

RENAL PHYSICIANS ASSOCIATION



2017 ANNUAL
MEETING March 17-19

Nashville

The Year in Nephrology: Key Papers in 2016

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Sunday, March 19, 2017, 11:00am



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Lessons from 2016 with High Likelihood of Affecting Clinical Practice

Hypertension

Chronic Kidney Disease

Glomerulonephritis

Acute Kidney Injury

CKRD & Dialysis

Transplantation

Hypertension



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PE-3

trial to evaluate whether blood pressure reduction reduces the risk of CV events in patients with intermediate risk and lower blood pressure.

randomly assigned 12,705 subjects with intermediate risk, no CV dz to 2 groups: Candesartan 8mg/day + HCTZ 12.5mg/day vs. placebo

1st coprimary outcome: death from CV causes, nonfatal MI, or nonfatal stroke. Second primary outcome: also included cardiac arrest, heart failure, revascularization
The median follow-up was 5.6 years.

Therapy with candesartan + HCTZ was not associated with a lower rate of major CV events than placebo among persons at intermediate risk who did not have CV disease.

This result is different from SPRINT, perhaps b/c blood pressures were taken differently.

N Engl J Med 2016; 374: 2009-2020.

Chronic Kidney Disease

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empagliflozin

EMPA-REG OUTCOME trial [NEJM 2015; 373]

Randomized >7000 type 2 diabetics to empagliflozin vs. placebo, in addition to standard treatment
Empagliflozin significantly reduced all-cause mortality, CV mortality, and hospitalization from heart failure

POST HOC analysis in subset of patients with prevalent kidney disease from EMPA-REG OUTCOME [NEJM 2016; 375]

Studied long-term effects of empagliflozin on the progression of kidney disease
Pts in the empagliflozin arm had a 39% reduction in new onset or worsening nephropathy
Common adverse events were UTIs and genital infections

SUMMARY:

SGLT2 inhibitors have shown mortality benefit (both all-cause and CV mortality)
SGLT2 inhibitors appear to be safe and tolerable in pts with CKD at baseline

Finerenone in Diabetic Nephropathy

3rd generation highly selective nonsteroidal mineralocorticoid antagonist

[Lipatopoulos Eur Heart Journal, 2016; 37]

Randomized patients with CHF, Type 2DM, and CKD to finerenone vs. eplerenone

Pts in the finerenone 10-20mg dose had the greatest reduction of the composite outcome [death from any cause, CV hospitalization, or emergency presentation to a hospital]

Incidence of hyperkalemia (serum potassium > 5.6 mmol/L) was 4.3%, and equally distributed between the groups

SUMMARY: Finerenone is a new MR antagonist that may treat proteinuria as well as improve CV outcomes in type 2 diabetics

Metformin in Advanced CKD

Risks of adverse outcomes in CKD remain controversial, particularly lactic acidosis

April 8, 2016 Revised FDA warning

Metformin can be used safely in mild renal impairment as well as in some patients with moderate kidney dysfunction

Use of metformin is contraindicated in pts with $eGFR < 30 \text{ mL/min/1.73 m}^2$

RTUE-CKD Trial

trial to study the individual and combined effects of paricalcitol and dietary sodium restriction on residual albuminuria in CKD.

Multicenter, randomized, placebo-controlled crossover trial in which 45 patients with nondiabetic CKD stages 1-3 and albuminuria > 300 mg/24 hr despite ramipril at 10 mg/d and BP < 140/90 mmHg were treated for 4 8-week periods with paricalcitol or placebo, each combined with a low sodium diet or a regular sodium diet.

Moderate sodium restriction substantially reduced residual albuminuria, and the additional effect of paricalcitol was small and nonsignificant.

J Am Soc Nephrol. 2016

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Glomerulonephritis



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Rituximab in IgA nephropathy [Lafayette RA JASN 2016]

The goal of the trial is to determine whether depleting antibody-producing B cells with Rituximab improves outcomes in IgA nephropathy.

This is an open label, multicenter study of 34 adult patients with biopsy-proven IgA nephropathy and proteinuria > 1gm/day, randomized to maintenance with an ACE-inh or to rituximab.

Primary outcome measures included change in proteinuria and change in GFR.

At 1-year of follow-up, Rituximab did not alter the level of proteinuria compared to baseline or the control group.

Rituximab therapy did not significantly improve renal function or proteinuria assessed over 1 year.

Acute Kidney Injury



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Initiation of RRT in the ICU

Goal of the study was to compare early versus delayed renal-replacement initiation in patients with severe acute kidney injury.

The trial assigned 620 patients with Stage 3 severe acute kidney injury who required mechanical ventilation, catecholamine infusion, or both, and did not have a potentially life-threatening complication directly related to renal failure to either an early or a delayed strategy of renal-replacement therapy.

