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Abbreviations used in this issue:

- CKD = chronic kidney disease; eGFR = estimated glomerular filtration rate;
- ESRD = end-stage renal disease; HD = haemodialysis; HR = hazard ratio;
- OR = odds ratio; PUFA = polyunsaturated fatty acids.

Welcome to the latest issue of Nephrology Research Review.

In this issue, real-world evidence supports the cautious use of metformin in patients with type 2 diabetes and CKD, a population-based study compares the use of percutaneous ablation and nephrectomy (partial or radical) for stage T1a renal cancer, and an analysis of the MADRAD study shows that low dialysate potassium concentrations are associated with higher mortality in HD patients, particularly those with high pre-dialysis serum potassium. A meta-analysis reports that psoriasis may be associated with an increased risk for CKD and ESRD, an analysis from the data from the Australia and New Zealand Dialysis and Transplant Registry identifies risk predictors and causes of technique failure within the first year of peritoneal dialysis, and a meta-analysis suggests that peri-operative omega-3 PUFA supplementation may have beneficial effects on vascular access patency in HD patients.

We hope you find these and the other selected studies interesting and look forward to any feedback you may have.

Kind Regards,

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Association of metformin use with risk of lactic acidosis across the range of kidney function

Authors: Lazarus B et al.

Summary: This community-based cohort study examined the association between metformin use and hospitalisation for acidosis in patients with diabetes and a range of kidney function. 75,413 diabetic patients with eGFR data were followed up for a median 5.7 years, during which time 2335 patients were hospitalised with acidosis. Compared with alternative diabetes management, metformin use was not associated with incident acidosis in patients with eGFR 45–59 or 30–44 ml/min/1.73m², but increased the risk of acidosis in patients with eGFR <30 ml/min/1.73m² (adjusted HR, 2.07).

Comment: This large analysis of administrative data supports the more recent recommendations for metformin use in CKD down to an eGFR of 30 ml/min/1.73m² with no evidence of an increased risk of acidosis overall in this population. In contrast, a doubled risk of acidosis was observed in people with an eGFR below 30 treated with metformin. In the absence of data from randomised trials (that do not appear likely in the foreseeable future), these data argue against the use of metformin in people with an eGFR below 30.

Reference: JAMA Intern Med 2018;178(7):903-10
Abstract

Percutaneous ablation versus partial and radical nephrectomy for T1a renal cancer

Authors: Talented A et al.

Summary: This population-based analysis compared the use of percutaneous ablation (PA), partial nephrectomy (PN) and radical nephrectomy (RN) in patients with stage T1a renal cell carcinoma (RCC). 4310 patients who received treatment for T1a renal cancer in 2006–2011 were followed for a median of 52 months for overall survival and 42 months for RCC-specific survival. The 5-year RCC-specific survival rate was 95% vs 98% after PA vs PN, and 96% vs 95% after PA vs RN. The 5-year overall survival rate was 77% vs 86% after PA vs PN, and 74% vs 75% after PA vs RN. Cumulative rates of renal insufficiency 31–365 days after PA, PN, and RN were 11%, 9%, and 18%, respectively. Rates of nonurologic complications within 30 days after the procedures were 6%, 29%, and 30%, respectively. 10% of patients in the PN group had intraoperative conversion to RN, and 7% of patients in the PA group received additional PA within 1 year of treatment.

Comment: The treatment of localised RCCs often involves nephrologists particularly in people with any of reduced kidney function, advanced age or frailty. This observational analysis describes quite reasonable outcomes for people treated with radiofrequency ablation, partial or total nephrectomy and reports similar outcomes overall. It suggests that radiofrequency ablation may have a role in selected patients, particularly those with reduced kidney function and/or where surgery might be very high risk. This would appear to be an ideal opportunity to conduct a randomised trial and generate definitive data.

Abstract
Dialysate potassium and mortality in a prospective hemodialysis cohort

Authors: Ferrey A et al.

Summary: This analysis of data from the MADRAD study investigated the association between dialysate potassium concentration and mortality in 624 haemodialysis patients. Compared with reference dialysate potassium concentrations of 2 mEq/L, adjusted Cox models showed that dialysate potassium concentrations of 1 mEq/L were associated with higher mortality (HR, 1.70) and concentrations of 3 mEq/L were associated with similar mortality (HR, 0.95). In analyses stratified by serum potassium, baseline dialysate potassium concentrations of 1 mEq/L were associated with higher mortality in patients with serum potassium >=5 mEq/L (HR, 2.87) but not in those with serum potassium <5 mEq/L.

