after transplantation.
- Tacrolimus has two times the risk of causing PTDM than Cyclosporine A.
- The survival of the graft is maximized and the risk of developing PTDM minimized when the levels of Tacrolimus are < 10ng/ml during the first year after transplantation.

Table 1: Meta-analysis of 123 papers from 30 random clinical trials (4102 patients) Tacrolimus vs. Cyclosporine A as a primary immunosuppressant in renal transplants (adapted from Webster et al.)*

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**mTor Inhibitors: Sirolimus and Everolimus**

**Mechanism of Action**

Sirolimus is a macrolide product from the fermentation of an actinomycete that was the first mTOR inhibitor developed as an immunosuppressant. Everolimus is a derivative of Sirolimus, with a substitution in the two hydroxyl group in
position 40, developed to have a better oral bioavailability. Their mechanisms of action and possibly their safety profiles are similar.

The last decade witnessed some excellent results regarding short-term graft survival, but not a parallel development of long-term results. A shift in the ideals of immunosuppression has been observed, now paying closer attention to the unresolved question of long-term graft and patient survival. A new family of immunosuppressants, proliferation signal inhibitors, also called mammalian target of Rapamycin (mTOR) inhibitors, Sirolimus and Everolimus seem to have great potential in this respect. mTOR inhibitors have a way of acting that is clearly different from the CNIs. They block the proliferation signal that provides the T-cell growth factors and therefore stop T-cell proliferation.

The anti-proliferative actions of the mTORs are not limited to the immune system; these medicines also inhibit stimulated cell proliferation by general growth factors. The anti-proliferative effects on smooth muscle prevent the vascular restructuring that is a key component in the development of arteriosclerosis and peripheral vascular disease that can generate progressive allograft dysfunction.

Sirolimus is administered orally and has a low bioavailability (20%). Its half life is rather long (60 hours) which allows for a once daily dose. Everolimus has a greater intestinal bioavailability and a shorter half life (36 hours) which requires its administration every 12 hours.

Use of Sirolimus/Everolimus in de novo patients:

Clinical studies have shown that Sirolimus can be used in both induction and maintenance therapy. Recent studies show that Sirolimus/Everolimus can be used in immunosuppressive
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therapy as a base (without calcineurin inhibitors) or in combination with either Cyclosporine A or tacrolimus.30-35

Sirolimus/Everolimus’s immunosuppressive efficiency seems to be equal to that of Cyclosporine A, with similar rates of acute rejection. It can also be used as a substitution in patients that experience toxicity with calcineurin inhibitors and in the presence of chronic graft dysfunction. It is very important to note that patients switched to Sirolimus or Everolimus should be switched early with serum creatinine less than 2 mg/dl and proteinuria < 1g/24h or 0,5g/24h.

Conversion to mTOR

<table>
<thead>
<tr>
<th>Benefits of Sirolimus/Everolimus Immediately Following Transplant</th>
<th>Reasons for conversion to Sirolimus/Everolimus</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Low incidence of acute rejection</td>
<td>• Chronic graft nephropathy</td>
</tr>
<tr>
<td>• Better blood pressure control</td>
<td>• Malignant neoplasms</td>
</tr>
<tr>
<td>• Improvement of renal function</td>
<td>• Severe hypertension</td>
</tr>
<tr>
<td>• Anti-fibrosis effect and prevention of arteriosclerosis</td>
<td>• Post-transplant diabetes</td>
</tr>
<tr>
<td>• Anti-tumour effect</td>
<td>• Haemolytic-uremic Syndrome due to CNIs</td>
</tr>
<tr>
<td>• Prevention of haemolysis</td>
<td>• Aesthetic effects due to CNIs</td>
</tr>
</tbody>
</table>

Side effects:

• Dyslipidaemia, especially hypertriglyceridaemia and hypercholesterolaemia
• Presence of moderate myelotoxicity in the form of: thrombocytopenia, leucopenia and microcytic anaemia
Less frequent side effects:
- A worsening of pre-conversion proteinuria
- Lymphocoeles
- Delayed wound healing; need to switch to CNI to cover planned surgery
- Oedema
- Anaemia

Monoclonal and Polyclonal Antibodies

**Mechanism of Action**

Monoclonal and polyclonal antilymphocyte antibodies are biological products that attack the proteins on the surface of the lymphocyte membrane in order to block the powerful and temporary immune response. They are used to prevent acute rejection during induction therapy and in the treatment of corticosteroid-resistant acute rejection.

**Polyclonal versus Monoclonal Antibodies**

Over the last 10 years, the way in which different regimens of antilymphocyte antibodies are used in induction therapy has varied.

In 1992, the majority of renal transplant patients did not receive antilymphocyte antibodies during induction therapy. From 1992 to 2001 their implementation gradually increased, and in 2001 close to 60% of organ recipients received some sort of antilymphocyte medication. Since 1995 OKT3 was the most commonly used antibody and later the anti-thymocyte globulin Atgam (ATG, horse-derived). In 1998 the antagonist antibodies for the IL-2 receptor Basiliximab and Daclizumab were introduced into the market, and since then their use has become increasingly more widespread. The anti-thymocyte
rabbit globulin Thymoglobuline(R) (ATG) was introduced in 1999 and is currently the polyclonal antilymphocyte antibody most frequently used.

**Recommendations for the use of polyclonal and monoclonal antibodies**

There is no general consensus on how to establish a successful induction therapy in renal transplant patients; however, there are recommendations and strategies according to the clinical and immunological profiles of recipients and donors. In high risk patients like paediatric patients, African-Americans, patients with hypersensitivity to anti-HLA antibodies, re-transplant patients (principally with early graft failure) and in renal-pancreas transplantation ATG demonstrates greater efficiency than anti-IL-2Rα antibodies with respect to the prevention of acute rejection. Following the advice of European guidelines and clinical experience, many nephrology centres, for high risk patients, opt for a quadruple therapy: ATG, Tacrolimus, MMF and Steroids. This is a powerful immunosuppression therapy that diminishes the possibility of early acute rejection.

The use of expanded criteria donors is increasingly common. The term “expanded” includes donors with a risk of developing delays in graft function, such as: elderly donors, donors with prolonged cold ischemia, asystolic donors and donors with previous acute renal insufficiency. A delay in the recovery of renal function is a factor that predisposes the patient to early acute rejection. The association between acute rejection and delayed graft function is probably the worst prognostic factor regarding the survival of the graft. As a consequence, the immunosuppression therapy of less favourable donors should always, when possible, avoid the use of nephrotoxic agents and simultaneously offer a powerful immunosuppressive action. The addition of monoclonal or polyclonal antilymphocyte antibodies is one of the leading therapies to avoid acute rejection and reduce the incidence of delayed renal function in this transplant group.56-63
Belatacept

Belatacept (LEA29Y) is a research medicine and a selective blocker of the co-stimulation pathway that unites the CD80 and CD86 ligands of the antigen cell. During recognition of the antigen (signal 1), the interaction between CD80 and CD86 with the surface of the co-stimulator receptor CD28 of the T-cell (signal 2) is necessary in order to carry out the complete costimulation of the T-cell (Fig. 1). By blocking signal 2, the activation of the T-cell is stopped, provoking clonal anergy and apoptosis (Fig. 2). A randomized multi-centre study was carried out comparing Cyclosporine A and Belatacept grouped with steroids, MMF and Basiliximab. This study showed that Belatacept was not inferior to Cyclosporine A in preventing acute rejection. It preserves renal function by obtaining optimum glomerular filtration rates, reduces the risk of developing chronic graft dysfunction, and reduces the metabolic effects derived from CNIs and in turn cardiovascular problems.

Due to the absence of nephrotoxicity in this new class of immunosuppressant medicines they have the potential to be the primary immunosuppressant option for expanded criteria donors. Currently, there is still little clinical experience with this drug.

Immunosuppression Protocols

The introduction of new medicines has broadened the arsenal of available immunosuppressants, and has made it possible to individualize treatment and design therapeutic protocols dependent on the clinical and immunological characteristics of donors and recipients. The choice of an ideal immunosuppressive treatment is based on preventing acute rejection, prolonging the long-term survival of graft and patient and minimizing the appearance of negative side effects. This therapeutic process must always be flexible and adaptable to
the needs of the transplant patient. It is necessary to specify that the immediate post-transplant immunosuppressive needs are different from the long-term needs. Hence, both an induction treatment and a long-term maintenance therapy need to be developed and defined. During the induction period there is greater risk of acute rejection; therefore, the immunosuppressant treatment needs to be more aggressive and more effective. Subsequently, the risk of acute rejection, although it never completely disappears, will be reduced while new risk factors for the patient develop such as chronic graft nephropathy, cardiovascular morbimortality or the appearance of neoplasms. Immunosuppressive treatment must be individualized and adapted to the patient's characteristics and the transplant's evolution.

