Canadian Society of Nephrology/
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Abstracts - Oral Presentation

Friday May 13th, 2016 / 15:30 – 17:00 / WTCC-Room 200E

O-001

HDAC6 INHIBITION PREVENTS AGGRESOME ACCUMULATION AND PRESERVES KIDNEY FUNCTION IN CHRONIC KIDNEY DISEASE

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Background
Cellular pathways that are similarly perturbed in experimental rodents and humans, resistant to conventional therapy and dysregulated in multiple disease states represent ideal treatment targets to slow renal decline in chronic kidney disease (CKD).

Objectives and Methods
Here we combined bioinformatic analyses, disease association studies and a pharmacological intervention to identify, validate and test the efficacy of a novel treatment in CKD.

Results
Using a bioinformatic strategy that combines transcriptomic changes with protein-protein interactions, we discovered that pathways common to multiple neurodegenerative diseases are enriched in the kidneys of people with diabetic nephropathy and Type 2 diabetic db/db mice despite "standard-of-care" therapy with renin-angiotensin system blockade. A common feature of neurodegenerative diseases is the pathological formation of aggresomes, misfolded protein aggregates that cannot be disposed of by the ubiquitin-proteasome system. To determine the extent of aggresome formation in CKD, we probed kidney sections from humans and multiple experimental models for the aggresome marker p62, observing an increase in staining in humans with diabetic kidney disease, subtotally nephrectomized (SNx) rats, streptozotocin-diabetic mice and db/db mice (where it was unaffected by ACE inhibition, despite attenuation of albuminuria). Finally, we administered an inhibitor of a pivotal regulator of aggresome formation, HDAC6 to SNx rats (a rodent model that develops GFR decline analogous to humans with CKD) and observed an attenuation of p62 accumulation, proteinuria, glomerulosclerosis and tubulointerstitial fibrosis.

Conclusions
Pathways that are typical of neurodegenerative diseases and associated with aggresome accumulation are also active in CKD, where they may contribute to the development of renal dysfunction. In an experimental model of progressive proteinuric kidney disease, a pharmacological strategy that prevented aggresome accumulation also attenuated renal injury. These observations suggest that therapeutic approaches that redirect the misfolded protein response may slow renal decline in CKD.

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O-002

DONOR-RECIPIENT WEIGHT MISMATCH AND THE RISK OF GRAFT LOSS IN RENAL TRANSPLANTATION

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Background: Relatively smaller kidney donor to recipient size is proposed to result in increased graft loss due to nephron underdosing and hyperfiltration injury but few studies have investigated the outcomes associated with donor-recipient body weight mismatching. The purpose of this study was to determine if donor and recipient absolute weight mismatch was associated with graft loss in a cohort of deceased donor kidney transplant recipients.

Methods: The relationship between kidney donor and recipient absolute body weight difference and death-censored graft loss was explored using a cohort of United States deceased donor recipients between 2000-2014 through the Scientific Registry of Transplants Recipients (SRTR). Absolute weight differences between donor and recipient were categorized as >30 kg, 10-30 kg, or <10 kg. Time to death-censored graft loss was evaluated using multivariable Cox Proportional Hazards models adjusting for known literature predictors of graft loss.

Results: 21,261 of 115,124 kidney transplant recipients developed death-censored graft failure, (median graft survival time was 3.8 years (Q1-Q3 0.0-14.8 years)). After multivariable adjustment for donor, immunological, surgical and recipient factors, a weight difference of >30 kg (donor<recipient) was associated with an increased risk of graft loss (relative hazard 1.25, 95% confidence interval 1.19-1.31). The highest risk was observed with sex mismatch between donor and recipient and concurrent absolute weight difference of >30 kg (donor<recipient).

FIGURE 1

Conclusions: A mismatch in donor and recipient weight (donor<recipient) is associated with an increased risk of death-censored graft loss. This knowledge may better inform the selection of recipients for deceased donor kidney transplant.

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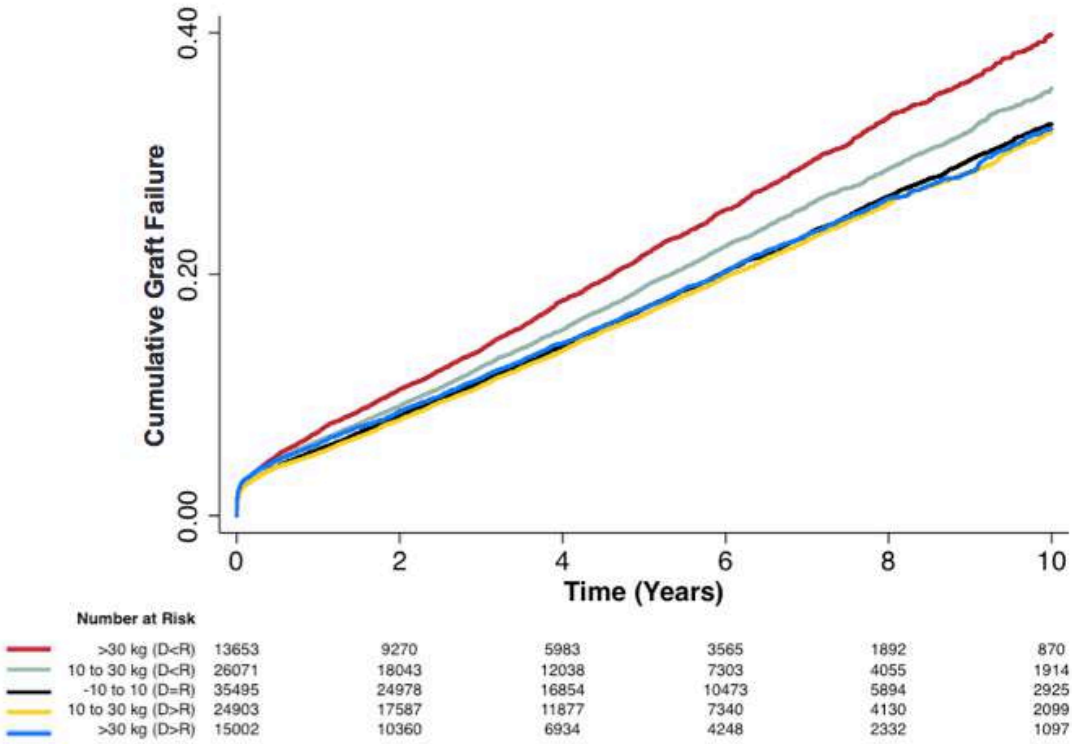
O-002



Number at Risk

>30 kg (D<R)	13653	9270	5983	3565	1892	870
10 to 30 kg (D<R)	26071	18043	12038	7303	4055	1914
-10 to 10 (D=R)	35495	24978	16854	10473	5894	2925
10 to 30 kg (D>R)	24903	17587	11877	7340	4130	2099
>30 kg (D>R)	15002	10360	6934	4248	2332	1097

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O-003

THE COST-EFFECTIVENESS OF PRIMARY SCREENING FOR CHRONIC KIDNEY DISEASE IN RURAL AND REMOTE FIRST NATIONS

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Background: Chronic Kidney Disease (CKD) is a risk factor for cardiovascular disease, early mortality, and kidney failure. First Nations (FN) are at increased risk of CKD and its associated complications. The cost-effectiveness of screening for CKD and treatment in FN or other high-risk indigenous populations has not been described.

Methods: We constructed a Markov model comparing screening in adult FN for CKD by both proteinuria and eGFR to usual care from the perspective of the health care payer. Patients were assigned an initial risk classification based on urine albumin-to-creatinine ratio and eGFR using the Kidney Disease Improving Global Outcomes (KDIGO) heat map. We obtained screening tests results on 1346 participants from the First Nations Community Based Screening to Improve Kidney Health and Prevent Dialysis (FINISHED) initiative. Our analysis was further stratified into communities accessible by road and communities accessed by air travel. Our primary outcome of interest was the incremental cost per quality-adjusted life-year (QALY).

Results: Overall prevalence of CKD in FN was 26.7%. Screening for CKD was associated with an ICER of $33,500/QALY in comparison to usual care. Restricting the model to screening in the remotest air access communities (prevalence of CKD 36.0%), this ratio fell to an ICER of $16,180/QALY. In less remote road access communities (CKD prevalence 18.4%) this ICER was $63,780/QALY. Primary model drivers included the cost of dialysis, assumed treatment effectiveness, and rates of progression towards kidney failure.

Conclusions: Targeted screening for CKD in rural and remote First Nations is likely cost-effective. These findings may be translatable to other high-risk indigenous groups with elevated rates of CKD and kidney failure.

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O-004

POTENTIAL BIOMARKERS AND TREATMENTS FOR BK VIRUS INDUCED FIBROSIS: A MECHANISTIC APPROACH

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Background: BK polyomavirus (BKV) reactivation in kidney transplants is associated with significant fibrosis. It is important to study the mechanism of fibrogenesis due to BKV.

Objective: To determine key epigenetic mechanisms regulating the expression of genes involved in BKV induced fibrosis and necroptosis, and to assess DNA methyl transferase 1 (DNMT1) as a potential therapeutic target.

Methodology: Human Proximal Tubular Epithelial Cells (HPTCs) were infected with BKV and RNA/DNA was isolated. Gene expression was studied with RT-PCR and hypermethylation of promoters assessed by Bisulfite Sequencing (BS) and Methylation Specific PCR (MSP). Flow-cytometry assays and Western blots were done to study necroptosis.

Results: BS and MSP showed hypermethylation in the promoters of E-cadherin and Collagen IV genes following BKV infection. As expected with increases in DNA methylation, both collagen IV (COLIVA1) and E-cadherin (CDH1) gene expression was downregulated (p-value<0.029). Collagen I, however, was increased. Loss of E-Cadherin, a decrease in the basal membrane collagen component, and increases in collagen I all favour the process of epithelial to mesenchymal transition (EMT). BKV increased the expression of DNMT1, suggesting a mechanism of increased methylation. Treating BKV infected cells with DNMT1 inhibitor RG108 increased transcription of COLIVA1 (mean factor of 40.368).

BKV induced necroptosis was inhibited with Necrostatin-1. BKV infection increased the expression of Receptor-interacting serine/threonine-protein kinase 3 (RIPK3), phospho-Mixed Lineage Kinase Like pseudokinase (pMLKL) and High Mobility Group Protein B1 (HMGB1). Treatment of BKV infected cells with RG108 reduced the expression of these genes, conferring that BKV may induce necroptosis epigenetically in renal tubular cells.

Conclusion: Our results suggest that BKV epigenetically induces EMT and necroptosis in HPTCs. RG108 inhibits DNMT1 and prevents these epigenetic events. Further studies of DNMT inhibitors as potential treatments in BK virus induced fibrosis are warranted.

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O-005

CHRONIC KIDNEY DISEASE IN RURAL AND REMOTE INDIGENOUS CHILDREN: RESULTS FROM MANITOBA'S FINISHED SCREEN/TRIAGE/TREAT PROGRAM

Allison Dart (1), Barry Lavallee (1), Caroline Chartrand (2), Lorraine McLeod (2), Claudio Rigatto (1), Thomas Ferguson (1), Audrey Gordon (3), Navdeep Tangri (1), Tom Blydt-Hansen (4), Paul Komenda (1)
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(3) Winnipeg Regional Health Authority
(4) University of British Columbia

Background: Indigenous populations have high rates of chronic kidney disease (CKD), and progress to end-stage at a younger age. We aimed to evaluate the prevalence of CKD and associated risk factors in youth from the The First Nations Community Based Screening to Improve Kidney Health and Prevent Dialysis (FINISHED) project.

Methods: After community engagement, an interdisciplinary team screened for CKD risk in 11 rural and remote Manitoba communities in 2014/15 including blood pressures, urine albumin-to-creatinine ratios (ACRs), CKiD Schwartz eGFRs and hemoglobin A1cs (A1cs). The results for children (ages 10 – 17) are reported here.

Results: 353 youth were screened, with a median age of 12 years (IQR 10 – 13). Fifty-five percent of youth were overweight or obese, and 21.2% were identified with hypertension, CKD and/or diabetes. A total of 15% of the screened cohort had CKD including 10.5% with an ACR >3mg/mmol and 6.2% with an eGFR <90ml/min/1.73m^2. In addition, 5.4% had hypertension and 11.9% had pre-hypertension. Diabetes was identified in 1.4%, and an additional 1.4% had A1cs between 6.1 and 6.49%. Although 32% of the overweight/obese group had hypertension or CKD, 61% of the group with albuminuria had no risk factors.

Conclusions: Early CKD and associated risk factors are highly prevalent in youth in rural and remote First Nation communities. The early onset of risk likely contributes to the younger age of end stage kidney disease in this population. Evaluation of the efficacy of screening and intervention strategies in Indigenous children is needed to address this population health issue.

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O-006

COGNITIVE IMPAIRMENT IN ADVANCED CKD: THE CANADIAN FRAILTY OBSERVATION AND INTERVENTIONS TRIAL (CANFIT)

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Background: Chronic kidney disease (CKD) affects more than one third of older adults, and is a risk factor for vascular disease and cognitive impairment. Cognitive impairment can have detrimental effects on quality of life through decreased treatment adherence, poor nutrition, and results in increased costs of care and early mortality. Little is known about cognitive decline in patients with pre-dialysis CKD.

Methods: We aimed to determine the prevalence and risk factors for cognitive impairment in patients with CKD stages 4-5 (non-dialysis). Cognitive function was measured with a validated tool called the Montreal Cognitive Assessment as part of a comprehensive frailty assessment in the Canadian Frailty Observation and Interventions Trial (CanFIT). Participants in this multicenter study included patients with CKD stages 4-5 attending one of four Canadian renal health clinics. Cognitive impairment was defined as a MoCA score of ≤ 24.

Results: We studied 500 participants with CKD Stages 4-5 and found that 60.2% (301/500) had cognitive impairment. When compared to controls, participants scored lower in all domains of cognition, with pronounced deficits observed in recall, attention, and visual/executive function ($p<0.01$ for all comparisons). Older age, recent history of falls, and a history of stroke were independently associated with cognitive impairment.

Conclusions: Our study uncovered a high rate of unrecognized cognitive impairment in an advanced CKD population. This impairment is global, affecting all aspects of cognition and is likely vascular in nature. The longitudinal trajectory of cognitive function and its effect on dialysis decision making and outcomes deserves further study.

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P-007

ARE HOME BLOOD PRESSURE DEVICES ACCURATE? A SYSTEMATIC REVIEW OF THE EVIDENCE

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BACKGROUND: Hypertension is a major risk factor of Kidney diseases. Little data exist on the accuracy of home blood pressure (BP) device in actual use. We undertook this systematic review to summarize the accuracy of home BP monitors as reported in the literature.

METHODS: We undertook a literature search of MEDLINE and EMBASE from 1946 and 1947 respectively, until April 2015. Studies were included if they compared BP values measured by a home device with those measured by a gold standard device (mercury sphygmomanometer). Two reviewers independently selected studies, extracted data and assessed quality. Disagreements between the two reviewers were resolved by a third author.

RESULTS: 13 studies involving 2 646 devices were included. The threshold used to report accuracy (difference between home BP device and mercury) ranged from 2 mm Hg to 15 mm Hg. For studies that have reported inaccuracy of home BP devices as proportion, the home BP devices inaccurate ranged from 39% to 76% and from 36% to 88% respectively for systolic BP and diastolic BP values. For those that measured mean difference between home BP devices and mercury readings, the mean difference ranged from 1.9 to 9.5 mmHg and from 0.6 to 9.4 mmHg for systolic BP and for diastolic BP values respectively.

CONCLUSION: Irrespective of the definition used to determine the accuracy of home BP monitors, we observed a high prevalence of inaccurate devices. The accuracy of home BP devices should be considered as home BP monitoring is integrated in the management of hypertension.

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P-008

THE PREVALENCE OF CHRONIC KIDNEY DISEASE IN RURAL AND REMOTE CANADIAN INDIGENOUS PEOPLES: RESULTS FROM THE FINISHED SCREEN/TRIAGE/TREAT PROGRAM

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(2) Diabetes Integration Project
(3) Seven Oaks General Hospital

Background: Indigenous Canadians have high rates of proximate risk factors for Chronic Kidney Disease (CKD), in particular elevated rates of diabetes. The prevalence of CKD is not well defined in this population. We aimed to determine the prevalence of CKD in this population using data from The First Nations Community Based Screening to Improve Kidney Health and Prevent Dialysis (FINISHED) project, an initiative completed in 2015 that accomplished community wide screening in 11 rural and remote communities in Manitoba, Canada.

Methods: An interdisciplinary team screened for CKD, using both urine-albumin-to-creatinine ratio (ACR) and eGFR, and its associated risk factors, including diabetes and high blood pressure, in community members over 10 years of age. We present here the cross-sectional data on demographics, risk factors for CKD, and the prevalence of CKD in the adult (age 18+) screening cohort.

Results: A total of 1346 adults were screened. 26.7% had CKD defined as elevated urine ACR (micro- or macroalbuminuria) or eGFR <60 ml/min/1.73m^2. Road access communities had a lower prevalence of CKD (18.4%) than more remote air access only communities (36.0%). 4.2% of adults screened had reduced kidney function by eGFR <60 ml/min/1.73m^2. Macroalbuminuria was present in 5.0% of those screened.

Conclusions: We found over a two-fold higher prevalence of CKD in comparison to the general population and a prevalence of macroalbuminuria that was five-fold higher. This is comparable to patients with diabetes and/or hypertension. Interventions to screen, triage, and treat Canadian indigenous peoples with CKD should be considered.

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P-009

PHARMACOLOGICAL AUGMENTATION OF NEPHRIN PHOSPHORYLATION PRESERVES THE FUNCTION OF BOTH PANCREATIC BETA-CELLS AND PODOCYTES IN DIABETES

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Background: Recent clinical trials have highlighted the advantages of developing blood glucose lowering therapies that independently prevent kidney damage in diabetes. The immunoglobulin superfamily member nephrin is present in both glomerular podocytes and pancreatic ß-cells and can be post-translationally modified through phosphorylation. However, the effects of pharmacological augmentation of nephrin signalling are mostly unknown.

Objectives: Here, we hypothesized that pharmacological induction of nephrin phosphorylation preserves ß-cell function and prevents albuminuria development in diabetes.

Methods: To induce nephrin phosphorylation, we employed a first-in-class agonist of the IP receptor, MRE-269 and its pro-drug form, selexipag in cultured MIN6 ß-cells and human podocytes and in streptozotocin-diabetic wildtype and $eNOS^{-/-}$ mice.

Results: In MIN6 ß-cells, IP receptor agonism induced nephrin phosphorylation through a cAMP/protein kinase A (PKA)-dependent signalling pathway. This induction of nephrin phosphorylation both increased ß-cell viability and augmented glucose-stimulated insulin secretion (GSIS), with both of these effects being abrogated by the mutation of phosphorylated nephrin tyrosine residues 1176 and 1193. In newly diabetic mice, IP receptor agonism similarly preserved ß-cell mass and augmented GSIS. Unlike in ß-cells, the presence of the IP receptor in podocytes has been uncertain. We identified expression of the IP receptor in mouse and human podocytes in culture by immunoblotting and RTQ-PCR and in mouse podocytes *in vivo* by immunogold electron microscopy. As was observed in ß-cells, MRE-269 promoted nephrin phosphorylation in podocytes in an IP receptor/cAMP/PKA-dependent manner and, in these cells, nephrin phosphorylation was accompanied by cytoskeletal rearrangement and a reduction in albumin transcytosis. *In vivo*, the heavy albuminuria that occurred in diabetic $eNOS^{-/-}$ mice was reduced with IP receptor agonism independent of glucose-change.

Conclusions: Collectively, these findings demonstrate the feasibility of developing a pharmacological strategy that post-translationally modifies nephrin and highlight the importance of nephrin phosphorylation to normal ß-cell and podocyte function in diabetes.

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P-010

ACTIVITY BASED PROTEIN PROFILING OF SERINE HYDROLASES IN CARDIAC-SURGERY ASSOCIATED ACUTE KIDNEY INJURY.

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(2) University of Manitoba

Background: Changes in enzyme activity are physiologically relevant and may be independent of enzyme quantity. Activity-based protein profiling (ABPP) is a novel proteomic approach to assess the functional status of selected enzymes. ABPP may offer insight into the pathophysiology of ischemia-reperfusion injury (IRI) and identify novel markers for acute kidney injury (AKI) following cardiopulmonary bypass (CPB).

Objectives: To determine serine hydrolase activities and composition throughout IRI in AKI versus non-AKI urines.

Methods: Pooled urines from a nested case-control cohort (8 AKI & 8 non-AKI patients) drawn from a prospective cohort study of 326 adult cardiac surgery patients, was collected and evaluated at: baseline, start of CPB, 1-hour CPB, arrival to intensive care unit, post-operative day 1 and 3-5. ABPP was visualized by SDS-PAGE and protein by Sypro Ruby. Serine hydrolase composition was determined in 1-hour CPB AKI urines by MS/MS. Active serine hydrolases were isolated with affinity purification from 1-hour CPB AKI urines and identified on LC-MS/MS.

Results: Serine hydrolase activity remained stable throughout IRI in non-AKI patients. AKI patients demonstrated early differential intraoperative serine hydrolase activity that may relate in part to protein compositional changes (**Figure 1**). Intraoperative AKI urines contained 43 serine hydrolases, but only 17 were identified in their active state, which have diverse functions including complement activation and lipoprotein metabolism.

Conclusions: This analysis demonstrated novel, early intraoperative changes in serine hydrolase activity in AKI versus non-AKI patients and identified 17 active serine hydrolase candidates. Enzyme specific activity assays are underway to validate their involvement in IRI.

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P-010

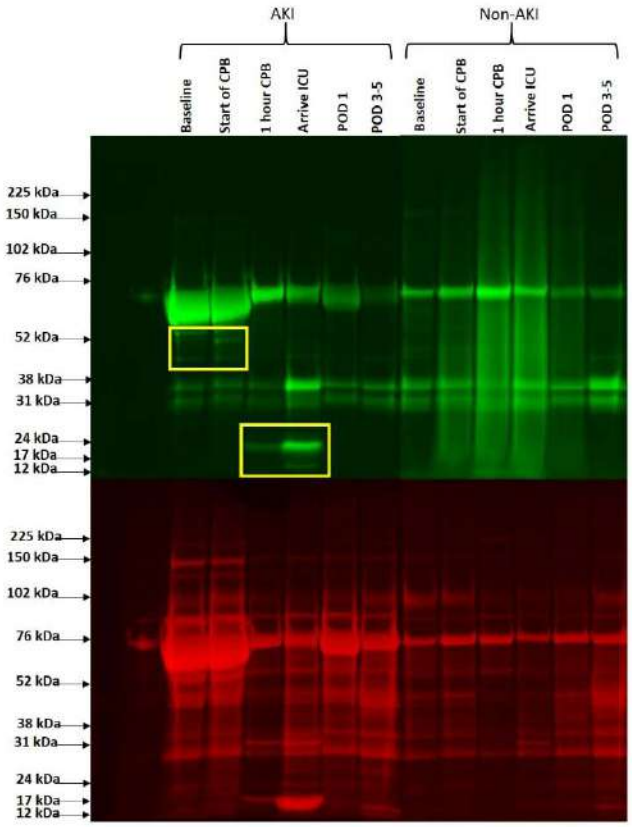

Figure 1 : Serine hydrolase activity-based protein profiling (ABPP, upper panel - green) demonstrated early differential intraoperative serine hydrolase activity in AKI patients (left panel- highlighted, n=8) versus stable activity in non-AKI patients (right panel, n=8). Total protein (Sypro ruby, bottom panel – red) showed more compositional changes in AKI versus non-AKI patients.

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P-011

DETERMINANTS OF ALBUMINURIA IN YOUTH WITH TYPE 2 DIABETES

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Background: Youth with type 2 diabetes (T2D) have a high burden of renal injury and comorbidities; determinants of risk are unknown.

Objectives: To evaluate relationships between biological factors, mental health, inflammation, and albuminuria in The *I*mproving renal *C*omplications in *A*dolescents with T2D through *RE*search (iCARE) Manitoba cohort.

Methods: Based on univariate analyses from 187 youth (10-25 yrs) with T2D, a structural equation model was fitted by weighted least squares. The main outcome was microalbuminuria (non-orthostatic urine albumin:creatinine ratio ≥2 mg/mmol; MA). Latent factors included psychological health (8 indicators including distress (K6 score), stress (PSS-14), positive mental health and measures of resilience), hypertensive load (4 indicators; 24 hr ambulatory monitoring), and inflammation (CRP, ESR and fibrinogen). Glycated hemoglobin (A1c) and duration of T2D were covariates. Parameter estimates were based on standardized variables and interpretable as correlations.

Results: 30.1% of youth with T2D had MA, median age 15 (IQR 13.3-16.8), duration of T2D 2.3 yrs (IQR 0.9-4.1), 66.8% female. Youth with MA had higher A1c's (11.1 vs 8.6%; p<0.001), more hypertension (94.2 vs 78.2%; p=0.02), distress (8 vs 7; p=0.02), stress (28 vs 27; p=0.03), and inflammation (CRP 4.9 vs 3.1mg/L; p=0.01, Fibrinogen 3.5 vs 3.2g/L ; p=0.02, ESR=NS), and longer duration of T2D (2.7 vs 1.8 yrs; p=0.01); age, sex, positive mental health and resilience; NS. Factor loadings were plausible and significant, as was the correlation between psychological health and inflammation (-0.20;p<0.001); significant coefficients were hypertension (0.25;p=0.001), inflammation (0.36;p<0.001), and A1c (0.41;p<0.001) in the structural model for MA.

Conclusions: Albuminuria is highly prevalent in youth with T2D. These results suggest a multifactorial causal model linking hypertension, inflammation, psychological distress, and glycemic control in the pathogenesis of MA. A broader approach to assessment of risk and treatment should be considered in these high risk youth.

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P-012

THE COMPARATIVE EFFECTIVENESS AND SAFETY OF WARFARIN INITIATION IN OLDER ADULTS WITH NEWLY DIAGNOSED ATRIAL FIBRILLATION ACCORDING TO LEVEL OF KIDNEY FUNCTION

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(4) Baylor College of Medicine

Background
There is clinical uncertainty regarding the effectiveness and safety of warfarin use among patients with atrial fibrillation (AF) and reduced kidney function.

Objective
To assess the association between warfarin therapy and adverse clinical outcomes by level of kidney function in AF.

Methods
We conducted a community-based cohort study of adults aged ≥66 years in Alberta, Canada, with AF and a measure of kidney function. Propensity scores were used to construct a matched-pairs cohort with incident AF patients who did and did not have a warfarin prescription dispensed within a 60-day period of their AF diagnosis. Patients were matched within eGFR categories ≥90, 60-89, 45-59, 30-44, and <30 mL/min/1.73m^2. Chronic dialysis or kidney transplantation recipients were excluded. We assessed, within 1 year of warfarin initiation (or the matched date for non-users), the (1) risk of the composite outcome of death, ischemic stroke, or transient ischemic attack and (2) first hospitalization or emergency department visit for a major bleeding episode.

Results
Among the 14892 matched patients, 2104 (14.1%) developed the composite outcome and 1023 (6.9%) experienced a major bleed. Across eGFR categories, warfarin therapy was associated with lower risk of the composite outcome compared to non-use (adjusted HRs [95% CI] for eGFR categories: 0.59 [0.35-1.01], 0.61 [0.54-0.70], 0.55 [0.47-0.65], 0.54 [0.44-0.67], and 0.64 [0.47-0.87]). Warfarin therapy was not associated with a higher risk of major bleeding except for those with eGFR 60-89 ml/min/1.73m^2 (HR 1.36, 1.13-1.64).

Conclusions
Among older adults with AF, warfarin initiation was associated with a significantly lower 1-year risk of the composite outcome across all strata of kidney function, with no appreciable increase in bleeding risk except for those with eGFR 60-89 ml/min/1.73m^2. Sufficiently powered trials in atrial fibrillation patients with reduced kidney function are needed to confirm the potential efficacy and safety of warfarin in this group.

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P-013

UPDATE OF THE PAN-CANADIAN ABLE STUDY: BIOMARKERS OF PEDIATRIC CISPLATIN ACUTE KIDNEY INJURY

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(4) Cincinnati Children's Hospital Medical Center

Background: Cisplatin is well known to cause acute kidney injury (AKI). Serum creatinine (SCr) is a late AKI marker. Novel biomarkers (NGAL: neutrophil gelatinase-associated lipocalin, KIM-1: kidney injury molecule-1) may allow earlier AKI diagnosis than SCr. ABLE is a Canadian study of childhood cancer treatment toxicities, including nephrotoxicity.

Objective: Describe biomarker excretion and AKI phenotype in children currently enrolled in the ABLE cisplatin nephrotoxicity study.

Methods: Prospective cohort study of 150 children receiving cisplatin(12 centres). Exclusion: advanced CKD. Protocol: two “acute” visits (AV) surrounding an early cisplatin infusion (AV1) and a late cisplatin infusion (AV2) (pre-infusion, post-infusion, discharge blood/urine sampling). Measures: SCr, cystatin C, urine NGAL/KIM-1. Outcomes: SCr-AKI: ≥Kidney Disease Improving Global Outcomes(KDIGO) Stage 1; Electrolyte-AKI: ≥National Cancer Institute(NCI) Grade 1 electrolyte abnormality(low serum potassium, phosphate or magnesium). Proportions with AKI were calculated. Biomarker concentrations were compared using Mann-Whitney-U tests.

Results: Data available in up to 71/94 recruited (AV1 median[IQR] age 5[2-13] years; hospital stay 5[3-15] days; 51% male). AV1: 21% SCr-AKI, 51% electrolyte-AKI, 59% with either. AV2: 14% SCr-AKI, 74% electrolyte-AKI, 78% with either. Stage 1 SCr-AKI and hypophosphatemia are most predominant during cisplatin. AV1 NGAL excretion pattern varies by AKI definition used and KIM-1 tends to drop post-cisplatin and rise at discharge(Figure).

Conclusions: This is a novel study of AKI biomarker excretion in cisplatin-AKI. Electrolyte-AKI is more common than SCr-AKI. There are specific biomarker excretion patterns associated with cisplatin. Our larger sample size will allow further characterization of biomarker excretion and biomarker associations with AKI definition and outcomes.

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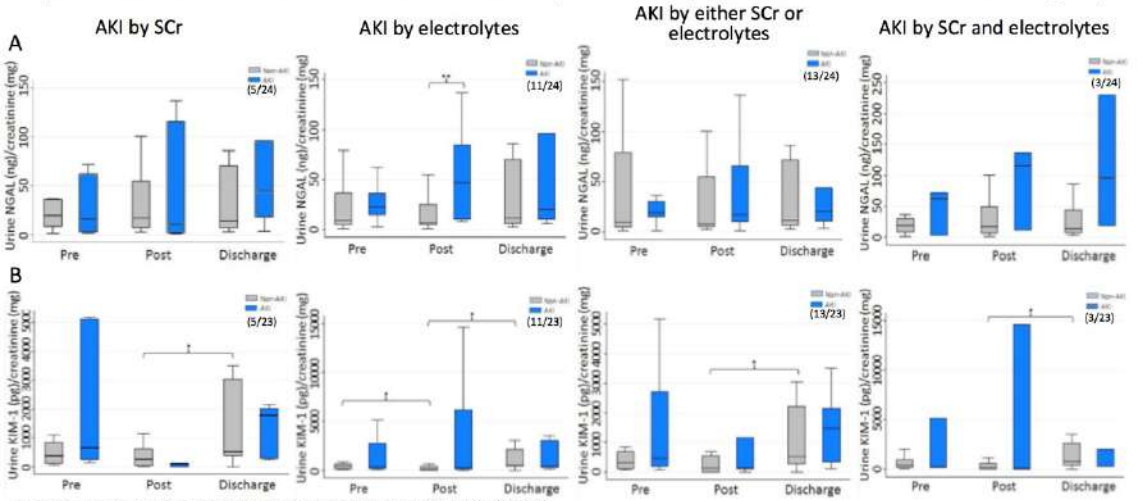
Figure: Urine biomarker excretion during early cisplatin cycle (acute visit 1) by each AKI definition: 1) AKI by SCr criteria of KDIGO guidelines (SCr rise ≥ 50% from baseline), 2) AKI by electrolyte abnormalities of NCI criteria (either low K, P, or Mg for age), 3) AKI by either definition, 4) AKI by KDIGO and NCI criteria. Biomarkers collected at 3 time points: pre-infusion, post-infusion, before discharge. Panel A: Urine NGAL. Panel B: Urine KIM-1. Results shown are for 24 patients that have have biomarker data available. Proportion of subjects with AKI is shown under the AKI group.



*Indicates significant difference from other time point by Mann-Whitney test (p<0.05)
** Indicates significant difference between AKI and Non-AKI groups by Mann-Whitney test (p<0.05)

Abstracts - Poster Presentation

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P-014

CHOP DEFICIENCY INHIBITS FIBROSIS AND PROTEINURIA IN A CKD MOUSE MODEL.

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Background: Endoplasmic reticulum (ER) stress occurs due to the accumulation of misfolded proteins in the ER and is associated with proteinuria in chronic kidney disease (CKD). CHOP (GADD153/DDIT3) is a pro-apoptotic transcription factor that is upregulated during ER stress.

Objective: Analysis of genes upregulated in a mouse model of CKD showed a significant increase in CHOP early in the model and its inhibition by 4-PBA, an ER stress inhibitor that prevented disease progression. Here, we investigated the role of CHOP in an experimental model of murine CKD.

Methods: Our model of CKD combines a uninephrectomy and subcutaneous implantation of a slow release deoxycorticosterone acetate (DOCA) pellet and Angiotensin (Ang) II osmotic infusion pump in C57BL/6 male mice. Mice were also given 1% sodium chloride in their drinking water. Mice with total CHOP knockdown were used to test the role of CHOP in CKD development. CKD was assessed using blood pressure and 24h total urinary protein and albumin measurements. On day 21 post-implantation, mice were sacrificed. PAS and a-smooth muscle actin (SMA) staining was used to evaluate renal intertubular cast formation, glomerular damage and fibrosis.

Conclusions: In response to the CKD model, both $CHOP^{-/-}$ and wild type mice experienced significant increases in systolic and diastolic blood pressure. However, $CHOP^{-/-}$ mice showed significantly lower proteinuria and albuminuria. In addition, CHOP deficiency significantly decreased intertubular cast formation and glomerular damage in response to the model compared to wild type. CHOP deficiency also resulted in lower a-SMA deposition indicating decreased fibrosis. This data suggests that CHOP inhibition may be a viable therapeutic target to halt the progression of CKD.