Comment: The relationship of potassium levels to the risk of death and other adverse outcomes is an area of great interest in an era where new potassium-lowering drugs have been developed. This is particularly true in haemodialysis patients where the risk of death is markedly increased in the peridialysis period, particularly after the long period, possibly implicating potassium level. This analysis shows that the risk of death was higher in people treated with low-potassium dialysate, especially if they continued to have a serum potassium level above 5 mEq/L. Assessing whether potassium-lowering agents might reduce potassium fluctuations and improve outcomes in dialysis patients would appear to be a priority for the future.


Psoriasis and risk of incident chronic kidney disease and end-stage renal disease

Authors: Ungprasert P & Rakasuk S

Summary: This systematic review and meta-analysis investigated the risk of CKD and ESRD in patients with psoriasis. A search of MEDLINE and Embase identified 4 retrospective cohort studies that evaluated the risk of incident CKD and/or ESRD in 199,808 patients with psoriasis. Pooled analysis of the data showed that the risk of incident CKD and ESRD was significantly higher in patients with psoriasis than in those without psoriasis (pooled ratio ratios, 1.34 and 1.29, respectively).

Comment: Psoriasis is common in the community but has not been widely recognised to be a risk factor for kidney disease. This pooled analysis supports a relationship between psoriasis and both CKD and ESRD, and suggests that further exploration to understand the mechanism would be worthwhile.

Reference: Int Urol Nephrol 2018;50(7):1277-83

Impact of a primary care CKD registry in a US public safety-net health care delivery system

Authors: Tu et al.

Summary: This study examined the impact of a team-based primary care CKD registry on clinical measures and processes of care in patients with CKD. 79 primary care providers and their patients (n=746) were cluster-randomised to a CKD registry or a usual-care registry for 1 year. The CKD registry identified at point-of-care all CKD patients with blood pressure (BP) >140/90mm Hg, those without albuminuria quantification, but no improvement in BP control. This cluster-randomised trial assessed the impact of a point-of-care approach to flagging individuals who were not receiving guideline-based care, and led to a doubling of the number of people receiving renin-angiotensin system (RAS) blockade and having albuminuria quantification, but no improvement in BP control. Finding better ways to implement proven treatments should be a priority area for research in kidney disease.


Risk predictors and causes of technique failure within the first year of peritoneal dialysis

Authors: See E et al.

Summary: This analysis of data from the Australia and New Zealand Dialysis and Transplant (ANZDATA) registry evaluated risk predictors and causes of technique failure within the first year of peritoneal dialysis. 16,748 adult patients who initiated peritoneal dialysis therapy in Australia and NZ in 2000–2014 were included; 4390 of them had early technique failure. Factors associated with increased risk of technique failure included age >70 years, diabetes or vascular disease, prior renal replacement therapy, late referral to a nephrology service, or management in a smaller centre. Asian or other ethnicity and use of continuous ambulatory peritoneal dialysis were associated with reduced risk, as was initiation of peritoneal dialysis in 2010–2014.

Comment: Peritoneal dialysis technique failure is a major limitation of the treatment modality. This analysis from the ANZDATA registry identified a number of factors associated with higher or lower risk of technique failure. Awareness of these factors will help clinicians to mitigate the risk, and support the development of targeted future trials.


Coffee consumption and incident kidney disease: results from the Atherosclerosis Risk in Communities (ARIC) study

Authors: Hu E et al.

Summary: This analysis of data from the ARIC study examined the association between coffee consumption and CKD. 14,209 participants aged 45–64 years were assessed for coffee consumption at visits 1 (1988–1989) and 3 (1993–1995) using food frequency questionnaires. 3845 cases of incident CKD were reported during a median 24 years of follow-up. Men, whites, current smokers, and participants without comorbid conditions were more likely to consume higher amounts of coffee per day. After adjustment for confounding factors, higher categories of coffee consumption were associated with lower risk for incident CKD compared with those who never consumed coffee. Each additional cup of coffee per day was associated with a 3% decline in risk of incident CKD.

Comment: Caffeinistas rejoice! Not only is coffee intake associated with lower risks of diabetes, cardiovascular disease and death (among other conditions), this analysis from the ARIC cohort found that each cup of coffee drunk per day on average was associated with a 3% lower risk of developing CKD. This study cannot prove causality, and mechanistic studies would be of interest, but it certainly gives me comfort as I sit here cradling my precious latte!


Contact

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A randomized trial of a multicomponent intervention to promote medication adherence

Authors: Foster B et al.