**Induction Treatment**

In this stage of great activity and immune response, the immunosuppressive treatment must be more intense and effective. Accordingly, the combination of immunosuppressants is crucial, enabling the of use quadruple therapies in cases with greater immunological risk and poly and monoclonal antibodies during the induction treatment. In general the recommended immunosuppressive treatment for a standard recipient (one who does not present high immunological risk or increased risk of delayed graft function) is based on a triple therapy with steroids, a CNI and an anti-proliferative (MMF or mTOR). The choice of which CNI to use must be patient specific and will ultimately depend on the characteristics of the patient; however, Tacrolimus is the most frequently used nowadays. This is due in part to the fact that Tacrolimus has a lower rate of acute rejection, offers a more favourable cardiovascular profile and produces less cosmetic side effects.
Nevertheless, Cyclosporine A should be indicated for older patients and those with the risk of developing post-transplant diabetes mellitus. The same should be considered for anti-proliferatives, therefore the choice between MMF or mTOR will also be made depending on the clinical profile of the patient and their future immunosuppressive maintenance plan. If withdrawal of CNIs is planned it is best to use Sirolimus, because it is the most effective and efficient immunosuppressant. If reduction of CNIs is planned, but not elimination, then MMF can be used just as well as Sirolimus.

Induction therapies that use poly and monoclonal antibodies should not be restricted to patients with an elevated immunological risk, hypersensitive patients, second or third transplant patients or combined renal-pancreas transplant patients. They should also be considered for patients with a risk of delayed graft function such as with elderly donors, donors with acute renal failure or uncontrolled non-heart beating donors with the idea of using low dose or CNI - free combinations of MMF and Sirolimus and future use of a costimulation inhibitor with good results. Special care must also be taken when individualising immunosuppression therapy for the specific population of transplant patients with the hepatitis C virus (HCV). HCV infection is associated with a greater post-transplant morbidity and mortality especially when virus replication is active. There are not enough clear clinical findings that suggest which immunosuppressive treatment is more suitable.\textsuperscript{64-69}

The table below offers an example of the different alternatives for immunosuppression as established in a single, large nephrology centre (Table 4).
### Immunosuppression Protocol

<table>
<thead>
<tr>
<th>Patient Type</th>
<th>Clinical Characteristics</th>
<th>Immunosuppression</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Standard Patients</strong></td>
<td>• First transplant&lt;br&gt;• Average donor-recipient age 20-55 years old</td>
<td>TAC+MMF+S</td>
</tr>
<tr>
<td><strong>Patient with high immunological risk</strong></td>
<td>• Previous acute rejection&lt;br&gt;• &gt; 50% Panel Reactive Antibodies or positive cross-match&lt;br&gt;• Re-transplants&lt;br&gt;• Renal-pancreas transplantation</td>
<td>TAC+MMF+S+ATG</td>
</tr>
<tr>
<td><strong>Less favourable donors</strong></td>
<td>• Advanced age &gt;60 years old&lt;br&gt;• Donors &gt;55 years old with cardiovascular risks (HTN, DM) during 10 or more years&lt;br&gt;• Prolonged cold ischemia&lt;br&gt;• Asystolic donors&lt;br&gt;• Donors with acute renal insufficiency</td>
<td>TAC or CsA (reduced doses or delayed introduction) +MMF+S+ATG/Anti-CD25</td>
</tr>
<tr>
<td><strong>Neoplasms</strong></td>
<td>• Recipients with a history of neoplasms</td>
<td>MMF+SRL+S +Anti-CD25 or TAC (3 months) +SRL+S+Anti-CD25</td>
</tr>
<tr>
<td><strong>Patient HCV+</strong></td>
<td>• Patients with HCV infection (&gt;60 years)</td>
<td>TAC vs CsA (short-term)+MMF+S+Anti-CD25</td>
</tr>
</tbody>
</table>

CsA: Cyclosporine A; TAC: tacrolimus; SRL: sirolimus; MMF: mycophenolate mofetil; S: steroids; HCV+: hepatitis C virus positive, Anti-CD25: Basiliximab or Daclizumab ATG: anti-thymocyte globulin

Table 4: Immunosuppression Treatment Protocol based on clinical and immunological profile of donor and recipient.
Maintenance Treatment

The objective of maintenance treatment is to obtain long-term survival of the graft and minimize the side effects of immunosuppressant treatment with visible improvements in the patient’s quality of life. In this phase the objectives change and acute rejection is no longer a primary concern, although it should never be ignored. Efforts in this stage are focused on avoiding the appearance and progression of chronic allograft nephropathy and minimizing cardiovascular morbidity and mortality and the appearance of neoplastic processes. For all of these reasons, the maintenance treatment should be the least aggressive possible and have a good safety profile, but achieving this balance is sometimes difficult. As the field of renal transplantation evolves, the use of immunosuppressants with severe negative long-term effects should be eliminated or reduced. Modification of treatment should be done prudently, slowly and progressively, weighing the risks and benefits for each patient:

- The first step should be directed at a mid-term elimination of steroid treatments, especially among paediatric patients. The advantage of this strategy is elimination of the negative side effects, mainly the cardiovascular risks such as diabetes, hypertension and dyslipidaemia. These steroid-free protocols are growing increasingly stronger thanks to the efficiency of the current immunosuppressant guidelines, with the growing use of anti-lymphocyte globulins and monoclonal antibodies anti-CD25 in the induction phase.

- The possible reduction or suspension of a second immunosuppressant, depending on the clinical situation of the patient and graft function, should be considered. The ultimate objective of maintenance treatment, in the majority of patients, should be a therapy with low doses of both immunosuppressants or in select patients (low immunological risk, immediate renal function, no
Consideration should always be given to the fact that the ideal immunosuppressant should be efficient and safe and should not induce nephrotoxicity, cardiovascular risk factors or neoplasms.
References


Renal Transplantation: A Guide to Clinical Practice


35. Grinyo JM, Campistol JM, Paul J, garcia-Martínez J, Morales JM, Prats D y cols.: Pilot Randomized Study of Early Tacrolimus Withdrawal from


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Immunology and Immunosuppression


Bibliography


Long term care of Renal Transplant Patients
Learning Outcomes

- To learn about the ways we can help patients to help themselves after transplantation
- To understand the need for long-term monitoring of patients after transplantation

Introduction

Once a newly-transplanted patient is discharged from hospital their follow-up as an outpatient begins. Healthcare professionals must work in partnership with the patient to maximise graft survival and minimise the problems which are associated with renal transplantation.

Although patients will need to be followed up for as long as the kidney is working, the first few months after the transplant are the most critical. Appointments often start at thrice weekly, and become less frequent as the months go on, decreasing after several years to four monthly. An example of a clinic follow-up schedule is:

<table>
<thead>
<tr>
<th>Weeks</th>
<th>Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-2</td>
<td>Daily review while inpatient</td>
</tr>
<tr>
<td>3-4</td>
<td>x3/ week after discharge from hospital</td>
</tr>
<tr>
<td>5-8</td>
<td>x2/ week</td>
</tr>
<tr>
<td>9-12</td>
<td>x1/ week</td>
</tr>
<tr>
<td>4-6</td>
<td>Blood test fortnightly, clinic monthly</td>
</tr>
</tbody>
</table>
Long term care of Renal Transplant Patients

<table>
<thead>
<tr>
<th>Months</th>
<th>Clinic Frequency</th>
<th>Blood Test Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>7-12</td>
<td>Blood test monthly, clinic 6-8 weeks</td>
<td></td>
</tr>
<tr>
<td>&gt; 12 months</td>
<td>Clinic 2-3 monthly, blood test only 4-6 weekly</td>
<td></td>
</tr>
<tr>
<td>&gt; 3 years</td>
<td>Clinic 4 monthly, blood tests 2 monthly</td>
<td></td>
</tr>
</tbody>
</table>

After any problem with graft function, such as a rejection episode, or other medical problem such as infection, the patient’s follow-up may be more frequent, as clinically indicated.

In clinic patients have routine blood tests to monitor renal and liver function, bone profile, glucose, blood count, Cytomegalovirus (CMV), CRP, cholesterol and therapeutic drug levels. Urine is also tested for infection and protein. Patients are particularly at risk of rejection, infection and ureteric stenosis in the first few months. Blood pressure, weight and temperature are checked each visit.

Patients must be aware that Cyclosporin, Tacrolimus and Rapamune drug monitoring must be done on trough levels. A decision is made on any dose changes, usually on the same day for recently transplanted patients, and the patient telephoned at home.

**Rejection**

It is important to recognize the signs of acute rejection. About 10-15% of transplant patients experience mild episodes of rejection in the first few months, and require treatment. Patients should be made aware of the signs of rejection which are listed below:

**Fever:** some patients develop an elevated temperature when they go through a rejection episode. This is often associated with chills and muscle aches, similar to the symptoms of flu.
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**Graft Tenderness:** this is most common in rejection episodes occurring in the first few weeks after transplantation, but can happen later.

**Decreased urine output or oedema:** ankle oedema is common but should improve; if it is only on the same side as the graft it may indicate a lymphocele. However it may also indicate rejection.

Additional signs include rising or persistently raised serum creatinine and trough drug levels below the therapeutic range.

**Rehabilitation of the patient**

Although most patients feel quite well and are fairly active during their last few days of hospitalisation, they usually feel surprisingly tired when they get home. In general, patients should be encouraged to do anything they feel up to.

