Nephrology Research Review™

Making Education Easy

Issue 10 - 2012

In this issue:

Abbreviations used in this issue:

CRF = chronic renal failure
CKD = chronic kidney disease
eGFR = estimated glomerular filtration rate
ESRD = end-stage renal disease
OR = odds ratio

Welcome to the latest edition of Nephrology Research Review.

Highlights this month include findings that patients with CRF have an increased prevalence of co-morbid eye disease. Other interesting studies found that CKD hastens cognitive decline in the elderly, colonoscopy is the best screening test for colorectal cancer in kidney transplant recipients, sirolimus reduces the risk of secondary skin cancers in kidney transplant recipients, and the rate of non-skin cancers in living donors is lower than that in nondonors.

We hope you find this issue interesting and look forward to hearing any feedback you may have.

Kind Regards,

Professor Neil Boudville

neil.boudville@researchreview.com.au

Increased risk of co-morbid eye disease in patients with chronic renal failure: a population-based study

Authors: Wang T et al

Summary: This study examined the prevalence and risk of ocular co-morbidities in patients with CRF. 9,149 patients with CRF were selected from the Taiwan Longitudinal Health Insurance Database and matched with 27,447 control patients who didn't have CRF. Patients with CRF were found to have a significantly higher prevalence of retinal disorders (16.62% vs 9.70%), uveitis (1.38% vs 0.95%), glaucoma (7.56% vs 5.70%), and cataract (33.08% vs 28.90%) than patients without CRF (all p<0.001), but the prevalence of dry eye did not differ between groups. After adjustment for potential confounders, patients with CRF were still more likely to have retinal disorder (OR 1.84), uveitis (OR 1.33), glaucoma (OR 1.48) and cataract (OR 1.24) than patients without CRF. In conclusion, patients with CRF had a higher prevalence of retinal disorders, uveitis, glaucoma and cataract than patients without CRF.

Comment: The relationship between CKD and eye disease has been poorly investigated with this study providing some valuable insight. This study utilises a unique dataset of 1,000,000 people randomly selected in 2000 in Taiwan from which a matched cohort was generated for comparison. The prevalence of eye disease in a group of patients with CKD was compared with randomly selected matched group. Three people were selected for every CKD patient and they were matched for sex, age group and diabetes. This study demonstrated that patients with CKD had a significantly higher prevalence of retinal disorders, uveitis, glaucoma and cataracts. Clearly more investigation is required to explore this association.

Reference: Ophthalmic Epidemiol 2012;19(3):137-43
http://informahealthcare.com/doi/abs/10.3109/09286586.2012.680531

Kidney function and cognitive and functional decline in elderly adults: findings from the Singapore Longitudinal Aging Study

Authors: Feng L et al

Summary: This study investigated whether lower eGFR or CKD are associated with subsequent cognitive and functional decline in older patients. 1315 adults aged ≥55 years who were participating in the Singapore Longitudinal Aging Study were followed for up to 4 years. CKD was defined as eGFR <60 mL/min/1.73m^2, cognitive decline was defined as a ≥2-point drop on the Mini-Mental State Examination (MMSE), and functional decline was defined as a ≥2-point drop in instrumental activity of daily living (IADL) score. Multivariate analysis adjusted for confounding factors showed that decreasing levels of eGFR and the presence of CKD were associated with a greater risk of cognitive decline at follow-up (OR 1.94; p=0.004 for CKD vs non-CKD). The risk of cognitive decline increased in 14% increments for each 10 mL/min/1.73m^2 decrease in eGFR. CKD, but not eGFR, was significantly associated with higher risk of IADL decline. In conclusion, CKD was significantly associated with cognitive and functional decline in older patients.

Comment: I have always wondered if there is a relationship between kidney function and cognition and this study is the largest prospective study to date to explore this. All eligible Singaporean citizens over the age of 55 years were followed for 4 years. This study demonstrated that CKD was associated with a 2.24 unadjusted odds ratio of cognitive decline compared to those without CKD, which maintained significance after adjustment. A similar relationship was seen between CKD and decline in activities of daily living. It is easy to imagine that the comorbidities of CKD that cannot be accounted for in this analysis maybe the mechanism behind this association.

