Expert Forum
Nephrology Meeting
Making Education Easy
October 2010

In this review:

Welcome to this review of the Annual Nephrology Meeting held in Wellington in October 2010.

The meeting was chaired by Drs Ian Dittmer, Tonya Kara, Philip Matheson and Walter van der Merwe. We have summarised the presentations made at the meeting for your information.

A discussion regarding live kidney donation

Financial assistance for live organ donors

Presented by: Dr Kelvin Lynn, Medical Director Kidney Health New Zealand

Kidney transplantation, when compared to dialysis, results in improved survival and quality-of-life for the recipients and, over time, a reduction in healthcare costs. Over the past two decades, the number of deceased kidney donors in NZ has remained unchanged and increases in transplant rates have been due to transplants from live donors. Factors that have increased living donation rates are laparoscopic donor nephrectomy and altruistic donation. Furthermore, Work and Income NZ (WINZ) financial assistance for live donors, paired kidney exchange and ABO blood group incompatible transplants have a potential influence on the rate of donation.

Whereas the deceased donor rates are low in NZ compared with similar countries, and did not rise significantly with the implementation of the donor registration programme linked to motor vehicle driver licensing in 1986, our living donation rates are high. At the end of 2008, there were 2099 people on dialysis and >350 on the deceased donor waiting list (waiting times for a deceased donor transplant average 3 to 5 years). During that year, there were 65 kidney transplants from deceased donors and 58 from live donors.

ANZDATA indicate that, in general, living-donor transplants, including those from unrelated donors, function for longer than those from matched deceased donors. The 10-year graft survival rate for current living donor kidneys is likely to be ≈80%.

Live kidney donation in NZ

The counselling and medical assessment process for living donors is managed by transplant coordinators to agreed protocols. Live kidney donors can be members of the recipient's family (including those genetically unrelated), friends or strangers (non-directed donation).

Potential non-medical barriers to live donation include the fact that the recipient needs to find their own donor, that there is a lack of knowledge in the community regarding who can be a donor, that there may be delays in the medical assessment of the donor or potential recipient, and that there may be delays in getting access to surgical and operating theatre time. Furthermore, there may be financial barriers for the donor.

NZ legislation

The Human Tissue Act 2008 is predominantly concerned with deceased donation; the Ministry of Health suggests that existing legislation and common law will cover most issues related to live organ donation. The Act is silent on financial assistance for live donors, but emphasises that transplantation is to be considered a 'health treatment' and states that trading in human tissue is generally prohibited, as is advertising for tissue donation.

International guidelines on organ donation

- The World Health Organization Guiding Principles on Human Organ Transplantation (1991) state a preference for deceased over living donors
- The 57th World Health Assembly (2004) urged member states to extend the use of living kidney donations when possible, in addition to donations from deceased donors
- The Declaration of Istanbul on Organ Trafficking and Transplant Tourism 2008 encourages each country to have a legal and professional framework to govern organ donation and transplantation activities, as well as a transparent regulatory oversight system that ensures donor and recipient safety and the enforcement of standards and prohibitions on unethical practices. The declaration also encourages the initiation or enhancement of deceased donor transplantation to minimise the burden on living donors

Financial assistance for donors

The Declaration of Istanbul states that *"Reimbursement of the documented costs incurred during the evaluation & performance of the donor procedure is part of the legitimate expense of transplantation and does not constitute a payment for organs."*

In NZ, a scheme for financial assistance for live donors, set up following lobbying from Kidney Health NZ (KHNZ), is administered by WINZ and provides payment for people who are donating a kidney (or liver) and incur a loss of income and/or childcare costs; the scheme pays $129.41 - $323.52/week for up to 12 weeks. WINZ states that "*Financial support for donors is intended to reduce financial barriers to donation, rather than to provide full compensation for loss of income or act as an incentive.*" Dr Lynn says that the scheme was not exactly what KHNZ wanted, but that it is a start.

A recent review of legislation and programmes that facilitate reimbursement for donors in 40 countries was undertaken by Sickand et al.[1] In 16 countries, reimbursement for donors was expressly legal, in 18 reimbursement occurred but the conditions were unclear, in 6 it was unspecified and in 1 it was expressly prohibited; overall, 21 countries had donor reimbursement programmes. The nature of the reimbursement was for lost income in 17 countries and for travel, accommodation, meals and childcare in 12-19 countries. In 9 countries, there were conditions on the reimbursement; 7 conditional on donor income, 2 conditional on recipient income.

In June 2010, The Financial Assistance for Live Organ Donors Bill was submitted to Parliament. The Bill is endorsed by KHNZ and the National Renal Advisory Board (NRAB). The purpose of the Bill is to provide financial assistance to people who, for altruistic reasons, donate kidney or liver tissue for transplantation purposes, by providing income assistance to those who forgo income from employment during their convalescence, by ensuring that those in receipt of certain income-tested benefits will retain their entitlement to those benefits, and by providing payment for childcare assistance. The Bill would provide an increase in the support for donors who forgo income during their convalescence to the equivalent of 80% of the donor's pre-operation earnings (the same formula applied to income support for ACC recipients) or the rate of the sickness benefit, whichever is higher.

Financial assistance for live organ donors

The following are some pros and cons that have been put forward regarding financial assistance for donors.

Pros: we have a static deceased organ donor rate with at least 350 people on the waiting list, many of whom will die while waiting for a kidney; increasing live donation is the only practical way to increase transplants; it also brings many advantages to the recipient, family, community and health system including personal, social and fiscal benefits.

Cons: potential donors are poorly informed of the risks (Dr Lynn doesn't believe this to be the case in NZ); potential donors could be coerced by the amount of financial assistance (not likely with the amount being offered in NZ); it may deflect efforts from increasing deceased donation; potential donors may be exploited; live donors must be altruistic; organ trafficking may reduce deceased organ donation.

Kidney Health New Zealand's Position

In NZ, there is strong community support for live kidney donation, and donors and recipients appear to be in favour of financial compensation for donors. In doing so, increasing transplant rates will 'reward' recipients and the community. KHNZ believes that harm to donors must be minimised, including financial hardship. A major goal for KHNZ is an increase in kidney transplant rates and they recognise that for some potential donors loss of income may be a barrier. KHNZ also supports the proposed increase in financial assistance as outlined in the Financial Assistance for Live Organ Donors Bill.

Reference:

1. Sickand M et al. Reimbursing live organ donors for incurred non-medical expenses: a global perspective on policies and programs. Am J Transplant. 2009;9(12):2825-36.

Incentives in organ donation

Morally repugnant, the lesser of two evils or ethically sound?

Presented by: Professor Stephen Munn, New Zealand Liver Transplant Unit, Auckland City Hospital

Professor Munn will attend a meeting in Manila in November 2010, where the possibility of incentivising organ donation from living and deceased donors will be explored. Subjects to be discussed include: removing disincentives, principles of a system of incentives, allocation of organs within a system of incentives; what incentives should be considered for deceased donation; addressing some of the arguments against incentives; what incentives should be considered for living donation; the Philippine experience (strengths and weaknesses); difficult questions in considering incentives.

The Istanbul Declaration makes it very clear that transplant commercialism (which targets the vulnerable), transplant tourism and organ trafficking should be prohibited. Professor Munn agrees with that statement, but does feel that work in this area is not complete. He points out that often, living organ donors do not seek or need reimbursement.

Reimbursement of donors in NZ

The WINZ scheme, which was put in place as a financial safety net for living donors, is increasingly being used (1/3 donors are on the scheme, but many struggle to meet their regular expense payments on the allowance). This, however, is not surprising given that many NZers only get 4 weeks annual leave and 2 weeks sick leave which may be insufficient to cover the period of recovery following organ donation. Reimbursement levels allowed and encouraged by the Istanbul Declaration would mean payments of NZ$5,000 - 10,000 for NZers who donate, which is considerably more than the WINZ allowance. In the US, donors are entitled to up to ≈US$6,000 to cover expenses, such as transport, accommodation and loss of income. In Pennsylvania, an initiative was put forward to provide a payment of US$300 to assist with funeral expenses for those families who agreed to deceased donation.

Discrepancies

Professor Munn points out that there are a number discrepancies in our thinking about the donation of non-renewable tissues. He highlights the following;

- In the US it is perfectly legal to pay human egg donors between US$5,000 - 10,000 for what is a non-renewable tissue
- It is assumed that, when done for 'love', organ donation is a noble and laudable act but, when done for money, that it is tainted and somehow akin to prostitution. This is in spite of the fact that there is a viable commercial activity associated with the act (transplantation medicine and surgery) and, indeed, dependent upon it
- There already exists a commodities market in the US, and it is about to commence here in NZ and in Australia – it is called the paired kidney exchange scheme. The value of one kidney from a living donor has been determined to have the exact same value as a kidney from another living donor. We apparently see nothing wrong with donation to a stranger when the reward is a pay-back kidney for a beloved recipient. The benefits to that recipient, as we all know, are considerable and can be measured in health metrics (quality-adjusted life years) but also in direct economic terms to the extended family of that recipient, the local hospital and the country as a whole
- The total economic value of a kidney for transplant purposes is considerable. It has been estimated that cost-neutrality, in the US, would be maintained if such a kidney had to be purchased for US$100,000. Using crude figures in NZ (post-transplant survival, on-dialysis survival, costs of dialysis) and our own transplant costings, an estimated overall economic contribution of NZ$100,000 would not be unreasonable
- The most morally repugnant aspects of selling human organs are the dual concerns of exploitation (persons coerced into taking unnecessary and poorly perceived risks for money) and the sullying of altruism

- Interestingly, we do not think it unreasonable or exploitative to encourage young people to join the army, pay them a wage and send them to a war zone where they may well perish whilst protecting others. We consider this noble and courageous even though such persons are paid, and are not infrequently from lower socioeconomic groups
- The assumption that the unpaid are altruistic, and that the paid are not, is proven to be false in many situations. Unpaid volunteers often have clear secondary motives and paid persons are perfectly capable of using the money they earn to altruistic ends

A question to vote on

Professor Munn asked attendees for feedback, by voting on their preferred choice from four options relating to reimbursement for living donors:

(1) The status quo.

