ABSTRACTS – ORAL PRESENTATIONS
FREE COMMUNICATIONS – Friday, April 25th, 2014 – 13:00 – 14:30 – Ballroom I

O-001

THE UNRECOGNIZED POTENTIAL FOR DECEASED ORGAN DONATION IN CANADA

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The extent that recent stagnation in deceased organ donation in Canada is due to a decrease in the number of medically eligible potential organ donors is unclear.

Using data from the Discharge Abstract Database, we estimated the number of potential deceased organ donors (PDs) among Canadian in-hospital patient deaths between 2005-2008. PDs were identified among mechanically ventilated patients aged ≤ 70y, with diagnoses compatible with neurological death, and without contraindications to donation defined by Canadian Standards. We compared our estimates of PDs to a gold standard (chart audit of in-hospital deaths in Manitoba). Finally information on the actual number of organ donors was obtained from the Canadian Organ Replacement Register to calculate the donor conversion ratio (actual donors ÷ potential donors).

N= 8,274 of 335,793 deaths (2.5%), were identified as PDs; and this proportion was similar between provinces. Compared to the gold standard, our study method resulted in a two-fold overestimate of PDs. The overall conversion ratio of PDs to actual donors was 15%, but varied between provinces (Table). After accounting for the two-fold overestimate of PDs, N=2,928 identified PDs were not converted to actual donors during the study period.

These findings suggest that organ donation is limited by failure to convert potential donors to actual donors, rather than low numbers of potential donors. Estimating potential donors using administrative data from hospital separations in conjunction with periodic chart audits can provide timely information regarding the performance of Canada's organ donation system, and may inform strategies to increase deceased organ donation.

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O-002

RISK BASED TRIAGE OF NEPHROLOGY CONSULTATIONS: THE MANITOBA EXPERIENCE

Navdeep Tangri (1), Peter Wojciechowski (1), Brett Hiebert (2), Sean Armstrong (3), Joe Bueti (3), Mauro Verrelli (3), Claudio Rigatto (3), Paul Komenda (3)
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Background: Routine reporting of the estimated glomerular filtration rate (eGFR) has increased the awareness of chronic kidney disease (CKD), at the expense of increasing nephrology referrals and wait times for outpatient consultation. Public health campaigns and physician education efforts have failed to reduce these wait times. The purpose of this study was to evaluate the impact of a centralized risk based triage system on nephrology referrals and wait times for a provincial program. Methods: We compared the number of new outpatient consults and wait times pre and post implementation of a risk based triage system. Our triage process used the Kidney Failure Risk Equation (KFRE) to evaluate the 5 year risk of kidney failure for all consults, and patients with a KFRE < 3 % over 5 years were referred back to their family physician with guideline based recommendations. We compared monthly consult volumes and wait times for calendar years 2011 and 2013 using paired T tests. Results: From Jan 2011 to Dec 2011, the numbers of referral to nephrology clinic increased from 60 per month to 75 per month. After a 12 month implementation and run in period, the number of referrals increased to 90 per month, but only 50 were seen, with the remainder triaged as low risk. ($p<0.001$ vs 2011) Median wait times in 2013 decreased to 58 days, compared to 230 days in 2011 ($p<0.001$). Conclusions: A centralized risk based triage process based on the KFRE can reduce wait times for nephrology consults, and thereby improve access to care for high risk individuals. The impact of risk based triage on long term outcomes, and patient and provider satisfaction needs further study.

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O-003

THE PILOT TRIAL OF HEMODIALYSIS PATIENTS UNDERGOING ALDOSTERONE ANTAGONISM WITH EPLERENONE (PHASE) TRIAL

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Background: Aldosterone antagonism reduces morbidity and mortality in patients with heart failure without severe kidney disease. It is unclear if aldosterone antagonism is safe in patients with end-stage renal disease. Objective: To determine if aldosterone antagonism with eplerenone in patients with end-stage renal disease is limited by excess hyperkalemia and hypotension. Methods: We randomly allocated 154 prevalent patients receiving hemodialysis from 5 Canadian centres to 13 weeks of either eplerenone 50 mg daily or a matching placebo. The primary outcome was permanent discontinuation of the study drug due to hyperkalemia or hypotension. Aldosterone antagonism was considered non-inferior if a relative discontinuation rate for hyperkalemia or hypotension of greater than 20% could be excluded. Secondary outcomes included rates of hyperkalemia and effects on blood pressure and cardiovascular events. Results: Seventy-seven participants were allocated to each group and had similar baseline characteristics. The per protocol group (i.e., those taking medication for at least one week) included 74 participants in the eplerenone group and 70 in the placebo group. The primary outcome occurred in 3 (4.1%) in the eplerenone group and 2 (2.9%) in the placebo group for an absolute risk difference of 1.2% (95% confidence interval -4.8% to 7.1%). Eplerenone was therefore considered non-inferior to placebo with respect to the primary outcome. In the eplerenone group, 9 (12.1%) developed hyperkalemia (>6.5 mmol/L) compared to 2 (2.8%) in the placebo group (relative risk 4.3, 95% confidence interval 1.0 to 19.0). No significant differences in fatal or non-fatal cardiovascular events were seen. Conclusion: We did not find a substantially increased risk of permanent discontinuation of eplerenone due to hyperkalemia or hypotension. Serum potassium concentrations should be carefully evaluated when aldosterone antagonism is initiated. Large studies are required to determine if aldosterone antagonism reduces cardiovascular morbidity and mortality among chronic dialysis recipients.

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O-004

LONG-TERM CHRONIC KIDNEY DISEASE (CKD) AND HYPERTENSION (HTN) IN CHILDREN PREVIOUSLY ADMITTED TO THE INTENSIVE CARE UNIT (ICU)

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Background: Acute kidney injury (AKI) in ICU children is associated with poor hospital outcomes. AKI may also be a risk factor for CKD, an important cardiovascular risk factor.
Aims: Determine the extent to which previously admitted ICU children are at risk for CKD and HTN at follow-up.
Methods: This is a preliminary analysis of an ongoing cross-sectional longitudinal follow-up study of previously ICU-admitted children from two Canadian centres, identified by mailing and from participation in previous studies (exclusions: known pre-ICU renal disease, transplant, dialysis, geographical distance). Protocol: a study visit 6 years±6 months from ICU admission (blood for creatinine and cystatin C, urine for albumin and creatinine, physical exam, clinical data). Outcomes: CKD [low (<90ml/min/1.73m^2) estimated glomerular filtration rate (eGFR) or high (>2.4) urine albumin/creatinine (ACR)], HTN (≥90th age-gender-height percentile). Prevalence of outcomes is reported (n,%) on subjects with measures thus far.
Results: 276 patients have consented (recruitment ongoing), with outcome data available from 105 (mean 5.2±1.3 years post-ICU, age 8.6±4.1years old, 60% male). Follow-up eGFR=135±50 ml/min/1.73m^2, ACR=2.8±6.8, systolic BP percentile=60±40th %le, diastolic BP percentile=49±23rd %le. Prevalence of CKD and high BP was high relative to expected during childhood (Figure).
Conclusion: HTN, low eGFR and microalbuminuria prevalence is high in previously admitted ICU children, with implications on future cardiovascular risk. Our project will elucidate the extent to which AKI increases CKD and HTN risk, allowing for suggestions of evidence-based guidelines for post-ICU renal follow-up and future treatment and prevention studies.

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O-005

THE ASSOCIATION BETWEEN KIDNEY FUNCTION AND MAJOR HEMORRHAGE IN PATIENTS WITH ATRIAL FIBRILLATION INITIATING WARFARIN THERAPY

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Background: There is limited data regarding the safety of warfarin in people with reduced kidney function.
Objective: To assess the association between kidney function and major hemorrhage in patients with atrial fibrillation (AF) initiating warfarin.
Methods: We conducted a community-based cohort study of patients aged ≥66 years in Alberta, Canada, with AF who initiated warfarin therapy between 2003-2010 and had a measure of serum creatinine. Patients were grouped into estimated glomerular filtration rate (eGFR) categories based on their baseline eGFR. The risk and rate of major hemorrhage (first hospitalization for intracerebral, gastrointestinal, or other hemorrhage assessed using administrative data) was assessed according to eGFR categories using adjusted Poisson regression.
Results: 12989 AF patients with a measure of kidney function, initiating warfarin were identified. 1325 (8.8%) patients experienced a major hemorrhage over a mean follow-up of 2.61 years. Lower eGFR was associated with an increased risk of hemorrhage in the first 30 days of warfarin therapy (category 5 vs 1: incidence rate ratio 5.04, 95% CI: 1.19-21.34). Across all eGFR categories, adjusted hemorrhage rates were higher during the first 30 days of therapy compared to the remainder of the follow-up (Figure 1).
Conclusion: In this cohort of AF patients initiating warfarin, the risk of a major hemorrhage was significantly increased in patients with lower levels of kidney function. Rates were higher in the first 30 days of therapy. Our study suggests the need for more careful monitoring of patients with reduced kidney function receiving warfarin compared to the general population.

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O-006

ASSOCIATION OF ERYTHROPOIESIS STIMULATING AGENTS AND THE RISK OF CANCER AMONG CHRONIC DIALYSIS PATIENTS: A NESTED CASE-CONTROL STUDY

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Background and objectives: Erythropoiesis stimulating agents (ESA) are the first line of treatment for anemia among end-stage renal disease (ESRD) patients. While ESAs have been associated with increased tumors' growth in patients with cancer, whether they are associated or not with a higher risk of cancer among chronic dialysis patients is unclear. Methods: We conducted a nested case-control study in a cohort of 4574 patients initiating chronic dialysis between January 1, 2001 and December 31, 2007 in Quebec, Canada, using dialysis registry and administrative databases. Patients with prior diagnosis of cancer were excluded. We identified cases of a first cancer diagnosis on the hospital's discharge sheet or during an outpatient physician visit. Up to ten controls were randomly selected for each case. The exposure to ESA was evaluated between 6 and 9 months prior to the first cancer diagnosis. Epoetin alpha was converted to equivalent doses of darbopoetin using a 200UI:1µg ratio. Mean weekly exposure to ESA was categorized as low dose (<30 µg/week), moderate dose (30 to 70 µg/week) and high dose (>70 µg/week). Association between ESA and risk of cancer was estimated using conditional logistic regression. Results: We identified 419 cases of cancer and 3895 matched controls during the study period. ESA use was associated with an increased risk of cancer (OR, 1.04; 95%CI, 1.02-1.07). We also found that being in the high exposure group (> 70 µg/week) was associated with an increased risk of developing a cancer (OR, 1.77; 95%CI, 1.18-2.66) compared to the non-exposed group. Conclusion: High doses of ESA were associated with increased risk of cancer among chronic dialysis patients.

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O-007

DRUG REPURPOSING FOR THE TREATMENT OF EXPERIMENTAL ALPORT SYNDROME UTILIZING CONNECTIVITY MAP AND DRUG PAIR SEEKER

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BACKGROUND: Alport syndrome (AS) is a hereditary disorder resulting from mutations in any of the genes encoding collagen-IV-a3a4a5 chains in the glomerular basement membrane, leading to glomerular injury and disease progression. There are few treatment options for AS. Accordingly, we sought to identify existing drugs for the repurposed treatment of AS by studying gene expression in the kidneys of Col4a3-/-mice. METHODS: We performed gene profiling of renal cortices from male 129/Svj Col4a3-/-mice (KO) and wild type (WT) mice at 4 and 7 weeks of age (N=8/group). Gene expression was analyzed with the Affymetrix_Mouse_Gene2.0_ST array. We used Significance Analysis of Microarrays (SAM) and 2-way ANOVA to identify differentially expressed genes. These genes were utilized for in silico drug repurposing by Connectivity Map (CMAP) and Drug Pair Seeker (DPS) to find drugs that reverse AS gene expression changes. RESULTS: We first used SAM to identify the "disease signature", composed of 769 significantly up-regulated and 113 significantly down-regulated genes in 7-week-old KO versus WT mice (FDR<1%). The top drug combination that reversed this disease signature in DPS included vorinostat and genistein. We next identified the "progression signature", composed of 426 differentially up-regulated and 501 down-regulated genes in 7-week-old compared to 4-week-old KO mice, when adjusted for age. The top drug that reversed the AS progression signature in CMAP was vorinostat (p=0.00032). Data reanalysis with 2-way ANOVA, accounting for the interaction between age and genotype, revealed that vorinostat and genistein were among the top drug combinations that reversed the AS progression signature. Both vorinostat and genistein inhibit tyrosine kinase activation. CONCLUSIONS: Gene expression profiling and in silico analysis in a murine model of AS identified a novel drug combination that may reverse gene expression profile associated with renal disease progression. In vivo studies of this drug combination will determine if it impacts disease progression.

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O-008

MFG-E8 LIMITS TISSUE DAMAGE THROUGH INFLAMMASOME MODULATION IN RENAL INJURY.

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Background: Renal diseases are characterized by tubulo-interstitial fibrosis due to the loss of renal parenchymal cells. In the early phases of inflammation, macrophages kill renal parenchymal cells leading to renal fibrosis. Apoptosis of these cells characterizes kidney injuries. Mediators released by the apoptotic renal resident cells (epithelial and endothelial) play a crucial role in the modification of the renal microenvironment. We recently demonstrated that milk fat globule-epidermal growth factor E8 (MFG-E8) was released by apoptotic cells, resulting in a reduced pro-inflammatory cytokine production by macrophages.
Objectives: The present study is designed to study the role of MFG-E8 on the modulation of tissue damage and fibrosis in an unilateral ureteral obstruction (UUO) model.
Methods: C57BL/6 WT or MFG-E8 KO mice underwent ureteral ligation for 3, 7 and 14 days to evaluate the progression of renal damage and fibrosis. MFG-E8 (30µg/kg) was administered intra-peritoneally 1 day before and every 3 days subsequently. Kidneys were harvested and tissues were PAS stained to evaluate the obstructive associated damage. We also used Sirius Red stain to evaluate fibrosis. Macrophages exposed to MFG-E8 were administred to UUO MFG-E8 KO mice.
Results: MFG-E8 administration reduced kidney damage and fibrosis compared to control whereas its absence in the MFG-E8 KO mice was associated with a worse disease. Moreover, MFG-E8 administration was associated with a decreased protein expression of inflammasome activation in the kidney. Furthermore, administration of MFG-E8 stimulated macrophages prior to UUO conferred protection in kidney obstruction by reducing inflammasome activation and renal injury.
Conclusions: We propose that the protective role of MFG-E8 is mediated through the decrease of inflammasome activation and the attenuation of pro-inflammatory macrophage programming preventing severe tissue damage. These data provide valuable insight to identify MFG-E8 as a novel target for the regulation of renal inflammation and CKD progression.

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ABSTRACTS – POSTER PRESENTATIONS
With Presenters – Saturday, April 26th, 2014 – 11:00 – 12:30 – Ballroom II

P-009

NEWER BIOMARKERS IMPROVE PREDICTION OF CARDIOVASCULAR EVENTS IN CKD PATIENTS - CANPREDDICT STUDY OUTCOMES

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Background: Cardiovascular risk stratification/prediction tools for chronic kidney disease (CKD) population have poor performance. Better prediction models are needed.
Objective: To assess if the inclusion of newer biomarkers (NBM) improves risk prediction of cardiovascular events in the CKD cohort, over and above conventional clinical, demographic and laboratory predictors.
Methods: Pan-Canadian multicentre prospective cohort study of 2544 referred CKD patients in nephrology centres. NBM tests at baseline included asymmetric dimethylarginine, high sensitivity C-reactive protein (hsCRP), interleukin-6, pro-brain natriuretic peptide (NT-proBNP), troponin I, transforming growth factor beta-1, cystatin C and fibroblast growth factor-23 (FGF-23). Main Outcome: Adjudicated ischemic and congestive cardiovascular events within 3-years. We compared discrimination and classification of proportional hazards models based on conventional predictors (base model) vs. models based on combination of conventional and NBM predictors.
Results: Mean age of the cohort is 68yrs; median eGFR was 28 ml/min/1.73m^2 (20%<20ml/min, 38% 20-29ml/min and 41% 30-45mil/min); 62% were male. There were 409 cardiovascular events during 3-yr follow up, resulting in the rate of 63.9 events per 1000-person years (95%CI:58.0-70.4). Base model, base+NBM models and model based on 'best' predictors are presented in table, including the associated measures of discrimination (C-statistic) and net reclassification index (NRI). After adjusting for conventional predictors, NT-proBNP yields the highest improvement in cardiovascular events prediction (NRI=13.8;95%CI: 5.1-2.1), followed by Troponin I (NRI=11.8; 95%CI:1.7-19.4) and Cystatin C (NRI=4.5;95%CI: 0.5-11.0).
Conclusions: Inclusion of NBMs in risk prediction models significantly improves precision of cardiovascular outcomes prediction. The NBM-based risk prediction models need to be validated in similar cohorts.

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P-010

PROGNOSTIC VALUE OF PREDICTION EQUATIONS AND "SURPRISE QUESTION" IN CKD PATIENTS IN IDENTIFYING NEED FOR RENAL REPLACEMENT – CANPREDDICT STUDY

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Background: The intensity of care for patients with chronic kidney disease (CKD) is often based on an overall intuitive, qualitative assessment. Health resources and surgical risks are taken for renal replacement therapy (RRT) planning, and are unnecessary in patients who do not progress. We explore here the value of evidence-based prediction equations compared to physician qualitative assessment in guiding the timing and planning for RRT. Objective: To assess the accuracy of physicians qualitative assessment of CKD patients risk of needing RRT and compare it with a validated prediction equation (Kidney Failure Risk Equation, KFRE). Methods: Pan-Canadian prospective cohort study of 2544 referred CKD patients, from 25 rural, urban, academic and non-academic nephrology centres, followed every 6-months. A survey was implemented in 2011 for physician to indicate if they would be surprised if the patient required RRT within 1-year. Demographic, clinical, and laboratory data was collected at each visit and used to generate a risk score. Discrimination and reclassification were compared between the qualitative survey and the KFRE. Primary Outcome: Need for RRT within 1-year from survey. Results: We surveyed 90 nephrologists who followed 564 patients, with the median eGFR of 25 ml/min (IQR18-34), for a period of 1-year post physician survey. Of the 161 patients predicted to require RRT by nephrologists, 38 (24%) actually required RRT within the year. Identification of patients requiring RRT by qualitative assessment poorly discriminated progressors vs non-progressors [(AUC) of 69.4% (95%CI:61.1-77.6) for surprise question vs. AUC 91.2% (95%CI:88.5-94.9) for KFRE] . The continuous net reclassification improvement with the KFRE was 0.96 (95%CI:0.45-1.29) and integrated discrimination improvement was 0.19 (95%CI:0.133- 0.35). Conclusions: Physicians greatly overestimate risk of CKD patients needing RRT. There is a need for evidence-based prognostic tools in guidelines to better allocate resources in preparing CKD patients for RRT.

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P-011

PERCEPTIONS OF PEDIATRIC NEPHROLOGISTS IN CANADA REGARDING TIMING OF DIALYSIS INITIATION

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Background: Data guiding timing of dialysis initiation in children is scant. Physician's perceptions significantly influence their decision-making. We therefore assessed providers' perspectives and practice regarding timing of dialysis initiation in children in Canada. Methods: A cross-sectional web-based survey was administered to all 59 pediatric nephrologists in Canada. It evaluated stated perspectives and practices of providers regarding timing of dialysis initiation. We also explored the importance of eGFR vs. symptoms and patient and provider factors influencing decisions. Results: Thirty-five nephrologists (59%) completed the survey. Most care for advanced CKD patients in a multidisciplinary clinic (85.7%) and no centers have a formal policy on timing of dialysis initiation. Seventy-five percent of centers follow 30 patients. Discussions about dialysis initiation are generally informal (74.5%) and the decision to start is made by the nephrologist (37.1%), or team (57.1%). Fifty percent agreed GFR was important when deciding when to start, 41.1% were neutral and 8.8% disagreed. Variability exists in the threshold that nephrologists considered early (vs. late) dialysis initiation: >20 ml/min/1.73m2 (21%), >15 (38.2%), >12 (26.4%) and >10 (11.8%). Practitioners typically start asymptomatic patients at eGFR's of 7-9 (8.8%), 10-11 (41.1%) 12-14 (38.3%) and 15-19 (5.9%). Patient factors important for >90% of nephrologists in decision making were fatigue, >10% weight loss, nausea, increasing missed school and awaiting a pre-emptive transplant. Age was only a factor for 50%. Seventy five percent agreed with the statement that early initiation of dialysis decreased emergent starts. Conclusions: Variability exists in Canada regarding the importance and threshold of eGFR guiding the decision as to when to start dialysis in children with kidney failure, whereas patient factors are almost universally important to pediatric nephrologists. Additional studies evaluating the outcomes of children starting early vs. late are needed to guide decision making.

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P-012

ARTERIOVENOUS FISTULAS AND CENTRAL VENOUS CATHETERS IN ELDERLY HEMODIALYSIS PATIENTS: A PROPENSITY SCORE ANALYSIS

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Background: Arteriovenous fistulas (AVF) are considered the preferred dialysis access for all patients on hemodialysis, but their survival advantage over central venous catheters (CVCs) may be diminished with age. The purpose of this study was to compare the effect of AVF on survival when compared to CVCs in a national incident dialysis cohort. Objectives: To evaluate the effect of age on the relationship between AVF use and mortality in an incident dialysis cohort. Methods: Survival analysis, propensity-adjusted models, and propensity-matched models. All hemodialysis patients in the Canadian Organ Replacement Register (CORR) database who were incident hemodialysis patients between January 24th, 2000 and December 31st 2009 were included. Patients without a known vascular access type were excluded from the analysis. Results: 22189 patients were included in the study and 8103 had an AVF as method of vascular access. AVFs were associated with lower all-cause mortality in the univariate (HR 0.632, 0.607-0.658 95% CI), multivariable (HR 0.701, 0.672-0.732 95% CI), propensity-adjusted (HR 0.702, 0.673 – 0.733 95% CI), and propensity-matched cohorts (HR 0.633, 0.593 – 0.675). There was a positive interaction between age, AVF and diabetes status. In particular, no statistically significant relationship in the propensity-matched cohort for those aged 70-79 with diabetes (HR 0.688, 0.468 – 1.009 95% CI), and those aged over 79 without diabetes (HR 0.667, 0.376 – 1.174 95% CI), and with diabetes (HR 0.875, 0.317 – 2.413). Conclusions: AVFs are generally associated with reduced all-cause mortality in hemodialysis patients in comparison to CVCs. In those aged over 69 with diabetes and those aged over 79 the protective effect of AVFs on survival may be diminished, but definitive conclusions require further evaluation.

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P-013

SURVIVAL ASSOCIATED WITH HOME DAILY DIALYSIS USING LOW DIALYSATE FLOW RATES COMPARED TO PERITONEAL DIALYSIS

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Background: Daily hemodialysis with low dialysate flow (DHD^L) is an emerging home dialysis option, but its efficacy compared to home peritoneal dialysis (PD) is unknown.
Methods: We identified 3359 consecutive adult patients receiving DHD^L from a large US dialysis provider between January 2004 and December 2011. All patients received hemodialysis ≥5 days/week for ≥3 hours/day. Using a validated data-linkage cross-walk, we matched 2668 DHD^L patients by propensity scores to 2668 contemporaneous USRDS patients receiving home PD. Comorbidities, demographics, and outcomes were ascertained from USRDS. We used Cox regression including the robust covariance estimator, to compare all-cause mortality between groups. All patients were followed to October 31, 2012 or death; transplants were censored.
Results: After matching, between-group standardized differences for baseline variables were <10%. Mean age was 51 years, 66% were male, 72% were white, and 29% had diabetes. During 10221 patient-years, 1493/5336 patients died. Compared to PD, DHD^L was associated with a significantly lower risk of death (PD vs. DHD^L: 16.7 vs. 12.7 deaths per 100 patient-years; HR 0.75 (95% CI 0. 68– 0.82); p<0.001). During follow-up, 20% of DHD^L and 59% of PD patients switched to another therapy. Censoring modality switches at 90 days yielded HR 0.83 (95% CI 0.74–0.95; p=0.005) favouring DHD^L. There was no significant interaction between dialysis type and vintage, age, weight, diabetes or heart failure.
Conclusion: Compared to PD, DHD^L was associated with lower all-cause mortality. While we cannot exclude residual confounding, these results may have implications for those considering home dialysis options.

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P-014

PERCEIVED FACILITATORS OF AND BARRIERS TO THE USE OF HOME DIALYSIS USE: A CANADIAN NATIONAL SURVEY OF NEPHROLOGISTS

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Background:
Barriers to and facilitators of home dialysis (peritoneal dialysis and hemodialysis) are numerous and complex.

Objectives:
In order to better understand these factors in the Canadian context, we developed a *de novo* survey to measure nephrologists' attitudes and perceptions regarding factors affecting home dialysis use.