Patients should anticipate being off work for at least 6 weeks, but this will depend on how they are doing and the demands of their job. Physical exercise is very important after the transplant for general well being. It can be helpful in preventing excessive weight gain, keeps the patient fit and can bring great enjoyment. The amount of exercise taken should be gradually increased. Patients should be advised to keep themselves upright and not stoop over the wound, thus worsening posture and increasing the risk of back pain. Heavy weights should not be lifted for the first few weeks following the transplant, and only gradually increased. Walking is an excellent exercise form for general fitness. Extreme athletic exercise should be avoided for twelve weeks. The only sports which are recommended to be avoided are those where the kidney might suffer a direct blow, for example rugby and some types martial arts.

Patients are advised not to drive for about four weeks following the transplant. They must be able to perform any emergency
manoeuvre, such as a sudden stop or rapid change of direction. National agencies may require that motor insurance companies are informed or specify when driving may resume, subject to medical advice. Different rules are likely to apply to drivers of minibuses, goods vehicles and buses.

Diet & Fluid Advice

Patients usually need to drink at least two litres of fluid per day and more in hot weather or if pyrexial to maintain good kidney function. If patients are feeling unwell, vomiting or having diarrhoea they should inform the Renal Unit, because they could become dehydrated and this could affect kidney function. Also, if Muslim patients previously observed fasting for religious reasons during Ramadan they should be advised that people with medical conditions that make fasting injurious to health, for example if they need to take medication, are exempt. To compensate, they should make a donation to the poor (fidyah).¹

Following the transplant, if blood results are normal, patients should eat a normal healthy diet: a balanced, low fat, low sugar, high fibre, low salt diet. A Renal Dietitian will be able to advise on specific dietary requirements, and follow up as appropriate. Many patients with good kidney function have low serum phosphate for the first few weeks after the transplant; they should increase their phosphate-rich foods (dairy products, sea-food) and may need short-term supplements.

It is important that during the first few months after the transplant, patients avoid eating foods that may contain the Listeria bacterium. Patients are highly immunosuppressed for the first few months, with higher doses of immunosuppression, and are more vulnerable to infections. Listeria usually presents with no symptoms or very mild flu-like symptoms. Headache, diarrhoea or a sore throat can also occur and a more serious infection can arise if the Listeria spreads in the body. Foods
that may contain Listeria include the following: unpasteurised cheese, pate, live yoghurt, foods containing raw eggs e.g. mayonnaise. Patients are also more vulnerable to other food poisoning bacteria.

Patients should be advised to avoid eating grapefruit or drinking grapefruit juice, because the enzyme pathways it uses interferes with the level of cyclosporine, tacrolimus or sirolimus in the blood.

**General Health**

Illness and steroid treatment may change the condition of the hair. Permanent hair dyes, tints, wave lotions and bleach may cause hair to become brittle and break, patients should be advised to use a mild shampoo and a good conditioner. Unwanted facial and body hair growth might be a problem as a result of ciclosporin. Patients can be offered advice on hair removal or the option of switching to another immunosuppression regime once graft function is stable. Patients should be advised to wait for several months, until immunosuppression has been reduced, before purchasing new glasses/ contact lenses, as vision can alter in the first few months. It is advisable that patients have routine dental examinations, this is particularly important because of the risk of gum disease in patients on ciclosporin.

**Sexual Activity:** Normal sexual activity may be resumed as soon as the patient feels ready. Both patient and partner may need time to readjust. Following a successful kidney transplant many people experience a return of libido (sex drive) and energy. Patients who are sexually active and do not have a long-term sexual partner should be advised to use condoms to reduce the risk of sexually transmitted diseases such as HIV, syphilis, herpes, hepatitis, chlamydia or gonorrhoea. Contraception should also be used to avoid unplanned pregnancy. Women of child bearing age usually resume a normal menstrual cycle and
Long term care of Renal Transplant Patients

along with it normal fertility. Both men and women should be aware of the possible need for some method of birth control.

It is not usually advisable for women to become pregnant in their first year following a kidney transplant, because of the higher doses and type of immunosuppression, and diabetic transplant patients should ideally wait two years. Patients must be encouraged to discuss any plans in clinic as some common transplant medicines will need to be stopped, and alternatives found, because of the risk of foetal harm. Patients should have a good level of renal function before they become pregnant.

Malignancy: The anti-rejection therapy causes an increased risk of developing some cancers. With careful surveillance the impact of this can be markedly reduced.

Cervical Cancer: Routine check ups, including cervical smears, are very important.

Breast Cancer: Patients should be encouraged to self-examine their breasts each month (one week following the menstrual cycle) and to report any lumps or discharge from the nipple to the clinic immediately.

Testicular cancer: Self-examination is important to detect cancer as testicular cancer is almost always curable if detected early. Self-examination should ideally be carried out in a warm bath or shower. Any lumps or change in size should be reported immediately.

Skin cancer: Squamous Cell Carcinoma (SCC) is the most common cancer seen after transplantation, and patients with low skin pigment and increased exposure to sunlight are most at risk. It is associated with Human Papilloma Viruses (HPV). Patients should cover up, wear a hat and use a high factor sun protection cream when exposed to the sun. A sunscreen lotion and lip balm can be used daily if going outside, especially on the head, neck and hands. Patients should have their skin
checked regularly for signs of malignancy and solar keratoses which can be a precursor to SCC. Basal Cell Carcinomas are also fairly common. Dermatologists can use various treatments for these lesions.4

Patients originating from regions with high prevalence of Human Herpes Virus 8 (HHV8) virus (Mediterranean, Sub-Saharan Africa) are at increased risk of Kaposi’s Sarcoma, which usually manifests as limb oedema and/or purple-black patches on the skin.

The Epstein Barr Virus (EBV) is linked to Post Transplant Lymphoproliferative Disorder which can occur early in the post-transplant period.

**Cardiovascular disease**

Cardiovascular disease is the greatest cause of mortality in renal transplant patients.5

Smoking is discouraged, especially after transplantation. Apart from the normal risk of cancer, smoking causes gradual blockage of the blood vessels, and is associated with proteinuria and reduced renal function.6 This is exacerbated by the side-effects of some immunosuppressants – hyperlipidaemia and hypertension. Reduction of cardiovascular risk can be achieved by the use of statins, ACE-Inhibitors/ARBs and aspirin and are generally recommended.7 The patient should also be encouraged to maintain a healthy lifestyle.

**Travelling:** Patients are discouraged from long-distance travel for at least the first few months after transplantation. Kidney function should be stable and risk of rejection or other complications low. Patients must be aware that they need an adequate supply of all drugs, carried in their hand luggage, know how to seek expert assistance in case of problems, and have adequate health insurance. Certain vaccinations are advised for transplant patients but are not usually given
in the first few weeks after transplantation because the high level of immunosuppression reduces their effectiveness. Immunosuppressed patients should not receive live vaccines such as: Polio, BCG, Yellow fever or Typhoid (TAB) vaccines. The following vaccines are recommended for transplant patients and are quite safe: Influenza and Pneumovax vaccine. The following vaccines may be given if necessary: Cholera, Diphtheria, Hepatitis A and B, Meningococcus and Tetanus. Malaria prophylaxis varies according to the region visited. Some anti-malarial treatment can affect the levels of immunosuppression drugs and some may require a dose reduction according to graft function.

Infections

Immunosuppression means that transplant patients are at risk of infection. Prophylaxis against Pneumocystis carinii in the form of co-trimoxazole is usually given for a few months after transplantation when immunosuppression is at a maximum.

The most common infection in the first months after transplantation is Cytomegalovirus (CMV). This can be transmitted from the transplanted kidney or reactivated from past infection in the recipient. Less commonly it can be community-acquired or transmitted via blood transfusion. Signs include fatigue, high temperature, aching joints and headaches. Less common but more serious symptoms are shortness of breath/dry cough (CMV pneumonitis) or abdominal pain (CMV gastroenteritis). 60 % of the general population have been exposed to CMV. The anti-viral drug Valganciclovir can be used as prophylaxis in those at high risk of infection (such as CMV positive donor/CMV negative recipient or CMV positive recipient having anti-thymocyte globulin) or as treatment. It is advisable to monitor recipients’ CMV replication activity (by Polymerase Chain Reaction) so that treatment can be commenced in good time.
BK virus is less common but is difficult to treat except by reduction of immunosuppression. It can cause graft dysfunction or failure. The Human Papilloma viruses are associated with warts as well as cancers of the mucous membrane and skin. Patients with previous exposure to Chicken pox (Varicella) are more susceptible to shingles, but systemic Varicella infection in an immunosuppressed patient is a life-threatening disease.

Bacterial infection of the urinary tract (UTI) can be a recurring problem, particularly in female transplant patients. If a patient maintains good hygiene, and has a normal kidney-ureter-bladder ultrasound, but has repeated UTIs, then regular antibiotic prophylaxis may be necessary.

Immunosuppressed patients are at risk of various other opportunistic infections and have a low threshold. Investigating possible infections is wise.