(2) Better reimbursement of lost income (between 80-100% with a maximum level as per ACC practice). This might amount to NZ$5,000 - 10,000 per donor.

(3) A pilot research project (within a countries borders) using incentives that might include money, plus assistance with insurance (health and life), plus financial planning advice.

(4) Government regulated incentive scheme (fully implemented, without a pilot project) that aimed at eliminating or drastically reducing renal transplant waiting times.

The vast majority of attendees voted for option (2).

Donor outcome

Presented by Dr John Schollum, Department of Nephrology, Dunedin Hospital

Many retrospective analyses have addressed the issue of short- and long-term outcome in living kidney donors. However, many are poorly designed and biased. A recent retrospective review of outcome in 3698 living donors who had undergone nephrectomies between 1963-2007 in the US, revealed that their survival rate was similar to that of the general population.[1] GFR, BP and urine protein levels were measured in 255 donors and findings compared with data from age-matched controls from the National Health And Nutrition Examination Survey (NHANES). Among the 255 donors, the mean age at nephrectomy was 41.1 years and the mean post-transplant follow-up time was 12.2 years. Analysis revealed that the longer the time since donation the higher the GFR, and a higher GFR was associated with microalbuminuria. Eleven of the donors had developed end-stage renal disease (ESRD); all had donated to a sibling and three lost their kidney due to the same disease as their sibling. However, overall, the incidence of ESRD was lower than that for the general population (186 vs 268 per million person years).

Another recent retrospective analysis compared death rates of 80 347 live kidney donors in the US who had undergone nephrectomy between 1994 and 2009, with death rates of a matched cohort of 9364 NHANES III participants who would have been considered 'fit' enough for donor nephrectomy.[2] The median follow-up time was 6.3 years. The risk of death in the first 90 days following a live donor nephrectomy was 3.1/10 000, compared with 0.4/10 000 in the control group; the mortality rate in the first 90 days did not change over the 15-year analysis period. Risk factors for perioperative mortality included hypertension, age, smoking, male sex and black race. However, the long-term risk of death was not increased in the donor group compared with the matched cohort. These findings have been seen in many other similar analyses.

Hypertension following nephrectomy?

Most follow-up studies have demonstrated a BP increase associated with nephrectomy. One such study, undertaken in Germany, showed that in 135 kidney donors mean BP had increased significantly ($p<0.001$) from 125/79 mmHg before donation to 134/81 mmHg at evaluation (mean follow-up time 11 years; range 1-28 years).[3] The question arises as to whether such increases in BP are just age-associated changes.

A subsequent meta-analysis of 48 donor studies with control participants, from 28 countries, followed a total of 5145 normotensive donors and measured BP at least 1 year post-nephrectomy.[4] The analysis revealed that in donors, BP increases 5/4 mmHg above what is expected with aging. Another study involving 148 consecutive kidney donors at the Mayo clinic, including 24 who were hypertensive (mean BP >135/85 mmHg), revealed that while normotensive donors had no change in arterial pressures at a mean of 282 days post-nephrectomy, the hypertensive group had a significant drop in BP to normal levels with both pharmacological and non-pharmacological therapy.[5]

Cardiovascular disease

In the general population, it is well known that an increase in BP is associated with an increased risk of cardiovascular disease (CVD). A Canadian study investigating the risk of CVD and hypertension in 1278 donors (mean age at nephrectomy 41 years) and 6369 matched controls, found that after a mean follow-up of 6.2 years, there was no difference in the incidence of CV events between the groups (2 vs 2.7/1000 person years).[6] However, there was an increased incidence of hypertension in donors (29.1 vs 20.6/1000 person years).

The Caring for Australasians with Renal Impairment (CARI) guidelines suggest that hypertensive donors with a BP >140/90 should have ambulatory BP measurements or at home BP monitoring, and that an average >135/85 is a relative contraindication to donor nephrectomy.

Should we ever accept hypertensive donors?

Possibly in older individuals with isolated hypertension and with personal gain (i.e donation to spouse or child), after careful discussion regarding potential long-term risks. More long-term data is required.

Obese donors

Obese donors are on the increase, with up to 16% of Australian donors and 20-30% of US donors being obese. There is clear evidence that the risk of ESRD increases with increasing BMI, and a Spanish study involving 73 patients who were followed up a median of 13.6 years after unilateral nephrectomy, revealed that obesity (BMI >30 kg/m^2) at the time of nephrectomy was the greatest predictor for chronic kidney disease (CKD) and proteinuria.[7]

A study by Tavakol et al involving 98 kidney donors (16 obese) and matched controls from NHANES, revealed that after a mean follow-up of 10-11 years, obese subjects had a higher BP and more proteinuria than those who were non-obese; there was no difference in renal function between the two groups.[8] However, whether this increase in BP is more than you would expect in obese subjects over time is not clear. Similar findings were seen in a study from Pakistan.[9]

The CARI guidelines suggest the following regarding obese donors;

- BMI >30 kg/m^2 relative contradiction to donor nephrectomy
- BMI >30 kg/m^2 with any other vascular risk factor should be considered a contraindication to donor nephrectomy

Take-home points

- In carefully selected donors, living donation appears to be safe in the long term with a low rate of perioperative complications
- BP rises after donor nephrectomy in normotensive donors and this rise is probably greater than would be expected with age alone
- The long-term significance of such a BP rise is uncertain
- In the general population, a similar difference in BP is associated with a 10-15% higher incidence of CVD
- There is no increased incidence of CVD in the short term
- Very little data is available on hypertensive donors
- Obesity is associated with morbidity and mortality in the general population
- Higher perioperative morbidity in obese donors
- Obese donors may have a higher BP and more proteinuria than non-obese donors; whether this is due to obesity or nephrectomy is unknown

References:

1. Ibrahim HN et al. Long-term consequences of kidney donation. N Engl J Med. 2009;360(5):459-69.
2. Segev DL et al. Perioperative mortality and long-term survival following live kidney donation. JAMA 2010:303(10):959-66.
3. Gossmann J et al. Long-term consequences of live kidney donation follow-up in 93% of living kidney donors in a single transplant center. Am J Transplant. 2005;5(10):2417-24.

4. Boudville N et al. Meta-analysis: risk for hypertension in living kidney donors. Ann Intern Med. 2006;145(3):185-96.
5. Textor SC et al. Blood pressure and renal function after kidney donation from hypertensive living donors. Transplantation 2004;78(2):276-82.
6. Garg AX et al. Cardiovascular disease and hypertension risk in living kidney donors: an analysis of health administrative data in Ontario, Canada. Transplantation. 2008;86(3):399-406.
7. Praga M et al. Influence of obesity on the appearance of proteinuria and renal insufficiency after unilateral nephrectomy. Kidney Int. 2000;58(5):2111-8.
8. Tavakol MM et al. Long-term renal function and cardiovascular disease risk in obese kidney donors. Clin J Am Soc Nephrol. 2009;4(7):1230-8.
9. Rizvi SA et al. Living kidney donor follow-up in a dedicated clinic. Transplantation 2005;79(9):1247-51.

Y-TEC®: physician-implanted PD catheters – technique and audit

Presented by: Dr David Voss, Specialist Renal Physician, Middlemore Hospital, Auckland

The Y-TEC® system is a non-surgical procedure for the peritoneoscope placement of peritoneal dialysis (PD) catheters. This direct-vision procedure is being increasingly used by renal physicians and, since the beginning of 2010, the procedure has been undertaken in the procedure room of the renal ward at Middlemore Hospital, a non-sterile, but 'clean' environment. Dr Voss explained the Y-TEC® technique and presented the PD catheter audit undertaken by his group in order to obtain an early comparison of this new technique with the established surgical and radiological techniques for PD placement. Dr Voss says that his group has been relatively selective with choosing patients for this procedure, choosing thinner patients initially. However, his group is now attempting this procedure on more difficult patients.

