Nephrology Research Review™

Making Education Easy

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In this issue:

Abbreviations used in this issue:

AKI = acute kidney injury; **BP** = blood pressure; **CABG** = coronary artery bypass grafting; **CKD** = chronic kidney disease; **ESKD** = end-stage kidney disease; **ICU** = intensive care unit; **SBP** = systolic BP.

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Welcome to the latest issue of Nephrology Research Review.

Highlights include a report of the future global burden of ESKD that all nephrologists need to read. This is followed by disappointing findings for an automated, electronic alert system for AKI in hospitalised patients, but positive findings for renal denervation and central iliac arteriovenous anastomosis in patients with resistant hypertension, and for remote ischaemic preconditioning in patients undergoing cardiac surgery.

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

Kind Regards,

Professor Neil Boudville

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Worldwide access to treatment for end-stage kidney disease

Authors: Liyanage T et al.

Summary: This systematic review estimated the global burden of ESKD in the next decade. Medline was searched for observational studies and renal registries, and national experts were contacted for renal replacement therapy (RRT) prevalence data. Poisson regression was then used to estimate the prevalence of RRT for countries without reported data. The gap between needed and actual RRT was estimated, and needs were projected to 2030. In 2010, 2.618 million people received RRT worldwide. The number of patients needing RRT was estimated to be between 4.902 million in a conservative model and 9.701 million in a high-estimate model, suggesting that at least 2.284 million people might have died prematurely because RRT could not be accessed. The largest treatment gaps were seen in low-income countries, particularly Asia (1.907 million people needing but not receiving RRT; conservative model) and Africa (432,000 people; conservative model). Worldwide use of RRT is projected to more than double to 5.439 million people by 2030, with the most growth in Asia (projected 2.162 million).

Comment: While this paper will not directly affect clinical practice in Australia, it is still a critical paper that I believe all nephrologists need to be familiar with. It documents the current state of dialysis and transplantation in the world through an exhaustive search of available data. As such, it demonstrates considerable regional differences and the future potential spectacular growth of ESKD in the world, in particular in our closest neighbours. It is difficult to imagine how we are going to be able to cope with this tsunami unless we have a paradigm shift in how we deliver treatment.

Reference: Lancet 2015;385(9981):1975-1982

Abstract

Automated, electronic alerts for acute kidney injury

Authors: Wilson F et al.

Summary: This study determined whether an automated electronic alert for AKI in hospitalised patients would reduce the severity of AKI and improve clinical outcomes. 1201 patients in hospital with stage 1 or greater AKI were randomly assigned to an AKI alert group (a text-based alert was sent to the covering provider and unit pharmacist in the event of a new AKI) and 1192 were assigned to the usual care group. The primary outcome, a composite of relative maximum change in creatinine, dialysis, and death at 7 days after randomisation, did not differ significantly between groups. Stratification by medical versus surgical admission, and ICU versus non-ICU location, did not alter the results.

Comment: Clinical decision support systems have been shown to improve clinical outcomes in a number of disease states e.g. venous thromboembolism prophylaxis and drug interactions. This is the first randomised trial to test its utility for improving the outcome following AKI. Maybe somewhat surprisingly, in this single-centre study, automated electronic alerts for AKI did not show any improvement in clinical outcomes compared to standard care. In fact, they may have resulted in increased cost. We need to develop alternate ways to manage AKI in the hospital setting.

Reference: Lancet 2015;385(9981):1966-1974
Abstract

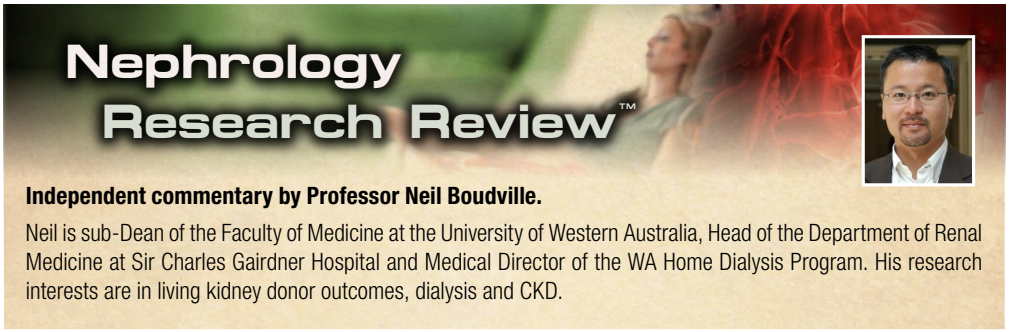
Optimum and stepped care standardised antihypertensive treatment with or without renal denervation for resistant hypertension

Authors: Azizi M et al.