**Chronic Allograft Nephropathy (CAN)**

Many grafts begin to deteriorate after a period of stability, with no obvious acute cause. CAN is multi-factorial and can include both immunological and non-immunological damage. Diagnosis is made by renal biopsy. Some factors cannot be modified at this stage, such as a previous rejection (acute or sub-clinical), donor factors or previous infections. However, good blood pressure control and avoidance of CNI toxicity are vital in prolonging renal function in the long-term.

**Bone disease**

Many transplant patients suffer from bone disease, shown as a reduction in bone mineral density, either as a result of their renal history and/or steroids used in immunosuppression. In severe cases this can lead to necrosis of the head of femur. Weight bearing exercise can increase bone-density, but most patients will also benefit from calcium and vitamin D
supplementation, control of hyperparathyroidism and the use of biphosphonates in the early post-transplant period when steroid doses are high.\textsuperscript{10}

**Poorly functioning graft**

Transplant patients with poor function should have the usual measures taken to deal with their stage of chronic renal failure. For example, counselling and the possible need for access surgery, correction of calcium-phosphate imbalance and so on. Immunosuppression may contribute to anaemia in transplant patients, this should be approached in a systematic way.\textsuperscript{11}

**Conclusion**

In terms of maximising the health of the patient and the graft, Sahadevan, M and Kasiske\textsuperscript{12} list the most important things to do to in the long-term follow-up of renal transplant recipients:

- Minimise immunosuppression
- Reduce non-adherence
- Monitor renal function closely
- Accurately diagnose renal dysfunction
- Aggressively treat hyperlipidaemia and hypertension
- Encourage a healthy lifestyle
- Screen for malignancies
- Prevent infection
- Protect the bones
- Treat patients with poorly functioning grafts the same as other CKD patients

Renal transplantation continues to present old and new challenges for the transplant team. By addressing these issues, in partnership with the patient, there is great potential to improve graft and patient morbidity and mortality.
References

2. Lessan-Pezeshki, M. Pregnancy after renal transplantation: points to consider Nephrology Dialysis Transplantation 2002; 17: 703-707
7. ERA-EDTA European Best Practice Guidelines for Renal Transplantation (Part 2) Nephrology Dialysis Transplantation 2002; 17 (Suppl 4)
8. Fehr, T., Bossart, W., Wahl., Binswanger, U. Disseminated varicella infection in adult renal allograft recipients: four cases and a review of the literature Transplantation 2002;73(4):608-611
Long term care of Renal Transplant Patients
Psychosocial issues in Renal Transplantation
Learning Outcomes

- To raise awareness of the psychosocial issues of renal transplant patients
- To emphasise the importance of a patient-family centred approach throughout the transplant process from assessment to post transplantation
- To introduce the Donor perspective

Introduction

Renal transplantation is considered to be the optimal treatment choice transplantation for patients who have been diagnosed with Chronic Kidney Disease (CKD) stage 5, and hence require Renal Replacement Therapy (RRT). In comparison to the various RRT modalities it has been shown that renal transplantation is the most cost effective and best quality treatment. It provides the patients and their family members with an improved quality of life both in the physical and psychosocial domains. Successful renal transplantation gives patients a longer lifespan with reduced morbidity, hope of freedom from dialysis treatment restrictions, enhanced stamina and physical ability, improved rehabilitation options both in employment and in the family role and quality of life.1-4

For some patients, transplantation would not be appropriate due to poor general health status, co morbidities, and/or a high possibility of negative outcome from the transplant operation resulting in the patient's death. A few patients are not motivated to be transplanted because they have adjusted to the dialysis lifestyle and feel safe, are reluctant
to have surgery and face possible financial loss due to being transplanted. Additional contraindications to transplantation include: uncontrolled psychosis, nonadherence, current substance abuse, insufficient living arrangements, lack of adequate social support, and specific contraindications of the Transplant Centre.5-9

Major advances have occurred in the Transplantation field, yet it does not provide a complete cure for patients, and transplants may fail, requiring a return to dialysis.

Most donated kidneys are retrieved from suitable donors in whom death has been certified as defined by Acts of law, Regulations, Standards of Practice and parameters in each Transplantation centre country.

The growing numbers of patients on the waiting list on one hand, and the worldwide shortage of renal donors on the other hand, have become a concern for patients, families, medical teams as well as health organization and insurance companies. The existing imbalance worldwide is presented in Table 1.

Continuous efforts and programmes are being made worldwide to enlarge the number of opportunities for renal donation. “The Spanish Model” is an example of an outstanding programme representing continuous improvement in the cadaveric organ donation rate.22, 23 Additional efforts are made via Living Kidney Donor Programmes: 1. Blood related family member - such as: a parent, an adult child, a sibling, or from “emotionally related” such as a spouse, friends, and co-workers. 2. The Altruistic (Non-directed) donors – people who are unknown to the patient, yet wish to anonymously help someone in need of a kidney transplant. 3. The Paired Organ Exchange programme, 4. Transplant Tourism and Organ trafficking.

Donation issues are addressed in a separate section of this chapter.
Number of patients on dialysis in comparison to renal waiting list, Cadaver and living donors in various countries for 2007

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<th>Country</th>
<th>No. of Patients on Dialysis</th>
<th>No. of Patients on Dialysis per million</th>
<th>No. of renal Patients on the Active waiting list</th>
<th>No. of cadaveric renal TX.</th>
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<td>Transplant Deaths</td>
<td>Rejection Rates</td>
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Sources:
Jitka Panicirova EDTNA/ERCA President • Maria Cruz Casal /Executive Committee
Key members: Martha Girak/Austria • Marianna Eleftheroudi/Greece • Susan Rogers/Netherlands • Carmen Reiher/Germany
Psychosocial issues

The psychosocial aspects of patients diagnosed with CKD stage 5 have been dealt extensively elsewhere, and are beyond the scope of this chapter.24, 25

This chapter presents the general psychosocial issues of renal patients ranging from the candidacy for renal donation, throughout the transplantation process, up to the post transplant period.

The importance of the psychosocial aspect lies in the provision of:

- Psychosocial data as part of the transplant team’s evaluation of suitability for transplantation. It is prepared by a social worker, psychologist or counselor, where required.
- Psychosocial counselling services and or social interventions.
- Referrals to additional services such as: Mental Health, Vocational rehabilitation, Alcohol and substance abuse rehabilitation, support groups, financial resources etc.

The main psychosocial factors

**Demographic data:** age, marital situation, employment status, adequacy of housing, level of education ethnic/ cultural background, legal guardian.

**Economic status:** sources of income, health and insurance coverage, eligibility for state benefits and entitlements.

**Cognitive status:** perception of CKD and its implications, the capability to understand the transplant process and to provide informed consent. Cognitive status is sometimes complicated due to various impairments such as mental retardation, prior neurologic insult etc.
Family, Social and Support systems: marital situation (or significant other relationship), number of children, quality of nuclear family relationship, available and/or additional support from significant others such as: extended family members, friends, neighbours, spirituality and religion, support groups in the community, Internet based support groups. Psychosocial status of the primary carer is significant.

Quality of life: functional status including ability to perform activities of daily living, personal care, assistance device(s), presence of physical impairments: vision, hearing and speech.

Patient’s life goals, interests, and patient’s global life satisfaction.

Adherence/compliance History and current status: adherence on dialysis and to previous medical history. For dialysis regimen: fluid and food restrictions, medication, attendance at medical appointments and treatment, coping with changes in the medical regimen, behavioural and emotional reactions to CKD detection and upon starting dialysis.

Mental Health History and current status: current and past mental health history may need to be evaluated by a psychiatrist.

Substance Use History and current status: past and current behaviour, history of relapses and availability of rehabilitation.


From the psychosocial perspective, transplantation creates alterations in the patient psychosocial equilibrium. It requires a period of both body adjustment as well as the psychological adaptation for the patient and the patient’s support system—mainly the family. It includes crisis and turning points, patient
motivation, willingness to change, psychosocial background etc.

In order for the transplant to be a successful one, a process of psychological adjustments is crucial. The adjustment or adaptive process, as the term implies, is not a static but a dynamic and ongoing process. It is of a complex nature and poses unique challenges for the patient and family. It combines paradoxical situations such as loss and revitalization in multiple dimensions: changes in body image, new perceptions of the self, hope and setting new life-style goals.

The psychosocial issues of transplantation coincide with and follow the physical consequences of renal failure, starting with the deterioration of CKD to stage 5, throughout the transplant process commencing with assessment for suitability for transplantation. It is usually presented in 2 periods:

1. The Pre-Transplant period: this period includes 2 stages: the Evaluation for renal Transplant stage (where necessary), then once approved the Waiting stage.

2. The Post-Transplant period: this period includes: the Surgery, the Perioperative Recovery stage, the First Post Transplant year and the Long term adjustment-adaptation.

1. The Pre-Transplant period

Similar to other populations who live with chronic disease, patients diagnosed with CKD stage 5 are at risk of several types of psychological distress and clinically significant depressive and anxiety related disorders compared with the general population.

The Evaluation Stage

Psychosocial assessment goals are:

- Provision of information to maximize the probability of a successful transplant outcome.
Consideration of patient’s individual suitability for transplant candidacy.

Development of an individualized management to address special candidate needs.