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P-015

TEN-YEAR TRENDS IN KIDNEY DIALYSIS AND TRANSPLANTATION TREATMENT FOR PATIENTS WITH END-STAGE KIDNEY DISEASE IN CANADA

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(2) University of Toronto Toronto General Hospital, University Health Network
(3) University of Alberta

Background: The Canadian Organ Replacement Register (CORR) is a pan-Canadian information system for organ failure and is an important resource for examining trends in end-stage kidney disease (ESKD) and renal replacement therapies.

Objectives: Present trends in kidney dialysis and transplantation treatment statistics and patient outcomes in Canada, including stratification by cause of ESKD, dialysis modality, presence of diabetes, late referral status and geography.

Methods: CORR data were used to calculate incidence and prevalence rates for ESKD patients who received dialysis or kidney transplants. Data from 2005 to 2014 for all provinces and territories in Canada was included (except Quebec, due to under-reporting between 2011 and 2014). Rates were calculated using the Statistics Canada published population estimates.

Results: In 2014, the incidence rate of patients on dialysis in Canada was 187 per million population (N=5,116), 12% greater than in 2005. Similarly, the prevalence rate was 757 per million population (N=20,690), 18% greater than 2005. While the number of kidney transplants performed per year has increased by 320 between 2005 and 2014 (N=1,376), the waiting list for a kidney transplant has also increased by 618 between 2005 and 2014 (N=3,377), with the number of patients on the waiting list at the end of the year exceeding the number of transplants performed during that year by approximately 2.5 times.

Conclusions: The need for renal replacement therapy is steadily rising in Canada, and increases in kidney transplantation have not kept pace with demand. This puts pressure on the health care systems to improve the efficiency of kidney transplantation and the organ donation process while ensuring all dialysis modalities are accessible for ESKD patients. Innovation and improvements in clinical practice are continually needed to provide efficient treatment that maximizes patient-important outcomes.

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P-016

CLINICAL CHARACTERISTICS OF CHILDREN WITH STEROID RESISTANT AND STEROID DEPENDENT NEPHROTIC SYNDROME IN MARITIME CANADA

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Background: Steroid-resistant and steroid dependent nephrotic syndrome is a chronic relapsing illness that is difficult to treat in children. Published reports of renal biopsies from children with a relapsing or resistant course have predominantly featured minimal change nephrotic syndrome (MCNS), and to a lesser extent focal segmental glomerulosclerosis (FSGS).

Objectives: To determine the incidence and clinical profile of each pathological diagnosis in children in the Maritimes with idiopathic nephrotic syndrome who were steroid-resistant or dependent.

Methods: A chart review was conducted of patients aged 1 to 18 years with chronic relapsing nephrotic syndrome, admitted to the IWK Health Centre, Halifax, Canada, for a renal biopsy. Clinical and laboratory data at the time of biopsy, and their status at one-year post-biopsy were recorded from the chart review.

Results: 55 patients had a renal biopsy due to steroid-resistant/dependent nephrotic syndrome from 1998-2015. All but one child had normal renal function at the time of biopsy. 49% of the children had MCNS, of which 30% had additional features (mild proliferation/deposition). 29% had membranoproliferative glomerulonephritis type 1 (MPGN1), of which 37% had overlapping features of IgA/IgM nephropathy. 11% had IgA/IgM nephropathy alone, 5% had a rapidly progressive glomerulonephritis, 4% had FSGS, and 2% had non-specific changes. 24 children were in remission on medication in one year, while 27 had continued relapses on medication. Three children had a family history of nephrotic syndrome, and eleven children had other co-morbidities as a result of or prior to their nephrotic syndrome.

Conclusions: The incidence of MPGN1 seems to be increased in the Maritime provinces in children with steroid-resistant nephrotic syndrome compared to reports from other centres. Further research is required to elucidate the reasons for this finding, which may include genetic or environmental factors in the local population.

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P-017

ASSISTED PD IN BRITISH COLUMBIA: RESULTS OF A 12-MONTH PILOT PROJECT

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Background: PD is challenging to patients with compromised strength, dexterity, vision and/or cognitive deficits yielding high attrition from the therapy. Assisted PD (PDA) has been used in other jurisdictions to maintain patients on PD instead of switching to facility-based HD.

Objectives: To examine the effect of PDA on technique survival on PD, clinical outcomes and cost.

Methods: Eligible CCPD patients for PDA service were identified by standardized criteria at 4 pilot sites. Participating patients received daily assistance with cycler dismantle and setup provided by an external service provider, but remained responsible for other aspects of PD including connections and choice of dialysate. Outcomes for the PDA cohort were compared against: the general CCPD cohort and patients who met criteria for PDA but did not utilize the service (PDA eligible) in BC.

Results: 53 PDA patients had an 88% (95% CI: 78-97%) 1-year death and transplant censored technique survival on PD, which was similar to the general CCPD cohort (84% [95% CI: 81-87%]) and PDA eligible cohort (86% [95% CI: 77-96%]). PDA cohort had lower peritonitis rates (0.18 episodes per patient-year vs 0.22 and 0.36), but higher hospitalization (55% vs. 34% and 35%). Qualitative feedback from patients and PD clinicians was overwhelmingly positive for PDA. The cost of PDA was approximately $15,000/year in addition to existing dialysis costs. The estimated additional annual cost for transfer to HD is $44000, and cost of long term care is $38000.

Conclusions: PDA was an effective way to support independent CCPD patients who were identified as at risk of PD technique failure and yielded acceptable clinical outcomes for this at risk group. The annual PDA cost is less than transfer to HD or placement in long term care, which represents a cost-minimization for a failing self-care PD patient.

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P-018

HCARG IMPROVES KIDNEY REPAIR BY REGULATING EGF RECEPTOR ENDOCYTOSIS IN AN ACTIN CYTOSKELETON-DEPENDENT MANNER

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Acute kidney injury (AKI) is a common clinical problem associated with high mortality rates. The kidney has a high capacity to regenerate after injury that is intrinsic to tubular cells. Our group has identified *HCaRG* (*Hypertension-related, Calcium-Regulated Gene*) whose overexpression in renal proximal tubules of transgenic mice increased survival after AKI by stimulating mesenchymal to epithelial transition (MET) of tubular cells and recovery of renal tissue integrity and function. Tissue repair after injury involves cell differentiation, remodeling of actin cytoskeleton and regulation of such key receptors as the Epidermal Growth Factor Receptor (EGFR). We identified several proteins interacting with HCaRG by a yeast 2-hybrid screening of a human kidney cDNA library, including actin and proteins associated to vesicles trafficking.

Our goal is to demonstrate that HCaRG regulates MET through EGFR endocytosis and transport, in an actin cytoskeleton-dependent manner.

HCaRG and EGFR intracellular localization were analyzed by cell fractionation and confocal microscopy. Co-immunoprecipitations were used to investigate interactions between HCaRG and proteins known to be involved in vesicle trafficking (actin, tubulin, Rab proteins). HCaRG was silenced by a specific siRNA and EGFR activation and endocytosis were evaluated in renal cell lines treated with EGF.

We demonstrated that HCaRG regulates endosomal trafficking of EGFR and its delivery to cell surface by controlling actin polymerization in endosomal tubules. Silencing of HCaRG reduced EGFR expression and delayed activation of this receptor induced by EGF. Confocal analysis showed that HCaRG co-localizes with G-actin and EGFR and with endosomal markers (EEA1, Rab11, 5) at specific time points during cell treatment with EGF.

Our results suggest that HCaRG plays a crucial role in MET process and kidney repair by controlling EGFR signaling/trafficking. This receptor is a key regulator of cell differentiation involved in tissue repair. HCaRG could be a novel therapeutic target for kidney repair after injury.

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P-019

THE RELATIONSHIP BETWEEN URINARY RENIN ANGIOTENSIN SYSTEM MARKERS AND CARDIORENAL FUNCTION IN ADOLESCENTS WITH TYPE 1 DIABETES

Yuliya Lytvyn (1), Kevin Burns (2), Farid Mahmud (3,4), Denis Daneman (3,4), Livia Deda (3,4), David Dunger (5), John Deanfield (6), Neil Dalton (7), Yesmino Elia (3,4), Ronnie Har (1), Julie Van (1), Timothy Bradley (3), Cameron Slorach (3), Fengxia Xiao (2), Joe Zimpelmann (2), Luc Mertens (3), Rahim Moineddin (8), Heather Reich (1), Etienne Sochett (3,4), James Scholey† (1), David Cherney† (1)
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(2) Kidney Research Centre, Ottawa Hospital Research Institute, University of Ottawa
(3) The Hospital for Sick Children, University of Toronto
(4) JDRF-Canadian Clinical Trial Network (JDRF-CCTN) SickKids Multicenter Clinical Trial Center
(5) University of Cambridge
(6) University College Hospital
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(8) University of Toronto

Background: The relationship between urinary renin-angiotensin aldosterone system (RAAS) markers and cardiorenal pathophysiology in type 1 diabetes mellitus (T1D) is unclear.

Objectives: To assess (1) levels of urinary RAAS markers and (2) the association between RAAS components and HbA1c, urine albumin/creatinine ratio (ACR), estimated glomerular filtration rate (eGFR) and peripheral vascular function in otherwise healthy adolescents with TID vs. healthy controls (HC).

Methods: Urinary angiotensinogen and ACE2 levels, activity of ACE and ACE2, blood pressure (BP), eGFR, flow-mediated dilation and carotid-femoral pulse wave velocity were measured in 65 HC and 194 T1D from the AdDIT Trial.

Results: Urinary levels of all RAAS components were higher in T1D vs. HC (Figure 1, $p<0.0001$). Higher HbA1c was associated with higher urinary angiotensinogen, ACE2, and higher activity of ACE and ACE2 ($p<0.0001$, $p=0.0003$, $p=0.003$ and $p=0.007$ and respectively) in T1D. Higher ACR was associated with higher urinary angiotensinogen ($p<0.0001$) and ACE activity ($p=0.007$), but not with urinary ACE2 activity or ACE2 levels. These observations were absent in HC. Urinary RAAS components were not associated with BP, eGFR or vascular function in T1D or HC.

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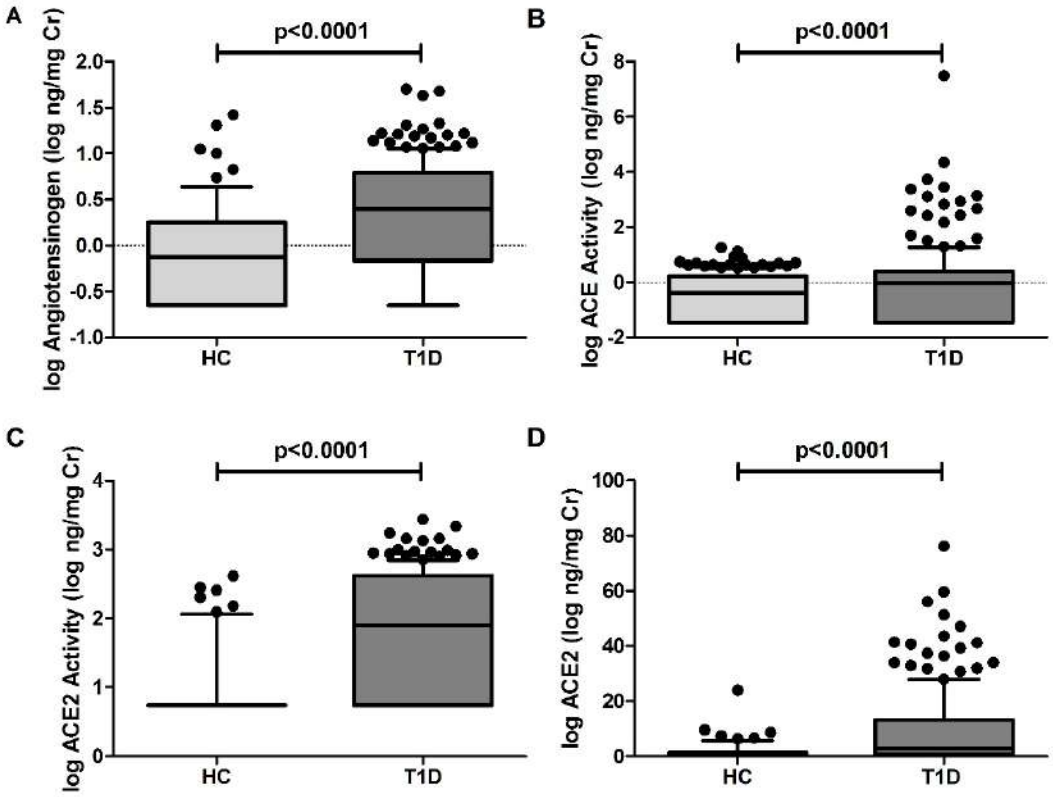
Conclusions: Otherwise healthy adolescents with T1D exhibit higher levels of urinary RAAS markers compared to HC. Urinary RAAS markers correlate with HbA1c and ACR in T1D but not in HC, suggesting that these factors reflect an intermediary pathogenic link between hyperglycemia and albuminuria within the normal range.

Figure 1



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P-020

THE THREE-YEAR CUMULATIVE INCIDENCE OF GOUT IN CHRONIC KIDNEY DISEASE

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(2) ICES Western
(3) University of Alberta

Background: Knowledge of the incidence of gout across stages of chronic kidney disease can be used for risk stratification and sample size estimates in clinical trials.

Objective: To determine the 3-year cumulative incidence of gout according to estimated glomerular filtration rate (eGFR) and sex.

Methods: In 282,925 adults aged ≥66 years, we used healthcare databases from Ontario, Canada to assess the 3-year cumulative incidence of diagnosed gout accounting for the competing risk of death. We stratified results at cohort entry by sex and eGFR (≥90 mL/min/1.73 m^2, 60-89, 45-59, 30-44, 15-29, and chronic dialysis). We also examined the incidence rate of gout per 1000 person-years, the risk of gout adjusted for clinical characteristics, results stratified by eGFR and albuminuria, and the incidence of gout defined by the receipt of allopurinol or colchicine.

Results: Older adults with a lower level of eGFR had a higher 3-year cumulative incidence of diagnosed gout (P for trend <0.001); however, persons on chronic dialysis had a lower incidence of gout compared to those with moderate reductions in kidney function. The 3-year cumulative incidence of gout across six groups of women with progressively lower eGFR was 0.6%, 0.7%, 1.3%, 2.2%, 3.4% and 2.0%. Corresponding numbers in men were 0.8%, 1.2%, 2.5%, 3.7%, 4.6% and 2.9%. The association between a greater loss of kidney function and a higher risk of diagnosed gout was evident in all additional analyses. For example, after adjustment for clinical characteristics, women with an eGFR between 15 and 29 mL/min per 1.73 m^2 had over a 5-fold higher risk of gout compared to women with an eGFR ≥90 mL/min/1.73 m^2 (hazard ratio 5.6, 95% confidence interval 4.2-7.5).

Conclusions: Many patients with a lower level of kidney function will be diagnosed with gout. Strategies should be developed to reduce gout risk in these patients.

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P-021

EFFECT OF RENAL BIOPSY ANGLE OF ATTACK ON SPECIMEN ADEQUACY AND COMPLICATIONS

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(2) Saskatoon Health Region

BACKGROUND: Although *medical* factors such as hypertension have been identified that are associated with an increased risk, little is known about the role of *technical* factors in renal biopsy.

OBJECTIVE: To examine the role of angle of attack (AOA), site of biopsy, and direction of the needle towards the medulla on complications and specimen adequacy.

METHODS: This was a retrospective study of all adult renal biopsies performed at a single center (n=189) in 2012 and 2013. The radiological image from the time of the biopsy was printed to paper. A line was drawn tangential to the point of entry into the kidney and the angle between this line and the needle was recorded as the AOA. Radiographic information was cross-referenced to the official pathology report and the patient chart.

RESULTS: Ultrasound-guided biopsies with an AOA of ≤60° yielded more glomeruli (24.5 vs. 16, p=0.003) than biopsies with AOA >60°. There were also fewer significant hemorrhagic complications with an AOA of ≤60° (9/61 vs. 0/26, p=0.039). Biopsies directed at the kidney pole yielded more glomeruli than in the interpolar region, while biopsies directed towards the medulla showed increased significant hemorrhagic complications (9/56 vs. 0/31, p=0.046). Regression analysis showed that AOA >60° is predictive of complications (p=0.015), while interpolar biopsy predicts specimen inadequacy (p=0.05). There were no significant findings for any of the technical factors in CT-guided renal biopsies, possibly related to limited range of AOA.

CONCLUSIONS: Renal biopsy directed at a kidney pole and an AOA of <=60° are technical factors that may yield better specimens and fewer complications. While biopsy directed at the medulla is necessary for some pathological diagnoses, this may come with increased risk, emphasizing the need for communication between nephrologist, pathologist and radiologist.

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P-022

TWO PHOSPHATE TARGETS IN END-STAGE RENAL DISEASE (TARGET): A RANDOMIZED CONTROLLED TRIAL OF INTENSIVE VS. LIBERALIZED PHOSPHATE CONTROL IN HEMODIALYSIS RECIPIENTS

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(4) McMaster University
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Background: Hyperphosphatemia is common among dialysis recipients and is associated with a higher risk of mortality and cardiovascular events. Phosphate binders are prescribed to most patients to reduce their serum phosphate concentrations. It is uncertain whether targeting a lower phosphate concentration with binders improves patient-important outcomes.

Methods: We conducted a randomized controlled trial of prevalent hemodialysis recipients already receiving calcium carbonate as a phosphate binder at 5 Canadian centres. Participants were randomly allocated to 26 weeks of a phosphate goal of either 0.75 to 1.50 mmol/L (intensive group) or 2.00 to 2.50 mmol/L (liberalized group) by titrating calcium carbonate using a dosing nomogram. The primary outcome was the difference in serum phosphate at 26 weeks.

Results: 53 participants were randomized to the intensive group and 51 to the liberalized group. The median (interquartile range) dose of elemental calcium at 26 weeks was 1.8 (1.4 to 3.0) g/day in the intensive group, and and 0 (0 to 0.3) g/day in the liberalized group. The mean (SD) serum phosphate at 26 weeks was 1.49 (0.36) mmol/L in the intensive group and 1.94 (0.49) mmol/L in the liberalized group. The mean difference (95% confidence interval) in phosphate concentration between the two groups was 0.36 (0.19 to 0.53, $p<0.001$) mmol/L. Hypocalcemia was more common in the liberalized group ($p=0.02$). There were no statistically significant differences between the two groups in the risk of hypercalcemia, parathyroid hormone, parathyroidectomy, or major vascular events.

Conclusions: It is feasible to achieve a difference in serum phosphate concentrations in hemodialysis recipients by titrating calcium carbonate. A large, long-term trial is needed to determine if targeting a lower serum phosphate concentration improves patient-important outcomes.

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P-023

REASONS FOR PRACTICE VARIATION IN THE MANAGEMENT OF CHILDHOOD NEPHROTIC SYNDROME IN CANADA

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(2) University of Calgary

Background: Treatment protocols for childhood nephrotic syndrome are highly variable among physicians and care centres. Lack of consistency in the management of nephrotic syndrome leads to poor satisfaction with care for patients and families. The reasons for practice variation in nephrotic syndrome are not studied.

Objectives: We conducted a qualitative study to understand the complex multi-level processes that lead to practice variation and influence physician decision-making in treatment of nephrotic syndrome. This qualitative study is part of a larger national mixed-methods research study, which includes a longitudinal cohort study of children with nephrotic syndrome (from 12 Canadian centres) to determine centre-, physician-, and patient-level factors leading to variation in care.

Methods: Ten focus groups with pediatric nephrology health care providers (physicians, nurses, and allied health, 67 total participants) were performed across Canada (one in each major pediatric health centre). The interviews were guided by the Ottawa Model for Research Use, a comprehensive framework of elements that affect the process of health care knowledge transfer. Discussions in focus groups were transcribed, and analysis occurred concurrently using qualitative content analysis in three phases (coding, categorizing, and developing themes).

Results: Emerging themes were grouped into two categories: a) physician-level, or b) centre-level. Under the physician level category two themes, guiding treatment decisions, emerged: a) use of physician experiential knowledge versus empirical knowledge, and b) physician interpretation of patient characteristics. At the centre-level three themes, influencing care, emerged: a) model of care, b) structures and resources in clinic and c) lack of communication and collaboration within and across centres.

Conclusions: Physician and centre factors play a major role in shaping practice differences in nephrotic syndrome. Further research is needed to determine whether variation in care is associated with disparities in outcomes and whether harmonization of protocols based on best evidence will reduce these disparities.

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P-024

THE EFFECT OF CYCLOOXYGENASE-2 INHIBITION ON RENAL SODIUM HANDLING IN HUMANS

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Background: Cyclooxygenase-2 (COX-2) inhibitors are associated with increased cardio- and renovascular risk, with altered renal sodium handling suggested in animal studies as a contributing factor. We examined the effect of COX-2 inhibition on the fractional excretion of lithium, a marker of proximal tubular function in healthy humans.

Methods: Twelve healthy subjects (42% female, 37±10 years) were studied in high-salt balance pre- and post-14d daily ingestion of the COX-2 inhibitor celecoxib 200mg. The set-point of proximal renal tubular sodium excretion was estimated by fractional excretion of lithium (FELi, calculated as $lithium_{urine}$ x $creatinine_{serum}$/ $lithium_{serum}$ x $creatinine_{urine}$), hence not altered by changes in diet. Endogenous serum and urine lithium was measured by graphite furnace atomic absorption spectroscopy. In addition, fractional excretion of sodium (FENa, calculated as $sodium_{urine}$ x $creatinine_{serum}$/ $sodium_{serum}$ x $creatinine_{urine}$) was calculated for comparison.

Results: No significant changes in blood pressure, salt balance, or renal hemodynamics were observed pre- vs post-COX-inhibition. Similarly, COX-2 inhibition was not associated with any significant change in FELi (6.97±2.94 vs 6.48±2.94, p=0.4; pre- vs post-celecoxib) (Figure 1). There were no sex differences in FELi at baseline (7.17±2.67 vs 6.83±3.33; p=0.8) or in response to COX-2-inhibition (ΔFELi: 0.01±2.54 vs 0.84±1.97; p=0.6; all values women vs men). FENa did not change in response to COX-2 inhibition (0.72±0.28 vs 0.66±0.47; p=0.7, pre- vs post-celecoxib)

Conclusion: In healthy humans, short-term COX-2 inhibition is not associated with changes in proximal tubular function. Whether these same findings apply to the chronic kidney disease population is unknown.

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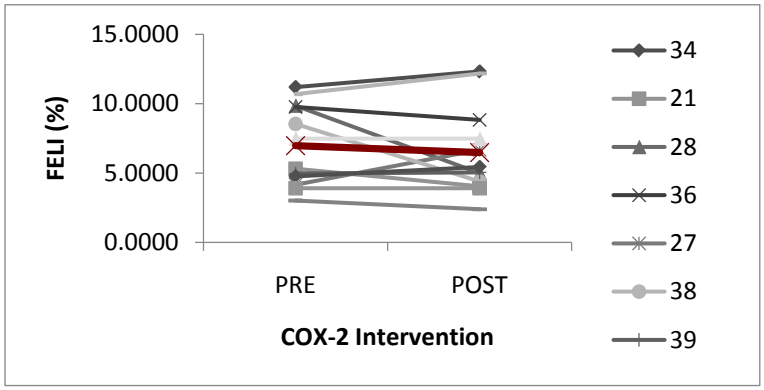
P-024

A



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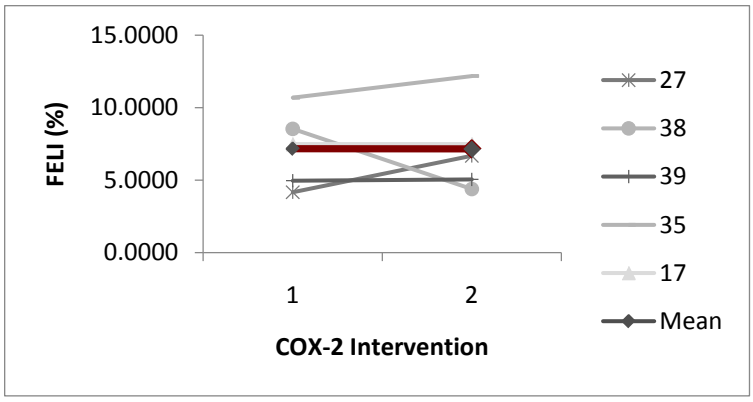

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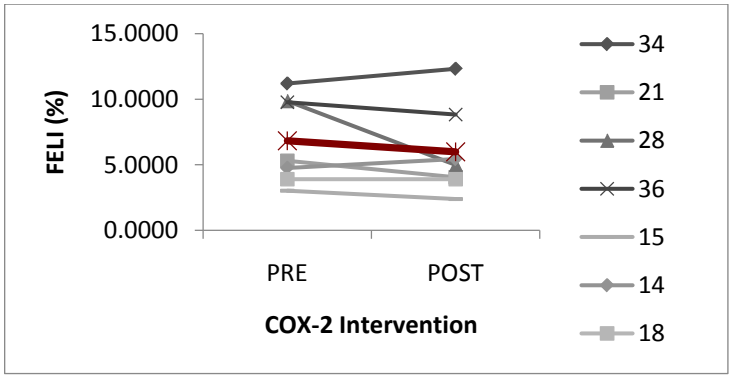

Figure 1. The fractional excretion of lithium pre and post COX-2 inhibition in **A)** all participants **B)** in women only and **C)** in men only.

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P-025

URINARY PODOCYTE MICROPARTICLES IN NORMOTENSIVE PATIENTS WITH TYPE 1 DIABETES: A PILOT STUDY

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(2) Mount Sinai Hospital, University of Toronto
(3) Kidney Research Centre, Ottawa Hospital Research Institute, University of Ottawa

Background: Microparticles (MPs) are small (0.1-1.0 µm), membranous vesicles shed from the surface of cells in response to injury. We recently reported that MPs are released from podocytes and may be detected in the urine of diabetic mice in advance of albuminuria.

Objectives: To determine whether podocyte MPs are detectable in human urine samples, and whether their levels are altered in the presence of diabetes.

Methods: In this *post-hoc*, exploratory analysis, we assessed urinary podocyte MPs in archived urine samples obtained from patients with uncomplicated type 1 diabetes (T1D, n=25) studied under clamped euglycemia (4-6 mmol/L) and hyperglycemia (9-11 mmol/L) compared to healthy controls (HC, n=20). Patients were >18 years of age, >10 years diabetes duration, normotensive, normoalbuminuric without history of renal or macrovascular disease. Patients were not taking anti-hypertensive or lipid lowering agents that can influence MP formation. Podocyte MPs were isolated from frozen urine specimens and quantified by podoplanin labeling and flow cytometry. MP levels were log-transformed and normalized to urinary creatinine. Non-parametric Mann Whitney and Wilcoxon tests were used to analyze the data.

Results: In T1D, urinary podocyte MP levels were higher compared to HC (Figure 1A). In response to clamped hyperglycemia in the T1D cohort, urine microparticle levels increased (Figure 1B).

Conclusions: Urine podocyte MPs are detectable in human urine. In this analysis, MP levels were significantly higher in normotensive, normoalbuminuric patients with T1D vs. healthy controls. Further work is required to determine whether urinary podocyte MPs predict the development of diabetic kidney disease.

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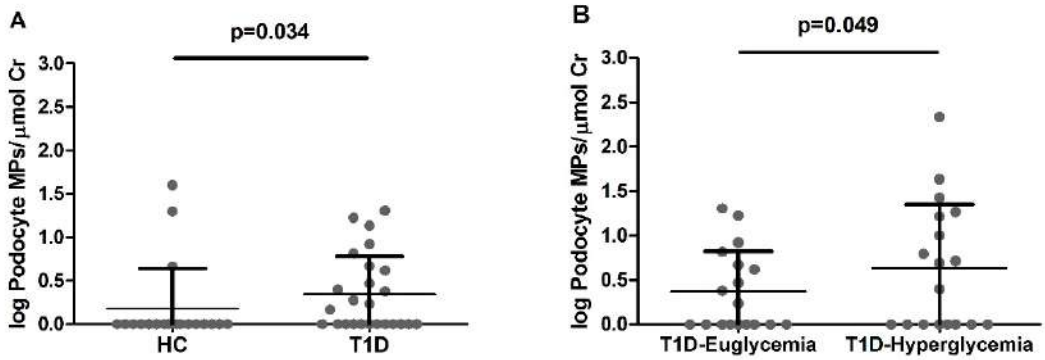
P-025

Figure 1



Abstracts - Poster Presentation

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P-026

BARRIERS AND FACILITATORS TO ENHANCING CONSERVATIVE/PALLIATIVE KIDNEY MANAGEMENT IN THE PRIMARY CARE SETTING: A POPULATION-BASED SURVEY

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Background: Conservative/palliative (non-dialysis) kidney management is increasingly provided in the primary care setting for patients with stage 5 chronic kidney disease (CKD).

Objectives: The objective of this population-based survey was to examine perceived barriers and facilitators to improving primary care physicians' ability to conservatively manage stage 5 CKD patients across Alberta.

Methods: All primary care physicians in Alberta who had experience providing care for older adults aged ≥75 years with stage 5 CKD (eGFR <15ml/min/1.73m2) not planning on initiating dialysis were invited to complete a self-administered questionnaire. Questionnaire items were based on a qualitative descriptive study and informed by the Theoretical Domains Framework, which were subsequently tested for face and content validity. Physicians were contacted via postal mail and/or fax, based on a modified Dillman method. Data were analyzed descriptively.

Results: 409 primary care physicians completed the questionnaire (9.6% response rate). The most common barrier was the ability to access support to maintain the patient in the home setting; 39% of respondents reported that it was often/always a barrier to care. This was followed by 32% of respondents that reported the ability to work with non-physician providers with limited renal-specific clinical expertise was often/always a barrier to care. Approximately 85% indicated that having the ability to contact a nephrologist or clinical staff from a Conservative Care Clinic by telephone would likely/definitely enhance care. In contrast, 68% reported that their ability to access a nephrologist by electronic methods (e.g. email) and access to an online conservative care clinical pathway would likely/definitely enhance patient care.

Conclusions: We identified important areas to inform clinical programs to reduce barriers and enhance facilitators to improve primary care physicians' provision of kidney conservative care, particularly in relation to resources available to maintain patients at home and telephone access to experts in conservative care.

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Abstracts - Poster Presentation

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P-027

EFFECTIVE KNOWLEDGE BUILDING THROUGH A DIALYSIS BOOTCAMP IN NEPHROLOGY FELLOWSHIP TRAINING

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Background: An essential component of nephrology fellowship training is developing proficiency in peritoneal dialysis (PD), hemodialysis (HD) and dialysis access. With increasing clinical demands and delegation of dialysis care to other professionals such as vascular access coordinators, clinical exposure for trainees can become limited. In response, novel approaches are required to incorporate essential dialysis education into the nephrology curriculum.

Objectives: To demonstrate the feasibility and effectiveness of an intensive Dialysis Bootcamp in delivering dialysis education.

Methods: After a needs assessment, we developed a station-based Dialysis Bootcamp utilizing guiding principles from Kolb's experiential learning model. This consisted of six 30-minute stations, led by experts in HD, PD and vascular access. Participants included Canadian and international nephrology fellows from adult and pediatric programs in a single academic nephrology program. All fellows completed at least 2-4 months of home dialysis and in-centre dialysis. The bootcamp was delivered at the end of an academic year to trainees at all levels. Pre- and post-tests targeting essential content were administered, as were anonymized surveys documenting experience level and self-assessment.

Results: Fourteen and 21 participants completed pre- and post- tests, respectively. Data were analyzed in aggregate form using a Cohen's d statistic to determine effect size based on difference between scores. Mean scores for pre- and post- tests were 43.6% (SD=10.5%) and 58.4% (SD=15.6%), respectively. The Cohen's d=1.50 represented a large effect size. Seventeen pre-intervention surveys were collected, with self-assessments ranging across the spectrum of novice to highly experienced.

Conclusions: The Dialysis Bootcamp is a feasible, effective method of delivering dialysis education, resulting in measurable gains on testing. Future work should examine methods of incorporating competency-based metrics into assessment. Self-assessment in this cohort of advanced trainees may be more accurate than those in earlier stages, and should be further evaluated.

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Abstracts - Poster Presentation

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P-028

ATTITUDES AND OPINIONS OF NEPHROLOGISTS TOWARDS CONTINUOUS QUALITY IMPROVEMENT OPTIONS

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(2) Humber River Hospital
(3) University of Toronto
(4) McMaster University

Background: Accountability and public reporting are increasingly prominent in health care. At the present time, quality improvement in Canadian nephrology is based on reporting of facility-wide performance.

Objectives: The objective of the study was to determine the attitudes and opinions of nephrologists towards a potential shift of improvement efforts from facility based to the individual physician level.

Methods: A web-based survey instrument was used to administer a survey to 330 nephrologists across Canada, through the Canadian Society of Nephrology (CSN).

Results: Out of the initial 320 eligible nephrologists contacted, 137 nephrologists responded (43%). Amongst all respondents, 48% agreed or strongly agreed that “there is significant variation in physician performance in my facility”. 79% agreed or strongly agreed that “there are quality metrics that nephrologists should be responsible for”. More than 80% agreed or strongly agreed that “there are some appropriate and valid measures that should form a basis for CQI activities”. 82% agreed or strongly agreed to “receive a confidential, personalized score card reflecting my individual patient care”. Only 30% agreed or strongly agreed that “public reporting of physician performance is likely to improve patient outcomes”. Of note, compared to staff nephrologists, medical directors were twice as likely to agree or strongly agree that “shifting from program to physician level measurement and reporting is likely to improve care”.

Conclusions: Overall, the majority of nephrologists were not supportive of shifting from program to physician-level measurement and public reporting. Leadership level physicians were more likely to support this shift. As modern medicine evolves towards more accountability and public reporting, the Canadian nephrology community must grapple with how to adapt to these trends and apply those methods that are validated and proven to improve patient care and outcomes.

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P-029

PHOSPHATE CONTAINING PRESCRIPTION MEDICATIONS CONTRIBUTE TO THE DAILY PHOSPHATE INTAKE IN A THIRD OF HEMODIALYSIS PATIENTS

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Objective: Cardiovascular disease in dialysis patients is associated with hyerphosphatemia which is primarily managed by restriction of dietary phosphate intake to 800-1000 mg/day and phosphate binders. Phosphate salts are used as excipients in tablets that function in the dispersal of the active ingredient. The contribution of prescribed medications to the daily oral phosphate load is unknown.

