Assessment of self-reported prognostic expectations of people undergoing dialysis

Authors: O’Hare A et al.

Summary: The USTATE study evaluated prognostic expectations in dialysis patients. 1434 patients undergoing regular dialysis at 31 nonprofit dialysis facilities in the US were asked to complete a survey (69.5% response rate). Mean age of the 996 respondents was 62.7 years, and 44.0% were women. When asked “How long would you guess people your age with similar health conditions usually live?” – 11.2% of respondents selected a prognosis of <5 years, 15.1% selected 5–10 years, 33.1% selected >10 years, and 40.6% were not sure. In a comparison cohort of 307,602 patients undergoing in-centre haemodialysis, 60.3% died within 5 years, 19.0% died within 5–10 years, and 20.7% lived >10 years. Survey respondents with a prognostic expectation of >10 years (vs <5 years) were less likely to report documentation of a surrogate decision-maker and treatment preferences and to value comfort over life extension, and were more likely to want cardiopulmonary resuscitation and mechanical ventilation.

Comment: This important study suggests many people with ESKD have unrealistic, overly positive views of their likely life expectancy. It also suggests this may in turn be associated with a higher likelihood of aggressive treatment choices. There are serious practical and ethical challenges in translating this research directly into actionable clinical information, but it does suggest that we might consider providing more realistic information to patients with kidney failure, in order to allow them to make informed choices. It will be important to learn whether people with kidney failure would like to hear more realistic (and negative) views of likely prognosis.


Abstract

In this issue, a US study finds that many dialysis patients have overly optimistic prognostic expectations that may affect their care planning. The AMBER trial reports that treatment with the potassium binder patiromer enables patients with resistant hypertension and CKD to stay on spironolactone without developing hyperkalaemia, and a US study suggests that the ASK1 inhibitor selonsertib slows progression of diabetic kidney disease. An Australian cohort study finds that preterm Indigenous infants are highly vulnerable to renal dysfunction and should be monitored long-term, a meta-analysis suggests that a healthy dietary pattern may prevent CKD, and an open-label trial reports that treatment of metabolic acidosis with sodium bicarbonate is safe and improves kidney and patient survival in patients with CKD.

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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Abbreviations used in this issue:
AF = atrial fibrillation; ASK1 = apoptosis signal-regulating kinase 1; CKD = chronic kidney disease; eGFR = estimated glomerular filtration rate; ESKD = end-stage kidney disease; HR = hazard ratio; NOAC = nonvitamin K antagonist oral anticoagulant; RAS = renin-angiotensin system; SGLT2 = sodium-glucose transport protein 2; SOLVD = Studies of Left Ventricular Dysfunction.

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Association of family ratings of quality of end-of-life care with stopping dialysis treatment and receipt of hospice services

Authors: Richards C et al.

Summary: This study determined family-rated quality of end-of-life care in ESKD patients who did or did not stop dialysis treatment before death. Of 3369 patients with ESKD, 937 (27.8%) stopped dialysis before death and 2432 (72.2%) continued dialysis treatment until death. Patients who stopped dialysis were more likely to have been receiving hospice services at the time of death than patients who continued dialysis (58.1% vs 17.7%). Overall, 1701 patients (50.5%) had a family member who responded to the Bereaved Family Survey. Families were more likely to rate overall quality of end-of-life care as excellent if the patient had stopped dialysis before death (54.9% vs 45.9%; \( p = 0.002 \)) or continued to receive dialysis but also received hospice services (60.5% vs 40.0%; \( p < 0.001 \)).

Comment: This study adds to the growing literature that suggests patients and their families are happier with their care if they make active decisions about it, and maintain autonomy. While it is important not to over-interpret the data, they suggest that families of people choosing to stop dialysis will not have more negative views on their care overall.

Reference: JAMA Netw Open 2019;2(10):e1913115
Abstract

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Patiromer versus placebo to enable spironolactone use in patients with resistant hypertension and chronic kidney disease (AMBER)

Authors: Agarwal R et al.

Summary: The use of spironolactone in patients with CKD can be restricted by hyperkalaemia. The AMBER trial evaluated the use of the potassium binder patiromer to enable use of spironolactone in patients with CKD and resistant hypertension. 295 patients with CKD and uncontrolled resistant hypertension were enrolled from 62 outpatient centres in 10 countries and were randomised to receive either placebo or patiromer (8.4g once daily) in addition to open-label spironolactone (starting at 25mg once daily) and their baseline blood pressure medications. Dose titrations were permitted after 1 week (patiromer) and 3 weeks (spironolactone). At week 12, 66% of patients in the placebo group and 86% in the patiromer group were still taking spironolactone at week 12 (\( p < 0.0001 \)). Adverse events were mostly mild or moderate in severity and were reported by 53% and 56% of patients in the placebo and patiromer groups, respectively.