The technique: The belt line and exit site are marked on the patient. After draping, a small amount of local anaesthetic is administered and the trocar, which has a plastic sheath around it, is inserted. The peritoneoscope is then inserted and the peritoneum visualised. The patient is then placed in the Trendelenburg position and approximately 500-1000mL of air instilled. The dilator is inserted following removal of the trocar and the stylette with the Tenckhoff catheter is then pushed straight down the tunnel to the level of the second cuff. With the aid of a cuff implanter tool, the inner cuff is driven down into the rectus muscle sheath area. Once the catheter is in place, it is flushed with 20-30 mL of saline and observed to make sure the solution runs out freely (the patient may need to be in the flat or pelvis down position). The exit tunnel is then fashioned, ideally in a downwards-facing position. The catheter is then hooked up as per any other Tenckhoff procedure and approximately 400-500 mL of solution drained in and out to make sure that catheter is patent (the solution should be relatively free from blood and free of faeces). The patient is then sutured. The whole procedure takes approximately 1 hour (40-45 minutes on a good day!).

The audit: A total of 60 PD catheters have been placed by Dr Voss' group since the beginning of 2010; 9 radiologically guided, 21 using the Y-TEC® procedure and 31 surgically inserted. Removal of the catheter was necessary in 40% of the surgical group, 20% of the Y-TEC® group and approximately 10% of the radiological group. Of the 4 catheters removed in the Y-TEC® group, one removal was due to infection, one due to incorrect placement (abdominal wall cavity), one due to failure to work and one due to persistent tunnel leak. The rate of infection at 1-month follow-up in the Y-TEC® group was approximately 14%, comparing favourably with the radiological and surgical groups, which both had a much higher incidence (≈33% and 26%, respectively). The rate of infection over the entire duration of the catheter life was similar between the Y-TEC® and surgical groups (≈40%) and less than that for the radiological group (78%). With regard to peritonitis, the rate at 1 month was high in the Y-TEC® group with nearly ¼ of recipients experiencing this infection; rates for the radiological and surgical groups were approximately 11% and 6%, respectively. Over the entire catheter life, the rates of peritonitis were approximately 28% in the Y-TEC® group, 29% in the surgical group and 22% in the radiological group.

Dr Voss says that his group suspected that the high rate of peritoneal infection was due to the large numbers of observers that were coming in and out of the procedure room and the associated potential flow of bugs. They now limit the numbers of spectators and do not allow entry following the start of the procedure, but are yet to determine the effects of this on the rate of infection. They also now clean the room before the procedure and suggest that it may be beneficial to double-glove, a procedure where the second glove is taken off just before picking up the catheter for insertion.

Take-home points

- Y-TEC® is a physician-directed catheter insertion
- The procedure is successful, but adverse events are an issue
- Allows for timely catheter insertion and possible avoidance of haemodialysis
- May be an interventional procedure that will attract trainees to renal medicine

Laparoscopic versus radiological Tenckhoff insertion

Presented by: Dr Emad Maher, Advanced Trainee, Middlemore Hospital, Auckland

Dr Maher was awarded the Morrison award at the meeting for this presentation.

Dr Maher described laparoscopic insertion as the commonest technique for the placement of PD catheters. However, he pointed out that radiological (fluoroscopic) PD catheter placement has the advantage of being able to be undertaken in a timely manner (within approximately 1 week at Middlemore) while the laparoscopic waiting list is much longer. Some patients waiting for laparoscopic PD catheter insertion require haemodialysis while they wait for their procedure. Dr Maher presented data comparing the outcomes of the two techniques. He also outlined the 2010 International Society for PD (ISPD) guidelines which recommend that >80% of catheters should be patent at 1 year and give the following as additional audit standards for catheter-related complications: bowel perforation <1%; significant haemorrhage <1%; exit-site infection within 2 weeks of catheter insertion <5%; peritonitis within 2 weeks of catheter insertion <5%; functional catheter problem requiring manipulation or replacement, or leading to technique failure <20%.

RCT comparing laparoscopic and radiological PD catheter insertion

A randomised controlled trial (RCT) comparing laparoscopic versus radiological PD catheter insertion was undertaken by Dr David Voss and colleagues between April 1999 and August 2004 at Middlemore Hospital. They randomised 113 patients to either laparoscopic (56 patients) or fluoroscopic (57) Tenckhoff (TK) insertion. Patient characteristics were similar to that of the source population except that Pacific people were under-represented, accounting for 14% of the fluoroscopic group and 19.6% of the laparoscopic group, compared with 26% of the source population (49/187). The study groups also had higher mean eGFR levels at dialysis inception and a lower rate of late referrals than the source population. In terms of incidence of comorbidities, the study population was similar to that of the source population. At one year, the probability of complication-free catheter survival was higher in the fluoroscopic group compared with the laparoscopic group (40% vs 25%, $p<0.05$). The probability of overall catheter survival at one year was similar between the two groups, as was the the probability of patient survival. The incidence of peritoneal dialysate leak and hernia was somewhat higher in the fluoroscopic versus the laparoscopic group (7% vs 17.9% [$p = 0.08$] and 7% vs 14.3% [$p = 0.21$], respectively). However, the incidence of both peritoneal dialysate leak and hernia was higher in the study population than that seen in the literature.

Study conclusions:

- Fluoroscopic insertion is equivalent to laparoscopic insertion
- Neither technique achieved standards
- TK survival marginally adequate
- High rates of hernia and leaks
- Not a real-life situation

Follow up audit

Dr Maher points out that the RCT does not represent a real-life situation; the RCT involved one surgeon, one radiologist, no late referrals, few Pacific people and virgin abdomens. The group therefore set out to investigate the real-life situation and undertook a retrospective audit, collecting data between 2004 and 2009 from multiple sources to capture all the fluoroscopic and laparoscopic PD catheter insertion procedures undertaken at Middlemore Hospital during that period. This data was back validated against ANZDATA and the renal database. A total of 286 procedures were identified (133 fluoroscopic, 153 laparoscopic) and patient demographic and outcome data were collected. Patient characteristics and incidence of comorbidities were similar between the two groups. The probability of complication-free survival at 1 year was similar between the fluoroscopic and laparoscopic groups (≈25%), as was the probability of overall catheter survival at 1 year (≈75%). With regard to probability of patient survival at 1 year, there was a trend for a lower survival rate in the fluoroscopic group (although not statistically significant). Predictors for catheter complications were Māori ethnicity and cerebrovascular disease. Predictors for catheter removal were Māori ethnicity and female gender. A trend towards higher mortality was seen with fluoroscopic insertion, but the only statistically significant predictor for death was coronary artery disease. The rates of catheter inflow/outflow failure were similar between the fluoroscopic and laparoscopic groups (19.6% vs 18.3%), as was the incidence of peritoneal dialysate leak, being 9.8% for both groups (overall, this value was lower than that seen in the RCT outlined above). The incidence of hernia was also high in the fluoroscopic and laparoscopic groups (9% and 10.5%, respectively), but the rate was slightly less than that seen in the RCT. The incidence of exit-site infection was 43% for both groups (the median time to infection occurrence was 45 days in the fluoroscopic group and 21 days in the laparoscopic group). Peritonitis occurred at a rate of 33% in the fluoroscopic group and 32% in the laparoscopic group.

Study conclusions:

- Fluoroscopic insertion is equivalent to laparoscopic insertion
- Neither technique achieved standards
- TK survival marginally adequate
- Lower rates of hernia and leaks than in RCT but remained high
- Higher rate of catheter blockage
- Māori patients, female patients, and those with cerebrovascular disease have a lower catheter complication-free and/or actual TK survival

Kidney Health New Zealand

Presented by: Dr Kelvin Lynn, Medical Director Kidney Health New Zealand

Kidney Health NZ (KHNZ) is a consolidating organisation with very strong links with kidney units, patient support groups and the NRAB (of which Dr Lynn is an *ex officio* member), and is starting to work very closely with Diabetes NZ. The Board has a Strategic Plan for 2008-2011 and this can be viewed on their website (http://www.nzkidneyfoundation.co.nz). Current members of the Board are Dave Henderson (Chair), Richard Robson (Treasurer), Nora Van der Schrieck, David Voss, Linda Grenell and Humphry Rolleston. Key priorities for KHNZ are outlined below.

Key priorities for KHNZ

- Increasing kidney donation
- Improving support for kidney donors
- Streamlining assessment of donors and recipients
- Assistance with costs of home dialysis
- Improving information for and about people with kidney disease
- Support for local patient support groups
- Working with Diabetes New Zealand
- Community education, targeting groups at high risk of kidney disease
- Kidney awareness Week and World Kidney Day activities

A specific area of focus for KHNZ is improving financial assistance for live organ donors (presented by Dr Lynn in his previous talk; see page 1). The organisation has focused on renal service improvement by working on improving primary care CKD management, improving rates of renal transplantation, initiating regional co-ordination in planning to address demand and access, and undertaking national co-ordination in renal workforce development. The organisation has also improved information about, and for, renal patients by putting together seven web-based patient information resources and informing all GPs of their availability (the downloadable information resources can be found at http://www.kidneys.co.nz).

Furthermore, the organisation talks to a variety of community and professional groups, undertakes workplace kidney checks to raise awareness and undertakes media interviews. A key activity of the KHNZ since its inception has been the funding of research and this year, $75,000 has been made available for research projects and summer studentships. KHNZ liaises with other community groups, including patient support groups, and is currently working on enhancing their Māori liaisons.