For many patients the formal evaluation procedure for renal transplantation candidacy is a milestone in the exhausting road of coping with CKD. As patients start the evaluation process, both they and their family share a strong motivation to present themselves in a positive way in order to be approved.

Patient concerns are:

• Medical decision regarding approval for the waiting list.
• Fears about the risk of surgery and complications.
• If and when a suitable donor will be found.
• How it will be to live with someone else’s kidney.
• Transplant failure /rejection.
• Some family members share concerns on whether they will provide an adequate home environment and care for the patient.

All of these concerns are combined with a strong sense of hope to have a healthy future and resume to a normal life-style.

Staff Concerns are:

• Obtaining the fullest relevant data about the patient in order to provide an accurate assessment for transplantation suitability, and a successful outcome.
• Identifying special psychosocial needs as soon as possible in order to ensure that appropriate support and/or intervention will be carried out. Psychosocial special needs include: alcohol and active substance abuse, and uncontrolled psychiatric problems. An additional category is those patients who have been diagnosed as mentally handicapped. Special education is required to ensure that patients have an
The issue of whether patients should be deemed unsuitable for transplantation due to psychological and or psychosocial factors remains controversial. Moral and Ethical issues arise when transplantation is offered or denied on the basis of psychosocial and behavioural history and/or current status. Yet, it is important to bear in mind the scarce supply of available kidneys which affect the criteria for organ allocation in the public eye and in Public policy decisions.

Psychosocial assessment is required only in some Transplant Centres. The criteria for assessment may vary from one country to another or from one Transplant Centre to another.8, 9

The Waiting Stage

This stage ranges from several days up to many years. Patients may also be removed from the waiting list due to medical reasons or die.

While being on the waiting list most patients start to adapt to the importance of adherence to RRT medical recommendations and the costs of not subscribing, learn new rules regarding the optimal health style required of them on RRT and take responsibility for their health condition.

The Waiting stage is often characterized as a period of uncertainty. It is sometimes named the “dance with death” period. Happy occasions, such as holidays and weekends may become a source of black humour about the violence of events. For some of the patients and family the black humour is a form of relief, others become distressed and withdrawn or even depressed.
Patient concerns are:

- Difficulties understanding how the transplant list works.
- Maintaining optimal health status while on dialysis.
- Coping with uncertainty.

Staff concerns are:

- Maintaining the patient’s optimal health status and performing the medical tests and procedures.
- Educating the patient and family about what to expect after the transplant, including discussions about unrealistic expectations post transplantation.
- Coping with patient’s stressors regarding dialysis, the “ups and downs”, and accepting emotional support and practical assistance, when needed.
- Facilitating communication channels about patient’s concerns with family and medical teams.

Just before Transplant surgery

In most cases patients are overjoyed and excited about the invitation to the transplant surgery. Some patients and family share fears regarding the operation.

Renal staff availability and emotional support in this time is helpful and appreciated by patients and family, as non-scheduled dialysis is sometimes being done at short notice and or at unusual hours as part of preparations for the transplant surgery.

2. The Post-Transplant period

Significant physical and emotional transitions characterize the post Transplant period for the patient and the family.
Surgery and the Perioperative recovery stage

Most of the recipients and families report high levels of optimism during the first several weeks after the transplant surgery. They share tremendous appreciation and gratitude to the donor and/or to the donor’s family, desire to know details about the donor and to communicate with his family, appreciation for the medical teams involved in their care: (the staff on the dialysis centre, the transplantation team), hope and a sense of purpose. In more Transplantation than a few cases expression of grief, and feelings of guilt about the death of the individual whose kidneys were donated have been expressed.

Recipient concerns are:

- Whether the “new kidney will work”: acute rejection, delayed graft function, infections, and acute medication side effects.
- Surgical complications and how much time is needed for recovery.
- Management of the new post transplant regimen including: multiple medications, exercise and dietary prescriptions, regular follow-up, laboratory tests and the new lifestyle restrictions.
- Getting to know new staff in the Post Transplant medical team.
- In the case of living donations it was found that recipients expressed fears and concerns regarding that they can never live up to the worthiness of the donation, and fears for the living donor’s comfort and health.10

Staff concerns are:

- Overcoming the patient’s difficulty in focussing. Patients and family are sometimes so overjoyed by the transplant; they may be less focused on absorbing new information about self-management and the importance of adhering to the new regimen.
For patients who have exhibited emotional and or behavioral difficulties during their hospital admission, it can be useful to consider a reassessment of the psychiatric status, in order to determine the need for mental health counselling or, other psychosocial support services.26

The First Post-Transplant year

The First year is best characterized as a period of readjustment and rehabilitation, with gradual improvement in all domains of quality of life: physical, emotional and social.

Recipient concerns are:

- Graft rejection.
- Learning and implementing the new lifestyle required of them and adjusting to the emotional “highs and lows” that sometimes occur.
- Psychosocial adaption process: to shift from the “sick role” - a dependant individual as a patient - to an active role, for example, as a provider, or to be more involved in family life. These shifts are not always realistic and may be a source of frustration and tension in the family relationship.
- Pre-transplant marital tensions, which existed during dialysis, may surface. A patient may feel physically stronger and vital, expect to return to the previous physical intimacy with partner, yet the partner, while relieved about the successful transplant, may be reluctant to resume to physical intimacy.
- Unrealistic expectations that the recipient will behave as if they are “completely cured,” and pose demands that are beyond the recipient’s capacity, for example to earn more money.

Rehabilitation and Vocational Rehabilitation

Patients who were working prior to transplantation usually return to work after recovering from the surgery. For patients
who became disabled before receiving a transplant, and have been out of the workforce for a couple of years, vocational rehabilitation services will be required so they can re-enter the workforce. It is important to know that some patients might lose insurance and social benefits because they have been transplanted.

Depression

A successful renal transplant is an achievement and a cause for celebration renal for the recipients, family and the medical team. Yet, to the surprise of recipients and the medical team “paradoxical” behaviours and reactions have been detected after a successful transplant such as non compliance, resulting even in graft rejection and signs of depression.

Approximately 50%-80% of transplant patients show heightened levels of depression, and over 30% have increased levels of anxiety compared to standard norms. Renal transplant candidates also report heightened levels of emotional stress over the first year and a worsening of compliance in most areas. The emotional distress is more frequent during the first post transplant year then during later years.29-31

According to Ferztiger 32 depression among renal recipients could be understood by the failure of some recipients to grieve over the loss of the sick organ and to express the feelings associated such as sadness. This may be expressing itself in a number of pathological or self destructive ways. Usually everyone around the recipient expects him to be very happy, however, he may be still experiencing a sense of loss or closeness to death. The recipients probably see themselves as crazy for experiencing this kind of sadness when they knew they should be happy. This type of unsanctioned grief can wreak havoc with transplant recipients. They have almost no way to understand or to explain such overwhelming feelings. When the psychological pressure created by this type of inner
chaos is added to the psychological stress to adjusting to a fairly radical change in life style, the combination can be daunting.

As the body must be aided in providing a suitable host environment for the new organ, so must the mind be aided in providing a healthy environment.

**Long term Adjustment- Adaptation**

Recipients who have gone through a successful physical recovery process share feelings of happiness about freedom from the dialysis treatment and improved quality of life. They express strong motivations to volunteer to educate others by acting as advocates for organ donations.8, 26

**Recipient Concerns are:**

- Chronic Graft rejection.
- Implications of the long term medication regimen.
- Financial issues: costs of medications (where demanded) and continuing healthcare expenses.

**Staff concerns are:**

- Chronic Graft rejection.
- Maintaining regular contact with patients and family.26

**Loss of graft and return to dialysis**

Graft loss causes tremendous emotional turmoil for the patient and family. Though it may happen slowly and gradually, it is a source of major disappointment and frustration to the patient. The various stressors associated in this situation are: the loss of the favoured form of treatment, losing an object of attachment, guilt at having wasted the donated kidney, guilt and shame at failing the expectations of others and sense of control.33
Renal Transplantation: A Guide to Clinical Practice

The family support system

Like in every discussion of coping with a chronic disease the availability of family support is a crucial component. So is the case for every patient diagnosed with CKD stage 5, throughout the transplant process ranging from evaluation of suitability up to the Post-Transplant period.

The Systems-Illness Model developed by Rolland provides a theoretical foundation that addresses the family efforts to cope with the various stages of the illness and levels of uncertainties attached to it, while sustaining hope. The Systems-Illness Model provides the concepts of family life: belief system and cohesion - expectations, adaptability - adjustment and communication.34

The Pre-Transplant period

The majority of the family share worries about the medical procedures, possible complications and risks including death. These feelings are shared in combination with a strong sense of hope for their family member to transplanted and relieved from the strains of the dialysis treatment. Financial considerations and insurance benefits are also a source of concern and anxiety.

The Post-Transplant period

After the patient has become a stable transplant recipient, some family members have experienced difficulties adjusting to possible role change. For example: the recipient has much more spare time and energy to return to outside activities, yet the family is still engaging in old medical routines and limitations, or the recipient and partner have different expectations about their intimate life.

