Irish Nephrology Society

Annual Scientific Meeting

8th May 2015

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Book of Abstracts

Abstracts 1-6: Free Communication Session 1

Basic Science

Abstract 01

Towards the Glomstix test: urine sCD163 as a biomarker of active renal vasculitis

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Introduction: A specific biomarker which can separate active renal vasculitis from other causes of renal dysfunction is lacking, with a kidney biopsy often being required to resolve the issue. We have previously presented data relating to serum sCD163 as a vasculitis biomarker. We hypothesised that shedding into the urine of sCD163, which is expressed on crescent macrophages, would provide an estimate of active glomerular inflammation and have extended our analysis to investigate urine sCD163.

Methods: To investigate the link between vasculitic glomerulonephritis and urinary sCD163 excretion, immunohistochemistry and rtPCR was performed on renal tissue from patients with SVV and from rats with MPO-ANCA vasculitis. Using the Rare Kidney Diseases (RKD) Biobank, urine and serum samples from 430 patients with systemic small vessel vasculitis (SVV), disease controls and healthy controls were then assayed for sCD163 by ELISA. Clinical data were derived from the linked RKD registry. The gold standard for active vasculitis was the clinician assessment >1 month after sampling, with active disease in most cases being supported by biopsy and invariably followed by an escalation in immunosuppression.

Results:

In human renal tissue, the degree of glomerular CD163 expression was tightly correlated with the level observed in the urine but not the serum. Serum sCD163 levels were not significantly different in patients with SVV and disease or healthy controls in the expanded cohort. There was no correlation between serum and urinary sCD163. In an inception cohort which included 176 patients with SVV, urinary sCD163 levels in patients with active renal vasculitis were markedly elevated compared to both healthy and disease controls, and to patients in remission. Of note, urinary sCD163 was undetectable in those with active non-renal vasculitis. ROC curve analysis disclosed an AUC of 0.95 (95% CI 0.9-0.99) for differentiation of active renal vasculitis from remission, and defined an optimum cutoff of 0.33ng/mL/mmol creatinine. Applying this to a validation cohort which included 155 patients with SVV allowed differentiation of active renal vasculitis with a sensitivity of 83%, specificity of 98% and positive likelihood ratio of 21.9.

Conclusion: Urinary sCD163 associates very tightly with active renal vasculitis. A positive result can therefore be used to guide treatment for renal flare in place of renal biopsy.

Abstract 02

Title: Immunometabolism in ANCA vasculitis

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Background: Anti-neutrophil cytoplasmic autoantibody (ANCA) vasculitis (AAV) is an autoimmune condition characterised by inflammation of the microvasculature. It can manifest with rapidly progressive glomerulonephritis and vasculitis of the respiratory tract. The Warburg effect (switch from oxidative phosphorylation to glycolysis for the production of energy, in the presence of oxygen) first noted in cancer cells, has been described in pro-inflammatory immune cells. We investigated if this switch to aerobic glycolysis occurs in the pathophysiology of AAV.

Methods: Peripheral blood mononuclear cells (PBMCs) were obtained from AAV patients (active disease and remission) and age-matched healthy donors. Metabolism was measured by Seahorse extracellular flux analysis. Glucose uptake was analysed using 2NBDG (a fluorescently-labelled deoxyglucose analogue) and flow cytometry. Cell populations were identified by cell surface marker expression. Mitochondrial content of cells was quantified by a combination of flow cytometry and PCR-based assays.

Results: We report that. basal respiration, oxygen consumption for ATP production and maximum respiratory capacity are decreased in PBMCs from patients with active disease compared to those in remission, and also to healthy controls. Conversely, we have detected increased glucose uptake in cells from patients with active disease, supporting our hypothesis that peripheral immune cells undergo a metabolic shift in AAV. Despite decreased capacity for oxidative phosphorylation in PBMCs from active patients we found increased mitochondrial mass is these cells suggesting mitochondrial dysfunction.

Conclusions: Using state of the art technologies we have found that peripheral immune cells from patients with active disease display a metabolic switch to aerobic glycolysis that may in part be due to mitochondrial dysfunction.

Abstract 03

Candidate gene study of skin cancer in renal transplant recipients

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Background: Multiple robust genetic loci for skin cancer have been identified via large genome-wide association (GWA) studies. We wished to test the hypothesis that these loci are risk factors for skin cancer in post-transplant populations. We were also interested in determining if the odds ratio changed in the transplant population, compared to the general population in which they were discovered.

Methods: We identified 21 robustly associated SNPs from the GWA studies and tested these SNPs in a cohort of 325 cadaveric kidney transplant recipient patients. The cohort was cross referenced with the Irish cancer registry resulting in the identification of 94 cases that developed skin cancer post-transplantation and 231 controls. Illumina 660K bead-chip data was available for all 325 individuals. Logistic regression and survival analysis was applied to test for correlation with skin cancer.

Results: A nominally significant association was found with rs885479, a SNP found in the *MC1R* gene (p= 0.0157) in the survival analysis. The variant was found to have the same direction of affect as described in the original study and the odds ratio was higher. The presence of one or more copies of the minor allele caused a significant decrease in time to develop skin cancer post renal transplant (hazard ratio = 2.06). None of the variants survived Bonferroni correction for multiple testing.

Conclusion: *MC1R* was found to be associated with increased time to developing skin cancer. We are now seeking to extend this analysis to additional patient cohorts.

This work is funded by the IRCSET.

Abstract 4

The divergence of HIF isoforms in regulation of renal inflammation

Masterson E, Godson C & Higgins D

The kidney is highly susceptible to hypoxic injury making it prone to an exacerbated inflammatory response and increased macrophage recruitment. Functional versatility is an innate characteristic of macrophages mediating both tissue damage and repair, exemplified by M1 and M2 phenotypes respectively. Macrophage recruitment is a feature of response to tissue hypoxia resulting in accumulation of hypoxia inducible transcription factors [HIFs]. Different forms of HIF exist (e.g. HIF-1α and HIF-2α) regulating expression of overlapping and unique target genes. We hypothesise that HIF1α drives an M1 pro-inflammatory phenotype and HIF2α drives an M2 pro-resolution phenotype.

Expression of endogenous HIF-1α and HIF-2α protein in THP-1 and peripheral blood myeloid cell (PBMC) monocytes and macrophages subjected to hypoxic or normoxic conditions was examined. The effect of HIF-1α and HIF-2α over-expression on macrophage polarisation and phagocytic function was examined in THP-1 cells transfected with HIF-1α or HIF-2α and differentiated into macrophages post-transfection. THP-1 and PBMC derived macrophages were stimulated to M1 or M2 phenotypes and HIF isoform expression examined.

HIF-1α expression was detected in both hypoxic monocytes and macrophages, whereas HIF-2α levels were diminished on differentiation of THP-1 monocytes to macrophages. M1 polarized macrophages had increased HIF-1 expression while M2 polarized macrophages had increased expression of HIF-2. ELISA analysis of secreted proteins revealed HIF-2α over-expressing macrophages had decreased levels of MCP-1 with increased IL-10 which correlated with an increase in phagcoytic capacity.