Summary: The Renal Denervation for Hypertension (DENERHTN) trial investigated the BP-lowering efficacy and safety of radiofrequency-based renal denervation added to a standardised stepped-care antihypertensive treatment (SSAHT) in patients with resistant hypertension. 106 patients with confirmed resistant hypertension were randomised 1:1 to receive either renal denervation plus an SSAHT regimen (renal denervation group) or SSAHT alone (control group). For SSAHT, spironolactone 25 mg/day, bisoprolol 10 mg/day, prazosin 5 mg/day, and rilmenidine 1 mg/day were sequentially added if home BP remained ≥135/85mmHg. At 6 months, the mean change in daytime ambulatory SBP was −15.8mmHg in the renal denervation group and −9.9mmHg in the control group (a baseline-adjusted difference of −5.9mmHg; p=0.0329). The number of antihypertensive drugs needed at 6 months did not differ between groups.

Comment: The enthusiasm for renal denervation as a treatment for resistant hypertension was in free-fall following the Symplicity HTN3 trial demonstrating no difference in BP control. Many still believe that it has a role in some patients, however we just don't know who those patients are. This small French study included patients with much lower BP than previous studies (≥135/85 on ambulatory BP monitor), after 4 weeks of triple antihypertensive therapy. A criticism of previous studies has been a lack of introducing adequate additional antihypertensives, especially the use of spironolactone. This study helps to overcome this by using a standardised treatment plan but the dose of spironolactone I think is still lower than I would use for hypertensive patients. They demonstrated a lower BP with renal denervation with the use of the same amount of antihypertensives. Notably some patients seem to respond very well to renal denervation, the problem is we still don't know how to identify these patients.

Reference: Lancet 2015;385(9981):1957-1965
Abstract



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.

Central arteriovenous anastomosis for the treatment of patients with uncontrolled hypertension

Authors: Lobo M et al., for the ROX CONTROL HTN Investigators

Summary: This study investigated the use of a central iliac arteriovenous anastomosis in patients with uncontrolled hypertension. 83 patients (baseline office SBP ≥140mmHg and average daytime ambulatory BP ≥135/85mmHg despite antihypertensive treatment) were randomised to undergo implantation of an arteriovenous coupler device in addition to current antihypertensive treatment or to maintain current treatment alone (control group). At 6 months, mean office SBP had decreased by 26.9mmHg in the arteriovenous coupler group (p<0.0001) and by 3.7mmHg in the control group (p=NS); mean 24h ambulatory SBP had decreased by 13.5mmHg (p<0.0001) and 0.5mm Hg (p=NS), respectively. 29% of patients who received the arteriovenous coupler developed late ipsilateral venous stenosis; this was treatable with venoplasty or stenting.

Comment: This study examines a novel intervention for controlling hypertension. This intervention produces a 4mm arteriovenous anastomosis between the external iliac vein and artery. In this small randomised controlled trial, antihypertensive medication doses were left unchanged for the 6-month follow-up period. At the end of follow-up there was a significant reduction in BP with the intervention group but there was no sham-group and numbers are small so further larger trials are required before there is widespread use of this treatment option. In addition, examination of the relatively common complication of venous stenosis needs exploration.

Reference: Lancet 2015;385(9978):1634-1641
Abstract

Effects of acute kidney injury and chronic kidney disease on long-term mortality after coronary artery bypass grafting

Authors: Han S et al.

Summary: This retrospective study examined the impact of AKI and CKD on long-term mortality in patients undergoing coronary artery bypass grafting (CABG). Outcomes for 1,899 patients undergoing CABG were reviewed. The presence of AKI, CKD, or both increased the hazard ratios for mortality compared with the absence of both: hazard ratios were 1.84 for AKI alone, 2.46 for CKD alone, and 3.21 for AKI and CKD together. The impact of AKI was primarily on early mortality (particularly within 3 years), whereas CKD had a relatively constant effect over time. AKI and CKD were found to have a synergistic additive effect on early mortality.

Comment: This study examines the differential effect of AKI and CKD on mortality following CABG, comparing it to one another (AKI in 633 out of 1899; CKD in 217 out of 1682) and in combination (101 had both AKI and CKD). The combination of AKI and CKD was associated with an increased mortality compared to the presence of either AKI or CKD alone. In addition, even with recovery of AKI outcomes were worse than if AKI did not happen.

Reference: Am Heart J 2015;169(3):419-425
Abstract

Effect of remote ischemic preconditioning on kidney injury among high-risk patients undergoing cardiac surgery

Authors: Zarbock A et al., for the RenalRIPC Investigators

Summary: This German study examined whether remote ischaemic preconditioning reduces the rate and severity of AKI in patients undergoing cardiac surgery. 240 patients due to undergo cardiac surgery at 4 hospitals in Germany who were considered to be at high risk for AKI (Cleveland Clinic Foundation score ≥6) were randomised to receive remote ischaemic preconditioning or sham remote ischaemic preconditioning (control). They then completed follow-up 30 days after surgery. The primary end-point was the rate of AKI within the first 72 hours after cardiac surgery. Remote ischaemic preconditioning significantly reduced the rate of AKI compared with controls (37.5% vs 52.5%; p=0.02). It also reduced the need for renal replacement therapy (5.8% vs 15.8% of patients; p=0.01), and intensive care unit stay (3 vs 4 days; p=0.04). It had no effect on myocardial infarction, stroke, or mortality rates.