Note each recipient is coping in a unique way with the process of transplantation and every family has its own individual dynamics and communication system. Cultural components are important to remember and the way they reflect on family cohesion and belief systems.
Patients who survived longer post transplantation had more social support, were more cooperative with medical care pre-transplant and exhibited less dependency behaviour. 26, 35

**Sexuality, Physical Intimacy and Fertility**

For most people sexuality and physical intimacy are considered a healthy positive aspect in their adult lives, yet for most medical care teams discussing it with patients and partners seems frightening and not easily carried out. Concerns regarding age bias, limited staff education, cultural diversity and perception of intrusion to patient’s personal life are found. CKD like any other chronic disease often disrupts some parts human sexual response, but rarely does it disrupt it entirely. Many patients retain functioning in at least one of the major phases: desire, excitement or orgasm. Patients who have enjoyed sexuality and physical intimacy as part of their relationship often express interest to resume it especially after a successful transplant. 36

**The Pre-Transplant period**

It is most likely that patient's sexual activity will be declining in the time leading up to the diagnosis of CKD 5. Many patients share the feelings that they are no longer sexually attractive because of: disfiguring of their body, changing colour of skin and nails, and body odour smell. Sexual problems and dysfunction are common among patients diagnosed with CKD stage 5. For the **Male** patients the most frequently reported symptoms include: decreased libido, difficulty with sexual arousal, erectile dysfunction, premature or delayed ejaculation, difficulty achieving orgasms and infertility. 28, 36

For **Female** patients menstrual irregularity and infertility are found. Additional symptoms include: reduced libido, difficulty with sexual arousal, lack of vaginal lubrication, pain during intercourse and difficulty achieving orgasms. By the time women reach CKD stage 5, most are amenorrhoeic and pregnancies are rare. 28, 36
The Post-transplant period

For Male Transplant patients it is reported that about two-thirds observe improved libido and a return of sexual function to predialysis levels. In some patients, there is no improvement, and occasionally sexual function deteriorates. Fertility improves in half of patients and family planning must be considered.

For Female patients it is reported that within a year of successful transplantation, menstrual functioning and ovulation typically return. All women of childbearing years should be counselled concerning the possible risks of pregnancy after renal transplantation.

Psychosocial considerations include genetic counselling to be provided for those with hereditary renal disease.

Pregnancy

Some women diagnosed with CKD seek transplantation in the knowledge that a well functioning graft will give them their only chance for natural motherhood. It has been estimated that 2% of women of childbearing age conceive after transplantation.

The prevalence of normal sexual functioning among transplanted patients has been reported to be 50-55%; mild to severe problems with predictors such as older age and lower patient perception of physical health and well being has been found for the other recipients.

It is important to remember that sexual functioning is just one aspect of the patient-partner relationship. The difficulties described above may also be symptomatic of tensions in the marital relationship which pre-date CKD and transplantation.

Financial and Economical considerations

For most patients and family the financial implications of RRT are a source of concern and stress to young or old, male or female, providers as well as retired. Patient income, insurance
and state benefit and entitlements and benefits are the components to be considered when addressing the issue of financial consideration.

The Pre-Transplant period
Patient financial concerns lie in how the medical expenses associated with the RRT treatment will affect their household budget: medications, special diet, transportation to and from the medical setting and loss of time due to medical tests. Eligibility for State entitlements and benefits should be sought to maintain the family’s standard of living.

For patients at working age concerns lie whether their source of income will be reduced or their employment status changed due to physical limitations. Insurance coverage may be changed as result of being on RRT.

The Post-Transplant period
Common concerns are divided into 2 main categories: the short and the long term. The first include paying for the transplant surgery (where necessary), living expenses while out of work after the surgery and recovery, and nonmedical expenses such as travel to and from medical settings and accommodation expenses near the Transplant centre. The long term concerns include: paying for the various required medications (where obliged), and the risk of losing State entitlements and insurance coverage or both post transplant.

Vocational Rehabilitation
Employment provides not just income, but also socialization, self esteem, and financial security and in some cases insurance coverage.

For patients who were able to have a living donor transplant before they became disabled, it easier for them to remain in their roles at work.
For patients who become disabled on dialysis before receiving transplant, they may need vocational rehabilitation services so that they can re-enter the workforce.

Although many transplant recipients are interested in vocational rehabilitation and employment, they may be fearful of losing State entitlements and or benefits. 8,39

**Paediatric Transplantation**

Children diagnosed with CKD require one of the RRT modalities. They too have to adhere to the strict regimen of dialysis care: medications, food and fluid intake. In considering the psychosocial aspects of children on dialysis it is vital to include physical growth, psychological development, family background and structure, parent-child relationship, siblings, availability of extended family support, school attendance, socialization possibilities, age appropriate emotional maturation, availability of community services and rehabilitation.41

It is recommended that all children diagnosed with CKD should be on the waiting list for transplantation, unless contraindicated. Children are usually prioritized on the waiting list.

**The admission for Transplant surgery**

Children attending dialysis treatments are sometimes provided with fewer opportunities to socialize with their peers, hence lack socialization skills. The period of isolation required at the Transplantation ward to prevent infections creates a further sense of isolation and may impair development of social skills.

**The First Post-Transplant year**

It is reported that within a year of successful transplantation the majority of transplanted children and their families return to their routine prior to being diagnosed with renal failure. More
than 90% of children attend school, and less than 10% are not involved in any age-appropriate program.40

Staff and parent’s concerns

Adherence issues: a major concern for staff and parents is maintaining the adherence to the medical regimen in the post Transplant period.40 It is estimated that about a half of transplanted children demonstrate significant noncompliance behaviours. In adolescents this rate is up to 60%.40

Noncompliance behaviour varies from partial to complete nonadherence. Partial compliance includes occasional to persistent missed doses of medications. It is most commonly the result of forgetfulness, misunderstanding of a dose change or modification, presence of events that lead to the belief that medications are not helping and a power struggle in the case of adolescence. In children, complete noncompliance is often the result of underlying emotional or family stress. 40

Unrealistic expectations: parents, or extended family members expectation that the transplanted child will be completely healthy after transplantation is met with a different reality, causing sadness among parents and sometimes signs of depression.

Strain and tension in the family system: Due to the tremendous amount of attention given to the patient child, tensions among siblings may rise. Another source of tension may come from differences of attitudes between the parents as to how the transplanted child should be treated: more or less protected, how much is the child responsible for managing his medications regimen etc.

With pre-existing difficulties these situations may cause conflicts and additional pressures in the family.
Long term Adjustment- Adaptation

A three year follow up study found that 90% of children are in appropriate school or job placement. Surveys of 10 years of paediatric renal transplant survivors report that most patients consider their health to be good, engage in appropriate social, educational and social activities, and experience very good or excellent quality of life.

Financial Considerations

Short term considerations includes loss of income while the child is hospitalized or needs to be escorted to medical check-ups, extra child care payments for other children at home, paying for transplant surgery (where necessary), living expenses after the surgery and recovery time, nonmedical expenses such as travel from and housing near, the Transplant Centre. Long term issues include paying for the various medications and possible loss of state benefits and entitlements.

The Living Donor

The act of living renal donation is an act of human generosity and altruism. When appropriate considerations are given to donor safety alongside medical and psychosocial considerations, it can be a source of gratification for all the individuals involved.

The living donation process involves a detailed physical and psychosocial investigation, surgery and a life thereafter with a single kidney.

Once the possibility of living donation has been raised, the following issues must be addressed:

1. Donor safety: providing the donor with the best possible environment for making a voluntary and informed decision.
2. Option to withdraw: donor’s option to withdraw from the process should be respected at any stage and the reasons should remain confidential.

3. Informed consent: the need to provide an informed consent should be explained to the potential donor and discussions should include:
   a) Information about the nature of the risks of renal donation: the extent and limits of potential risks to the donor.
   b) The Acts of law and Regulations regarding living donation according to the national and local Transplant Centre.

4. Financial considerations: providing information about leave of absence from work, possible additional loss of earnings and expenses as part of the assessment process. Concerns may be raised about the validity of pre-existing health and life insurance policies during the immediate perioperative period and the availability of new policies following donation.

5. Living donor reimbursement of expenses and loss of earnings varies from country to country.

The psychosocial assessment of potential donors must focus wholly on the needs and issues relevant to the donor’s well being. It should be carried out in a confidential relationship, while maintaining good communication with the prospective donor.

Psychological stressors in potential donors should be identified at an early stage in the evaluation to ensure appropriate support and/or intervention, up to and including referral to a mental health professional if necessary. Access to specialist psychiatric/psychological services should be available for donors who need to be referred for consultation. Issues related to the decision-making process and previous psychological problems should be explored, as should the
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donor’s relationship with the recipient and within the context of the wider family.

Living renal donation is associated with generally positive donor and donor-recipient relationship psychological and psychiatric outcomes. Psychological problems reported after renal donation are infrequent and most donors share increased self-esteem, whilst donor and recipient relationships are enhanced. The majority of donors express no regrets after donation.10

Family Living Donation

The possibility of living donation from a family member poses sensitive challenges to both the potential donor and the patient. Issues in family life such as cohesion and belief systems are being tested, resulting sometimes favourably and sometimes in major disappointments and crisis. Societal attitudes, along with the pre-donation relationship with the recipient, affect living donors’ expectations and motives.