These findings support our hypothesis that HIF-1α promotes an M1 phenotype and HIF-2α promotes an M2 phenotype and highlights the divergent roles of HIF-1α and HIF-2α in inflammation and resolution.

Abstract 5

Attenuation of diabetic kidney disease following Roux-en-Y gastric bypass in the Zucker Diabetic Fatty rat

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Background: Roux-en-Y gastric bypass (RYGB) ameliorates hyperglycaemia in type 2 diabetes. Its' effect on diabetic kidney disease (DKD) is underexplored. Glucotoxic and proinflammatory effects of hyperglycaemia drive DKD. Monocyte-chemoattractant protein 1 (MCP-1) generation is associated with macrophage infiltration and DKD progression.

Methods: Using the Zucker diabetic fatty rat (ZDF) model of DKD, we investigated weight dependent and weight-independent effects of RYGB on proteinuria, glomerular architecture, MCP-1, and macrophage infiltration. We used data from a randomised controlled trial to determine the effect of RYGB on patients with DKD and class I obesity.

Results: Ab libitum fed sham operated controls demonstrated progressive proteinuria that was attenuated by RYGB, and to a lesser extent by diet-induced weight loss. RYGB reduced hyperglycaemia to a greater extent than diet-induced weight loss. Both interventions improved glomerular architecture. This was paralleled by reductions in urinary MCP-1, renal MCP-1 expression and macrophage infiltration. Human data demonstrate that in the context of comparable short-term improvements in glycaemic control, RYGB and best medical treatment are equally efficacious in reducing albuminuria.

Conclusion: Non-surgical weight loss remediates renal inflammation to the same degree as RYGB. However, RYGB has a greater effect on reducing proteinuria. The extent and duration of this effect may be contingent on improved glycaemic control.

Abstract 06

Time Dependent Evolution of Enteric Hyperoxaluria following Roux-en-Y Gastric Bypass in the Rat and its Attenuation by *Oxalobacter Formigenes* Colonisation

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Background: Roux-en-Y gastric bypass (RYGB) is associated with a calcium oxalate urolithiasis incidence rate of 8% at 1 year post-surgery. *Oxalobacter formigenes* is a gut anaerobe, which metabolizes dietary and endogenously derived oxalate. We conducted a pilot study in adult male Wistar rats to ;1) describe the time-course of changes in urinary oxalate excretion following RYGB 2) establish its dependence on dietary oxalate and 3) examine the impact of colonisation with *Oxalobacter formigenes* (OF) on 24 hour urinary oxalate excretion (24UOE).

Methods: Twenty seven adult male Wistar rats underwent Roux-en-Y gastric bypass (RYGB, n=20) or Sham surgery (n=7). At 23 days post-surgery diet was switched to 1.5% oxalate chow. Six and eight days later RYGB animals were gavaged with 150mg wet weight of pure OF culture (OF) or vehicle (VEH). At pre-operative day 7 and post-operative days 21, 28 and 49 24UOE was tracked and compared between groups. OF colonisation was confirmed by faecal PCR.

Results:. No differences were observed in 24UOE pre-operatively or at 21 days post-operatively between RYGB and SHAM. Oxalate chow significantly increased 24UOE in all animals. At post-operative week 7, RYGB VEH animals showed a significant increase in 24UOE versus Sham (31±8.1 v 6.5 ±3.4µmol/24h p=0.03). In RYGB OF treated animals a bimodal pattern of 24UOE was observed with a discrete cohort of animals showing complete attenuation of hyperoxaluria.

Conclusions: Hyperoxaluria following RYGB in the rat occurs in a time and dietary oxalate dependent fashion. OF colonisation may be a means of attenuating post-RYGB hyperoxaluria.

Abstracts 7-12: Free Communication Session 2

Clinical Nephrology

Abstract 7

The association between antihypertensive agents and orthostatic hypotension using beat-to-beat blood pressure measurements: Results from The Irish Longitudinal Study on Ageing

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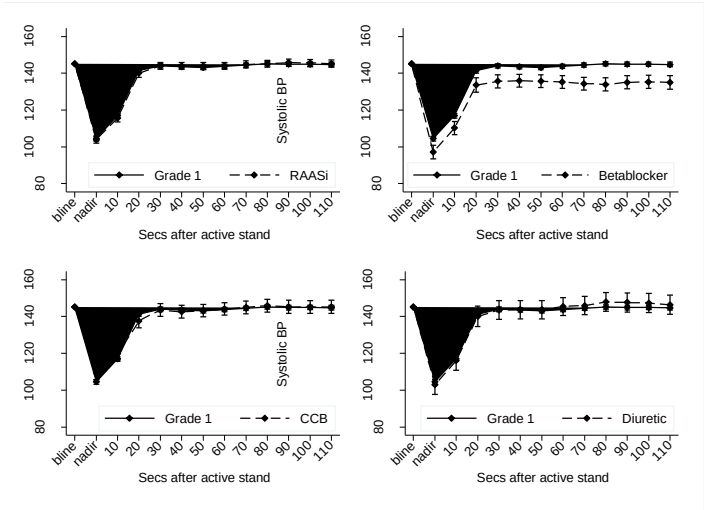
Background: Hypertension is an important cardiovascular risk factor however benefits of treatment are often outweighed by adverse events including orthostatic hypotension (OH) which is associated with significant morbidity and mortality. Beat-to-beat blood pressure (BP) technology provides a dynamic picture of BP behaviour that could influence choice of therapy.

Methods: Cross-sectional analysis from The Irish Longitudinal Study on Ageing, a nationally representative cohort study of adults ≥50 years. Beat-to-beat systolic (SBP) and diastolic (DBP) readings were recorded in participants undergoing an active stand. We defined grade 1 hypertension according to European Society of Cardiology criteria (SBP 140-159mmHg and/or DBP 90-99mmHg). OH was defined as a drop in SBP ≥20mmHg ± DBP ≥10mmHg. Outcomes were "sustained OH" (OH throughout the active stand) and OH at each 10-second (s) interval (total 110s). Logistic regression models were adjusted for potential confounding variables.

Results: A total of 536 hypertensive participants were receiving monotherapy with a renin-angiotensin-aldosterone-system inhibitor (317), beta-blocker (89), calcium channel blocker (89) or diuretic (41). Beta-blockers were associated with increased risk of sustained OH vs untreated grade 1 hypertension (OR 3.36, 95% CI 1.87-6.03). This was evident from 20s and remained statistically significant at 110s (figure 1). Multivariate adjustment did not attenuate this association. No increased risk of OH was detected among the other agents.

Conclusions: Beta-blocker monotherapy was associated with a >3-fold increased risk of OH compared to untreated grade 1 hypertension. The effect was evident within 20s of standing and was sustained. This should inform decision-making regarding choice of antihypertensive agent in older adults.



Abstract 8

The Irish Kidney Gene Project- prevalence of family history in patients with kidney disease in Ireland

DM Connaughton[1], S Bukhari[1], P Conlon[1], E Cassidy[1,2], M O'Toole[2], M Mohamad[1], J Flanagan[2], T Bulter[4], A O'Leary[3], L Wong[1], J O'Regan[1,4], S Moran[3], P O'Kelly[1], V Logan[5], B Griffin[3], MD Griffin[4], P Lavin[2], MA Little[2, 5], P Conlon[1].