During the National Just Water Week in schools, held in conjunction with World Kidney Day (11 March 2010), KHNZ was able to achieve publicity regarding the link between CKD and diabetes, and undertook CKD checks in the community. Members of Parliament were sent information packs on CKD along with their own urine testing kit (annual kidney screening at Parliament is now undertaken). The focus of World Kidney Day March 10th 2011 will be on 'protecting your kidneys to save your heart', recognising the relationship between the increased risk of CVD in individuals with CKD. This message is a difficult one to get across, with many GPs not recognising that individuals with moderate kidney disease may be at increased risk of CVD.

Dr Lynn says that KHNZ is grateful for the excellent support of doctors and nurses from local renal units, and the support from patient support groups.

CKD-EPI versus MDRD for the estimation of GFR in an Australian and NZ cohort

Presented by: Dr Firoz Hossain, Advanced Trainee, Middlemore Hospital, Auckland

The accurate estimation of renal function is extremely important to nephrologists. Dr Hossain presented data from a study comparing the CKD Epidemiology collaboration (CKD-EPI), Modification of Diet in Renal Disease (MDRD) and the Cockcroft and Gault (CG) equations for the estimation of GFR in an Australian and NZ population cohort. Data was obtained from the EPO AUS–14 study, a prospective, multicentre, randomised study conducted from 1998-2002 to determine if maintenance of serum haemoglobin between 120 and 130 g/L prevented and/or delayed the development of left ventricular hypertrophy in patients with advanced CKD. The study cohort comprised 178 patients, aged 18-75 years, with CKD (GFR 15-50 mL/min and a historic decline in haemoglobin concentration of 110-130 g/L for males and 100-120 g/L for females) from 12 centres in Australia and NZ. Measured GFR (mGFR) by radioisotopic EDTA clearance was used as the gold standard. For MDRD, both four variable (4v) and seven variable (7v) calculations were undertaken and the CG equations were performed according to actual and ideal body weight. A total of 441 radioisotope measurements of GFR were undertaken. The ethnic make-up of the study population was 89% white race, 2% Asian and 9% black race (Māori, Pacific people, Aboriginal, or not specified). GFR was measured for all patients at the beginning of the study and then at yearly intervals. Concordance correlation coefficient (ccc) measurements to measure the degree to which pairs of observation fall on the line of identity and the Bland and Altman plot to assess the level of agreement between mGFR and estimated GFR (eGFR) were undertaken.

In NZ Māori, Pacific people and Aboriginals, the mean mGFR was 18.73 mL/min. In this group, 4v-MDRD and CKD-EPI both with black correction factor were found to be the best predictors of mGFR [4v-MDRD with black correction factor; mean eGFR 19.39 mL/min/1.73m^2 (ccc 0.729): CKD-EPI with black correction factor; mean eGFR 18.18 mL/min/1.73m^2 (ccc 0.724)]. For whites and Asians, the mean mGFR was 22.94 mL/min. In this group, the best predictors of mGFR were 4v-MDRD (mean eGFR 19.72 mL/min/1.73m^2, ccc 0.733), 7v-MDRD (19.15 mL/min/1.73m^2, 0.721) and CKD-EPI (19.16 mL/min/1.73m^2, 0.719), all of which underestimated GFR. Overall the best predictor of mGFR (22.60 mL/min) was found

to be 4v-MDRD with black correction for all races (mean eGFR 23.49 mL/min/1.73m^2, ccc 0.767).

Take-home points

- 4v-MDRD with black correction factor for all races is overall the most accurate formula for estimating GFR
- eGFR with black correction factor marginally underestimates GFR in NZ Māori, Pacific peoples and Aboriginals
- eGFR without black correction factor considerably underestimates GFR in whites and Asians
- A NZ national study is needed

Home haemodialysis training

Presented by: Dr Alvin Ng, Advanced Trainee, Middlemore Hospital, Auckland

Dr Ng presented data from a home haemodialysis study undertaken in conjunction with Dr Mark Marshall. The study assessed factors that are associated with training time and training failure. Data was collected from the Counties Manukau District Health Board (CMDHB) home haemodialysis programme between 2000 and 2009. During that time period, 162 patients underwent home dialysis training. Of those patients, 135 were successfully trained, 22 failed training, 1 underwent a kidney transplant and 4 were still undergoing training at the end of 2009. The majority (63%) of patients were between 45 and 64 years of age, while 6% were ≥65 years. The ethnicity of the study population was as follows; 40% NZ Māori, 30% NZ European, 27% Pacific Islander and 4% Asian.

Approximately 40% of patients exhibited a comorbidity, with the most frequent comorbidity being diabetes mellitus (≈55%). The majority of patients had good English proficiency (89%); 2% had poor English proficiency. With regard to type of vascular access, 63% of patients had an AV fistula, 30% had a tunnelled line, 5% an AV graft and 2% a temporary central line at the start of training (by the end of training, 50% of patients with a tunnel line would have a functioning AV fistula). The NZDep Score, a weighted average of nine census indicators of socioeconomic status for a specific area, showed 59% of patients with a score of 9-10 (most deprived) and 9% with a score of 1-2 (least deprived). With regard to prior modality, 52% of patients were dependent (i.e. in-centre patients), 34% independent (self-care haemodialysis), 14% intermediate.

Time to train

The study revealed that the median home haemodialysis training time (excluding failures) was 100 days, with the 25th percentile being approximately 70 days and the 75th percentile being approximately 120 days. Of those patients who failed training, 50% failed training in the first 70 days and the rest failed after 100 days. Multivariate linear regression analysis revealed that time to train was significantly increased for those patients aged 45-65 years (3 x longer to train), age >65 years (6 x), Māori ethnicity (2 x), Pacific Island ethnicity (4 x), male gender (3.6 x), those with central lines (3.23 x), those who were in intermediate category of modality pre-training (4.2 x) and those who had already been on dialysis for >7 months (2.68 x). Interestingly, the NZDep score and English proficiency were not associated with time to train.

Training failure

The odds ratios for training failure were 10.16 for patients aged >65 years, 9.19 for males, 13.51 for those with poor English and 3.46 for Māori (not significant). Those who had been on dialysis between 7-24 months were 14-fold less likely to fail training compared to those who started earlier (the reason for this is unknown). As with time to train, the NZDep score was not related to training failure.

Take-home points

- Home haemodialysis training time longer for; Māori and Pacific Island people, males, older patients, those with central lines, those 7-24 months on dialysis, those who are intermediate category of modality pre-training
- NZDep score and level of English proficiency not associated with time to train
- Increased incidence of training failure in; patients with poor English, older patients, males, Māori (trend only)
- Lowest training failure rates in those >7 months on dialysis
- NZDep score and modality of pre-training not associated with training failure

Live donor exchanges

Presented by: Professor Justin Roake, University of Otago, Christchurch School of Medicine

Approximately 30% of kidney donor-recipient pairs in the living donor setting are incompatible either due to ABO incompatibility or HLA sensitisation. Strategies to increase living donor kidney transplantation include non-directed (altruistic) organ donation, ABO incompatible transplantation, desensitisation programmes and donor exchange (paired kidney exchange involving either single pairs or multiple pairs, and unbalanced donor chain programmes).

Conventional paired kidney exchange

Conventional paired living donor exchange programmes involve two donor-recipient pairs with incompatibility and involve the exchange of donors. Such an exchange is normally undertaken simultaneously in order to avoid defaulting and this type of exchange is relatively straightforward to organise.

Multiple paired kidney exchange loops

Multiple paired kidney exchange loops are more difficult to organise, require sophisticated software to achieve optimal matching from a pool of pairs, and have an increase risk of the donor defaulting. The procedures are normally undertaken simultaneously, but this can be difficult from a logistics perspective. Evidence suggests that the optimal number of pairs for such a closed-loop exchange is three.[1] The pool size is important in this type of exchange and it is estimated that with 100 donor-recipient pairs it is possible to achieve ≈60% match for non-O recipients and ≈15% match for O recipients. A substantial population is required to generate the pool. Prof. Roake says that it may be a possibility for NZ if linked with Australia.

Non-simultaneous donor chains

This type of chain is initiated by an 'unbalanced' donor (either a non-directed living donor [NLD] or a deceased donor). This can be a sequential system and simultaneous donation is not required. Default disadvantages the system but not individuals. The chain can remain open for a long time, but can be closed at any time by donation into the deceased donor waiting list. This domino-type chain has been successfully demonstrated in The Netherlands[2] and Australia[3].

Attitudes to use of non-directed donors

A study by Ratner et al investigated donor and recipient attitudes to the use of NLD.[4] They found that survey respondents indicated a general willingness amongst a proportion to participate in an altruistic unbalanced paired kidney exchange that was circumstantial rather than static. The willingness of donors and recipients was shown to be influenced in favour of participation if there was a perceived benefit to the recipient, and both were more willing to participate if their intended recipient or donor was enthusiastic about participating.