Methods:
We used in-depth interviews and rigorous qualitative methods to develop a theoretical framework, which led to an initial item (N=60) pool. We used preference ratings and a Delphi process to reduce and refine candidate items into a 47-item survey, which we administered to all Canadian nephrologists providing dialysis and predialysis care to adult (>18 years) patients.

Results:
We received 199 complete and 6 partial responses (response rate 41%). We examined item-level responses and used factor analysis to reduce items into domains. An 11-factor solution explained 67% of the variance across 41 item scores, denoting excellent construct validity. Test-retest reliability was 0.70; Crohnbach's α was 0.60-0.95. Domain-level median scores for barriers were low (12-19; possible range 0 to 100), indicating that respondents were unconcerned about most barriers. The highest median domain scores were for facilitators related to nephrologist training (75), funding for personnel and infrastructure (64), physician reimbursement (42), and offering home dialysis to most patients (38). The highest-ranked items included: nurse and lay caregiver-assisted home dialysis, PD in long-term care facilities, pre-dialysis nurse case-managers, multi-disciplinary modality rounds, public funding of water and electricity for home HD, and mandatory fellowship training in home HD. There was little support for home dialysis targets or a mandatory "PD first" policy.

Conclusions:
We identified several potential target interventions for national and provincial initiatives to promote appropriate use of home dialysis, as well as several priorities for future research. We also established the reliability and validity of a barrier assessment tool for potential use in other jurisdictions.

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P-015

SLIT2-ROBO4 SIGNALLING AS A POTENTIAL TARGET FOR ATTENUATING EARLY DIABETIC RENAL HYPERFILTRATION

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Background: Diabetes is the leading cause of kidney failure in Canada. One of the principal targets for diabetic kidney disease is the endothelium, manifesting initially as pathological glomerular neovascularization. Neovascularization leads to increased filtration surface area, resulting in hyperfiltration that can promote disease progression. No clinically available therapies safely target this pathologic process. Slit2 has emerged as an important regulator of endothelial function, eliciting either pro-angiogenic or anti-angiogenic effects through its Robo1 and Robo4 receptors respectively. Objectives: To examine whether Slit2-Robo signaling regulates glomerular endothelium responses in diabetes in vivo and in vitro. Methods: Changes in expression of Slit2, Robo1, and Robo4 induced by high glucose (25 mM) were analyzed in human renal glomerular endothelial cells (HRGEC), and two rodent models of diabetic nephropathy (db/db mice, streptozotocin (STZ)-induced diabetic Wistar rats). Additionally, the effects of Slit2 administration (2 µg thrice weekly i.p. injections) on diabetic glomerular neovascularization and hyperfiltration were analyzed in STZ-diabetic rats 3 weeks after diabetes induction. Results: Robo4 mRNA and protein levels fell while Robo1 levels remained unchanged in HRGEC grown in high glucose medium. While healthy glomerular endothelium expressed high levels of Robo4 and low levels of Robo1 in vivo, in db/db mice and STZ-diabetic rats, Robo4 levels fell while Robo1 levels remained unchanged, leading to a reduction in the ratio of Robo4:Robo1. Similarly, Slit2 levels were reduced in rat glomeruli 3 weeks after STZ-diabetes induction. These changes in expression of Slit2-Robo signaling components were accompanied by STZ-diabetes-induced glomerular capillary growth and hyperfiltration, both of which were attenuated by exogenous Slit2 administration. Conclusions: Our observations suggest that diabetic glomerular angiogenesis is regulated by a reduction in anti-angiogenic Slit2-Robo4 signalling. Slit2 therapy can overcome this effect, suggesting that Robo4 activation by Slit2 or other analogs might represent a novel therapeutic strategy for diabetes-induced glomerular angiogenesis and hyperfiltration.

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P-016

RELATIONSHIP BETWEEN ESTIMATED SODIUM AND POTASSIUM EXCRETION AND SUBSEQUENT RENAL OUTCOMES: ANALYSIS OF ONTARGET AND TRANSCEND

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Background: Patients with and without chronic kidney disease (CKD) are often advised to reduce sodium & potassium intake, but supporting evidence is limited.
Objective: To determine the association between sodium & potassium intake, measured by urinary excretion, and renal outcomes.
Methods: We estimated 24 hour sodium and potassium excretion in 28,879 participants at high cardiovascular risk, followed for a mean of 4. 5yrs in the ONTARGET & TRANSCEND trials. The primary outcome was eGFR decline ≥30% or chronic dialysis; secondary outcomes were eGFR decline ≥40% or chronic dialysis, doubling of creatinine or chronic dialysis, >5%/year loss of eGFR, progression of albuminuria and hyperkalemia. Multinomial logit regression with multivariable fractional polynomials, adjusted for confounders, determined the association between sodium & potassium and renal outcomes, with death as a competing risk.
Results: The primary outcome occurred in 2,052 (7.6%). There was no significant association between sodium and any of the renal outcomes (primary outcome OR 0.95; 95% CI 0.86-1.05 for highest [median 6.2g/day] v lowest third [median 3.3g/day]) (Figure A-C). Higher potassium was associated with a lower risk of all renal outcomes (primary outcome OR 0.71; 95% CI 0.64-0.78 for highest [median 2.7g/day] v lowest third [median 1.7g/day], except hyperkalemia (increased risk) (Figure D-F).
Conclusions: Potassium, but not sodium, excretion predicted clinically-important renal outcomes. Our findings do not support routine low sodium and potassium diets for prevention of renal outcomes in people with vascular disease with or without CKD.

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P-017

ECULIZUMAB INHIBITS THROMBOTIC MICROANGIOPATHY AND IMPROVES RENAL FUNCTION IN ADULT PATIENTS WITH ATYPICAL HEMOLYTIC UREMIC SYNDROME

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Background: Atypical hemolytic uremic syndrome (aHUS) is a rare, genetic, life-threatening disease of uncontrolled, chronic complement activation leading to thrombotic microangiopathy (TMA) and end-organ damage. Within 1 year, up to 65% have permanent renal damage, end-stage renal disease, or die despite plasma exchange/plasma infusion (PE/PI). Early diagnosis and effective treatment are critical to prevent TMA. Eculizumab, a terminal complement inhibitor, is approved for aHUS.
Objective: To report safety and efficacy of eculizumab from the largest prospective aHUS study.
Methods: This was an open-label, single-arm, Phase 2 trial of adult aHUS patients with platelet count <150 x10^9/L and lactate dehydrogenase ≥1.5 upper limit of normal. Shiga toxin + *E. coli* HUS and severe ADAMTS13 deficiency were excluded. Identified complement gene mutations were not required. The primary endpoint was complete TMA response (defined in Table) at 26 weeks.
Results: Forty-one patients enrolled; 38 (93%) completed 26 weeks. Most were newly diagnosed (median, 2 weeks to first dose). At week 26, 30 (73%) achieved complete TMA response; most achieved other efficacy outcomes (Table). Platelet count and estimated glomerular filtration rate increased significantly from baseline through week 26. Twenty of 24 (83%) discontinued dialysis; 2 initiated and remained on dialysis. Quality of life significantly improved. Eculizumab was generally safe and well tolerated. Two patients had meningococcal infections (1 continued eculizumab). None died.
Conclusions: Results of this ongoing, prospective study confirm that eculizumab inhibits complement-mediated TMA in adult aHUS patients and validate guidelines recommending eculizumab as first-line treatment in adults with unequivocal diagnoses.

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P-018

ETHNIC DIFFERENCES IN THE LIKELIHOOD OF LIVING KIDNEY DONATION AMONG REGISTERED POTENTIAL DONORS

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Tonelli et al (KI, 2007) have reported that South Asian and East Asian Canadian ESRD patients are 58% and 73% less likely to receive a living donor kidney transplant, but the reasons for lower living donation among South and East Asian Canadians remains unclear. We identified all n=2,368 individuals who registered as directed potential living kidney donors within our program between 2000-2008 and compared their likelihood of proceeding with kidney donation and reasons for non-donation as a function of ethnicity. All registered potential donors were stratified into the following 3 groups: South Asians (n=225,9%); East Asians (n=156, 7%); Other (n=1987,24%).
Results: Compared to non-Asians, South and East Asian potential donors were younger, included more females, and were more likely to be related to their intended recipients ($p<0.001$). South Asians were the least likely to proceed to donation (crude donor conversion ratio of 10%), while East Asians were the most likely (19%), followed by non-Asians (17%), ($p<0.001$). Compared to non-Asians, more South and East Asians were excluded from donating due to ABO/HLA incompatibility, whereas fewer South Asians were found medically or psychologically unsuitable to donate (Table).
Conclusion: South Asians who registered as potential living donors were half as likely to actually donate compared to East Asians and non-Asians. ABO and HLA incompatibility rather than medical suitability appears to be a greater barrier for both South and East Asians, suggesting that initiatives to promote kidney paired donation or ABO incompatible donation may be especially effective in increasing donation in these populations.

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P-019

THE COMBINED USE OF ANTIPLATELET AGENTS AND STATINS IS ASSOCIATED WITH DECREASED TITERS OF ANTI-LG3 ANTIBODIES IN PATIENTS WITH CHRONIC KIDNEY DISEASE

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Background: Endothelial apoptosis triggers the release of LG3, a C-terminal fragment of the vascular basement membrane proteoglycan perlecan. Anti-LG3 autoantibodies are present before transplantation and are associated with the occurrence of acute vascular rejection in kidney transplant recipients. Objectives: The aim of this study was to evaluate whether factors that are associated with endothelial injury correlate with anti-LG3 titers in patients with chronic kidney disease (CKD). Methods: We performed a cross-sectional study of CKD patients in the Canadian Prevention of Renal and cardiovascular Endpoints Trial (CanPREVENT). We used Spearman correlation coefficients or Wilcoxon rank sum statistics to assess the associations between anti-LG3 titers and other variables. Linear regression was then performed to identify determinants of anti-LG3 titers (after natural log transformation). Results: Anti-LG3 titers were determined in 449 CKD subjects. Age (ρ: -0.12, 95% confidence interval (CI): -0.21, -0.03) and HBA1c (ρ: -0.09, 95% CI: -0.19, 0.00) were inversely correlated with anti-LG3 titers, whereas diastolic blood pressure (ρ: 0.10, 95% CI: 0.00, 0.19) showed a positive association. Unexpectedly, patients with evidence of atherosclerotic coronary artery disease exhibited lower anti-LG3 titers (-18, 95% CI: -32, -3). However, patients who used antiplatelet agents (-17, 95% CI: -29, -5), a renin-angiotensin system inhibitor (-13, 95% CI: -25, 0), or a statin (-15, 95% CI: -27, -3) had lower anti-LG3 titers. When age, HBA1c, diastolic blood pressure and smoking history were adjusted for, patients who were treated with a statin and an antiplatelet agent exhibited lower anti-LG3 titers (-0.18 ln unit, 95% CI: -0.35, -0.02). Conclusion: We observed an association between lower anti-LG3 titers and the use of combined therapy with an antiplatelet agent and a statin. Larger human studies or animal models are needed to evaluate whether these drugs can affect the production of anti-LG3 antibodies.

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P-020

EXPLORING NEW METHODS FOR THE EARLY IDENTIFICATION OF ESRD PATIENTS WITH HIGH INTENSITY ACUTE HOSPITAL USE

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Background: A minority of ESRD patients require a disproportionately large degree of high intensity (HI) acute care during their first year of dialysis. We used administrative data to proactively identify modifiable factors leading to HI resource use among incident dialysis patients. Study Design: Bayesian network modeling Patient Cohort: FY10/11 Ontario incident adult patients (2,659 patients) Methods: HI patients were identified as the top 10% of the patient cohort with regards to Resource Intensity Weight (RIW; a proxy of cost) in their first year of dialysis, and were found to account for 55% of the total patient cohort's cumulative RIW. We randomly split HI patients 80/20% into derivation and validation cohorts. We ascertained patient demographic, comorbidity, hospitalization and clinical variables (N=80) drawn from provincial datasets, including DAD, ORRS, and NACRS with a one-year look-back window from the date of first dialysis. These patient-level data were fed into a machine learning package (Bayesialab), along with HI patient status during the first year of dialysis. A Bayesian Network of top predictor variables, the values of which collectively defined the probability that a patient would be HI during the first year of dialysis, was developed. Results: Seven variables were selected as the top predictors of HI patient status: inpatient admissions in pre-dialysis year, and quarter; creatinine, and serum albumin at dialysis start; access to nephrologists in pre-dialysis year; emergency visits in pre-dialysis year; and dialysis crash start indicator. The gains charts on the validation cohort revealed that the top 20% of the HI patients as identified by the model comprise 65% of the HI patients. Conclusions: Late referral and crash starts to dialysis represent potentially modifiable outcomes that are potent predictors of HI use. Measurement efforts to better understand and control these factors may translate into better outcomes and reduced resource use.

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P-021

IMMUNE SENSITIZATION AND MORTALITY ON THE WAITING LIST FOR KIDNEY TRANSPLANTATION

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Background: Cardiovascular mortality is the leading cause of death in end-stage renal disease (ESRD) patients. Inflammation has been shown to play a role in cardiovascular disease. Anti-HLA antibodies, measured as panel reactive antibodies (PRA), may also be a marker of inflammation. PRA is routinely monitored in ESRD patients on the waiting list to facilitate transplantation with a compatible donor. Objective: To assess whether PRA is a risk factor for cardiovascular mortality in ESRD. Methods: Using the Scientific Registry of Transplant Recipients, we conducted a retrospective cohort study in first-time adult kidney transplant candidates. The relationship between PRA modeled as a time-varying categorical variable and cardiovascular mortality was assessed in Cox proportional hazards models. All-cause mortality was a secondary endpoint. The analysis was repeated in a subcohort of transplant candidates at low risk for significant comorbidity. Competing risk analyses evaluating the effect of time-fixed PRA category upon activation on study endpoints while considering transplantation and non-cardiovascular mortality as competing events, were also conducted. Results: Among 161,308 patients, Cox models showed an increase in the hazard ratio (HR [95% confidence interval]) for cardiovascular mortality (HR 1.04 [0.95, 1.13], 1.23 [1.12, 1.36], and 1.45 [1.28, 1.65]) and all-cause mortality (HR 1.01 [0.95, 1.08], 1.11 [1.02, 1.21], and 1.17 [1.05, 1.31]) in PRA 1-19%, PRA 20-79%, and PRA 80-100% categories compared with PRA 0%, respectively. The relationship was accentuated in the low risk subcohort and in competing risks models (cardiovascular mortality in PRA 80-100% vs. PRA 0%: HR 3.90 [2.21, 6.90] and 1.58 [1.37, 1.84], respectively; all-cause mortality: 1.53 [1.18, 2.00] and 1.52 [1.44, 1.62], respectively). Conclusion: Our findings suggest that PRA may be an independent risk factor for mortality on the waiting list for kidney transplantation. Organ allocation schemes may need to consider this additional risk of mortality in sensitized patients.

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P-022

CLASS II HLA EPLET LOAD IS A RISK FACTOR FOR TRANSPLANT GLOMERULOPATHY

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Background: Transplant glomerulopathy (TG) is an important contributor to kidney transplant failure. Currently, there is no adequate therapy to reverse the effects of TG. Objective: To assess the risk of developing TG as a function of donor and recipient class II HLA incompatibility at the eplet level. Methods: We conducted a nested case-control study from a cohort of adult kidney transplant recipients transplanted at the University Health Network January 1, 2000 to December 31, 2012. Cases (n=52) were defined as patients diagnosed with TG based on biopsies showing glomerular basement membrane duplication without immune complex deposition. Controls (n=104) were randomly selected from the remaining cohort at the time of case diagnosis. HLAMatchmaker was used to ascertain the number of class II eplet mismatches ("eplet load"), from donors and recipients' 4-digit HLA typing. DRB1, DR3/4/5, DQA, and DQB typing was updated using molecular methods when absent. Class II eplet load was modeled both as categorical (eplet load: 43) and continuous variables. We fit conditional logistic regression models adjusting for recipient, donor, and transplant characteristics to assess the association between TG and eplet load. Results: A significant increase in the odds of TG was observed across ascending categories of eplet load. The fully adjusted model showed odds ratios of TG of 2.84 (95% confidence interval: 1.03, 7.84) and 4.62 (95% CI: 1.51, 14.14) in the presence of 27 to 43 and >43 class II eplet mismatches vs. <27 eplet mismatches, respectively. When the eplet load was modeled as a continuous variable, the odds ratio for TG was 1.25 (95% CI: 1.04, 1.50) for every 10 additional class II eplet mismatches. Conclusions: Class II eplet load is an independent risk factor for TG. Minimization of class II eplet load may decrease the incidence of TG in kidney transplant recipients.

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P-024

IMPACT OF BIOCOMPATIBLE PERITONEAL DIALYSIS SOLUTIONS ON RENAL FUNCTION, URINE VOLUME AND ULTRAFILTRATION: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Biocompatible peritoneal dialysis (PD) solutions, which are neutral-pH and low in glucose degradation products (GDPs), were developed in an attempt to abrogate the adverse effects of conventional PD solutions. We performed a systematic review evaluating the impact of biocompatible solutions on residual renal function (RRF), urine volume, peritoneal ultrafiltration and peritoneal small solute transport (D/P Cr). Methods: Medline, Embase, Biosis and Scopus electronic databases were searched from 1995 onwards without any language restrictions. Randomized trials which reported on any of our 4 pre-specified outcomes were selected by consensus amongst multiple reviewers. Results: 13 trials of 1137 patients were included. Trials were of low to average quality. Biocompatible solutions resulted in a higher RRF when studies of all durations were combined (13 studies, 843 patients, standard mean difference 0.15 mL/min, 95% CI 0.01-0.29) as well as during the first 6 and 12 months of treatment. We observed no significant difference in RRF after 12 months. There was an increase in urine volume when studies of all durations were combined (10 studies; 806 patients; mean difference 129.45 ml/day; 95% CI 65.27-193.64). Up to 12 months of therapy, peritoneal ultrafiltration fell significantly (9 studies; 694 patients; mean difference -160.1 ml/day; CI -288.2 to -32.22). D/P Cr was significantly greater with the use of biocompatible solutions during the first 12 months of treatment (4 studies, 426 patients, SMD 0.34, 95% CI 0.15 to 0.53). Conclusion: The use of biocompatible solutions results in improved preservation of RRF only during the first 12 months of therapy. The improved RRF coincides with a simultaneous reduction in peritoneal ultrafiltration, which may be due to increased peritoneal small solute transport. Based on these findings, we believe the use of these novel solutions may result in inadequate volume control and cannot recommend their routine use in clinical practice.

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P-027

INCIDENCE OF SUDDEN CARDIAC DEATH IN PATIENTS WITH END-STAGE RENAL DISEASE: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Objective: Although sudden cardiac death (SCD) is emerging as a distinct cause of death among patients with end stage renal disease (ESRD), current estimates of sudden cardiac death vary widely. We conducted a systematic review and meta-analysis of cohort studies reporting on the incidence of SCD in patients with ESRD.
Design and Methods: We searched MEDLINE and EMBASE (1950 to October 2013) for cohort studies reporting on the incidence of SCD in patients with ESRD, including those receiving hemo- or peritoneal dialysis. Random effects models were used to create summary estimates of the incidence of SCD. Heterogeneity was assessed using stratified meta-analysis and univariate meta-regression.
Results: Among 5062 articles, we included 21 cohort studies that reported on 4038 events of SCD in 56,790 patients. The cumulative incidence of SCD among ESRD patients ranged from 2.5% to 27.3%, with an overall pooled incidence of 7.67% (95% CI, 6.48% to 8.87%). There was evidence of significant heterogeneity (I^2=98.2; p<0.001). Although the heterogeneity could not be explained by differences in mean age, BMI, or systolic or diastolic blood pressures among the included studies, length of follow-up and the percentage of the cohort with diabetes and hypertension appeared to exhibit a positive trend in SCD incidence (p=0.08).
Conclusion: There is a need for further studies to more accurately estimate the incidence of SCD in the ESRD population to better understand and elucidate this relationship. This may allow clinicians to better stratify ESRD patients into risk groups based on prognosis.

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P-028

FEMALE SEX HORMONES ARE ASSOCIATED WITH CARDIAC AUTONOMIC TONE IN SUBJECTS WITH IGA NEPHROPATHY

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Background: Dysfunctional cardiac autonomic tone (CAT), a cardiovascular risk factor, is common in the chronic kidney disease (CKD) population. Low testosterone is associated with increased cardiovascular risk in men with end-stage kidney disease, though has not been studied in non-dialysis CKD patients. We sought to determine the association between sex hormones and CAT in non-dialysis CKD patients.

Methods: Thirteen normotensive subjects with Class 1-2 CKD due to IgA nephropathy (IgAN) (39±27y, 85% male, 29±5 kg/m2, eGFR 103±27 ml/min) were studied in high-salt balance. CAT was determined by spectral power analysis (Low Frequency (LF), a measure of sympathetic modulation, high frequency (HF), a measure of vagal modulation). CAT was assessed at baseline and in response to graded Angiotensin II(AngII) infusion (3ng/kg/min×30min, 6ng/kg/min×30min). The primary analysis assessed associations between endogenous sex hormones and measures of cardiac autonomic tone at baseline and in response to the stressor.

Results: All sex hormones were within age and sex-specific normal ranges. No associations were found between testosterone or estradiol and baseline CAT. Higher progesterone levels were associated with a trend towards a more favourable cardiac autonomic tone profile, with lower cardiosympathetic (r=-0.4, p=0.06) and higher cardiovagal (r=0.4, p = 0.09) tone. When examining the CAT response to AngII challenge, no association was observed between testosterone and the change in CAT. However, estradiol was inversely associated with the change in cardiosympathetic (r= -0.6p=0.08) and positively associated with the change in cardioprotective vagal (r=0.7, p=0.045) tone. Conversely, higher progesterone levels were associated with a greater increase in cardiosympathetic (r=0.5, p=0.05) and decrease in cardiovagal (r= -0.5, p=0.05) tone in response to AngII.

Conclusions: Testosterone is not associated with any measure of CAT in early CKD, though estradiol and progesterone may play a role in modulating CAT, both at rest and in response to a stressor.

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P-029

FRAILTY AND MORTALITY IN DIALYSIS: EVALUATION OF A CLINICAL FRAILTY SCALE

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Background/Aims: Frailty is associated with poor outcomes for dialysis patients; however, the severity of frailty is not captured by previous measurement tools. The purpose of this study was to assess if frailty (as defined by a clinical frailty scale) was associated with mortality among incident dialysis patients.
Methods: We conducted a prospective cohort study of incident, chronic dialysis patients at a large tertiary care institute between Jan 2009 and Apr 2013, (last follow-up Dec 2013). Based on overall clinical impression, the Canadian Society of Health and Aging Clinical Frailty Scale (CSHA-CFS) score, was determined for patients at the start of dialysis by their primary nephrologist. The CSHA-CFS allocates a single point to different states of frailty (1:very fit, 2: well, 3: managing well, 4: vulnerable, 5: mildly frail, 6: moderately frail, 7: severely frail, 8: very severely frail) based on physical, functional and cognitive status. The primary outcome was time to death.
Results: The cohort consisted of 365 patients (mean age 63±15 years). The majority were male (68%) and 48% had diabetes. The median frailty scale score was 4 (IQR 2-5). There were 94 deaths over 717 patient-years at risk. In an adjusted analysis, the HR associated with each one-point increase in the CSHA-CFS was 1.25 (95% confidence interval 1.07-1.46, p=0.004, table 1).
Conclusions: Frailty as defined by the CSHA-CFS is associated with mortality in incident dialysis patients.

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P-030

AN INTEGRATED, DATA-DRIVEN MODEL FOR CAPITAL AND OPERATIONAL PLANNING AT THE ONTARIO RENAL NETWORK

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Background: The Ontario Renal Network is responsible for infrastructure and resource planning for Ontario's Chronic Kidney Disease (CKD) care system, with a strategic priority around increasing the appropriate use of home dialysis. Objectives: To forecast the growth of the prevalent chronic dialysis patient population in Ontario to 2025, and estimate consequent future need for hemodialysis (HD) stations at Ontario's treatment facilities. Methods: We identified CKD patients who received dialysis in Ontario from 1999 to 2013, and their region of residence, using two separate data sources: the Ontario Renal Reporting System, and the Ontario Health Insurance Plan Claims History Database. We used a mathematical modelling technique, integer programming, to minimize the discrepancies between the two datasets, and then joined them to form a single set of historical patient volumes. To predict the prevalent patient population in each region over the next 12 years, we used a variety of time series forecasting models. A patient flow model was developed that translated forecasted regional prevalent patient population, historical regional patient to facility assignment patterns, and expected movements between in-facility and home dialysis into HD station requirements. Results: From 2013 to 2025, the provincial prevalent chronic dialysis patient population is expected to grow by between 29.57% and 35.34%, resulting in a need for additional HD stations at 26 to 28 of the province's 97 treatment facilities. A provincial shortage between 111 and 141 stations (6.61% to 8.4% of the current provincial capacity) is estimated by 2025. Conclusions: Expansions in HD station capacity will be required, and capital projects in a number of affected programs are underway to help address the expected shortage. Future work on this model will also forecast the annualized amounts of bundled patient funding that the province will require for chronic dialysis patients.