Sibling decision-making is considered one of the most complex areas. Motivational factors such as altruism, manipulation of familial relationships, coercion and covert pressure are reported. Donor advocacy is essential to address these issues as robustly as possible.10, 41

Tensions may arise, usually around the gift exchange elements of the donation. Recipients suffer psychological distress from feelings of indebtedness, which they can never repay, and donors exhibit proprietary interest in the health, work, and private life of the recipient that can cause damaged relationships.10
The unsuitable donor

These are individuals who started the donor evaluation process, but do not donate for various reasons. If this is due to potential donor’s health risks, it is essential that appropriate arrangements be made for any necessary further investigations and management. If further emotional reactions include excessive self blame, further counselling is required.

Ethical dilemmas in Renal Transplantation

Since the first human renal transplant in 1954, followed by medical advances in the Transplantation arena, most countries have engaged in public discussions about the ethics of organ transplantation on the following major issues:

- The significance of removing organs from both living and deceased donors lies in the human context. This raises the issues of body integrity and “do no harm”. The response to that is the value of autonomy of the donor and the requirement to provide informed consent in living donations.

- If the answer to transplantation is positive, what are the criteria for determining when death occurs and thus when the donor organs might be procured.

- Whose wishes should ultimately be respected on whether organs are used or not used? What kind of consent is required, and in case of family objection who finally decides?

- The conflicting values of organ procurement and allocation policies, or what are the recommended criteria for equity of access to donor organs for all patients, or for only those that adhere to the medical regimen, and how priority for allocation is calculated.
Good Practice

General

1. Learn and be updated about Dialysis and Transplant Centre policies, rules, regulations, expectations, contact details and availability of services regarding transplant issues.
2. Be aware of the patient’s support system resources, as well as their needs, strength and sensitivities.
3. Gain data and understanding about the patient’s method of communication with others close to him to determine whether the patient will ask for assistance and support when appropriate and needed.
4. Liaise with the Social worker/Counsellor in providing the patient and family with information regarding possible changes of state benefits, referrals to support groups and mentor groups etc.

The Pre-Transplant period

1. Conduct the evaluation in a confidential and reassuring atmosphere in order to put the patient at relative ease.
2. Encourage patients to provide full medical and psychological data. This can be facilitated by promising confidentiality (if possible). Encourage honesty as the best policy.
3. Support patients to maintain optimal health condition and adherence to the routine medical lab tests necessary for the waiting list.
4. In accordance with the Transplant Centre policy:
   a. Provide access to transplant education including post transplant side effects. Be aware of special education needs such as: language barriers, illiteracy etc.
   b. Remind patients and their families they have not been forgotten, and are still on the waiting list.
The Post-Transplant period

1. Educate patients and family about the Post-Transplant medical regimen: multiple medications, exercise and dietary prescriptions, regular follow-up and lab tests and the new lifestyle restrictions. This could be done with written materials, face-to-face didactic presentation, videos, computer based programs, and discussion. Be aware of any special educational needs such as: language barriers, audio and visual impairments, illiteracy etc.

2. Balance undue optimism by regular reminders about what is realistic to expect regarding physical recovery, graft function, and emotional status during the immediate perioperative period.

3. Patients and families must understand that the Transplant team will continue to be the most important source of information regarding medical issues concerning the transplant, general physical and mental health concerns.

4. Encourage patients to contact other transplant recipients. This has been found be useful from psychosocial and psychological perspectives. Support groups could be used for this.

5. For patients who have exhibited extreme emotional reactions, it can be useful to consider a reassessment of the psychiatric status, in order to determine the need for mental health counselling or, other psychosocial support services.

Sexuality

1. Convey the message that sexuality and physical intimacy are natural and normal aspects of the patient’s life, starting at the initial contact with the patient and his relevant partner.

2. Handle the conversation in a safe environment regarding the patient/partner perspective.

3. Consider referring the patient for further medical consultation or sex therapy consultant.
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Paediatric:

1. Multi Disciplinary Team work is necessary when treating a CKD patient child on the waiting list and following transplantation.

2. The Multi Disciplinary Team should include a child psychologist, social worker and psychiatrist. Psychosocial follow up is necessary if the transplanted child is to be rehabilitated both medically and psychosocially. The best outcome will be achieved when there is close coordination between the medical and psychosocial team.

3. Provide emotional support for the family coping with the special needs of the CKD patient child.

4. Frequent follow-up visits decreases noncompliant behaviours.

5. Coordinated preparation for school re-entry after transplant is required for the transplanted child, family, school personal and classmates.

The Living Donor

1. In order to promote donor safety, independence between the clinical teams responsible for the evaluation (potential recipient and donor) is recommended.

2. Allow the prospective donor to address their concerns to appropriate medical care professionals, provide referrals to psychological or psychiatric counselling for additional emotional support when needed.

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Psychosocial issues in Renal Transplantation

References


11. European Transplant Coordinators Organization (ETCO) Homepage: www.etco.org [26/12/08]

12. European Society for organ Transplantation (ESOT) Homepage: www.esot.org [26/12/08].

13. NHS/Blood and Transplant Homepage: www.uktransplant.org.uk [26/12/08].

Renal Transplantation: A Guide to Clinical Practice

15. US transplant Scientific Registry of Transplant Recipients Homepage: www.ustransplant.org [26/12/08].
17. Medical Information Network Society Homepage:www.medi-net.or.jp [26/12/08].
19. Deutche Stifung Organtransplantation(dso) Homepage: www.dso.de [26/12/08].


Renal Transplantation in Children
Learning Outcomes

- To gain knowledge and understanding of clinical outcomes, medical and nursing care in paediatric renal transplantation
- To be able to describe specifically paediatric renal transplantation in comparison to adult care

Introduction

Clinical research in paediatric nephrology is continuing to expand dramatically, with an increased understanding of renal development and the molecular and cytogenetic aetiology of diseases. However, the challenges for the future are to increase worldwide evidence-based practice.¹ The scientific community has recognised that indications, procedures, complications, pharmacological prescription and transplant outcomes are different in children; for this reason now there are databases dedicated specifically to child kidney transplants.

Kidney transplantation is the treatment of choice for children with end-stage renal disease (ESRD). Children with a well functioning graft have a better quality of life, improved cognitive development and near normal growth in comparison with dialysis.²

The only contraindication to kidney transplant is a pre-existing metastatic tumour, whilst there is no contraindication in urological diseases correlated to complex malformations with bladder dysfunctions. Improvements in surgical technique in recent years have achieved good results with these pathologies,
and consequently the functionality of transplanted kidneys in children with enlarged bladders, or with urinary diversions or reconstructed urethras, can be compared to those children without such complications. With the introduction of new pharmaceuticals to kidney transplant therapy, we have seen exceptional improvements in transplant results, even in children.

Among living donors recipients, patient survival rates were 98.2%, 97.4% and 95.6% at one, three and five years post-transplantation. Among deceased donors patient survival rates were 97.1%, 96% and 92% at one, three and five years post-transplantation. Recipient age has been identified as an important determinant of outcome. Among living donor recipients, adolescents have the worst five-year graft survival rates. Among deceased donor recipients, excluding the immediate post-operative period, where infants had an increased incidence of graft loss secondary to technical complications, adolescents have the worst long-term graft survival. Adolescents have the highest rates of late initial rejection. The causes of death are infections (28.9%), cardiopulmonary complications (15.7%) and malignancy (11%).

Recipient and donor

There is no age limit for kidney transplantation in children, only a weight limit. Weight increase in nephropathic children is slowed by a decreased appetite correlated with high dosages of BUN. Low weight is considered unadvisable when the child’s weight is less then 5 or 6 kg at one year old. The recommended weight is about 8 kg, a weight reached at around two years of age. Doctors take into account also the risks for patient’s life and the durability of the transplanted kidney; risk is very high during the first months of life. When the risk to the patient’s life is severe, the transplant is carried out also on children with low weight, but when the child has a
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desirable weight, a dramatically reduced number of surgical and medical complications has been noted.

Surgical risks for the survival of the transplanted organ are correlated to vascular calibres and the physical space available for the implant; these risks are progressively reduced with an increase in the child’s weight and body mass. For this reason, the new kidney can be implanted in the peritoneal cavity. Even when the donor is much larger than the recipient the same surgical techniques need to be adopted.

It is usually considered that the optimum ratio is that of recipient’s weight/donor’s weight (DR) of 1 to 3 or 1 to 4. For paediatric recipients, the ratio D/R is a valuable adjunct when determining long-term graft survival. A recent study concludes that paediatric donor kidneys should be given preferentially to paediatric recipients due to better long term function. The only contraindication is related to the donor’s age, that must be at least two years older, to avoid an immature nephron and a diminished capacity of the transplanted kidney to adapt to the pressure rates of the recipient.

Worldwide a potential recipient can be included in a transplant list only if already about to commence, or is undergoing, renal replacement therapy (haemodialysis or peritoneal dialysis). Mostly, the waiting list allocates organs taken from heart beating deceased donors. Due to the shortage of deceased donors, or because of the wish of the family, sometimes the transplant is carried out with an organ donated by the parents themselves or by close relatives, including adult brothers or sisters. It is routine for tests to search for potential histological or pathological incompatibilities of the donor that may impede a donation.