Methods: In this observational study, the Health Canada Drug Database was used to determine if phosphate salts were included as non-medicinal ingredients of prescribed medications. The manufacturers of the medications containing phosphate were contacted directly to determine how much phosphate was present in the tablets. Prescription bottles of 101 dialysis patients were evaluated to determine the manufacturer of the prescribed medications.

Results: In 101 dialysis patients, the median [IQR] of medications prescribed was 8 [5.5, 10] and the median daily tablet burden was 13 [10,18]. 196 of 1744 (11%) of drugs reviewed contained a phosphate salt. Central nervous system acting medications and cardiovascular acting medications accounted for 61% and 22% of phosphate containing medications, respectively. 73% of amlodipine, 76% of bisoprolol and 98% of codeine formulations contained phosphate. 30% of patients in our dialysis unit were taking medications that contained phosphate and the total amount ranged from 9.3 to 251 mg/day (mean 88.3±58.3 mg/day).

Conclusion: Medications containing phosphate are frequently prescribed to dialysis patients and can provide a significant portion of the recommended daily phosphate intake. Alternate manufacturers of certain frequently prescribed medications such as amlodipine, bisoprolol and codeine should be considered in this patient group to reduce oral phosphate exposure.

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P-030

REDUCTION OF THE LONG-TERM PATHOLOGICAL EFFECTS OF ISCHEMIA-REPERFUSION INJURY BY CLUSTERIN ON RENAL INFLAMMATION AND FIBROSIS

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Background: One of long-term outcomes after acute kidney injury (AKI) is linked to chronic kidney disease (CKD); however, the mechanisms underlying the progression of AKI to CKD remain largely unknown. Clusterin (CLU) is a chaperone-like protein that reduces ischemia-reperfusion injury (IRI) and enhances tissue repair after IRI in the kidney. This study investigated the effects of CLU expression on the transition of IRI to renal fibrosis.

Methods: IRI was induced in the left kidneys of wild type (WT) C57BL/6J (B6) versus CLU knockout (KO) B6 mice by clamping the renal pedicles for 28 min at the body temperature of 32^{o}C. Tissue damage was examined by histology, the phenotypes of infiltrates by FACS analysis, and the fibrosis-related gene expression profile by PCR array.

Results: Here, we showed that the renal atrophy induced by IRI was no different between WT kidneys and CLU null controls, but at the end of 3 months WT kidneys preserved better function, indicated by the lower levels of both serum creatinine and BUN in WT mice than those in CLU KO controls, which were associated with less cellular infiltration (CD8 cells and macrophages), less tubular damage and less tissue fibrosis including glomerulopathy, interstitial fibrosis, vascular fibrosis and α-SMA expressing cells. PCR array showed the beneficial effect of CLU in WT was associated with up-regulation of EGF and down-regulation of CCL12, Col3a1, MMP9 and TIMP1.

Conclusion: the data suggest that expression of CLU is required to preserve the renal function and structural integrity after IRI, which are associated with reduced infiltrating effector cells (CD8 T cells, macrophagies and myofibroblasts) and tissue fibrosis.

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P-031

PLA2R ANTIBODIES IN A SERIES OF PATIENTS WITH MEMBRANOUS NEPHROPATHY: A SINGLE CENTRE EXPERIENCE

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Background/Aims: In this study we describe the differences between membranous nephropathy patients who are PLA2R antibody positive compared to those who are antibody negative.

Methods: A series of 188 patients with proteinuria were screened for PLA2R antibodies in a tertiary care centre, from May 2008 to Oct 2015. Patients who did not have a membranous lesion on kidney biopsy were excluded. Serum PLA2R antibodies were measured by ELISA at the University of Manchester. Positive PLA2R antibody was defined as levels 40 U/mL or greater. Relevant clinical and biological were analyzed .

Results: Among 160 patients with native kidney membranous nephropathy screened for PLA2R antibodies, 92 patients were positive PLA2R antibodies (68 were negative). Age, estimated GFR, and time from biopsy were comparable between the two groups –Table 1. On average patients with positive PLA2R had greater proteinuria and lower serum albumin at peak PLA2R levels. Compared to patients who were PLA2R antibody positive, more malignancy and connective tissue disease were present in patients with negative PLA2R antibody.

Conclusion: Patients with positive PLA2R antibodies may have worse proteinuria and lower serum albumin compared to those who are negative. A substantial number of patients with positive PLA2R antibodies have malignancy and connective tissue disease (8.6%), screening for which should be undertaken even with PLA2R antibody positivity.

P-031

Table 1. Comparison between PLA2R positive and PLA2R negative patients

Results	PLA2R Positive (≥40 U/ml) n=92 Mean ± SD	PLA2R Negative (< 40 U/ml) n=68 Mean ± SD
Time from biopsy, *months*	38.7 ± 53.5	42.7 ± 57.8
Estimated GFR, *ml/min/1.73m^2*	70.3 ± 37.9	71.5 ± 34.8
Urine protein, *grams per day*	7.21 ± 5.67	3.86 ± 3.78
Serum Albumin, *g/L*	30 ± 8	34.8 ± 7
Malignancy, n (%)	3 (3.2%)	5 (7.4%)
Connective Tissue Disease, n (%)	5 (5.4%)	7 (10.3%)
Viral Infections, n (%)	1 (1%)	2 (2.9%)

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P-032

EXOSOME-MEDIATED TRANSFER OF MICRORNA-486-5P TO ENDOTHELIAL CELLS AS A PROTECTIVE MECHANISM IN ACUTE KIDNEY INJURY

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Background: We have shown that infusion of cord blood endothelial colony forming cell (ECFC)-derived exosomes protects mice against kidney ischemia/reperfusion injury. Exosomes are enriched in microRNA-(miR)-486-5p, and their delivery increases kidney miR-486-5p levels, decreases phosphatase and tensin homologue (PTEN), and activates Akt, a pro-survival protein. We postulated that the protective effects might be due to exosomal transfer of miR-486-5p.

Objectives: i) To determine if ECFC exosomes transfer miR-486-5p to endothelial cells *in vitro,* and ii) To study if miR-486-5p directly targets PTEN.

Methods: ECFCs and Human Umbilical Vein Endothelial Cells (HUVECs) were co-cultured and miR-486-5p transfer was determined by qPCR. Confocal imaging identified exosomes labeled with the dye PKH26. Targeting of PTEN by miR-486-5p involved transfection of HUVECs with a luciferase reporter containing the PTEN-3'-untranslated region (UTR).

Results: Co-culture of HUVECs with ECFCs significantly increased HUVEC miR-486-5p levels, compared to HUVECs alone ($P<0.001$ n=5). Incubation of co-cultured cells with GW4869 (an exosome release blocker) or 5-*N*-ethyl-*N*-isopropylamiloride (EIPA) (an exosome uptake inhibitor) blocked this increase ($P<0.001$ vs vehicle, n=5). Transfection of ECFCs with a miR-486-5p precursor (pre-miR-486-5p) prior to co-culture with HUVECs, led to marked increases in HUVEC miR-486-5p (~700-fold), which were inhibited by adding GW4869 or EIPA to the co-culture. Confocal imaging revealed cytoplasmic localization of ECFC exosomes in HUVECs, and uptake was blocked by EIPA. When HUVECs transfected with the PTEN-3'UTR luciferase reporter were incubated with ECFC exosomes, luciferase activity was significantly reduced ($P<0.01$), an effect blocked when HUVECs were first transfected with antagomiR to miR-486-5p.

Conclusions: These data show that ECFC exosomes transfer miR-486-5p to human endothelial cells, where it directly targets PTEN. Inhibition of PTEN expression may activate cell pro-survival pathways. The results suggest that exosomes enriched in miR-486-5p could represent a therapeutic tool in human acute kidney injury.

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P-033

BETA BLOCKER DIALYZABILITY IN CHRONIC HEMODIALYSIS PATIENTS

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Objectives: There is a paucity of data available to describe beta-blocker dialyzability. Of the available information, most were obtained prior to implementation of high-flux dialysis membranes. This study aims to characterize the dialyzability of four of the most commonly prescribed beta-blockers in patients undergoing conventional high-flux hemodialysis (HD). Based on physiochemical properties, we hypothesize atenolol and metoprolol to be extensively removed by HD, while bisoprolol and carvedilol to be poorly dialyzed.

Methods: HD patients from the London Health Sciences Centre were recruited for a pharmacokinetic, crossover study. Atenolol (50mg), bisoprolol (5mg), carvedilol (6.25mg) and metoprolol (50mg) were administered separately to each patient over four hemodialysis sessions. Arterial and venous blood samples and total spent dialysate were collected. Beta-blocker concentrations were measured by mass spectrometry, and dialytic clearance was determined by the dialyzer and recovery clearance methods.

Results: Following dialysis, 6.17 mg of atenolol, 1.19 mg of bisoprolol, 0.03 mg of carvedilol, and 0.88 mg of metoprolol were recovered in spent dialysate. These amounts of dialyzed beta-blockers were applied in the recovery clearance method to produce dialytic clearance values of 117.1, 110.1, 17.78, and 148.4 mL/min for atenolol, bisoprolol, carvedilol, and metoprolol, respectively.

Conclusions: Beta-blocker efficacy can be hindered if substantial dialytic clearance occurs. Accordingly, atenolol and metoprolol were extensively cleared by HD, while carvedilol displayed low dialyzability. Contrary to previous literature, our data suggests moderate dialyzability for bisoprolol. With recent studies indicating heightened mortality risk in HD patients prescribed highly-dialyzable beta-blockers, drug dialyzability data is critically important to optimize pharmacotherapy in HD patients. Definitive characterization of beta-blocker dialyzability can allow for determination of post-dialysis supplemental drug doses, or alternative drug therapies.

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P-034

ELBASVIR/GRAZOPREVIR (EBR/GZR) TREATMENT OF HEPATITIS C VIRUS (HCV) INFECTION IN PATIENTS WITH CHRONIC KIDNEY DISEASE STAGE 4/5: FINAL RESULTS OF THE C-SURFER PHASE 3 STUDY

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(6) Houston Methodist Hospital
(7) Hôpital Purpan
(8) Merck & Co., Inc.

Background: Limited options are available for treating HCV infection in patients with advanced kidney disease. C-SURFER is the first randomized, placebo-controlled phase 3 study to evaluate an all-oral, ribavirin-free regimen in CKD 4/5 patients.

Methods: 224 patients with HCV genotype (G)1 and CKD 4/5 ± hemodialysis (HD) were randomized to EBR/GZR 50/100mg (immediate treatment group, ITG; N=111) or placebo for 12 weeks. Placebo subjects (deferred treatment group, DTG; N=113) received EBR/GZR after placebo. 11 additional subjects received EBR/GZR with intensive pharmacokinetic (PK) sampling. The primary safety comparison was EBR/GZR versus placebo. The primary efficacy endpoint was sustained virologic response (SVR) 12 weeks post-therapy in the ITG+PK group. Here we report the final results, including subjects who received EBR/GZR after placebo therapy.

Results: In the placebo-controlled phase, serious adverse events (AEs) occurred in 16 (14%) EBR/GZR and 17 (15%) placebo subjects; discontinuation due to an AE in EBR/GZR and placebo subjects was 0% and 4%. SVR12 in all subjects who received EBR/GZR was 94.6% (ITG+PK, 94.3% [115/122]; DTG after placebo, 95.0% [96/101]). Twelve subjects failed to attain SVR12: virologic relapse, n=3; discontinuation for AE, n=1; administrative reason, n=8. Excluding subjects who discontinued for reasons unrelated to drug, overall SVR12 was 98.6% (211/214). PK data indicate no need for dose adjustment in HD patients (geometric mean ratio [HD/non-HD] ranged from 0.67-0.85 for GZR and 1.43-1.67 for EBR).

Conclusion: Once-daily EBR/GZR for 12 weeks was highly effective with a low rate of AEs in patients with advanced kidney disease and HCV G1 infection.

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P-035

HOSPITAL READMISSIONS AND EMERGENCY DEPARTMENT VISITS AFTER ACUTE KIDNEY INJURY

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(6) Mount Sinai Hospital, University of Toronto

Background and objectives: Patients who survive a hospitalization complicated by acute kidney injury (AKI) are at risk for adverse events, including readmission to hospital and emergency department (ED) use. The objective of this study was to determine characteristics of patients with readmissions or ED visits within 30 days of a hospitalization complicated by AKI.

Methods: We conducted a population-based study of all patients who survived a hospitalization complicated by AKI between June 1, 2003, and December 31, 2013 in Ontario, Canada. Key outcomes included the proportion and characteristics of patients with a non-elective hospital readmission or an ED visit within 30 days of hospital discharge. We used a cause-specific proportional hazards model to identify determinants of hospital readmission within 30 days of hospital discharge.

Results: Of the 156,690 patients who survived a hospitalization complicated by AKI, 27,475 (18%) were readmitted to hospital, 41,307 (26%) visited the ED, and 11,856 (8%) died within 30 days of hospital discharge. Congestive heart failure was the most common reason for hospital readmission (3,443 patients; 13% of readmissions) and ED visits (3,354 patients; 8% of ED visits) within 30 days of discharge; 6,999 (26%) readmissions were complicated by AKI. No patient or hospital characteristic had a hazard ratio for 30 day hospital readmission above 1.20, except for discharge from hospital with a persistent need for renal replacement therapy (hazard ratio 1.94; 95% confidence interval 1.80- 2.08).

Conclusions: Survivors of AKI are readmitted to hospital within 30 days of discharge at the third highest rate in Ontario after congestive heart failure and chronic obstructive pulmonary disease. These two diagnoses were not strong determinants of hospital readmission after a hospitalization complicated by AKI, suggesting survivors of AKI represent a distinct at risk population.

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P-037

MANAGEMENT OF STROKE RISK IN PATIENTS ON HEMODIALYSIS WITH NON-VALVULAR ATRIAL FIBRILLATION: A COMPARISON OF CARDIOLOGISTS AND NEPHROLOGISTS IN CANADA

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Background: Antithrombotic therapy for stroke prevention in atrial fibrillation (AF) is a standard of care. For hemodialysis (HD) patients, the benefits are not clear and adverse outcomes more common. Our study objectives were to determine cardiologists' and nephrologists' stroke prevention practices in this population and associated decisional uncertainty across levels of stroke and bleeding risk.

Methods: A cross-sectional online survey was distributed to members of 3 Canadian societies (Nephrology, Cardiovascular, Heart Rhythm), and to cardiologists at the Universities of Alberta, Calgary and Toronto. Three reminder emails were sent at two-week intervals. The questionnaire included 4 cases of AF in HD patients with varying bleeding and stroke risks. Respondents selected from 3 treatment options (no drug therapy, antiplatelet, anticoagulant). Decisional uncertainty was measured on a 0-10 rating scale. Multinomial regression analysis was performed on drug therapy choice and an analysis of variance on uncertainty with physician specialty, bleeding risk and stroke risk as independent variables for both analyses.

Results: Response rates were 25.8% (103 of 400) for nephrologists and 3.9% (50 of 1297) for cardiologists. Both groups recommended anticoagulant therapy less when bleeding risk was high and more often when stroke risk was high. Cardiologists were 3 times more likely than nephrologists to recommend anticoagulant compared to no drug therapy (OR = 3.11, p=0.001) and to antiplatelet (OR = 2.99, p=0.001), regardless of bleeding or stroke risk. When bleeding risk increased, cardiologists' certainty decreased (6.8 to 5.4, p<0.001) and nephrologists' certainty increased (6.2 to 6.7, p=0.03). Stroke risk did not affect certainty.

Discussion: Cardiologists were more likely than nephrologists to recommend drug therapy with a higher bleeding risk. However, an increase from low to high bleeding risk had opposite effects on cardiologists' and nephrologists' decisional certainty. Because of the low response rate, particularly from cardiologists, these findings must be considered tentative.

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P-038

A DESCRIPTION OF THE PATIENT POPULATION IN AN URBAN CENTER UNDERGOING CONSERVATIVE CARE FOR THE TREATMENT OF ADVANCED CHRONIC KIDNEY DISEASE.

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Background: Comprehensive conservative/palliative (non-dialysis) management is chosen as a treatment option by some individuals for treatment of stage 5 chronic kidney disease (CKD). Little is known about individuals choosing this treatment in the Canadian setting.

Objective: The objective of this study was to describe the characteristics of patients who choose conservative care for the treatment of stage 5 CKD, and managed by a conservative care program, in a Canadian context.

Methods: A retrospective chart review of individuals enrolled in the conservative care program in an urban nephrology center between January 1, 2009 and June 30, 2015 was undertaken. Patient characteristics, as well as information about conservative care follow-up, advanced care planning, and death were abstracted for descriptive analysis.

Results: One hundred fifty-four patients were enrolled in the conservative care program. The average age was 81 years and 46% were male. The mean modified Charlson Comorbidity Index Score was 3.4 (95% confidence interval, 0.65 to 6.17). The median duration of conservative care participation was 11.5 months. Seven (4%) patients changed their modality to dialysis. One hundred three (67%) patients died during the study period. Eighty-two (80%) patients completed at least some advanced care planning before death. Sixty-six (80%) deceased patients died at their preferred place. Twenty-seven (26%) individuals died in hospital.

Conclusion: We found that individuals who chose conservative care were very old and did not have high levels of comorbidity. Few individuals who chose conservative care changed modality and accepted dialysis. Rates of engaging in advanced care planning and death in place of choice were high in this population. Death in hospital was uncommon in this population managed by an urban nephrology center.

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P-039

ABNORMAL MYOCARDIAL PERFUSION SCANS ARE NOT ASSOCIATED WITH INCREASED MORTALITY IN ASYMPTOMATIC INDIVIDUALS AWAITING RENAL TRANSPLANTATION

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Background: Risk assessment for asymptomatic patients awaiting renal transplantation is controversial.

Methods: Patients awaiting renal transplant in Southern Saskatchewan from 2005 to 2015 were retrospectively reviewed. Patients underwent risk stratification with stress myocardial perfusion scan. Baseline clinical characteristics, nuclear scan results and cardiovascular morbidity and mortality were analyzed. Abnormal scans were defined as studies with fixed/reversible defects, wall motion abnormalities, lung uptake, or transient ischemic dilation. Descriptive statistics and survival analysis were calculated.

Results: Charts from 285 consecutive patients with 608 nuclear scans were analyzed. Mean age was 55.2 ± 11.7 years and 34.7% were female. Twenty-seven (9.5%) patients were transplanted and 98 (34.4%) patients died while awaiting renal transplantation. One hundred and sixty-two patients (56.8%) had at least one abnormal scan. Of these 162 patients, 30.9% had 2 abnormal scans, 21% had 3 abnormal scans and 13% had ≥4 abnormal scans. Compared to those with normal scans, patients with abnormal scans were more likely to be revascularized (OR: 3.22, 95% CI: 1.61-6.41, p=.001). The mean follow up period was 5.47 ± 3.11 years. An abnormal scan was not associated with decreased survival (Figure).

Conclusion: Patients awaiting renal transplantation in Saskatchewan with abnormal myocardial perfusion scans were not associated with a greater risk of death.

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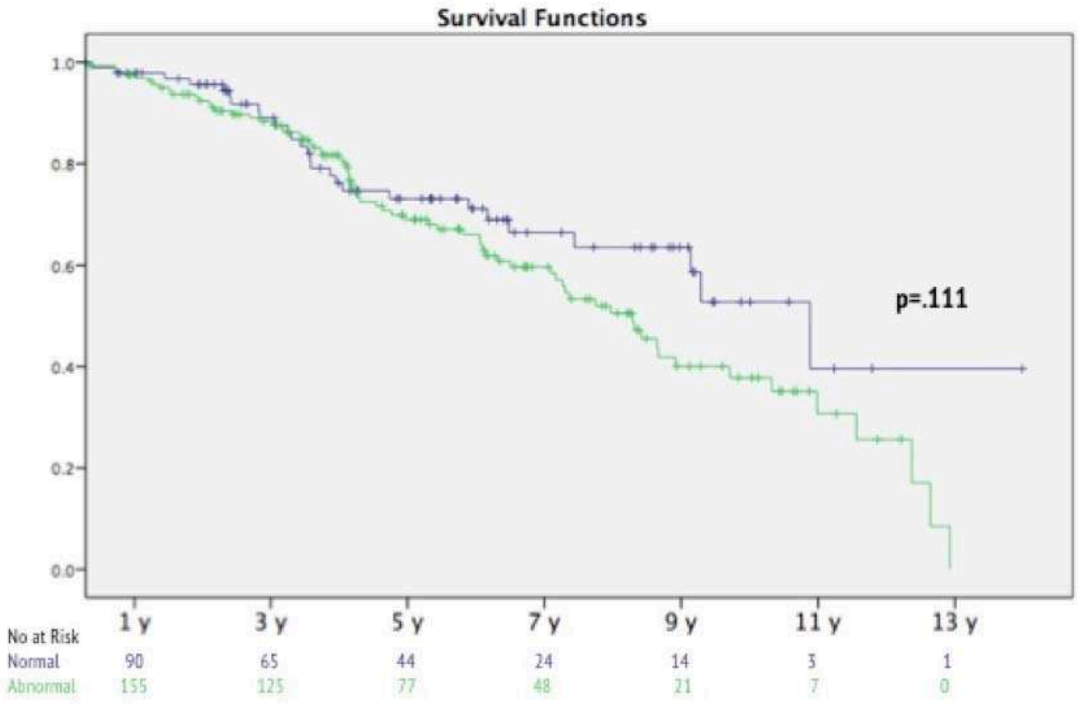

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P-040

NUTRITIONAL STATUS PREDICTS FRAILTY IN MAINTENANCE HEMODIALYSIS PATIENTS

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Background: Patients with chronic kidney disease(CKD) are at risk for premature frailty which is associated with a higher risk of hospitalization and death.Previous studies have shown a high prevalence(67.7%) of frailty among maintenance dialysis patients over the age of 65.

Objectives: To identify the nutritional factors which predict frailty in the chronic hemodialysis population.

Methods: Fat mass and muscle mass were measured with whole-body bioimpedance spectroscopy in 135 prevalent hemodialysis patients using Body Composition Monitor (BCM).We also measured biceps,triceps,suprailiac and subscapular skinfold thicknesses and calculated fat mass based on the equation of Dumin and Womersley. We measured waist circumference as surrogate of abdominal fat. As surrogates of muscle mass mid-arm muscle circumference(MAMC) was calculated as follows:MAMC=mid-arm circumference-3.142×triceps-skinfold thickness.We ascertained frailty based on Fried's definition: low walking speed, low grip strength, weight loss, exhaustion, and low level of physical activity. Patients who met three or more criteria were considered frail. Logistic regression was employed to investigate the association between tertiles of each nutrition characteristic with the risk of frailty.

Results: 47% of our population were considered frail, based on Fried's definition.After adjustment for age, race, gender, diabetes and dialysis vintage, low muscle mass and high fat mass, based on both BCM and anthropometry, were associated with higher risk of frailty (Table 1).MAMC was not correlated with the risk of frailty.Frailty score was significantly correlated with body percentage of fat mass($r=0.33, p<0.001$) while the correlation with muscle mass was not significant($p=-0.14$).

Conclusions: Our data suggest that the nutritional parameters especially fat mass are potential predictor of frailty.

P-040

Table 1. Odds ratio and 95% confidence interval of frailty across tertiles of different nutritional factors in 135 maintenance hemodialysis patients

	Tertile 1	Tertile 2	Tertile 3	P for trend
Serum Albumin	1	1.28(0.46-3.54)	0.73(0.27-1.96)	0.49
BMI[1]	1	2.36(0.86-6.51)	3.50(1.27-9.47)*	0.05
BCM[2] **Fat mass percent**[3]	1	2.31(0.82-6.46)	4.25(1.49-11.87)*	0.02
BCM Muscle mass percent[3]	1	0.42(0.15-1.17)	0.23(0.06-0.94)*	0.10
Waist circumference	1	2.32(0.85-6.36)	4.53(1.66-12.39)*	<0.01
Skin-fold fat mass	1	1.78(0.64-4.97)	4.65(1.61-13.39)*	<0.01
Mid-Arm Muscle circumference	1	2.17(0.84-5.63)	2.07(0.79-7.49)	0.38

*p<0.01
[1]BMI:Body mass index
[2]BCM:body composition monitor
[3]percent of body weight

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DYSNATREMIA IN RELATION TO FRAILTY AND AGE IN COMMUNITY-DWELLING ADULTS: AN NHANES STUDY

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BACKGROUND: Frailty represents an age-related state of increased risk of adverse health outcomes due to compromised repair processes. Dysnatremia is more common with age, suggesting that it may reflect a general imbalance in damage and repair and thereby be more common in frailty. Our objectives were to establish whether frailty is associated with dysnatremia; whether this explains the previously established association between age and dysnatremia, and; to assay the impact of each on mortality.

METHODS: The relationship between age, health status and dysnatremia was investigated across the adult life course in 8898 respondents from the 2003-2004 and 2005-2006 cross-sectional National Health and Nutrition Examination Survey (NHANES) datasets. A frailty index (FI) was calculated for each respondent, and related to dysnatremia (sodium values outside a 135-144 mmol/L reference range). Mortality follow-up data came from the National Center for Health Statistics. The relationship between FI, dysnatremia and mortality was assessed using Kaplan Meier statistics and Cox regressions.

RESULTS: Dysnatremia was significantly related to both age and health status: as the degree of frailty increased, so did the proportion with dysnatremia. Adjusted for frailty, the relationship with age was no longer significant, Figure 1. In the age and sex adjusted Cox models, both FI (for each 0.01 in the FI, the hazard ratio increased by 1.07 (95% confidence interval 1.06-1.08) and dysnatremia (HR 1.42; 1.12-1.80) were significant predictors of death.

CONCLUSION: Increasing frailty severity is associated with dysnatremia, and appears to confound the association between age and dysnatremia.

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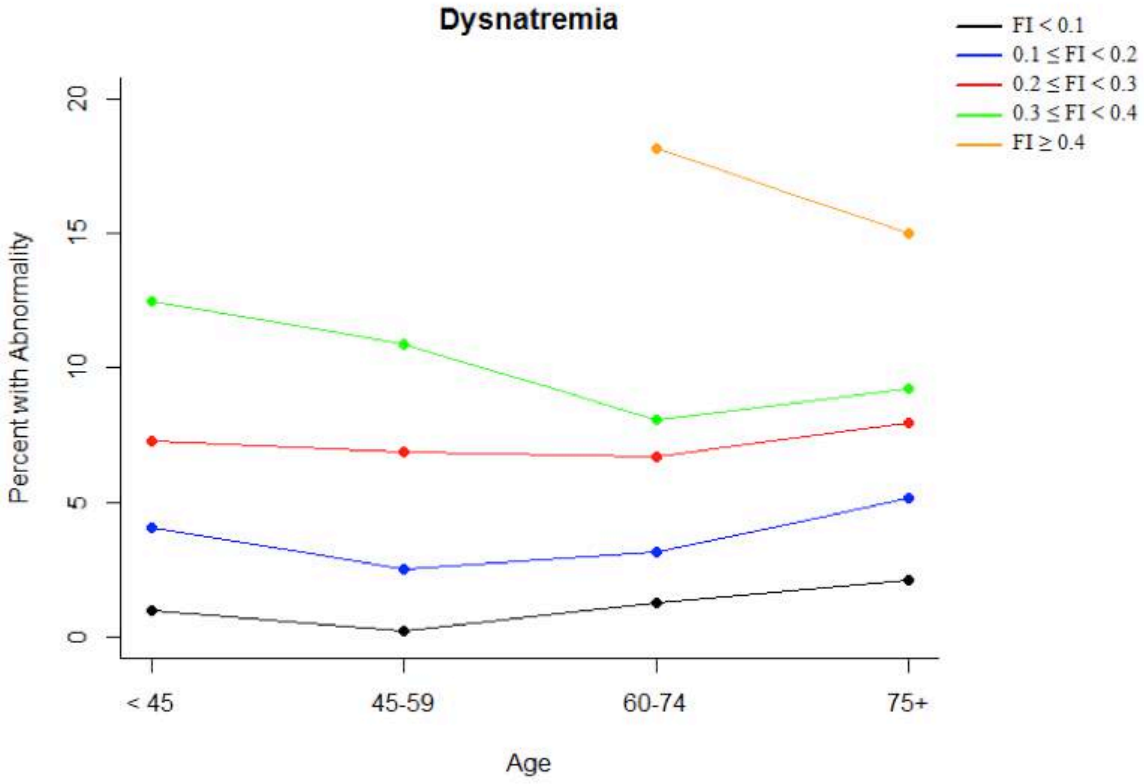

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P-044

EARLY MORTALITY ON CONTINUOUS RENAL REPLACEMENT THERAPY (CRRT): PRAIRIE CRRT STUDY

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Background:

Patients with acute kidney injury (AKI) requiring Renal Replacement Therapy (RRT) have an increased short-term and long-term risk of mortality. In most North American ICUs, these patients require continuous renal replacement therapy (CRRT). CRRT is resource intensive and the natural history of patients requiring CRRT in the ICU is poorly understood.

Methods:

We conducted a prospective cohort study of patients undergoing CRRT for AKI in three ICU's of the Regina Qu'Appelle Health Region (RQHR). We collected data on demographic, laboratory and clinical measures and followed patients from admission to the ICU to 9 months post discharge in the community.

Results:

Of the 2634 patients admitted to the ICUs in the study period (April 2013 to September 2014), (2201/2634) 83.6% had no AKI. 269 or 10.2% had stage III AKI. 106/269 (40%) were started on CRRT. Of those on CRRT, 66/106 died in ICU whilst on CRRT. 17/66 (26%) died within 24 hours of initiating therapy. Patients who died within 24 hours had a higher FiO2 (0.8 ± 0.2 vs. 0.6 ±0.2, p: 0.011); higher epinephrine (32.0 ± 29.9 vs. 6.5 ± 9.3, p: 0.005); higher norepinephrine levels (39.4 ± 23.5 vs. 19.6 ± 14.2, p:0. 005); lower pH (7.1 ± 0.2 vs. 7.3 ± 0.1, p: 0.005) when compared to those who survived the first 24 hours of admission.

Conclusion:

Patients admitted to the ICU with AKI requiring CRRT have a high risk of early mortality. In these patients, vasopressor use and hypoxia were independently associated with adverse short-term survival.

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P-045

DIAGNOSIS AND OUTCOMES OF ACUTE KIDNEY INJURY USING SURROGATE AND MULTIPLE IMPUTATION METHODS FOR MISSING PREADMISSION CREATININE VALUES

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Background. Missing preadmission serum creatinine (SCr) values are a common obstacle to assess acute kidney injury (AKI) diagnosis and outcomes. The KDIGO guidelines suggest using a SCr computed from MDRD (estimated glomerular filtration rate of 75 ml/min/1.73m^2).

Objectives. We aimed to identify the best surrogate method for estimating baseline SCr to assess AKI diagnosis and outcomes.

Methods. We compared the use of 1) first SCr at hospital admission 2) minimal SCr over 2 weeks after intensive care unit admission and 3) MDRD computed SCr to assess AKI diagnosis and outcomes. We then performed linear regression models to predict preadmission SCr and multiple imputation strategies to assess AKI diagnosis.

Results. Our one-year retrospective cohort study included 1001 critically ill adults; 498 of them had preadmission SCr values. In these patients, AKI incidence was 25.1% using preadmission SCr. First SCr had the best agreement for AKI diagnosis (22.5%;kappa=0.90) and staging (kappa=0.81). MDRD and minimal SCr overestimated AKI diagnosis (26.7% and 43.2%;kappa=0.86 and 0.60). However, MDRD SCr had a better sensitivity than first SCr for AKI (93% vs. 87%). Seventy-percent of patients experienced renal recovery. MDRD SCr was the only method associated with lower renal recovery (54.1%;p=0.01). In a multivariate model, age, male gender, hypertension, heart failure, undergoing surgery and log first SCr best predicted preadmission SCr (adjusted R^2=0.56). Imputation methods with first SCr increased AKI incidence to 23.9% (kappa=0.92) but not with MDRD computed SCr (26.7%;kappa=0.89).

Conclusions. In our cohort, first SCr performed better for AKI diagnosis and staging than MDRD or minimal SCr. MDRD SCr improved AKI diagnosis sensitivity but performed worse for renal recovery. Imputation methods minimally increased agreement for AKI diagnosis.

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P-047

SEVERE RENAL ISCHEMIA-MEDIATED DAMAGE IS REDUCED WITH GENETIC KNOCK OUT OF CHOP

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Background: Acute kidney injury (AKI) is a significant cause of morbidity and mortality in North America, and is typically characterized by a sharp rise in serum creatinine levels. Renal ischemia, which causes AKI, can induce endoplasmic reticulum (ER) stress, leading to activation of the unfolded protein response and increased expression of the pro-apoptotic gene CHOP. Genetic knockout of CHOP prevents ER stress-induced acute tubular necrosis, suggesting an important role for CHOP in the adverse effects of AKI.

Objective: The objective of this study was to determine if genetic knockout of CHOP protects the kidneys from ischemia-induced damage.

Methods: Male C57BL/6 and CHOP$^{-/-}$ mice on a C57BL/6 background underwent bilateral renal ischemia/reperfusion (I/R). Severe renal damage was induced by 55 minutes of ischemia, followed by 48 hours of reperfusion/recovery time. Serum creatinine was measured with an enzymatic assay, and kidneys were stained with periodic acid-Schiff (PAS) and TUNEL to assess damage in the cortex, pars recta, and medulla. Kidney sections were scored for damage (0-5), apoptosis, and total cell count.

Results: Serum creatinine levels were increased in wild type and CHOP$^{-/-}$ mice that underwent renal I/R. However, CHOP$^{-/-}$ mice revealed serum creatinine levels significantly lower than wild type mice. PAS-stained kidney sections showed significantly less structural damage in the cortex and medulla, but not the pars recta, of CHOP$^{-/-}$ mice compared with wild type mice. Further, apoptosis was found to be significantly higher in the medulla of wild type kidneys compared with CHOP$^{-/-}$ kidneys. Cellular sloughing was found in the cortex of wild type kidneys, but not CHOP$^{-/-}$ kidneys, as demonstrated by total cell count.

Conclusions: These results suggest that CHOP plays a major role in ischemia-induced AKI, and new methods of reducing or preventing its expression may provide therapeutic strategies to protect against AKI.

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CONVERTING FROM UNFRACTIONATED HEPARIN (UFH) TO DALTEPARIN FOR EXTRACORPOREAL CIRCUIT (ECC) ANTICOAGULATION: IMPACT ON DIALYSIS EFFICACY

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Background: Low Molecular Weight Heparins (LMWH) are used as the extracorporeal circuit (ECC) anticoagulant of choice in Europe. Although LMWHs are also indicated for ECC anticoagulation in Canada, UFH is more commonly used.