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P-032

THE STEROIDS IN THE MAINTENANCE OF REMISSION OF PROLIFERATIVE LUPUS NEPHRITIS (SIMPL) PILOT TRIAL

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Background: Patients with proliferative lupus nephritis (PLN) may experience relapses that reduce kidney function and quality of life. Uncertainty exists as to whether long-term, low-dose prednisone prevents relapses. We undertook a pilot randomized controlled trial to determine the feasibility of a larger trial testing this hypothesis. Methods: We conducted a blinded, two parallel-group randomized controlled trial of prednisone 7.5 mg/day (continuation) compared to placebo (prednisone withdrawal over 12 weeks). Adults with class III or IV lupus nephritis that achieved at least partial remission and remained on prednisone were eligible. Patients were followed for up to 36 months for the primary outcome: occurrence of a renal or major non-renal relapse. Results: Of 19 eligible patients, 15 (79%) were recruited and randomized; 8 to prednisone continuation and 7 to prednisone withdrawal. Seven (88%) patients in the prednisone continuation group and 7 (100%) patients in the prednisone withdrawal group achieved their allocated dose. Baseline characteristics were similar, except patients in the prednisone continuation group were older (39 vs 28 years), and a higher proportion were in complete remission (88% vs 29%). Over a median follow-up of 11 months, the primary outcome occurred in 4 (50%) patients in the continuation group (3 renal and 1 major non-renal), compared with one patient (14%, renal) in the withdrawal group (p=0.24). Three participants (38%) in the continuation group had minor flares, while no patients in the withdrawal group did (p=0.45). Conclusions: The high proportion of eligible patients recruited, absence of protocol violations, and adherence to the protocol suggest a large trial comparing prednisone maintenance with prednisone withdrawal in patients with PLN in remission is feasible. Given the equipoise in the community and the lack of randomized trial data available, a large trial to inform the efficacy and safety of long-term low-dose prednisone is urgently needed.

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P-033

CAROTID ULTRASOUND WITH PLAQUE QUANTIFICATION IS PREDICTIVE OF OCCLUSIVE CORONARY ARTERY DISEASE IN PATIENTS WITH AND WITHOUT CKD

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Introduction: Coronary angiography is diagnostic of occlusive coronary disease, but can be nephrotoxic. Quantification of the maximal carotid artery plaque height is an emerging surrogate for coronary intimal atherosclerosis, and has been correlated with coronary events in the general population. Our primary objective was to determine if carotid artery disease quantified by carotid intimal media thickness (CIMT) and maximal carotid artery plaque height (MCAH) are predictive of occlusive coronary artery disease in patients with and without CKD.
METHODS: 320 consecutive outpatients were referred for coronary angiography, and of these, 266 had data to estimate kidney function. MCAH and CIMT were measured by carotid ultrasound. CKD was defined as MDRD eGFR < 60 ml/min/1.73 m^2. Coronary artery disease was defined as at least 1 coronary artery with > 50% stenosis by angiography.
RESULTS: Patients with coronary stenosis (es) had significantly increased MCAH (2.64 mm versus 1.81 mm; P<0.0001), whereas CIMT was not significantly different between groups. By adjusted multivariable logistic regression, MCAH was a predictor of coronary artery stenosis of 50% or more (Odds ratio 3.15; 95% confidence interval 1.99 to 4.98; P<0.0001). In considering only patients with renal disease (eGFR < 60; N=76) this relationship remained robust (Odds ratio 4.5; 95% CI 1.6 to 13; P=0.005).
CONCLUSIONS: MCAH and not CIMT, was associated with coronary artery stenosis in patients with and without CKD. Carotid ultrasound with plaque quantification may aid the selection of patients who would benefit from coronary angiography, and results appear to be generalizable to the CKD population.

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P-034

FGF-23 IS ASSOCIATED WITH INSULIN RESISTANCE IN OBESE NON-CKD PATIENTS AND IN PRE-DIALYSIS CKD PATIENTS

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INTRODUCTION AND AIM: Previously, we reported an association between insulin resistance and fibroblast growth factor 23 (FGF-23) in pre-dialysis CKD patients (Garland J et al, *Journal of Diabetes and its Complications*, 2013). FGF-23 reduces renal phosphorus re-absorption (increasing renal phosphorus excretion) by decreasing the expression of renal proximal tubule NaPi-II co-transporters. In CKD, as renal phosphorus elimination becomes impaired, FGF-23 increases to maintain normo-phosphatemia. In contrast, insulin directly induces NaPi-II, promoting renal phosphorus retention. Aim: Our primary objective was to determine if FGF-23 and insulin resistance are associated in a non-CKD cohort as well as CKD patients.

Methods: Cross sectional study of 72 predialysis stage 3-5 CKD patients and 66 obese, non-diabetic, non-CKD patients receiving care in Ontario, Canada. Insulin resistance was assessed by the homeostasis model assessment of insulin resistance (HOMA-IR) and plasma carboxyl terminal FGF23 (ctFGF-23) was measured in duplicate by enzyme-linked immunosorbent assay. Kidney function was estimated (eGFR) using the abbreviated MDRD formula.

RESULTS: CKD patients had higher HOMA-IR and FGF-23 levels compared to the non-CKD population (see table). By partial correlation, in CKD patients (N=72), accounting for kidney function and phosphorus level, log ctFGF-23 was positively associated with log HOMA-IR (r=0.4; P=0.001). This association remained non-CKD patients (N=66) (r=0.26;P=0.04), and when considering all patients together (N=138) (r=0.25; P=0.003).

CONCLUSIONS: HOMA-IR and ctFGF-23 are associated in CKD and in obese non-CKD patients, suggesting insulin resistance may impact on renal phosphorus handling. Studies directly evaluating urinary renal phosphorus excretion in insulin resistance are needed.

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P-035

BENEFITS AND HARMS OF CITRATE LOCKING SOLUTIONS FOR HEMODIALYSIS CATHETERS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Citrate may be a cost-effective alternative to heparin based locking solutions for hemodialysis catheters.
Objective: To compare the benefits and harms of citrate versus heparin locking solutions among patients undergoing hemodialysis through central venous catheters.
Methods: We searched CENTRAL, MEDLINE, EMBASE, and CINAHL. We included randomized, parallel arm clinical trials that enrolled adult patients (>18 years) receiving chronic hemodialysis through central venous catheters using a citrate locking solution. We exclude studies in which citrate was combined with other agents, such as antibiotics. Two reviewers performed data extraction independently and in duplicate with standard data extraction forms. We pooled count data using generic inverse variance with random-effects models, but used fixed-effect models when combining only two studies. Subgroups included low (4% or lower) vs. higher (>30%) citrate.
Results: We screened 600 citations. Forty-one proceeded to full-text screen; 5 met inclusion criteria. Studies included between 19 and 291 participants (Median N = 61) followed for a total of 174.6 catheter-years; 2 were multi-centred trials. Three studies assessed all-cause mortality; the pooled relative risk was 0.71 (95% CI=0.42-1.24; p=0.21; I^2=0%). The rate ratio for bacteremic episodes was 0.54 (95% CI=0.23-1.29; p=0.16; I^2=65%) while the rate ratio for bleeding was 0.48 (95% CI=0.3-0.75; p=0.001;I^2=5%). Rates of catheter exchange/replacement and in-situ thromboslysis were not significantly different between groups in any of the pooled analyses. Risk of bias within pooled studies was low; however, imprecision due to small sample sizes and low event rates reduce our overall confidence in the pooled effect estimates.
Conclusions: Compared with heparin, citrate provided similar or better rates of death, bacteremia, and bleeding; however, larger trials are needed to confirm these findings. Given its lower unit cost, citrate may represent a dominant treatment strategy over heparin.

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P-036

SECULAR TRENDS IN CARDIOVASCULAR DISEASE AMONG KIDNEY TRANSPLANT RECIPIENTS

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Background: Cardiovascular death remains the number one cause of mortality in kidney transplant recipients. Cardiovascular events alone are associated with significant morbidity. Unfortunately, current trends in cardiovascular events after kidney transplantation are poorly understood. Methods: We conducted a retrospective observational study using Ontario's linked healthcare databases to follow all first-time kidney-only transplant recipients between 1994 to 2009. Our primary outcome was a composite of death or first major cardiovascular event defined as one of myocardial infarction, coronary angioplasty, coronary bypass surgery, or stroke within three years of the transplant date. Results: There were 4954 first-time kidney-only transplant recipients during the study period, of which 63% were male. The median age steadily increased from 43 years (interquartile range [IQR] 33-54) in 1994 to 53 years (IQR 42-62) in 2009 as did the proportion of recipients aged 65 years old older (3.8% in 1994 to 20.4% in 2009). There was also an increase in the proportion of recipients with diabetes (19.2% in 1994 to 29.9% in 2009) and coronary artery disease (23.7% in 1994 to 37.7% in 2009). A total of 444 recipients (8.8%) died or experienced a major cardiovascular event within three years of transplantation and this incidence remained stable throughout the study period. Conclusion: Despite transplant centers accepting recipients who are older with more co-morbidities, the three-year incidence of death or major cardiovascular event has remained stable from 1994 to 2009. These results are reassuring for transplant programs.

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P-037

OLDER PATIENTS WITH HERPES ZOSTER INFECTION, ANTIVIRAL DOSE, AND THE RISK OF MAJOR ADVERSE DRUG EVENTS

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Background: Higher versus lower doses of antiviral drugs used to treat herpes zoster infection may lead to more adverse drug events in older adults, particularly those with chronic kidney disease. Methods: We conducted a matched retrospective population-based cohort study of older adults (mean 77 years) in Ontario, Canada who initiated in the outpatient setting a higher (n=23,256) or lower (n=3876) dose of one of three oral antivirals for the treatment of herpes zoster between 2002 and 2011. The primary outcome was 30-day hospitalization with evidence of a computed tomography (CT) scan of the head (a proxy for acute central nervous system toxicity). The secondary outcome was 30-day all-cause mortality. Results: A higher compared to lower dose of antiviral drug was not associated with an increased risk of hospitalization with an urgent CT scan of the head (247 [1.06%] events with higher dose versus 43 [1.11%] events with lower dose, relative risk 0.96, 95% confidence interval 0.69 to 1.33, p-value 0.79) and was not associated with a higher risk of all-cause mortality (63 [0.27%] events versus 15 [0.39%] events, relative risk 0.70, 95% confidence interval 0.40 to 1.23, p-value 0.21). Results were consistent in all subgroups, including those with and without chronic kidney disease. Interpretation: Initiating a higher compared to a lower dose of an antiviral drug for the treatment of herpes zoster was not associated with an increased risk of adverse drug events. The findings support the safety of these drugs in older adults as currently prescribed in routine care.

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P-038

ECULIZUMAB INHIBITS THROMBOTIC MICROANGIOPATHY AND IMPROVES RENAL FUNCTION IN PEDIATRIC PATIENTS WITH ATYPICAL HEMOLYTIC UREMIC SYNDROME

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Background: Atypical hemolytic uremic syndrome (aHUS) is a rare, genetic, life-threatening disease of uncontrolled, chronic complement activation, leading to systemic thrombotic microangiopathy (TMA) and end-organ damage. The terminal complement inhibitor eculizumab is approved for aHUS, and was safe and effective in a retrospective pediatric study.
Objective: To report safety and efficacy at 26 weeks from the first prospective trial of pediatric aHUS patients.
Methods: This was an open-label, single-arm, Phase 2 trial of eculizumab in pediatric aHUS patients with platelet count less than the lower limit of normal at screening and baseline, lactate dehydrogenase ≥1.5 times upper limit of normal at the current manifestation start, and elevated creatinine at screening. Identified complement gene mutations were not required. Shiga toxin + *E. coli* HUS or severe ADAMTS13 deficiency (<5%) was excluded. Dosing was based on weight. The primary endpoint was complete TMA response (defined in Table).
Results: Twenty-two patients enrolled; 19 completed 26 weeks. Most were newly diagnosed. Twelve (55%) had no plasma exchange/plasma infusion (PE/PI) during the current manifestation. At week 26, 14 (64%) achieved complete TMA response (Table). Platelets and estimated glomerular filtration rate increased significantly through week 26. Nine of 11 patients (82%) discontinued and none initiated dialysis. All 10 on baseline PE/PI discontinued. Quality of life significantly improved. Eculizumab was safe and well tolerated. One patient withdrew (serious adverse event of agitation). None had meningococcal infection or died.
Conclusions: Eculizumab was safe and effective as first-line therapy in the first, ongoing, prospective trial of pediatric aHUS patients.

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P-039

INCREASING INDEPENDENT DIALYSIS UPTAKE: ROLE OF A NOVEL TRANSITIONAL CARE UNIT

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Background: Various interventions aim to increase the uptake of independent dialysis (ID), including multidisciplinary pre-dialysis clinics (PDC). More recently, we opened a 6-station Transitional Care Unit (TCU) providing approximately six weeks of enhanced focus on clinical and psychosocial issues during dialysis initiation. With a nurse-to-patient ratio of 1:2, the TCU provides individualized support and education for patients and families.
Objectives: To assess the effectiveness of the PDC and TCU in fostering ID by examining patients' dialysis modalities within six months of dialysis initiation.
Methods: Between October 2011 and March 2013, we assessed 180 newly initiated dialysis patients' ultimate dialysis modalities, and we compared patients who were, and were not, followed in the PDC and TCU.
Results: Of the 180 patients, mean age of 66 years, 39% percent selected ID (61% peritoneal dialysis, 39% home hemodialysis). Comparing PDC vs. non-PDC patients, 49% vs. 15% ($p < 0.001$) chose an ID modality. Similarly, comparing TCU vs. non-TCU patients, 56% vs. 21% ($p < 0.001$) chose an ID modality. With respect to patients' care pathway (i.e., whether kidney disease was known vs. unknown, and whether dialysis initiation was planned vs. unplanned), 54% of patients were known/planned, 15% were known/unplanned, and 31% were unknown/unplanned. More importantly, of the unplanned patients (known and unknown, 46%), ID uptake in those with TCU treatment vs. those without was 50% vs. 5%, $p < 0.001$.
Conclusions: Receiving care in the PDC and/or novel TCU significantly increased the likelihood of patients selecting an ID modality, highlighting the need and benefit of individualized support and education during the highly stressful period of dialysis initiation. This is all the more significant among unplanned patients, who are more likely to remain in the in-centre hemodialysis unit. Future research needs to focus on modes of enhancing psychosocial care during dialysis initiation.

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P-040

QUALITY OF LIFE ASSESSMENT DURING DIALYSIS INITIATION

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Background: The initiation of dialysis is a physically and emotionally stressful period in a patient's life. However, limited attention has focused on this difficult period and its impact on patient-reported quality of life (QOL).
Objectives: To assess the QOL of dialysis patients at various time points during the dialysis initiation phase. We also sought to validate the National Institutes of Health (NIH) Patient-Reported Outcomes Measurement Information System (PROMIS), which has been validated in many chronic conditions but not yet in renal disease, by comparing it with the Kidney Disease Quality of Life (KDQOL-36) survey, a highly reliable and validated nephrology questionnaire. PROMIS utilizes a unique computer adaptive testing methodology, whereby subsequent questions are selected based on participants' previous responses.
Methods: 76 patients initiating dialysis used an iPad to complete the KDQOL-36 and five selected PROMIS questionnaires (anxiety, depression, cognition, positive impact and negative impact of disease) at two time points, 1.4±1.4 and 13.2±1.8 weeks, after initiating dialysis.
Results: In the 76 patients, mean age of 62 years, QOL scores significantly improved in terms of anxiety ($p < 0.001$), depression ($p < 0.001$), cognition ($p < 0.05$), physical health ($p < 0.001$), mental health ($p < 0.001$), and symptoms ($p < 0.001$). In addition, PROMIS was highly correlated with the KDQOL-36, with r-values ranging from 0.19 to 0.67 (0.40 to 0.64 in directly comparable instruments), and the direction of change was similar across all instruments, thus validating the use of PROMIS in renal patients.
Conclusions: Dialysis initiation is associated with a highly disturbed emotional state, which improves over time. Initial high levels of anxiety and depression correlated with reduced cognition, highlighting the need for early interventions in order to maximize rehabilitation and independent dialysis uptake. PROMIS questionnaires may be useful adjuncts in evaluating parameters not currently assessed by the KDQOL-36.

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P-041

THE EFFECTS OF CINACALCET IN OLDER AND YOUNGER PATIENTS ON HEMODIALYSIS: THE EVOLVE TRIAL

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Background: The calcimimetic cinacalcet reduced the risk of death or cardiovascular (CV) events in older, but not younger, hemodialysis patients with secondary hyperparathyroidism (sHPT). To determine whether age-related differences in CV risk and co-interventions that reduce parathyroid hormone (PTH) may have influenced this result, we compared CV risk, use of kidney transplantation, parathyroidectomy (PTX) and commercial cinacalcet, and the effect of cinacalcet on mortality, CV events and severe unremitting HPT in older (≥ 65 years) and younger (< 65 years) patients. Methods: A double blind, multicenter clinical trial, 3883; patients on hemodialysis with moderate to severe sHPT randomized to cinacalcet or placebo, 2878 (74%) < 65 years and 1005 (26%) ≥ 65 years; primary composite endpoint (death or and CV events), a composite outcome representing severe unremitting HPT. Results: At baseline, older patients had higher prevalence of diabetes mellitus and CV co-morbidity than younger patients. By year 3, 32% of older patients randomized to placebo had received kidney transplant, PTX or commercial cinacalcet compared to 50% of younger patients. In older patients, the adjusted relative hazard (RH) (95% confidence interval) for the primary (CV) endpoint (cinacalcet vs placebo) was 0.70 (0.60, 0.81) and in younger patients, it was 0.97 (0.86, 1.09). After censoring for kidney transplantation, PTX or commercial cinacalcet use, in younger patients was 0.89 (0.78, 1.02). Relative hazards for severe unremitting HPT were 0.46 (0.31, 0.69) in older and 0.43 (0.36, 0.51) in younger patients. Conclusion: Cinacalcet nominally significantly reduced the risk of death and of the primary CV endpoint in older hemodialysis patients with sHPT, but not in younger patients. Cinacalcet reduced the risk of severe unremitting HPT in all patients. Effect modification by age may be explained by differences in CV risk, differential application of co-interventions that reduce PTH, and/or diminished power to observe an effect.

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P-042

CARDIAC BIOMARKERS AND HEALTH-RELATED QUALITY OF LIFE IN NEW HEMODIALYSIS PATIENTS WITHOUT SYMPTOMATIC CARDIAC DISEASE

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Background and Objectives. Health Related Quality of Life (HRQOL) is impaired in hemodialysis patients and cardiac biomarkers are elevated, but their relationship is uncertain. Our objective was to determine whether the cardiac biomarkers, troponin T and N terminal pro-B type natriuretic peptide (NT-proBNP), predict deterioration in the physical domains of HRQOL. Methods. This a prospective cohort study of patients in a randomized controlled clinical trial, enrolled maintenance hemodialysis patients who started dialysis within the previous 3-18 months, with no clinical evidence or prior history of symptomatic cardiac failure or ischemic heart disease, and left ventricular volume 0.05 ng/mL, were significantly associated with the change from baseline to 96 weeks follow-up for vitality and fatigue scores, and approached statistical significance for physical function (0.056). Conclusions. In hemodialysis patients without prior symptomatic cardiac disease and without a dilated left ventricle at baseline, elevated baseline Troponin T levels are associated with deterioration in the physical domains of HRQOL.

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P-043

CATHETER-RELATED BLOODSTREAM INFECTIONS CAN BE ACCURATELY REPORTED FROM THE HEMODIALYSIS CIRCUIT WHILE DIAGNOSIS BY DIFFERENTIAL TIME TO POSITIVITY DOES NOT ADD FURTHER INFORMATION

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Background: Most hemodialysis (HD) units diagnose HD catheter-related bloodstream infections (CRBSI) by obtaining blood cultures (BC) from the HD bloodline concurrent with clinical exclusion of other sources of infections. Guidelines from the Infectious Diseases Society of America (IDSA) recommend making the diagnosis of CRBSI by cultivating the same organism from a peripheral vein and from the catheter hub, meeting criteria for differential time to positivity (DTTP) >120 minutes. IDSA criteria for CRBSI have not been validated in HD patients. Hypothesis: BC taken from a peripheral vein during HD will yield the same result as BC taken from the dialysis bloodline. Methods: Four sets of BC (peripheral vein, both catheter hubs and HD bloodline) were obtained from adult patients who were suspected of having a CRBSI. Sensitivity, specificity and accuracy were calculated. DTTP was determined from HD bloodline and blood samples from a peripheral vein as gold standard. Results: 91 complete blood sample sets from patients with suspected CRBSI were obtained. Bacteremia was found in 35% of these patients and these BC consistently grew the same bacteria from all culture sites, with 98% specificity, 84% sensitivity and 93% accuracy. DTTP 120 was 129-1505 minutes (mean 716 minutes, median 567 minutes). Conclusion: Addition of DTTP to the current standard of practice of obtaining BC from the HD bloodline does not improve the accuracy of the results obtained through standard practice, suggesting that peripheral blood cultures for this testing is not necessary.

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P-044

Risk of Death following Kidney Allograft Failure: A Systematic Review and Meta-analysis of Cohort Studies

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Background: Although advances in immunology and surgical techniques have improved short- and medium-term outcomes of kidney transplantation, most kidney allografts will fail during the lifetime of the recipient. People with kidney allograft failure represent an increasing fraction of all those starting dialysis therapy. Purpose: To summarize prognosis following kidney allograft failure and identify potentially beneficial interventions or modifiable risk factors. Data sources: MEDLINE and EMBASE (inception to October 1, 2013) and article reference lists without language restriction. Study selection: Cohort studies of all-cause mortality and fatal infection-related and cardiovascular events in people starting dialysis following kidney allograft failure. Data extraction: Two reviewers independently extracted data on study design, participant characteristics, dialysis modality, transplant nephrectomy, immunosuppression strategy, transplant-naïve comparators, and risk of bias. Data synthesis: Forty studies comprising 249,716 participants met the inclusion criteria. The first year of dialysis therapy was associated with the highest mortality. By random-effects meta-analysis annual risk of death, from years 1 to 4, was 0.12 (0.09-0.15), 0.06 (0.05-0.07), 0.05 (0.04-0.06) and 0.05 (0.04-0.06), respectively. Limitations: We found high heterogeneity in each meta-analysis, which remained unexplained by pre-specified subgroup analyses. We could not find sufficient information to summarize the risk for fatal infection-related and cardiovascular events, or to test the role of transplant nephrectomy or different immunosuppressive strategies. Risk of bias was high, especially participation bias. Conclusions: Mortality is higher during the first year of dialysis treatment following kidney allograft failure than in subsequent years. Insufficient data are available to assess factors potentially impacting prognosis and strategies that may improve outcomes during this high-risk transition period. In a culture promoting transplantation, clinical research of different models of care, as well as medical and surgical interventions in this growing high-risk population should be a research priority.

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P-045

DIALYSIS VASCULAR ACCESS CREATION AND USE AFTER KIDNEY TRANSPLANT FAILURE

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Background and objectives: Patients initiating hemodialysis after kidney transplant failure is an increasing cohort with unique clinical characteristics. We describe the timing of creation and use of arteriovenous (AV) vascular access type(fistula or graft) in this population and the clinical variables associated with these outcomes. Methods: We conducted a population-based cohort study of adult Ontario patients (age ≥ 18 years) starting hemodialysis after kidney transplant failure between 2001 and 2010. Using four linked healthcare databases we determined: 1) the proportion of patients with an arteriovenous vascular access created within 36 months (12 months prior to and 24 months post) of initiating dialysis after kidney transplant failure 2) the proportion who used the vascular access in the 24 months after dialysis initiation, and 3) patient characteristics associated with vascular access creation. We used multivariable generalized estimation equation models, to define the associations with access creation. Results: Our cohort included 683 patients with an average age of 47.6 years with 13.5% older than 65 years. Of these 15.6% and 40% had an AV access creation 12 months prior to and 24 months after kidney transplant failure respectively. Characteristics associated with decreased likelihood of a vascular access creation: coronary artery disease (Odds Ratio (OR) 0.68, 95% confidence interval (CI) 0.52-0.89), diabetes mellitus (OR 0.63, CI 0.45-0.88), and undergoing peritoneal dialysis prior to transplant (OR 0.586, CI 0.37-0.94). Conclusions: Despite of being younger and healthier few patients get an aretriovenous access created prior to the return to dialysis after transplantation and with less than 50%. Having a creation after 2 years on dialysis.. Our findings highlight suboptimal hemodialysis vascular access planning in patients with transplant failure and emphasizes the opportunities to improve the hemodialysis access planning, care and outcomes for these individuals by the transplant team.