Paired kidney exchange and non-directed living donation in NZ

NZ has a paired kidney exchange register with 8 pairs registered. The programme has agreed donor and recipient criteria and agreed protocols. So far, no transplants have been undertaken. However, NZ has a relatively high rate of non-directed donation. NLD allocation is undertaken using the National Kidney Allocation Scheme, but is focused on local area recipient pools. In Auckland, ≈1 NLD transplant is undertaken per year and 10 have been undertaken in total. In Christchurch, 19 NLD transplants have been undertaken since 1998 (this makes up ≈10% of the living donor programme; a total of 176 living donor transplants have been conducted in Christchurch since 1998). In Christchurch, there has been no significant donor morbidity, all transplants have functioned well and there has been one death with a functioning graft 10 years post transplant. Overall, in NZ, there have been 509 living donor transplants and 21 (4.1%) of these have had a NLD.

Proposals

Prof. Roake proposed that NZ consider amalgamation of a paired kidney exchange programme with Australia and that all NLD are assessed for initiation of domino paired kidney exchange chains (this would mean that donation would not be restricted to the local waiting list). He does not see these two proposals as mutually exclusive, but acknowledges that there may be problems trying to initiate both.

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College matters: PREP Advanced Training Program

Presented by: Jacqui Hall, Executive Officer, The Royal Australasian College of Physicians

The Physician Readiness for Expert Practice (PREP) Advanced Training Program has been developed by The Royal Australasian College of Physicians. The PREP Program comprises a Basic Training curricula, an Advanced Training curricula and Continuing Professional Development (this will be mandatory). The PREP Training Program aims to develop a physician or paediatrician competent to provide consultant level, unsupervised comprehensive medical care in one or more sub specialties of Internal Medicine or Paediatrics. Jacqui Hall says that a lot of the tools used for PREP will be things that physicians and paediatricians will already be undertaking in everyday supervision, but the College has put a framework in place outlining specific items in training. Each specialty decides which assessments that specialty will use and how often they will be carried out. Jacqui Hall says it is important that physicians who are supervising give feedback to the College as to what specific needs NZ has with regard to the Program, as the needs in NZ may be different to those in Australia.

Analysis of the implementation of PREP in Basic Training has assisted with Advanced Training PREP development. Portal development has been initiated and handbooks for each specialty are being developed. The curriculum for Nephrology Medicine has been ratified. 2010 has been a transition year for Basic Training PREP and 2011 will see advanced trainees start to use some elements of PREP. The College acknowledges that Supervisors need training in order to implement PREP and this is being arranged.

Key features of PREP

Key features of PREP are that it is a workplace-focused, learner-centred approach, covers comprehensive educational curricula to guide learning, provides for education supervision, has an emphasis on exemplary patient care within the context of a complex, multi-disciplinary, team-based working environment, has an E-learning environment (Advanced Training portals), ensures that the nature, focus and direction of the learning experience is owned and managed by the trainee as a mature adult learner, allows for regular, formative assessments that will monitor progress and inform feedback to the trainee, and allows for an open and transparent assessment strategy.

Learning is guided by two curricula: the Professional Qualities Curriculum used throughout Basic and Advanced Training and the Specialty-Specific Curriculum with >40 specialty-specific curricula.

Professional qualities curriculum

The Professional Qualities Curriculum focuses on non-clinical/non-discipline specific aspects of physician's workplace practice, spans and integrates into Basic and Advanced training and is taught, learnt and assessed within the context of daily clinical/professional practice. The following are the domains of the Professional Qualities Curriculum: communication, quality and safety, teaching and learning (scholar), cultural competency, ethics, clinical decision-making, leadership and management, health advocacy and the broader context of health. Tools for learning within the curriculum include the Professional Qualities Reflection in which the trainee reflects on a clinical encounter of significance to his/her learning to further develop understanding, insight and new knowledge.

Specialty Curriculum

Within this curriculum, the Learning Needs Analysis tool allows for the trainee to create a learning plan for a rotation based on the curriculum and to reflect on learning at the end of the rotation. This could form part of a specialty program and could be included at the start of the year and then mid-year.

Formative and summative assessments

The program is based largely on formative assessments and includes staged implementation of several formative assessment tools. Two of these, the case-based discussion and the mini clinical examination tool, assess clinical skills. Procedural skills are assessed with the direct observation of procedural skills assessment and professional qualities will be assessed with the multi-source feedback tool. Research projects form a further part of the assessment. Results from formative assessments will be included in the trainee's file but are designed to provide feedback to assist trainee learning. Supervisor's reports on progress make up the summative assessment for accreditation.

Getting more than you bargained for – tumour in a donor kidney

Presented by: Dr Philip Matheson, Renal Physician, Wellington Hospital

Dr Matheson presented a renal transplant case in which, upon nephrectomy, the donor kidney was found to have a tumour. The ethical dilemma faced by the transplant team in this case is discussed.

The recipient was a 40-year-old woman with interstitial nephritis and focal glomerulonephritis since 2002. Peritoneal dialysis had been started in 2009. She was a smoker, had osteopenia and depression, but was otherwise well and was considered to be a good recipient.

The donor was the woman's 45-year-old brother. He was a non-smoker with no significant past medical history. There was no HLA mismatch. Ultrasound imaging showed normal kidneys bilaterally, but the CT angiogram showed an 18mm cyst in the upper pole of the left kidney.

The dilemma

Upon donor nephrectomy, the cyst was found to be solid and did not look like a cyst at all. A frozen section indicated that it was indeed a cancerous tumour. Dr Matheson explained that the transplant team considered several options;

A. Wake up donor and discuss

B. Proceed with partial nephrectomy and no transplant

C. Undertake total nephrectomy and no transplant

D. Undertake nephrectomy with bench surgery to remove tumour and transplant

E. Undertake nephrectomy, transplant and then monitor closely

Dr Matheson asked for feedback from the audience whether they would have at least considered continuing with the transplant; ≈ 60% of attendees said they would have.

During the procedure, the team searched the available literature to see if such a procedure had been undertaken before. They identified a report by Nicol et al in which 43 kidneys from donors with small renal tumours were successfully transplanted.[1] The literature also showed that with a prognosis of renal cancer, the overall survival rate may be better with partial nephrectomy than with radical nephrectomy.[2]

The team (donor surgeon and anaesthetist, recipient surgeon and three transplant physicians, one of whom is also a clinical ethicist) was faced with the dilemma that the recipient had been sedated. However, they considered her capable of making an informed decision and presented her with all the available facts. They offered her the chance to continue with the transplant after partial nephrectomy (bench surgery in this case). After discussion with her family (but not with the

donor who was still anaesthetised) she decided to go ahead with the transplant following partial nephrectomy. The procedure went well and the recipient felt that she had made the right decision. The donor continues to feel anxious that he may have given his sister cancer.

Dr Matheson explains that his team was faced with a crisis decision and explains that, as they saw it at the time, they had two options. Either take the 'easy option' and undertake a partial nephrectomy and no transplant or do the 'right thing' with the best outcomes for the donor and recipient with informed consent.

Has anyone done this before?

A subsequent search of the literature identified 88 similar renal transplants (including the Nicol series).[1, 3-10] Over a median follow-up of >24 months (range 1-210), one recurrence of renal cancer had been identified in a transplanted kidney.

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Deceased donor issues

Evaluation of comorbid disease in renal transplantation

Presented by: Drs Chris Hood and Jamie Kendrick-Jones,
Renal Physicians, Middlemore Hospital, Auckland

The waiting list in NZ for deceased donor kidneys is increasing and is currently ≈5 years for blood group O and 2 years for blood group A recipients. A contributing factor is the increasing comorbidity-challenged and older population. A major factor affecting the benefit one receives from their kidney transplant is comorbidity, and death with a functioning graft is becoming more common as patients with an increasing number of comorbid conditions are undergoing transplantation. The Auckland transplant protocol is currently being rewritten. The issue of evaluating potential recipients for the deceased donor list, and specifically the burden of comorbid disease, is being readdressed and Drs Hood and Kendrick-Jones took the opportunity to canvas opinion from those at the current Nephrology meeting. The current NZ renal transplant guidelines state that to be eligible for a transplant the recipient needs to have a ≥80% chance of 2-year survival.

The meeting attendees (n ≈ 40) were asked to vote on the following questions:

Q: In the NZ context of limited graft availability, should we utilise a defined rate of expected patient survival following transplantation as a limiting criteria for listing on the deceased donor list?
A: The vast majority voted 'Yes'

Q: What should this defined rate be?

1. ≥80% at 2yrs
2. ≥80% at 5yrs of more
3. Somewhere between the above figures
4. Not appropriate

A: 9 voted for option 1; 9 voted for option 2; none voted for option 3 or 4

Comorbidity indices

Various comorbidity indices, such as the Index of Coexistent Disease (ICED) and the Khan, Davies and Charlson comorbidity index (CCI) have been applied to the ESRD population. However, the consequences of patient comorbidity on kidney transplant outcomes have not been well studied. The first description and analysis of the impact of baseline comorbid conditions on kidney transplant outcomes using a simple comorbidity index came from a study involving 715 kidney recipients.[1] In that study, a version of the CCI was used that excluded age to assess and describe their comorbid conditions; the primary outcome measure was graft failure and death. For analysis, patients were divided into two groups depending on their CCI score (<5 or ≥5; a higher score indicating greater comorbidities). Of the study population ≈80% had a CCI <5, while ≈20% had a CCI ≥5. Heart failure, diabetes and diabetes with end-organ failure were the most common comorbidities (11.9%, 13% and 17.3%, respectively). After adjustment, patient death was significantly associated with a CCI ≥5 (HR 2.67; 95% CI 1.75-4.08). Multivariate analysis showed that high comorbidity was significantly associated with an increased risk for patient death in both the perioperative period and >3 months after transplantation. There was also a trend for CCI ≥5 to be associated with graft failure (although this did not quite reach statistical significance). Although the study had several limitations, the findings suggest that CCI is a simple and practical tool for the evaluation of comorbidity and patient outcomes.