Summary: The TAKE-IT trial assessed the efficacy of a clinic-based adherence-promoting intervention in kidney transplant recipients aged 11–24 years at 8 kidney transplantation centres in Canada and the US. Adherence was electronically monitored in all participants during a 3-month run-in, followed by a 12-month intervention. Participants assigned to the TAKE-IT intervention (n=81) could choose to receive text message, e-mail, and/or visual cue dose reminders and met with a coach every 3 months to review adherence data from the previous 3 months. “Action-Focused Problem Solving” was used to address any adherence barriers. Participants assigned to the control group (n=88) met with coaches every 3 months but did not receive any feedback about adherence. Electronic adherence data were available for 64 intervention and 74 control participants. Participants in the intervention group were more likely to take their prescribed medications (OR, 1.66) and were more likely to take them at or near the prescribed time (OR, 1.74) than controls.

Comment: The precious nature of kidney transplants highlights the importance of developing approaches that reduce the risk of graft loss, and medication adherence is a particular problem in this regard in younger individuals. This randomised trial demonstrated that a range of electronic or visual medication reminders led to substantially improved medication adherence and timeliness. Given its simplicity, implementing an approach like this might help reduce preventable graft loss.


Abstract

Omega-3 polyunsaturated fatty acid supplementation to prevent arteriovenous fistula and graft failure

Authors: Viecelli A et al.

Summary: This systematic review and meta-analysis investigated the use of omega-3 PUFAs for preventing arteriovenous fistula and graft failure in adults undergoing haemodialysis. A search of CENTRAL, MEDLINE, and Embase databases identified 5 trials (n=833) that compared peri-operative omega-3 PUFAs supplementation with placebo in patients requiring haemodialysis via arteriovenous fistula or graft. During a median follow-up of 12 months, omega-3 PUFAs supplementation prevented primary patency loss with moderate certainty (relative risk [RR], 0.81). Low quality evidence suggested that omega-3 PUFAs may have had little or no effect on dialysis suitability failure, access abandonment, need for interventions, or all-cause mortality.

Comment: Improving the patency of vascular access is an area of great focus for haemodialysis patients. This comprehensive review found that omega-3 PUFAs supplementation improved vascular access patency. A benefit for dialysis suitability of the access, abandonment or further interventions could not be demonstrated but this may be an issue of study power as the point estimates for these outcomes also suggested possible benefit. It would appear that the use of these agents may be helpful, particularly in high risk patients.


Abstract

Everolimus with reduced calcineurin inhibitor exposure in renal transplantation

Authors: Pascual J et al.

Summary: This multicentre, noninferiority study investigated the efficacy and safety of everolimus after renal transplantation. 2037 de novo kidney transplant recipients were randomised to receive everolimus with reduced-exposure calcineurin inhibitor (CNI), or mycophenolate with standard-exposure CNI. All patients also received induction therapy and corticosteroids. The primary end-point of treated biopsy-proven acute rejection or eGFR <50 ml/min/1.73m² at post-transplant month 12 occurred in 48.2% of patients in the everolimus group and 45.1% of patients in the mycophenolate group (between-group difference was within the 10% noninferiority margin). Treated biopsy-proven acute rejection, graft loss, or death at post-transplant month 12 occurred in 14.9% and 12.5% of patients in the respective groups.

Comment: This large randomised controlled trial compared everolimus with reduced dose CNI to mycophenolate with standard exposure CNI. There was no clear difference in the primary outcome, and discontinuations of everolimus were high at 23%, but there was some evidence of a lower infective risk (cytomegalovirus and BK virus). These data suggest that everolimus may have a role in selected renal transplant recipients.


Abstract

Independent commentary by Professor Vlado Perkovic

Professor Perkovic is Executive Director of The George Institute, Australia, Professor of Medicine at UNSW Sydney, and a Staff Specialist in Nephrology at the Royal North Shore Hospital. His research focus is in clinical trials and epidemiology, in particular in preventing the progression of kidney disease and its complications. He leads several international clinical trials, and has been involved in developing Australian and global treatment guidelines. He has played a central role in the development of an affordable dialysis system, which was a Eureka Prize finalist in 2017. Vlado is a member of the National Health and Medical Research Council Principal Committee on Research Translation, and is on the Board of the Australian Clinical Trials Alliance and the Association of Australian Medical Research Institutes. He is Chair of the International Society of Nephrology Advancing Clinical Trials (ISN-ACT) group; and is a Fellow of the Royal Australasian College of Physicians, and the Australian Academy of Health and Medical Sciences. He serves on the Editorial Boards of a number of leading specialist and general journals, including the Journal of the American Society of Nephrology, Circulation, and the New England Journal of Medicine.


Abstract