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P-048

VASCULAR ACCESS CREATION AND USE AMONG INCIDENT HEMODIALYSIS PATIENTS

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BACKGROUND AND OBJECTIVE: Although clinical practice guidelines promote appropriate fistula use for all patients, in Canada, use of an arteriovenous access (fistula or graft) among incident patients starting chronic hemodialysis is on the decline. We aimed to describe the proportion of patients with an arteriovenous (AV) access creation any time in the five years prior to starting chronic hemodialysis between January 1st 2001 and December 31st 2010. We also examined patient characteristics associated with AV access creation, and when created its use. DESIGN, SETTING, PARTICIPANTS, AND MEASURMENTS: We conducted a retrospective cohort study of adult patients (≥18 years) who started hemodialysis as the first form of renal replacement therapy, using linked health care databases in the province of Ontario, Canada. RESULTS: Our study included 17,183 incident patients starting chronic hemodialysis. Of these patients, 27% had ≥1 AV access created and 20% used an AV access at dialysis. When late referrals (followed by a nephrologist < 3 months prior to dialysis) were excluded, 37% of patients had ≥1 AV access created and 27% used an AV access at hemodialysis start. Patient characteristics associated with a lower likelihood of AV access creation and use (two separate models) were female sex, end-stage kidney disease comorbid index ≥5, late nephrology referral, and rural residence. CONCLUSIONS: An AV access was created in just over a quarter of incident patients in Ontario, with two thirds of these patients using an AV access at the start of hemodialysis. These findings were only slightly higher among those who received nephrologist care at least 3 months prior to dialysis initiation. These findings can inform quality improvement initiatives to ensure each patient has an optimal dialysis vascular access plan before starting hemodialysis.

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P-049

RATE OF ARTERIOVENOUS ACCESS CREATION AFTER STARTING HEMODIALYISIS: A POPULATION-BASED COHORT STUDY

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BACKGROUND: There remains uncertainty around the timing and the likelihood of patients having an arteriovenous (AV) access creation after starting hemodialysis. OBJECTIVE: We aimed to examine the rates as well as patient and facility level predictors of AV-access creation among adults (>18 years) starting hemodialysis between 2001 and 2010 for the first time via catheter. METHODS: We conducted a retrospective cohort study of adult patients who started hemodialysis as the first form of renal replacement therapy with no previous evidence of AV-access creation. Using linked administrative health care databases in Ontario, we followed patients for two years from the day of hemodialysis start to ascertain any AV-access creations. RESULTS: Our cohort included 8,229 patients who started hemodialysis via a catheter. By the end of our follow-up period, 46% had =1 AV-access creations after hemodialysis start. Of those patients, 51% used an AV-access for hemodialysis within the 2-year follow-up. Patients 3 months pre-dialysis nephrology care, and 1.72). However, after 1-year following hemodialysis, the relative rate for AV-access creation was more than 29% (RR50% of patients starting dialysis via a catheter never receive an AV-access creation after a two year-follow-up. For those who received an AV-access creation, there was ~50% non-use. Special care and follow-up should be placed on those individuals receiving an AV-access to reduce the high risk of AV-access non-use.

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P-050

INCREMENTAL APPROACH TO PERITONEAL DIALYSIS

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Abstract: Background: Incremental peritoneal dialysis (PD) reduces the workload and cost of PD for patients with well preserved residual renal function but its use has not been well described. In this observational cross sectional study we describe how we use incremental PD in a large patient population. Design: Cross-sectional study conducted July 2013 using most recent PD prescription and clearance achieved in all 124 PD patients at one academic centre. Method: We recorded basic demographic and prescription information and the most recent residual renal and peritoneal Kt/V. We then classified the patients into those who are on incremental and on standard prescriptions. Incremental PD was defined as total weekly Kt/V > 1.7 but with peritoneal component < 1.7 plus being on a 'day-dry' or 'night-off' schedule for APD, or < 8L/day prescription for CAPD. Results: Of the 124 PD patients, 10 were on CAPD and 114 on APD. 54 patients (43.5%) were on an incremental prescription while 70 (56.5 %) were on the standard approach. 68% (34) of APD patients were able to achieve Kt/V 1.7 weekly without a day dwell. 32%(16) were able to take at least one night off a week. 40%(4) of CAPD patients could achieve Kt/V 1.7 weekly with < 8 L/day of PD solution. Outcome measures from our program, including standardized mortality ratio, peritonitis rate and percentage of patients achieving clearance targets all suggest that excellent outcomes can be achieved with incremental PD. Conclusion: Incremental PD is feasible in a large program. It reduces the workload of dialysis for PD patients and decreases cost, particularly by reducing use of day dwells in APD. It does, however, require close monitoring of residual renal function in order to avoid under-dialysis.

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P-051

COGNITIVE IMPAIRMENT IN ADVANCED CHRONIC KIDNEY DISEASE

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Background: Chronic Kidney Disease (CKD) disproportionately affects the elderly and is associated with frailty and impaired quality of life. Patients with CKD suffer from multiple comorbid conditions putting them at risk of developing cognitive impairment. The purpose of this study was to describe the prevalence of cognitive impairment in patients with advanced CKD (eGFR< 30ml/min). Methods: We approached all patients with advanced CKD who attended an interprofessional non-dialysis CKD clinic at a tertiary care center for enrollment in our study. We excluded patients who did not speak English or were unable to provide informed consent. We collected demographic variables, physical examination measurements, laboratory values, and performed an assessment of cognitive function using the Montreal Cognitive Assessment (MoCA).Results: We studied 141 patients. Their mean age was 68.5 years (Standard Deviation [SD]+/- 12.4), and 57 patients were female (40.4%). The mean eGFR was 21.2 mL/min/1.73m^2 (SD +/- 7.8). One hundred and fourteen patients (80.9%) scored < 26 on the MoCA and were thus defined as cognitively impaired. In particular, the recall, visual/executive and language domains were impaired in >60 % of the participants. In contrast, naming and orientation were relatively well preserved (> 70 % achieving perfect score). Conclusions: Patients with advanced CKD have a high burden of cognitive impairment. Further studies on the pathophysiology of cognitive decline and its impact on patient decision making and outcomes are needed.

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P-052

EXOSOMES DERIVED FROM HUMAN ENDOTHELIAL COLONY FORMING CELLS PROTECT AGAINST HYPOXIA-INDUCED ENDOTHELIAL CELL INJURY

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BACKGROUND We have recently shown that human endothelial-colony forming cells (ECFCs) protect against renal injury in a mouse model of ischemia-reperfusion (I/R) acute kidney injury (AKI). Cell-derived microvesicles (MVs) have been reported to diminish apoptosis by horizontal miRNA transfer. Since two main classes of MVs exist with distinct properties (microparticles and exosomes), the purpose of this study was to determine the role of ECFC-derived MVs and miRNAs in endothelial protection. METHODS Mice subjected to renal I/R were injected with ECFCs (106/mouse i.v.) at reperfusion. Human umbilical vein endothelial cells (HUVECs) were rendered hypoxic for 24 hr, followed by reoxygenation (H/R), in the presence or absence of conditioned media from ECFCs (CM), conditioned media without vesicles (CM-), ECFC-derived microparticles, or ECFC-derived exosomes. Apoptosis was determined by caspase-3 activity and expression in both models. The expression profiles of miRNAs isolated from microparticles and exosomes were constructed using next-generation sequencing, followed by bioinformatic pathway analyses. RESULTS I/R increased renal caspase-3 activity and expression ($P<0.05$ vs sham $n=6$) while treatment with ECFCs blocked I/R-mediated increases in apoptosis. In the cell model, H/R increased caspase-3 activity and expression ($P<0.001$ vs control, $n=4$). Incubation with CM or ECFC-derived exosomes decreased both activity and expression of caspase-3 ($P<0.01$ vs H/R alone). By contrast, treatment with CM- or treatment with microparticles alone had no effect on apoptosis. Next-generation sequencing revealed miRNAs mainly expressed in the exosome fraction that are related to antiapoptotic and pro-survival pathways (mir486, mir381, mir25), while microparticles contained miRNA associated with pro-apoptotic and pro-inflammatory pathways (mir Let7 family, mir155, mir125b). CONCLUSIONS These data indicate that the protective effects of ECFC-derived MVs are mediated by exosomes activating pro-survival pathways, possibly due to horizontal transfer of antiapoptotic miRNAs. Our results suggest that exosomes from human ECFCs may represent a therapeutic strategy for the treatment of ischemic AKI.

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P-053

HEALTH CARE COSTS ASSOCIATED WITH ACUTE KIDNEY INJURY

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Background: The association of AKI with health care costs is unclear.
Objectives: To quantify health care costs of AKI by severity and renal recovery.
Methods: We identified a cohort of adults hospitalized in Alberta for <60 days between November 2002 and December 2008, and used serum creatinine to define AKI. Patients with ESRD or eGFR <15ml/minute/1.73m^2 were excluded. Costs were determined from inpatient, outpatient, and physician claims data over index hospitalization, renal recovery period (1-90 days) and 3-12 months post admission. A fully adjusted GLM regression model with bootstrapping was used, and sensitivity analysis was performed.
Results: Of 229869 subjects (mean age 62.8 years, 47% male), 24494 (10.7%), 4401 (1.9%), 2390 (1.0%) and 847 (0.4%) had AKIN stages 1, 2, 3 without dialysis, and 3 with dialysis, respectively. Increasing severity of AKI was independently associated with length of stay and costs (Table 1). Over 3-12 months, AKIN 3 requiring dialysis that either recovered, or did not recover was associated with the greatest costs ($18096 and $30166 respectively), with dialysis specific costs accounting for 43.1% of costs for those that did not recover at 90 days.
Conclusions: Graded increases in costs are observed with increasing severity of AKI, greatest with AKI requiring dialysis. AKI is associated with increased cost over 3-12 months, most pronounced for AKIN 3 requiring dialysis with non-recovery. The costs associated with AKI warrant evaluation of potential strategies to prevent and attenuate AKI or promote renal recovery.

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P-054

ISO-OSMOLAR COMPARED TO LOW-OSMOLAR CONTRAST MEDIA FOR PREVENTING CONTRAST-INDUCED ACUTE KIDNEY INJURY: A COST-EFFECTIVENESS ANALYSIS

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Contrast-induced acute kidney injury has major implications including morbidity and health resource utilization. Published literature supports a greater protective effect of iso-osmolar contrast media (such as iodixanol) as compared to low-osmolar contrast media, albeit at a higher cost per unit. We conducted a cost-effectiveness analysis to assist clinicians and health policy makers to compare between the two.

A systematic review was conducted to estimate the risk of acute kidney injury after iso- and low-osmolar contrast media. A Markov model was then created, taking into account peri-procedural risks, the differential risk of acute kidney injury, need for dialysis and subsequent mortality risk,cost of the contrast media itself and of downstream clinical events. Parameters for the model were identified from the meta-analysis and literature search. A base-case analysis and multiple sensitivity analyses were performed.

In the base case analysis, the iso-osmolar strategy was optimum (29.19 versus 28.87 quality adjusted life years). In the cost effectiveness analysis, the iso-osmolar strategy dominated over the low-osmolar, by virtue of being both, less expensive and more effective than the low-osmolar strategy. This result was robust across most sensitivity analyses (including: cost of contrast media, baseline risk of acute kidney injury, volume of contrast used, risk of dialysis). The exception was the sensitivity analysis with the differential risk of acute kidney injury with iso-osmolar versus low-osmolar.

Iso-osmolar contrast media, such as iodixanol, are cost saving and more effective compared to low-osmolar contrast media in a health economic analysis. This is robust across multiple sensitivity analyses.

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P-055

VASCULAR ACCESS OUTCOMES IN THE VERY ELDERLY

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The arteriovenous fistula is the vascular access of choice for hemodialysis patients given the superior survival rate seen in patients with a fistula compared to a central venous catheter. However, outcomes in the very elderly are not well known.

A retrospective chart review was done of all patients aged > 80 years who underwent fistula creation; data about comorbidities, interventions and duration of patency were abstracted from the administrative database. Survival analysis was carried out to calculate patency rates; functioning fistulas at time of modality change, death or transplant were censored.

249 arteriovenous fistulas were created in patients age > 80 years, 60% of them being men. The median age was 83.3 years (range 80 to 95 years). 128 fistulas (52%) required at least 1 intervention to establish or maintain patency, of whom 86 (35%) required atleast 2 interventions and 60 (24%) required 3 or more interventions. Of these, 117 fistulas were never successfully needled, a failure to mature rate of 47%. The primary patency rate for the remaining 133 at 1 year was 23% and at 2 years was 12% (figure). The assisted patency rate at 1 year was 79%, at 2 years was 59% and at 5 years was 28%.

Arteriovenous fistula outcomes in the very elderly are associated with high rates of failure to mature and high burden of interventions with modest patency outcomes. These data should be considered while making decisions about vascular access creation in the very elderly.

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P-056

IS CONVERSION FROM A THIAZIDE TO A THIAZIDE-LIKE DIURETIC A SIMPLE AND EFFECTIVE MEASURE TO TREAT RESISTANT HYPERTENSION?

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Thiazide-like diuretics (indapamide, chlorthalidone) are longer acting than thiazide diuretics and direct comparisons show a greater blood pressure lowering effect with chlorthalidone compared to hydrochlorothiazide. Despite this, most patients with resistant hypertension referred to a tertiary care hospital-based Renal Hypertension clinic are often on a thiazide diuretic.One of the common interventions done in improving control of these patients blood pressure is a conversion from the Thiazide diuretic to a thiazide-like diuretic.The objective of this project is to study the efficacy and safety of this approach.

We conducted a retrospective chart review of all the patients referred to the Renal Hypertension clinic at our tertiary care hospital. We included patients who were switched from a thiazide to a thiazide-like diuretic, with no other concomitant medication changes, and with atleast one follow-up visit. Primary outcome was change in systolic blood pressure (SBP); safety outcomes were changes in potassium and creatinine.

1169 charts were reviewed to identify 62 patients (mean age 65 years, 68% men), with the dose change from hydrochlorothiazide to chlorthalidone being 1:1 in 32 patients (52%). There was a significant decrease in SBP, (mean difference -11 mm Hg, 95%CI -6, -16; p <0.001). The difference was significant whether the dose ratio was 1:1 (difference -12, p 0.002) or not (difference - 10, p 0.02). There was no significant change in creatinine (1.5, p = 0.72) or potassium (-0.3, p = 0.29).

Changing thiazide to a thiazide-like diuretic appears to be a simple and efficacious step for treating resistant hypertension

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P-057

SUCCESSFUL IMPLEMENTATION OF A TRACKER TOOL TO IDENTIFY BARRIERS TO APPROPRIATE VASCULAR ACCESS AND INDEPENDENT DIALYSIS CHOICES AMONG PATIENTS WITH CKD IN ONTARIO

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Background: Increase in the uptake of Independent Dialysis (ID) and catheter reduction with appropriate use of arterio-venous (AV) access represent strategic priorities for the province. Identification of the barriers to the use of ID and appropriate vascular access (VA) will help shape provincial policy.
Objectives: To create ID and VA tracker tools capturing reasons for which patients are ineligible or reject ID and AV access choices at critical decision points; to evaluate early implementation of these tools.
Methods: ID and VA tools were created as electronic forms to document reasons for eligibility and choice around ID modality and AV accesses. They were grouped into patient, program and province-wide related reasons. The choice of a primary and secondary reasons was permitted. The data in the tools are updated electronically in a renal database when a change in the patient status is observed and are available for ongoing analysis. The use of the tools is triggered when chronic kidney disease (CKD) providers report patient encounters tied to funding, hence enhancing compliance.
Results: The tools were well received by the 26 regional programs. The initial 2 months of data collection resulted in 22% of potential encounter updates. Main barrier to AV access was unexpected start to dialysis and to ID was lack of home support. With assessments to continue to be completed, initial barriers are being identified and will be reported.
Conclusions: ID and VA tracker tools have been created successfully and are in the early phases of implementation in the province of Ontario. It is expected that the collected information will help to mitigate barriers to the strategic initiatives and will shape provincial policy.

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P-058

INCREASING UPTAKE OF INDEPENDENT DIALYSIS (ID) IN ONTARIO

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Background: Uptake of ID represents one of the strategic initiatives of Ontario. ID is defined as dialysis independent of in-centre facilities. The key metric of success is the 6-month incident ID rate (6MIIDR). It is defined as the patients on ID within 6 months of starting dialysis, over the patients who stayed on dialysis long enough (6 months) to be given such an opportunity. The goal for the 6MIIDR is 40% by 2015. Some of the supportive initiatives launched to date are: patient-based funding (including frequent home hemodialysis); promotion of patient education; creation of a 'collaborative' network for newly funded ID coordinators; establishment of a yearly ID conference.
Objectives: To report the interim results of the ID strategic initiative including the 6MIIDR as well as conventional home dialysis incident and prevalent rates.
Methods: Data reported were analyzed on a quarterly basis. Metric rates from Q3 FY11/12 onwards were included.
Results: Attrition rate from home dialysis was 25% per year. Patient follow up in CKD clinic >1 year associates with higher ID incident rate.
Conclusion: Provincial wide strategic initiatives led to the 6-month ID incident rate increase from 30% to 34%. Similar trends were observed in home dialysis rate at initiation of dialysis.

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P-059

USE OF PERSONAL SUPPORT WORKERS (PSW) FOR HOME HEMODIALYSIS (HHD): AN INDUSTRY DISRUPTIVE APPROACH

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Background: Despite good clinical outcomes and low cost, HHD is underutilized mainly due to an inability of patients to do it. Patient-based bundle funding in Ontario supports frequent dialysis both in-centre and at home.
Objectives: A pilot to use PSWs to perform HHD using a financially attractive model.
Methods: To allow future wider adoption and economies of scale, an industry partner assumed the human resource organizational role and risk. Three employed PSWs were trained to support 3 patients. The project was approved by the hospital risk management and legal teams, and insurance provider. The hospital assumed the risk for training and clinical care as usual.
Results: Three patients have been dialyzed at home for one year by 3 PSWs. No clinical problems were encountered. There was a high level of satisfaction among patients and nursing staff. The hospital team provided back-up support as needed. The projected yearly cost, including administrative cost, assuming economies of scale of 30 patients is seen below (PSW cost in hatched columns).
Conclusion: Based on this pilot, use of PSWs to provide HHD is safe, feasible, and based on provincial rates, projected to be less expensive than in-centre HD. This model needs to be evaluated including more patients to confirm the financial predictions.

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P-061

Thyroid Function and Chronic Kidney Disease in the CARTaGENE cohort

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Background: Hypothyroidism is common in patients with CKD and TSH levels are negatively correlated with eGFR in the general population. However, the effect of levothyroxine (LT) treatment on this association is uncertain.
Methods: We analyzed biological and clinical data from a random cohort of 20,004 participants aged 40 to 69 years from the general population. This cross-sectional study is part of the CARTaGENE data bank, a research infrastructure contributing to diagnosis, treatment and prevention of chronic diseases.
Results: Among subjects with measured serum TSH and creatinine, we observed a negative correlation between TSH and eGFR in both LT treated and untreated individuals. In addition, at equal TSH, the eGFR was on average 4 mL/min/1.73 m2 lower in subjects under LT (cf. Table). In reference to a normal TSH without LT, the odds ratio (95% CI) for CKD (eGFR<60 mL/min/1.73m2 was 2.04 (1.28-3.24) for an elevated TSH without LT, 1.49 (1.15-1.94) for a normal TSH under LT and 2.09 (1.10-3.98) for an elevated TSH under LT, after adjustment for gender, age, BMI, diabetes and dyslipidemia.
Conclusions: In summary, the negative correlation between eGFR and TSH exists in both treated and untreated subjects. In addition, at equal TSH, patients under LT therapy have a lower eGFR than untreated subjects, even after adjusting for confounders. These results suggest an association between thyroid disease and CKD regardless of current thyroid function status and therapy.

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P-062

MENTORSHIP PILOT PROGRAM: THE MENTEE PERSPECTIVE

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Background: The Mentorship Pilot Program was a 1-year Ontario based program linking primary care providers (PCP) with nephrologists in a collaborative mentor-mentee relationship to improve primary care for patients with chronic kidney disease (CKD). Objectives: This evaluation describes PCPs experiences as mentees and self-reported impact of the pilot program. Methods: An open call was conducted to recruit PCPs to participate as mentees. Prior to implementation, a pre-survey was distributed to capture mentee demographics, frequency of contact with CKD patients, perceived comfort/knowledge in CKD care, barriers to CKD care, and ease/satisfaction of nephrologist consultation using a modified Likert scale. At the close of the pilot, a post-survey with the same measures was distributed to mentees. It also asked mentees to provide their perceived usefulness of the program. Measures in both the pre and post survey were compared using paired t tests while measures in only the post-survey were reported on using frequencies. Results: Of 154 enrolled mentees, 138 and 98 completed the pre and post surveys, respectively. Over 75% of mentees reported increased knowledge/comfort in screening, identifying, and managing CKD patients post-program. 64% reported the program helped reduce barriers to providing CKD care. Significant improvements were observed from pre-pilot to pilot completion in ease of accessing a nephrologist (2.91 vs 4.28; P value <0.001) and level of satisfaction with a nephrologist encounter (3.37 vs 4.51; P value <0.001). Post-program, 75% felt the program was "very"/"extremely helpful", 43% felt program education was "always applicable" to their practice, 53% were "extremely likely" to recommend the program to a colleague/friend, and 87% would utilize the program if re-offered in the future. Conclusions: Survey results suggest the pilot program was effective in increasing knowledge/comfort in CKD care, reducing barriers to providing CKD care, and increasing ease and satisfaction of nephrologist consultation. Findings support continuation and expansion of the program.

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P-063

Urinary ACR and PCR are prognostically equivalent: Implications for clinicians and Laboratories

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Introduction: Proteinuria is an important prognostic variable in patients with chronic kidney disease (CKD). Both albumin-to-creatinine ratio (ACR) and protein-to-creatinine ratio (PCR) are widely used to estimate proteinuria. No study has directly compared the ability of these measures to predict progression to end-stage renal disease (ESRD).
Patients and methods: We examined the ability of baseline measures of ACR and PCR to predict progression to ESRD over one year in 2544 patients participating in CanPREDDICT, a prospective cohort study of adult patients with advanced CKD from multiple causes. ACR and PCR were log transformed for analysis. We created a base Cox multivariable model (BCM) for prediction of RRT using standard clinical variables, and then compared differences in the performance (discrimination [c statistic, IDI] and reclassification [NRI]) of enriched Cox models (ECM) created by addition of either logACR or logPCR.
Results: Both ACR and PCR independently predicted need for RRT at one year, and each remained highly significant after adjustment for the BCM variables. Both log ACR and log PCR improved BCM performance significantly and to the same degree (Table 1). Sensitivity analyses using alternate choices for BCM variables did not change these results.
Limitations: I year follow-up, single baseline measure, predominantly Caucasian cohort
Conclusions: ACR and PCR are equally and interchangeably valid predictors of progression to RRT at 1 year. Clinicians can choose whichever test is most appropriate for the specific renal diagnosis, without loss of general prognostic information applicable to CKD

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P-064

THE ASSOCIATION BETWEEN POSTOPERATIVE TROPONIN AND MORTALITY IN PATIENTS WITH AND WITHOUT IMPAIRED KIDNEY FUNCTION

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Background: Postoperative cardiac troponin T (cTnT) is an important risk factor for 30-day mortality in patients undergoing noncardiac surgery. Whether cTnT has the same association with mortality for patients with low kidney function compared to normal kidney function is uncertain. Objective: To evaluate the association between an abnormal cTnT after noncardiac surgery at different levels of kidney function. Methods: We performed a post-hoc analysis of an international, prospective cohort study that included patients at least 45 years old, undergoing noncardiac surgery that required an overnight hospital admission. cTnT was measured for three days after surgery and considered abnormal if the peak was ≥0.02 ng/mL. Kidney function was characterized by the estimated glomerular filtration rate (eGFR). We examined the interaction between an abnormal cTnT and eGFR. Results: A total of 14,037 patients were included of which 267 (1.9%) died within 30 days of surgery. 11,266 (80.3%), 1,488 (10.6%), 763 (5.4%), 274 (2.0%) and 246 (1.7%) had an eGFR of eGFR ≥60, 45 to <60, 30 to <45, 15 to <30, and <15 ml/min/1.73m2 or on dialysis, respectively. The adjusted hazard ratio (aHR) for death with an abnormal cTnT was 4.37, 6.15, 6.30, 1.33 and 1.46 for an eGFR ≥60, 45 to <60, 30 to <45, 15 to <30, and <15 ml/min/1.73m2 or on dialysis respectively. Compared to the ≥60 ml/min/1.73 m2 eGFR group, the aHR was significantly lower for the 15 to <30 eGFR group (interaction p-value=0.02). These results were unchanged by redefining an abnormal cTnT as ≥0.03 ng/mL or as a change in cTnT of at least 0.02 ng/mL. Conclusion: The risk associated with postoperative cTnT may be different for patients with an eGFR <30 ml/min/1.73 m2. Further research is required to determine how to interpret perioperative cTnT values for patients with low eGFR.