Objective: To determine if converting from UFH to Dalteparin (a LMWH) impacts hemodialysis efficacy.

Methods: 107 hemodialysis outpatients previously on UFH were converted to Dalteparin 2,500 IU / dialysis treatment regardless of weight or previous UFH dose. Dalteparin dosing was increased in a stepwise manner if consistent clotting impacting dialysis was observed. Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines define a minimally adequate hemodialysis session of <5 hours as a Urea Reduction Ratio (URR) of 65%; with a target URR of 70% suggested. As a surrogate measure of hemodialysis efficacy, URR and clotted dialysis circuits / 100 treatments were recorded for 3 months prior to and 3 months after converting from UFH to Dalteparin.

Results: 3 months after converting from UFH to Dalteparin, 79% of all patients remained on Dalteparin 2,500 IU / treatment; a dose less than that recommended for ECC anticoagulation on the product monograph. When comparing data collected 3 months prior to and 3 months after converting from UFH to Dalteparin, the percentage of patients with inadequate URRs (<65%) did not differ (11.85% vs 11.97%). The average URRs prior to and after converting to Dalteparin also did not differ (73.54% vs 73.26%). The number of completely clotted dialysis circuits / 100 treatments did not increase after converting to Dalteparin (1.37 vs 1.18).

Conclusion: 79% of hemodialysis patients were maintained on the Dalteparin 2,500 IU / treatment for ECC anticoagulation after switching from UFH. There was no difference in dialysis efficacy after conversion; based on our findings of no change in the URR nor increase in clotted dialysis circuits.

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P-049

IMPORTANCE OF HEALTH LITERACY IN ACCESS CHOICE FOR PATIENTS WITH END STAGE KIDNEY DISEASE TREATED WITH HEMODIALYSIS

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Background: Hemodialysis (HD) patients make decisions about vascular access and diet. We hypothesized that patients with low health literacy would be more likely to choose a CVC and have higher potassium (K), phosphorus (P) and interdialytic weight gain (IDWG).

Methods: Consenting adult HD patients on treatment for > 6 months were included. Health literacy was assessed with the Newest Vital Sign Test (NVS). Vascular access type and reasons for CVC use were determined. Serum K, P and IDWG were collected retrospectively for 6 months. T-tests and logistic regression was used to determine the association between health literacy (NVS score <4 versus ≥4) and CVC choice, K >6, P >2 and IDWGs > 5% of the target weight (TW).

Results: Fifty-six HD patients 62.6 (15.8) years, mostly male (63%) participated. 66% of the patients had a CVC; 1/3 had chosen this access. The average NVS was 2.95 (2.14). Poor control of K, P and IDWG was experienced by 27%, 55% and 36% of patients respectively. The average NVS score was different for patients choosing a CVC (P=0.001) but not those with higher K, P or IDWG gain (Table 1). None of the patients who chose a CVC had a NVS ≥4 (could not calculate OR). NVS was not associated with poor control of K [0.95 (0.30-3.06)], P [1.05(0.36-3.03)], or IDWG [1.34(0.44-4.07)].

Conclusion: Patients with low health literacy are more likely to choose a CVC compared to patients with adequate health literacy. Educational strategies for less advanced learners may be warranted.

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Table 1: NVS Test Average For CVC Choice, High Potassium, High Phosphate and High Interdialytic Weight Gain

Variable	Yes	No	P
CVC Choice	1.17	3.64	0.001
Potassium (>6mmol/L)	3.13	2.88	0.697
Phosphate (>2mmol/L)	3.16	2.68	0.409
High IDWG (>5% TW)	2.75	3.06	0.614

TW=target weight, IDWG=interdialytic weight gain

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P-050

DIABETES MELLITUS IS A RISK FACTORS FOR HYPERPHOSPHATEMIA IN PERITONEAL DIALYSIS PATIENTS

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Background: Hyperphosphatemia has been associated with adverse outcomes in patients with end stage kidney disease (ESKD). The purpose of this study was to determine risk factors for hyperphosphatemia in ESKD patients treated with peritoneal dialysis (PD).

Methods: Consenting adult PD patients documented their food, beverage, and phosphate binder intake for 3 days using a dietitian developed food journal prior to their clinic visit. Phosphate content of meals was calculated using the ESHA Food Processor SQL Software. Clinic biochemistry tests and an adequacy assessment (Baxter Adequest program) were done. Univariate logistic regression was used to determine predictors of serum phosphate >1.78mmol/L; repeated controlling for the phosphate intake/binder intake ratio in this treated population. A multivariable logistic regression model was then fit including those variables that achieved a significance level of p< 0.20 in univariate analyses.

Results: 60 patients (38 men, 22 women) completed the protocol. On average patients were 60 ±17 years old, Caucasian (85%) and 50% had a history of diabetes mellitus (DM). The variables associated with an increased risk of phosphate > 1.78mmol/L were DM, binder dose taken, and dialysate phosphate removal. Those factors associated with a decreased risk of phosphate > 1.78mmol/L included phosphate intake, percent absorption, and urinary phosphate clearance. When the phosphate intake/binder intake was controlled for in the analysis, only dialysate phosphate clearance was statistically significant. In multivariable logistic regression analysis, after controlling for the phosphate intake/binder intake ratio, the factors that were associated with a serum phosphate > 1.72mmol/L included: diabetes mellitus [OR 3.63 (1.00, 13.17) p=0.05), total phosphate removal [1.04 (0.99, 1.08) p=0.03] and, phosphate dialysate clearance [0.77 (0.59, 1.01) p=0.06].

Conclusion: To our knowledge this is the first time that diabetes mellitus has been shown to be a risk factor for hyperphosphatemia.

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SYMPTOMS INDUCED BY HEMODIALYSIS

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Background: Hemodialysis induces symptoms in many patients that take time to recover from (recovery time). The symptoms induced and how they vary over time and between patients is unclear. We conducted a prospective cohort study to describe how recovery time symptoms vary over time and between patients.

Methods: We recruited prevalent in-center hemodialysis patients and measured their recovery time using multiple instruments. Instrument A presented a global question regarding how long it took to recover from the last dialysis treatment. Instrument B addressed the recovery time for each of 10 symptoms. Participants completed each instrument for each dialysis treatment for one week. We compared the distribution of recovery time found with each instrument.

Results: One hundred twenty participants from 2 centres completed 914 recovery time assessments. Fewer participants required no recovery time with Instrument A (14 to 17% of participants depending on day of week) as compared with identifying no symptoms with Instrument B (20 to 34% of participants depending on day of week) (p=0.002 for difference between groups). However, the maximum recovery time from any symptom in Instrument B was longer than the recovery time identified with Instrument A (p=0.001). Lack of energy was the most common symptom following dialysis (65% of all patients), with muscle cramps (41%), bone and joint pain (25%), shortness of breath (19%), and muscle soreness (18%)the next most frequent. The median duration of these each of these symptoms was >12 hours with the exception of muscle cramps which was <6 hours. The median duration of recovery time measured with Instrument A was <6 hours.

Conclusions: Recovery time is a common, complex of different symptoms that vary in duration. Further research is required to understand how dialysis induces each type of symptom in order to reduce the burden of recovery time.

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P-052

ANALARMIN MFG-E8 ACCELERATES TISSUE REPAIR IN REVERSIBLE UNILATERAL URETERAL OBSTRUCTION

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(2) CRCHUM
(3) CHUM, Université de Montréal

Mediators released by the renal resident cells play a crucial role in the modification of the microenvironment. The resulting renal microenvironment can reprogram macrophages and modify their functions that can promote renal repair. Macrophages play a crucial role in the renal repair, but the exact mechanisms of the interactions between the microenvironment and the pro-repair reprogramming are still ill-defined. We identified MFG-E8 as a reprogramming factor released by apoptotic cells that can reprogram macrophages by reducing pro-inflammatory proprieties. In renal obstruction, we showed that MFG-E8 reduced tissue damage through a reduction of inflammasome activation. However, its role in renal repair is unknonwn.

MFG-E8 KO and WT mice underwent unilateral ureteral obstruction for three days and the obstruction was reversed. At time of reversal and q3 days, the animals received PBS or MFG-E8 ip. The mice were then followed for 7 days. At the end of the experiment, the kidneys were harvested for immunohistochemistry and immunoblotting. Administration of MFG-E8 reduced leucocyte infiltration and was associated with reduced tissue injury in mice (more brush borders in epithelial renal tubules and reduced inflammation). CD206+ cells were quantified as surrogate markers for M2 macrophages. MFG-E8 treatment increased the numbers of CD206+ cells in WT mice. The implication of the inflammasome activation in renal repair with MFG-E8 administration was also evaluated. MFG-E8 treatment reduced the activation of the inflammasome in WT mice.

Our data suggest that MFG-E8 attenuates renal inflammation, inflammasome activation and renal inflammation to promote tissue repair. A better understanding of the regulation of macrophage reprogramming by the MFG-E8 during renal repair could lead to the development of more specifically targeted therapeutics aimed at promoting an ordered resolution of inflammation and repair.

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P-053

2013 BANFF CRITERIA FOR CHRONIC ACTIVE ANTIBODY-MEDIATED REJECTION: ASSESSMENT IN A REAL LIFE SETTING

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Background : Significant changes in the criteria for chronic active antibody-mediated rejection (CAABMR) were made at the 2013 meeting, which is of major concern for clinical management. Here we compared the 2007 *vs.* 2013 criteria with regards to clinical outcomes.

Methods : Single-center, observational retrospective cohort study of all patients who received an indication biopsy between January 2006 and October 2014, during which EM evaluation, ptc scoring and C4d scoring by IH and IF was routinely performed. Patients were included if they met the criterion 1 for CAABMR: score cg1a>0, cg1b>0 or severe peritubular capillary basement membrane multilayering. Patients with GN, immune deposits, HCV+ status or suspicion of TTP-HUS were excluded. The endpoint was a composite of doubling of serum creatinine and death-censored graft loss.

Results : 123 patients were included. 18% met the full 2007 criteria, whereas an additional 18% fulfilled the complete 2013 criteria. Only 25% of patients met the 2007 criterion 2-C4d, in contrast to 82% for the 2013 criterion 2-microvascular injury (MVI): 67% were C4d-positive and 55% were g+ptc positive, with substantial overlap. 45 patients experienced the endpoint at a median of 22 months post-biopsy. Overall, only a 2013 diagnosis of CAABMR was associated with the endpoint (adjusted HR=2.5 [1.2-5.2] for 2013 *vs.* HR=1.6 [0.7-3.8] for 2007 diagnosis). Adjusted Cox modelling revealed that the 2013 criterion 2-MVI was more strongly associated with the endpoint than the 2007 criterion 2-C4d (HR=4.0 [1.1-14.1] vs. HR=2.3 [1.03-5.3]). When the 2013 criterion 2 was dissected by component, the C4d-component was significant (HR=2.5 [1.1-5.4]), but not the g+ptc (HR=1.1 [0.5-2.3]).

Conclusions : Compared to the 2007 criteria, applying the 2013 criteria doubled the proportion of patients with CAABMR. Importantly, it improved the association with clinical outcomes. This is due to the new C4d threshold, but not to the g+ptc component.

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KIDNEY INJURY MOLECULE-1 (KIM-1) INTERACTS WITH THE DYNEIN LIGHT CHAIN TCTEX-1 TO MEDIATE EFFEROCYTOSIS

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(2) Lawson Health Research Institute
(3) Western University

After tissue injury, the phagocytic clearance of apoptotic cells, or efferocytosis, attenuates inflammation and enables tissue repair. KIM-1 is an efferocytosis receptor specifically upregulated on proximal tubular epithelial cells during acute kidney injury (AKI). We previously showed that, after renal ischemia-reperfusion injury, mice deficient in KIM have impaired efferocytosis, with greater tissue damage, renal dysfunction and death, compared to wild-type mice. To uncover the phagocytic signalling pathway downstream of KIM-1, we utilized a yeast two-hybrid screening system and identified a potential KIM-1-interacting protein, the 14-kDa dynein light chain protein, Tctex-1. Tctex-1 is a component of the dynein microtubule motor complex involved in directly linking dynein to its cargo as an adaptor protein, or it plays dynein-independent roles in diverse cellular functions. Thus, we hypothesized that Tctex-1 is required for KIM-1-mediated engulfment of apoptotic cells. First, we confirmed the direct interaction between Tctex-1 and Kim-1 using co-immunoprecipitation, GST-Tctex-1 pull-down assay and immunofluorescence staining. When we stimulated KIM-1-expressing cells with apoptotic cells, the interaction between KIM-1 and Tctex-1 was sustained until the later stages of the efferocytosis. Knockdown of endogenous Tctex-1 expression with siRNA significantly inhibited efferocytosis by KIM-1-expresisng cells. To test if Tctext-1 the inhibitory effect caused by Tctex-1 knockdown was related to impaired cargo binding for dynein transport (i.e. dynein-dependent), we utilized a Tctex-1 mutant construct in which we replaced Threonine-94 with glutamic acid (T94E) to mimic the phosphorylated form that cannot bind dynein. Surprisingly, the phospho-mimic Tctex-1-T94E displayed decreased binding to Kim-1, but did not influence KIM-1-mediated uptake of apoptotic cells. Our studies have uncovered a novel role for Tctext-1 in efferocytosis, which is crucial to tissue repair following AKI.

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P-055

PERITONEAL DIALYSIS EXIT SITE INFECTION RATES

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Background

Patients on peritoneal dialysis (PD) are subject to high rates of infectious complications. Current evidence suggests a pathophysiologic link between PD catheter exit site (ES) infections and peritonitis. As a result, the International Society of Peritoneal Dialysis (ISPD) guidelines suggest topical ES prophylaxis to reduce the risk of ES infection. Presently, Saskatoon Health Region (SHR) does not have a standardized ES strategy; we hypothesized that SHR will have higher rates of ES infections when compared with data published from centers utilizing prophylactic therapies.

Methods

We retrospectively assessed data from all peritoneal dialysis patients within the SHR from 2013 (150 patients) and 2014 (168 patients). ES infections were defined as a positive culture and one of the following: antibiotic prescription within 5 days of the swab result, clinic notes describing a purulent ES, or clinic notes labeling the ES as 'infected'.

Results

In 2013 there were 150 patients with 275 ES swabs, and in 2014 there were 168 patients with 311 ES swabs completed. Despite the number of swabs, only 85 in 2013 and 75 in 2014 met our definition of an ES infection. Data collected showed ES infection rates as high as of 0.791/patient-year. In contrast, the ISPD reports ES infection rates of 0.154/patient-year when mupirocin is used for ES prophylaxis.

Conclusions

Given the results of this retrospective review, we suggest the implementation of an ES infection prophylaxis strategy in SHR. In addition, we found numerous swabs that did not lead to treatment, suggesting a high reliance on ES swabs to define infection, rather than ES appearance. We advocate for a more objective method of assessing ES, using one of the available ES scoring systems available. Further, we feel that SHR documentation of ES infections could be improved, and we advocate for a standardized method of tracking ES infections.

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P-056

PREDICTION OF 6-MONTH MORTALITY AMONG PATIENTS WITH END-STAGE KIDNEY DISEASE: AN EXTERNAL VALIDATION IN A BRITISH COLUMBIA COHORT

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Background: End-stage kidney disease (ESKD) is associated with a poor prognosis. Health care providers must be prepared to address end-of-life issues; hence, identifying patients at higher risk of death is recommended. A 6-month mortality prediction model for prevalent patients undergoing hemodialysis as derived by Cohen *et al.* (2010) has yet to be validated outside of the United States.

Objective: We aimed to validate this model in a Canadian cohort and assess its clinical utility.

Methods: 374 prevalent patients undergoing hemodialysis in two regions of BC were followed for 6 months. Data including serum albumin (ALB), age, peripheral vascular disease (PVD) and dementia captured when the surprise question (SQ) was asked was used to validate this 6-month mortality prediction model. Model performance was evaluated through discrimination, calibration and decision-curve analysis.

Results: The observed mortality in our cohort was 11.5% at 6 months. The prediction model had reasonable discrimination (c-stat=0.70) but poor calibration (calibration-in-the-large=-0.53 [95% CI: -0.88, -0.18]; calibration slope=0.57 [95% CI: 0.31, 0.83]) in our data. Decision curve analysis showed the model only has added value in guiding clinical decision in a small range of threshold probabilities: 8%-20%.

Conclusion: The prediction model by Cohen *et al.* has relatively limited clinical utility despite reasonable discrimination; this may partly due to its inaccuracy on estimating predicted risks. The model may be engaged in non-invasive clinical decision such as workload prioritization in advance care planning and shared decision making conversations. However, we do not recommend the model be used in guiding clinical decisions or interventions that apply to higher threshold probability. Further research is needed before the model can be applied to guide a wider range of clinical decisions.

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P-057

FOLLOW-UP OF SERUM CREATININE (SCR) AFTER INTENSIVE CARE UNIT (ICU) AND HOSPITAL DISCHARGE IN CHILDREN ADMITTED TO THE ICU

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Background: Acute kidney injury (AKI) in the pediatric ICU (PICU) may be associated with long-term chronic kidney disease (CKD). The extent to which children with AKI are followed for renal function post-discharge is unclear.

Objectives:

Determine if:
1) Post-PICU SCr measurement is more common in children with vs. without AKI.

2) Patients with PICU-AKI and SCr above baseline at hospital discharge are more likely to have SCr measured after hospital discharge.

Methods: Prospective cohort study of children in Montreal Children's Hospital PICU (excluded: primary renal disease). PICU-AKI was ascertained by KDIGO SCr-definition. SCr values from PICU discharge to hospital discharge and within 5 years post-hospital discharge were collected. Main outcome: presence of a SCr measurement a) between PICU and hospital discharge, b) within 3 months and 5 years of hospital discharge. Return to baseline SCr was defined as last hospital SCr <10% above baseline SCr. Group comparisons were made using Chi-square tests.

Results: 67/180 (37.2%) patients developed PICU-AKI. AKI vs. non-AKI PICU to hospital discharge SCr measurement occurred in 58.2% vs. 31.9% of patients, respectively (p=0.001); within 3 months of hospital discharge, SCr was measured in 35.8% vs. 13.3%, respectively (p<0.001); within 5 years SCr was measured in 53.7% vs. 38.1%, respectively (p<0.05). In AKI patients, those with vs. without hospital discharge SCr returned to baseline, 44% vs. 31% (p=0.28) of patients, respectively, had SCr measured within 3 months and 68% vs. 45.2% (p=0.07) of patients, respectively, had SCr measured within 5 years of discharge.

Conclusion: Patients with PICU-AKI have SCr measured more commonly after PICU discharge and hospital discharge, than patients without AKI. There appears to be no relation between discharge SCr in AKI patients and occurrence of long-term renal function measurement. This information is useful for devising future knowledge translation strategies on appropriate follow-up of post-AKI renal function.

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P-058

A CASE OF PURPLE URINE BAG SYNDROME

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Case Description

A 95 year old female presented to the hospital with an altered mental status and purple urine for one day. The patient had a past medical history significant for urinary retention being treated with a long-standing indwelling foley catheter. On physical examination the patient appeared to be in no acute distress. She was speaking in garbled sentences with no focal neurological deficits. She had no abdominal or suprapubic tenderness. Foley catheter bag had bright purple urine present. Abnormal laboratory findings included leukocytosis, urine pH of 8.0, and urine cultures positive for E.Coli and proteus mirabilis. Patient was started on piperacillin for UTI and after 3 days of treatment her mentation improved and urine returned to a light yellow hue.

Discussion

The colour of urine can be clinically significance as it may represent various pathological and physiological states. Purple urine bag syndrome (PUBS) is a rare phenomenon characterized by an intense purple discolouration of the urine in catheter bags, which is manifested by a urinary tract infection (UTI).The first case was described in 1978 and since that time only 78 reported cases have been documented in literature. The pathogenesis of PUBS is shown in figure 1 and has been associated with long-term urinary catheterization, increased tryptophan diet, alkaline urine, and constipation . This case elucidates a typical presentation for PUBS with a severe complication of altered mental status, which can lead to a costly and time consuming work-up if the condition is not familiarized and managed effectively.

P-058

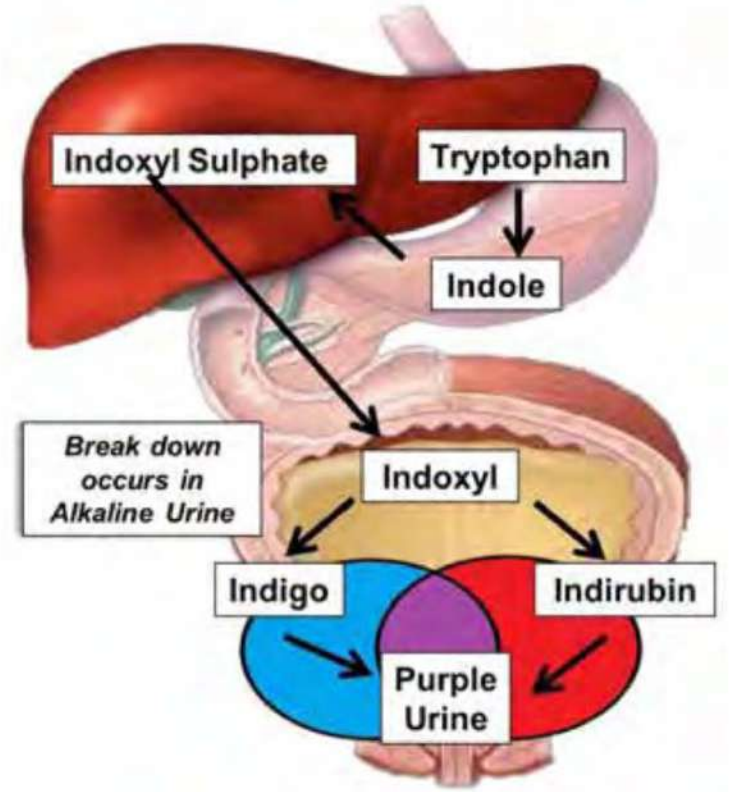

Figure 1: Biochemical conversion of tryptophan to indigo and indirubin

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P-059

UTILIZING ESTIMATED CREATININE EXCRETION TO ESTIMATE 24 HOUR ALBUMIN AND PROTEIN EXCRETION IMPROVES PERFORMANCE OF SPOT URINE SAMPLES FOR ESTIMATION OF ALBUMINURIA AND PROTEINURIA IN RENAL TRANSPLANT PATIENTS

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Background: Quantification of albuminuria and proteinuria is commonly utilized to monitor patients with renal transplant. Many centers utilize single voided specimen to estimate 24 hour urine protein and albumin excretion because of convenience and cost. We performed the current study to investigate if utilizing expected creatinine excretion (eCER) to calculate albumin or protein excretion rate (eAER or ePER) as compared to standard ACR or PCR on single voided sample would improve estimation of 24 hour urine albumin (mAER) and protein (mPER) excretion in renal transplant patients.

Methods: 181 patients met the inclusion criteria. mAER and mPER was the reference standard. eAER and ePER was calculated by spot urine samples by multiplying standard ACR and PCR by eCER (calculated by six different equations). Bias, precision and accuracy was determined for ACR, PCR, eAER and ePER.

Results: The ACR and PCR had the highest bias and significantly underestimated albumin and protein excretion (for ACR; Bias -57.5 mg, 95% CI -91 to -24; p=0.001 and for PCR; Bias -110 mg, 95% CI; -150 to -60; p<0.001). Accuracy (within 30%) for ACR was 38.1% and for eAER ranged from 45.9 to 49.2% depending on formula utilized. Accuracy (within 30%) for PCR was 42.5% and for ePER ranged from 46.4% to 53.6% depending on formula utilized.

Conclusion: Utilizing estimated creatinine excretion to calculate eAER and ePER improves the bias and accuracy of single voided samples for estimation of mAER and mPER in renal transplant patients.

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P-060

SUNITINIB TREATMENT INDUCES THE FORMATION OF STEM CELL-LIKE CANCER CELLS IN CLEAR CELL RENAL CELL CARCINOMA

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Background: Sunitinib (SU) is the first line treatment for advanced renal cell carcinoma (RCC). SU prolongs PFS by about 6 months; however, patients eventually develop resistance by a largely unknown mechanism.

Objectives: To investigate previously unknown mechanisms of SU resistance *in vitro* and in animal model.

Methods: *In vitro*: RCC cell lines were treated with SU. Proliferation, self-renewal and transcriptome were assessed. *In vivo*: Isogenic model and NSG mice were used as xenograft recipients. Mice were randomized to vehicle treated, SU sensitive and SU resistant groups. Tumorgenicity was assessed by limiting dilution assay (LDA). Metastasis assay was based on tail-vein injection of RCC cells. Gene- and miRNA expression was assessed by NGS (Illumina MiSeq), microarray (Illumina HumanHT12) or by Nanostring. Expression was validated by qPCR and by ICC.

Results: *In vitro*: SU sensitive cells showed increased stem cell marker and cancer stem cell marker expression; enhanced self-renewal and RCC sphere formation ability. SU-treated RCC spheres expressed high level of stem cell and cancer stem cell markers and were highly clonogenic, indicating potent self-renewal. *In vivo*: SU-treated RCC spheres were highly tumorigenic and metastatic. Differentially expressed genes and miRNAs were grouped into expression patterns. Significant functional categories included ‘stem cell’, ‘cell differentiation’, ‘development’, ‘proliferation’, ‘cell-cell and cell-ECM interactions’ and ‘metabolic processes’. Significant signaling pathways were ‘hypoxia-related pathways’, ‘BMP signaling’ and ‘canonical and non-canonical WNT signaling’.

Conclusion: RCC cells gain stem cell characteristics early in SU treatment, which could potentially contribute to SU resistance in advanced RCC.

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P-061

ASSOCIATION OF BONE MINERAL DENSITY WITH FRACTURES ACROSS THE SPECTRUM OF CHRONIC KIDNEY DISEASE- THE PRAIRIE DXA STUDY

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Regina Qu Appelle Health Region

Introduction: The value of Dual energy X ray Absorptiometry (DXA) scans in postmenopausal women in predicting fractures is robust. However, its role in patients with chronic kidney disease (CKD) stages III-V is controversial.

Methods: 410 consecutive patients who underwent DXA scan at the point of entry into our multidisciplinary CKD program were included. Bone mineral density (BMD) data, T score and Z scores were collected at four sites: the lumbar spine, total hip, mean of left and right femoral neck, and the proximal radial region (Radius 33%). We collected data on demographic, lab markers of mineral metabolism and fractures (identified through self-reported questionnaires, hospital electronic medical records and physician billing records).

Results: 35.9% stage III CKD, 28.4 % stage IV CKD, and 32.4% stage V CKD experienced a clinical fracture during the study period. On multivariate analysis, we observed a decline of 1.0 SD in T-score is associated with a statistically significant increase in the risk of fracture after addition of biochemical parameters such as Parathyroid hormone (PTH), Alkaline Phosphatase (ALP), calcium and phosphorus and estimated- Glomerular filtration rate (e-GFR) of <30 (OR= 1.36, 95% CI: 1.02, 1.72). In patients with a GFR of >30 mls/ minute, the odds ratio (OR) of identifying a fracture was 1.54 in comparison to OR of 1.14 in patients with GFR <29 mls/minute.

Conclusions: We conclude that there is a role for DXA scans in all patients with CKD although the ability of the T scores to predict fractures is more robust in stage III CKD, as compared to stages IV and V.

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P-062

SUCCESSFUL TREATMENT OF HYPOMAGNESEMIA IN A PERITONEAL DIALYSIS PATIENT WITH INTRAPERITONEAL MAGNESIUM SULFATE

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Magnesium is an important modulator of the electrical activity of cardiac cells. Its homeostasis is maintained through absorption, mainly in the small intestine, storage in the bone, and excretion via the kidneys and feces. In patients with advanced chronic kidney disease or on hemodialysis, hypermagnesemia is common due to decreased renal excretion. However, a high incidence of hypomagnesemia, occasionally requiring magnesium supplementation, has been reported in the peritoneal dialysis (PD) population. One of the contributing factors may be the daily use of low magnesium dialysate solutions. Coexisting hypokalemia, which happens frequently in these patients, further increases the risk of life threatening arrhythmias. In this paper, we report the successful treatment of critical hypomagnesemia with intraperitoneal (IP) magnesium sulphate ($MgSO_4$) in a 70 year old female PD patient with a history of celiac disease and recurrent atrial fibrillation. The patient was initially started on hemodialysis, then switched to PD. At PD initiation, her Mg level was 0.51 mmol/L. She was initiated on oral potassium and magnesium supplements because of hospitalizations for uncontrolled atrial fibrillation. However, due to gastrointestinal intolerance, the oral magnesium supplement was replaced with intravenous $MgSO_4$. As a result of fluctuations in the patient's serum magnesium levels and inconvenience of intravenous administration, we trialed the patient on IP $MgSO_4$. The patient was taught to instil 4 grams of $MgSO_4$ into a 2 L bag of Dianeal 2.5% solution with a dwell time of 6 hours once weekly. A series of peak and trough serum magnesium levels were obtained to assess the adequacy of the dosage regimen. Her mean peak serum magnesium concentration was 1.13 mmoL/L and mean trough magnesium concentration was 0.7 mmol/L. No adverse effects were reported by the patient and she has had no further admissions to hospital for atrial fibrillation.

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P-063

PREDICTING PATIENT-BORNE WATER AND ELECTRICAL COSTS IN HOME HEMODIALYSIS: A REGIONAL CANADIAN PERSPECTIVE

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Background:
There is increasing interest in the use of home hemodialysis (HHD) as an alternative renal replacement therapy to facility-based conventional hemodialysis. HHD can result in better physiological parameters, quality of life, and overall survival for patients with end stage renal disease (ESRD). While HHD is associated with lower costs to the healthcare system due to lower staffing and overhead costs, it transfers the treatment costs of utilities (water and power) to the patient.

Objectives:
The purpose of this work was to determine the utility costs of HHD and create a model such that patients and renal programs can predict the annual patient-borne dialysis utility costs involved with this type of treatment.

Methods:
Seven common HHD prescriptions were replicated 5 times using various combinations of HHD machines and reverse osmosis units. Real time electrical and water consumption was monitored during these dialysis simulations.

Results and Conclusions:
Using typical 2014 utility costs for Edmonton, Alberta, the most expensive prescription was for nocturnal HHD (8 hours, 6 days/week; Qd 300mL/min), which resulted in a utility cost of $1220/year, while the least expensive prescription was for conventional HHD (4 hours, 3 days/week; Qd 500mL/min) costing $482/year. A generic formula is presented to allow patients/programs to calculate a more precise estimate of utility costs based on individual combinations of dialysis intensity, frequency and utility costs unique to any individual patient. We demonstrate a significant cost burden of hemodialysis is transferred to the patient on HHD, which would otherwise be borne by the renal program.

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P-064

PREVIOUS FISTULA FAILURE AND OUTCOME OF THE SECOND FISTULA ATTEMPT: A MULTI-CENTRE LONGITUDINAL COHORT STUDY.

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***Background**:* Arteriovenous fistulas (AVFs) are considered the preferred form of vascular access for hemodialysis. Patients who experience failure of a first arteriovenous fistula (AVF) must decide whether or not to attempt a second AVF and there are few data to guide clinical decision-making. We hypothesized that the outcome of the first AVF attempt could be used to predict the success of a second attempt.

***Objective**:* To determine whether the outcome of the first AVF attempt influences the likelihood of success of a second AVF attempt.

***Methods**:* We prospectively assembled an incident cohort of adults receiving hemodialysis therapy who were enrolled in five Canadian dialysis programs between 2004 and 2012 and who had undergone a second AVF attempt. For both the first and the second AVF, we defined the attempt as successful if it resulted in a period of at least one month of catheter-free use. We used logistic regression to study the odds of a successful second AVF attempt as a function of the outcome of the first AVF attempt (success versus failure), while controlling for potential confounders.

***Results**:* Among 2388 eligible people in this cohort, 190 underwent a second AVF attempt and were included in this study. Of these patients, 34 (18%) had a successful first AVF attempt. People with a successful or failed first AVF attempt were similar in age (63±14 years), sex (64.2% male) and diabetes status (63.7%), whereas peripheral vascular disease was more common in patients with a failed first AVF attempt. Use of the first AVF for at least one month was not associated with increased odds of a successful second AVF attempt (Odds Ratio 1.17; 95% confidence interval [0.52 - 2.62]).

***Conclusion**:* The outcome of the first AVF attempt does not predict the outcome of the second AVF attempt.

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P-065

COMANAGEMENT BY NEPHROLOGISTS IS ASSOCIATED WITH INCREASED LIKELIHOOD OF APPROPRIATELY DOSED PRESCRIPTIONS IN PATIENTS WITH CHRONIC KIDNEY DISEASE

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(2) Department of Nephrology

Background: Two-thirds of patients with chronic kidney disease (CKD) are commonly prescribed drug doses that are excessive for their kidney function. Studies have shown improved outcomes when CKD patients are followed by nephrologists in addition to family physicians.

Objective: To determine whether care by both a nephrologist and family physician (i.e. comanagement) versus family physician alone is associated with increased appropriately dosed prescriptions in patients with stage 4 or 5 CKD.

Methods: We performed a retrospective cross-sectional study of antibiotic prescriptions from family physicians in Ontarians aged ≥66 years, with estimated glomerular filtration rate (eGFR) <30 mL/min/1.73 m^2 using linked healthcare databases from 2003-2014. Patients were categorized by comanagement, defined as having at least one outpatient visit with a nephrologist in the 1 year prior to prescription date. The outcome was whether antibiotic prescriptions were appropriately renally dosed for a patient's eGFR. The groups were matched one to one via propensity score matching to balance 34 baseline characteristics. Conditional logistic regression modelling was used to determine the independent association between comanagement and appropriate dosing.

Results: After propensity score matching, 3937 patients were included in each group. The median age of these patients was 81 (IQR 76-86), and 63% were female. Patient comorbidities included: hypertension (92%), diabetes (51%), coronary artery disease (48%), and congestive heart failure (40%). Comanagement was significantly associated with appropriately dosed prescriptions with a conditional odds ratio of 1.20 (95%CI 1.09-1.32). Neither eGFR reporting nor degree of kidney dysfunction significantly modified the association between comanagement and appropriate dosing.

Conclusion: In patients with stage 4 or 5 CKD prescribed an antibiotic, patients who were comanaged had 20% greater odds of having appropriately dosed prescriptions from their family physicians. Decreased medication errors may, in part, explain the improved patient outcomes associated with seeing a nephrologist in observational studies.