Reference: J Am Geriatr Soc 2012;60(7):1208-1214
http://onlinelibrary.wiley.com/doi/10.1111/j.1532-5415.2012.04043.x/abstract

Contact RESEARCH REVIEW

Email geoff@researchreview.com.au

Phone 1300 132 322

RESEARCH REVIEW™
the Australian perspective

Screening for colorectal cancer and advanced colorectal neoplasia in kidney transplant recipients: cross sectional prevalence and diagnostic accuracy study of faecal immunochemical testing for haemoglobin and colonoscopy

Authors: Collins M et al

Summary: This Australian study determined the prevalence of advanced colorectal neoplasia in a population of average-risk kidney transplant recipients and compared the diagnostic accuracy of faecal haemoglobin testing with that of colonoscopy. 229 kidney transplant recipients aged ≥50 years who were ≥6 months post-transplant (and otherwise at average risk of colorectal cancer) underwent faecal immunochemical testing for human haemoglobin, followed by colonoscopy. Advanced colorectal neoplasia was found in 29 (13%) patients, including 4 (2%) with high grade dysplasia and 5 (2%) with colorectal cancer. Faecal testing for haemoglobin was positive in 28 (12%) patients. Sensitivity, specificity, and positive and negative predictive values of faecal haemoglobin testing compared with colonoscopy were 31.0%, 90.5%, 32.1% and 90.1%, respectively. It was calculated that 8 colonoscopies would be needed to identify 1 case of advanced neoplasia, In conclusion, faecal haemoglobin screening for colorectal neoplasia has poor sensitivity in transplant recipients, so surveillance colonoscopy might be a more appropriate approach.

Comment: This South Australian study compares the diagnostic accuracy of faecal occult blood (FOB) testing with colonoscopy in detecting advanced colorectal cancer in kidney transplant recipients over the age of 50 years. There was a high prevalence of positive findings with 13% of participants having advanced colorectal neoplasia on colonoscopy, and 12% having a positive FOB. Of the 5 patients that were later diagnosed as having cancer, only 3 had a positive FOB, suggesting that FOB testing may not be the best screening test for kidney transplant patients.

Reference: BMJ 2012;345:e4657
http://www.bmj.com/content/345/bmj.e4657

Prevalence and risk factors for colonic perforation during colonoscopy in hospitalized end-stage renal disease patients on hemodialysis

Authors: Navaneethan U et al

Summary: This US study determined risk factors for and prevalence rates of colonic perforation during colonoscopy in ESRD inpatients on haemodialysis. Data for haemodialysis patients who had undergone colonoscopy in 2006 were retrieved from the Nationwide Inpatient Sample. The control group comprised patients without ESRD who underwent colonoscopy. Colonic perforations occurred in 51/17,000 (0.3%) ESRD inpatients on haemodialysis and 3,951/564,428 controls (0.7%). The risk of colonic perforation among ESRD inpatients was not significantly higher than that in controls. Older age (OR 1.007) and female gender (OR 1.18) were identified as independent risk factors for the risk of perforation in ESRD inpatients. In conclusion, ESRD inpatients on haemodialysis were not at increased risk for colonic perforation during colonoscopy.

Comment: There has been some suggestion that colonoscopy may have increased complications in end-stage kidney disease patients. This study utilises an administrative database from a US healthcare payer which covers about 20% of US community hospitals. They demonstrated in their large dataset that the incidence of colonic perforations was not significantly increased in ESRD patients compared to those without ESRD. In addition, undergoing a colonic biopsy did not lead to a differential in perforations between groups. However, the effect of polypectomy could not be assessed.