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P-065

INCIDENCE OF CT CONTRAST-INDUCED NEPHROPATHY: TOWARDS A MORE ACCURATE ESTIMATION

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Background: Acute kidney injury (AKI) in patients not receiving contrast CT is common, likely leading to inflated reports of the true incidence of CT contrast-induced nephropathy.
Objectives: For a more accurate estimation of contrast-induced nephropathy incidence, we compare the incidence of AKI immediately before and after contrast administration in the same population. We also control for a creatinine rise starting prior to and continuing after a contrast study being incorrectly associated with the scan itself.
Methods: We included all CTs from January 2006 to May 2013 in our city's health region with adequate lab data. We excluded patients <18 and current dialysis patients. The incidence of AKI (stage 1 AKIN or worse) was calculated in the 12H period before and the 24-48H after the scan. New AKI occurred if creatinine had increased at a greater rate than in the previous 24H period. The incidence of post-scan AKI and post-scan dialysis was calculated by subtracting the post-scan from the pre-scan incidence. Results were stratified by contrast usage and baseline GFR (CKD-EPI equation).
Results: See Table for results. Analysis of non-contrast scans showed similar incidences pre and post-scan. For contrast scans, incidence of AKI stage 1 or worse was 0.9% (-0.1% - 1.9%), 5.6% (2.8% - 8.4%), 0% (-9.6% - 9.6%) and -11.4% (-27.8% - 5.5%) for GFR > 60, GFR 30-60, GFR 15-30 and GFR <15 mL/min/1.73 m^2 respectively. The risk of dialysis after post-contrast AKI was statistically insignificant.
Conclusions: The incidence of post-CT contrast-induced nephropathy appears less than commonly reported.

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P-068

KIM-1 INTERACTS WITH GA12 AND SUPPRESSES ITS ACTIVITY TO MEDIATE EFFEROCYTOSIS

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Background: Efferocytosis, the phagocytic clearance of apoptotic cells, serves to attenuate inflammation and enable tissue repair following injury. Kidney injury molecule-1 (KIM-1) is a type I transmembrane protein that is upregulated on renal proximal tubular epithelial cells (PTECs) following acute kidney injury. KIM-1 is a phagocytic receptor that specifically recognizes phosphatidylserine, an "eat me" signal, displayed on the surface of apoptotic cells. The signalling mechanisms of how KIM-1 carries its efferocytic function is not known. Previously, we used immunoprecipitation and mass spectrometry to identify Gα12 as a potential novel KIM-1-interacting protein in PTECs. We hypothesized that KIM-1 interacts with Gα12 to mediate efferocytosis. Objective: To decipher how KIM-1 mediates phagocytic signalling in PTECs. Methods: Human embryonic kidney (HEK293) cells expressing high levels of endogenous Gα12 and stably overexpressing GFP-tagged human KIM-1, and PTECs isolated from wild type and Kim-1 knockout mice were used as cell culture models. Results: First, we established that Gα12 interacts with the cytosolic domain of KIM-1 via co-immunoprecipitation. Using confocal microscopy, we observed the co-localization of KIM-1 with GFP-tagged Gα12. Next, using an active Gα12 pull-down assay, we determined that Gα12 activity (GTP-binding) is significantly reduced in KIM-1-expressing cells upon exposure to apoptotic cells. To determine the role of Gα12 during KIM-1-mediated efferocytosis, we overexpressed a constitutively active mutant of Gα12 and found a significant decrease in uptake of apoptotic cells. Conversely, an increase in apoptotic cells uptake was found when we silenced Gα12 expression via siRNA. In addition, we observed that KIM-1 inhibited Gα12 activation in HEK293 cells loaded with non-hydrolyzable GTP in the absence of apoptotic cells. Similarly, PTECs isolated from wild type and Kim-1 knockout mice confirmed the later findings where KIM-1-expression inhibited GTP-loading onto Gα12. Conclusions: These experiments suggest that KIM-1 interacts with and inhibits Gα12 activation in PTECs to mediate efferocytosis.

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P-069

VERTEPORFIN: A NOVEL INHIBITOR OF TGF-ß SIGNALLING THAT BLOCKS FIBROBLAST MECHANOSENSATION

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Kidney fibrosis is the final common pathway of injury initiated by nearly all forms of CKD. The principle culprit of fibrosis is the myofibroblast, a matrix-forming cell type derived predominantly from fibroblasts. Fibroblast-myofibroblast transition requires transforming growth factor-β (TGF-β) and its canonical Smad signalling pathway. Anti-TGF-β therapies have failed to safely prevent fibrosis due to important pleiotropic effects of TGF-β on non-fibroblast cells. Recent observations suggest that fibroblasts are regulated by environmental stiffness, with stiffer surfaces promoting increased responsiveness to TGF-β via unknown mechanisms. TAZ/YAP are closely related mechanosensitive transcription co-factors, whose nuclear localization is regulated by substrate stiffness. Since TAZ/YAP are Smad nuclear retention factors promoting TGF-β signalling, we hypothesized that TAZ/YAP inhibition might attenuate stiffness-mediated, TGF-β-induced pro-fibrotic responses. Consistent with this assumption, we found that TAZ/YAP are in an active nuclear location in fibroblasts grown on stiff substrates similar to fibrotic kidneys (100 kPa), whereas they are primarily in an inactive cytosolic position in fibroblasts grown on soft surfaces akin to healthy kidneys (2 kPa). Importantly, cells grown on soft surfaces exhibited strongly attenuated nuclear Smad2/3 translocation and Smad3-depenedent transcription upon TGF-β stimulation, indicating impaired pro-fibrotic signalling. To test the role of YAP in reduced TGF-β signaling, we applied verteporfin (VisudyneTM), a clinically used drug for the treatment of macular degeneration with recently identified YAP inhibitory properties. Verteporfin reduced TGF-β-induced nuclear Smad2/3 accumulation and Smad3-mediated transcription in fibroblasts grown on stiff surfaces. Verteporfin treatment did not affect Smad2 phosphorylation levels suggesting that it primarily affects nuclear Smad retention. Our data suggests that soft, healthy kidney-like substrates inhibit, whereas stiff fibrotic-like substrates promote, pro-fibrotic TGF-β Smad signalling. Verteporfin is a YAP inhibitor that diminishes the stiffness-augmented responses of fibroblasts to TGF-β through blockade of Smad signalling, and therefore may be a novel anti-fibrotic agent for the treatment of CKD.

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P-070

LEFLUNOMIDE (LEF), AN ALTERNATIVE SECOND-LINE AGENT FOR THE TREATMENT OF IDIOPATHIC NEPHROTIC SYNDROME (INS) AND RECURRENT FSGS (rFSGS)

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Background: 50% of children with INS receive second-line agents for frequent relapses (FR), glucocorticoid dependence (GCD-NS) or GC resistance (GCR-NS). Limitations of newer agents are costs and/or adverse effects (AE). LEF promotes anti-inflammatory Th2-cells and suppresses T and B-cell expansion and production of pro-inflammatory cytokines, such as TNFα and IFNγ. Based on this profile, we hypothesized that LEF may be effective in NS.
Objectives: To report our initial experience with LEF in pediatric NS.<
Methods: Observational study/retrospective review of clinical and laboratory data. Results are described as medians (and ranges).
Results: Ten children age 9.9 (4.7-18.4)years received LEF over 8.9 (2.9–34.1)months: eight patients with FR/GCD-NS (n=6 minimal change disease [MCD]/INS, n=2 FSGS), one with treatment-recalcitrant collapsing glomerulopathy (CG), and one with rFSGS post-kidney transplantation (KT). LEF starting dose 20mg/d was titrated to steady-state trough levels of 40-80mg/L. Five/6 MCD/INS patients and two with GC-responsive FSGS were in remission with LEF monotherapy over 8 (1-28)months, with a dose of 20 (20-50)mg/day (12.5-50.8mg/m^2) and drug levels of 70 (26-95)mg/L. Four patients stopped treatment due to lack of response (GC) or relapse associated with inadequate trough levels (CG, GCD-NS, n=2), and oral ulcers or palmar eczema (n=2). The rFSGS patient achieved stable, partial remission (Upc 1-2g/g, GFR>110mL/min/1.73m^2) with LEF added to conventional post-KT immunosuppression. Two/10 patients revealed a small, transient rise of ALT, and one of indirect bilirubin <2fold upper normal; all resolved spontaneously after <4weeks without dose change. Average costs for LEF in this population is <5% of costs for tacrolimus or MMF, comparing Canadian wholesale and retail generic drug prices.
Conclusions: LEF represents an effective, mechanistically and economically interesting, therapeutic agent in FR/GCD-NS and potentially, rFSGS. Its clinical efficacy and absence of important AEs need be independently corroborated, and indications refined in view of its teratogenicity, long half-life and high protein-binding.

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P-071

VARIABLE COMPLEMENT ACTIVATION IN PNEUMOCOCCAL HEMOLYTIC UREMIC SYNDROME

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Background: Hemolytic uremic syndrome is a rare, but serious complication of invasive pneumococcal infection (pnHUS). Its pathogenesis is poorly understood, and treatment remains controversial. The emerging role of complement in HUS warrants a new look at this "old" disease.
Objectives: To examine evidence of complement activation and the nature of antibodies against the Thomsen-Friedenreich (T) antigen in children with severe pnHUS.
Methods: Retrospective analysis of clinical and laboratory features of three sequential cases of pnHUS since 2008 associated with pneumonia/pleural empyema, two due to *Streptococcus pneumoniae* serotype 19A.
Results: Profound depletion of complement was observed in two of the three patients affecting mainly C3 and CH50/AH50. Consumption of C3 was transient, during the first week of HUS. One patient was Coombs test positive. ABO blood group compatible donor serum and monospecific anti-C3d antibody strongly agglutinated the patient's RBC at 0° C, but not at 37°C. All patients received hemodialysis, packed RBCs, and platelets. Patient 2 received frozen plasma for hepatic failure with depletion of liver-dependent coagulation factors. Patient 3 was treated with intravenous immunoglobulin intended to neutralize pneumococcal neuraminidase. Two of the patients recovered without sequelae or disease recurrence. One patient died within 2½ days of admission due to complicating *Pseudomonas aeruginosa* sepsis and multiorgan failure.
Conclusions: We show early complement depletion mainly of C3 indicating alternative pathway activation in pnHUS. Complement activation appears to be variable and limited to the early course of the disease. RBC agglutination on ice, but not at 37°C, argues against a role of anti-T antibodies in the pathogenesis of this disease. Detailed mechanistic studies are needed to better characterize the biological roles and cellular effects of bacterial neuraminidases and the activation of complement in pnHUS, and to explore rationale treatment approaches for this rare, but potentially fatal disease.

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P-072

HIGH GLUCOSE STIMULATES FORMATION OF ENDOTHELIAL MICROPARTICLES AND INCREASES THEIR PRO-OXIDATIVE ACTIVITY

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Background: Microparticles (MPs) are small (0.1-1.0 μm) membrane fragments released from cells following stress or injury. In individuals with diabetes plasma endothelial MP levels are increased and predict risk of future cardiovascular events. Moreover, emerging evidence suggests that MPs may themselves exert deleterious biological effects. However, the stimuli responsible for increased MPs in diabetes, and the impact of diabetic conditions on the biological activity of endothelial MPs are not clear. Methods: Human dermal microvascular endothelial cells (ECs) were cultured in media containing 5.6 mM glucose, 25 mM D-glucose, or 25 mM L-glucose (osmotic control). MP levels were assessed by Annexin V labeling and flow cytometry as well as nanoparticle tracking analysis (NTA). Finally, the effects of endothelial MPs, formed under normal and high glucose conditions, on formation of reactive oxygen species (ROS) was assessed by dichlorofluorescin fluorescence. Results: Exposure of ECs to high glucose conditions was associated with a significant increase in MP formation over 24 hrs as assessed by flow cytometry (~2.5-fold vs. osmotic control, $P<0.05$, $n=4$) and NTA (~2.5 fold vs. osmotic control, $P<0.01$, $n=6$). Similarly, high glucose increased MP formation from human vascular smooth muscle or proximal tubule epithelial cells, although it had no effect on human mesangial cell MP formation.
Interestingly, exposure to 25 mM glucose increased the mean size of endothelial MPs (5.6 mM: 203±7 nm vs. 25 mM: 260±14 nm, $P<0.05$ $n=6$). Moreover, MPs generated under high glucose conditions were more potent inducers of endothelial cell ROS production than MPs generated under normal glucose (25 mM MPs: ~6-fold vs untreated control, 5.56 mM MPs: ~2.5 fold vs. control, $P<0.05$, $n=4$). Conclusions: Our results suggest that elevated glucose is a potent inducer of endothelial MP formation while also increasing the pro-oxidative effects of endothelial MPs. Such effects may contribute to progressive endothelial injury in diabetes.

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P-073

PODOCYTE MICROPARTICLES STIMULATE REACTIVE OXYGEN SPECIES PRODUCTION AND INDUCE P38 ACTIVATION IN CULTURED HUMAN PROXIMAL TUBULE CELLS

Dylan Burger (1), Shareef Akbari (1), Maddison Turner (1)
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Background: Microparticles (MPs) are small (0.1-1.0), membranous vesicles shed from the cell surface following stress/injury. Our laboratory and others have shown that endothelial MPs are increased in hypertension and diabetes and exert biological effects (i.e. oxidative stress, inflammation) on target cells through paracrine signaling. More recently, we reported that MPs are produced in podocytes following mechanical stretch (a mimic of intraglomerular hypertension. However whether podocyte MPs interact with the proximal tubule and influence function is unknown. Methods: Cultured human proximal tubule cells were exposed to podocyte MPs (105/ml) and phosphorylation of p38, ERK 1/2, and JNK were examined by Western blot analysis. Reactive oxygen species (ROS) production was assessed by lucigenin chemiluminescence. Results: p38 phosphorylation was increased (~3 fold) after 30 minutes exposure to podocyte microparticles. By contrast, JNK and ERK phosphorylation levels were unchaged over 24 hours. In addition, ROS production was shown increased by podocyte MP treatment at 16 hours (control: 7.2±1.6 vs treated 15.5±1.4 AU/mg protein). Fluorescence microscopy revealed cell surface binding of podocyte MPs to proximal tubule cells suggesting a paracrine effect. Conclusion: Our results suggest that podocyte MP interact with proximal tubule epithelial cells and induce intracellular signaling and ROS production. Such effects may play a role in the development of tubular injury in hypertensive and diabetic nephropathy.

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P-074

FORMATION OF CILIARY TRANSITION ZONE BY MKS5/RPGRIP1L ESTABLISHES A PIP2-ENRICHED CILIARY ZONE OF EXCLUSION (CIZE) NEEDED FOR COMPARTMENTALISING SIGNALLING PROTEINS

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Cilia are thought to harbour a membrane diffusion barrier at their transition zone (TZ) that compartmentalises signalling proteins. How this 'ciliary gate' assembles and functions remains largely unknown. Contrary to current models, we present evidence that C. elegans MKS-5 (orthologue of human Mks5/Rpgrip1L/Nphp8 and Rpgrip1) is an assembly factor for building the TZ—rather than simply a scaffold—for >10 different TZ proteins, helping form TZ ultrastructure comprising Y-shaped axoneme-to-membrane connectors. Coiled-coil and C2 domains within MKS-5 enable ciliary localisation and functional interactions with two TZ modules, consisting of Meckel syndrome (MKS) and Nephronophthisis (NPHP) proteins. Discrete roles for these modules at basal body-associated transition fibers and TZ explain their redundant functions in sealing the ciliary compartment. Furthermore, MKS-5 establishes a CIliary Zone of Exclusion (CIZE) at the TZ that confines signalling proteins, including GPCRs and NPHP-2/inversin, to distal ciliary subdomains. This CIZE, enriched in the phosphoinositide PIP2, defines a previously unknown ciliary lipid subdomain needed for signalling. Together, our findings suggest a new model for Mks5/Rpgrip1L in TZ assembly and function that is essential for establishing the ciliary signalling compartment.

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P-075

PHOSPHATE HANDLING IN PATIENTS WITH CARDIOVASCULAR DISEASE

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Background: Patients with chronic kidney disease (CKD) have reduced capacity to enhance the appearance of phosphate in the urine following an oral challenge. Phosphate and FGF-23 are being increasingly linked to the development of vascular calcification (VC) and cardiovascular disease (CVD) in people without CKD. Extra-skeletal manifestations directly linked to phosphate metabolism may begin at substantially higher levels of GFR than previously thought. Objectives: To determine the absolute and percent change in urine phosphate to urine creatinine ratio (Uphos/Ucr) at 1and 2 hours following a 500 mg oral phosphate test solution in patients with CVD and an estimated GFR (eGFR) of greater than 60 ml/min as well as healthy subjects. Methods: Ten subjects with CVD and stable kidney function were recruited from the cardiology ward. Seventeen healthy subjects were recruited from hospital staff. After an over-night fast, participants consumed 500 mg of phosphate. Blood samples were taken at baseline and urine samples were obtained at baseline, 60 and 120 minutes. Results: FGF-23 was significantly higher in the patients with CVD (99.2, [61.6,131.9]) compared to healthy controls (56.4, [40.5,75.5], $p<0.01$) but there was no difference in eGFR or baseline phosphate. In CVD patients, the Uphos/Ucr at 2 hours (2.55±0.86) was not different than baseline (2.28±1.03) nor was the mean (SD) relative change of 14.51%±40.5%. In healthy subjects, the 2-hour Uphos/Ucr (3.12±1.02) was significantly higher than baseline (1.98±0.58, $p<0.001$) with a mean (SD) relative change of 62.4% (53%) ($p<0.001$). There was a non-significant difference between groups in the absolute and relative change in Uphos/Ucr at 2 hours over baseline ($p=0.09$).Conclusions: The non-renal clearance of phosphate into soft tissue compartments could accelerate VC and may be an under-recognized risk factor for CVD in the non-CKD population despite normal serum levels of phosphate.

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P-077

EXERCISE TRAINING DURING HEMODIALYSIS IS NOT ASSOCIATED WITH INTRADIALYTIC HYPOTENSION

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Background: Intradialytic exercise is associated with improved HD efficacy, physical function, and quality of life. However, concerns regarding exercise induced hypotension have limited its widespread use.
Objectives: To demonstrate that intradialytic exercise is not associated with an increased frequency of intradialytic hypotension (IDH).
Methods: We performed a 12-week observational study of 48 maintenance HD patients. Hemodynamically stable patients performed intradialytic exercise (cycle ergometer) up to 3-times per week at moderate intensity (Borg scale 5), with duration at the patient's discretion. Hemodynamic parameters, fluid removal, exercise duration, single-pool urea kinetics (spKt/V), a numerical count of symptomatic (chest pain, shortness of breath, nausea/vomiting, dizziness, fatigue, cramps or anxiety) and asymptomatic IDH episodes were recorded. The duration of exercise (minutes exerted and in stratums [presence or absence of exercise; no exercise, <30 minutes, ≥30 minutes]) and IDH were analyzed using a random-effects model.
Results: A total of 1727 HD sessions were recorded with 827 involving exercise. Symptomatic and asymptomatic IDH occurred in 8.3% and 33.5% of all HD sessions, respectively. The rates (number of episodes/ 100 HD sessions) of symptomatic and asymptomatic IDH were similar with intradialytic exercise (Table 1). Symptomatic IDH and asymptomatic IDH were not affected by intradialytic exercise after adjustments for demographics, comorbidities, and intradialytic fluid removal (<0.01 symptomatic IDH episode per 10 minute exercise, P>0.10). The results were consistent when analyzed across the stratums. The dialysis efficacy was not affected by the presence or duration of intradialytic exercise.
Conclusion: Intradialytic exercise is not associated with hemodynamic instability or IDH.

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P-078

BIOMARKERS FOR EARLY ACUTE KIDNEY INJURY DIAGNOSIS AND PREDICTION OF AKI DURATION IN THE PEDIATRIC INTENSIVE CARE UNIT

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Background: Acute kidney injury (AKI) occurs early in pediatric intensive care (ICU) admission and increases risk for poor outcomes. Urine biomarkers may provide early AKI diagnosis, increasing opportunities for intervention. Objectives: Evaluate several biomarkers to predict AKI and AKI duration. Methods: Data from a single-centre prospective observational study (2007-2010) was enriched by data from an ongoing 4-centre prospective study (inclusion: 1 month-18 years; exclusion: cardiac surgery, prior severe kidney disease, unavailable urine/ serum in first 3 ICU days. Urine biomarkers: liver fatty acid binding protein (LFABP), neutrophil gelatinase-associated lipocalin (NGAL), kidney injury molecule (KIM-1), interleukin-18 (IL-18). AKI definition: (a) KDIGO serum creatinine (KDIGO-SCr), (b) KDIGO SCr- urine output criteria (KDIGO-SCr&UO). Analysis: ICU day 2 biomarkers to predict AKI (area under curve [AUC], 95%CI); biomarkers on day of AKI diagnosis to predict AKI duration (Spearman correlation, only NGAL, IL-18). Biomarker data were available from the first enrolled centre. Results: 182 patients had clinical data (mean±SD age 5.9±6.2 years, ICU stay 9.2±10.5 days, PRISM score 5.86±4.12; 107 (58%) males; 54% KDIGO-SCr&UO AKI, 37% KDIGO-SCr AKI. ICU day 2 NGAL and IL-18 predicted AKI (AUC's ≥ 0.70 (Table)); KIM-1 and LFABP had lower AUC's (0.63-0.69)(Table)). Biomarkers from AKI day 1 weakly correlated with number of AKI days (Table). Conclusion: Biomarkers from early ICU admission predict AKI development. More research is required to evaluate biomarkers for predicting AKI severity. We will perform the first multicentre PICU AKI biomarker study to evaluate these and other novel biomarkers.

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P-079

EVALUATING OUTCOMES OF PATIENTS WITH BEDSIDE PERITONEAL DIALYSIS CATHETERS PLACED BY NEPHROLOGISTS COMPARED TO SURGEONS.

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Background: Traditionally, surgeons have inserted catheters for patients receiving peritoneal dialysis (PD) for kidney failure in the Regina Qu'Appelle Health Region (RQHR). Since 2007, nephrologists have also begun to perform PD catheter placements for non-complex patients. The purpose of this project was to evaluate whether nephrologists can also successfully insert PD catheters but within a shorter time period compared to surgeons in order to improve access for PD patients to receive a catheter. Methods. We reviewed data from 78 charts of patients who received a PD catheter placement from 2007-2012 (Surgeon n=39; Nephrologist n=38). Our primary analyses examined the wait-time from referral to physician consult and the wait-time from physician consult to procedure between patients treated by a surgeon compared to a nephrologists. We also examined the percentage of patients with immediate (within one-month) and delayed complications following the procedure. Results. The complication rate for nephrologists was 18% for immediate and 16% for delayed. Patients had to wait significantly less time to see a nephrologist (median 1.36 weeks) compared to seeing a surgeon (5.71 weeks; $p<.05$). Similarly, patients only waited a median 1.14 weeks from the time of consult to have the procedure by a nephrologist but 6.29 weeks for a surgeon placement ($p<.05$). Conclusions. This research shows that nephrologists can successfully insert PD catheters with few patients experiencing immediate or delayed complications. The rates of complications were similar or lower than previous studies examining insertion of PD catheters. Given the current discrepancies in access to OR time and resources, this research suggests that nephrologists could continue to place PD catheters in non-complex cases, which would reduce wait-times without increasing the risk of complications for these patients. Decreasing the wait-time for PD catheters could also avoid some patients having to go on hemodialysis, which is more costly to the region.

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P-080

A RETROSPECTIVE REVIEW OF BONE DENSITY SCANS IN DIFFERENT STAGES OF CHRONIC KIDNEY DISEASE.

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Background. Our renal program undertook a retrospective chart review of all patients who underwent a baseline dual-energy X-ray absorptiometry (DXA) scan in our multidisciplinary CKD clinic from Jan 2001 to Jan 2010. The purpose of the study was to determine if there was a preferential site of bone loss in CKD patients across different disease stages. Methods. A total of 410 patients were included in the dataset. Measures included demographics, bone density measurements including T-scores and Z-scores for the lumbar spine, both hips, and the one-third distal radius, as well as the number of fractures. We compared these measures across patients in CKD Stages 2 through 5. Results. We found a significant decline in median bone density across Stages 2 through 5 for total hip (Χ2 (3) = 16.73, p=.001) and femoral neck (Χ2 (3) =12.76, p=.005) sites, but not lumbar spine or one-third distal radius. This decline was similar across CKD stages for both males and females but females generally had lower bone density overall. Similar results were found using bone mineral density T-Scores and Z-Scores. The percentage of patients suffering from a fracture, however, did not significantly change with CKD stage using a between-groups analysis (Χ2 (3) = 6.42, p=.09, Cramer's V = .13, p=.09). Conclusions. There is a demonstrable decline in total hip and femoral neck bone density with progression of CKD staging. In contrast, lumbar spine and distal radius bone mineral density were not affected by CKD stage. Although DXA scans provide information on BMD, they do not comment on trabecular and cortical microarchitecture and the resolution is too low to distinguish between cortical and trabecular bone. Future research will determine whether decreased bone density as determined by DXA scan is associated with increased fracture risk over time in the same patients.