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P-066

ESTIMATED GFR USING BETA TRACE PROTEIN (BTP) IS IMPACTED BY ASSAY TYPE

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Background: BTP is an emerging marker of GFR and several equations exist to convert it into an estimate of GFR. There are two available BTP assays: an ELISA assay (Cayman Chemical) and a nephelometric assay (Siemens). Differences between them have never been examined. The aim of this study was to determine the difference in BTP concentrations using the 2 assays and examine its impact on GFR estimation.

Methods: Serum from 105 subjects was split. BTP was measured using both assays. GFR was estimated using the new EPI BTP equation: BTP eGFR=55 * BTP $^{-0.695}$ * 0.998 ^{age} * 0.899 if female. Differences between paired BTP values were compared using paired student t-tests. The percentage of samples with paired values within 10%, 20% and 30% of each other was calculated. A similar analysis was performed using the EPI BTP GFR for the whole cohort and after stratification by eGFR.

Results: Mean Cr was 77 ± 25 umol/L. The mean Siemens BTP was 0.62 mg/dL (0.39-0.84, 95% CI) lower than the mean Cayman BTP (p<0.0001). Only 14%, 21% and 30% of paired values were within 10%, 20% and 30% of each other. The differences between the eGFR using the 2 BTP assays are shown below.

Conclusions: Significant differences in GFR estimation result from differences in BTP assays. Equations developed using one assay should not be used with the other assay. BTP assay standardization should be a priority as this novel analyte becomes increasingly utilized.

Wws	Siemens eGFR (SD) ml/min/1.73m^2	Cayman eGFR (SD) ml/min/1.73m^2	Siemens eGFR – Cayman eGFR (95% CI) ml/min/1.73m^2	% within 10%	% within 20%	% within 30%
Whole cohort (n=105)	49.7 (11.8)	45.2 (47)	4.5 (-4.7-13.7)	17	37	63
EPI BTP > 45 ml/min/1.73m^2 (n=52)	57.2 (9.7)	61.2 (62.2)	4.7 (-23.1-13.6)	35	58	79
EPI BTP < 45 ml/min/1.73m^2 (n=53)	42.3 (8.6)	28.7 (8.4)	13.5 (11.0-16.0)*	0	17	47

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P-067

EVERY OTHER DAY HEMODIALYSIS SCHEDULING: A COST UTILITY ANALYSIS

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Background: Mortality rates on hemodialysis (HD) are excessively high, possibly related to the episodic nature in which HD is delivered. More intensive HD strategies may provide more physiologic renal replacement and lead to improved outcomes at the expense of increased resource utilization.

Objectives: To predict if an alternate day HD schedule is likely to be cost effective compared to the conventional thrice weekly HD schedule.

Methods: We developed a Markov state transition model to perform a cost utility analysis comparing conventional thrice-weekly HD scheduling to an alternate day HD schedule (EODD, Every Other Day Dialysis). Cost inputs were derived from Ontario Renal Network data. State transition probabilities were derived from event rates obtained from a local database of Hemodialysis patients. Estimates for other model inputs were obtained from literature sources. A two-dimensional Monte Carlo simulation was conducted with 1000 outer-loop iterations each with 1000 inner-loop iterations allowing for both parameter- and individual-level uncertainty to be modelled. Outcome measures were discounted (3%/yr) quality-adjusted life years (QALYs), discounted lifetime costs, and incremental cost effectiveness ratios (ICERs).

Results: The mean (SD) costs of conventional HD and EODD were $129377 ($22171) and $199033 ($32686), respectively. The mean (SD) QALYs for conventional HD and EODD were 3.08 (0.22) and 3.63 (.24) respectively, yielding an ICER of $127809 per QALY gained by adopting EODD.

Conclusion: With current model inputs, EODD would lead to increased patient survival but also increased costs. EODD would only be cost effective if the willingness to pay threshold exceeded $125,000 per QALY gained.

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P-068

HYPERBRANCHED POLYGLYCEROL IS SUPERIOR TO GLUCOSE FOR LONG-TERM PRESERVATION OF PERITONEAL ULTRAFILTRATION IN A RAT MODEL OF CHRONIC PERITONEAL DIALYSIS

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(3) University of British Columbia
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Background: Replacing glucose with a better biocompatible osmotic agent in peritoneal dialysis (PD) solutions is needed in PD clinic. We previously demonstrated the potential of hyperbranched polyglycerol (HPG) as a replacement for glucose. This study further investigated the long-term effects of chronic exposure to HPG as compared to a glucose-based conventional PD solution on the peritoneal membrane (PM) structure and its function in rats.

Methods: Adult male Wistar rats received once-daily intraperitoneal injection of 10 mL of HPG solution (1 kDa, HPG 6%) compared to PhysionealTM 40 (PYS, glucose 2.27%) or electrolyte solution for 3 months. The overall health conditions were determined by blood chemistry test. The PM function was determined by peritoneal equilibration test (PET), and its injury by histological analyses.

Results: Here, we showed that there was no difference in the blood chemistry between rats receiving the HPG and the control electrolyte solution, while daily administration of PYS increased serum alkaline phosphatase, globulin and creatinine and decreased serum albumin. Unlike PYS, HPG did not significantly attenuate PM function, which was associated with smaller change in both the structure and the angiogenesis of the PM with less number of cells expressing vascular endothelial growth factor (angiogenetic factor), α-smooth muscle actin (myofibroblast marker) and MAC387 (macrophagy marker).

Conclusions: The results from this experimental study indicate the superiority of HPG to glucose in the preservation of the functions of the peritoneum during a long-term exposure to hyperosmotic PD solution, suggesting the potential of HPG as a novel osmotic agent for PD.

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P-069

PERITONEAL DIALYSIS: A SCOPING REVIEW OF STRATEGIES TO MAXIMIZE PD UTILIZATION

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(2) University of Toronto

Background: The percentage of end-stage renal disease patients treated with peritoneal dialysis has declined in many countries since the mid-1990s. Barriers to peritoneal dialysis have been reviewed extensively in the literature, but evidence about strategies to address these barriers and maximize the safe and effective use of peritoneal dialysis is lacking.

Objective: To conduct a scoping review identifying strategies to increase peritoneal dialysis use in adults with end-stage renal disease.

Methods: Our search strategy was developed in consultation with an experienced librarian and included the following online databases: MEDLINE (OVID), EMBASE, PubMed, Cochrane Controlled Trials Register, Current Controlled Trials, and Cochrane Database of Systematic Reviews for articles published from 1974 to November 2013. Experts in the field were contacted for information about other ongoing or unpublished studies. A complementary search was conducted in the grey literature. Websites of national, provincial or regional agencies were searched for documents regarding policies surrounding the use of peritoneal dialysis.

Results: A total of 5,856 papers were identified using our search; 52 studies met inclusion criteria and were included in our scoping review. We found a total of three randomized controlled trials that had limited sample size and limited follow-up. The remaining studies were retrospective or narrative reviews, with no controlled before-after studies or interrupted time series analysis. The majority of studies focused on pre-dialysis education programs, PD-first policies, unplanned PD starts, switching from HD to PD, addressing barriers to PD use in rural areas and among elderly patients, and insertion of PD catheters by nephrologists.

Conclusions: Individual dialysis centers need to identify barriers to increasing PD in their program and direct targeted strategies to increase PD utilization. Our review highlights some effective strategies that may be used. Our review also highlights the need for further research into strategies to increase PD utilization.

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P-070

CPAP TREATMENT FOR OBSTRUCTIVE SLEEP APNEA IMPROVES THE HEART RATE VARIABILITY RESPONSE TO ANGIOTENSIN II

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Background

Obstructive sleep apnea (OSA) is common in chronic kidney disease (CKD). Both conditions are associated with decreased heart rate variability (HRV) and increased renin-angiotensin system activity, each a risk factor for progression of kidney and cardiovascular disease.

Objectives

To determine the effect of continuous positive airway pressure(CPAP) treatment on HRV at baseline and in response to a physiological stress.

Methods

Twenty normotensive, non-diabetic, newly diagnosed OSA subjects with normal kidney function(75% male; 50±2y; respiratory disturbance index[RDI]>15hr^{-1}) and hypoxia(oxyhemoglobin saturation[SaO_2]<90% for >12% of night) were studied in high-salt balance pre- and post-CPAP(1 month). Utilizing a 3-lead Holter monitor with a sampling frequency of 125Hz, HRV was calculated by spectral power analysis (low-frequency[LF], high-frequency[HF], standard deviation of the normal R-R wave[SDNN]) at baseline and in response to graded Angiotensin II(AngII) infusion(3ng/kg/min·30min, 6ng/kg/min·30min).

Results

CPAP corrected OSA and hypoxia(RDI, 43.1±4.1 vs 3.8±0.6hr^{-1}, p<0.001; SaO_2<90%, 36.3±5.0 vs 5.6±2.0%, p<0.001). There was no change in baseline LF(45±2 vs 46±3nu[normalized units], p=0.4) or HF(81±4 vs 83±10nu, p=0.8), but improved SDNN(63±6 vs 75±9ms, p=0.087) post-CPAP. There was a greater reduction in LF(Δ30min, -1±2 vs -6±2nu, p=0.047; Δ60min, -2±3 vs -6±2nu, p=0.2), no change in HF(Δ30min, -7±5 vs -16±7nu, p=0.3; Δ60min, -9±5 vs -16±10nu, p=0.5), and SDNN was maintained(Δ30min, 14.1±6.8 vs 8.2±8.2ms, p=0.022; Δ60min, 14.9±6.1 vs 5.5±7.7ms, p=0.082) in response to AngII post-CPAP(Figure 1). Norepinephrine decreased post-CPAP(2.6±0.3 vs 1.9±0.2nmol/L, p=0.001).

Conclusions

Treatment of OSA, a common condition in CKD, with short-term CPAP improved HRV and may have important implications in mitigating cardiovascular risk in CKD patients.

P-070

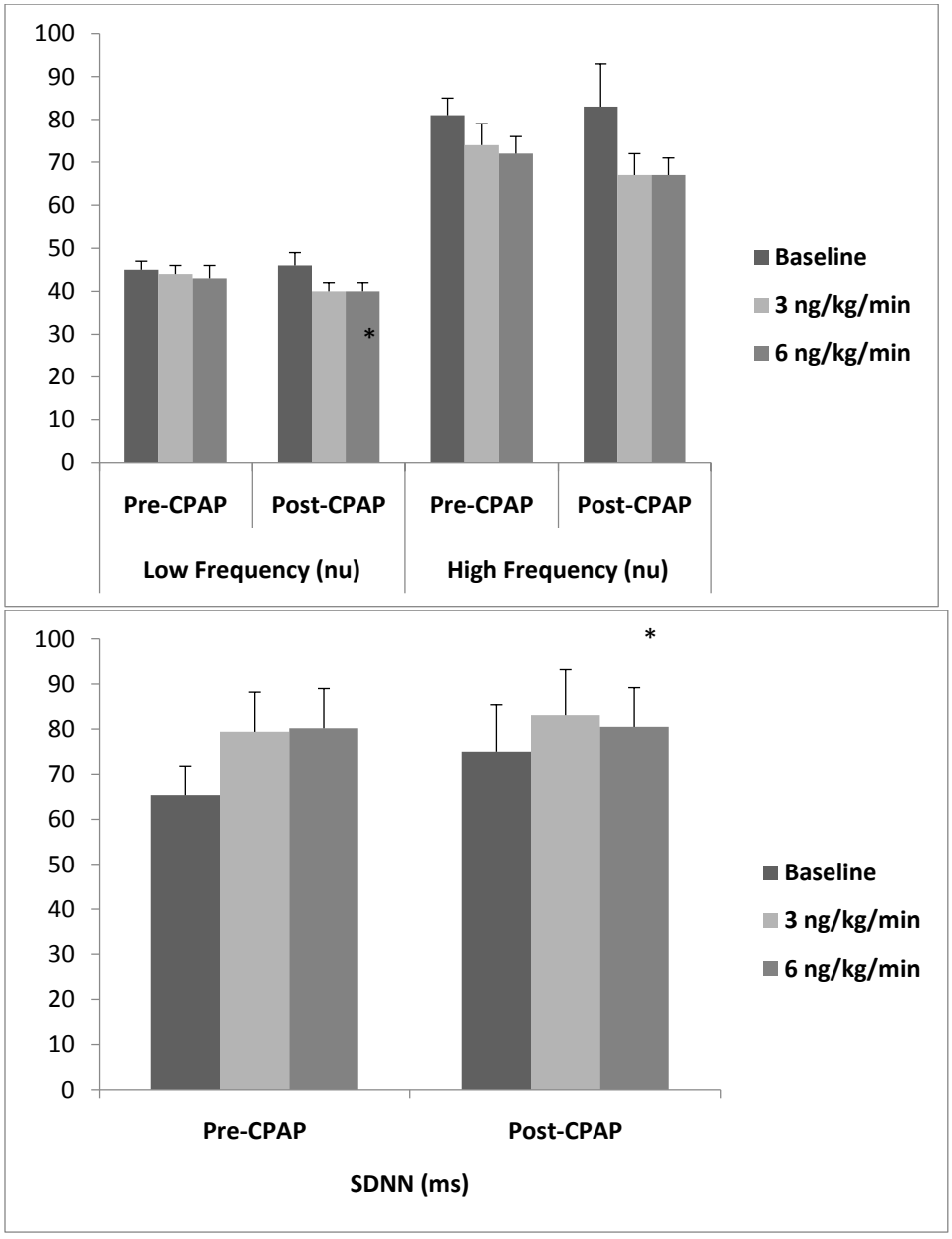

Figure 1. Heart Rate Variability Pre- and Post-CPAP at Baseline and in Response (Δ) to Angiotensin II. *P<0.05 vs Pre-CPAP. CPAP, continuous positive airway pressure; nu, normalized units; SDNN, standard deviation of the normal R-R wave.

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P-071

BONE MICROARCHITECTURE ANOMALIES AND EXPRESSION OF OSTEOCYTE MARKERS IN LOW SERUM PARATHORMONE CKD RATS WITH VASCULAR CALCIFICATION

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INTRODUCTION: The mechanisms underlying bone and vessels anomalies are poorly understood in chronic kidney disease (CKD). The aim of this study is to determine the anomalies of bone microarchitecture in CKD rats with vascular calcification and to evaluate whether if calcified vessels express osteocytes markers.

METHOD: CKD, low serum parathormone (PTH) level and vascular calcification in Wistar rats were induced by 5/6 nephrectomy and high calcium, phosphate and vitamin D (Ca/P/VitD) supplementation. These rats were compared to CKD and normal rats fed with a normal diet. The markers of vascular remodeling, osteoblastic differentiation and the expression of osteocytes markers were assessed on the tibia bones and thoracic aortas. Cortical and trabecular bone microarchitecture were performed by Micro-Ct and histomorphometry analysis.

RESULTS: In the thoracic aortas, markers of osteoblastic differentiation (RunX2, BMP-2, osteocalcin) were increased only in CKD rats with vascular calcification while α-SMA was significantly reduced. Sclerostin, DMP-1 and DKK-1 were all highly expressed in areas of vascular calcification (Figure 1). Furthermore, serum levels of sclerostin were increased only in rats with vascular calcification. Cortical bone mineral content and thickness were decreased in CKD rats with vascular calcification as compared to control while trabecular thickness, osteoid volume and surface were dramatically increased.

CONCLUSIONS: In this CKD model of vascular calcification and low serum PTH levels, there is increased expression of osteocytes markers in calcified vessels. Furthermore, cortical and trabecular bone compartments are differently affected. Our results emphasize the central role of bone metabolism and osteocytes in vessel anomalies in CKD.

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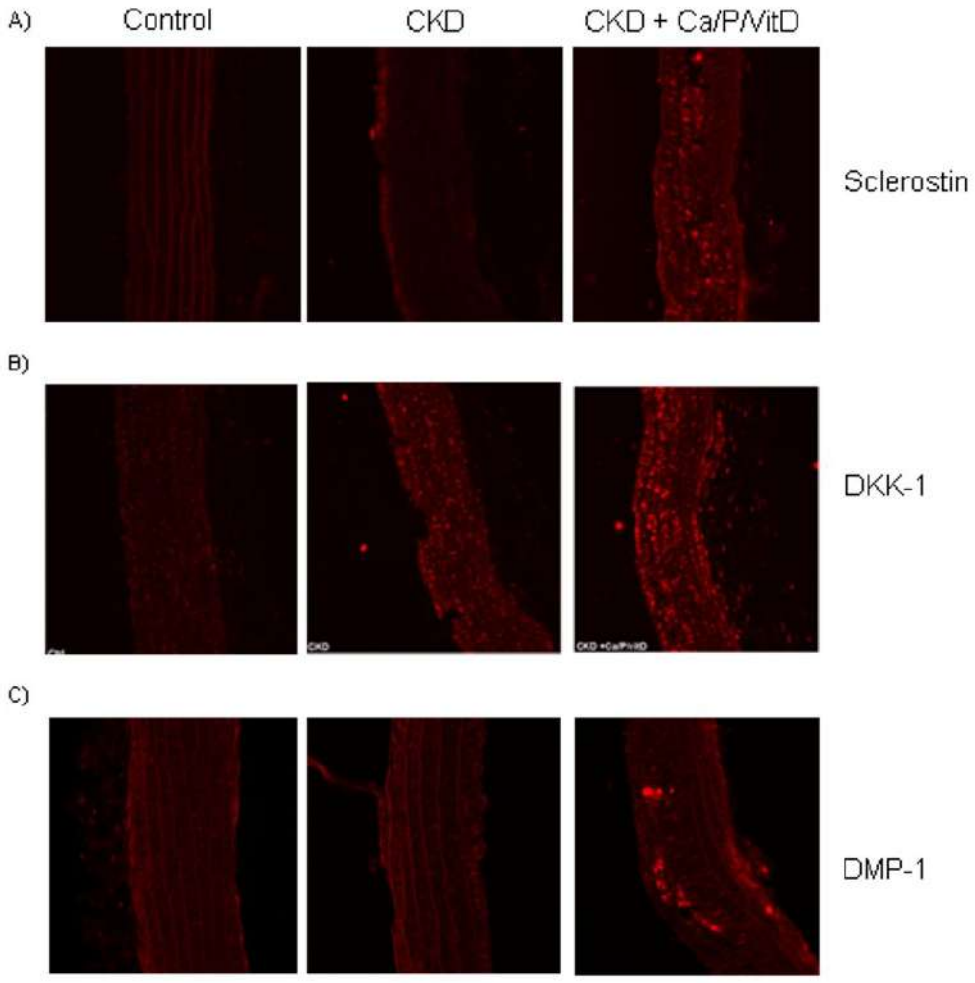
Figure 1. Expression of sclerostin, DKK1 and DMP1 in thoracic aortas from CKD rats with vascular calcification



CTL: control; Ca/P/VitD: calcium, phosphorus and vitamin D supplementation. There is significantly increased immunofluorescence expression of A) sclerostin, B) DKK1 and C) DMP1 in thoracic aortas from CKD rats with vascular calcification as compared to control and CKD rats without vascular calcification

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P-072

URINARY HEPCIDIN-25 IS ELEVATED AFTER CARDIAC SURGERY

Nora Choi, Claudio Rigatto, Ang Gao, Brett Hiebert, Carly Fraser, Simon Christie, Rakesh Arora, Julie Ho
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Background:
Acute kidney injury (AKI) following cardiac surgery results in increased morbidity and mortality. Biomarkers of AKI may allow for early intervention. Using proteomic techniques, we previously identified urinary hepcidin-25 as an independent predictor for AKI avoidance.

Objective:
Independently validate urinary hepcidin-25 as a novel biomarker for early AKI diagnosis in patients undergoing cardiopulmonary bypass (CPB).

Methods:
A prospective observational cohort of cardiac surgery patients (n=326) with serial urines was collected at: baseline, start CPB, 1 hour CPB, arrival to intensive care unit (ICU), post-operative day (POD) 1 and 3-5. A nested case-controlled cohort (n=42) of AKI versus non-AKI patients was evaluated for urinary hepcidin-25 using ELISA. AKI was defined using KDIGO (creatinine >50% from baseline and/or increase 26.5umol/L/48hrs).

Results:
AKI patients had more diabetes (47.6% vs. 14.3%, p=0.02) and lower baseline renal function (76.4 vs. 86.4 ml/min, p=0.03). The groups were otherwise balanced including CPB and cross-clamp time; EURO-score II; and intraoperative urine output. Urine hepcidin-25 remained low from baseline till arrival at ICU. Urine hepcidin-25 increased by POD1 and POD3-5, but there were no differences between AKI versus non-AKI (Figure 1).

Conclusion:
Urine hepcidin-25 is an important regulator of iron homeostasis, and these results suggest that iron sequestration pathways may be relevant following CPB, irrespective of AKI status. The lack of difference between groups may be due in part to the different AKI definition used in this cohort compared to the original studies (AKI defined: creatinine >50% from baseline). Urine creatinine data are pending to correct for dilution.

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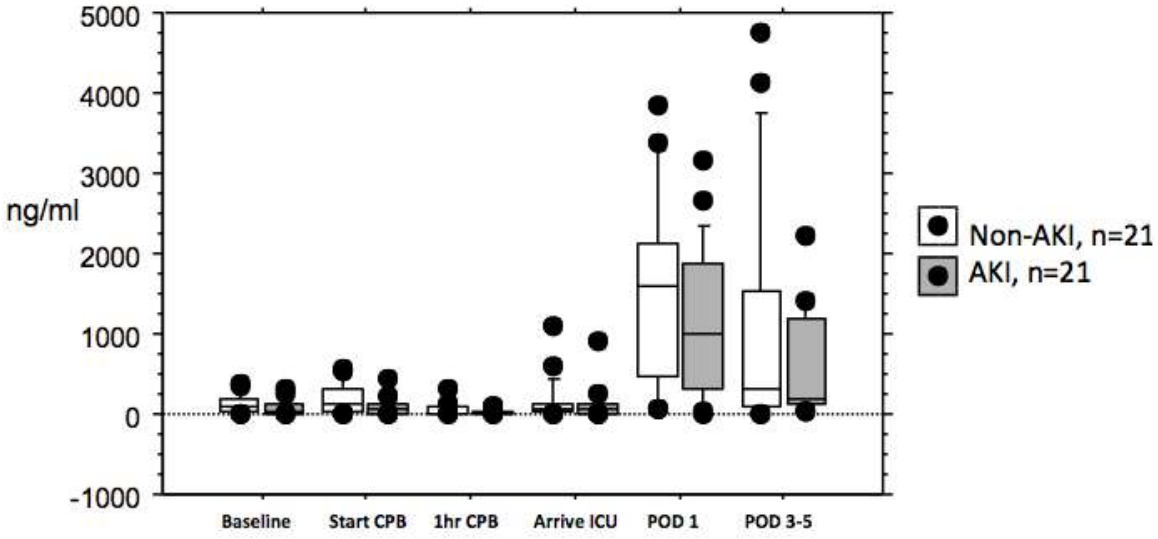
Figure.1: Urinary hepcidin-25 in AKI versus Non-AKI cohorts



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P-073

A MULTIFACETED EDUCATIONAL INTERVENTION TO INCREASE UPTAKE OF A URINARY TRACT INFECTION GUIDELINE

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Objective:
To evaluate whether a multifaceted educational intervention would increase adherence to the 2011 American Academy of Pediatrics guideline regarding voiding cystourethrogram (VCUG) use in first urinary tract infection (UTI) in young children.

Methods:
We conducted a prospective interventional study at one centre using a pretest-posttest design. We included all VCUGs ordered to exclude vesicoureteral reflux in 2-24 month old children with clinical documentation suggesting a preceding UTI. Using a health promotion model for effecting physician behaviour change, we constructed a multifaceted intervention including an interactive lecture, clinical pathway and faxed reminder. Pediatricians received all interventions; non-pediatricians received only the reminder. Our outcomes were the proportion of adherent VCUGs and VCUG ordering rate during each intervention phase. We also evaluated physician and patient characteristics associated with adherence.

Results:
Overall, 109 physicians ordered 219 VCUGs for 219 children. Using analysis of variance, pediatricians ($F(2,29) = 3.38$, $p = .048$) and non-pediatricians ($F(2,28) = 14.71$, $p < .001$) demonstrated a significant increase in the monthly proportion of adherent VCUGs. There was a significant decrease in the pediatrician monthly ordering rate of VCUGs (linear trend incidence rate ratio 0.74, 95% confidence interval (CI) [0.54, 0.99], $p = .046$). Utilizing logistic regression, the odds of adherence to the guideline were 2.91 times greater among pediatricians than non-pediatricians (95% CI [1.5, 5.5], $p = .001$).

Conclusions:
Following a multifaceted educational intervention, pediatricians were more likely to adhere to VCUG guideline recommendations than prior to the intervention. Pediatricians were more likely to be adherent than non-pediatricians.

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P-074

PARTICIPATION IN THE OPEN, ONLINE, TWITTER-BASED, NEPHROLOGY JOURNAL CLUB, #NEPHJC

Swapnil Hiremath (1), Joel Topf (2), Matthew Sparks (3), Edgar Lerma (4), Thomas Oates (5), Francesco Iannuzzella (6), Suzanna Norby (7), Graham Abra (8), Hector Madariaga (9), Nikhil Shah (10)

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(8) Satellite Healthcare
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(10) University of Alberta

Background: We established an online nephrology journal club, #NephJC in April 2014, with the addition of a European chat in December 2014, that meets twice monthly to discuss recently published research and clinical practice guidelines. We invite content experts and manuscript authors to the discussion. The meeting occurs on the public forum Twitter, allowing any interested individual to join. The purpose of #NephJC is to provide a recurring, academically-minded event on Twitter and to help establish this communication channel as one for serious nephrology discourse. In addition, online journal clubs are becoming a critical route for post publication peer review. In order to assess the impact of #NephJC we reviewed participation in the discussions since its inception, and the impact of the additional European chat.

Methods: We searched the Symplur analytics database for all tweets with the hashtag #NephJC from March 16 2014 to Jan 15 2016. We measured the number of participants, number of tweets and assessed participation over the first 41 NephJC sessions.

Results: From April 29th 2014 to Jan 15 2016, 41 topics were discussed, 17 initially and 24 since addition of the European chat. Overall, 1717 unique participants tweeted 21,277 tweets over the period. The overall median participation for each chat was 46 individuals (interquartile range, IQR, 36 to 65) and 540 tweets (IQR 299 to 684). The addition of the European chat has resulted in a significantly higher number of participants (from median 32 to 64, $p < 0.05$) and tweets (median 270 to 668.5, $p < 0.05$)

Conclusions: NephJC has established itself as an integral part of the online digital mentorship curricula. The sustained usage and growth in participation of #NephJC demonstrates the positive value of Twitter in medical education.

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P-075

ARE AUTOMATED BLOOD PRESSURE MONITORS ACCURATE COMPARED TO AMBULATORY BLOOD PRESSURE MONITORS? A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background:
Accurate blood pressure (BP) measurements are crucial for management of hypertension, a modifiable risk factor for cardiovascular events and mortality. 24-hour ambulatory BP monitoring (ABPM) provides an accurate assessment of BP, and CV risk. However ABPM is cumbersome and not reimbursed in most jurisdictions. BpTRU and other automated oscillometric BP monitors (AOBP) have been proposed to replace ABPM. Their accuracy in comparison to ABPM has not been systematically assessed.

Objective:
To perform a systematic review and meta-analysis to determine the accuracy of AOBP, as compared to the current gold standard, 24-hour ABPM

Methods:
A literature search was performed using Medline, Embase and CINAHL databases until July 16, 2015. We selected all studies that included intra-individual comparisons between AOBP and ABPM. Study selection was done in duplicate with disagreements resolved by consensus. Demographics and BP values including details of BP measurement techniques were also abstracted in duplicate. Quantitative synthesis was performed to report the weighted mean difference between the two methods.

Results:
From the 203 non-duplicate citations from the search, 16 full text articles were selected for the systematic review. 14 studies were Canadian, with 2 from Europe. The median sample size was 226 (range 17 to 654). The study-level difference in means for systolic BP (SBP) ranged from -9.7 to +9 mm Hg, with 5 studies reporting a higher average SBP and 10 studies reporting a lower average SBP with AOBP than ABPM (and one reporting exactly the same average). Thus there was significant heterogeneity (Cochran's Q = 261, I-squared 94, $p < 0.001$) not allowing for pooled analysis. 11/16 studies reported correlation coefficients (range 0.34 to 0.864). Very few studies reported measures of accuracy or Bland-Altman plots.

Conclusions:
The limited data available does not suggest that AOBP should replace ABPM in routine clinical practice.

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P-077

THE USE OF BIOIMPEDANCE ANALYSIS TO PREDICT CARDIOVASCULAR OUTCOMES IN PATIENTS WITH CHRONIC KIDNEY DISEASE: A PROSPECTIVE STUDY

Mohammed Tawhari (1), M. Omair Rahman (2), Azim Gangji (1), Trevor Wilkieson (1), Cathy Moreau (1), Mila Tang (3), Brenda Hemmelgarn (4), Charmaine Lok (5), Louise Moist (6), Steven Soroka (7), Sheldon Tobe (5), Marcello Tonelli (4), Adeera Levin (3), Catherine Clase (1)

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(2) University of Ottawa
(3) University of British Columbia
(4) University of Calgary
(5) University of Toronto
(6) Western University
(7) Dalhousie University

Background: Chronic kidney disease (CKD) leads to volume status abnormalities, which is a major cause of cardiovascular morbidity and mortality. The ability to routinely assess hypervolemia in patients with CKD in a reliable, non-invasive manner would facilitate management and potentially decrease adverse outcomes.

Objective: To determine if volume overload, as measured by bioimpedance, predicts a composite endpoint of myocardial infarction, stroke, congestive heart failure, amputation due to peripheral vascular disease, and death from all causes in patients with CKD.

Methods: We performed bioimpedance analyses on patients at baseline and followed them prospectively for the primary outcome. We measured bioimpedance using the Quadscan 4000 (Body Stat, Isle of Man, British Isles) and categorized patients as volume overloaded or not using an operationalization of the methods of Piccoli, with a reference population. We analyzed data using Cox regression.

Results: Of the 417 patients who underwent bioimpedance, 5 had uninterpretable readings. The remaining 412 patients were 61.5% male; mean age 68.1y; mean eGFR 26.2 mL/min/1.73m^2; mean urine albumin-creatinine ratio 40.8 mcg/mmol; 42.9% had diabetes. The follow-up was 11772.9 patient months. The hazard ratio (HR) for the primary outcome in patients who were overloaded compared with those who were not was 2.57 (95% CI 1.58, 4.18). This remained significant when adjusted for age, gender, diabetes, and CHF (HR = 1.85 [95% CI 1.12, 3.07]). Adjusting for NT-proBNP and Troponin T attenuated the effect to 1.28 (95% CI 0.73, 2.24) and 1.44 (95% CI 0.82, 2.52), respectively.

Conclusion: Bioimpedance is a non-invasive technique that predicts fluid-related outcomes in patients with CKD. The effect remains strong with adjustment for multiple clinical variables. Reduction of the effect when adjusted for NT-proBNP or Troponin T suggests shared variance and adds to the construct validity of bioimpedance, interpreted using the Piccoli method, as a method of assessing volume status.

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P-078

ECULIZUMAB PREVENTS THROMBOTIC MICROANGIOPATHY IN ATYPICAL HEMOLYTIC UREMIC SYNDROME PATIENTS: LONG-TERM FOLLOW-UP

Christoph Licht (1), Larry Greenbaum (2), Yahsou Delmas (3), Fadi Fakhouri (4), John Kincaid (5), Enrico Minetti (6), Chris Mix (5), François Provôt (6), Eric Rondeau (7), Neil Sheerin (8), Jimmy Wang (5), Laurent Weekers (9), Jan Menne (10)
(1) The Hospital for Sick Children
(2) Emory University and Children's Healthcare of Atlanta
(3) CHU de Bordeaux
(4) CHU de Nantes
(5) Alexion Pharmaceuticals, Inc.
(6) Careggi University Hospital
(7) Hôpital Tenon and Université Paris VI
(8) Newcastle University
(9) CHU de Liège
(10) Klinik für Nieren- und Hochdruckerkrankungen

Background: In previous prospective clinical trials and a retrospective study, eculizumab effectively prevented TMA and improved renal and hematologic parameters in 130 patients with aHUS. Subsequently, patients could enroll in a long-term follow-up study.

Objective*:* To evaluate TMA event rates during treatment and discontinuation from eculizumab.

Methods: This is an ongoing, observational, multicenter study (NCT01522170) of aHUS patients treated with eculizumab in 5 prior clinical studies. The primary endpoint is TMA event rate during on-treatment (ON; among patients receiving eculizumab) and off-treatment (OFF; among patients who discontinued eculizumab) periods. A secondary endpoint is TMA event rate ON per label (dose and interval) vs OFF.

Results: Eighty-seven patients enrolled: 76 with ON and 39 with OFF periods (median follow-up, 26.1 and 20.1 months in the current study) (Table). At discontinuation, OFF patients had higher eGFR than ON. After discontinuation, 17/39 (44%) reinitiated eculizumab. TMA event rates were higher among patients with genetic mutations (9.8/100 patient-years for ON vs 34.5 for OFF) vs no mutation (2.8 vs 7.8) (hazard ratio, 4.5; *P*=0.0082). The TMA event rate was 63% lower ON vs OFF, and 74% lower during labeled dosing vs OFF (Table).

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Conclusions: The TMA event rate was 3.8-fold higher for OFF vs labeled eculizumab dosing. Patients who discontinued had more severe disease at baseline, shorter disease history, and responded well to eculizumab. Patients with aHUS, particularly those with identified mutations, have increased risk of TMA events during non-labeled dosing or eculizumab discontinuation compared with labeled therapy.