Vaccinations are recommended in these patients as in healthy children, and administered during the first two years, in accordance with the national plan. It means that it’s usual to transplant after that vaccinations are already carried out. If the
transplant had been carried out before, live vaccines, such as rubella, measles, mumps, chickenpox and BCG are banned by reason of their immunosuppression that renders defences void, especially during the first period after transplant.

Pre-operative preparation

The selected patient is contacted by the surgical centre and he/she should arrive as soon as possible. At the patient’s arrival in the unit, doctors and nurses establish the timing necessary to prepare for the intervention. Feelings of anxiety and fear are the usual reaction of family members, mixed with hope for the possible resolution of the child’s illness. Health personnel should manage and support the patient and the family.

After health examination to assess the patient’s clinical condition, a nurse inserts a blood catheter to obtain blood samples for biochemistry and microbiologic tests and for administering anti-rejection drugs shortly before the surgical operation. An ECG and chest x-ray is performed for anaesthetic evaluation, and also dialysis treatment, bowel preparation, antiseptic shower, and renewal of peritoneal catheter and eventual central line medication.

Admission of the child to the operating theatre

The time between the entrance into the operating theatre and the start of anaesthesia is usually short, but very intense. The patient and the family present emotions such as the fear of the intervention, and tension caused by the uncertainty over the transplant’s final outcome. The nurse has to be aware of these feelings, reassure the child and give support to the parents.

The child is usually used to the hospital environment from his earliest years, and he/she knows well all the health care workers and procedures practiced in hospital. These patients are attentive observers and they monitor whether procedures
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have been carried out correctly. The nurse’s approach should be skilled and professional.

The smallest children need their attachment figure by their side at all times. For this reason, it’s a common rule that one parent can stay near the child until the first anaesthetic is given. In some centres, the parent is dressed with a gown, shoes and mask, and he/she enters into the procedure room in the operating department. When the child sleeps and he/she is taken to the operating theatre, the parent can go to the waiting room. Before the anaesthesia, toys are a useful distraction. For older children it is vital to establish a relationship of trust, with active listening and good communication.

Surgical technique

Generally the kidney is transplanted as in the adult. The surgeon produces a “hockey stick” skin incision, from the hypogastrium to the inguinal region, rising up to the hip. It can reach laterally to the ribs and edge towards the rectus abdominal muscles. After accessing the retroperitoneal space, the external and common iliac arteries are isolated from the aortic bifurcation. The sectioning of the veins is carried out (nowadays the time taken to complete this part is strongly reduced using high-power ultrasonic dissection). The new kidney is carried to the operating area, wrapped in a netting, and is kept cold using a cold saline solution.

After having positioned a vessel clamp on the external or common iliac artery, a small venous excision is carried out. The renal vein/vessel is anastomosed to the common iliac or external vessel by non-absorbable suture. By analogy, an anastomosis follows for the renal artery and for the selected iliac artery. Vessels are irrigated with saline solution and heparin before closing the anastomosis. The netting is removed as well as the vascular clamps and haemostasis controlled using hot cotton swabs. During the ureter-bladder anastomosis, the
vascular anastomoses are protected by cotton pads dipped in 1% lidocaine. The implant of the ureter is carried out by placing traction stitches on the front wall of the selected portion of the bladder; then a small incision is made into the muscle and bladder wall mucosa. After having tunnelled the ureter, the anastomosis is completed and a ureteral catheter is inserted. The dilators are removed after having checked the haemostasis and a closed wound drain is located (calibre should be adequate to the age and weight).

At the end, the surgeon sutures the abdominal wall layer by layer. In very small children, the kidney, after the shifting of the right colon to create a space, could be implanted with a lateral anastomosis to the inferior vena cava and the distal aorta. In general, native nephrectomy is not performed. This procedure is reserved only to infected kidneys, or organs enlarged by polycystic kidney disease, for the high risk of hypertension or kidney cancer.

The donor kidney, during surgical preparation, is perfused with cold liquid (Lactated Ringer solution), and inspected for the number of vessels and the possible presence of lesions, before the removal of superfluous tissues (such as fat, adrenal gland). The presence of vascular, ureteral and bladder abnormalities and their multiple or complex repair does not represent a theoretical disadvantage even in paediatric patients.6

The organ implant has to be carried out within the first 24 hours after removal, and during the surgical procedure it is important to keep the little patient’s temperature under control, because the intensive use of cold solutions can alter the homeostasis.

**Postoperative nursing care**

After the surgery, the patient is admitted for few days to the paediatric intensive care unit and then is treated in paediatric surgical unit. Nurses monitor frequently vital signs (body temperature, pulse rate, respiration rate and blood pressure),
pain intensity and fluid volume balance. They collect blood samples for evaluating renal function, control patency of the drains, dressing and surgical wound, and ureteral catheter and bladder catheter functioning. Pharmacological treatments are administered intravenously and by mouth. Vital signs are initially monitored every 15-30 minutes and then every four hours.

A small child cannot understand the importance of nursing procedures, such as the monitoring of vital signs or the renewal of a medication, so sometimes the child doesn’t accept the contact with health care workers. There are often present fears and suspicion, in particular during treatments that may have been unpleasant in the past. Paediatric nurses try to make procedures less traumatic using games and distractions with the younger patients and compromises with the older children. Nursing interventions are concentrated into a short time, so the day in the surgical unit can pass as easily as possible (for example, personal hygiene and vital signs are monitored at the same time).

Pharmacological treatment

The immunosuppressive drugs used in renal transplantation have evolved during the past two decades. Data from several trials have been used to provide evidence-based guidelines on immunosuppressive treatment for renal transplantation in children and adolescents. This treatment is vital for avoiding kidney rejection. Paediatric nurses are involved in dosage preparation and family education.

Drugs available are not always produced with paediatric dosages and some patients are not capable of swallowing pills, entire tablets or even a portion. If the hospital pharmacy does not prepare paediatric doses, tablets or pills have to be dissolved and a dosage calculation is required (this topic is included in family’s education). It should be considered that
part of the dosage remains in the container and adhered to the walls of the syringe used to draw out the solution. Some drugs need also to be handled under an extraction hood; it means that they should be prepared in hospital.

**Non adherence to immunosuppressive regimen**

The literature on therapeutic adherence includes many studies, but there are few articles about paediatric patients, and risk factors in this population are not well known. It seems that compliance with medications is affected mainly by social class and age. When the problem is severe and persistent, nurses should consider the use of counselling and more extensive education programs. Education should be tailored to the age, and the whole family is involved in therapy management. It is necessary to train the caregiver about drugs, dosages and way of administrations. In some cases, diet is correlated to drugs administration (e.g. tacrolimus requires fasting before and after administration). If the family is incapable of managing these tasks, the intervention of home care nurses is required.

Adolescence represents a critical phase. After the transplant, there are many changes in the style of life correlated to physical aspects, drugs and dietary restrictions. Young patients can experiment and have difficulties with friends and at school. Non adherence is particularly problematic in adolescent females, where the side effects of immunosuppressants, for example the moon face and weight gain associated with high dose corticosteroids and the hirsutism associated with cyclosporin, may cause problems with body image. Some girls become responsible and autonomous in therapy management, they accept routine tests and medical controls, and they also maintain the recommended lifestyle (the fear of a return to dialysis has a high impact). Other patients, responsible at the beginning, after some months, when they have acquired a self-confidence and physical well-being, decide not to assume
responsibility for the therapy. This choice can mean kidney loss and return to dialysis.

Psychological aspects

Quality of life, social integration and psychological topics are important issues in paediatric kidney transplantation, much as in all chronic diseases. For many children, the kidney transplant represents a ‘liberation’ from restrictions imposed by dialysis and frequent relationship with health care workers. Waiting for the kidney, the patients can present doubts, anxiety and anguish. These feelings are present also during the post-operative phase, where frequently they manifest fear of infection, trepidation for a rejection, loss of hope and preoccupation with collateral effects and complications. The patient’s anxieties seem to be reflected within the entire family, even if sometimes it’s not clearly expressed. The psychological sufferance experienced can influence clinical outcomes and therefore must be handled in a competent and adequate manner.

Psychological care is adapted to each stage of the transplant. Pre-transplant, the admission to the waiting list provokes disquiet, insecurity, ambivalence, fear, expectations, and frustrations, such that in certain patients, when these feelings are combined with a high level of psychological suffering can give rise to consequences that can lead to a refusal of the transplant itself, or to the renouncement by the parent to the donation of his/her own kidney. In the post-operative stage, the patient feels that he/she has never been so close to death, but he/she begins a new life integrating the transplanted kidney in the self-image.

Conclusion

Advances in surgical procedures, immunosuppressive therapy and critical care nursing are relevant in improving standard
of care and the children’s quality life. Paediatric critical care nurses must be aware of possible correlations with events that may lead to graft loss. It is necessary to support the development of general guidelines for care in paediatric renal transplantation.¹⁰
References


Bibliography


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