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P-081

VALIDATING A SCORING TOOL TO PREDICT ACUTE KIDNEY INJURY FOLLOWING CARDIAC SURGERY

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Background: Acute kidney injury (AKI) after cardiac surgery is associated with increased mortality. Pre-operative risk scores help identify AKI patients to improve patient management. Current validated scoring tools can predict AKI requiring dialysis (AKI-D); it is unclear whether these tools predict less severe forms of AKI. The purpose of this study was to evaluate the Cleveland Clinic scoring tool in predicting both AKI-D and less severe AKI in patients in the Regina Qu'Appelle Health Region (RQHR). Methods: Data on risk factors for AKI were collected from a retrospective chart review of 2343 cardiac surgery patients (2007- 2011) in the RQHR. The primary outcomes were AKI and AKI-D. AKI was defined as an increase of serum creatinine 50% over baseline during the post-operative period in hospital; AKI-D was defined as patients who had at least one post-operative dialysis session in hospital. We assessed the performance of a modified version of the Cleveland Clinic tool using all available risk factor data. Results: The overall incidence of AKI was 9.7% and AKI-D was 5.4%. Patients with either type of AKI were older, more likely to have higher baseline serum creatinine, Type 1 diabetes, previous cardiac surgery, congestive heart failure, preoperative use of an intra-aortic balloon pump, and longer bypass time. Using ROC analyses, the area under the curve (AUC) for the Cleveland score was 0.79 (95% CI 0.75 to 0.83; $p<.001$) for the AKI-D group, and 0.65 (95% CI 0.62 to 0.69; $p<.001$) for the AKI group. The score was also a predictor of mortality for all patients (AUC=0.77; 95% CI 0.73 to 0.80; $p<.001$). Conclusions: We found the Cleveland Clinic tool to be valid in identifying patients with both AKI and AKI-D in the RQHR, which could help improve patient management following cardiac surgery.

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P-082

INTERVENTIONS TO REDUCE RESTLESS LEG SYNDROME SYMPTOM SEVERITY IN CHRONIC DIALYSIS PATIENTS: A SYSTEMATIC REVIEW

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Background and Objectives: Restless legs syndrome (RLS) is common amongst patients receiving dialysis. It is unclear how to optimally treat RLS in dialysis patients. We conducted a systematic review to identify therapies to reduce the severity of RLS. Methods: We systematically searched MEDLINE and EMBASE and hand searched narrative reviews for randomized controlled trials that assessed the use of pharmacological or non-pharmacological interventions to reduce the severity of RLS among patients receiving dialysis. The primary outcome was RLS symptoms. Results: Of 621 abstracts identified, 11 studies that included 13 interventions met the inclusion and exclusion criteria. All trials reported interventions that significantly improved RLS severity. The interventions included dopamine agonists (n=6), gabapentin (n=2), intradialytic exercise (n=2) intravenous iron (n=1), and vitamins (n=2). In studies that compared two interventions, ropinirole gabapentin, and intradialytic exercise each appeared more effective than L-dopa in single studies. However, all studies were at high risk of bias with the most common causes due to lack of allocation concealment, high losses to follow-up, and missing data. Further, follow-up for these studies was short-term ranging from 1 to 24 weeks. Conclusions: Ropinirole, gabapentin, and intradialytic exercise are promising agents to reduce RLS in patients that require dialysis. However, methodologically rigorous, appropriately powered, longer term RCTs are required to determine the optimal treatment strategy for RLS in this patient population.

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P-084

BIOIMPEDANCE ASSESSMENT OF VOLUME STATUS IN REFERRED PATIENTS WITH CHRONIC KIDNEY DISEASE: BASELINE DATA FROM BIO-CANPREDDICT

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Background. Volume status in patients with chronic kidney disease is difficult to assess. Establishing construct validity for new methods of assessment is challenging because no criterion measure exists. A modest correlation with other methods of assessment would suggest that the methods assess the same underlying construct, and confirm the potential for bioimpedance to provide more accurate information than the comparator studied. Methods. We measured bioimpedance, in triplicate, in patients with CKD who were already participating in CANPREDDICT. We analyzed the data according to the method of Piccoli, classifying patients based on the resistance (R) – reactance (Xc) graph. Results. We recruited 416 patients, median age was 70 (IQR 17) and 61 % were male. Median MDRD GFR was 28 mL/min/1.73 m2 (IQR 16), median urine albumin-creatinine ratio was 107 mg/L (IQR 391), 44% had diabetes, 26% ischaemic heart disease and 10% a history of congestive heart failure. Median physician-assessed volume status was 1 on a 1-to-7 scale (IQR 1) and volume status by bioimpedance was 1 on a 0-to-3 scale (IQR 2). For both scales higher values reflect worse volume overload. By bioimpedance, 179 (44%) of patients had normal volume status (0), 91 (22%) status of 1, 108 (26%) status of 2 and 33 (8%) status of 3. Correlation between physician-assessed and bioimpedance- measured volume status was 0.31 ($p < 0.001$). In multivariate analysis, volume status by bioimpedance was associated with age (OR 1.07 per year, 95% CI 1.05-1.10), gender (OR 0.56 for women, 95% CI 0.34-0.92) and diabetes (OR 2.3, 95% CI 1.26-4.09). Conclusion. Volume overload by bioimpedance is prevalent in referred patients with CKD. The moderate correlation with physician-assessed volume overload establishes construct validity for this method.

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P-085

PRE, POST AND DELTA SERUM POTASSIUM AND ASSOCIATION WITH MORTALITY IN HEMODIALYSIS PATIENTS

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Background: Electrolyte changes with hemodialysis have been implicated in sudden cardiac death.

Objectives: Primary - To determine if pre, post and/or delta K were associated with mortality. Secondary - To determine if post dialysis serum K could be predicted using commonly available parameters (usually not measured).

Methods: Data were from the MISSION Hemodialysis study; prospective observational 2-year study. Inclusion: 1) adult patients treated with HD for < 2 years, 2) expected to be treated for >3months. Basic demographic data, co-morbid illnesses and laboratory investigations from baseline were used for this study. Mortality was documented during the study. Logistic regression was used to determine the predictors of mortality. Linear regression was used to predict post dialysis K.

Results: The study included 99 participants. Average age of the patients was 66 years; 65% male. The median CCI score was 7 (IQR 5-9). In multivariable analysis, the predictors of mortality included predialysis K, use of beta-blockers and albumin (p=0.048, 0.026, 0.01 respectively). The prediction equation for post dialysis K can be seen in Figure 1.

Conclusions: Although we did find that pre-dialysis K was associated with mortality, this association did not exist for delta K or post dialysis K. It is unclear if these results are due to small sample size and a limited number of events. We have developed a prediction equation for post dialysis K that requires external validation before utilizing in a larger data set to explore the importance of post dialysis K in sudden cardiac death.

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P-086

INTRADIALYTIC EXERCISE TRAINING IN HEMODIALYSIS PATIENTS – IMPACTS ON FUNCTIONAL CAPACITY: A PILOT STUDY

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Background: Exercise has been shown to be beneficial in chronic kidney disease (CKD) patients with improvements in cardiac function, blood pressure and quality of life. The functional capacity of hemodialysis, HD patients can be determined using a simple validated patient survey – the Duke Activity Status Index (DASI).

Objective: The primary objective of this pilot study was to explore the impact of a twelve-week intradialytic exercise program on the functional capacity of chronic HD patients.

Methods: A prospective cohort of 45 stable, chronic HD patients was evaluated at baseline and after twelve weeks of intradialytic exercise to assess functional capacity (DASI), strength (STS, sit-to-stand, grip strength right and left hands), urea clearance (URR) and phosphate level. Patient demographics, pre and post blood pressures on dialysis and the number of symptomatic and asymptomatic episodes of intradialytic hypotension were tracked. Patients performed intradialytic biking 3-times per week at moderate intensity (Borg scale 5). The duration of exercise achieved per dialysis session was documented.

Results: The mean age was 55 years, 82% male, with co-morbidities of hypertension (84%), diabetes (53%), coronary artery disease (38%), peripheral vascular disease (27%), congestive heart failure (20%) and cancer (18%). There was no change in the primary outcome, DASI score with intradialytic biking. The STS score increased with the 12 week exercise program (Table).

Conclusion: Intradialytic exercise was associated with an increase in lower limb strength and no change in the score for the global subjective function (DASI).

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P-087

TARGETING THE LOSS OF THE VON HIPPEL-LINDAU GENE IN RENAL CELL CARCINOMA: QUANTITATIVE PROTEOMIC TO IDENTIFY CANDIDATE EFFECTORS OF A SMALL MOLECULE

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P-088

ADVANCING QUALITY IN END-OF-LIFE CARE FOR PATIENTS WITH KIDNEY DISEASE IN BRITISH COLUMBIA

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Background: Acknowledging the needs and importance of delivering quality end-of-life (EOL) care for renal patients, the BC Provincial Renal Agency (BCPRA) developed a provincial EOL framework which articulated four pillars of EOL care: Patient identification, advance care planning, symptom assessment & management and care of the dying patient and bereavement. As set out in the framework, the need to assess both processes and outcomes are essential to quality improvement in each of these four areas of EOL care. Objectives: To develop and implement an evaluative framework which will provide data for strategic planning and continuous quality improvement in EOL care for renal patients. Methods: An environmental scan was conducted to assess current state and perceptions of EOL care among care providers using a survey and interviews with individual EOL champions in the Health Authority Renal Programs (HARPs). Literature review was carried out to identify tools for measuring the quality of dying and death from various perspectives. Results: Implementation of the EOL framework varies across the HARPs with each having formalized strategies to facilitate ongoing growth in EOL care. Specifically, prominent improvements were shown in symptom care & management and advance care planning. The majority of survey respondents deemed standardizing agreed-upon measures (79%) and evaluating EOL care at a provincial level (93%) provincially as "very" and "moderately" important on a 5-point Likert scale. Key challenges identified include enabling the organizational culture, sustaining quality EOL care and continual improvement. Conclusions: From the environmental scan, we were able to identify enablers, barriers and opportunities in advancing EOL care provincially. Our next steps include selection and testing of tools for measuring quality of death, establishing provincially agreed-upon outcome and process measures for population-based monitoring of progress for continual improvement in EOL care for renal patients, their families and caregivers.

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P-089

DONOR-SPECIFIC ANTIBODIES, C4D AND THEIR RELATIONSHIP WITH THE PROGNOSIS OF LATE TRANSPLANT GLOMERULOPATHY

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Background and objectives: Transplant glomerulopathy (TG) is included in the Banff classification as a diagnostic criterion for chronic active antibody-mediated rejection (CAABMR), with C4d, antidonor antibodies (DSA) and other lesions of chronic tissue injury. However, TG often presents without C4d or DSA. Until recently, such cases were termed suspicious for CAABMR, and their prognosis remains unclear. Design, setting, participants, and measurements: To better understand the contribution of TG, C4d and DSA on outcomes, we retrospectively studied 61 patients with late TG for the composite endpoint of death-censored graft failure or doubling of serum creatinine. Cases were matched to controls based on age, year and number of transplant, type of donor and the availability of an indication biopsy during the same time post transplant. Analyses were performed using unadjusted and adjusted proportional hazards models. Results: Compared to matched controls, patients with TG had a more than 5-fold increased risk of reaching the endpoint (adjusted hazard ratio (aHR) 5.3; 95% CI:1.5-18.4). The proportion of patients with isolated TG, TG suspicious for CAABMR (C4+/DSA- or C4d-/DSA+) and TG with definite CAABMR (C4d+/DSA+) were 63, 20 and 17% respectively. Suspicious and definite CAABMR had a similar prognosis, significantly worse than isolated TG (aHR 4.5, 95% CI:1.1-18.9 and 5.9, 95% CI:1.1-31.3 respectively). 29% of patients with suspicious or definite CAABMR who received intensive therapy with plasma exchange and/or rituximab reached the endpoint compared to 89% in patients who received less intensive therapy (p=0.006). Conclusions: Late TG is associated with poor prognosis beyond other chronic changes. This prognosis is similar whether there is evidence of tissue or peripheral alloantibody reactivity. These findings are relevant to the development of clinically meaningful criteria for CAABMR, for its clinical management and in the future selection of population for clinical trials.

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P-090

PREVALENCE OF FRAILTY IN PATIENTS ON HOME DIALYSIS

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Background: Patients with kidney failure on dialysis are often elderly and have a diminished quality of life. Frailty is common in patients on in-center hemodialysis and is associated with adverse outcomes. Little is known about the burden of frailty in the home dialysis population. The purpose of this study was to examine the prevalence of frailty in the home hemodialysis (HHD) and peritoneal dialysis (PD) populations. Methods: We approached all patients on either home hemodialysis or peritoneal dialysis attending a multidisciplinary clinic at a tertiary care center for enrollment in the study. We excluded patients who did not speak English or were unable to provide informed consent. We collected demographic variables, laboratory values, and performed a detailed assessment of frailty using a modified Fried frailty criteria and Short Physical Performance Battery (SPPB) in addition to physician and nurse evaluations. Results: We evaluated 46 PD patients and 27 HHD patients at the baseline study visit. The mean ages for the PD and HHD patients were 55.1 and 59.3 years respectively. The prevalence of diabetes in the PD population was 50%, and in the HHD population was 37%. Frailty was common in both populations, with 41 % of the PD patients and 44 % of the HHD patients deemed frail. Both physicians and nurses underestimated the burden of frailty in the PD population (Physician evaluation 22 % vs. SPPB 41 %). Conclusions – Frailty is common in patients on home dialysis (peritoneal and home hemodialysis). Physician and nurse evaluations may underestimate the burden of frailty in these populations. Longitudinal assessments of frailty and physical function in patients on home dialysis are needed.

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P-091

RENAL REPLACEMENT THERAPY FOLLOWING PEDIATRIC CARDIAC SURGERY: A LOCAL REVIEW OF OUTCOMES AND RENAL RECOVERY

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Objectives: 1) Describe the outcomes of patients requiring renal replacement therapy (RRT) following cardiac surgery including mortality, duration of RRT and likelihood of renal recovery 2) Explore the potential predictors of renal recovery following RRT.

Methods: We reviewed our PICU database for all patients between 2008-2013 who required cardiac surgery and received RRT post-operatively. A detailed chart review was then performed using a standardized data extraction form.

Results: 1184 (3%) patients required RRT following cardiac surgery. The median age and weight at surgery was 66 days and 4.29 kg respectively. 28/37 (76%) patients received PD, 5/37 (14%) continuous renal replacement therapy (CRRT), and 4/37 (10%) both during their admission. 16/37 (43%) required ECMO post-operatively. The overall mortality rate was 32% (12/37) and was significantly higher in patients requiring ECMO (10/16, 62%). 10/37 (27%) patients failed to recover renal function, all of whom died. In patients who recovered function the median length of RRT was 5 days with a maximum of 19 days (Figure). The following variables were significantly associated with a failure to recover renal function: lowest diastolic pressure intra-operatively, number of blood transfusions, post-operative chest compressions, requirement of ECMO, suspected or confirmed necrotizing enterocolitis, re-intubation and re-initiation of inotropes ($p<0.05$).

Conclusions: RRT following cardiac surgery in the pediatric population is a relatively uncommon event, but carries a high mortality. Our local results suggest that the majority of patients recover renal function before 2 weeks. Confirmation in larger cohorts is needed before reliable prognostication can be made.

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P-092

The Canadian Society of Nephrology Methods in Developing and Adapting Clinical Practice Guidelines: A review

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Introduction: The Canadian Society of Nephrology (CSN) was established to promote the highest quality of care for patients with renal diseases and to encourage research related to the kidney and its disorders. The CSN Clinical Practice Guideline (CPG) Committee develops guidelines with clear recommendations to influence physicians' practice and improve the health of patients with kidney disease in Canada. Review: In this review we describe the CSN process in prioritizing CPGs topics. We document the CSN experience using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach. We then detail the CSN process in developing de novo CPGs and in adapting existing CPGs and developing accompanying commentaries. We also discuss challenges faced during this process and suggest solutions. Furthermore, we summarize the CSN effort in disseminating and implementing their guidelines. Additionally, we describe recent development and partnerships that allow evaluation of the effect of the CSN guidelines and commentaries. Conclusion: The CSN follows a comprehensive process in identifying priority areas to be addressed in CPGs. In 2010, the CSN adopted GRADE, which enhanced the rigor and transparency of guideline development. This process focuses on systematically identifying all available evidence and carefully assessing its quality, balancing benefits and harms, considering patients' and societies' values and preferences, and when possible considering resource implications. Recent partnership allows wider dissemination and implementation among end users and evaluation of the effects of CPG and commentaries on the health of Canadians.

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P-093

PHARMACOKINETIC STUDY OF CEFAZOLIN IN SHORT DAILY HEMODIALYSIS

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Background: A number of centres across Canada offer short-daily hemodialysis (SDHD) treatments. Dialysis sessions are on average two hours in duration performed six times per week. As with intermittent hemodialysis, infections requiring treatment with cefazolin are common. To date, cefazolin pharmacokinetics have not been described in patients undergoing SDHD. The primary objective of this study was to investigate the effect of SDHD on the pharmacokinetics of cefazolin. Methods: Prospective, observational, single-centred study. Five non-infected adults undergoing SDHD were enrolled. Participants received a 1 g intravenous infusion of cefazolin after SDHD on study day one, and a second dose after SDHD on day two. To determine the concentration of cefazolin, six blood samples were drawn at 0, 1, 2, 2.3, 4, and 24 hours after initiation of dialysis on day two, and two dialysate samples were drawn at 1 and 2 hours after initiation of dialysis on day two. Samples were analyzed using high-performance liquid chromatography (HPLC) and pharmacokinetic parameters were determined. Results: Median off-dialysis clearance was 3.6 mL/min (IQR: 2.6-4.8 mL/min) and median on-dialysis clearance was 41.9 mL/min (IQR: 37.7-87.3 mL/min). Median off-dialysis half-life was 25.8 hours (IQR: 22.7-27.3 hr) as compared to a median on-dialysis half-life of 1.6 hours (IQR: 1.6-2.2 hr). The percent removal of cefazolin during dialysis varied between patients, ranging from 34.2 to 93.3 % with a median of 56.2% (IQR: 34.2-56.2%). Conclusion: Estimated cefazolin dialysis clearance is higher than previous estimates with thrice weekly regimens. Current dosing recommendations appear to achieve serum drug concentrations that meet existing standards for microbiological eradication. Further study is warranted in a larger cohort of patients.

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P-094

EVALUATING TIME IN THERAPEUTIC RANGE FOR HEMODIALYSIS PATIENTS ON WARFARIN

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Warfarin is frequently used in the hemodialysis (HD) population for patients with atrial fibrillation (AF) and venous thromboembolism (VTE); however, there is a lack of literature to support this practice. Given that HD patients have a 3-10 times higher risk for both stroke and bleeding than the general population, anticoagulation in these patients is controversial. Time in therapeutic range (TTR) has been accepted as a surrogate outcome of clinical effectiveness and safety of warfarin and is used extensively as an endpoint in clinical trials with a benchmark goal of 66%. To evaluate TTR in an HD population, a six-year retrospective chart review was performed in 46 HD patients with AF or VTE on warfarin. One year of individual patient data was collected, which included weekly INR values, demographics, medication histories and clinical outcomes. TTR was calculated using the Rosendaal, fraction of INRs in range (FIR) and cross-section-of-the-files methods. The mean TTR using Rosendaal and FIR was 49.2%±14.6 and 44.2%±13.5, respectively. The cross-section-of-the-files method captured INR data for 35 patients and TTR was 33.3%, 36.4%, 31.4% and 43.3% at four points during 2011. The percentage of time spent below and above target INR was 39.3%±16.2 and 10.0% (6-15.5) respectively for the Rosendaal method, suggesting that more often patients were at risk of inadequate efficacy rather than toxicity. There were 9 serious bleeding and 9 thrombotic events; these all occurred in patients with a TTR <60%. A survey of nephrologists in the unit revealed that they often target an INR range lower than 2-3 due to insufficient evidence and higher bleeding risk. In conclusion, our data suggests this HD unit is not meeting the TTR goal previously established and that clinicians are conservative with INR management. Ultimately, a prospective study evaluating the safety and efficacy of warfarin in HD patients is needed.

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P-095

SUCCESS OF AN URGENT-START PERITONEAL DIALYSIS PROGRAM IN A LARGE CANADIAN CENTRE

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Background: Many patients start renal replacement therapy urgently on in-centre hemodialysis via central venous catheters, which is suboptimal. An alternative approach to manage these patients is to start them on peritoneal dialysis. In this report, we describe the first reported Canadian experience with an urgent-start peritoneal dialysis (PD) program. Additionally we reviewed the literature in this area. Methods: In this prospective observational study we report on our experience in a single academic centre. This program started in July 2010. We included patient who initiated PD urgently, that is within 2 weeks of catheter insertion. We followed all incident PD patients until October 2013 for mechanical and infectious complications. PD catheters were inserted either percutaneously or laparoscopic and dialysis was initiated in either an inpatient or outpatient setting. Results: Thirty patients were started on urgent PD during our study period. Follow up ranged from 28 to 1050 days. Twenty insertions (66.7 %) were done percutaneously and ten (33.3%) were laparoscopic. Dialysis was initiated within two weeks (range:0-13 days, median=6 days). Twenty-four patients (80%) started PD in outpatient setting and six patients (20%) required immediate inpatient PD start. Three patients (10%) developed a minor peri-catheter leak during first week of training that was managed conservatively. There were no episodes of peritonitis or exit site/tunnel infection during first 4 weeks post insertion. Four patients (13.3 %)from the percutaneous insertion group and two patients (6.7%)from laparoscopic insertions developed catheter dysfunction due to migration, which was managed by repositioning without need for catheter replacement or modality switch. Conclusions: Our results are consistent with other studies in this area and demonstrate that urgent-start PD is an acceptable and safe alternative to hemodialysis in patients who need to start dialysis urgently without established dialysis access.

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ACUTE CHANGE IN GLOMERULAR FILTRATION RATE WITH INHIBITION OF THE RENIN-ANGIOTENSIN SYSTEM AS A PREDICTOR OF FUTURE RENAL AND CARDIOVASCULAR OUTCOMES.

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Background. Initiation of blockade of the renin-angiotensin system (RASi) can cause acute decrease in glomerular filtration rate (GFR). This acute decrease may predict long-term renal outcomes. Objective. To investigate the relationship between acute RASi-induced change in GFR and subsequent renal & cardiovascular outcomes in a cohort with vascular disease. Methods. Cohort analysis of ONTARGET & TRANSCEND trials. Patients with, or at high risk for, vascular disease; mean follow-up 56 months, 9340 with initiation of RASi,. We estimated GFR at initiation of RASi (week 0), and week 2, week 8, 2 years, and study end, and measured urine albumin-creatinine ratio. We analyzed the relationship between the primary renal outcome (chronic dialysis or doubling in creatinine) and primary cardiovascular outcome (cardiovascular death, myocardial infarction, stroke, or hospitalization for heart failure) from (A) week 8 to study end and (B) from week 0 to study end. Results. Analysis A: A rise in GFR within 2 to 8 weeks after initiation of RASi was associated with a significant increase in subsequent (after week 2-8) primary renal outcomes and new micro-& macroalbuminuria. A fall in GFR was associated with a non-significant trend for fewer subsequent renal outcomes but not with albuminuria. Analysis B: When renal outcomes were analyzed from week 0 to study end, a initial rise in GFR was associated with fewer, and a fall with more renal outcomes, mainly doubling in serum creatinine. Cardiovascular outcome exhibited a U-shaped association with the initial change in GFR: both a rise and a fall in GFR predicted more outcomes. Conclusions. In people with vascular disease and little change in GFR (mean < 1mL/min/1.73m2 per year) over 56-months follow up, RASi-induced change in GFR was associated with contrasting long-term renal outcomes, depending on whether the doubling-in-creatinine outcome was calculated from baseline, or from 2 or 8 weeks

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ALBUMINE/CREATININE RATIO AND ITS VARIATION ACROSS FIRST AND SECOND TRIMESTERS AS A PUTATIVE MARKER OF HYPERTENSIVE DISORDERS OF PREGNANCY

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Introduction: Albuminuria, a known risk marker for renal and cardiovascular morbidity in the general population, is associated with an increased risk of hypertensive disorders of pregnancy (HDP). As of today, there are no optimal tests to predict the occurrence of HDP. Objectives: To assess albumin/creatinine ratio (ACR) and its variation across first and second trimesters as a marker of HDP. Methods: This was a prospective observational and longitudinal pilot study. From March 2010 to June 2011, pregnant women were recruited during their first trimester at the Blood Sampling in Pregnancy Clinic at our Clinical Research Centre. Obstetrical/medical history, blood pressure, renal and diabetes laboratory values were collected at first and second trimester visits. Pregnancy outcomes and severe maternal/fetal complications were abstracted from medical charts. Standard descriptive/comparative analyses then univariate/multivariate logistic regressions were performed. Results: Among 489 women, 44 (9,0%) were diagnosed with an HDP. 33 (6,7%) women had gestational diabetes (GDM), of those, only 4 had an HDP. Mean systolic and diastolic blood pressures were significantly higher from the first trimester in women with an HDP compared to those without an HDP ($p<0.001$). ACR levels for both visits, as well as variation of ACR, were very low (median 0, interquartile range 0-0) without significant difference between groups with and without HDP, as well as for women with GDM. In the latter group, there was a trend for increased uric acid levels in the first trimester ($p=0.056$). Univariate and multivariate logistic regressions showed no association between ACR levels at both visits or variation of ACR and the occurrence of maternal or fetal complications. Conclusion: In this small sample, ACR levels in first or second trimesters and its variation were very low and not associated with the occurrence of HDP or GDM, nor predicted maternal or fetal complications.