Another larger study (n = 6324) used data from the Canadian Organ Replacement Registry to test the ability of four comorbidity indices including the CCI to predict patient survival by using a Cox regression model.[2] The study showed that after adjusting for cause of renal disease, age and sex, increased comorbidity was strongly associated with reduced patient survival. Of the four comorbidity indices examined, the model containing the CCI offered the best fit.

A new comorbidity index

A 2010 study using data from the United States Renal Data System derived and validated a new prognostic index to accurately quantify survival for the various treatment options available to patients requiring renal transplantation.[3] The study incorporated data from 169 393 patients (divided into derivation and validation groups) with a mean observation time of 3.6 years. The regression model looked at 30 variables. Those variables with the strongest detrimental effect on survival were diabetes, chronic obstructive pulmonary disease, being non-ambulatory and smoking. Variables with a protective effect were polycystic kidney disease and being of non-caucasian origin. Of all the continuous factors, the association between age and death was the strongest (especially post-transplant). The study showed a HR of death associated with increasing age of between 16% and 18% per decade. The concordance probability of the index in the validation group was 0.746 (95% CI 0.741-0.751).

While this study involved large numbers and appears to be a robust analysis, it also has several limitations. Furthermore, it uses data not routinely collected in ANZDATA and it is not clear how the index may translate to the NZ population.

The attendees were then asked to vote on the following questions:

Q: Are you in favour, in principal, of a comorbidity index/scoring system and selecting renal transplant recipients based in part on this?
A: The majority voted 'Yes'

Q: Should we (and can we ethically/legally) incorporate age in any scoring system?
A: The vast majority voted 'Yes'

Q: Should the scoring system include a definite cut-off (i.e. cannot be listed if beyond threshold)?
A: A small majority voted 'Yes'

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Deceased donor kidney recipient selection

Presented by: Dr Nick Cross, Nephrologist, Christchurch Public Hospital

Dr Cross says that while he doesn't disagree with having a comorbidity scoring system as discussed above, his main concern is the fact that there is a grey zone around the number, with the estimation of survival being exactly that, an estimation. He raises the question that if a person calculates at 75% chance of survival at 5 years, but the cut off is 80%, can we deny them a kidney transplant based on that value, when we know that there is an error rate associated with its calculation?

Key ethical concepts

The key ethical concepts in the allocation of deceased donor kidneys are justice, beneficence and efficiency (health economic concept).

Guidance for the ethical allocation of organs and tissues has come from the Australian Government's National Health and Medical Research Council. The Transplantation Society of Australia and NZ (TSANZ) has put together a consensus statement on eligibility criteria and allocation protocols for all organ transplantation from deceased donors. The TSANZ states that the distribution should be 'just' and take no account of race, religion, gender, marital status, sexual orientation, social status, capacity to pay, past behaviour or location. It also states that account should be taken for relative urgency, success factors (e.g. matching), relative severity, relative waiting time and likelihood of compliance. With regard to age, the TSANZ states that age should not be taken into account, except where it may affect outcome.

The TSANZ has also put together specific criteria for kidney transplantation. Inclusion criteria are as follows; ESRD, anticipated low risk of perioperative mortality, an 80% likelihood of 5 year survival. Dr Cross separates the TSANZ exclusion criteria into two categories, absolute criteria and relative criteria. Absolute criteria include contraindications to transplantation; infection, malignancy and inability to comply. Relative criteria are conditions where their severity dictate whether or not they are a contraindication to transplantation; cardiac disease, diabetes, other medical conditions and age.

Current paradigm: who's listed?

The current paradigm for selection onto the deceased donor list works as follows: A patient presenting with ESRD requests a transplant following education about their illness. If there is no suitable living donor, the patient undergoes medical and surgical assessment and additional tests. Their case is reviewed by a committee. The patient will then be either considered well enough to list or too sick to list.

Data from the 2009 ANZDATA Annual Report has been used to show the NZ ESRD population (n = 2100) by deceased donor list status and age (see **Figure 1**). It is clear that those individuals who are younger have an increased chance of being included on the list. Those individuals not listed tend to be older and sicker. In total, only 14% of the NZ ESRD population is currently on the deceased donor waiting list. However, ≈ 30-50% of the paediatric ESRD population is on the list and a large proportion of the remainder of the paediatric ESRD population will have living donors being organised.

Every year in NZ, ≈20% of the kidney donor waiting list (including those on the living-donor list) receive a transplant (≈2.6% of all those on dialysis get transplanted each year). It appears that NZ transplant recipients do really well, with the 5-year survival rate being ≈90%, while the 5-year survival rate for those who remain on dialysis is only ≈40%. However, Dr Cross points out that this is not surprising given that we choose the patients who are most well to undergo transplantation, while sicker patients may not get selected and remain on dialysis.

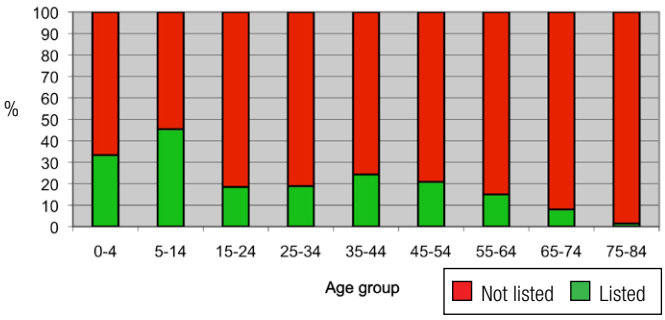

Figure 1: The proportion of the NZ ESRD population who are currently on the deceased donor waiting list (green) and the proportion who are not (red); based on data from the 2009 ANZDATA report.

So who should we choose to transplant to maximise incremental benefits to ESRD group?

Dr Cross and colleagues, including Dr Germaine Wong, have recently undertaken a study investigating the comparative survival and economic benefits of deceased donor kidney transplantation and dialysis in people with varying ages and co-morbidities (Wong et al., unpublished data). Their study involved 10 000 hypothetical patients, incorporated data from ANZDATA and used a Markov model. The findings indicate that all groups benefit from listing and that the young and fit gain the most years. Furthermore, transplantation was not cost saving but was cost effective. The study also indicated that the relative mortality benefits of transplantation are smaller than possibly expected and that transplant waiting time has a large negative effect on benefit, especially for those in their 40s and 50s.

Some further points

Dr Cross says that the current 5-year survival rate for deceased donor transplant recipients is high at 90%. He suggests that this may mean that we are being too selective with recipients. He also points out that if more marginal recipients were to be accepted on to the waiting list, we must expect a reduction in the 5-year survival rate. We would need to realise that this would not indicate a failing in our transplant system, but rather just a reflection of transplant into more patients with comorbidities who will benefit from transplantation.

Take-home points

- Ability to predict 80% 5-year survival is poor
- Current 5-year survival rate better than stated aim
- Current practice emphasises utilitarianism
- All patients listed benefit to a similar degree (0.5–3 years)
- Possible benefit/egalitarian arguments for accepting more onto waiting list

Mortality of ICU patients by modality of renal replacement therapy: an analysis adjusting for time-varying confounding and modality

Presented by: Namrata Khanal, Nephrology Fellow, Middlemore Hospital, Auckland

Up to 65% of Intensive Care Unit (ICU) patients develop evidence of acute kidney injury (AKI) and this has been shown to be an independent risk factor for death. Approximately 5% of ICU patients receive acute renal replacement therapy (RRT) and the mortality rate in such patients is up to 50%. Acute RRT is performed in a variety of ways, including intermittent haemodialysis (iHD), continuous renal replacement therapy (CRRT), prolonged intermittent renal replacement therapy (PIRRT) or acute PD. PIRRT is becoming increasingly popular world-wide and particularly in the Asia-Pacific region, but little data is available on outcomes with PIRRT compared with other modalities.

At Counties Manukau District Health Board, PIRRT has become the most common modality and has largely supplanted CRRT. Typically dialysis is undertaken for 8-12 hours daily or at least on alternate days. A retrospective study by Dr Khanal and colleagues was undertaken with the aim of determining if PIRRT was associated with different risks of patient mortality (i.e. death at hospital discharge) or renal mortality (i.e. death or dialysis at hospital discharge) than CRRT. The study used Robin's Marginal Structural Modeling technique. All patients >18 years of age who were treated with acute RRT in the ICU from 2002 to 2008 were identified and a total of 142 patients who were free from ESRD were included for analysis. Within the cohort, there were 839 patient (pt)-days of PIRRT, 209 pt-days of CRRT and 82 pt-days of iHD. Overall, there were 56 deaths and 69 renal deaths. For analysis, those patients receiving PIRRT and iHD were grouped together and compared with those receiving CRRT. Baseline characteristics and risk of death on admission were similar between the groups.