The prevalence of kidney disease (KD) due to inherited genetic conditions in Ireland is unknown. The aim of this study is to characterise an adult kidney disease population and to identify familial clusters of kidney disease.

Multi-centre cross-sectional study of patients with kidney disease in Ireland from January to September 2014, recruiting from dialysis units and out-patient renal departments. A survey was administered collecting data on aetiology of kidney disease and whether a family history of kidney disease exists. Medical records were cross-referenced to confirm aetiology.

1840 patients were recruited; mean age 55.97 years (range 17-94.5 years) with a male predominance (n=1095, 59.5%). A positive family history was reported by 629 (34.2%). Excluding polycystic kidney disease (n=134, 7.3%), a positive family history was reported by 495 (26.9%) with kidney disease aetiology unknown the commonest aetiology within this group (10.6%, n=67). Kidney diseases not classically associated with familial inheritance, such as tubulo-interstitial kidney disease and glomerulonephritis demonstrated familial clustering. Patient characteristics associated with a positive family history included younger age of diagnosis and female gender whereas the stage of kidney disease or modality of renal replacement therapy did not differ between groups. Adjusting for age and gender, diabetic nephropathy, hypertensive nephropathy, CAKUT and IgA nephropathy were also associated with a positive family history.

26.9% of an Irish non-polycystic kidney disease population report a positive family history. Examining families with kidney disease provides an opportunity to better understand the disease pathogenesis and potentially identify genetic predisposition to kidney disease.

Abstract 9

Long-term consequences of transient acute kidney injury on risk of death and kidney failure in the irish health system.

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Background: Recent studies have shown that acute kidney injury (AKI) independently predicts mortality and risk of end stage kidney disease (ESKD). However, the effects of transient bouts of AKI on major outcomes are less well understood. We investigated the long-term consequences of transient AKI episodes within the Irish Health System.

Methods: Clinical data from health information systems in the Midwest and Northwest regions were linked with mortality data from 1999 to 2011 (n=502, 641). AKI events were identified as per KDIGO guidelines using mean standardized creatinine measurements over a 3-month window as baseline. Transient AKI events were identified as acute elevations in creatinine which fell to below 1.1 times baseline within 48 hours of the initial event. Multivariate Cox regression modelled the associations with death and risk of ESKD (first eGFR < 10 ml/min.1.73m^2).

Results: Overall rate of transient AKI (per 1000 person yrs) in the population was 6.6, increasing from 3.9 in CKD 1 & 2, to 165.7 in CKD 4. Unadjusted death rates (per 1000 person yrs) were 8.4 (CI 8.2-8.6) for patients without AKI and 91.8 (CI 90.3-93.3) for patients with a transient AKI. The adjusted hazard ratios (HR) and 95% CI from the multivariable model (n=122, 634) are shown.

			Risk of Death		**Risk of eGFR<10 ml/min/1.73m²**	
	N	N_{AKI}	No AKI	Transient AKI	No AKI	Transient AKI
CKD 1	70,412	739	1.00	3.16 (2.48-4.02)	1.00	6.66 (0.95-46.71)
CKD 2	41,466	1,687	1.00	1.94 (1.68-2.24)	1.00	9.02 (3.66-22.22)
CKD 3	9,662	9662	1.00	1.35 (1.18-1.55)	1.00	6.26 (3.50-11.22)
CKD 4	1,094	236	1.00	1.29 (0.87-1.92)	1.00	0.53 (0.33-0.86)

Conclusions: Transient AKI is associated with excess mortality and progression to ESKD. Risks were present for all CKD stages but were substantial for those with mild impairment. These findings would suggest that regular follow-up be considered for all patients following a transient AKI event even after kidney function returns to baseline.

Abstract 10

Post-Mortem Renal Findings in Critically Ill Patients that Required Continuous Renal Replacement Therapy

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Introduction: Acute kidney injury (AKI) is common in critically ill patients but they are rarely biopsied. The underlying aetiology is often assumed and not well defined.

Methods: We retrospectively reviewed the electronic records of all patients who required CRRT during admission to a 35 bed medical-surgical ICU, died before discharge and had a post-mortem (PM) over a two-year period (2012-2013). Renal tissue was examined by light microscopy only.

Results: Thirty-two subjects were identified. PM autolysis precluded analysis in 4 patients and these were excluded. ATN was a component of the clinical renal diagnosis in 21/28 (75%) patients however histological features of ATN were only seen in 5 of these. There was significant discordance between the clinical and histological renal diagnosis in 6 patients: 3 had unexpected chronic pyelonephritis, 1 had bilateral renal infarction, 1 had septic emboli and 1 had acute interstitial nephritis. Background atherosclerotic reno-vascular disease was common (32%). Nine patients had normal kidneys at PM examination (32%).

Conclusions: ATN was seen less often than anticipated on renal PM suggesting a different pathophysiological mechanism for AKI in critically ill patients. One fifth of patients had unanticipated renal pathology indicating a greater role for renal biopsy in the ICU.

Abstract 11

Mortality Discrimination based on Health Related Quality of Life, Symptom Burden and Self-Rated Health in a prospective Haemodialysis Cohort.

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Background: Little is known about the ability of impaired health related quality of life (HRQOL), or symptom burden to predict mortality in haemodialysis.

Methods: A prospective cohort study in haemodialysis (N=362). The Euro Quality of Life Questionnaire (EQ5D), the self-rated EQ visual analogue scale (EQVAS) and the Palliative Care Outcome Scale Renal (POS-S Renal) were used to assess HRQOL, self-rated health and symptom burden, respectively. Participants were followed from instrument completion to death or study end.

Results: Over a median (25^{th}-75^{th} centile) of 2.6 (1.41-3.38) years, 32% (N=116) of participants died. Shortness of breath, vomiting, restless legs, depression or problems with mobility, self-care or usual activities at baseline were associated with mortality. Survival analysis factors most associated with mortality adjusted hazard ratio (AHR 95%CI) included: higher POS-S Renal score 2.4 (1.3, 4.3) P=0.004 (highest tertile), lower EQ5D score 2.6 (1.3, 5.3) P=0.01 (lowest tertile), lower EQ VAS rating (figure 1.) 2.7 (1.4, 5.2) P=0.004 (lowest tertile). After age adjustment AUC 95%CI for mortality were: 0.71 (0.63, 0.80) for POS-S Renal, 0.76 (0.68, 0.84) for EQ5D and 0.71 (0.62, 0.79) for EQ VAS self-rating. AUC 95%CI was highest for our third model at 0.80 (0.75, 0.85) comprised of elements from both instruments and established mortality risk factors.

Conclusions: HRQOL, symptom burden, and self-rated health were independently associated with all-cause mortality. Age adjusted EQ5D, POS S Renal scores, EQ VAS self-rating and models based on combinations of elements from each instrument may aid in mortality prediction and palliative input planning in haemodialysis.