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ACCELERATED RECEPTOR SHEDDING INHIBITS KIDNEY INJURY MOLECULE-1 (KIM-1)-MEDIATED EFFEROCYTOSIS

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Efficient clearance of apoptotic cells (efferocytosis) prevents inflammation and permits repair following tissue injury. Kidney injury molecule-1 (KIM-1) is a receptor for phosphatidylserine, an "eat me" signal exposed on the surface of apoptotic cells that marks them for phagocytic clearance. KIM-1 is upregulated on proximal tubule epithelial cells (PTECs) during ischemic acute kidney injury (AKI), enabling efferocytosis by surviving PTECs. KIM-1 is spontaneously cleaved at its ectodomain region to generate a soluble fragment that serves as a sensitive and specific biomarker for AKI, but the biological relevance of KIM-1 shedding is unknown. Here, we sought to determine how KIM-1 shedding might regulate efferocytosis. Using cells that endogenously and exogenously express KIM-1 we found that hydrogen peroxide-mediated oxidative injury or phorbol-12-myristate-13-acetate (PMA) treatment accelerated KIM-1 shedding. Moreover, accelerated shedding or the presence of excess soluble KIM-1 in the extracellular milieu significantly inhibited efferocytosis. We also identified that tumor necrosis factor alpha-converting enzyme (TACE or ADAM17) mediates both the spontaneous and PMA-accelerated shedding of KIM-1. While accelerated shedding inhibited efferocytosis, we found that spontaneous KIM-1 cleavage does not affect the phagocytic efficiency of PTECs. Our results suggest that KIM-1 shedding is accelerated by worsening cellular injury, and excess soluble KIM-1 competitively inhibits efferocytosis. These findings may be important in AKI when there is severe cellular injury.

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THE POTENTIAL IMPACT OF FINANCIAL INCENTIVES ON PARTICIPATION OF DIRECTED COMPATIBLE LIVING DONORS IN KPD

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The use of financial incentives to encourage medically suitable compatible donors already approved for directed donation, to participate in KPD may be a non-coercive strategy to increase transplants. To inform this strategy we surveyed previous living donors and recipients regarding their willingness to participate in KPD with and without financial incentives.

An anonymous survey was mailed to previous directed donors and recipients in our program between 2001-2009.

93% (78/86) of donors and 95% (35/38) of recipients indicated that they would have participated in KPD had it been offered at the time of their transplant. The table shows the proportion of donors and recipients who would be more willing to participate in KPD with the provision of different types of financial incentives.

The survey also identified non-financial considerations that would limit participation including: delays in transplantation >3 months, inability to complete a preemptive transplant, or a requirement to travel. The potential to obtain a better donor kidney (younger donor, higher HLA match) was rated important by 87% of donors, while helping multiple recipients was important to 80% of donors. Irrespective of the amount offered, a direct cash reward did not increase willingness to participate in KPD.

We conclude that >90% of previous directed donors and their recipients reported a willingness to participate in KPD if they had been provided the opportunity. Reimbursements for travel and lost wages, but not direct cash rewards may increase participation, while delays in transplantation > 3 months may decrease participation of directed compatible donors in KPD.

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INCIDENCE, RISK FACTORS, AND OUTCOMES OF PREGNANCY-RELATED ACUTE KIDNEY INJURY TREATED WITH DIALYSIS

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Background: Acute kidney injury (AKI) is a rare complication of pregnancy, but may be associated with significant morbidity and mortality in young and often otherwise healthy women. As renal dysfunction in pregnancy may be missed or misclassified using serum creatinine based definitions of AKI, we report the incidence of AKI treated with dialysis and describe the associated risk factors and short-term maternal and fetal outcomes. Methods: We used data from universal health care databases to study all consecutive pregnancies in Ontario over a 15-year period. Maternal outcomes included acute dialysis during the peripartum period, 90-day mortality, and dialysis dependence among women who survived beyond 90 days. Fetal outcomes included low birthweight, small for gestational age or intrauterine growth restriction, premature birth, stillbirth, neonatal death, and perinatal mortality. Results: There were a total of 1,918,789 pregnancies in Ontario between 1997 and 2011. The cumulative incidence of acute dialysis during pregnancy was 1:10,000 over the study period. Among women who received acute dialysis, 4.3% died within the 90-day postpartum period and 3.9% of survivors were dialysis dependent. Adverse fetal outcomes associated with AKI treated with dialysis during pregnancy included low birthweight (unadjusted relative risk [RR] 4.7, 95% confidence interval [CI] 3.6 – 6.0), small for gestational age (RR 3.2, 95% CI 1.9 – 5.3), and premature birth (RR 2.5, 95% CI 2.0 – 3.1). Conclusions: The incidence of AKI treated with dialysis is low, but adverse maternal and fetal outcomes exist. These results provide important prognostic information for patients and reinforce the role of the nephrologist in pre-conception counseling, risk factor reduction, and monitoring during pregnancy for women at risk.

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SYSTEMATIC IMPLEMENTATION OF A PROTOCOL TO IMPROVE SYMPTOM MANAGEMENT IN HEMODIALYSIS PATIENTS AT VANCOUVER GENERAL HOSPITAL.

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Background: Dialysis patients experience a high symptom burden, which has historically been under-reported and not systematically assessed. Symptom assessment tools like the Edmonton Symptom Assessment Scale (ESAS) are increasingly being used in chronic patient care settings as a way to engage patients in the symptom assessment process, resulting in improved identification and management of symptoms. Objectives: To systematically implement a protocol to improve symptom assessment and management in hemodialysis patients at Vancouver General Hospital using a patient centered approach. Methods: A rapid process improvement testing method was used to optimize the process for systematic symptom assessment using the modified ESAS (mESAS). Surveys were used to gather ongoing feedback from frontline staff and patients to inform this effort. Results: Initial Plan-Do-Study-Act (PDSA) cycles were carried out with promising progress on the uptake of the mESAS in the VGH HD unit. Outcome and process measures have also been established for monitoring the improvement process. To date, approximately 50% of patients on the hemodialysis units have completed the mESAS with a completion rate of 80%. Following brief explanation of the mESAS, most patients have been willing to complete the checklist. Patient and staff surveys have provided constructive and practical information to guide continuous improvement in symptom care. Conclusion: Routine patient-centered symptom assessment can help to reduce overall symptom burden. Although not all problematic symptoms can be eliminated, increased discussion about symptoms may reduce symptom burden and generally improve patient's health related quality of life. Systematic introduction of mESAS into our unit has resulted in significant progress to date with high patient involvement and good staff engagement. We will continue to document the process as well as impact on both patients and staff as the initiative progresses. Source of Funding: Vancouver General Hospital Hemodialysis Education Fund.

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BLOOD OUTGROWTH ENDOTHELIAL CELLS (BOECS) AS A MODEL TO STUDY ATYPICAL HEMOLYTIC UREMIC SYNDROME

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Background Atypical hemolytic uremic syndrome (aHUS) is due to defective regulation of the alternative complement pathway which is constitutively active and requires a multi-layered defense system. It remains unclear how this multilayered system functions as a whole to protect injured cells and why loss or diminished function of one of these regulators results in disease. Objectives We aimed to establish the technique of BOEC culture, endothelial cell precursors that can be grown from patients, and use BOEC in an ex vivo model to study cellular and humoral elements involved in aHUS and to assess the contribution of these biologically relevant components. Methods BOECs were cultured from control subjects by a standard protocol. Endothelial phenotype and presence of endothelial cell (EC) complement regulators was confirmed by immunofluorescence (IF), western blot (WB), qPCR and flow cytometry. Cells were challenged with complement, in both static and microfluidic conditions with or without functional blockade of complement regulators. Readouts included IF and flow cytometry demonstration of complement product deposition, EC activation and platelet aggregation. Results BOECs were cultured from 4 adult donors and colonies appeared at a mean of 12.8 (range 9-19) days. BOECs were positive on IF and WB for EC markers (including von Willebrand Factor (VWF), CD31/PECAM-1 and Caveolin-1). BOECs were characterized by flow cytometry (positive for CD31/PECAM-1 and CD144/VE-cadherin; negative for the haemangioblast marker CD45 and immature endothelial progenitor cell marker CD14). Surface expression of EC complement regulators (including CD46/MCP, CD59/Protectin, and CD55/DAF) was confirmed by IF, flow and PCR. Complement deposition, confirmed by IF and flow cytometry, could be further enhanced by blocking complement regulators resulting in a prothrombotic phenotype of the cells. Conclusion We have established an ex vivo method to model aHUS pathogenesis that can now be expanded to use patient-derived BOECs.

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USE OF IPADS TO ASSESS HEALTH-RELATED QUALITY OF LIFE IN CLINICAL NEPHROLOGY NURSING PRACTICE

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Background: Given the need for integration of patient reported outcomes (PROs) into research, electronic capture of PROs are important aspects of clinical nephrology research initiatives. It is particularly important because health-related quality of life (HRQOL) for patients with end-stage renal disease is compromised and assessment by patients of their HRQOL in practice is relatively uncommon. Objective: The aim of this study was to evaluate the feasibility of administering HRQOL and symptom assessment measures using iPads in outpatient home hemodialysis and peritoneal dialysis clinics. Methods: Fifty-six patients from two home dialysis clinics participated in the study: 35 males (63%) and 21 females (37%) with a mean age of 66 ± 12 (36-90 years old) were included. Forty-nine participants were on peritoneal dialysis (87%), 6 on home hemodialysis (11%), and 1 on nocturnal home hemodialysis (2%). They completed the Kidney Disease Quality of Life-36 questionnaire online, and the modified Edmonton Symptom Assessment Scale and Participant's Level of Satisfaction in using a Tablet Computer using newly created apps. Patients were also interviewed about their experiences with using the iPad for the study. Direct access to the health authority's internet network was not possible, so data collection proceeded using a 3G connection. Results: Participants' level of satisfaction using an iPad was high. There were no significant correlations between their level of satisfaction and age, gender, HRQOL, time taken to complete surveys, computer experience, or comfort with technology, and none of these independent variables explained satisfaction. Comfort with technology and computer experience were highly correlated, $r = .62$, p (two-tailed) $< .01$. Conclusions: It is feasible to administer HRQOL measures using iPads. Routine use of HRQOL for clinical purposes may be facilitated through use of iPads. The ease of data collection may offer opportunities to use HRQOL data for patient care and/or quality improvement programs.

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INCIDENCE OF BLOOD STREAM INFECTIONS IN APHERESIS: COHORT STUDY

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Background: Patients receiving apheresis are at risk of infectious complications because of their illnesses and the access required for the procedure.

Objectives: To determine the incidence of blood stream infections (BSI) in a cohort receiving apheresis.

Methods: Patients receiving apheresis between 2000-2011 were identified and all BSI episodes were ascertained from a regional microbiology database. BSI incidence was calculated within 30 and 90 days of the first procedure. Risk ratios (RR) for BSI were calculated according to access type and indication for the procedure.

Results: 1097 patients (6618 procedures) with an average age of 53 years (45% female) were analyzed. 175 BSI (17% of patients) were identified. In the cohort, there were: 11.8% healthy allogeneic donors (Allo), 56.2% autologous donation patients (Auto), 28.1% plasma exchange patients (TPE), and 3.9% photopheresis (Photo) patients. Access types included: 2.7% arterio-venous fistulas, 51.9% temporary central venous catheters (CVCs), 39.5% permanent CVCs, and 5.9% used peripheral veins. The incidence of BSI did not differ when all other access types were compared to peripheral venous access. The risk of BSI was significantly increased for Auto, TPE, and Photo patients compared to Allo patients (Table 1).

Conclusions: Access type does not appear to be associated with the risk of BSI in apheresis. Compared to Allo patients, those undergoing TPE, Auto, and Photo are at increased risk. This suggests that patient characteristics (including underlying diseases and other treatments) are more important risk factors for BSI in apheresis than the access itself.

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THE EFFECT OF AN EXERCISE COUNSELING CLINIC ON PHYSICAL FUNCTION IN INDIVIDUALS WITH CHRONIC KIDNEY DISEASE (CKD)

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Background: Individuals with CKD have low levels of physical function (PF) which decline over time. We investigated the impact of attending a formal exercise counseling clinic (ECC) on PF in individuals with CKD within a large provincial renal program using a retrospective observational cohort design.

Methods: Individuals who attended the ECC from Jan 1, 2011 – May 31, 2013 and provided consent for data entry into the research database were eligible. Primary outcome was change in PF from baseline to 1 year, measured by Short Physical Performance Battery (SPPB). PF over time was compared using the Wilcoxon Signed Rank Test. We also compared baseline characteristics and PF of ECC patients with a convenience control group (CG) of patients not referred to ECC.

Results to date: Baseline and 1-year follow-up ECC visits occurred in 174 and 67 individuals, respectively. ECC attendees were predominately male (54%) and diabetic (55%) with mean age 60 (SD 14.5)

Forty-three per cent of patients were on dialysis and 29% had CKD Stage 4-5. Baseline characteristics for ECC and control cohorts were similar, except a smaller proportion of the control group was on dialysis and ECC attendees had higher baseline SPPB scores (10 (IQR: 9-12) vs. 9 (IQR: 6-11), respectively; p <0.001). At 1 year, physical function was maintained overall in the ECC group and slightly improved in several subgroups (Table 1).

Conclusions: Attendance at an ECC may prevent the progressive decline in PF in CKD patients. Further analyses of follow-up data in the CG are planned.

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HEALTH PROFESSIONALS' PERSPECTIVES ON THE GIFT EXCHANGE IN ALTRUISTIC UNBALANCED PAIRED KIDNEY EXCHANGE AND KIDNEY PAIRED DONATION

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Background: The gift exchange cycle is characterized by a triple set of norms: to give, receive and repay. Do new modalities of living organ donation such as kidney paired donation (KPD) and altruistic unbalanced paired kidney exchange (AUPKE) alter the gift relationship? The aim of this study is to examine how health professionals view the gift relationship in AUPKE and KPD. Methods: A total of 19 transplant professionals working in 4 Canadian transplant programs, and 19 non-transplant professionals (referring nephrologists and pre-dialysis nurses) working in 5 Quebec dialysis centres took part in semi-structured interviews between 11/2011 and 06/2013. The content of these interviews was analyzed using a qualitative data analysis method. Results: To give: Respondents mentioned that the principal motivation to donate in AUPKE would be altruistic, since the donor would help more individuals than in living related donation. To receive: Respondents were divided on the issue of receiving a kidney from a loved one or stranger. For some, the priority was for the recipient to get a functioning kidney; others acknowledged the importance of receiving a kidney from a known donor because of the emotional relationship and knowledge of the donor's lifestyle. To repay: For many respondents, AUPKE or KPD would not alter the obligation to repay, since the recipient's gratitude would be the same, regardless of the donor. Also, AUPKE or KPD could mitigate the "tyranny of the gift" that can occur in living related donation. On the other hand, some respondents believed that being related to the donor could be an added incentive for recipients to adhere to their treatment regimens. Conclusion: The results of this study show that respondents were divided on how AUPKE and KPD could alter the gift exchange in living organ donation.

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IS IT ETHICAL TO PRESCRIBE GENERIC IMMUNOSUPPRESSIVE DRUGS TO OUR TRANSPLANTED PATIENTS?

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In various countries, drug patents for immunosuppressive drugs have recently expired or are about to expire. As a result, generic versions of these immunosuppressive drugs have emerged on the market. The use of generic drugs is widely accepted for chronic diseases such as hypertension and dyslipidemia. In organ transplantation, the use of generic drugs is debated. Some transplant societies discourage their use while others recommend extreme caution. This reluctance to use generic drugs in organ transplantation is partly related to the fact that most of these drugs are "critical dose drugs" and either low dosing of the drug or overdosing could have serious adverse consequences for the patient. This situation led us to question whether it was ethical to prescribe generic immunosuppressive drugs to transplanted patients. How much evidence and how many bioequivalence studies are needed to ensure the safety of generic drugs? Do the beneficence and nonmaleficence principles require the use of brand name immunosuppressive drugs? Given that transplant physicians are stewards of a precious resource (organs), should they prescribe brand name immunosuppressants in order to minimize the risk of rejection? Should patients be involved in the debate and how should physicians help them make informed decisions? Are there any conflicts of interest that might influence the debate? From a societal point of view, is the use of brand name immunosuppressive drugs a fair allocation of resources? Our review of the literature and ethical analysis led us to conclude that it would be ethical, under certain circumstances, to prescribe generic immunosuppressive drugs. That said, further health economics studies are needed to look at all of the costs related to the substitution (e.g., frequent and closer monitoring of patients).

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RETROSPECTIVE COHORT STUDY OF ANTIMICROBIAL USE AMONG OUTPATIENT HEMODIALYSIS PATIENTS IN A CANADIAN TERTIARY CARE HOSPITAL

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Rationale: Current guidelines emphasize developing antimicrobial stewardship programs for hemodialysis (HD) centers. Stewardship may be challenging as infection is the second leading cause of death among this medically complex population. Previous studies underestimate exposure by only focusing on intravenous antimicrobials prescribed by nephrologists. Objectives: This study aimed to determine 1) the frequency and pattern of antimicrobial prescribing among HD outpatients; 2) the current level of documentation accompanying antimicrobial prescriptions including clinical presentation and presumed site of infection. Methods: A retrospective cohort study was conducted among prevalent HD outpatients at a tertiary-care center in Toronto, Canada. Data on antimicrobial prescriptions from both nephrology and non-nephrology prescribers between 1 December 2012 and 1 June 2013 were gathered through review of patient charts and electronic medical records. Information was collected on whether or not the clinical presentation prompting initiation of the antimicrobial and presumed site of infection were documented within the chart. Results: Of the 210 patients, 88 (42%) were prescribed at least one antimicrobial during the 6 month period. Overall 204 antimicrobials were prescribed, with an average of 17.7 prescriptions per 100 patient months. Ninety prescriptions (44%) were intravenous and 114 (56%) oral. Nephrologists prescribed 126 (62%) antimicrobials with the remaining from non-nephrologists. Overall, cefazolin (24%), amoxicillin (11%) and azithromycin (9%) were most commonly prescribed. Forty-four percent of intravenous prescriptions were ordered as a single dose. The median duration of therapy was 7 days. Fifty-four (43%) prescriptions by nephrologists had accompanying documentation on clinical presentation but few (15%) had documentation on the presumed site of infection. Conclusion: We found extensive antimicrobial use among HD patients. The presumed site of infection was poorly documented. Oral antimicrobials and prescriptions from non-nephrologists contributed significantly to overall exposure. A prospective study is required to adequately examine indications and appropriateness of antimicrobial prescriptions among Canadian HD patients.

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DEVELOPMENT, IMPLEMENTATION AND EVALUATION OF A WEB-BASED CLINICAL PATHWAY FOR CHRONIC KIDNEY DISEASE IN PRIMARY CARE

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Background: Identification and management of Chronic Kidney Disease (CKD) is complex and the Kidney Disease Improving Global Outcomes (KDIGO) Clinical Practice Guideline (2012) provides direction to improve the care of patients with CKD. Primary care physicians play a key role in identification, management and referral of patients with CKD, and are an important target population for the CKD guidelines. Using the knowledge-to-action cycle framework, we identified a clinical pathway for CKD as a potential tool to increase uptake of the CKD guidelines in primary care.

We are developing an electronic CKD clinical pathway in close collaboration with key stakeholders, decision makers and knowledge users, including provincial renal programs, primary care physicians, and Chronic Disease Management programs. This CKD clinical pathway will be aimed at primary care physicians, and will incorporate evidence from the guidelines, including targeted testing, identification and management of CKD, and referral to specialist care. Working in collaboration with our knowledge user and decision maker partners we will implement the CKD clinical pathway across the province of Alberta and evaluate its clinical benefits in primary care.

Objectives: To determine (using an interrupted time series design) whether the CKD clinical pathway implemented as a web-based online tool in primary care improves guideline-concordant care of patients with CKD.

Methods: The clinical pathway will be implemented as an online tool, and a multifaceted education strategy will coincide with the release. We will evaluate the impact of the clinical pathway using quantitative and qualitative methodology.

Future work: We will use a cluster randomized trial design to determine whether a web-based CKD clinical pathway combined with an electronic reminder and clinical decision support system (personalized CKD care plan) improves guideline-concordant care of CKD patients, compared to the web-based clinical pathway alone. The CKD clinical pathway will be available for use by interested groups.

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MENTORSHIP PILOT PROGRAM: PREDICTORS OF PRIMARY CARE PROVIDER UTILIZATION

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Background: A one-year Ontario based pilot study was conducted to evaluate the feasibility of linking primary care providers (PCP) with nephrologists in a collaborative relationship to improve chronic kidney disease (CKD) patient care.

Objectives: To determine the characteristics and predictors of PCP-nephrologist interactions.

Methods: 154 PCPs were recruited to participate in the pilot with 7 nephrologists throughout Ontario. 138 PCPs provided sufficient information for study inclusion. PCP demographics, practice characteristics, and type of interactions were recorded. Logistic regression models were constructed to assess potential independent predictors of PCP-nephrologist interactions.

Results: 68.8% of mentees were family physicians. PCPs had been in practice 3.2 (1.9) years and 31.2% were males. 292 interactions (87.3% via email) occurred over the study (mean 2.1 ± 3.5). No univariate predictors of increased interactions taking place were identified. A multivariate logistic regression model of predictors of interest demonstrated that increased PCP time in practice (> 5yrs vs ≤ 5 yrs) was associated with increased frequency of interactions (O.R. 2.33 [95% C.I. 1.02, 5.29]; P=0.044). A trend was observed to a decreased number of interactions in those PCPs with more frequent CKD patient encounters.

Limitations: Self-reported data. Sample size may be insufficient to detect clinically important differences.

Conclusions: This pilot study demonstrated that PCPs in practice greater than 5-yrs were more likely to access a nephrologist for advice on CKD patients. These findings will help to inform the creation of a provincial-wide program providing PCP mentorship on CKD patient care.

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ACID- BASE BALANCE IN HEMODIALYSIS PATIENTS RECEIVING A STANDARD BASE-BUFFER DIALYSATE

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Background: Guidelines recommend maintaining serum bicarbonate concentrations between X and Y in patients with end-stage renal disease on hemodialysis to avoid the complications of chronic acidemia. However, many hemodialysis programs utilize a standard bicarbonate bath in all patients with little individualization for patient's acid-base balance. We undertook a retrospective review of a single dialysis program to determine the prevalence of acidemia and risk factors for acidemia. Methods: St. Joseph's Healthcare provides dialysis for approximately 700 patients in Ontario, Canada. We utilized laboratory data from hemodialysis patient's routine, monthly dialysis bloodwork drawn prior to commencing dialysis at a mid-week session. We excluded patients on peritoneal dialysis, who required acute dialysis only, or were admitted to hospital. We defined acidemia as a serum bicarbonate 26 mmol/L. We linked our laboratory database to electronic medical records to determine patients' characteristics. We performed multinominal probability regression to determine the association between acid-base status and patient characteristics. Results: Of the 546 in-centre hemodialysis patients, 452 (83%) had laboratory data. All patients received a dialysate bicarbonate of 31 mmol/L plus an acetate concentration of 4 mmol/L. Acidemia was present in 26% and alkalemia in 14% leaving 60% in the recommended serum bicarbonate range. In our multivariable model, acidemia was more common in patients that prescribed only twice weekly dialysis ($p=0.04$) and in younger patients ($p=0.007$). There were no measured characteristics associated with alkalemia. Conclusions: A serum bicarbonate concentration outside the recommended range is common with a fixed bicarbonate and acetate dialysate. Younger patients and patients receiving less frequent dialysis may merit particular attention to acid-base balance and the base concentration of the dialysate.