Kaplan-Meier estimates of 60 day mortality did not differ significantly between early and delayed therapy strategies

A total of 151 patients in the delayed-strategy group did not receive renal-replacement therapy

The rate of blood stream infections was higher in the early-strategy group than in the delayed-strategy group.

Conclusion: a delayed strategy averted the need for renal-replacement therapy in an appreciable number of patients.

N Engl J Med. 2016. 375:122-33.

1: Spironolactone and Cardiac Surgery

The goal of this study was to test whether short-term peri-operative administration of oral spironolactone could reduce the incidence of AKI in cardiac surgical patients.

A double-blinded placebo-controlled trial of 233 patients randomized to spironolactone at a dose of 100mg 12-24 hours before surgery and 3 doses of spironolactone 25mg on postoperative days 1, and 2, vs. placebo at each of those times.

The primary Endpoint was AKI incidence defined by KDIGO criteria. Secondary endpoints included need for RRT, ICU length of stay, and ICU mortality.

The incidence of AKI was higher for the spironolactone group. No significant differences were found for secondary endpoints.

ESRD & Dialysis



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Patiromer (Veltassa) in HD patients

The purpose of this study was to examine the effect of Patiromer, a gastrointestinal potassium binder, on serum K in HD patients.

Six hyperkalemic patients (5 anuric) were admitted to clinical research units for 15 days (1 pretreatment week and 1 patiromer treatment week), where they received a controlled diet.

Mean serum K⁺ levels decreased (maximum change 0.6 ± 0.2 mEq/l, and fecal K⁺ increased 20% during the treatment week.

Patiromer, Phos decreased from 7.0 ± 0.5 to 6.2 ± 0.5 mg/dl.

One patient discontinued patiromer because of adverse events, and there were no serious adverse events.

Conclusion: In 6 hyperkalemic HD patients, patiromer decreased serum K and Phos levels and increased fecal K.

Am J Nephrol. 2016;44:404-410.

TES Central Venous Catheter Study

randomly assigned a nontunnelled central venous catheter site in over 3000 adults treated in intensive care units, in France.

The subclavian site was associated with a lower rate of short-term complications, including catheter-related bloodstream infection and deep venous thrombosis, compared to the femoral or internal jugular site.

Implications for Nephrologists – need to be aware of this study, and the need to continue to advocate for alternatives to subclavian vein catheter placement in patients with CKD who are expected to require AV access for dialysis in the future.

N Engl J Med. 2015. 373:1220-1229.

Remodiafiltration and Mortality in End-stage Kidney Disease Patients

Goal of the study was to evaluate whether the additional clearance of larger toxins with HDF improved survival.

Study is a pooled individual participant data analysis of 2793 patients from four trials that compared online HDF with HD.

Over a median follow-up of 2.5 years, online HDF reduced the risk of all-cause mortality by 14% and cardiovascular mortality by 23%.

Nephrol Dial Transplant. 2016. 31:978-984.

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Ergocalciferol Supplementation in HD Patients with Vitamin D Deficiency

Goal of the trial is to assess the effects of supplementation with ergocalciferol on epoetin repletion and other secondary outcomes in patients on HD with serum 25(OH)D < 30 ng/ml.

Design: double-blind, placebo-controlled, randomized clinical trial of 276 patients randomized to 6 months of ergocalciferol or placebo.

Mean serum 25(OH)D increased from 16.0 ± 5.9 ng/ml at baseline to 39 ± 14.9 ng/ml in the ergocalciferol arm, with no change in the placebo arm.

There was no significant change in epoetin dose over 6 months in either arm.

Rates of all-cause, cardiovascular, and infection-related hospitalizations did not differ by study arm.