Table. Demographics and Disease Characteristics at Baseline of Parent Studies, and TMA Event Rates During Labeled Dosing, Non-Labeled Dosing, and OFF Treatment

Characteristic	Ongoing Eculizumab (n=48)	Discontinued (n=39)	Total (N=87)
Age at first-ever eculizumab infusion, years			
Median (range)	24.0 (0.0–65.0)	21.00 (0.0–80.0)	22.00 (0.0–80.0)
<12 years, n (%)	13 (27.1)	11 (28.2)	24 (27.6)
12–<18 years, n (%)	6 (12.5)	5 (12.8)	11 (12.6)
≥18 years, n (%)	29 (60.4)	23 (59.0)	52 (59.8)
Female, n (%)	30 (62.5)	23 (59.0)	53 (60.9)
Identified complement gene mutation or autoantibody, n (%)	31 (64.6)	21 (53.8)	52 (59.8)
Time from last pretreatment aHUS manifestation to first-ever dose of eculizumab, median (range), months	2.3 (0.0–47.4)	0.5 (0.0–19.2)	0.9 (0.0–47.4)
Time from aHUS diagnosis to first-ever dose of eculizumab, median (range), months	18.4 (0.0–313.3)	0.9 (0.0–178.1)	4.0 (0.0–313.3)
History of aHUS events, n (%)			
Single	29 (60.4)	27 (69.2)	56 (64.4)
Multiple	19 (39.6)	12 (30.8)	31 (35.6)
Prior renal transplant, n (%)	14 (29.2)	8 (20.5)	22 (25.3)
PE/PI sessions per patient, median (range)	13.3 (0.0–230.0)	7.0 (0.0–64.0)	11.0 (0.0–230.0)
Dialysis at baseline[a], n (%)	14 (29.2)	15 (38.5)	29 (33.3)
eGFR[b] at baseline, mL/min/1.73 m^2, median (range)	21.2 (8.4–128.3)	12.1 (5.3–105.5)	18.9 (5.3–128.3)

TMA Events[c]	OFF Treatment (n=39)	ON Treatment (n=76)	Dosing	
			Labeled (n=65)	Non-labeled (n=33)
Patients with event, n (%)	11 (28.2)	10 (13.2)	7 (10.8)	4 (12.1)
Total number of events	14	14	7	7
Total patient-years	70.5	192.8	135.0	57.9
TMA event rate per 100 patient-years	19.9	7.3[d]	5.2	12.1

Results as of March 28, 2015.
[a]Dialysis at baseline was defined as any dialysis that occurred within 7 days prior to or 14 days following the first eculizumab dose in the parent study.
[b]eGFR was defined as 10 mL/min/1.73 m^2 when a patient was on dialysis.
[c]A TMA event was defined as any one of the following: 1) the occurrence of a change in ≥1 laboratory parameter confirmed by a second measurement ≥28 days apart with no interruption (ie, platelet count decrease ≥25% compared with baseline[e] and less than the lower limit of normal; increase in serum creatinine or lactate dehydrogenase level ≥25% compared with baseline and greater than the upper limit of normal); 2) clinical signs and symptoms of TMA considered definitely related to aHUS, including: thrombosis, seizure, decreased renal function, proteinuria (new or worse compared with baseline and >1+ or >30 mg/dL), hematuria (new or worse compared with baseline and >50 red blood cells per high-powered field), increased hemolytic anemia, biopsy-proven TMA, or other (eg, extrarenal TMA manifestations including confusion, cardiovascular abnormalities, pericarditis, gastrointestinal symptoms, diarrhea); or 3) the patient received plasma exchange/plasma infusion, dialysis, blood transfusions, or renal transplant due to a TMA event.
[d]The hazard ratio during OFF compared with ON periods was 4.7 (*P*=0.0008) based on a Cox proportional-hazards model of time to first TMA event during each treatment status. Hazard ratios and *P* values were analyzed using Cox proportional-hazards models with treatment status as a time-dependent explanatory variable and the mutation status as a covariate.
[e]Baseline was defined for each ON period as the last laboratory value during the preceding OFF period, and for each OFF period as the last value during the preceding ON period.
aHUS, atypical hemolytic uremic syndrome; eGFR, estimated glomerular filtration rate; PE/PI, plasma exchange/plasma infusion; TMA, thrombotic microangiopathy.

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P-079

ONTARIO RENAL NETWORK PALLIATIVE CARE REPORT: RECOMMENDATIONS TOWARDS AN APPROACH FOR CHRONIC KIDNEY DISEASE

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(2) University of Western Ontario
(3) Ontario Renal Network

Background
Symptom control and palliative renal care are increasingly recognized as important to patients, their families and community and to health care personnel. World wide interest in altering the current delivery of palliative renal care is increasing with the need for change being emphasized through the Auditor General of Ontario's Report in 2014, and Kidney Disease: Improving Global Outcomes (KDIGO)'s recommendations for palliative care within Chronic Kidney Disease (CKD). In addition, within Ontario, the 2011 Declaration of Partnership and Commitment to Action presented a shared vision of palliative care across all of Ontario. With these priorities in mind, the Ontario Renal Network (ORN) identified Palliative and end of life care as a priority in its second Ontario Renal Plan (ORPII) for 2015-2019.

Methods
The ORN convened a multidisciplinary committee, including patients, families and healthcare stakeholders to address the unique palliative care needs of people with CKD, and further the provincial palliative care work within CKD. The findings and recommendations have been presented in the ORN Palliative Care Report.

Results
The report summarizes current state and evidence reviews, regional and provincial consultations, and patient and family interviews. Based on findings from a recent Ontario analysis on the impact of palliative care on end of life care within CKD, that suggest high emergency departments and intensive care unit admission rates in the last 14 days of life, the committee members have developed a provincial framework and six recommendations to advance high-quality, integrated palliative care in Ontario for people living with CKD over the next four years, regardless of chosen treatment modality (conservative care, dialysis, and transplant).

Conclusion
The recommendations support a collaborative and continuous approach to palliative care, focusing on education, system accountability, shared understanding of palliative care in CKD, ongoing support and accountability for advance care planning, and standard care models.

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P-080

BEDSIDE PERITONEAL DIALYSIS CATHETERS FOR THE MANAGEMENT OF REFRACTORY ASCITES: A SINGLE CENTRE EXPERIENCE

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(2) Seven Oaks General Hospital

Background: Refractory ascites is when fluid recurrently accumulates in the peritoneal cavity, and is a common complication of liver cirrhosis. It can result in symptoms of anorexia, early satiety, nausea and vomiting, shortness of breath, and cause limited mobility. The initial management typically involves sodium restriction and diuretic therapy. When ascites no longer can be controlled by these measures, large volume paracentesis (LVP) is the treatment of choice in many patients. We believe that tunneled, peritoneal dialysis catheters placed at the bedside by trained operators is a safe, effective alternative for the palliation of refractory ascites.

Methods: The Manitoba Renal Program interventional nephrology program has offered the service of placing bedside PD catheters in patients with refractory ascites since 2010. We have collected basic demographic and comorbidity data on these patients in addition to complications of the procedure and outcomes such as peritonitis and survival.

Outcomes: We have placed 29 PD catheters for the sole indication of refractory ascites since 2010. We have experienced no complications with the insertion procedure itself. Our patients had a mean age of 64 years and 52% were male. The median survival time from the time of insertion was 56 days. The rate of peritonitis was 1 case per 767 months. The reasons for ascites in each patient included cirrhosis (14), malignancy (10), cardiac event (4) and other (1). There were no cases of peritonitis among those whose ascites was caused by cirrhosis.

Conclusion: Bedside PD catheter insertion by trained operators appears to be a safe, effective option for the management of refractory ascites. Prospective, randomized trials are needed to assess survival and quality of life and patient satisfaction metrics for this palliative procedure.

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P-081

DIFFERENCE IN POST PARATHYROIDECTOMY OUTCOMES IN HEMODIALYSIS PATIENTS COMPARED TO PERITONEAL DIALYSIS PATIENTS - ONE CENTER EXPERIENCE

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(1) University of Western Ontario
(2) King Abdulaziz University

Background and objectives: KDIGO guidelines recommend parathyroidectomy for ESKD patients with severe hyperparathyroidism, without randomized controlled evidence of benefit. Recent studies indicate parathyroidectomy is associated with significant morbidity at both 30 days and one year post procedure. This study compares outcomes post parathyroidectomy between patients on peritoneal (PD) and hemodialysis (HD).

Methods: Single center, retrospective, observational study including dialysis patients receiving parathyroidectomy, between January 2011- December 2014, with available blood work and 1 year follow up. Patient characteristics and laboratory data were collected from patients' electronic record. Outcomes assessed include 30-day ER visits and hospitalizations. Time to normalized calcium (NCa) (2 readings of Ca > 2 mmol/L, 48 h post-surgery) were examined.

Results: Thirty patients,(20 HD and 10 PD), mean age 54years, 60% females and 40% diabetics, were reviewed. One HD and 1 PD patient died within 30 days. Thirty day ER visits were increased in PD (3/9 pts vs 3/19 pts HD), with no difference in 30-day admission rates (22% vs 26%). Average time to NCa was 34 days in PD and 13 days in HD. The frequency of Ca monitoring within 30 days post discharge, was less in PD vs HD (mean 4 vs 9).

Conclusion: Parathyroidectomy is associated with increased use of health care resources with higher ER visits in the peritoneal dialysis population. This may be related to the frequency of monitoring of calcium levels. Further studies are needed to define the optimal care plan for monitoring and treatment of dialysis patients post parathyroidectomy.

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P-082

COMMON ILIAC ARTERY STENOSIS: AN OFTEN OVERLOOKED CAUSE OF GRAFT DYSFUNCTION

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Background: Transplant renal artery stenosis is an increasingly recognized complication post kidney transplantation and a potentially reversible cause for hypertension and allograft dysfunction.

Objectives: This retrospective case series aims to describe five cases of upstream native common iliac artery stenosis, leading to similar clinical presentations as transplant renal artery stenosis, with resistant hypertension and graft dysfunction.

Methods: Five cases were identified over 15 years from a single Canadian centre. Baseline characteristics and known risk factors for transplant renal artery stenosis were abstracted from the electronic medical record, as well as blood pressure readings, medications and laboratory parameters pre and post intervention.

Results: Three cases were deceased donor kidney transplants; average presentation from transplantation was 7 years. Culprit stenotic lesions were proximal to the transplanted renal artery, located at the common iliac artery or aortic bifurcation. All were angioplastied and four were stented. One patient with declining graft function for months, who was dialysis dependent for over 3 weeks, recovered completely to baseline eGFR of 57 ml/min post stenting. The remaining four had mean improvements in eGFR of 26.5 ml/min. Systolic blood pressure was reduced by a mean of 16.8 mmHg and diastolic of 5.4 mmHg, allowing reduction of antihypertensives in three cases.

Conclusions: Upstream native vessel disease is likely linked to the gradual increase in age, comorbidities, and atherosclerotic arterial disease in transplant recipients. Prevalence is likely to rise and should prompt more aggressive investigation for common iliac disease in patients with otherwise unexplained allograft dysfunction.

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Abstracts - Poster Presentation

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P-083

URIC ACID LEVELS ARE ASSOCIATED WITH PERIPHERAL BUT NOT CENTRAL BLOOD PRESSURE PARAMETERS IN NORMOTENSIVE INDIVIDUALS

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Background:
Uric acid is increasingly recognised as a risk factor for cardiovascular disease. Whether this could be explained by changes in peripheral or central blood pressure (BP) profiles remains controversial. The aim of this study was to assess the association of uric acid levels with peripheral and central hemodynamic parameters in untreated normotensive individuals.

Method:
Of 20,004 CARTaGENE participants, 8,662 were normotensive individuals not treated for hyperuricemia or hypertension with valid pulse wave analysis (47% male, 52.6 yo). The associations between uric acid levels and peripheral systolic BP (SBP), pulse pressure (PP) central systolic BP (cSBP), central PP (cPP), pulse pressure amplification (PPA), augmentation index (AIx) and augmented pressure (AP) were tested with linear regressions.

Results:
In univariate analyses, uric acid levels were significantly associated with all parameters. In contrast, in multivariate analyses, only SBP and cSBP remained independently associated with uric acid levels. As cSBP is usually highly dependent of SBP, it was further adjusted for peripheral BP, where it was not independently associated with uric acid levels (β coefficient -0.003, p=0.51).

Conclusion:
In normotensive individuals, uric acid levels were independently associated with SBP, but not with other hemodynamic parameters. Whether the increased risks associated with uric acid levels are explained by these parameters remains uncertain and needs further study.

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Table 1: Association between uric acid levels and hemodynamic parameters.

	Univariate		Multivariate [a]	
Parameters [b]	**β coefficient [c]**	**p-value**	**β coefficient [c]**	**p-value**
SBP	0.260	<0.001	0.062	<0.001
PP	0.108	<0.001	-0.004	0.77
cSBP	0.167	<0.001	0.068	<0.001
cPP	-0.027	0.013	0.002	0.89
PPA	0.236	<0.001	-0.005	0.65
AIx	-0.272	<0.001	0.002	0.85
AP	-0.210	<0.001	0.006	0.60

[a] adjusted for gender, age, BMI, diabetes, cardiovascular disease, smoking history, eGFR, fasting glucose, total cholesterol, HDL, TSH, and heart rate.

[b] PPA expressed in 0.01 unit and AIx in %. All others in mmHg.

[c] expressed per 10 umol/L of uric acid.

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P-084

#NEPHPEARLS : NEPHROLOGY EDUCATION IN BYTE SIZED TWEETS

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(2) University of Illinois at Chicago College of Medicine
(3) Duke University
(4) Oakland University William Beaumont School of Medicine
(5) University of Ottawa

Background – The use of social media in medical education continues to grow. Increasingly, physicians are adopting social media platforms mainly Twitter and Facebook, for learning and dissemination of subject specific knowledge. Nephrology educators, being early adopters, have strived to take social media education mainstream. The twitter hashtag #NephPearls is one of the most commonly used nephrology hashtags on Twitter, and aims to convey 140-character sized nephrology pearls, using text, images and links. We undertook this study to measure the reach and explore the content diversity of this hashtag.

Methods – All tweets with the hashtag #NephPearls were collected over a 6-month period from July 2015 to January 2016, using a third party analytic website (Symplur.com). Individual tweets were analyzed for nephrology topic content.

Results – During the study period 6982 tweets were tagged #Nephpearls from 968 unique twitter accounts. These tweets were retweeted 21762 times at an average of 3.15 retweets/tweet. The theoretical reach of these tweets (impressions) was 6,664,168 (number of tweets x number of followers). The maximum number of tweets (n=1898) occurred in November 2015 coinciding with ASN Kidney Week 2015. The top topics are depicted in Fig 1.

Conclusions - #NephPearls hashtag is being used to label tweets as a source of nephrology knowledge. It covers a wide range of topics. The use of a single hashtag for nephrology content enables curation, discoverability and organization of medical knowledge.

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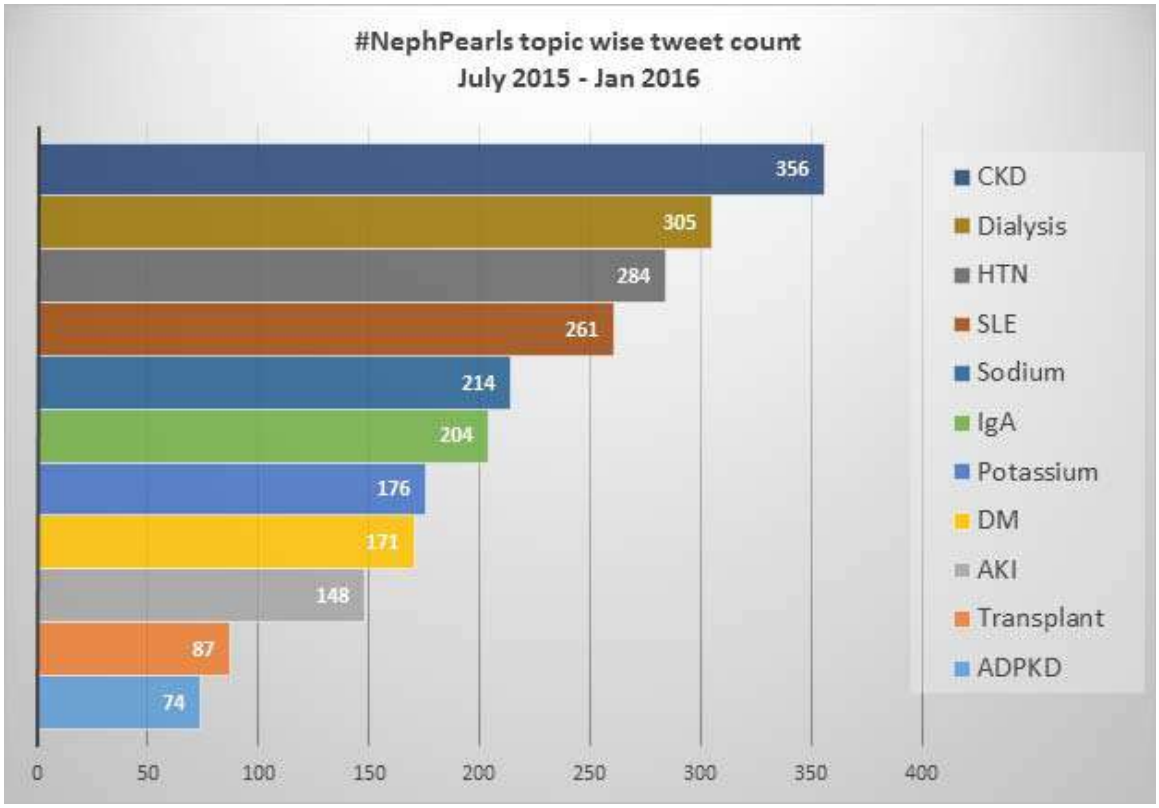

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P-085

RELATIVE CHANGE IN PTH IS ASSOCIATED WITH APPEARANCE OF PHOSPHATE IN THE URINE FOLLOWING AN ORAL PHOSPHATE CHALLENGE

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We determined whether acute changes in PTH and FGF-23 were associated with the appearance of phosphate in the urine (Uphos:Ucr ratio) following an oral phosphate challenge of 3.9 mls of Phoslax (500 mg) in 15 subjects with GFR measured by inulin clearance. Mean (SD) GFR was 68 (45.1) ml/min. Serial change in biochemical variables are presented in the Table. Uphos:Ucr was significantly higher at 120 and 180 minutes following the phosphate stimulus. The absolute increase in U_{phos}:U_{cr} at 120 minutes was inversely correlated with baseline PTH (r=-0.6, p=0.04) and FGF-23 (r=-0.6, p=0.04) and a positive trend was observed with GFR (r=0.5, p=0.07). There was a significant correlation between the relative, but not absolute, increase in PTH at 60 minutes and the increase in Uphos:Ucr (r-0.6, p=0.025) at 120 minutes. Subjects with higher levels of FGF-23 had lower % increase in PTH at 60 minutes (r=-0.750, p=0.05 and r=-0.77, p=0.07 at 15 and 30 minutes). This association was similarly observed in the sub-set of subjects with GFR > 30 ml/min (n=10). The relative increase in PTH in response to a phosphate stimulus was associated with increased phosphate appearance in the urine. The relative increase in PTH was attenuated in subjects with higher FGF-23 and lower GFR. Phosphate retention, due to delayed appearance in the urine following absorprtion, could be an under-recognized risk factor for vascular calcification that is not limited to people with recognized CKD.

	Time 0	15	30	45	60	120	180
Blood Data							
phosphate	1.1±0.2	1.1±0.2	1.2±0.2*	1.2±0.2*	1.3±0.2**	1.3±0.2**	
calcium	2.3±0.1	2.2±0.1	2.2±0.1	2.3±0.1^	2.2±0.1	2.2±0.1^	
PTH	8.2±7.7	8.6±7.4	8.5±6.9*	9.4±8.3**	11.2±10.3**	9.8±8.7*	
FGF-23	98.3±128.8	95.3±118.1	88.3±109.2	117.8±130.5	92.0±107.5	67.1±49.0	
Urine Data							
Uphos:Ucr	1.6±0.7					2.2±0.8^	2.9±1.2*

^ significantly different from baseline at p<0.05, * significantly different then baseline at p<0.01, ** significantly different from baseline at p<0.001

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P-086

PROVINCIAL SURVEY TO ASSESS CURRENT STATE OF GLOMERULONEPHRITIS CARE IN ONTARIO

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(2) Ontario Renal Network
(3) Trillium Health Partners

Background: As part of the second Ontario Renal Plan, Ontario Renal Network (ORN) is committed to implementing models for the delivery of safe, high-quality and accessible care to people requiring specialized care such as those with complex glomerulonephritis (GN). As part of a provincial needs assessment, an online survey was conducted to assess the current state of GN.

Objectives: To better understand 1) the current state of care for GN patients across Ontario; 2) factors contributing to known gaps in care; and 3) opportunities to improve care.

Methods: An online survey was distributed to Ontario nephrologists based on an internal ORN nephrologist contact list, collected in 2014. In addition, ORN Regional Medical Leads were encouraged to share the online survey with nephrologists in their jurisdiction. The survey primarily included closed-ended questions, with some opportunities to leave comments. Nephrologists affiliated with renal programs with an established specialized GN clinic were excluded from the survey.

Results: Sixty-eight eligible nephrologists completed the online survey, representing 21 of 26 renal programs in Ontario. The survey identified several gaps in care, including an overall lack of standardization in GN care, provincial GN expertise, access to drug therapy, resources and infrastructure to support specialized GN care (including support from multidisciplinary staff), access to non-renal services (such as plasma exchange and pathology), and patient supports.

Conclusions: Over the next five years, ORN will develop and implement a provincial GN strategy to address the identified gaps in care. This strategy will be guided by a panel of GN experts, with broad representation from academic and community renal programs in Ontario, physicians, administrations, front-line staff, and patients.

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P-087

SEDENTARY TIME AND CHRONIC KIDNEY DISEASE: A CROSS-SECTIONAL ANALYSIS OF THE CANADIAN HEALTH MEASURES SURVEY

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(2) Seven Oaks Chronic Disease Innovation Centre

Background: Studies have examined the association between CKD and sedentary time and shown that patients with CKD and kidney failure tend to be inactive. To date, most population based studies have used self-reported measures of physical activity, with only small studies using accelerometry, the gold standard for evaluation of physical activity. The Canadian Health Measures Survey (CHMS) included detailed physical activity evaluation for a representative sample of adult Canadians across 3 cycles from 2007 to 20XX. Here we report the results on physical activity in those with CKD.

Objectives and Methods: To determine the association between physical activity and CKD, we conducted a cross sectional analysis of all adult (18+) individuals (n=8444) from the activity monitoring component of the Canadian Health Measures Survey. Our primary outcome was sedentary time, divided into quartiles, based on accelerometry data.

Results: Older age, lower eGFR, lower serum albumin, and higher blood pressure and BMI were associated with increased sedentary time. Compared to patients with normal kidney function, patients with CKD Stages 3b and higher had a nearly 5-fold higher likelihood of being increasingly sedentary (OR 5X quartile 4 vs. quartile 3, $p < 0.05$). This association was independent of age, gender, and conventional risk factors for cardiovascular and kidney disease.

Conclusions: In this nationally representative cross sectional survey of Canadian participants, CKD was strongly and independently associated with a lack of physical activity. Further studies are needed to determine the aetiology for sedentary behaviour and potential interventions to increase physical activity in patients with CKD.

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P-088

DEVELOPING A MODEL FOR THE INTRAOPERATIVE PREDICTION OF CARDIAC SURGERY-ASSOCIATED ACUTE KIDNEY INJURY

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(2) Seven Oaks General Hospital
(3) St. Boniface Hospital
(4) St. Boniface Hospital Research Centre

Rationale
Acute kidney injury (AKI) is a potentially fatal complication of cardiac surgery. The inability to predict CSA-AKI is a major barrier to prevention and early treatment. Current models for prediction of cardiac surgery-associated AKI (CSA-AKI) are insufficient, particularly in patients without pre-existing kidney dysfunction.

Objective
To identify the perioperative variables that can improve Thakar risk score prediction of CSA-AKI.

Methods
A prospective, observational cohort (n=289) of adult cardiac surgery patients was recruited. CSA-AKI was defined using the 2012 KDIGO serum creatinine criteria. The area under the Receiver Operating Characteristic (AUC) curve was calculated for the Thakar score alone, and for the Thakar score plus different intraoperative variables to identify improvements in discrimination.

Results
The Thakar score alone gave an AUC of 0.721 (95%CI=0.619-0.824). Nadir hematocrit during the operative period was the only variable associated with improved model discrimination for post-operative AKI when added to the Thakar score, (AUC=0.770, 95%CI=0.682-0.857, p=0.031). Other intraoperative measures including arterial blood pressure, urine output, duration of procedure, blood transfusion and fluid balance did not improve model discrimination.

Conclusions
Nadir hematocrit appears to be a good predictor of CSA-AKI, and may provide a target for early intervention.

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P-089

RISK FACTORS FOR CLINICAL URINARY TRACT INFECTIONS IN KIDNEY TRANSPLANT RECIPIENTS WITH ASYMPTOMATIC BACTERIURIA

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(3) Centre de Recherche du Centre Hospitalier de l Université de Montréal
(4) Centre Hospitalier de l'Université de Montréal

Background: The factors that are associated with the development of symptomatic urinary tract infections (UTI) in kidney transplant recipients (KTRs) with asymptomatic bacteriuria (ABU) are unclear.

Objectives: We sought to identify patient or episode related characteristics associated with subsequent symptomatic UTIs and with antibiotic prescribing in KTRs with ABU.

Methods
We retrospectively recorded all episodes of bacteriuria (defined as ≥10^4 colony-forming units (CFU) /ml) in KTRs transplanted at our centre between January 1st 2008-2013. Through logistic regression models using generalized estimating equations, we assessed i) factors associated with occurrence of a symptomatic UTI within 3 months of an episode of ABU; ii) factors associated with antibiotic treatment of ABU.

Results
Among 318 study participants, there were 622 episodes of ABU in 156 patients. Symptomatic UTIs within 3 months occurred following 87 (14 %) of ABU episodes. Factors associated with an increased likelihood of a symptomatic UTI following ABU were younger age (OR: 1.38 per 10-year decrease in age; 95% CI: 1.12-1.70), previous symptomatic UTI (OR: 5.24; 95% CI: 2.18-12.59), the presence of leukocyturia or haematuria (OR: 3.38; 95% CI: 1.86-6.17), a ciprofloxacin resistant or extended-spectrum beta-lactamase (ESBL) producing strain (OR: 2.21; 95% CI: 1.03-4.75), and isolation of gram negative bacteria (GNB) (OR: 2.44; 95 % CI: 1.12-5.31). Antibiotics were prescribed in 24% of ABU episodes. The presence of leukocyturia or haematuria (OR: 2.02, 95% CI: 1.27-3.22), urinary nitrites (OR: 2.54, 95% CI: 1.08-5.99), GNB (OR: 2.08, 95% CI: 1.11-3.85),and bacterial count >10^5 CFU/ml (OR: 5.55 versus 10^4-10^5 CFU /ml, 95% CI: 3.44-8.33) were associated with an increased likelihood of receiving antibiotic treatment for ABU.

Conclusion
Younger age, leucocyturia or haematuria, bacterial strain, and a history of symptomatic UTI are predictors of progression of ABU to symptomatic UTI that can help in guiding management and designing future therapeutic trials.

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P-090

CENTRAL NERVOUS SYSTEM ACTING MEDICATION PRESCRIPTION PATTERNS IN HEMODIALYSIS PATIENTS

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(2) Kingston General Hospital

Background: Polypharmacy may reduce adherence and decrease quality of life (QOL).

Objectives: The purpose of this study is to examine prescription patterns of central nervous system (CNS) acting medications in hemodialysis patients.

Methods: We evaluated CNS prescription medication in 353 hemodialysis patients from a regional center (n= 206), a northern satellite (n=10) and 2 urban satellites (n=84, 53). CNS medications were sub classified according to the AHFS drug classification system.

Results: 207 patients (59%) were prescribed at least 1 CNS acting medication and 55 patients were prescribed more than 3 (16%). The most frequently prescribed classes were antidepressants (27%), analgesics (26%) and anxiolytics (18%). Patients prescribed more CNS acting drugs were more likely to have a higher burden of total prescribed medications ($p<0.001$) and over-the-counter medication use ($p<0.001$) but there was no association with age or dialysis vintage. When comparing those prescribed at least 1 CNS drug (207) versus none (146), there was a trend towards increased prescription in females (55% of males vs 64% of females, $p=0.06$). CNS prescription rate was highest in the regional center and northern clinic and there was a trend towards a higher number of CNS drugs prescribed in the northern clinic (1.50±1.43) versus the regional center (1.33±1.45, $p=0.078$).

Conclusion: CNS medication prescription contributes significantly to overall drug burden in dialysis patients. Patients in a regional center and at a remote, northern dialysis clinic were more likely to be prescribed CSN-acting drugs. Whether CNS prescription medication contributes to impaired QOL, falls, hospitalizations or mortality requires study.

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P-091

SUCCESSFUL PREGNANCY IN A PERITONEAL DIALYSIS PATIENT

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University of Alberta

Introduction – Pregnancy in End Stage Renal Disease (ESRD) is rare and frequently has adverse outcomes. Extended and frequent hemodialysis has the best outcomes while intensive peritoneal dialysis (PD) has mixed results.

Case report – We describe a successful pregnancy in a 41-year-old female with ESRD secondary to Type 1 Diabetes Mellitus. Patient had a buried PD catheter in place prior to conception. After extensive discussion regarding dialysis modality, she chose to continue with PD. PD was initiated at GFR of 12 ml/min and a urine output of approximately 1L/d. She started cycler dialysis from 12th week of gestation (5 exchanges, 2.5%, 1.5 lit volume, 9 hours & 2 twinbag exchanges). She was followed by a multidisciplinary team including nephrologists, nurses and specialists in obstetrics, endocrinology and fetal-maternal medicine. Clinically she tolerated the therapy well and mean values(SD) of key biochemical parameters were urea 16.09(±1.4)mmol/L, calcium 2.15(±0.05) mmol/L, phosphorus 1.62(±0.14) mmol/L, glucose 7.95(±2.53) mmol/L, and hemoglobin 109.5(±6.6) g/L. Her BP was ≤ 130/80 mm Hg without any medications.

At 30 weeks she underwent amnioreduction for worsening polyhydramnios and received two doses of steroids. She required a caesarean section at 34 weeks owing to placental insufficiency and a singleton live female child was delivered. Apgar scores of 9 and 9 at birth and 5 minutes birth weight was 2.15kg. The child was antenatally diagnosed with an absent left kidney but was otherwise normal. The patient initiated peritoneal dialysis the day after surgery and was discharged on Day3 on a standard CAPD prescription of 4 exchanges a day.

Conclusion – Successful outcome of pregnancy is possible in a patient with ESRD and substantial residual function treated with an aggressive PD prescription and close monitoring by a multidisciplinary team in a tertiary care setting.

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P-092

PILOT USE OF RESPITE ASSISTED PD FOR PATIENTS WITH ACUTE INTERRUPTIONS IN SELF-CARE PD

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(2) BC Provincial Renal Agency

Background:
Acute illness/injury or primary caregiver unavailability can render patients on PD temporarily unable to perform dialysis independently. These patients generally remain in hospitals, care facilities or are even transferred to HD.

Objectives:
To describe reasons for acute interruption and evaluate service, cost and impact of respite assisted PD (respite PDA) on self-care PD retention.

Methods:
This was part of a 12-month pilot study on assisted PD (PDA) service wherein patients with acute interruptions in CCPD were offered respite PDA. Patients received daily assistance with cycler dismantle and setup provided by an external service provider. Patients remained responsible for other aspects of PD, including connections and choice of dialysate.

Results:
Of the 64 PDA pilot patients, 11 (17%) received respite PDA. The most common reasons for duse were primary caregiver unavailability and musculoskeletal injury/fracture. Respite care ended with 64% (7/11) returning to self-care PD, 1 transfer to HD and 1 death where respite PD allowed for palliation. The median usage of respite PDA was 29 days with a range of 1 to 70 days. Cost of respite PDA (excluding pre-existing PD costs) was $43/visit which equates to $1,247 for the median enrollment of 29 days. The estimated cost of continued hospital admission or transfer to HD would each be approximately $7000-$10000.

Conclusions:
Respite PDA is an effective way to support patients with an acute interruption in self-care PD. The majority of patients returned to independent PD. Respite PDA is cost-effective compared to hospital admission or transfer to HD.

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Table for: **PILOT USE OF ASSISTED PD FOR PATIENTS WITH ACUTE INTERRUPTIONS IN SELF-CARE PD**

Reasons for initiating respite service	Frequency	Duration of respite required (days)
Primary caregiver away travelling	2 patients x 2 2 patients x 1	13, 16, 2,2 3, 32
Fall – fractured wrist	1 patient	40
Hand injury	1 patient	14
Fall – fractured tibia	1 patient	40 (remains on respite)
Neuro assessment for ability to self-manage	1 patient	1 (transferred to HD)
Palliative support prior to hospice placement	1 patient	12 (deceased following)
Surveillance for weakness	1 patient	55 (remains on respite)
Fractured rt arm	1 patient	70

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ANTI-LG3 ANTIBODIES ENHANCE RENAL MICROVASCULAR RAREFACTION,FIBROSIS AND DYSFUNCTION ASSOCIATED WITH ISCHEMIA-REPERFUSION INJURY

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Delayed graft function (DGF) is associated with decreased kidney graft survival. We have shown that pre-transplant anti-LG3 autoantibodies were associated with increased risk of DGF in kidney transplant recipients (KTR) and decreased renal function in a murine model of ischemia reperfusion injury (IRI). Now we ask whether pre-transplant titers of anti-LG3 and other transplant-relevant autoantibodies are associated with 1-year graft function in KTR with DGF, and whether anti-LG3 IgGs can enhance renal microvascular rarefaction and fibrosis. We performed a single center, retrospective cohort study in consecutive KTR transplanted between June 1st 2008 and 2013 without rejection. DGF was defined as the need for dialysis in the first week or failure of sCr to decrease by >10% on the first 3days post-transplant. Anti-LG3, anti-vimentin and anti-angiotensin II type 1 receptors (anti-$ATII_1R$) were measured immediately prior to transplantation using ELISA. 1year eGFR was estimated with the 4-variable MDRD equation. Unilateral renal artery clamping for 30min plus contra-lateral nephrectomy was performed in C57Bl/6 mice. Intra-venous injections of anti-LG3 IgGs or control IgGs were performed every other day starting 2days pre-surgery. Among 130 participants, 39 experienced DGF. There was no association between the titers of three autoantibodies. Elevated pre-transplant anti-LG3 titers (β: -13 ml/min/1.73m^2, 95% CI: -25, -1 for 3rd versus 1st tertile) were associated with reduced 1year eGFR in patients with DGF (adjusted for donor age) but not in those with immediate graft function, while anti-vimentin and anti-$ATII_1R$ were not. Mice injected with anti-LG3 IgGs had higher sCr (p=0.04), decreased CD31 staining (p<0.001) and increased alpha-SMA staining (p<0.001) on immunohistochemistry at day 7post-IRI. Together these results demonstrate that anti-LG3 antibodies but not anti-$ATII_1R$ or anti-vimentin are associated with decreased 1-year graft function in patients with DGF. This may be explained by anti-LG3 induced renal microvascular rarefaction and fibrosis in the context of IRI.