Reference: Int J Colorectal Dis 2012;27(6):811-6
http://link.springer.com/article/10.1007%2Fs00384-011-1400-8

Long-term follow-up of a randomised controlled trial of azathioprine/methylprednisolone versus cyclophosphamide in patients with proliferative lupus nephritis

Authors: Arends S et al on behalf of the Dutch Working Party on systemic lupus erythematosus

Summary: This long-term follow-up study investigated induction treatment with azathioprine/methylprednisolone versus high-dose intravenous cyclophosphamide in patients with proliferative lupus nephritis (LN). 87 patients with biopsy-proven proliferative LN were randomised to receive azathioprine/methylprednisolone (n=37) or intravenous cyclophosphamide (n=50); all patients also received prednisone. After 2 years, renal biopsy was repeated, and all patients then continued with azathioprine/oral prednisone. After a median follow-up of 9.6 years, the proportion of patients with sustained doubling of serum creatinine (16% vs 8%), ESRD (5% vs 4%) or mortality (16% vs 10%) did not differ significantly between azathioprine/methylprednisolone and cyclophosphamide groups, but renal relapses occurred more often with azathioprine/methylprednisolone (38% vs 10%; p=0.002). Clinical and laboratory parameters at baseline and 2 years, and renal biopsy parameters at baseline, were predictive of renal outcome. In conclusion, azathioprine/methylprednisolone appears to be a useful alternative to intravenous cyclophosphamide for induction in patients with proliferative LN who wish to avoid the adverse gonadal toxicity associated with cyclophosphamide.

Comment: This study is a long-term follow-up of patients originally enrolled in the Dutch Lupus Nephritis Study, where 87 patients with proliferative lupus nephritis were randomised to either azathioprine and methylprednisolone or IV cyclophosphamide for 2 years. Both groups received oral prednisolone and after 2 years the cyclophosphamide group was swapped to azathioprine. The median follow-up in this study was 9.6 years with only 6 participants being lost to follow-up. 11% of patients had a doubling of serum creatinine and 22% had a renal relapse with no significant difference between the two groups. In addition, there was no significant difference in serum creatinine or proteinuria at follow-up, despite the azathioprine group having a higher incidence of renal relapse.

Reference: Ann Rheum Dis 2012;71:966-973
http://ard.bmj.com/content/71/6/966

Sirolimus and secondary skin-cancer prevention in kidney transplantation

Authors: Euvrard S et al for the TUMORAPA Study Group

Summary: This study investigated the use of sirolimus for preventing secondary skin cancers in kidney transplant recipients with previous cutaneous squamous-cell carcinoma. 120 transplant recipients who were taking calcineurin inhibitors and had at least 1 cutaneous squamous-cell carcinoma were randomised to switch to sirolimus (n=64) or to maintain their initial treatment (n=56). During the 2-year follow-up period, 14 (22%) sirolimus recipients and 22 (39%) calcineurin-inhibitor recipients developed new squamous-cell carcinomas (relative risk in the sirolimus group was 0.56; 95% CI 0.32–0.98). Survival free of cutaneous squamous-cell carcinoma was significantly longer in the sirolimus group than in the calcineurin-inhibitor group (median onset of secondary skin cancer was 15 vs 7 months; p=0.02). In conclusion, switching from calcineurin inhibitors to sirolimus had an antitumoral effect in kidney transplant recipients with previous squamous-cell carcinoma.

Comment: 120 prevalent kidney transplant recipients on calcineurin inhibitors and at least one cutaneous squamous cell carcinoma were randomised to either continue their calcineurin inhibitor or to change to sirolimus. After 2 years, the adjusted hazard ratio of a new carcinoma was 0.38 for those on sirolimus, though this did not maintain significance in those with multiple cutaneous squamous-cell carcinoma at baseline. These results suggesting clear benefits when using sirolimus in these patients but they need to be weighed up against the increased adverse events seen with this medication.