Analysis showed that as the admission progressed, patients receiving CRRT became less physiologically stable relative to those receiving PIRRT/iHD. Sequential organ failure assessment scores at 24 hours were higher in the CRRT group compared with the PIRRT and iHD groups. However, there was no apparent difference in patient or renal mortality between those treated with PIRRT/iHD and those treated with CRRT. The Marginal Structural Modeling technique provided plausible estimates of both patient mortality and renal mortality.

Dr Khanal points out that their study did have limitations and that clinical trials are needed.

Use of nurse titration clinics to achieve target blood pressures

Presented by: Dr Dominic Taylor, Renal Registrar, North Shore Hospital, Auckland

Hypertension affects 26% of the adult population and is a significant cause of ESRD. In NZ, there are 3485 GPs and an estimated 260 cases of hypertension per GP; around 10% of those patients have resistant hypertension. In the Waitemata District Health Board region, out of a population of ≈530 000, there are an estimated 111 163 cases of hypertension and 11 116 cases of resistant hypertension. Even if 10% of these patients were referred per year, this would overload the current service of 1 consultant clinic per week seeing 3 new patients and 6 follow-ups.

Many studies have shown that rapid achievement of target BP leads to better outcomes in hypertensive patients and that BPs from the first few months of treatment are predictive of outcome.[1,2] There is also good evidence from the US that nurse titration clinics have good success rates in achieving target BP.[3]

The Waitemata Hypertension Service Pilot Audit is underway. The aim is to determine if GP-referred patients with difficult or resistant hypertension can be safely and effectively managed with an initial physician visit, followed by fortnightly nurse-clinic titration visits until at target BP. Data from 20 consecutive new patients (GP or specialist referrals) is being collected. Patients initially attend a registrar clinic, where a full assessment is made followed by initial medication adjustment, then attend nurse-led clinic visits approximately fortnightly until target BP is met. Once at target, they are discharged with a letter to their GP. During the nurse titration clinic, patients receive a thorough initial 60 minute assessment (including careful baseline automated office BP measurement) and education regarding medication and lifestyle modification. During subsequent 30 minute visits, antihypertensive medication is titrated. Patients are informed at the outset that they may require two or more drugs to reach their target BP.

Hypertension was classified according to the JNC 7 (2003) guidelines.[4] Treatment algorithms, also based on JNC 7 (2003) data, were produced for patients in 4 different groups: stage 1 hypertension and <60 years; stage 1 hypertension and 60-75 years; stage 2 hypertension and <75 years; stage 1 and 2 hypertension and >75 years. So far, 15 patients (mean age 49 years) have been seen at the Registrar clinic and each have attended at least 1 nurse-led clinic. The mean BP at first assessment was 159/94 mmHg (mean number of drugs per patient 2.07). Six patients have now been discharged with a mean BP of 134/77 mmHg after a median of 2 total visits. Nine patients are undergoing follow up and after a median of 3 total visits have a mean BP of 146/85 mmHg. The mean number of drugs received at discharge or last follow-up was 3.07. Dr Taylor says that they have added predominantly RAS blockers and thiazide diuretics, and have increased the number of patients taking maximum doses in each drug class.

Initial conclusions

- We appear to be able to reach target BP in the majority of patients by 8 weeks
- More time available for accurate, automated BP measurement, lifestyle advice, patient education and discussion of drug side effects in nurse-led clinics
- Faster patient turnover in registrar-led clinic
- Model likely to be useful in CKD and transplant patients
- Further results to come

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NZ dialysis audit 2009

Presented by: Dr Grant Pidgeon, The National Renal Advisory Board

Dr Pidgeon points out that this report is indicative only and that he needs further information from ANZDATA. Some of the 2009 data is not yet available and he stresses that it is important for data to be sent to ANZDATA in a more timely fashion.

An addition to the 2009 report included dialysis related demographic data, which highlights that there are differences (including ethnicity) in the patient populations treated in the different regions of NZ.

Summary of 2009 data available so far:

- Treatment modality rates (PD or HD) of incident patients differed greatly throughout the country as did the rate of automated peritoneal dialysis
- The rate of central venous catheter (CVC)-related bacteraemia is now reported by most units and was uniformly below the current standard of 4 episodes/1000 catheter days
- The rates of incident dialysis patients requiring HD for ≤90 days via a temporary CVC before starting PD were below the <20% standard at most units (8/10)
- Very few patients on HD received fewer than 3 sessions per week although the percentage of patients receiving HD sessions of <4.5 hours varied markedly across units
- The number of patients starting dialysis with an MDRD CrCl >10mL/min varied between 13% and 57%
- Transplantation rates, assessed either by total DHB population or dialysis numbers, varied considerably across units

Dr Pidgeon suggests that attendees consider what further data they would like to see being reported in the future.

Antibiotic resistance after introduction of antimicrobial catheter locks

Presented by: Dr Martin Wolley, Advanced Trainee, Auckland

Catheter-associated bloodstream infection (CABSI) causes significant morbidity. Rates of CABSI as high as 5/1000 catheter days have been reported, although typical rates in most units are closer to 1/1000. Catheter colonisation is generally the preceding event before CABSI and migration of organisms along the internal

surface of the catheter via a biofilm is the most common source of CABSI organisms in long-term CVCs. The standard procedure to prevent occlusion is to use heparin, but heparin has been found to increase the formation of biofilms.[1]

Effect of antimicrobial locks

A recent meta-analysis identified 16 trials investigating the efficacy of antibiotic-based catheter lock solutions at preventing CABSI (9 trials involved HD patients). A mean baseline CABSI rate of 3/1000 catheter days was found among the trials. The CABSI rate was higher in the heparin only group compared with the antibiotic/anticoagulant group; this reached statistical significance in 7/9 trials.[2] However, the trials included in this analysis all had limitations.

Auckland experience

Dr Wolley and colleagues undertook a 4-year audit of CABSI data from Auckland City Hospital, where a gentamicin 5 mg/mL plus heparin 5000 U/mL solution was introduced for all central venous haemodialysis catheters in 2006. They found that CABSI rates for tunnelled lines dropped significantly ($p = 0.03$) from 1.25/1000 catheter days pre antimicrobial lock (AML) to 0.75/1000 catheter days post AML; corresponding CABSI rates for non-tunnelled lines were 2.16 and 1.53/1000 catheter days but this difference was not significant. This drop was found to be due to significant ($p < 0.0005$) reductions in the rates of gram negative CABSI; *Staphylococcus aureus* and coagulase negative staphylococci (CNS) CABSI rates did not change significantly. Furthermore, a methicillin-sensitive *S. aureus* (MSSA) with isolated gentamicin resistance was found to have developed in the last 2 years of the study period; this doesn't appear to exist anywhere else in the hospital.

Middlemore experience

A study of the effect of antimicrobial locks for tunnelled HD catheters on bloodstream infection and bacterial resistance was undertaken using data from Middlemore hospital between 2003 and 2006.[3] AMLs with gentamicin 1 mg/mL plus heparin were introduced at Middlemore in 2004. The study found a 52% reduction in CABSI following the introduction of AML. Furthermore, there was a trend for increased gentamicin resistance in CNS isolates from 25% to 71% during AML use; in the non-ESRD population, the figures for the same period were ≈26%. In the follow up period, AML exposure was also associated with a trend to increased gentamicin resistance amongst CNS isolates; this was similar to the pattern observed for bloodstream infections (BSI) in the general HD population, in which tunnelled catheters were not the source of BSI, but this was different from that seen in the general non-ESRD population.

Take-home points

- Locally there is a trend to increased gentamicin resistance in CNS CABSI
- There is some evidence that gentamicin resistance in MSSA may be emerging in the HD population

References:

1. Shanks RM et al. Heparin stimulates *Staphylococcus aureus* biofilm formation. Infect Immun. 2005;73(8):4596-606.
2. Snaterse M et al. Antibiotic-based catheter lock solutions for prevention of catheter-related bloodstream infection: a systematic review of randomised controlled trials. J Hosp Infect. 2010;75(1):1-11.
3. Abbas SA et al. Effect of antimicrobial locks for tunneled hemodialysis catheters on bloodstream infection and bacterial resistance: a quality improvement report. AM J Kidney Dis. 2009;53(3):492-502.

A difficult case of anaemia in a renal transplant recipient

Presented by: Dr Penny Morgan, Nephrology Trainee, Christchurch

Case report

A 56-year-old man, who had received a living unrelated renal transplant in 2002, presented with recurrent anaemia in May 2010. He was lethargic with a Hb level of 47 g/L. He was transfused with 5 units of blood and was discharged with a Hb level of 110 g/L. The following month, he re-presented with lethargy and a HB level of 51 g/L. His work-up was unremarkable and he did not report a recent change in medications. Following his transplant, he had been receiving cyclosporin, mycophenolate mofetil (MMF) and prednisone, but had experienced acute rejection in late 2002 and received high-dose prednisone followed by muromonab-CD3. His graft function did not return to baseline; MMF was switched to azathioprine after 1 year and cyclosporin was switched to tacrolimus after 15 months. His graft had been stable in recent years. Current medications comprised prednisone 6mg, tacrolimus 2mg twice daily, azathioprine 150mg, quinapril 10mg, frusemide 40mg, calcium carbonate, ranitidine 150mg twice daily, omeprazole 40mg twice daily, multivitamins, humalog insulin, protaphane insulin and terbinafine.