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P-094

ABNORMAL SEX HORMONE PROFILE IN WOMEN WITH END STAGE KIDNEY DISEASE

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Introduction:
Women with ESKD often have menstrual irregularities and infertility, though the pathophysiology is incompletely understood. In healthy women, low estradiol and increased follicular stimulating hormone (FSH) is consistent with the diagnosis of menopause. We sought to characterize the sex hormone profile in women with ESKD initiating dialysis.

Methods:
Women who initiated hemodialysis since February, 2005 in 3 Canadian centres were studied. Serum estradiol, FSH and prolactin levels were measured within 3 months of dialysis initiation. Women were stratified according to age (> or ≤51 years, average age of menopause in North America), estradiol levels (> and ≤150pmol/L, upper limit of normal for menopause) and FSH levels (> or ≤33IU/L, levels indicating menopause).

Results:
Four hundred eighty-two women (60±16years, 40% diabetic) were studied (estradiol: 118±163pmol/L, FSH: 58±55IU/L and prolactin: 69±138ug/L). One hundred twenty-eight women were ≤51 years and 354 women were >51 years. In women ≤51 years, 50% had estradiol levels and 25% had FSH levels in the post-menopausal range, and 19% had postmenopausal levels of both estradiol and FSH. In women >51 years, 85% had estradiol levels and 71% had FSH levels in the postmenopausal range. Only 64% of women >51 years had postmenopausal levels of both estradiol and FSH. Prolactin levels were high but did not differ with age (54±7ug/L vs 74±8ug/L, p=0.17).

Conclusion:
Women with ESKD have an abnormal sex hormone profile irrespective of age which may contribute to poor clinical outcomes and increased cardiovascular risk. The effect of kidney disease on hypothalamic-pituitary-gonadal dysfunction warrants further study.

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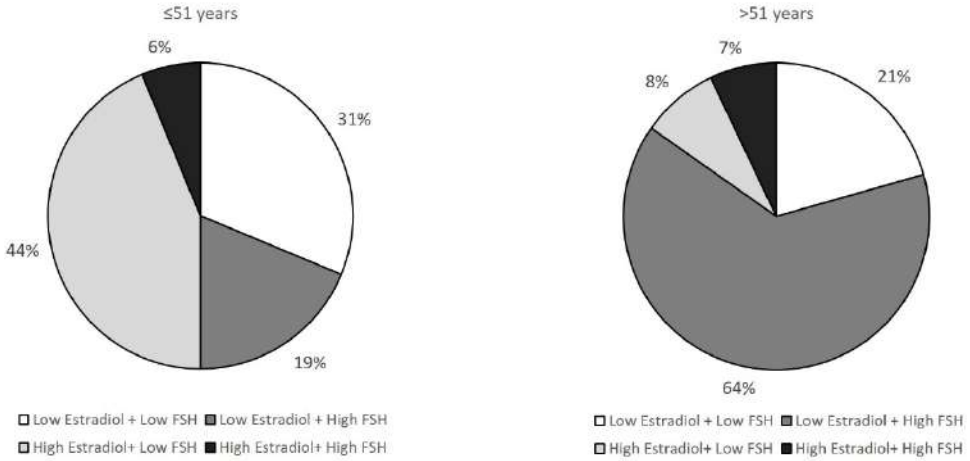
Figure 1. Estradiol and FSH levels in women with ESKD, by age



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BLOOD PRESSURE GUIDED BIOFEEDBACK ON HEMODIALYSIS AND THE REDUCTION OF INTRADIALYTIC HYPOTENSIVE EPISODES: A RANDOMIZED CROSS OVER TRIAL (BP-RIDH).

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(2) BC Provincial Agency
(3) University of British Columbia

Background:
Intradialytic hypotension, IDH is associated with increased morbidity and mortality. Blood pressure (BP) guided biofeedback monitors BP during dialysis and automatically adjusting the fluid removal rate.

Objective:
To determine if BP biofeedback (BioLogicRR, B Braun) can reduce symptomatic IDH.

Methods:
A randomized two-period crossover trial in hemodialysis (HD). Patients with symptomatic IDH were randomized to control (A) or BP biofeedback (B) for 8 weeks and then crossed over. Symptomatic IDH was defined as a decrease of systolic BP (SBP) ≥ 20 mmHg if SBP is > 100 mmHg and a decrease of ≥ 10mmHg if SBP is < 100 mmHg) with patient symptoms or nursing intervention . Primary outcome, proportion of HD sessions complicated by symptomatic IDH at week 8. A generalized mixed effect model was used to account for within-patient correlation.

Results:
30 patients were randomized; 22 completed the study. Median age was 81 yrs (76.8, 85.7), 60% diabetes and median duration of HD 4 years ((3.4, 9.6). There were 525 runs for A and 522 runs for B. Proportion of HD sessions with symptomatic IDH at week 8 decreased with biofeedback, Figure 1 (p=0.0039). The decline in the proportion of HD sessions with IDH with biofeedback at week 8 did not reach significance (p=0.053).

Conclusion: BP guided biofeedback may result in a reduction of symptomatic hypotension episodes but likely requires a longer duration of intervention.

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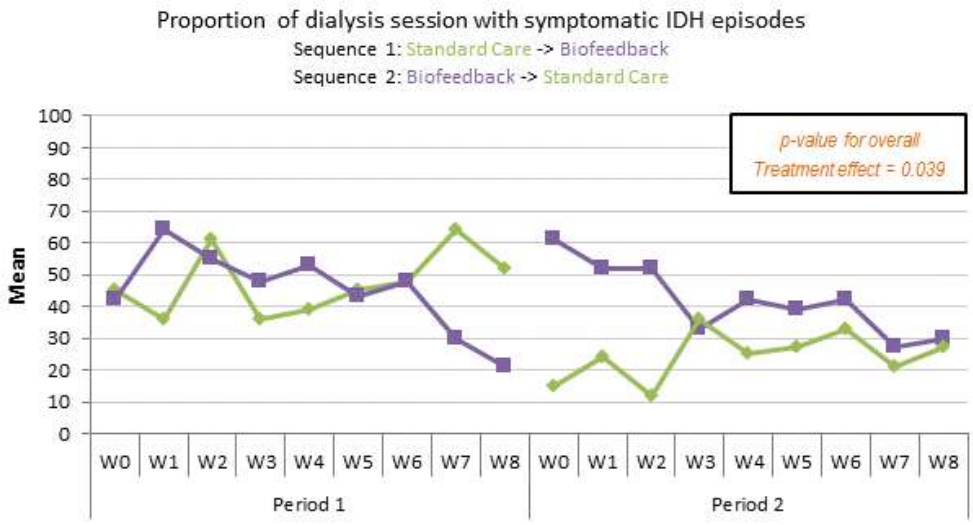

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ACUTE ELEVATION OF RENAL VENOUS PRESSURE INCREASES RENAL VASCULAR RESISTANCE VIA RENAL NERVES IN RATS

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(2) Simon Fraser University

Background:
The intimate connection between cardiac and renal function is of clinical concern due to significant, poorly explained mortality in heart failure (HF) patients with diminished renal function. Increased central venous pressure in HF leads to increased renal venous pressure (RVP) which may, in turn, impair renal function. We hypothesized that increases in RVP lead to increased renal vascular resistance (RVR) and involves renal nerves.

Objectives:
(1) Determine the impact of selective RVP increase of on renal hemodynamics,
(2) Elucidate the contribution of renal nerves.

Methods:
In anesthetized, male rats (300-400g, n=14) mean arterial pressure (MAP) and RVP were assessed using femoral artery and adrenal/supraspermatic vein catheters. FITC inulin in 0.9% NaCl to assess GFR was infused via femoral vein; timed urine samples were collected from each kidney. Left renal arterial blood flow (RBF) was directly measured by transit-time flow probe. Rats were intact or subjected to bilateral renal denervation (RD). Following baseline measurements, RVP was selectively increased to 10-12 mmHg by partial occlusion of the left renal vein for 120 min or not manipulated (time controls).

Results:
Elevation of RVP from 1.1±0.3 to 11.3±0.4 mmHg (n=9) did not alter MAP compared to time control in intact (93.8±4.0; n=5 vs 97.5±1.2 mmHg; n=3) or RD (81.4±5.0; n=4 vs 73.8±4.2; n=3) rats. RBF significantly decreased in intact ($p<0.001$, n=5) rats, which was absent in time controls ($p<0.05$, n=3). RVR (calculated by MAP-RVP difference) tended to increase in intact rats compared to controls ($p=0.085$). RD did not prevent a fall in RBF, but completely abolished the RVR increase. Modest increase in RVP does not appear to impact GFR.

Conclusions:
Elevated RVP directly modulates renal hemodynamics, inducing an immediate reduction in RBF followed by a steady increase in RVR over time, which appears to be mediated by renal nerves.

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DOES FISTULA PREVALENCE REFLECT DIFFERENCES IN ATTITUDE AMONGST VASCULAR ACCESS CLINICIANS IN CANADA?

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(1) University of Saskatchewan
(2) University of Manitoba
(3) University of British Columbia
(4) University of Calgary

Background
Vascular access (VA) is a key driver of quality of life, morbidity, mortality, and resource use. Improving VA care is a strategic priority of numerous organizations. There is marked variation in fistula usage across Canada, which may be due to differences in the attitudes of vascular access clinicians.

Objectives
To determine if opinions/attitudes towards VA differ between clinicians in centres with high versus low fistula prevalence.

Methods
The CSN Vascular Access Work Group surveyed health care providers who work with VA programs. Data collected included demographic information, vascular access opinions, and centre-specific practice patterns. Participants were asked to report if their fistula prevalence rate was ≥50% (high) or < 50% (low).

Results
83/88 (94.3%) of respondents reported fistula prevalence; 40/83 (48.2%) had a prevalence of ≥ 50%. Opinions regarding contraindications to fistula creation are shown in Table 1.

Respondents from high fistula centres identified high degree of comorbidity (37.5% disagree) and patient refusal for fistula creation (30.0% disagree) as the least valid reasons to dialyze with a catheter.

Clinicians from high fistula centres cited multidisciplinary teams (92.5%), timely access to interventional radiology (92.5%), and a dedicated access coordinator (90.0%) as factors to success. Clinicians from low fistula centres cited high primary failure rates (84.1%), lack of suitable vessels (81.8%), and long maturation time (75.0%) as barriers to using a fistula.

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Conclusion

Overall consensus was observed between high and low fistula centres regarding contraindications to fistula creation, suggesting that other factors may account for regional variations in fistula prevalence.

Table 1: Distribution of respondents who agree or strongly agree with the following statements regarding contraindications to fistula creation

Statement	≥ 50% fistula prevalence (n=40)	< 50% fistula prevalence (n=43)	p-value
Fistulas are the first choice in all patients	32 (80.0%)	28 (73.7%)*	>0.5
There are no contraindications to fistula creation	8 (20.0%)	5 (11.6%)	>0.5
The following is a contraindication to fistula creation:			
Age > 80 years	5 (12.5%)	6 (14.0%)	>0.05
Dementia	16 (40.0%)	26 (60.5%)	>0.5
Terminal malignancy with life expectancy < 12 months	36 (90.0%)	36 (83.7%)	>0.05
Living donor transplant anticipated in < 12 months	23 (57.5%)	22 (51.2%)	>0.05
Poor cardiac function with LVEF < 20%	24 (60.0%)	25 (58.1%)	>0.05
Poor cardiac function with LVEF < 10%	32 (80.0%)	35 (81.4%)	>0.05
History of stable angina	1 (2.5%)	2 (4.7%)	>0.05
History of unstable angina	18 (45.0%)	13 (30.2%)	>0.05
History of severe peripheral vascular disease	14 (35.0%)	20 (46.5%)	>0.05
History of pacemaker in same extremity	14 (35.0%)	13 (30.2%)	>0.05
History of central vein occlusion	22 (55.0%)	25 (58.1%)	>0.05
Poor vasculature on venogram or ultrasound	28 (70.0%)	39 (90.7%)	0.017

* Only 38 respondents for this question

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MULTI-COMPARTMENT MEDICATION COMPLIANCE AIDS AND ADHERENCE IN AN AMBULATORY HEMODIALYSIS SETTING

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Horizon Health Network

Background: The hemodialysis patient population is known to have low adherence to medications, due in part to large pill burden and complex medication regimens. Pharmacists commonly recommend medication adherence such as multi-compartment compliance aids (MMCAs), despite a lack of evidence for their efficacy in hemodialysis patients.

Objective(s): To assess the effect of MMCAs on adherence in ambulatory hemodialysis patients. Secondary outcomes were change in serum parathyroid hormone, phosphorus and calcium.

Methods: Thirty-five hemodialysis patients were divided into two groups: those using MMCAs at baseline and those not using any adherence aid at baseline. Those not using a device underwent a standardized education session teaching them to use the device. Those on a device received a standardized educational medication review alone. Medication adherence data was gathered for six months pre- and six months post intervention.

Results: For patients not using an MMCA at baseline, there was no difference in medication adherence post-intervention (multi-medication adherence ratio 71.8%±7.1% pre-intervention vs. 70.9% ±8.4% post)). Likewise in those already using an MMCA at baseline, there was no statistical difference in multi-medication adherence ratios post-education session (81.1%±5.8% at baseline versus 75.9%±8.8% post-education session.) There were no significant changes in serum calcium or phosphorous. Parathyroid hormone could not be evaluated.

Conclusions: MMCA devices did not increase medication adherence in the hemodialysis patient population.

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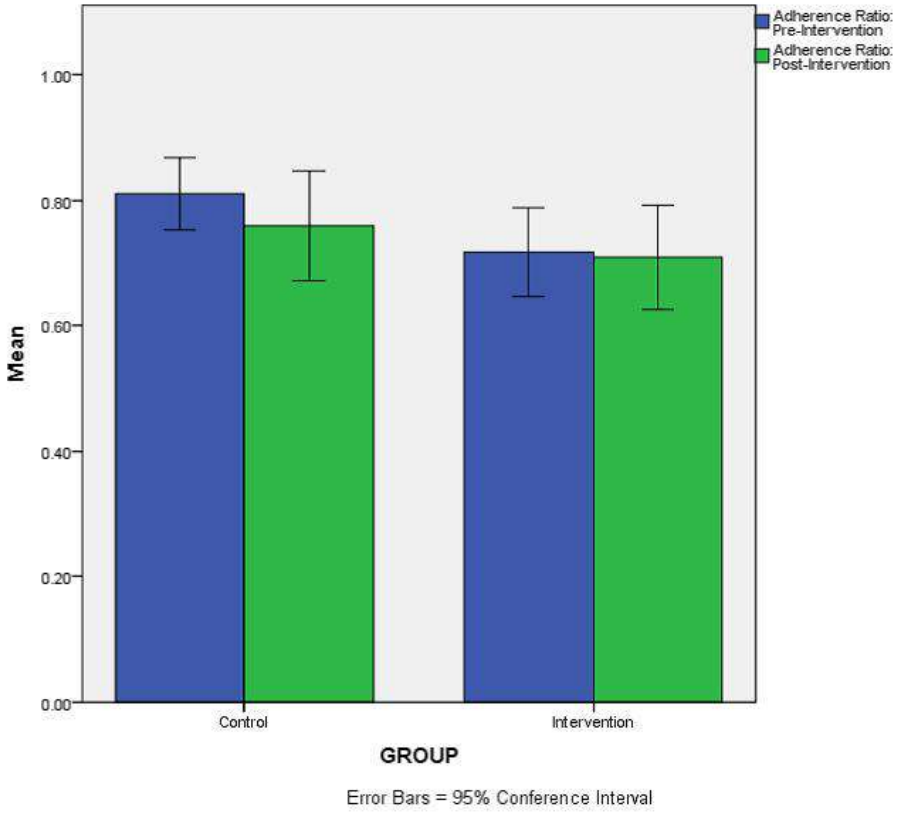
Mean Group Adherence Ratios by Time (Pre- and Post-Intervention)



Control: Those participants using an MMCA at baseline **Intervention:** Those participants not using an MMCA at baseline who were taught to use the device

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THE DETRIMENTAL EFFECTS OF BETA-BLOCKERS ON CENTRAL HEMODYNAMIC PARAMETERS: A PROPENSITY SCORE ANALYSIS

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(2) CHU de Québec, Hôtel-Dieu de Québec, Université Laval

Introduction:
Central blood pressure (BP) and aortic stiffness are better predictors of the cardiovascular burden than peripheral BP. Beta-blockers (BB) are known to reduce central BP to a lesser extent than peripheral BP, a hypothesized consequence of heart rate (HR) reduction. Therefore, the association between BB use, HR and central hemodynamics indices were studied in the treated hypertensive participants of the CARTaGENE study.

Methods:
Using propensity score analyses, BB users (n=605) were matched to controls having similar clinical characteristics with (Model 1) and without (Model 2) adjustment for HR. This resulted in 457 and 510 pairs with adequate balance, except for a different HR in Model 2 (62.5 ± 10.5 vs. 70.4 ± 11.5 bpm, $p<0.001$).

Results:
In Model 1, the difference between peripheral and central systolic BP (ΔSBP) was 8.3 mmHg (IQR 5.8, 11.6) with BB compared to 9.7 mmHg (7.1, 13.5) without ($p<0.001$), indicating that for any given peripheral BP, BB use resulted in higher central systolic BP. Pulse pressure amplification, augmentation index and augmented pressure were also less favorable with the use of BB. The different HR in Model 2 further increased the detrimental ΔSBP observed with BB to 7.9 (5.6, 11.0) vs. 10.6 (8.1, 14.3) without ($p<0.001$) and was associated with a higher central pulse pressure (46.5 ± 13.0 vs. 43.3 ± 11.3, $p<0.001$).

Conclusions:
This study shows that the unfavorable central hemodynamic profile of BB has both a HR-dependent and a HR-independent component.

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	Model 1 (HR matched)		
Central hemodynamic Parameters	**No BB n = 457**	**BB n = 457**	**p-value**
cSBP (mmHg)	120.0 ± 14.7	120.8 ± 16.3	0.07
ΔSBP (mmHg)	9.7 (7.1, 13.5)	8.3 (5.8, 11.6)	<0.001
cPP (mmHg)	45.4 ± 11.0	46.5 ± 12.9	0.045
PPA	1.25 (1.17, 1.34)	1.21 (1.14, 1.30)	<0.001
AIx (%)	28.7 ± 10.6	30.7 ± 10.6	0.005
AP (mmHg)	12.8 (8.5, 17.3)	13.4 (9.1, 19.1)	<0.001
	Model 2 (HR not matched)		
Central hemodynamic Parameters	**No BB n = 510**	**BB n = 510**	**p-value**
cSBP (mmHg)	118.1 ± 14.7	120.8 ± 16.5	0.006
ΔSBP (mmHg)	10.6 (8.1, 14.3)	7.9 (5.6, 11.0)	<0.001
cPP (mmHg)	43.3 ± 11.3	46.5 ± 13.0	<0.001
PPA	1.29 (1.20, 1.41)	1.20 (1.13, 1.29)	<0.001
AIx (%)	26.5 ± 10.5	31.2 ± 10.3	<0.001
AP (mmHg)	11.2 (6.9, 15.7)	13.7 (9.3, 19.7)	<0.001

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TARGETED ASSESSMENT AND OPTIMIZATION OF FALLS-RELATED MEDICATIONS IN AN OUTPATIENT HEMODIALYSIS UNIT: A PILOT STUDY

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(2) University of Toronto

Background: Patients undergoing hemodialysis (HD) are at high risk of falls, with subsequent complications including fractures, loss of independence, hospitalization, and death. Assessing and optimizing falls-related pharmacotherapies are important steps towards decreasing the rate of medication-related falls in this patient population.
Objectives: The objectives of this pilot study were to: (1) describe the use of falls-related medications by HD patients; (2) systematically assess and optimize falls-related medication therapies using a standardized process; and (3) determine the proportion and types of successful interventions.

Methods: Medication classes consistently associated with an increased risk of falls were identified through literature searches, and a list of medications was developed for use during pharmacotherapy work-ups. Patients who were considered to be at high risk of falling by the physiotherapist were approached. Best Possible Medication Histories were conducted for these patients, and falls-related medications were then assessed by a pharmacy team member. Recommendations for optimization were discussed with the nephrology care team and implemented upon agreement from the patient. Patients were monitored by the nephrology care team post-intervention according to usual clinical practice.

Results: Medication assessments were completed for 35 patients. In total, 103 falls-related medications were identified, and 37 recommendations were made. The overall rate of acceptance of interventions was 64% (93% for cardiovascular medications and 57% for psychotropic medications). The main reason for non-acceptance of interventions was patient preference (90% of cases of non-acceptance).

Conclusion: A large proportion of patients in the HD unit may be taking medications that increase their risk of falling. Pharmacists can play a key role in assessing and optimizing medication therapies, thereby potentially decreasing a patient's falls risk. This data may inform the development and validation of tools to aid clinicians in the assessment and optimization of falls-related medications with the aim of improving practice in the HD unit.

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THE IMPACT OF HEPATIC FUNCTION ON SERUM BTP CONCENTRATIONS

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(1) Queen's University
(2) University of Ottawa
(3) Ottawa Healt5h Research Insitute

Background: Beta Trace Protein (BTP) is a promising novel endogenous marker of glomerular filtration rate (GFR). New equations are being developed to convert its concentration into a GFR estimate. Very little is known about BTP's production and metabolism. It has been hypothesized that the liver metabolizes certain BTP isoforms. As such, hepatic dysfunction may influence serum levels independently of GFR. This would impact on the accuracy and precision of GFR estimates using BTP.

Objectives: The aim of this study was to determine whether patients with hepatic dysfunction have higher than expected serum BTP concentrations due to reduced hepatic clearance.

Methods: BTP, cystatin C (cysC) and creatinine (Cr) were measured in 99 cirrhotic subjects and in age, gender and diabetes status matched controls. BTP/cysC and Cr/cysC ratios were compared between cases and controls. This was repeated after stratification by Child Pugh category. Comparisons of ratios between Child Pugh category A and combined B and C case subjects were also performed. Prior studies reveal a lack of impact of cirrhosis on serum cysC suggesting that, unlike Cr, it is an acceptable surrogate for measured GFR.

Results: There were no differences in BTP/cysC ratios between cases and controls for the entire cohort (0.80 vs 0.79) or for any of the Child Pugh categories ($p > 0.10$ for all). There were significant differences between cases (1.09) and controls (0.73) for the BTP/Cr ratios ($p<0.001$). The BTP/Cr ratio was higher in those with more advanced cirrhosis as compared to those with less severe cirrhosis (1.20 vs 1.03, $p<0.01$). There were no differences in BTP/cysC ratios between those with less severe and more advanced cirrhosis ($p=0.25$).

Conclusions: This study suggests that hepatic dysfunction does not influence serum BTP concentrations and that BTP might be a particularly useful marker of GFR in cirrhosis.

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BETWEEN-CENTRE VARIATION IN THE MANAGEMENT OF TRANSPLANTATION: A SYSTEMATIC REVIEW

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(2) Ottawa Hospital Research Institute

Background: Kidney transplantation is the most effective therapy for patients with end stage renal disease with an improved quality of life and lower risk of death compared to dialysis. Although one-year graft and patient survival rates are now above 95% there has been little improvement in long-term outcomes. While certain patient-level factors that influence graft and patient survival have been established, the presence of variation in the management of kidney transplant patients and its influence on patient outcomes remains largely unknown.

Objective: This systematic review will focus on centre variation and centre/provider factors that impact patient and graft survival post renal transplantation.

Methods: A comprehensive and systematic search of published articles was performed by a trained and experienced librarian using both MEDLINE and EMBASE. Key words such as “kidney transplantation”, “centre effect” and “centre variation” “mortality” and “graft failure” were used. We included all study design types. The primary outcome was graft failure and patient survival post-transplant. Information was abstracted by three individuals independently. Risk of bias was assessed using the Ottawa Newcastle score.

Results: Our search yielded 6196 abstracts; 236 full texts were assessed for eligibility. Twenty-one studies published between 1985 and 2011 were included; 1 prospective and twenty retrospective studies. The number of centres in each study ranged from 1 to 258 with patient samples ranging between 480 and 141,406. Exposures assessed included centre effect (n=11), transplant volume (categorical/continuous) (n=11), cross match policy (n=1) and type of follow up (n=1). Studies varied in their approach to data analysis, patient factors they adjusted for and length of follow up.

Conclusion: This systematic review found mixed findings as to whether centre variation in patient and graft survival and a centre effect exists. No studies looked at provider differences. The association between kidney transplant volume and graft/patient survival remains unclear.

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IMPACT OF PERCUTANEOUS RENAL ARTERY DENERVATION (RDN) ON PATIENTS WITH LOIN PAIN HEMATURIA SYNDROME (LPHS): THE PRAIRIE LPHS STUDY

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(1) Regina Qu Appelle Health Region
(2) Cypress Health Region

Introduction:
Loin pain hematuria syndrome (LPHS) is a painful and incapacitating condition that typically afflicts young women. Treatment options are either opiates and/or surgical denervation of the renal nerves that includes auto transplantation or even nephrectomy with varying success.

Methods:
Three patients between the ages of 28-62 years (all female) with LPHS underwent endovascular ablation of the renal nerves between July and November 2015 using the Vessix ™renal denervation system. The number and frequency of pain medications, EQ-5D, McGill Pain Questionnaire, Geriatric Depression Score, Short Form (SF)- 36, and Oswestry Disability Index were measured at baseline and at 3 months post-procedure to evaluate changes in pain, disability, quality of life and mood.

Results:
There were improvements in pain (McGill Pain Questionnaire), disability (Oswestry disability index), and quality of life (EQ-5D and SF-36) from baseline to 3-months post-procedure. 2/3 patients were off tylenol # 3 and non steroidal anti inflammatories, whilst the third had a 70% reduction in the dose of morphine.

Conclusions:
We conclude that RDN is associated with decline in the number of pain medications and considerable improvement in quality of life. These results suggest that percutaneous catheter based delivery of radiofrequency energy is a safe, rapid, treatment option that should be considered in all patients with LPHS.

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CLUSTERIN-REGULATED TRANSCRIPTOME IN KIDNEY CELLS DURING HYPOXIA

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Background: Clusterin (CLU) is a chaperone-like protein and contributes to the resistance of the kidney to ischemia-reperfusion injury (IRI) causes acute kidney injury, however its pathways are not fully understood. This study was designed to investigate CLU-mediating pathways in kidney cells by using bioinformatics analysis.

Materials and Methods: CLU null renal tubular epithelial cells (TECs) expressing human CLU cDNA (TEC-CLU^{hCLU}) or empty vector (TEC-CLU$^{-/-}$) were exposed to hypoxic condition (1% O_2). Transcriptome profiling of these cells under both hypoxia and normoxia was performed using gene expression microarray, and the signaling pathways was identified by using Ingenuity pathway analysis.

Results: Here we showed that ectopic expression of human CLU in CLU null kidney cells enhanced cell survival under hypoxia, and promoted cell growth but inhibited migration under normoxia. Transcriptome profiling showed that under hypoxia, CLU was responsible to down-regulate more numbers of genes compared to TEC-CLU$^{-/-}$ cells and, more cell survival in TEC-CLU^{hCLU} cells compared to TEC-CLU$^{-/-}$ cells was associated with PI3K/AKT and with activation of endoplasmic reticulum (ER) stress-unfolded protein response (UPR) (up regulation of *FOXO3*, *IRE1, XBP1).*

Under normoxia, the promotion of cell growth or cell cycle progression in TEC-CLU^{hCLU} cells compared to TEC-CLU^{hCLU} cells was related to up-regulation of *p21*,AKT2 and *GSK3B* in PI3K/AKT and of *FBGFR1 and CREB1* in ERK/MAPK signaling, while the suppressed migration of TEC-CLU^{hCLU} cells was correlated with down-regulation of *RHOA* and up regulation of *AKT2.*

Conclusion: Data suggests that CLU expression in kidney cells regulates gene expression under hypoxia. CLU promotes the cell proliferation, restores cell cycle progression and inhibites cell migration under normoxia mainly through PI3K/AKT, and favored cell survival under hypoxia may through PI3K/AKT in addition to ER stress/UPR.

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REVERSIBILITY OF ACUTE KIDNEY REJECTION ACCORDING TO THE BANFF 2013 CLASSIFICATION: A RETROSPECTIVE COHORT STUDY

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(2) Hôpital Maisonneuve-Rosemont (HMR)
(3) Statsciences

Background: Vascular involvement of the allograft is a poor prognostic factor in acute kidney rejection. Cell-mediated endarteritis often coexists with antibody-mediated rejection. As previous studies have used older versions of the Banff classification, antibody-mediated rejections may have been misclassified as cell-mediated vascular rejections. Our aims were to determine the reversibility of acute rejection episodes according to the Banff 2013 grade and to assess the correlation between clinical and histological responses to treatment.

Method: We performed a retrospective cohort study in kidney transplant recipients who were transplanted between 2008 and 2014 and developed an episode of acute rejection diagnosed on biopsy. Rejections were graded according to the 2013 Banff classification. A clinical response was defined as a 1 month post-rejection creatinine that had returned within 25% of the best value in the month prior to rejection. A histological response was defined as the complete clearance of rejection on a control biopsy performed within 3 months of rejection.Clinical and histological responses were compared with Fisher exact's tests.

Results: We observed 126 rejection episodes. Amongst the 80 borderline, 1A or 1B pure cell-mediated rejections, a clinical response was observed in 77% (95%CI: 68-87%) of the episodes. Amongst the 22 episodes of pure cell-mediated Banff grade ≥2, a clinical response was observed in 73% (95%CI: 53-93%) of cases, a figure which fell to 43% (95%CI: 22-65%) in the 24 episodes of pure antibody-mediated or mixed rejection episodes (p=0,04). A control biopsy was performed in 50 cases. We did not observe a significant association between clinical and histological responses (p=0,14).

Conclusion: Pure cell-mediated Banff grade ≥2 rejections have a distinct rate of response to treatment when compared to antibody-mediated or mixed rejection episodes. Our findings argue for an increased use of control biopsies after rejection, as clinical responses do not correlate well with histological responses.

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A NATIONAL SURVEY OF NEPHROLOGISTS ASSESSING THE PERCEPTION OF PROGNOSTICATION IN PATIENTS WITH END-STAGE RENAL DISEASE (ESRD)

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(1) The University of British Columbia
(2) BC Provincial Renal Agency
(3) Island Health Authority

Background
Patients with ESRD have a relatively poor prognosis with higher risk of mortality. The care needs for these patients are unique as optimal care for these patients would depend on their prognosis. While prognosis is seen as an important issue in management of ESRD, little is known about how often and by what means Canadian nephrologists prognosticate for these patients, and how prognosis informs and guide clinical management.

Objective
To guide robust management strategies for patients, we aimed to better understand how nephrologists in Canada consider prognosis during routine care.

Methods
A web-based multiple choice survey was designed, refined and administered to all nephrologists in Canada through the e-mail list of the CSN. The core content of the survey consisted of two parts in which we asked the respondents about their routine practice of estimating survival and the perceived importance of prognostic practices and tools in patients with CKD and <15 ml/min not on dialysis and in those on dialysis. Descriptive statistics were used in analyzing the responses.

Results
The survey response rate was 43%. Less than 50% of the respondents indicated they “always” or “often” make an explicit attempt to estimate and/or discuss survival with ESRD patients not on dialysis, and ≤25% reported they do so “always” or “often” with patients on dialysis. Survival estimation is primarily based on clinical gestalt. Respondents indicated a wide range of issues that are influenced by prognosis, including advance care planning, transplant referral, choice of dialysis access, medication management, and consideration of conservative care. Quality of life was the most important factor for recommending conservative management. Respondents expressed the need for a validated prognostic tool to guide clinical management.

Conclusions
In conclusion, prognostication of patients with ESRD is an important issue for nephrologists and impacts management in fairly sophisticated ways.

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PERSPECTIVES OF NEPHROLOGISTS AND ALLIED HEALTHCARE WORKERS IN NEPHROLOGY ON THE IMPORTANCE OF SEX HORMONES AND HORMONE THERAPY IN WOMEN WITH KIDNEY DISEASE

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(2) Brigham and Women's Hospital
(3) University College London

Background: Chronic kidney disease (CKD) in women is often accompanied by menstrual and fertility disorders. We sought to determine nephrologists' and allied healthcare providers' perceptions of reproductive status, and hormone treatment in women with CKD.

Methods: An anonymous, internet-based survey was sent electronically to members of the Canadian, Australia and New Zealand Societies of Nephrology, British Renal Society and the Canadian Association of Nephrology Nurses and Technologists (February-November 2015). Respondents answered questions about demographics, and sex hormone status and hormone treatment in women with CKD.

Results: A total of 288 (175 nephrologists (21% response rate) and 123 allied healthcare workers (30% response rate)) individuals responded to the survey. Sixty-eight percent of nephrologists and 46% of allied workers were between the ages of 30-50 years and 38% of nephrologists and 89% of allied workers were female. Ninety-five percent of the nephrologists strongly agreed or agreed that kidney function has an impact on sex hormones. Only 35% of nephrologists often discussed fertility and 15% discussed menstrual irregularities with their patients of childbearing age. Female nephrologists were more likely to discuss menstrual irregularities with their patients than male nephrologists (57% vs 38%, p=0.03). Many physicians (43%) and allied workers (57%) did not know if there is a role for postmenopausal hormone therapy in this population.

Conclusion: Nephrologists recognize the impact CKD has on sex hormone status in women. They infrequently discuss fertility, menstrual regularity and menopause in practice. Our international survey highlights uncertainties around management of sex hormone disturbances in CKD.

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ERRORS IN HLA TYPE ASSIGNMENT AND EPLET LOAD ESTIMATION WHEN IMPUTING 4-DIGIT FROM 2-DIGIT HLA TYPES OF DONOR-RECIPIENT PAIRS

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Background: Eplet load, or the number of polymorphic structural mismatches between donors and recipients' HLA, is an independent predictor of donor-specific antibodies and allograft rejection. An important barrier for the consideration of eplet load for organ allocation, however, is the reliance on the availability of 4-digit HLA types to estimate eplet load. Such high-resolution typing is not readily available at the time of transplantation for most donor-recipient pairs.

Objective: We sought to assess the error rate in 2-digit to 4-digit HLA type assignment and the associated donor-recipient eplet load.

Methods: A convenience sample of 18 stem cell donor-recipient pairs form a single centre with 4-digit HLA-A, -B, -C, -DRB1, and -DQB1 typing by molecular methods was used. To simulate HLA type imputation, available donor and recipient 4-digit HLA types were rendered into 2-digit types. Two-digit HLA types were then haplotype-phased and reverse-imputed using HaploStats (http://www.haplostats.org) to obtain 4-digit HLA types. HLAMatchmaker (ABCMatchingvs1 and DRDQDPMatchingvs1) programs were then used to compare eplet load associated with verified and imputed donor-recipient 4-digit types.