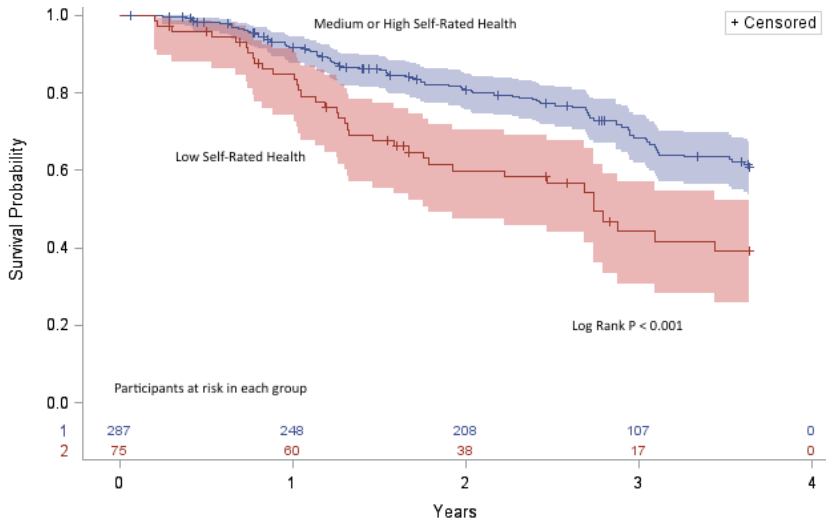

Figure 1. Survival probability curves for all-cause mortality comparing participant self-rated health based on visual analogue scale (EQ VAS) (N=362 total, N=116 deaths).

Abstract 12

Waiting, waiting, waiting…transplanted: enabling transplantation for the highly sensitised patients

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Background: Transplantation is the optimal form of renal replacement therapy for suitable patients with end stage renal disease. Long term outcomes improve when the time spent on dialysis is minimised, and individuals with prolonged waiting times can become unfit for transplantation. Those with pre-existing HLA antibodies often wait for a disproportionately long time.

Methods: All Northern Ireland patients active on the UK deceased donor renal transplant waiting list on 1 Jan 2013 were ranked according to waiting time. All waiting longer than 5 years were identified and those that were very highly sensitised were reviewed with the Histocompatibility & Immunogenetics staff. Antibodies that were currently not detectable or present at low titres were removed from the unacceptable antigens listed with NHS Blood and Transplant.

Results: There were 30 patients waiting longer than 5 years. The mean waiting time for transplantation was 8 years 5 months, (range 5 yr. 1 mth – 21 yr. 3 mth). The mean panel reactive antibody sensitisation was 71%, (range 0 – 100%); 16 (53%) were very highly sensitised (>95% antibodies). The registered unacceptable antigens were altered in 10 (33%). Within 24 months, there were 30 transplants in 28 (93%) patients, 8 (27%) were from living donors. Alemtuzumab was given in 9 and Rituximab in 2. 12 month graft survival was 87%, 4 failed: 2 had primary non-function due to poor donor quality, 1 non-recovery of recurrent episodes of AKI (5 months), 1 recurrent anti-GBM disease (10 months). Two of these patients have since been transplanted successfully. 12 month patient survival was 100%. In NI there are currently only 2 patients waiting longer than 5 years for transplantation.

Conclusion: A proactive approach to highly sensitised patients waiting for renal transplantation can enhance the opportunities for transplant. Such methods should be considered for those with high HLA antibody levels before they have had a prolonged period on dialysis.

Abstracts 13-18:

Moderated Prize Poster Session

Abstract 13

Association of substance abuse with mortality and kidney transplantation among new dialysis patients

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Background: It is unclear to what extent substance abuse contributes to adverse outcomes among dialysis patients. The goal of this study was to describe the impact of substance abuse on mortality and kidney transplantation among new dialysis patients.

Methods: We analysed data from a cohort of 1,226,461 US patients who began dialysis between 1995 and 2008 and were followed until December 2010. Hazard ratios (HR) for hospitalisation events and death were determined for each addictive behaviour (current smoking, alcohol use and illicit drug use) and combinations.

Results: In multivariate analysis, Smoking (HR=1.24, CI 1.23-1.26), alcohol (HR=1.59, CI 1.55-1.63) and drug use (HR= 1.79, CI 1.74-1.84) were each independently associated with higher risks of death. When assessed in combination, increases in mortality of 30% (95% CI 28 to 31%), 66% (95% CI 60 to 71%) and 81% (95% CI 67-96%) were found with rising number of addictive behaviours (1, 2 and 3 versus none) respectively. Similarly, risks of all-cause hospitalisation increased significantly by 13% (CI 12 to 14%), 12% (CI 9 to 16%) and 18% (CI 10 to 26%) with increasing numbers of addictive behaviours. In contrast, the risk of kidney transplantation declined significantly by 42 % (95% CI 40-44%), 80% (95% CI 77-83%) and by 87% (95% CI 80-92 %) for those reporting 1, 2 and 3 addictive behaviours respectively compared to none.

Conclusions: Substance abuse from smoking, alcohol and illicit drugs exerts a significant detrimental impact on patient survival following the onset of dialysis. Better awareness, detection, and treatment programmes for substance abuse are required to reduce the risk of adverse outcomes.

Abstract 14

Blood pressure (BP) trends during the short and long inter-dialytic periods in stable in-centre haemodialysis patients: A 24 hour ambulatory BP monitoring study

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Background: 3-day-a-week in-centre haemodialysis (HD) regimens involve two short (48hr.) and one long (72hr.) intervals between treatments. Recently, higher death risk following the long inter-dialytic period (IDP) was reported. Using ambulatory BP monitoring (ABPM) in a group of stable HD patients, we aimed to determine whether the final 24hrs. of the long IDP are associated with inferior BP control and higher cardiovascular (CV) biomarker levels compared to those of the short IDPs.

Methods: Inclusion criteria: 1. Stable HD regimen for ≥3 months. 2. Age >18yrs. 3. BP measured routinely on arm by automated cuff. 4. No hospital admission within 3months. 5. No active medical condition with life expectancy <6 months. 6. Enrolled by informed consent. Each subject underwent ABPM during the final 24hr. of the long IDP and one short IDP within the same week. Pre-dialysis cuff BP was recorded and blood was collected for CV biomarkers (CRP, Troponin T, BNP) following each ABPM.

Results: 23 subjects completed the study. Mean systolic and diastolic BP (SBP/DBP) did not differ for the long and short IDPs despite significantly greater weight gain during the long IDP. Similar observations were made for pulse pressure (PP), day-time SBP/DBP, night-time SBP/DBP, % “non-dipper” and pre-dialysis CV biomarker levels. (Table).