Tests revealed a haptoglobin level of 3.25. Bone marrow aspirate and biopsy showed findings consistent with pure red cell aplasia (PRCA). His WBC and platelet counts were normal. Tests were negative for possible causes of his PRCA, such as evidence of parvovirus B19, HIV, Epstein-Barr virus, hepatitis B or C virus, thymoma, autoimmune disorders, lymphoma or leukaemia.

Terbinafine was identified as a possible suspect agent in the cause of his PRCA and the agent was discontinued. He was discharged with weekly blood tests. Follow-up 3 weeks later revealed a further decline in his Hb level, to 65 g/L (reticulocyte count = 2), and he received a further 4 units of blood.

Azathioprine was then considered a possible suspect and was discontinued. His prednisone dosage was increased to 10mg. At follow-up 6 weeks later, his Hb level was 114, but he had had an extra 5 units of blood (his reticulocyte count was still only 4). Tacrolimus was discontinued and replaced with cyclosporin. Within a few weeks, his Hb level and reticulocyte count increased (see **Figure 2**).

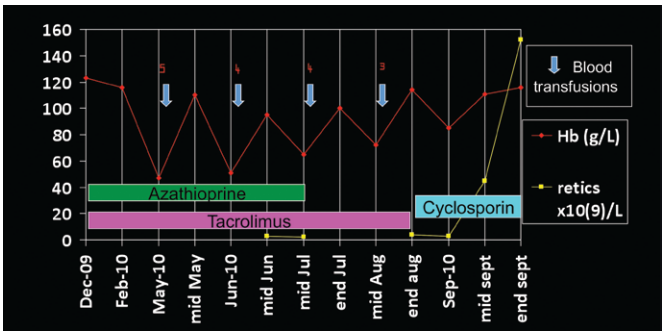

Figure 2: Time frame of events in a 56-year-old man who developed pure red cell aplasia during treatment with tacrolimus and azathioprine.

Calcineurin-inhibitor-induced pain syndrome

Presented by: Dr Caroline Chembo, Advanced Trainee, Wellington Hospital

Calcineurin-inhibitor-induced pain syndrome (CIPS) was first described in 2001 by Grotz et al.[1] CIPS was initially thought to be due to cyclosporin only, but is also seen with tacrolimus and affects up to 5% of patients following a solid organ transplant. Dr Chembo presented 3 cases of CIPS.

Case 1

A 50-year-old man who had undergone a living-donor transplant and was receiving cyclosporin 100mg twice daily, mycophenolate mofetil and prednisone, developed pain in his left knee with reduced exercise tolerance 3 months post-transplant. He was taking regular analgesia to little effect. A subsequent MRI revealed signs of possible calcineurin-inhibitor (CNI)-related bone marrow oedema (mainly on the left side). Cyclosporin was decreased to 50 mg twice daily and his pain resolved within ≈6 weeks.

Case 2

A 50-year old woman who had been receiving cyclosporin, mycophenolate mofetil and prednisone since her deceased-donor renal transplant presented 2 months post-transplant with bilateral knee pain, and painful shins and feet. An x-ray revealed degenerative changes. CNI-related bone marrow oedema was

suspected. Cyclosporin was replaced with tacrolimus with the dose subsequently reduced. Her pain resolved 2 months after a reduction in her tacrolimus dose.

Case 3

A 58-year-old man who was receiving cyclosporin 175mg twice daily, mycophenolate mofetil and prednisone following a deceased-donor transplant experienced debilitating bilateral knee pain 3 months after undergoing his surgery. He was taking ibuprofen for his pain. An MRI showed severe bone marrow oedema and subtle subchondral fractures. Cyclosporin was discontinued and subsequently restarted at a lower dose, with his prednisone dosage increased. His pain resolved after 2 weeks.

Symptoms and signs of CIPS

- Usually begins 2-4 months post-transplant
- Affects lower limbs – feet>knees>ankles
- Pain worse on standing or walking
- Mobility may be affected to extent of using aids
- Pain relieved by resting with limbs raised
- Hips or spine not involved
- No skin changes or signs of vasomotor instability
- Clinically nil to find
- Symptoms usually resolve within a few months
- Drug concentrations usually within therapeutic range
- Bone marrow oedema in areas of pain on MRI

Pathogenesis of CIPS

The pathogenesis of CIPS is not fully understood, but it is thought that calcineurin inhibitors provoke vascular changes leading to disturbance of bone perfusion and permeability, causing intraosseous vasoconstriction and bone marrow oedema. It is thought that the lower limbs are affected because they are subject to higher venous blood pressures.

Management of CIPS

The following are recommended for management; analgesia, rest, possible reduction of CNI, increase other immunosuppressants if CNIs decreased, give calcium channel blockers to reduce intraosseous hypertension, give bisphosphonates and calcitonin to help with pain.

Dr Chembo points out that the risks and benefits must be weighed for each patient before the CNI is reduced. Since the prognosis is good, some people advocate not to reduce the CNI, but Dr Chembo and colleagues believe that stopping the CNI or reducing the dose may alleviate the symptoms very quickly, as shown in Case 3.

Reference:

1. Grotz WH et al. Calcineurin-inhibitor induced pain syndrome (CIPS): a severe disabling complication after organ transplantation. Transpl Int. 2001;14(1):16-23.

About Expert Forums

Expert Forum publications are designed to encapsulate the essence of a local meeting of health professionals who have a keen interest in a condition or disease state. These meetings are typically a day in duration, and will include presentations of local research and discussion of guidelines and management strategies.

Even for local events it is not always possible for everyone with a similar therapeutic interest to attend. Expert Forum publications capture what was said and allows it to be made available to a wider audience through the Research Review membership or through physical distribution.

Paediatric nephrology in Auckland – the early years

Presented by: Drs Max Morris and Tonya Kara

The Hospitals

In Auckland, the first documented mention of any special hospital facilities for children was in 1890, when the Auckland Hospital Board discussed altering some of the wards in the main hospital to make them more suitable for children. Before this period, children were not generally admitted to hospital, but rather nursed at home. In 1898, plans were underway to built a children's hospital, the Costley building, named after Edward Costley who bequested £12500. The building had four wards each able to accommodate 12 children. However, within a few years it was being over-run by adults and the Board decided that it was too small. They subsequently built the Princess Mary Hospital which opened in 1918. The hospital had four wards each able to accommodate 25 children. Soon after it opened, it was swamped by adults with influenza from the pandemic, but by the following year had resumed service as a children's hospital. The hospital remained operational as a children's hospital until after World War II.

Another hospital, a second Princess Mary, was constructed for injured marines returning from the Pacific war in 1942. Following the war, the building, which was more like a prefab, lay empty until the Board decided to move children into it. Dr Morris says that when he came to Auckland in 1969, the hospital had three paediatric medical wards, a neurosurgery unit and a surgical ward. By 1972, the hospital had four medical wards and a specialised infectious diseases ward. Each ward was capable of holding ≈45 children and the hospital had x-ray facilities and its own labs. The hospital was demolished in 1991 following the building of the Starship Hospital.

Early days in Auckland

Dr Morris trained in paediatric nephrology and dialysis in Vancouver B.C. in 1974-76 and he trained in renal transplantation as a Registrar and Research Fellow at Guys Hospital London between 1978 and 1980. Upon his return to NZ, a multidisciplinary team was developed in paediatric nephrology. Between 1980 and 1985, five paediatric renal transplants were undertaken and between 1985 and 1989 a further nine were performed. During the 1980s, Dr Morris developed the PD programme; continuous ambulatory PD then automated PD. During the 1990s, a further 38 transplants were undertaken.

The first renal transplants

History suggests that the first renal transplants were undertaken in France in 1909 and were experimental, involved transplanting animal kidneys into children; both recipients and donors died. While the first successful renal transplant in an adult was performed in 1954, and is well documented, it is difficult to ascertain when the first paediatric transplant was undertaken. It may have been performed in France in the 1960s, but this is not clear. At that time, pediatricians were concerned about the ethics of transplantation in children and there was opinion expressed that it would be like housing kidneys in 'healthy dwarfs'.

The first documented paediatric renal transplant in Australia was undertaken in 1963. In NZ, teenagers were transplanted in Auckland in the 1970s. When Dr Morris first performed renal transplants in NZ in the 1980s, the average age of recipients was 10 years, and those under the age of 5 were excluded until the mid-late 1980s. Patients under two years were not transplanted until the mid 1990s. During the last 10 years, 48 paediatric renal transplants have been undertaken and now those under the age of two years are also being treated.

The mean graft survival at Auckland is 10.7 years (range 6 months to 22 years) and the 1-year survival rate is 94%. Furthermore, 70% of the group who underwent transplant in the first 10 years at Auckland are still alive.

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