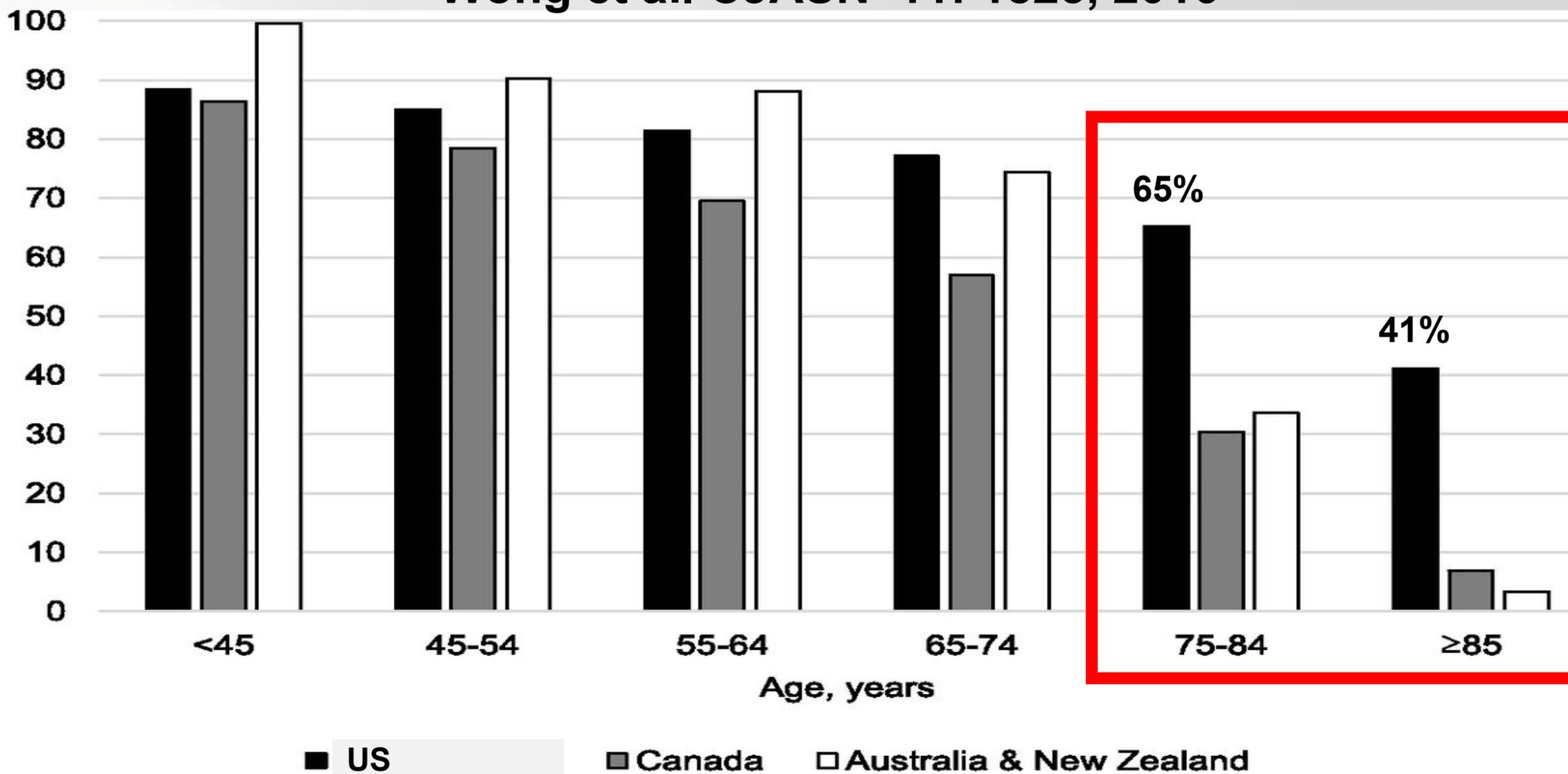
Conclusion: 6 months of supplementation with ergocalciferol increased serum 25(OH)D levels in patients on hemodialysis with Vit D insufficiency or deficiency, but had no effect on epoetin repletion or secondary biochemical and clinical outcomes.

J Am Soc Nephrol. 2016, 27:1801-10.

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International differences in use of RRT among patients with advanced CKD

Wong et al. CJASN 11: 1825, 2016



Does not include VA patients who have private insurance or MA.

Transplantation



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Hepatitis C and Renal Transplant

Background: HCV infection in kidney transplant patients reduces long-term patient and graft survival.

The University of Utah developed a protocol to allow HCV-infected pts with ESRD to receive interferon-free direct acting antiviral therapy after transplantation.

Sample of 12 HCV-positive pts listed for transplant, of those 7 received HCV-positive deceased donor kidney, and 1 received an HCV-negative organ.

Three to six months after transplant, 6 patients completed treatment and all achieved a sustained response, with one patient currently awaiting transplant.

7 patients have functioning kidney grafts.

Conclusions:

HCV-positive patients with ESRD can successfully receive an HCV-positive donor's kidney.

Once transplanted, these patients can receive DAA therapy and achieve SVR.

Use of HCV-positive organs reduced time on the waitlist by greater than three years and expanded donor organ pool.

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opra T, Rosner M. Recent Advances in CKD and ESRD: A literature update. Hemodialysis International 2017; 21:11-18.

lleagues at Vanderbilt

Dr. Lewis, Dr. Burgner, Dr. Siew (AKI)

edScape emails: “Journal Articles read most by Nephrologists in 2016”

phMadness 2017: <https://ajkdblog.org/tag/nephmadness2017/>

Additional Slides



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SPRINT Trial Intensive vs. Standard BP Control

Study population: SBP > 130mmHg, Age > 50

Excluded: diabetics, prior stroke, PKD, severe HTN

Randomly assigned 9362 pts to SBP target \leq 120mmHg or \leq 140mmHg

Intervention stopped early (median 3.26 years) because of significantly lower rate of primary composite outcome: MI, ACS, stroke, heart failure, CV death, in more intensive group

Higher rate of serious adverse events in more intensive group: hypotension, syncope, electrocardiogram abnormalities, AKI