Index	Long-IDP	Short-IDP	p
24hr. SBP (mmHg, mean ± SD)	147.5± 20	146.6±21	0.6
24hr. DBP (mmHg, mean ± SD)	80±11	80±12	0.5
24hr. PP (mmHg, mean ± SD)	62.6±16	60.4±15	0.3
Day-time SBP (mmHg, mean ± SD)	151±17	148±18	0.1
Day-time DBP (mmHg, mean ± SD)	83±11	82±10	0.4
Night-time SBP (mmHg, mean ± SD)	144±25	145±26	0.6
Night-time DBP (mmHg, mean ± SD)	76±12	79±16	0.2
Non-dipper (n / %)	13/56%	13/56	0.9
Inter-dialytic weight gain (kg, mean ± SD)	2.7±1.4	1.8±0.8	0.002
Pre-dialysis Troponin T (ng/mL, mean ± SD)	76±57	72±50	0.4
Pre-dialysis BNP (pg/mL, mean ± SD)	9801±10805	8628±9822	0.1
Pre-dialysis CRP (mg/L, mean ± SD)	9.5±12	6.6±9	0.2

Conclusions: 1. Overall ABPM results indicated SBP mildly above target. 2. ABPM revealed no evidence of inferior BP control during the final 24hrs of the long IDP despite greater fluid gain. 3. Pre-dialysis CV biomarker levels were not significantly higher following long vs. short IDP.

Risk of Acute Coronary Events and Coronary Interventions for Overweight and Obese Patients versus normal Weight Patients undergoing Dialysis; A National Study

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Background: Although elevated body mass index (BMI) is associated with increased risk of cardiovascular events in the general population, it is suggested that the converse may hold true for patients on dialysis.

Methods: We tested this hypothesis in a national cohort of 1,072,737 incident Medicare-eligible US patients, who began dialysis between 5/1995 and 12/2008. Hospitalizations attributed to first myocardial infarction (MI) [ICD 9 codes; 410] were obtained from the US Renal Data System and merged with treatment history and mortality files. Major coronary interventions following first MI, namely coronary angioplasty, stent, and coronary bypass surgery were also captured. Multivariable Cox regression compared hazard ratios [HR] of MI and subsequent coronary interventions among BMI categories.

Results: The adjusted HR of MI was highest for underweight patients and lowest for the most obese patients, decreasing significantly with increasing BMI category. The association of BMI with hazard of ACS followed a similar pattern. Following an MI, overweight patients (BMI 25-<30) were significantly more likely to receive a coronary intervention for either a STEMI (HR 1.31, 95% CI 1.11, 1.54) or non-STEMI (HR1.17, 95% CI 1.06,1.29) compared to normal weight individuals and this benefit did not extend to patients in the Class II and III Obesity groups or underweight patients.

Conclusions: In contrast to the general population, higher BMI is associated with lower risk of major coronary events in US dialysis patients suggesting a protective effect. Furthermore, access to coronary interventions following a major coronary event is not equal across BMI categories.

		N (%)	HR of MI[1]	Intervention post STEMI MI	Intervention post non-STEMI MI
			HR	HR	HR
BMI category (Kg/m²)					
Underweight	(< 18.5)	58,659 (5.7)	1.04 (1.00,1.08)	0.79 (0.56,1.12)	1.00 (0.82,1.24)
Normal	(18.5 to<25)	380,587 (37.0)	1.00 (1.00,1.00)	1.00 (1.00,1.00)	1.00 (1.00,1.00)
Overweight	(25 to<30)	290,542 (28.3)	0.96 (0.94,0.98)	1.31 (1.11,1.54)	1.17 (1.06,1.29)
Class I Obesity	(30 to<35)	159,895 (15.6)	0.90 (0.87,0.92)	1.24 (1.01,1.52)	1.01 (0.89,1.15)
Class II Obesity	(35 to<40)	75,823 (7.4)	0.85 (0.82,0.88)	1.20 (0.91,1.59)	1.05 (0.89,1.26)
Class III Obesity	(> 40)	63,027 (6.1)	0.84 (0.81,0.88)	1.04 (0.74,1.45)	0.89 (0.72,1.10)

[1] Multivariable model adjusted for: age, sex race, cause of ESKD, hypertension, diabetes, coronary disease, heart failure, peripheral vascular disease, malignancy, tobacco use, drug use, alcohol use, haemoglobin, serum albumin, eGFR at dialysis initiation, and employment status,

Abstract 16

Spatial and temporal modelling of anti-glomerular basement membrane disease: evidence to support an environmental trigger

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[1]Trinity Health Kidney Centre, St. James's TCD Campus, Dublin , [2]Mater Misericordiae Hospital, Dublin, [3]Beaumont Hospital, Dublin, [4]Waterford Regional Hospital, [5]St. Vincent's University Hospital, Dublin, [6]Limerick University Hospital, [7]Galway University Hospital, [8]Cork University Hospital, [9]Letterkenny General Hospital, Donegal, [10]St. James's Hospital, Dublin, [11]Department of Public Health and Primary Care, Trinity College Dublin

Background: The pathogenesis of anti-glomerular basement membrane (GBM) disease is well characterised at a molecular level but the inciting factor is unknown. An environmental trigger has been suspected however quality epidemiological studies are lacking to refine this hypothesis. The aims of this study were to robustly define country-wide incidence of anti-GBM disease and investigate clustering of cases in time and space.

Methods: Multi-centre retrospective observational study between 1.6.2003 and 31.5.2014. Inclusion criteria were based on 2012 Chapel Hill Consensus Nomenclature Criteria. We screened immunology laboratories for instances of positive anti-GBM antibody and the national renal histopathology registry for biopsy-proven cases. Clinical information was obtained by chart review at each centre. We defined the population at risk using published census figures. A variable-window scan statistic was used to detect temporal clustering. A Bayesian spatial model was employed to estimate standardised incidence ratios (SIR) for each county.

Results: Seventy-nine cases met inclusion criteria. National incidence rate was 1.64 (95% CI 0.82-3.35) pmp/year. A statistically significant temporal cluster (n=10) was identified from 10.12.2012 - 14.3.2013. Six of these cases occurred in the south-east. There was substantial regional variation in incidence (figure 1). Donegal had the highest SIR (1.71, 95% CI 1.02-3.06). These patients (n=7) were older than the rest of the cohort (66 v 61yrs), 71% were double-positive and none had lung involvement.

Conclusions: Country-wide incidence of anti-GBM disease using a robust screening process is higher than previously reported by single centre or regional studies. We detected clustering of cases in time and space which supports the hypothesis of an environmental trigger.

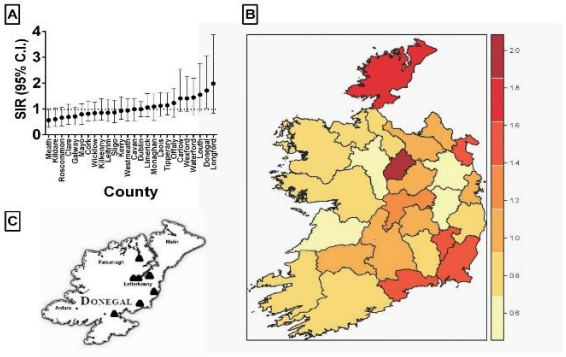

Figure 1. Standardised incidence ratios for each county (A), spatial map of incidence (B) and location of Donegal cases (C)

Abstract 17

Ten Year Experience of IgA Nephropathy in the South East.

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Background: Worldwide IgA nephropathy (IgAN) is the most common non-infectious glomerulonephritis[1]. Its presentation varies widely from asymptomatic urinalysis abnormalities to renal failure. There are few randomised controlled trials to guide its treatment.