Reference: N Engl J Med 2012;367:329-339
http://www.nejm.org/doi/full/10.1056/NEJMoa1204166

Cancer diagnoses after living kidney donation: linking U.S. registry data and administrative claims

Authors: Lentine K et al

Summary: This study determined the prevalence of cancer diagnoses among living kidney donors. Data from the US Organ Procurement and Transplantation Network for 4,650 living kidney donors (1987–2007) were linked to the records of a US private health insurer (2000-2007 claims) to identify postdonation cancer diagnoses. The median time from donation to the end of plan insurance enrollment was 7.7 years, with a median observation period of 2.1 years. Rates of skin cancer among prior living donors in the observation period were similar to those in age- and sex-matched nondonor controls (rate ratio 0.91; 95% CI 0.59–1.40). Rates of total non-skin cancers were significantly lower among donors than controls (rate ratio 0.74; 95% CI 0.55–0.99). Several cases of cancer diagnosis (e.g. uterine and melanoma) were identified in the first year after donation. Prostate cancer diagnosis was significantly more common among living donors than controls (rate ratio 3.80; 95% CI 1.42–10.2). In conclusion, follow-up health assessment of donors is warranted after kidney donation.

Comment: Some publications to date have suggested that the most common cause of death in living kidney donors is due to cancer. Follow-up data however is patchy at best and limited in its time since the donation. This paper utilises the US Organ Procurement and Transplantation Network linked to a national private health insurance providers' administrative database. Living kidney donors that donated between October 1987 and July 2007 and subsequently had a diagnosis of cancer were identified. The median time since donation in this study was 7.7 years. The rate of non-skin cancers was in fact significantly lower in living donors than age- and sex-matched nondonor controls. With respect to organ-specific cancer diagnoses, only prostate cancer was significantly more common in prior donors.

Reference: Transplantation 2012;94(2):139-44
http://tinyurl.com/a64lgb9

Awareness of kidney disease and relationship to end-stage renal disease and mortality

Authors: Whaley-Connell A et al for the Kidney Early Evaluation Program Investigators

Summary: This study determined the association between patient awareness of kidney disease and subsequent ESRD and mortality. 109,285 patients at high-risk for kidney disease were identified from the National Kidney Foundation's Kidney Early Evaluation Program. 28,244 (26%) patients had CKD defined by albuminuria or eGFR <60 mL/min/1.73m^2. Only 2660 (9%) patients were aware they had kidney disease. These participants had lower eGFR (49 vs 62 mL/min/1.73m^2) and a higher prevalence of albuminuria (52% vs 46%), diabetes (47% vs 42%), cardiovascular disease (43% vs 28%), and cancer (23% vs 14%) than those who were not aware. During 8.5 years of follow-up, aware patients had a lower rate of survival for end stage (83% vs 96%; p<0.001) and mortality (78% vs 81%; p<0.001) than unaware patients. Aware patients with CKD remained at increased risk for ESRD (hazard ratio 1.37; p<0.0123) and mortality (hazard ratio 1.27; p<0.0077) compared with unaware patients even after adjustment for demographics, socioeconomic factors, comorbidity, and severity of kidney disease. In conclusion, patients who were aware they had CKD were at a disproportionately high risk for mortality and ESRD.

Comment: The US National Kidney Foundation implemented the Kidney Early Evaluation Program (KEEP) to detect kidney disease among high-risk individuals. Prior to the screen participants were asked if they were aware of their CKD or not. This paper evaluates the outcome of the large cohort of patients that were screened and subsequently demonstrated to have CKD, comparing those that were and were not aware of their CKD prior to screening. 26% of people screened were demonstrated to have CKD, of which only 9% were aware of their disease. Those aware of their CKD were at a more severe stage of CKD and had more risk factors. Despite this, even with adjustment, those aware of CKD had significantly higher mortality and great risk of developing ESRD, suggesting that awareness of CKD on its own may not be sufficient to provide survival benefits.

Reference: Am J Med 2012;125(7):661-669
http://www.amjmed.com/article/S0002-9343(12)00074-5/abstract

Nephrology Research Review™

Independent commentary by Professor Neil Boudville.

Neil is sub-Dean of the Faculty of Medicine at the University of Western Australia, Head of the Department of Renal Medicine at Sir Charles Gairdner Hospital and Medical Director of the WA Home Dialysis Program. His research interests are in living kidney donor outcomes, dialysis and CKD. However, his real interest is snow skiing, and he hopes to complete 10 marathons in 2013 or 2014.