Comment: The role of potassium binders continues to be debated, and currently remains uncertain outside the management of acute hyperkalaemia. This study asks whether people are more likely to be able to stay on spironolactone for uncontrolled hypertension in the setting of CKD if they are randomised to concurrent patiromer, and found that 20% more people could indeed do so. Demonstrating benefits for hard outcomes is likely to be required for regulatory approvals, but will be difficult with these relatively small differences in spironolactone use between arms.

Reference: Lancet 2019;394(10208):1540-50
Abstract

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Rivaroxaban versus warfarin in patients with nonvalvular atrial fibrillation and severe kidney disease or undergoing hemodialysis

Authors: Coleman C et al.

Summary: This study evaluated the efficacy and safety of rivaroxaban compared with warfarin in patients with nonvalvular AF and stage 4 or 5 CKD (or undergoing haemodialysis) in routine practice. 1896 rivaroxaban users (38.7% received a dose <20 mg/day) and 4848 warfarin users were included, of whom 88% had stage 5 CKD or were undergoing haemodialysis. Compared with warfarin, rivaroxaban did not significantly reduce the incidence of stroke/systemic embolism or ischaemic stroke, but was associated with a significant 32% reduction in major bleeding risk.

Comment: The question of the risks and benefits of anticoagulation in advanced CKD is of great interest, and this observational analysis found lower bleeding with NOACs than with warfarin, without differences in stroke. But the study is limited by its non-randomised design. The more important question is still to be whether any anticoagulation is worthwhile in this population.

Abstract

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JINARC is the first and only treatment approved for slowing the progression of Autosomal Dominant Polycystic Kidney Disease (ADPKD).\(^1,2\)

Effects of selonsertib in patients with diabetic kidney disease

Authors: Chertow G et al., for the GS-US-223-1015 Investigators

Summary: This phase 2 trial evaluated the renal effects of the selective ASK1 inhibitor selonsertib in patients with type 2 diabetes and treatment-refractory moderate to advanced diabetic kidney disease. 333 adults were randomised 1:1:1:1 to receive oral selonsertib (2, 6, or 18 mg/day) or placebo for 48 weeks. Although mean eGFR at week 48 did not differ significantly between groups, piecewise linear regression revealed 2 dose-dependent effects of selonsertib: an acute and more pronounced eGFR decline from 0 to 4 weeks (creatinine secretion effect) and an attenuated eGFR decline between 4 and 48 weeks (therapeutic effect). The rate of eGFR decline from week 4 to 48 was reduced by 71% in the 18-mg group relative to placebo. Selonsertib appeared to be safe, with no dose-dependent adverse effects observed over 48 weeks.

Comment: This trial did not find overall renal benefits for the ASK1 inhibitor selonsertib compared to placebo, but the findings suggest a possible benefit that may have been masked by a dramatic effect on creatinine excretion. Whether this translates into long-term benefits remains uncertain, and will be studied in the ongoing MOSAIC trial.


Acute declines in estimated glomerular filtration rate on enalapril and mortality and cardiovascular outcomes in patients with heart failure with reduced ejection fraction

Authors: McCallum W et al.

Summary: This analysis of SOLVD data evaluated the impact of acute decreases in eGFR on mortality and cardiovascular outcomes in 6245 patients with heart failure who were assigned to the trial’s enalapril or placebo arms. Compared with the placebo group, any eGFR decline in the enalapril group after 2 or 6 weeks’ treatment was associated with lower risk of both all-cause mortality and heart failure-related hospitalisation. Using zero percent eGFR after 2 or 6 weeks’ treatment was associated with lower risk of both all-cause mortality and heart failure-related hospitalisation (HR, 0.78).

Comment: Acute eGFR declines seen with RAS blockade (and now with SGLT2 inhibition) often lead to withdrawal of the likely protective therapy, particularly in non-nephrological settings. This analysis of the SOLVD trial of enalapril vs placebo in heart failure adds to the growing literature that suggests acute declines in eGFR are not harmful in the context of RAS blockade. Promulgating this information is an important task for nephrologists, in order to maximise the benefits of these treatments.


Renal dysfunction is already evident within the first month of life in Australian Indigenous infants born preterm

Authors: Sutherland M et al.