Methods: We retrospectively reviewed all renal biopsies undertaken at our institution over ten years. Data collected included patient characteristics, clinical presentation, treatment and disease course.

Results: Between January 2005 and December 2014 425 native renal biopsies were performed. IgAN was diagnosed in 65 (15%); 51 (78%) male and 14 (22%) female, median age was 39years (IQR 18.5). Median creatinine was 139umol/L (IQR 146) at time of biopsy. Presenting features are detailed in table 1. 56 (86%) received ACEI +/or ARB, 19 (29%) fish oils, 18 (28%) steroids without mycophenolate, 11 (17%) mycophenolate +/- steroids. Follow-up data at 1 year was available for 58 (89%). Of these 6 (10%) were receiving RRT. Of the remaining 52, 12 received steroids alone and 9 received mycophenolate +/-steroids. At 1 year those receiving steroids had a median change in serum creatinine of +6umol/L (IQR 17.8) and in urinary PCR -259mg/mmol (IQR 253.8). Those receiving a mycophenolate-based regimen had a median change in creatinine of -18umol/L (IQR 47) and in urinary PCR -215mg/mmol (IQR 133).

Conclusions: Manifestations of IgAN vary widely. The mainstay of therapy consists of supportive measures, which the majority of our cohort received. Immunosuppressive regimens are reserved for a select group, and in our cohort both mycophenolate and steroid based regimens yielded a reduction in proteinuria.

Table 1

	Patient number (n=65)	Percentage (%)
Vasculitic rash	7	11
Frank haematuria	17	26
Nephrotic range proteinuria	25	38
Hypertension	44	68
Creatinine ≥ 200umol/L	19	29
Creatinine ≥ 300umol/L	11	17

References:1. Jurgen Floege and Frank Eitner: Current Therapy for IgA Nephropathy. J Am Soc Nephrol 22: 1785-1794, 2011.

Abstract 18

A Retrospective Survey of Rhabdomyolysis in an Acute Hospital in 2014.

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Background: Rhabdomyolysis is a state of skeletal muscle necrosis resulting in leakage of intracellular muscle content such as myoglobin and creatinine kinase (CK). It may result in acute kidney injury (AKI) via direct renal tubular toxicity of myoglobin, tubular obstruction and intrarenal vascoconstriction. We reviewed all cases of rhabdomyolysis admitted to Tallaght Hospital in 2014.

Methods: Rhabdomyolysis was defined as serum CK >5times upper limit normal. Data was collected retrospectively from medical records and analysed using SPSS version 22.

Results: We reviewed 317 cases with a mean(SD) age of 59(19) years; 68% were male. Median(interquartile range) for CK was 1726(1175-3347)IU/L. Median length of stay was 10(5-25) days. Total mortality was 16%. The main associations were acute coronary syndrome (19.2%), post-operative (18.0%), long-term confinement in the same position (16.7%), infection (9.1%), seizures (6.3%), trauma (5.7%) and drugs and toxins (5.4%). A secondary factor was evident in 36% of cases, with 54/115(46.9%) being infection. AKI was present in 42% of cases; of those, AKIN stages were as follows 1 (38%), 2 (21%), 3 (41%). Regarding AKIN3, 33/48(65%) required acute dialysis with a mortality of 20/48(42%). A nephrology consultation was requested in 22% of cases; 9% were already under the care of nephrology. Of note, 57% (76/134) of patients with AKI had neither a nephrology consultation nor were under nephrology care.

Conclusion: Rhabdomyolysis in an inpatient population occurs in conjunction with many other medical and surgical problems. It is associated with substantial mortality and morbidity. Nephrology consultation should be considered in AKI.

Abstracts 19-74:

General Poster Session

Abstract 19

The Polycomb repressor complex and Smad 3 constitute a switch enhancing complex that interprets TGF-β signaling to control cell fate in diabetic microvascular complications.

Letizia De Chiara, Darrell Andrews, Giorgio Oliviero, Hayley Beaton, Catherine Godson, Gerard Cagney, John Crean.

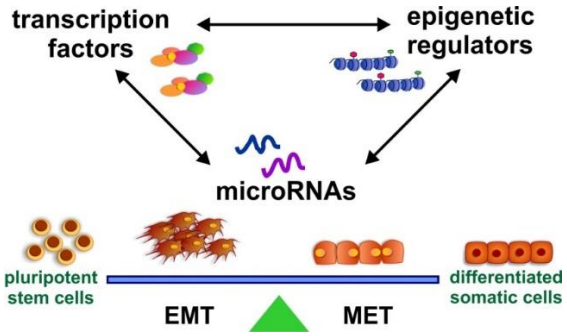
Diabetes Complications Research Centre, UCD School of Biomolecular and Biomedical Science and UCD School of Medicine and Medical Science, University College Dublin, Belfield, Dublin 4, Ireland

Background: Developmental cell fate decisions are controlled by the interplay of transcription factors and epigenetic modifiers which together determine cellular identity. During the initiation and progression of diabetic complications, cells within affected tissues undergo a process of reprogramming, evoking gene expression profiles reminiscent of ontogenesis. *In vitro* and *in vivo* studies have identified members of the Transforming Growth Factor-β superfamily as central to these processes and established this signaling network as a prime candidate for therapeutic manipulation.

Methods: Western Blot, Immunofluorescence, Microscopy, Immunoprecipitation, Mass Spectrometry

Results: We have identified a context dependent switch enhancing complex comprising Smad 3 and PRC2 that regulates cell fate during embryonic differentiation and is reactivated during fibrotic processes. Our data strongly suggests that the H3K27 methylating polycomb repressor complex 2 regulates the silencing of TGF-β activated genes during cell differentiation and commitment. Gene expression profiles of renal cells undergoing TGF-β mediated differentiation has revealed a number of transcription factors that co-segregate with Smad3 including the Yamanaka reprogramming factors Oct4, Sox2 and Nanog, while differential expression of these factors in response to TGF-β was clearly demonstrated by western analysis of chromatin associated proteins. Analysis of H3K27 trimethylation revealed that during the process of differentiation the histone mark is turned on, suggesting PRC2 mediated remodeling of the chromatin and switching of gene expression from a permissive or “ON” state to non-permissive or “OFF”. Intriguingly proteomic analysis of the EZH2 interactome revealed a number of direct associations with a transcription factor network including phosphorylated Smad 3, TEAD4, Oct 4 and Sox2, suggesting that cooperative recruitment of PRC2 regulates gene repression during TGF-β mediated differentiation. Furthermore, treatment of cells with the specific EZH2 inhibitor 3 deazaneplanocin, inhibited TGF-β mediated epithelial dedifferentiation and blocked the expression of genes associated with fibrosis.

Conclusions: This data demonstrates for the first time a functional association between Smad signaling and the polycomb repressor complex with potential for therapeutic manipulation during the progression of renal disease.