Comment: The potential benefits of remote ischaemic preconditioning have been considered for many years, even though the mechanism behind how it could achieve this is unknown. This randomised controlled clinical trial provides enticing evidence that it may indeed have a role in significantly reducing AKI, ESKD and ICU hospitalisation within 72 hours post-cardiopulmonary bypass. This does need to be followed up by another larger clinical trial and consideration for exploration in other conditions, such as post-transplantation.

Reference: JAMA 2015;313(21):2133-2141
Abstract

Comparison of different interdialytic intervals among hemodialysis patients on their echocardiogram-based cardiovascular parameters

Authors: Obokata M et al.

Summary: This study tested the hypothesis that a long interdialytic interval (IDT) alters echocardiographic parameters at rest and during exercise compared with other IDTs in stable maintenance haemodialysis (HD) patients. Echocardiograms for 80 stable Japanese outpatients on thrice weekly maintenance HD were assessed at 3 different IDTs: just after HD, after short IDT (1 day), and after long IDT (2 days). Resting left ventricular end-diastolic volume index and stroke volume index were larger after a 1-day IDT than just after HD, and were even larger after a 2-day IDT. End-systolic elastance (Ees), arterial elastance (Ea) and Ea/Ees ratio at rest were similar after short and long intervals, but stroke work (SW) and pressure-volume area (PVA) were higher after the long interval. During handgrip stress testing, a significant increase in Ea without a corresponding rise in Ees was seen only after long IDT. This resulted in decreased stroke volume index, SW, and SW/PVA efficiency.

Comment: This study performed resting and handgrip stress echocardiograms on 80 HD patients immediately after, 48 hours and 72 hours post-HD. The findings for this study suggest that resting cardiac function is no different at all these 3 intervals. However, there was some evidence to suggest that oxygen consumption increased and there was deterioration in exercise-induced echocardiogram changes during the long break. These findings may provide some reason for the increased cardiovascular events reported during the long break.

Reference: Am Heart J 2015;169(4):523-530
Abstract

Randomized clinical trial of dialysate cooling and effects on brain white matter

Authors: Eldehni M et al.

Summary: This study investigated whether the use of cooled dialysate could provide protection against haemodialysis-associated brain injury. 73 haemodialysis patients were randomised to dialyse with a dialysate temperature of either 37°C or 0.5°C below the core body temperature, and were followed up for 1 year. Brain white matter microstructure was assessed using diffusion tensor magnetic resonance imaging, and intradialytic haemodynamic stress was quantified using the extrema points analysis model. Haemodialysis patients exhibited a pattern of ischaemic brain injury (increased fractional anisotropy and reduced radial diffusivity). Changes in brain white matter were associated with haemodynamic instability. Patients who dialysed at 0.5°C below core body temperature showed complete protection against white matter changes at 1 year.

Comment: Another thought-provoking Chris McIntyre study challenging the things we do every day. Results suggest a simple change in what we do, cooling dialysate to 0.5°C below core body temperature may protect against brain injury and improve haemodynamics. An intervention ripe for a large scale clinical trial.

Reference: J Am Soc Nephrol 2015;26(4):957-65
Abstract

Association of mortality risk with various definitions of intradialytic hypotension

Authors: Flythe J et al.

Summary: This study investigated the associations between commonly used intradialytic hypotension (IDH) definitions and mortality. Data from 1409 patients in the HEMO Study and 10,392 patients from a single large dialysis organisation were analysed. IDH definitions were selected from a review of the literature. For each definition, patients were characterised as having IDH if they met the corresponding definition in at least 30% of baseline exposure period treatments. Overall and within subgroups of patients with predialysis SBP <120 or 120–159mmHg, an absolute nadir SBP <90mmHg was most potently associated with mortality. Within the subgroup of patients with predialysis SBP ≥160mmHg, nadir SBP <100mmHg was most potently associated with mortality.

Comment: IDH is a common phenomenon for all dialysis units but there have been multiple definitions of what IDH is. This study utilised data from the old HEMO study to examine various definitions that have been used previously. They found that a nadir SBP <90mmHg (even without symptoms) was the definition most strongly associated with mortality. Indeed, symptoms of IDH did not seem to predict mortality. A standardised definition for IDH is essential to enable intervention studies to try and reduce this adverse event.

Reference: J Am Soc Nephrol 2015;26(3):724-34
Abstract