Results: Eleven of the 36 (30.6%) imputed haplotype pairs deviated from the original 4-digit HLA types in at least one HLA locus. This 4-digit assignment error was related to errors in HLA-DR (7 loci), -DQ (5 loci) and –B (1-locus) four-digit type assignment. This 4-digit assignment error was associated with a modification in eplet load in only one of the donor-recipient pairs.

Conclusions: Our sample includes donor-recipient pairs matched at the 2-digit level on multiple loci. Consequently, the degree of error associated with 2- to 4- digit HLA type imputations and the eplet load associated with them are likely underestimated. A provincial population-based study is awaited to ascertain the error rate in 4-digit HLA types and eplet load estimations among solid organ donor-recipient pairs where less stringent matching is permitted.

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P-109

PROMOTING ARTERIOVENOUS FISTULA AS HEMODIALYSIS ACCESS: EXPECTED BENEFITS AND UNINTENDED CONSEQUENCES

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Background
Multidisciplinary vascular access teams (MDVATs) have been established in renal programs to maximizing fistula use while minimizing access-related procedures. The Southern Alberta Renal Program (SARP) implemented a MDVAT in 2005.

Objectives
To study the relationship between MDVAT implementation and:
1) probability of fistula use in people starting hemodialysis,
2) rates of vascular access-related procedures.

Methods
We assessed the probability of fistula use in people starting hemodialysis between January 1, 2004 and December 31, 2011. The primary outcome categories were: fistula never attempted; fistula used within the first year of hemodialysis for a) <= 6 months; or b) >6 months); or fistula used after the first year of hemodialysis. We defined exposure based on the year of hemodialysis start: 2004-2005 (pre-MDVAT); 2006-2008 (early MDVAT); and 2009-2011 (late MDVAT). Secondary outcome was the rate of access-related procedures.

Results
The study included 609 participants: 146 started hemodialysis before MDVAT implementation; 252 in 2006-2008 and 211 in 2009-2011. Participants in the three groups had similar characteristics (age 64.8±15 years; 61.6% male; 54.2% with diabetes and 49.6% with cardiovascular disease). The probability of each outcome was similar across the three periods, with the exception of fistula use for <=6 months, which increased in the early period relative to the pre-MDVAT period (Risk Ratio 3.45, 95% Confidence Interval 95%CI] 1.29 - 9.21). The rates of access-related procedures increased in both periods by the same amount (10% per patient-year), although were statistically significant only in the early period (Incidence Rate Ratio 1.11; 95%CI 1.01 - 1.22).

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Conclusions

MDVATs failed to increase use of fistulas in hemodialysis patients and may lead to an increased number of access-related procedures. Clinical trials are needed to determine the benefits and harms of such vascular access programs promoting fistula use in people receiving hemodialysis therapy.

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P-110

PROTEOMIC APPROACHES TO IDENTIFY DIFFERENTIALLY EXPRESSED PROTEINS IN CARDIAC SURGERY ASSOCIATED ACUTE KIDNEY INJURY

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Background: Acute kidney injury (AKI) after cardiopulmonary bypass (CPB) is an important cause of morbidity and mortality. Mass-spectrometry (MS)-based proteomics may allow us to improve our understanding of pathogenic processes in ischemia-reperfusion injury (IRI) and identify 'at-risk' individuals.

Objectives: To perform an in-depth analysis of patients undergoing CPB to elucidate proteomic changes during IRI.

Methods: A nested case-control cohort of AKI (n=5) and non-AKI (n=5) patients were selected from a prospective observational cohort of 326 adult CPB patients, and pooled urines from baseline, start of CPB, 1hr after CPB and arrival to the intensive care unit analyzed. Samples were processed using modified Filter Assisted Sample Preparation, separated and analyzed by 2D-LC-MS/MS for protein identification and to generate an ion library. A label-free approach was applied for protein quantitation. Protein identification accuracy was increased by analyzing the same samples using SWATH-MS (Sequential Window Acquisition of All Theoretical Fragment ion spectra Mass-Spectrometry). Protein relative abundance was compared between AKI and non-AKI using a combination of 2D-LC-MS/MS and SWATH data.

Results: Using a high-content MS approach we confidently identified 2,042 proteins (≥2 peptides, log(e)≤-3) across all time-points. For more complete comparison we used SWATH-MS to provide quantitative data on 730 proteins, which demonstrated some overlap with the 2D-LC-MS/MS data. Differential analysis detected 20 decreased and 4 increased proteins in AKI versus non-AKI patients, based on normalized Z-scores >1 across all time-points. Urinary MMP9 was validated as decreased in AKI versus non-AKI pooled urines using ELISA.

Conclusions: This study provides high quality data on comparative protein quantitation in AKI versus non-AKI patients throughout IRI. We established methods for urine sample processing, which contains low protein amount in large volumes, high salt concentrations, metabolites and interfering drugs. The differential proteomic changes identified may provide insight into the pathophysiology of IRI and potential novel biomarker identification.

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APPROACH TO ACUTE KIDNEY INJURY IN THE PREGNANT TRANSPLANT PATIENT: A COMPLEX CASE OF TWIN PREGNANCY AFTER SIMULTANEOUS PANCREAS KIDNEY TRANPLANT

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Background: With the success of kidney transplantation, pregnancy post-transplant has been steadily increasing. Currently the approach to acute kidney injury(AKI) in the pregnant transplant patient is not well defined. We present a complex case of AKI during pregnancy in the extraordinary clinical scenario of twin pregnancy after simultaneous pancreas-kidney transplant(SPK) and an approach to AKI in pregnant transplant patients.

Case: a 34 year old female with type 1 diabetes received an SPK and a repeat kidney transplant 3 years later, requiring incisional hernia repair with mesh and skin advancement flaps. One year later she conceived with twins. At 28 weeks gestation she presented with abdominal pain and mild hypovolemia. Investigations were non-diagnostic. On day 4 of hospitalization creatinine rose to 215µmol/L. Guided by our AKI approach(Table 1), investigations, including viral studies and donor specific antibodies were unremarkable, except for hypercalcemia and elevated tacrolimus level of 14.7µg/L. She became oliguric, with peak creatinine of 380 mmol/L. Allograft biopsy revealed mild tubular injury and thrombotic microangiopathy(TMA). As tacrolimus levels decreased, creatinine returned to her baseline, along with lack of proteinuria, suggesting TMA was secondary to tacrolimus toxicity. Her abdominal pain persisted, and creatinine later increased to 175 µmol/L. A bladder pressure was measured at 29 mmHg suggestive of abdominal compartment syndrome. An emergent Caesarean section was performed at 32 weeks gestational age, after which renal function normalized and abdominal pain resolved.

Conclusions: There are multiple unique factors to consider in the clinical scenario of AKI in the pregnant transplant patient.

Type of renal transplant dysfunction	Possible Etiology
Pre-Renal	Hypovolemia/Hypotension
	Hyperemesis gravidarum – first and second trimester
	Hemorrhage (placenta or uterine bleeding, abortion)
	Sepsis (chorioamnionitis, intra-abdominal infections)
	Amniotic fluid/pulmonary embolism
Vasoconstriction	
pre-eclampsia, calcineurin inhibitor, hypercalcemia	
	Diuretic use
	Heart Failure
Renal	Acute tubular necrosis
	Interstitial nephritis
	Recurrent or de novo glomerular disease
	Rejection – T cell mediated and antibody mediated
	Infection – BK virus, pyelonephritis
	Vascular Compromise
	Transplant renal artery stenosis
	Abdominal compartment syndrome
	Uterine compression of allograft vessels
	Pregnancy-specific thrombotic microangiopathy
	Pre-eclampsia, HELLP syndrome
	Disseminated intravascular coagulation
	Acute fatty liver of pregnancy
	Thrombotic thrombocytopenic purpura(TTP)
	Allograft-specific thromobotic microangiopathy
	Drug induced – calcineurin inhibitor, mTOR inhibitor
	Cytomegalovirus infection
	Antibody mediated rejection
	Thrombotic microangiopathy – others
	Cryoglobulinemia
	Lupus anticoagulant, anti-phospholipid antibody
Hydronephrosis	
Nephrolithiasis	
Uterine compression on allograft ureter	
Allograft ureteric stenosis	
	Neurogenic bladder

Table 1. Approach to differential diagnosis of acute kidney injury in pregnancy of kidney transplant recipients.

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PREVALENCE OF CHRONIC KIDNEY DISEASE IN CHILDREN: A POPULATION BASED STUDY IN MANITOBA

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(2) Manitoba Centre for Health Policy

Background: Risk factors for chronic kidney disease (CKD) are increasing in children, however the prevalence of pre-dialysis CKD in Canadian children remains unknown.

Objectives: To evaluate the prevalence of CKD in children in Manitoba, and to stratify children by risk for progression.

Methods: Administrative data housed at the Manitoba Centre for Health Policy was utilized to evaluate the prevalence of CKD in children <18 years of age in April, 2012 utilizing 3 years of health claim (1+ inpatient and/or 2+ outpatient and/or 1 CKD drug prescription) and laboratory data (CkiD Schwartz eGFR <90ml/min/1.73m2 and/or proteinuria X 2 90+ days apart). Sensitivity analyses were conducted to address the limitation that laboratory data was not available for the entire province. The first included only children with laboratory results, and the second was a capture-recapture method including administrative and laboratory data. Children were further stratified by risk of progression based on eGFR and albuminuria status according to KDIGO criteria.

Results: 4330 children were identified with CKD with an age and sex-adjusted prevalence of 1.49% (95% CI: 1.45-1.53). Sensitivity analyses revealed estimates of 3.41% (laboratory data) and 2.97% (capture-recapture). Laboratory data was available for 52.5% of the cohort. Three-quarters of this cohort was low-risk for progression (A1/G1-G3a and A2/G1-G2). A small proportion had eGFRs less than 45 ml/min/1.73m2 (G3b or worse; n=79) and fewer than 20 children had eGFRs less than 30 ml/min/1.73m2 (G4 or worse). Conversely, many had significant proteinuria (A2, n= 550 and A3 n= 457).

Conclusions: CKD prevalence is significantly lower in children than in adults. However, the lifetime risk of progression for affected children is currently unknown and could be significant. More research is needed to address the population health implications of this identified burden of low risk disease in early life.

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MINIMAL CHANGE DISEASE NEPHROTIC SYNDROME FOLLOWING INTRAVITREAL ANTI-VEGF THERAPY WITH RANIBIZUMAB

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University of Alberta

Ranibizumab (Lucentis®) is a monoclonal antibody F(ab) fragment directed against vascular endothelial growth factor (VEGF). This intravitreal medication is currently used for treatment of wet age-related macular degeneration, macular edema following retinal vein occlusion, and diabetic macular edema. In this report, we describe a 74-year-old woman who presented with acute onset of glomerular proteinuria, frank nephrotic syndrome, and renal failure, beginning seven days after intravitreal injection of ranibizumab for macular degeneration. Serologic studies were negative, and a subsequent renal biopsy showed podocyte foot process effacement as the only glomerular lesion. After treatment with prednisone, the proteinuria renormalized over 11 weeks. The close temporal relationship supports the central role for VEGF in the pathogenesis of minimal change disease, but also indicates this F(ab) antibody fragment was able to systemically dysregulate the action of VEGF. While glomerular proteinuria has been described as a consequence of treatment with the parent antibody bevacizumab (Avastin®), to date this concern has not been recognized in the clinical trials for ranibizumab. We believe this is the first report of nephrotic proteinuria resulting from ranibizumab. This case underscores the potential of anti-VEGF agents to have significant adverse effects on the kidney. Clinicians who treat patients with either systemic or intravitreal anti-VEGF therapy should be cognizant of the development of proteinuria and nephrotic syndrome as this would warrant a change in therapy.

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A NOVEL COMPUTERIZED DECISION SUPPORT TOOL FOR NON-DIALYSIS CKD ANEMIA MANAGEMENT

Janice Bissonnette, Ayub Akbari, Pierre Brown
The Ottawa Hospital

Background: The KDIGO group has produced comprehensive guidelines for the management of anemia in CKD patients. Yet, there is no generally accepted standardized dosing algorithm for treating anemia in CKD patients. In one study, a computerized decision support tool for the management of anemia in dialysis patients showed a 50% reduction in time spent by dialysis staff on anemia management, however no change in maintaining the hemoglobin within a targeted range. Clearly, anemia treatment with erythropoiesis-stimulating agents (ESA) is important for improving patients' quality of life. What remains unclear is the best method for monitoring treatment and reducing the risk associated with higher hemoglobin targets.
Methods: In this study, we implemented and trialed a unique patient call management (PCM) system for prescribing, monitoring, and triggering erythropoiesis-stimulating agent (ESA) dose changes in a group of non-dialysis CKD patients. A local PCM system triggered nurses to complete a post hospital discharge phone call to patients. We reprogrammed the PCM system and included a computerized decision support tool to initiate a standardized anemia management protocol for non-dialysis CKD patients.

Results: Implementation of a novel IT decision support system, which included 1) protocols for adjusting ESA dose based on 2 possible hemoglobin target ranges, 2) timed triggers for nurse review of monthly hemoglobin results or patient reminder calls, 3) protocols for notification of prescribing nephrologist with high risk range results, and 4) tracking system for quality assurance monitoring.

Conclusions: A computerized decision support system for use in ambulatory care settings is a feasible approach for standardization and monitoring of ESA's for non-dialysis CKD patients.
Further evaluation of outcome measures to include achievement of target ranges, iron indices, and adverse event reporting.

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INCREASING SERUM CHLORIDE IS ASSOCIATED WITH AKI IN CRITICALLY ILL PATIENTS

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Background

Physiologic studies have shown hyperchloremia may negatively affect kidney function. However, few studies have looked at the impact of hyperchloremia on adverse outcomes in critically ill patients. We examined the association between serum chloride levels and the development of acute kidney injury (AKI) and mortality in an intensive care unit (ICU) setting.

Methods

We conducted a retrospective, single-center, cohort study of 1866 adults admitted to an ICU between 2006 and 2011. Serum chloride values during the first 48 hours of ICU admission were collected and analysed for baseline levels, peak levels, and change in the first 48 hours. Adjusted logistic regression analysis was used to examine the association between serum chloride and the incidence of AKI (2012 KDIGO criteria) and ICU mortality.

Results

The incidence of AKI was 56.3% and ICU mortality was 12.8%. The mean (SD) baseline chloride was 106 (7.1) mmol/L and average peak chloride 106 (7.1). The mean change in chloride was -2.2 mmol/L, with 12.8% of patients showing an increase within the first 48 hours of admission. An increase in serum chloride was significantly associated with AKI and ICU mortality. In multivariate analysis adjusting for age, APACHE II score, ventilation status and pH value, the association remained significant between the serum chloride increase and severe AKI (OR 1.756, 95% CI 1.140-2.706, p=0.0107) and ICU mortality (OR 2.260, 95% CI 1.384-3.69, p=0.0011). There was no significant association between baseline or peak chloride and AKI or ICU mortality.

Conclusion

An increase in serum chloride in critically ill patients during the first 48 hours of admission is significantly associated with the development of severe AKI and ICU mortality, independent of disease severity (APACHE II score). Serum chloride increase may have a deleterious effect on kidney function. Whether this justifies the use of chloride-restrictive fluid strategies requires further evaluation.

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THE EQUIVALENCE OF EGFR BASED ON CKD-EPI TO MDRD FORMULA

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(2) Cancer Care Ontario

Background

Canadian CKD programs have recently adopted an 'intent-to-defer' strategy for chronic dialysis initiation. Although there is no defined eGFR at which dialysis should start, the proportion of patients initiating chronic dialysis with MDRD GFR < 10.5 ml/min/1.73m^2 is reported by various provincial health authorities to track adoption of this deferred initiation strategy. Given its better performance, the CKD-EPI formula has recently been adopted by commercial laboratories and by the Ontario Renal Network.

Objective

In order to adopt the CKD-EPI formula in reporting, we empirically derived an Ontario population-level estimate of the CKD-EPI equivalent of an MDRD GFR of 10.5 ml/min.

Method

Using incident chronic dialysis data (serum creatinine at initiation, age, sex and ethnicity) collected in the ORRS between Jan 2014 and Dec 2015 inclusive, we fitted a linear model to investigate the relationship between GFR estimated by the MDRD and CKD-EPI methods.

Result

We identified 5,073 patients with eligible MDRD and CKD-EPI eGFR values for the study. Mean eGFR values were 10.3 and 9.2 for MDRD and CKD-EPI respectively. The two sets of GFR estimates were highly correlated with correlation coefficients 0.93(Kendal), 0.96 (Pearson) and 0.99 (Spearman). When regressing CKD-EPI eGFR on MDRD eGFR, the estimated intercept and coefficients were 0.41 ($p < 0.0001$) and 0.86 ($p<0.0001$). The fit statistic r^2 was 0.93, indicating that 93% of variation in CKD-EPI eGFR can be explained by the MDRD eGFR. Using our regression model, we calculated that a CKD-EPI GFR of 9.5 mL/min/1.73 m^2 is equivalent to a MDRD GFR of 10.5 mL/min/1.73 m^2 at dialysis initiation..

Conclusion

A CKD EPI eGFR value of 9.5 mL/min/1.73 m^2 can be used in place of an MDRD GFR of 10.5 as a cut-point for calculating the proportion of deferred chronic dialysis starts.

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EVALUATING THE ASSOCIATION BETWEEN ACUTE KIDNEY INJURY AND LONG-TERM RENAL OUTCOMES USING ADMINISTRATIVE DATA IN CHILDREN

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(2) Université de Montréal
(3) StatSciences Inc
(4) Centre hospitalier universitaire Sainte-Justine

Background
Acute kidney injury (AKI) may be a risk factor for long-term chronic kidney disease (CKD) or hypertension. Provincial administrative healthcare data (PAHD), using International Classification of Disease codes (ICD-9/ICD-10), has been a rich resource to study long-term AKI outcomes in adults, but has not yet been explored in child AKI research.

Objectives
1. Develop a pediatric definition for CKD and hypertension using ICD-9/ICD-10, procedural, and billing codes in PAHD.
2. Evaluate the association between pediatric intensive care unit (PICU) AKI and 5-year post-discharge CKD and hypertension.

Methods
Clinical chart data from an existing retrospective PICU cohort (two Montreal PICUs, 2003-2005 [n=2500]; no health number, PICU deaths, pre-existing CKD excluded) was merged with Quebec PAHD from the 5 years post-PICU. Several CKD and hypertension PAHD algorithms were developed (detailed literature, expert opinion), tested, and discussed, followed by final algorithm selection. Main exposure: Kidney Disease Improving Global Outcomes serum creatinine AKI. Main outcomes: 5-year post-PICU CKD, hypertension, per PAHD. Analysis: univariate AKI *vs.* non-AKI comparisons using T-tests.

Results
Cohort: n=2457, 56.5% male, mean±SD age=6.0±5.8 years, PRISM (mortality) score=8.6±6.5. 477/1973 (24.2%) developed PICU-AKI. Figure 1 shows the PAHD CKD/hypertension algorithms. Seventeen CKD algorithms were evaluated; the selected algorithm represents the highest specificity algorithm. 8.10% developed CKD (AKI:15.7%, non-AKI:6%, $p<0.0001$) and 10.4% developed hypertension 5 years post-PICU (No AKI comparison performed).

Canadian Society of Nephrology/
Société canadienne de néphrologie
CSN/SCN

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Conclusions

AKI in the PICU seems to be associated with the development of PAHD-defined CKD and hypertension 5 years after discharge. Future research should evaluate validity of child PAHD-defined CKD and hypertension.

Figure 1: Pediatric CKD and hypertension algorithms for PAHD.

Proposed CKD definition: one or more inpatient or outpatient diagnostic codes, **or** CKD medication prescription, **or** fulfill nephrology visit criteria.

Proposed hypertension algorithm: one or more **outpatient** hypertension diagnostic codes **or** prescription for anti-hypertensive medication.

<table>
<tr><th colspan="4">CKD ALGORITHM</th></tr>
<tr><th colspan="3">Inpatient or outpatient diagnostic codes (ICD9 or ICD10)</th><th>Medications</th><th>Nephrology visits</th></tr>
<tr><td>Description</td><td>ICD-9</td><td>ICD-10</td><td rowspan="5">Erythropoietin
Activated Vitamin D
Potassium –removing agents
Phosphate binding agents</td><td rowspan="5">Two or more outpatient nephrology visits in a 16 month time period.</td></tr>
<tr><td>CKD</td><td>585</td><td>N18.x</td></tr>
<tr><td>Unspecified renal failure</td><td>586</td><td>N19</td></tr>
<tr><td>Proteinuria</td><td>791.0</td><td>R80</td></tr>
<tr><td>Outpatient Dialysis</td><td>V451</td><td>Z992</td></tr>
<tr><th colspan="5">HYPERTENSION ALGORITHM</th></tr>
<tr><th colspan="3">Outpatient diagnostic codes (ICD-9 or ICD-10)</th><th>Medications</th><th>Nephrology visits</th></tr>
<tr><td>Description</td><td>ICD-9</td><td>ICD-10</td><td rowspan="6">Diuretics
Loop Diuretics
Thiazide Diuretics
Thiazide-like Diuretics
Miscellaneous Diuretics
Beta-Blockers
Calcium Channel Blockers
Angiotensin-Converting Enzyme (ACE) Inhibitors
Angiotensin II Receptor Blockers (ARBs)
Alpha-Adrenergic Blockers
Renin Inhibitors</td><td rowspan="6">N/A</td></tr>
<tr><td>Primary Hypertension</td><td>401.x</td><td>I10.x</td></tr>
<tr><td>Hypertensive heart disease</td><td>402.9</td><td>I11</td></tr>
<tr><td>Hypertensive nephropathy</td><td>403.9</td><td>I12</td></tr>
<tr><td>Hypertensive cardionephropathy</td><td>404.9</td><td>I13</td></tr>
<tr><td>Secondary Hypertension</td><td>405.x</td><td>I15.x</td></tr>
</table>

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PRELIMINARY RESULTS OF THE CANADIAN MULTI-CENTRE ABLE STUDY: EVALUATION OF LONG-TERM RENAL OUTCOMES IN CHILDREN TREATED WITH CISPLATIN

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(3) University of Alberta

Background: Cisplatin causes acute kidney injury (AKI) and may lead to late chronic kidney disease (CKD) or hypertension. The pediatric late cisplatin renal outcome phenotype remains unclear. ABLE is a Canada-wide project evaluating late child cancer treatment effects and biomarkers of toxicity, including nephrotoxicity.

Objective: Describe the CKD and hypertension phenotype in the first year post-cisplatin in children in the ABLE cisplatin nephrotoxicity study.

Methods: Ongoing, 12-site, prospective cohort study of 150 children receiving cisplatin. Exclusion: severe baseline CKD(glomerular filtration rate(GFR)<30 ml/min/1.73m^2). Protocol: two “acute” visits (AV) around cisplatin infusion (AKI biomarkers, urine, blood); three “follow-ups” (FU) (3, 12, 36 months post-treatment; renal outcomes, urine, blood). AKI: SCr rise≥50% from baseline(≥Kidney Disease Improving Global outcomes(KDIGO) Stage 1). FU outcomes: CKD: estimated GFR(eGFR)<90ml/min/1.73m^2 or albumin-to-creatinine ratio(ACR)>30 mg/g(≥KDIGO Grade 2); Hypertension: blood pressure≥95th percentile for age, gender, height. Proportions with low eGFR, microalbuminuria or hypertension at 3 and 12 months were calculated. Chi-square or non-parametric tests were used to compare groups as appropriate.

Results: Characteristics and 3-month post-cisplatin renal outcomes are shown in Table. Hypertension and microalbuminuria were more common in patients with AKI.
Of 12-month data available (not shown), 2/12(17%) had microalbuminuria, 0/9 had eGFR<90, 2/14(14%) had hypertension.

Conclusions: ABLE will be the largest follow-up of children treated with cisplatin. 3-month post-cisplatin CKD and hypertension prevalence is high and appears more common in patients who develop AKI during therapy. Our complete sample size will help clarify late post-cisplatin CKD and hypertension and allow to develop evidence-based recommendations for renal follow-up post-cisplatin.

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Table: Long-term renal abnormalities 3 months after cisplatin treatment end in all patients, AKI patients and Non-AKI patients.

Characteristics	All	AKI	Non-AKI	P-value
Age (median [IQR] years)	5.8 [2.7-11.9] N = 42	3.5 [2.7-8.4] N=14	6.9 [3.3-13.5] N = 28	0.25
N Males	25/47 (53%)	9/15 (57%)	16/32 (50%)	0.52
ACR (median [IQR] mg/mmol)	1.8 [1.3-5.0] N = 45	5.0 [1.6-17.9] N = 13	1.7 [1.2-4.0] N = 30	**0.038**
N microalbuminuria	17/45 (38%)	7/13 (54%)	9/30 (30%)	0.14
Systolic BP percentile (median [IQR])	42 [29-50] N= 33	41 [36-50] N= 12	46 [15-50] N= 21	0.76
Diastolic BP percentile (median [IQR])	50 [40-74] N= 33	61 [45-83] N= 12	46 [40-67] N= 21	0.12
N Pre-hypertension or worse	7/34 (21%)	4/12 (33%)	3/22 (14%)	0.21
N Hypertension	3/34 (8.8%)	3/12 (25%)	0/22 (0%)	**0.037**
eGFR (mean ± SD mL/min/1.73m^2)	137 ± 39 N = 34	149 ± 52 N = 12	131 ± 29 N = 22	0.21
N with eGFR<90 mL/min/1.73m^2	5/34 (15%)	2/12 (17%)	3/22 (14%)	0.59
N with CKD (either low eGFR or microalbuminuria)	21/49 (43%)	8/15 (53%)	12/32 (38%)	0.31
N with hyperfiltration (eGFR>150 mL/min/1.73m^2)	13/34 (38%)	6/12 (50%)	7/22 (32%)	0.30

Abbreviations: AKI: Acute kidney injury, IQR: Interquartile range, ACR: Albumin-to-creatinine ratio, BP: Blood pressure, eGFR: Estimated glomerular filtration rate

*GFR is estimated by the updated CKiD formula; blood pressure is measured by an automated device

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IMPACT OF RENAL DENERVATION (RDN) ON CENTRAL BLOOD PRESSURES AND ARTERIAL STIFFNESS IN PATIENTS WITH CHRONIC KIDNEY DISEASE (CKD): THE PRAIRIE RDN STUDY.

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Background:
Accumulating evidence demonstrates that central aortic blood pressures (CBP) compared to the blood pressure (BP) measured at the brachial artery correlates better with adverse cardiovascular outcomes. We investigated the impact of RDN on central blood pressures and pulse wave velocities in patients with stage III and IV CKD with resistant hypertension.

Methods:
Twenty-six patients with resistant hypertension from our multidisciplinary CKD clinic underwent either unilateral or bilateral RDN from February 2013 to August 2014. CBP, 24-hour ambulatory blood pressures, average of 6 office BP readings on BP Tru, along with carotid-femoral pulse wave velocities were measured at 3,6,12 and18 months. Seven patients withdrew, died or transitioned to dialysis leaving a final cohort of 19 patients for analysis.

Results:
Baseline (mean ± standard deviation) central systolic/diastolic blood pressures (mm Hg) were 131±22.57/ 77.09±16.36 and at 18 months were 120.16±14.67/ 70.58±14.35 respectively. In contrast the 24-hr ambulatory blood pressures (mm Hg) at baseline and 18 month were 142.8±16.27/65.63± 11.59 and 145.34± 13.99/66.53±13.36. Central pulse pressures (mm Hg) at baseline and 18-month post-RDN were 55.59±25.17 and 49.54±20.07 respectively. Similarly, the augmentation pressures at baseline and 18 month were: 14.09±11.35 and 11.32±11.52 mm Hg respectively. Augmentation index (%) was 22.86±11.98 at baseline and 18.45±12.63 at 18 months. Pulse wave velocity was 15.95 (14.15) at baseline and 15.03 (4.93) at 18 months. MDRD GFR in mls/min/1.73m2 at baseline and 18 months were: 39.3±14.34 and 36.67±17.83 respectively.

Conclusion:
We conclude that RDN is associated with modest improvement in aortic pulse pressure, augmentation pressure, and augmentation index relative to the brachial ambulatory blood pressures in patients with stage III and IV CKD. The impact on pulse wave velocity was minimal. There was no negative impact on the GFR post procedure.

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ATYPICAL HEMOLYTIC UREMIC SYNDROME (AHUS) AND MEMBRANOPROLIFERATIVE GLOMERULONEPHRITIS (MPGN), DIFFERENT DISEASE OR A SPECTRUM OF COMPLEMENT- MEDIATED GLOMERULAR DISEASE? CASE REPORT

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Historically, patients with kidney diseases caused by genetic or acquired dysregulation of the complement alternative pathway (AP) have been grouped into clinical syndromes, C3 glomerulopathy (C3GN/DDD) versus thrombotic microangiopathy (TMA), specifically atypical hemolytic uremic syndrome (aHUS). Recent data suggest that these diseases share a common pathophysiology and patients can transition between glomerulopathies in this spectrum. Histopathologically, the main difference cited is the immunofluorescence (IF) findings, with C3 predominance in C3 glomerulopathy (compared to Immunoglobulins and complements in immune complex-mediated membranoproliferative glomerulonephritis (MPGN)) and negative IF in TMA. Mechanistically, the major difference is the site of complement AP dysregulation. In C3 glomerulopathy, it occurs in the fluid phase leading to deposition of C3 in the glomerular basement membrane, wheres, in aHUS it occurs at the cellular level targeting renal microvascular endothelium. We report a case that presented with hypertension, seizures, proteinuria, renal impairment and a picture of immune complex mediated MPGN on kidney biopsy. Months later she represented with classic TMA with microangiopathic hemolytic anemia, thrombocytopenia and worsening renal function. She failed to respond to steroids and plasmapheresis but then made a remarkable hematologic and renal recovery following treatment with Eculizumab supporting an underlying complement dysregulation and a diagnosis of aHUS.

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ECULIZUMAB FOR TREATMENT OF RECURRENT ATYPICAL HEMOLYTIC UREMIC SYNDROME IN KIDNEY TRANSPLANT PATIENTS- CASE REPORT AND REVIEW OF THE LITERATURE

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Atypical hemolytic uremic syndrome (aHUS) is a very rare disorder. More than 60% of patients with aHUS have complement genetic or acquired abnormalities most commonly associated with anti-CFH antibodies. Without appropriate management, those patients have a high rate of recurrence after kidney transplantation. The risk of recurrence strongly depends on the pathogenetic mechanism involved. Graft failure following recurrence is reported in up to 60-80% of patients. Over the past decade the advance in understanding the pathogenesis of aHUS led to the development of a humanized monoclonal antibody that suppresses the effector functions of the complement system (Eculizumab). This therapy represents the most notable therapeutic advance in patients with recurrent aHUS post transplant. Areas of uncertainty include, duration of therapy especially given the expense of the drug as well as how to monitor for optimal complement blockade. We present a challenging case of recurrent thrombotic microangiopathy (TMA) in the first month after kidney transplantation. Her pre-transplant presumed diagnosis was TMA related to thrombotic thrombocytopenic purpura (TTP), however, post-transplant she failed to respond to aggressive treatment with plasma exchange with an ADAMTS13 >10% and had a remarkable hematologic and renal recovery following treatment with Eculizumab supporting an underlying complement dysregulation and a diagnosis of aHUS. Our case highlights the challenges in managing this disease entity given the overlapping features of the different TMA categories. We provide a comprehensive review of the current strategies for treatment of aHUS recurrence post-transplant focusing on the role of eculizumab.

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HEALTH CARE COSTS OF HOSPITAL ACQUIRED COMPLICATIONS IN PATIENTS WITH CKD

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Background and objectives: Patients with CKD are vulnerable to hospital acquired complications (HACs), including those considered preventable. Understanding the economic burden of HACs can define the scope of strategies aimed at preventing complications.

Design, setting, participants, and measurements:

Subjects hospitalized from April 1, 2003 to March 31, 2008 from a population based cohort (Alberta Kidney Disease Network) were studied. KDIGO criteria were used to categorize CKD using serum creatinine and urine protein. Type II diagnostic flag and published literature were used to identify “all” and “potentially” preventable complications using hospital discharge information. Index hospitalization and readmission costs were determined using CIHI CMG methodology; physician claims and ambulatory care costs were also determined. The total cost of the index hospitalization, and within 90 days after discharge were determined. Purposeful multivariable regression, Tobit, and quantile models (where appropriate) estimated the incremental health care costs associated with preventable complications.

Results:

Of 45,336 subjects, 4,441 (9.80%) had ≥ 1 preventable complication, associated with median incremental cost of $8,435 (95% CI: 8,184 – 8,686). A graded association was observed for incremental cost with increasing number of preventable complications. The association of HAC and increased costs persisted when patients were subdivided into length of stay quartiles; e.g. the incremental cost of ≥ 1 preventable complication in the 0 - 25% quantile (≤3 days LOS) was $2,344 (95% CI: 1,976 – 2711). The 90 days post discharge incremental costs of readmission and ambulatory care was $1,429 (95% CI: 1,150 – 1,709) and $67 (95% CI: 48 – 87), respectively. Similar results were noted when all HACs were considered. No graded association by severity of CKD was observed.

Conclusion: Potentially preventable HACs are associated with significant increases in healthcare costs during the index hospitalization and after discharge. Targeted strategies to reduce preventable HACs may attenuate these costs.

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WHOLE-ORGANISM DEVELOPMENTAL EXPRESSION PROFILING IDENTIFIES RAB-28 AS A NOVEL CILIARY GTPASE WHICH UNDERGOES IFT

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Ciliogenesis in *Caenorhabditis elegans* occurs during late embryogenesis, when most ciliated sensory neurons being are born within a short timespan. Using available whole-organism RNA-Seq libraries, we identified a signature expression pattern specific to known ciliary genes. Using this cilia-related expression pattern we query the genome for genes that share the expression profile to identify novel cilia-related genes. We identify *C. elegans* proteins with human orthologs that localize to cilia, including FAM-161/FAM161B, MAP-9/MAP9, RP1L-1/RP1L1, CCDC-104/CCDC104, TZA-3 and RAB-28/RAB28 . We show that RAB-28, a small GTPase protein recently associated with Autosomal-Recessive Cone-Rod Dystrophy, is a novel ciliary GTPase which undergoes IFT.