Abstract 20

Exploiting renal oxygenation to develop novel strategies for detection and treatment of renal disease

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Cellular response to hypoxia (low oxygen) is mediated through stabilisation of hypoxia inducible transcription factors (HIFs). In the kidney, hypoxia promotes fibrogenesis through modulation of the extracellular matrix. The lysyl oxidase family of collagen cross-linking enzymes, consists of five members; LOX and LOXL-like 1-4 (LOXL1-4). Inhibiting HIF or LOX function attenuates renal fibrosis. As hypoxia is an early feature of kidney injury, we hypothesised that hypoxia-induced LOX proteins may represent novel urinary biomarkers for the early detection of renal injury and potential therapeutic targets for treatment of CKD.

LOX family gene and protein expression was analysed in two pre-clinical models of kidney injury; unilateral ureteral obstruction (UUO) and gentamicin-sulphate-induced (GS) renal disease (40 or 120 mg/kg/day for 9 days) and two independent kidney transplant nephropathy collections, GoCAR (Genomics of Chronic Allograft Nephropathy) and the North Dublin Renal Biobank.

Three of the five LOX isoforms were significantly increased in UUO and down-regulated with resolution of injury. Urinary levels of LOX isoforms correlated with gentamicin-induced injury and inhibition of LOX preserved renal function. LOX proteins are currently being evaluated in a CKD patient urine collection.

We conclude that LOX isoforms are differentially regulated during kidney injury, certain isoforms may be used as urinary biomarkers of kidney disease and are potential novel therapeutic targets for treatment of CKD.

Abstract 21

FRMD3: A Novel Modulator of Diabetic Nephropathy?

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Background: Genome-wide association studies have identified a single nucleotide polymorphism (SNP, rs1888747 C>G) in the extended promoter of the FERM domain containing 3 (FRMD3) gene associated with increased risk of diabetic nephropathy (DN) in type 1 and type 2 diabetes. Renal expression of FRMD3 decreases significantly with severity of DN. *In silico* analysis of the FRMD3 extended promoter sequence predicts that FRMD3 may be co-regulated with bone morphogenetic protein (BMP) pathway family members. Given the evidence for BMP agonists and antagonists in DN we propose that altered FRMD3 expression may be implicated in the pathophysiology of DN.

Methods: Expression of FRMD3 and fibrotic markers were measured in primary human mesangial cells (hMCs) and podocytes by quantitative Taqman PCR and western blot following: (i) transfection with FRMD3-targeting siRNA and (ii) stimulation with BMPs (BMP-2/4/6/7; 10ng/ml) or TGF-β1 (5ng/ml).

Results: Here we report that reduced FRMD3 expression in primary human mesangial cells (hMCs) is associated with increased expression of DN-associated connective tissue growth factor (CTGF), jagged 1 (JAG1) and fibronectin 1 (FN1) genes, this was further exacerbated by stimulation with TGF-β1 (5ng/ml). Inhibition of podocyte FRMD3 expression renders podocytes more vulnerable to TGF-β1-induced injury. We provide evidence for FRMD3-BMP co-regulation by demonstrating that FRMD3 gene expression is significantly up-regulated in hMCs following stimulation with BMPs (BMP-2/4/6 and 7). Additionally, we have found a correlation between serum creatinine and FRMD3 expression in renal biopsy material affected by disease of diverse aetiologies.

Conclusion: Taken together our findings suggest that altered FRMD3 expression may play a role in the pathogenesis of DN.

Abstract 22

Computational analysis of BMP-receptor and BMP-antagonist interactions with a view to designing BMP super-agonists and dominant negatives

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We have previously reported a role for the Bone Morphogenetic Protein [BMP] antagonist Gremlin as a driver of diabetic nephropathy and fibrosis in both kidney and lung. Bone Morphogenetic Proteins are integral regulators of bone and organ development. BMPs are secreted proteins and signal by associating with membrane bound receptors. The activity of BMP agonists is modulated by a family of secreted protein antagonists, including Noggin, Crossveinless-2 and Gremlin that limit BMP-receptor association by binding to the ligand and thereby inhibiting receptor binding. We have analysed BMP-receptor and BMP-antagonist interactions using a newly designed automated pipeline, Protein Complex Tool (PCT). Co-crystal structures of the BMP-BMP receptor and the BMP-antagonist complexes were submitted to PCT and in silico alanine substitution scans were performed to calculate the free energy contribution of each BMP-2, or BMP-7, residue to the stability of the complexes with receptors, BMPRIa (BMP-2 only) and ActRIIa, and antagonists, Crossveinless-2 (BMP-2 only) and Noggin (BMP-7 only). The free energy calculations identified the key contributions of BMP residues to both binding events and suggested mutations that might generate super-agonist and dominant negative molecules. Further in silico analysis was performed by mutating each residue to each of the other 19 amino acids. From this we identified potential super-agonist (SA) and dominant negative (DN) mutations for both BMP-2: L51V and N102T (SAs), S88G and L92D (DNs), and BMP-7: E60T, D119I, I124A and K127E (SAs), F117E and V122D (DNs). The super-agonists will bind and activate receptor but will be resistant to binding by antagonist; in contrast, the dominant negatives, bind antagonist but not receptor. Data will be presented from our investigations of these molecules as potential therapeutic leads for treating fibrotic diseases including DN.

Abstract 23

Wnt6 regulates epithelial cell differentiation and is dysregulated in renal fibrosis

Hayley Beaton, Darrell Andrews, Martin Parsons, Mary Murphy, Andrew Gaffney, David Kavanagh, Gareth J. McKay, Alexander P. Maxwell, Cormac T. Taylor, Eoin P. Cummins, Catherine Godson, Debra F. Higgins, Paula Murphy, and John Crean

Background: Diabetic nephropathy is the most common microvascular complication of diabetes mellitus. We have described the functional characterization of Wnt6, whose expression is progressively lost in diabetic nephropathy and animal models of acute tubular injury and renal fibrosis.

Methods: Mouse embryonic whole mounts at Theiler stage 17.5 were analysed by in situ hybridisation. Wnt6 expression was determined in the unilateral ureteral obstruction (UUO) mouse model of tubulointerstitial fibrosis. Wnt6 was overexpressed in renal epithelial cell lines and signalling networks were assessed by Western blot. Vimentin expression was assessed by Western blot in IKKα/β-/- and p65 NFκB-/- mouse embryonic fibroblasts to elucidate the mechanism of Wnt6 further.

Results: Developmental expression demonstrated prominent Wnt6 and FzD7 expression in the mesonephros of the mouse kidney, suggesting a role for Wnt6 in epithelialization. Importantly, TCF/Lef reporter activity is also prominent in the mesonephros. Expression analysis of Wnt family members in human renal biopsies identified differential expression of Wnt6, correlating with severity of the disease. In animal models of tubular injury and fibrosis, loss of Wnt6 was evident. Importantly, Wnt6 rescued epithelial cell dedifferentiation in response to TGF-β; Wnt6 reversed TGF-β-mediated increases in vimentin and loss of epithelial phenotype. Wnt6 inhibited TGF-β-mediated p65-NFκB nuclear translocation, highlighting crosstalk between the two pathways. The critical role of NFκB in the regulation of vimentin expression was confirmed in both p65-/- and IKKα/β-/- embryonic fibroblasts.

Conclusion: We propose that Wnt6 is involved in epithelialization and loss of Wnt6 expression contributes to the pathogenesis of renal fibrosis.