Summary: This observational cohort study determined the impact of preterm birth on renal function in Australian Indigenous and non-Indigenous infants. Renal function was assessed at 4–29 days postnatally in 60 Indigenous and 42 non-Indigenous infants born at 24–36 weeks’ gestation. Compared with non-Indigenous infants, Indigenous infants had impaired renal function, with significantly higher serum creatinine, fractional excretion of sodium, and urinary albumin levels after controlling for gestational/postnatal age, sex and birth weight z-score. Renal injury was associated with maternal smoking and postnatal antibiotic exposure.

Comment: This provocative study suggests that abnormalities in kidney function might be present in the first month post birth in Aboriginal and Torres Strait Islander preterm babies, compared to control preterm babies. Accepting that there are risks of residual confounding, the findings suggest that interventions to improve pregnancy care among Indigenous Australians might be needed to reduce the excess burden of kidney disease in this population.

Reference: Kidney Int 2019;96(5):1205-16

Healthy dietary patterns and incidence of CKD

Authors: Bach K et al.

Summary: This meta-analysis evaluated the impact of healthy dietary patterns on CKD incidence. A search of MEDLINE and Embase identified 18 prospective cohort studies that evaluated dietary patterns in 630,108 adults without CKD over a mean 10.4 years. The primary outcome in all studies was the incidence of CKD (eGFR <60 ml/min/1.73m^2). Meta-analysis of the data found that a healthy dietary pattern (higher intakes of vegetables, fruit, legumes, nuts, whole grains, fish and low-fat dairy, and lower intakes of red and processed meats, sodium, and sugar-sweetened beverages) was associated with lower incidences of CKD and albuminuria (odds ratios, 0.70 and 0.77, respectively).

Comment: This meta-analysis of observational studies found a clear relationship between healthy dietary patterns and lower rates of various markers of CKD. While unable to prove causation, and prone to confounding by factors related to socio-economic status, the findings suggest that dietary interventions are worthy of further study in randomised trials among people with CKD.


Treatment of metabolic acidosis with sodium bicarbonate delays progression of chronic kidney disease

Authors: Di Iorio B et al., for the UBI Study Group

Summary: The open-label UBI study investigated whether treatment of metabolic acidosis with sodium bicarbonate improves kidney and patient survival in CKD. 740 patients with stage 3 to 5 CKD and metabolic acidosis were randomised to receive sodium bicarbonate or standard care for 36 months. The mean daily dose of sodium bicarbonate was 1.13, 1.12, and 1.09 mmol/kg/day in the first, second and third year of treatment, respectively. or standard care reached the primary end-point of creatinine doubling (p<0.001), 6.9% and 12.3% of patients in the respective groups started dialysis (p=0.016), and 3.1% and 6.8% of patients in the respective groups died (p=0.004).

Comment: This randomised trial compared open-label sodium bicarbonate to control outcomes in people with stage 3 to 5 CKD. While there are a number of methodological concerns, the results add to the growing literature suggesting potential renoprotective effects in people with CKD. Large, multicentre, high-quality randomised trials are urgently required.

Direct delivery of kidney transplant education to black and low-income patients receiving dialysis

Authors: Waterman A et al.

Summary: This study examined the efficacy of two kidney transplantation education approaches delivered directly to patients. Black and white low-income patients receiving dialysis in Missouri were randomised to 1 of 3 educational conditions: 1) standard care (usual kidney transplantation education provided in dialysis centres); 2) patient-guided Explore Transplant @ Home (4 modules of kidney transplantation education sent directly to patients via print, video, and text messages); and 3) educator-guided Explore Transplant @ Home (the patient-guided intervention plus 4 phone calls with an educator). Patients receiving the educator- and patient-guided interventions had significantly greater knowledge gains of living donor kidney transplantation (LDKT) and deceased donor kidney transplantation (DDKT) than those receiving standard care, and more patients receiving the interventions versus standard care were able to make informed decisions about starting kidney transplantation evaluation, and pursuing DDKT or LDKT.

Comment: This nice trial demonstrates that randomised trials can be a potent tool for developing care strategies and education tools. It found that patient- or educator-based education settings improved their understanding of their options compared to standard care, in a low-income setting. It suggests this approach is likely to be valuable if rolled out more broadly.


PBS eligibility criteria

1. ≥18 years of age and
2. CKD stage 2 or 3 (eGFR 89 to 30 mL/min/1.73m²) at initiation of treatment and
3. Evidence of rapid progression determined by:
   - eGFR decline of ≥5 mL/min/1.73m² in one year or
   - eGFR decline of ≥2.5 mL/min/1.73m² per year over a period of 5 years

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