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IT'S BABY TIME: 3 PREGNANCIES ON INTERMITTENT HEMODIALYSIS

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Background: Patients with End stage renal disease (ESRD) are usually amenorrhic and infertile with 42% of women reporting at least one menstrual cycle after starting hemodialysis (HD). Conception is extremely rare in these patients with reported pregnancy rates between 1-7%. Survival of the fetus in this population has increased in the last decade with reported live birth rates of 50-87% We present two successful pregnancies and one current pregnancy on intermittent HD. Case 1 21yo with reflux nephropathy on dialysis for 8months, whose pregnancy was discovered at 4weeks and HD intensified to 18-21hours/week. The pregnancy was uneventful and delivered at 38weeks a healthy baby girl weighing 2780g (10-50thpercentile). Case 2 36yo with polycystic kidney disease, who in retrospect conceived prior to initiation of dialysis. Her pregnancy was discovered at 24weeks and HD intensified to 24hours/week. The pregnancy was uneventful and delivered a healthy baby boy at 35weeks weighing 2916g (50-90thpercentile). Case 3 32yo with focal segmental glomerulosclerosis on dialysis for 17months, whose pregnancy was discovered at 18weeks and HD intensified eventually to 36hours/week. Pregnancy was complicated by cervical incompetence and hypertension requiring anti-hypertensive medications. Delivery will be before March 2014. All patients were managed with intensified hemodialysis and a multidisciplinary team. Bloodwork was checked weekly to maintain predialysis urea <17 mmol/l, HCO3 18-22 mmol/l, K+ 3.5-5 mmol/l, Ca 2.2-2.5 mmol/l, PO4 0.8-1.6 mmol. Hemoglobin was maintained between 100-110 g/l with the use of venofer, darbepoetin and blood transfusions. Patients' diets were liberalized to ensure adequate caloric and protein intake for daily dialysis and pregnancy. Blood pressures were monitored to maintain a blood pressure <140/90. Conclusion: These cases illustrate that successful pregnancies on HD are possible with intensification of HD prescription, careful management of hemoglobin and electrolytes. Pregnancies on dialysis remain high risk and require frequent monitoring with a multidisciplinary team.

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DEVELOPMENT OF CHRONIC KIDNEY DISEASE QUALITY INDICATORS FOR PRIMARY CARE

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(5) Ontario Renal Network
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Background: A large body currently exists of Chronic Kidney Disease (CKD) Quality Indicators (QIs) and CKD guidelines, however, there is little guidance to determine the CKD QIs that are most appropriate to measure in primary care across Canada. This initiative is designed to address the gap. Objectives: To describe the methodology used to identify and confirm a set of CKD QIs for use in primary care in Ontario. Methods: A modified Delphi panel process is being used to identify and confirm CKD QIs. The panel will include representatives from primary care, nephrology and other relevant stakeholders. Established methodology will be used to conduct a scoping review in order to identify existing QIs, which will then be circulated to panel members for ranking against a number of predefined criteria. A separate search will also be conducted to identify and extract recommendations from relevant clinical practice guidelines in order to establish the evidence base for panel members' consideration. Three rounds of ranking, as well as one webinar meeting will be used to achieve consensus among panel members. Results & Conclusions: This methodology will be reported on and discussed to demonstrate the usefulness of this approach for future QI development. The resulting set of QI will be feasibility tested in a second phase of this work which will involve examining whether advanced EMR functions such as Clinical Decision Support Systems (CDSS) improve quality of care through a pragmatic cluster randomized controlled trial (RCT). In addition, the QIs will be leveraged to continue to address quality care for CKD in Ontario.

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CHECKLIST FOR THE SAFEST USE OF THE NEW ORAL ANTICOAGULANTS: INCLUSION & EXCLUSION CRITERIA

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BACKGROUND & RATIONALE: New oral anticoagulants could possibly replace warfarin safely for atrial fibrillation (AF) in 25% of warfarin patients. These anticoagulants must be screened systematically to decrease the risk of major/fatal bleeds in the highest risk patients, such as the elderly & renally impaired. Since dabigatran's AF approval, our community-based anticoagulation service [with point-of-care INR testing, certified anticoagulation pharmacists, case management & evidence-based medicine protocols], has received inquiries and prescriptions for high bleeding-risk & non-compliant patients. A quote from Dr. M. Crowther (McMaster University) at the 2011 Anticoagulation Forum conference: "A bad warfarin patient will be a very bad dabigatran (rivaroxaban or apixaban) patient." PURPOSE: A one-page checklist was developed to assist prescribers in hospital & community practice with the safest use of the dabigatran, rivaroxaban & apixaban in AF. CRITERIA: The inclusion criteria are: baseline SCr & AST, original CHADS2 score > 2 for moderate to high risk AF patients (not > 1 as per CCS), etc. The exclusion criteria are: stroke within 6 months, renal and/or hepatic dysfunction, unstable CHF, non-compliance, alcohol and/or substance abuse, major drug interactions (e.g. p-Glycoprotein interactions; cytochrome P450 interactions with rivaroxaban or apixaban), etc. For educational purposes, additional information was provided: (1) Numbers need to treat, (2) Numbers needed to harm, (3) Therapeutics Initiatives 2011 recommendation, and (4) CEDAC 2011 recommendations. CONCLUSION: This one-page checklist for the safest use of the new oral anticoagulants is practical & easy to use; with favourable feedback from health care professionals across Canada & the USA.

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TRADITIONAL VERSUS ONCE WEEKLY INTRAVENOUS IRON THERAPY IN HEMODIALYSIS PATIENTS

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Rationale: Although iron replacement is a key element in anemia management in stage 5 chronic kidney disease patients, studies evaluating novel iron dosing regimens are scarce. The purpose of this study was to compare the effectiveness of once weekly intravenous (IV) iron dosing strategy to that of a conventional iron dosing regimen.
Methods: A retrospective cohort study was conducted on 148 eligible patients who received hemodialysis (HD) between June 1st, 2010 and June 30th, 2012 at a regional kidney dialysis center in southwestern Ontario, Canada. The primary outcome was to compare haemoglobin (HB) concentration and erythropoiesis stimulating agent (ESA) utilization using once weekly IV iron regimen compared to traditional iron dosing in HD patients.
Results: Of the 148 patients, 99 (67%) received a traditional (every dialysis loading dose) and 49 (33%) received a once weekly IV iron regimen. Generalized estimating equations analyzed 313 observations, obtained from 148 patients, suggested that TSAT and iron concentration were both significantly higher in the weekly group versus traditional ($p = 0.01$ and 0.01, respectively). Further, ESA utilization was significantly lower in the once weekly IV iron regimen than the traditional dosing approach (means = 7679.02 and 6366.44 units respectively, $p = 0.04$). While HB (means = 110.46 and 111.51 g/L, $p = 0.46$) and ferritin concentrations ($p = 0.13$) were not found to differ significantly between the two groups.
Conclusion: HB and ferritin levels achieved by once weekly iron dosing approach were similar to those achieved by the traditional iron dosing approach. When compared to traditional dosing approach, once weekly iron dosing approach significantly reduced ESA consumption, increased TSAT, and increased iron concentration with the same utilized iron quantities.

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CD46-ASSOCIATED ATYPICAL HEMOLYTIC UREMIC SYNDROME WITH INITIAL FOCAL SEGMENTAL GLOMERULOSCLEROSIS

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Background: There are rare reports of focal segmental glomerulosclerosis (FSGS) preceding atypical hemolytic uremic syndrome (aHUS). However none had underlying complement mutations. We report a patient with FSGS who later presented with *CD46*-associated aHUS.

Case report: A 9 year old girl presented with a history of progressive edema, nephrotic range proteinuria and microscopic hematuria. Creatinine, hemoglobin, platelets, C3, C4, ANA, ANCA and ASOT were normal. She was initially steroid responsive but, after 5 weeks of 60 mg/m^2 steroid therapy, became steroid-resistant. Her renal biopsy showed FSGS. No disease-causing mutation was found in *ACTN4*, *CD2AP*, *NPHS1*, *NPHS2*, or *TRPC6*. Tacrolimus was started and steroid therapy discontinued after 5 months of 0.5 mg/kg on alternate days. She had two infusions of rituximab 375 mg/m^2 without effect. One year after diagnosis, a repeat biopsy showed FSGS progression. She continued to have nephrotic range proteinuria when her treatment was changed to mycophenolate mofetil. One month later, she developed HUS with anemia (Hb 56 g/L), low platelets (122 x 10^9/L), elevated LDH (560 U/L), low haptoglobin (<0.10 g/L) and elevated creatinine (peak 641 µmol/L). Serum complement and ADAMTS13 activity were normal. Her renal biopsy showed FSGS with thrombotic microangiopathy, acute tubular injury and C3c deposition. *CD46* (membrane cofactor protein (MCP)) gene sequencing showed a heterozygous missense mutation in exon 11 (c.1058C>T, p.Ala353Val). Other complement genes showed no mutation. She required 4 days of hemodialysis. After 16 plasma exchange sessions, she had recovery of renal function (creatinine 87 µmol/L) but ongoing hemolysis with low haptoglobin, mildly elevated LDH, and schistocytes on peripheral blood smear.

Conclusions: FSGS nephrotic-range proteinuria is associated with endothelial dysfunction which may trigger complement activation. Defective MCP is unable to protect the glomerular endothelium resulting in a prothrombotic microvascular state and kidney injury.

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PRIOTITIZING AND VALIDATING KIDNEY CARE QUALITY INDICATORS TO DRIVE PERFORMANCE IN ONTARIO: A ROADMAP

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Background: The Ontario Renal Plan (ORP), developed through extensive stakeholder engagement, provides a roadmap through which the Ontario Renal Network promotes optimal patient outcomes, experience of care, and sound stewardship of public dollars. An effective and evidence-based measurement framework is central to these efforts, yet rigorously developed quality improvement methods and tools in nephrology are lacking. Development of ORP-II, the next iteration of the ORN's strategy, is underway, with implementation planned for early 2015. Goals: 1) To improve outcomes for Ontario residents with chronic kidney disease by developing and applying a de novo provincial measurement strategy based on clinically meaningful, feasible, scientifically sound, and actionable measures. 2) To create a culture of quality improvement in the Ontario renal community. 3) To minimize data collection and reporting burden for renal programs. 4) To align measurement with quality improvement practices using the knowledge-to-action (KTA) cycle. Methods: Our project plan is comprised of 8 workstreams: 1) knowledge syntheses to identify outcome, process, and structure variables in each of the clinical domains outlined in the ORP-II; 2) development of a prioritization strategy for selecting the most useful measures; 3) construction of conceptual and statistical models to empirically validate candidate measures that have not been adequately evaluated, drawing on the Ontario Renal Reporting System (ORRS) and other provincial data-sets; 4) to construct comprehensive measurement sets drawing on the best validated measures; 5) to develop and apply primary data collection tools, including facility level surveys and the ORRS in the collection of selected measures; 6) ongoing integration of the measurement framework with database development and deployment; 7) application of the knowledge to action (KTA) framework at the regional program and facility level (including KTA gap and barrier mitigation); and 8) a formative and summative evaluation of the measurement framework.

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PLASMAPHERESIS AND RITUXIMAB FOR POST TRANSPLANT RECURRENCE FOCAL SEGMENTAL GLOMERULOSCLEROSIS IN A CHILD

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BACKGROUND: Post Transplantation Recurrence Focal Segmental Glomerulosclerosis (FSGS) has an incidence up to 30% with great effect in graft survival if not detected and treated early. There is no known single treatment protocol for such cases and their response is quite unpredicted.

CASE REPORT: A 11 year old girl with FSGS diagnosed at two year, she progressed to chronic renal failure with Peritoneal dialysis at 9 year. She underwent a deceased kidney transplantation from a pediatric donor with negative crossmatching. She was induced with Antithymocyte globulin and she started to pass urine immediately with serum creatinine decreased untill it reached 105 micromol/l by day 3. She was maintained on Tacrolimus, Mycophenolate and Prednisone . She was noticed to have proteinuria with protein/creatinine ratio of 2500-4000 mg/mmol and generalized oedema. Serum creainine increased to 324 micromol/l, allograft biopsy done and electron microscopy showed diffuse Foot Processes Effacement with no light microscopy changes. Plasmapheresis(PP) started with albumin/Fresh Frozen Plasma as replacement fluid for initial intensive 12 sessions. Renal function recovered, oedema resolved and creatinine dropped to 95 but she continued to show proteinuria so 4 doses Rituximab (375 mg/m2) given every other week without complication. Both enalapril and candesartan were added. she was discharge home and currently she is on once weekly PP with her Urea 3.4 mmol/l, Creatinine 48 micromol/l with protein/creatinine ratio between 800-1200 mg/mmol and stable graft and patient status.

CONCLUSION: Early aggressive treatment with PP and Rituximab can dramatically reverse recurrence FSGS and improved graft and patient survival.

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CONVERSION FROM EPOETIN ALFA TO DARBEPOETIN ALFA WITHIN HORIZON HEALTH NETWORK DIALYSIS UNITS: A COMPARISON OF DOSE RATIOS FROM CANADIAN SWITCH STUDIES

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Background: The erythropoiesis-stimulating agents epoetin alfa and darbepoetin alfa have similar efficacy when used to treat anemia of chronic kidney disease. The most appropriate dose conversion between intravenous epoetin alfa and darbepoetin alfa remains uncertain. Dose conversion ratios from previous switch studies range from 199:1 to 400:1.

Objectives: To describe the dose conversion ratio between epoetin alfa and darbepoetin alfa in hemodialysis patients after a program-wide switch and compare dose conversion ratios reported among other Canadian switch studies. Methods: In this prospective, open-label observational study, patients from five hemodialysis centres were converted from epoetin alfa to darbepoetin alfa (both given intravenously) over a two-month period (May and June 2011). Lab parameters and mean weekly doses of erythropoietin stimulating agents were collected for three months pre-conversion and post-conversion, respectively. The resultant dose conversion ratio was compared to ratios previously reported in two Canadian switch studies.

Results: A total of 42 patients receiving epoetin alfa at baseline were included. Mean hemoglobin and iron parameters did not differ significantly between the pre- and post-conversion periods. Conversion to darbepoetin alfa resulted in significant cost savings for the program. The mean dose conversion ratio between epoetin alfa and darbepoetin alfa was 296:1. In comparison, a mean dose conversion ratio of 244:1 (Manitoba) and median dose conversion ratios of 288:1 and 400:1 (Ontario) have been reported in other Canadian switch studies.

Conclusion: Conversion of patients from epoetin alfa to darbepoetin alfa demonstrated cost-efficiency without compromising clinical outcomes. The dose conversion ratio was observed to be greater than 200:1, which is comparable to the results of previously reported Canadian studies.

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A REAL-WORLD STUDY OF LANTHANUM CARBONATE AND SEVELAMER IN THE USA: COST-EFFECTIVENESS CONSIDERATIONS FOR ONTARIO

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Background: Drug costs associated with use of the non-calcium phosphate binders lanthanum carbonate (LC) and sevelamer could impact the management of patients with end-stage renal disease (ESRD) and hyperphosphatemia.

Objectives: To assess the cost impact of converting patients with ESRD from sevelamer hydrochloride (SH) monotherapy to LC monotherapy.

Methods: *Post hoc* economic analysis of a 16-week, phase 4, real-world US study investigating conversion from SH to LC monotherapy (n=950). LC doses were titrated to maintain the level of phosphate control achieved with SH. Daily doses were analyzed and costs calculated using Ontario Drug Benefit Prices from Q2 2013 (LC 1000mg:$4.72; SH 800mg:$1.84). Patients were stratified by baseline SH dose subgroup and also by clinically available doses of SH and LC.

Results: Analysis by SH dose subgroup, based on mean daily doses, showed that it becomes more cost-effective to use LC rather than SH in patients on SH >4800–7200mg (Table). Analysis by clinically available doses revealed that switching to LC 3000mg/day (3 pills/day; $14.16/day) from SH 6400mg/day (8 pills/day; $14.72/day) is more cost-effective and results in a lower pill burden. At study entry, ~60% of patients in the primary US study were on SH ≥6400mg/day.

Conclusions: Based on this real-world, economic analysis of patients with ESRD, LC is estimated to be more cost-effective than SH in approximately 60% of patients. For patients taking SH ≥6400mg/day, switching to LC 3000mg/day is more cost-effective and results in a reduced pill burden (≥8 vs 3 pills/day) while maintaining similar phosphate control.

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HIGH ACCESS FLOW IN CHRONIC HEMODIALYSIS (HD) PATIENTS AND PULMONARY HYPERTENSION (PH) – HAF-PHTEN STUDY.

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PH, defined by echocardiography as pulmonary arterial systolic pressure =35mmHg1,2, is prevalent in 38% of HD patients3 and is an independent predictor for all-cause mortality (HR 2.2; P<0.01). High arteriovenous fistula (AVF) blood flow (A/F) is the most statistically significant variable associated with PH in HD patients (P<0001), although its clinical difference was unimportant4. A defined high A/F cutoff is currently unavailable in literature and guidelines5.This study examines the prevalence of PH in HD patients with high A/F and the association between a specific A/F cutoff and PH development in HD patients at Kingston Hemodialysis Program, after obtaining Queen's Health Sciences Research Ethics Board approval.This is a cross-sectional study of 216 patients with AVF, out of 358 HD patients. Patients with A/F =1600ml/min, measured by Fresenius Conductivity Method, were retrospectively evaluated for PH, diagnosed by Echo done at least 6 months post AVF creation. Patients with PH prior to AVF creation or without standardized Echo were excluded. Student's t-test and Fisher's exact test were used to compare the means and differences of normally distributed and categorical variables, with a 0.05 level of significance. Standardized echoes were available only for 21 out of 37 HD patients with A/F =1600ml/min. PH was prevalent in 38% of patients (n=8, 95%CI: 0.2-0.6). The association between high A/F cutoff (A/F =1600-to-<2000 versus =2000ml/min) and PH was not significant (P=1.0). The results of this study showed a high prevalence of PH in HD patients similar to Agarwal et al.3, though we only included patients with high A/F. Although statistical significance was not identified between a high specific A/F cutoff and PH, this could be due to the small sample size, the selection bias, and the cross sectional design of the study. Future trials are required to define a specific high A/F cutoff and PH.

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A CLINICAL ALGORITHM FOR THE DETECTION, MONITORING, AND MANAGEMENT OF CHRONIC KIDNEY DISEASE IN PRIMARY CARE

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Background: Chronic Kidney Disease (CKD) affects approximately 2 million Canadians and is a recognized risk factor for all-cause mortality. Patients that progress to end-stage renal disease and require dialysis experience significant morbidity and a reduced quality of life. Primary care providers (PCPs) can play an important role in the early detection and prevention of progression of CKD. Objectives: To develop a clinical algorithm for PCPs that: (i) identifies which patients in a typical family practice are at higher risk for CKD; (ii) outlines investigations to order for patients at high risk for CKD and how to interpret the results; and (iii) describes the role of the PCP in managing patients with CKD and the criteria for appropriate referral to nephrology. Methodology: The Kidney Disease Informing Global Outcomes (KDIGO), Canadian Hypertension Education Program (CHEP), and the Canadian Diabetes Association CKD guidelines were reviewed for relevant content to produce, through an iterative process, a clinical algorithm. Results: A clinical algorithm that outlines a practical approach for PCPs to enhance their ability to identify, detect and manage patients both at high risk for, and with CKD. Plans to disseminate this algorithm as part of a clinical toolkit for PCPs are underway. Conclusions: Early detection and management of CKD at the primary care level can prevent progression to end stage renal disease. It is anticipated that this algorithm will help PCPs become more aware of CKD management issues and provide CKD care in a consistent evidence-informed manner.

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BIOMARKERS OF ACUTE AND CHRONIC RENAL DISEASE IN CHILDREN TREATED WITH CISPLATIN FOR CANCER: DESCRIPTION OF RATIONALE, METHODS AND PROGRESS OF THE PAN-CANADIAN ABLE STUDY

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Background: Cisplatin causes acute kidney injury(AKI) and may increase chronic kidney disease(CKD) risk. New biomarkers may allow early AKI diagnosis/treatment and late renal risk-stratification. ABLE, a pan-Canadian team project(CIHR) evaluating late child cancer treatment effects, comprises four arms: 1)ototoxicity, 2)nephrotoxicity, 3)thrombosis, 4)graft-versus-host disease. The nephrotoxicity arm is a prospective, 3-year longitudinal study of cisplatin-treated children.

ABLE Objectives: Overall: Evaluate biomarkers of late effects of childhood cancer therapy.

Nephrotoxic arm: Determine if: 1)novel biomarkers predict AKI, CKD, hypertension(HTN); 2)cisplatin-AKI predicts 3-year post-cancer CKD/HTN; 3)genetic variants predict nephrotoxicity.

Methods: The Nephrotoxicity arm is a Canadian inception cohort of 200 children receiving cisplatin in 8 centers. Exclusions: advanced CKD. Recruitment: near cancer diagnosis. Protocol(Figure): five visits: two "acute"(during cisplatin infusions: AKI biomarker validation, urine, blood, DNA, data); three "follow-ups"(3 months, 1, 3 years post-treatment; renal outcome evaluation, data, urine, blood). Measures: Blood for creatinine, CystatinC, urine for AKI biomarkers(acute phase), albumin-creatinine ratio(chronic phase), saliva for SNP analysis. Outcomes: AKI ≥KDIGO Stage 1(acute phase), low glomerular filtration rate, microalbuminuria, HTN(chronic phase). Biobanking for biomarker validation/discovery and data banking are centralized.

Results: Three sites are recruiting (6 patients recruited; 10 "acute", four 3-month visits complete); remaining sites have ethics approval. A national data/specimen collection infrastructure is established, personnel trained, data forms derived/tested.

Conclusion: This represents one of the first pan-Canadian pediatric nephrology studies and one of the largest evaluating late child cancer therapy renal effects. ABLE is multi-disciplinary, enabling effective knowledge translation, a major step forward to helping childhood cancer survivors lead long, healthy lives.

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ARTERIOVENOUS FISTULA RECIRCULATION - A RARE ETIOLOGY OF PERSISTENT SEVERE HYPERKALEMIA IN AN ESRD PATIENT

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BACKGROUND A 51 year old african american male presented to our institution with new onset chest pain, dyspnoea and weakness. He has history of end stage renal disease on hemodialysis(HD), Hepatitis C, hypertension and hyperparathyroidism but denies any cardiac history. His labs were significant for potassium of 8.3 and BUN of 55 and was treated with urgent hemodialysis and post dialysis potassium and BUN were 5 and 19. Within 12 hours, his potassium rebounded to 10. In a week long ICU course, various potential causes of hyperkalemia such as dietary excess, rhabdomyolysis, ischemia, mineralocorticoid deficiency, hemolysis, hyperkalemic periodic paralysis, medications and severe systemic infections were eliminated. In spite of daily HD, his potassium kept rebounding to maximum of 7.8 on 3 consecutive days. Arteriovenous fistula (AVF) recirculation secondary to stenosis was thought as the potential cause and a hybrid run of dialysis with arterial access from AVF and venous return through the new permanent catheter was attempted to eliminate recirculation. Subsequent potassium levels were always near normal limits with highest of 5.2. AV fistulogram revealed stenosis just distal to the arterial anastomosis which was treated by angioplasty. DISCUSSION AVF recirculation occurs when dialyzed blood returning through the venous needle reenters the extracorporeal circuit through the arterial needle, rather than returning to the systemic circulation, leading to inadequate hemodialysis and increased mortality1. Though current guidelines recommend pre and post HD urea levels and dilutional method to measure for recirculation, persistent severe hyperkalemia as seen in our patient should raise suspicion for AVF stenosis in end stage renal disease patients and prompt diagnostic workup should be initiated to avoid life threatening complications of severe hyperkalemia REFERENCES 1. Marzieh Beladi Mousavi et al; A Review Article: Access Recirculation Among End Stage Renal Disease Patients Undergoing Maintenance Hemodialysis; Nephrourol Mon. 2013 Spring; 5(2): 728–732

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PLASMA EXCHANGE FOR RENAL DISEASE: WHAT IS THE BEST EVIDENCE?

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Therapeutic plasma exchange (TPE) has been used as adjunctive therapy for a variety of renal diseases dating back to the 1970s. In many cases, support for TPE was on mechanistic grounds given the potential to remove unwanted large molecular weight substances such as autoantibodies, immune complexes, myeloma light chains, and cryoglobulins. More recently, growing evidence from randomized controlled trials, meta-analyses, and prospective studies has provided insights into more rational use of this therapy. This report describes the role of TPE for the six most common renal indications in the 2013 Canadian Apheresis Group (CAG) Registry and the evidence that underpins current recommendations and practice. These renal indications include thrombotic microangiopathy, anti-glomerular basement membrane disease, antineutrophil cytoplasmic antibody associated vasculitis, cryoglobulinemia, recurrence of focal and segmental glomerulosclerosis in the renal allograft, and kidney transplantation.

The use of plasma exchange for renal disease by the Canadian Apheresis Group correlates with published evidence. Early introduction of plasma exchange appears to be effective for a variety of immunologic renal diseases. However, plasma exchange primarily serves as an adjunct to other immunosuppressive therapies and is often expected to offer only a small incremental benefit. The strongest evidence for plasma exchange is for thrombotic microangiopathy in which it serves as the single most important therapy in most cases.