Abstract 24

Podocyte Architecture and Glomerular Basement Membrane Thickness in a Rat Model of Obesity and Type 2 Diabetes

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Background: Diabetic kidney disease (DKD) is postulated to arise secondary to podocyte injury. The Zucker Diabetic Fatty (ZDF) is a well-characterised model of DKD associated with obesity, progressive insulin resistance and the development of type 2 diabetes. The aim of this study was to describe and quantify ultrastructural changes in podocyte morphology in age matched ZDF *Fa/Fa* (diabetic) versus ZDF Fa/+ (non-diabetic control) rats at 31 weeks of age.

Methods: Ultrathin sections of renal cortex from each time point were viewed using a Technai 12 transmission electron microscope. Glomerular basement membrane (GBM) thickness, podocyte foot process diameter (PFPD) and podocyte foot process frequency (PFPF) per unit length of GBM were determined for each group (n=3-7 per group). Statistical comparison of data was performed using a Mann Whitney U test.

Results: Glomeruli from diabetic animals demonstrated GBM thickening, podocyte hypertrophy, cytoplasmic vacuolation, foot process effacement (FPE) and podocyte detachment. Significant differences between diabetic and control groups were observed: a 19% increase in median GBM thickness (262nm to 311nm); 21% decrease in median PFPF (3.17 to 2.5 per 3um unit length of GBM) and a 183% increase in median PFPD (343nm to 629nm) in *Fa/Fa* relative to *Fa/+* animals (all p=0.017).

Conclusion: The ZDF rat model of DKD is characterised by podocyte injury. Quantitative ultrastructural analysis of podocyte architecture may permit the elucidation of the basis for proteinuria remission following intensive interventions such as Roux-en-Y gastric bypass surgery.

Abstract 25

A novel platelet function assay detects alterations in platelet function pre and post kidney transplantation

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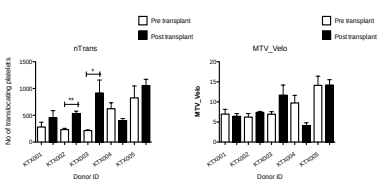
Background: Acquired platelet dysfunction in the setting of uraemia is a significant cause of morbidity and mortality in patients with end stage kidney disease (ESKD). The aetiology of platelet dysfunction in uraemic states is multifactorial including the direct effect of uraemic toxins on platelets, platelet signalling abnormalities, anaemia, von Willebrand factor dysfunction and blood vessel abnormalities. Kidney transplantation, by restoring renal function should restore platelet function however there is a paucity of research investigating the effect of kidney transplant on platelet function.

Methods: Five individuals with ESKD scheduled for live kidney donation with a mean age of 37±5.2 year (three female and two male) were recruited into this study following informed consent and approval by our institutional review board. Blood samples were collected pre and post-transplant (median 7.3 weeks, range 9 days – 8.7 weeks). Whole blood was labelled and perfused over immobilised VWF using a custom-designed microfluidic parallel plate flow chamber at arterial shear flow rates. Dynamic platelet-protein interactions were tracked and evaluated by a novel analytical method providing rapid data on five platelet translocation properties (the numbers of platelet tracks, stably-adhered platelets, translocating platelets, median speed travelled and platelet coverage on the final analysis frame, ***PCFF***).

Results: ESKD subjects demonstrated an altered profile of platelet-VWF interactions in four of five parameters measured despite similar platelet counts pre and post transplant. Specifically, increased numbers of platelet tracks, stably adhered platelets, translocating platelets and PCFF were observed post transplant (2 patients with statistically significant differences and other with trends only).

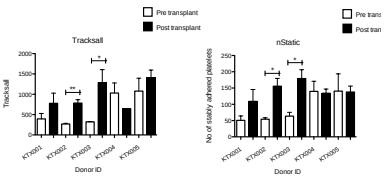
Conclusion: To the best of our knowledge, this is the first report of platelet activity when renal function has been restored post kidney transplantation. An increase in interaction with vWF (post transplant) may suggest restoration of platelet function.

Translocating platelets and speed travelled



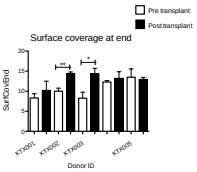
Translocating platelets tether, adhere and roll on the VWF - not static

Platelet tracks and stably adhered platelets



Represents platelet interactions with VWF

Surface coverage on final frame



Snapshot of platelet coverage on final frame (30 frames per second are recorded to reach a total of 1000 frames, analysis based on frame 1-500)

Abstract 26

Attitudes to organ donation amongst university students in the West of Ireland.

McDonnell TM*, O'Regan JA, Gleeson J, O'Connor S, Lappin DW.
Galway University Hospital, Galway

Background: Successful organ transplantation programs depend upon a regular supply of organs from deceased donors. Organ donation in Ireland operates on 'explicit-consent' basis whereas some European countries employ 'presumed-consent' policies. The aim of this project was to characterise the attitudes of university students towards organ donation.

Methods: We surveyed university students attending National University of Ireland Galway (NUIG) for the academic year 2014-2015. An invitation to participate in the 16-point questionnaire, which examined students' attitudes towards organ donation, was provided via an email request linked to SurveyMonkey® software.

Results: In total, 732 participants responded to the survey. Male participants comprised of 222 (30.3%) and the median age was 21 years (range 17-55 years). Ninety-six percent were generally in favour of organ donation, 71% were in favour of a 'presumed-consent' default system and 81% supported an online organ donor signatory registry. Medical students (totaling 395 participants) responded to the survey. Ninety-six percent of these participants were generally in favour of organ donation, 73% were in favour of a 'presumed-consent' default system and 80% supported an online organ donor signatory registry. Comprehensive results on data points are presented in Table 1.

Conclusions: Attitudes towards organ donation amongst the respondents were overwhelmingly positive. The attitudes of participants studying medicine were remarkably similar to the general university student population. A large proportion was in favour of a 'presumed-consent' (opt-out) default system and a national online donor signatory registry.

Abstract 27

Irish Experience of Participation in UK Paired Kidney Exchange (PKE) Scheme

Ryan H, Connaughton D, Wong L, Hart P, Higgins R, O'Neill D, Keoghan M, Conlon P, Magee C.

Background: In Ireland patients with a living donor, to whom they are deemed immunologically incompatible, are referred to the United Kingdom for enrolment into the PKE programme. This allows the incompatible donor-recipient pair to be matched with another incompatible pair in order to proceed with live kidney transplantation. Here we report the Irish experience.

Methods: Retrospective chart review of all patients enrolled in the PKE programme from 2010.

Results: In total 38 donor-recipient pairs have been listed in the PKE programme, with 14 pairs currently active on the list. The majority of patients referred are highly sensitised (76.4% (n=26) PGen >80%) and 47% of recipients are blood group O. Seven (18.4%) donor-recipients pairs have undergone successful PKE transplantation all of whom now have functioning grafts. Eight patients (21%) proceeded to direct living donor transplantation with 4 requiring desensitization prior to transplantation. Three recipients received a deceased donor kidney transplant from the Irish pool. The average number of runs in the PKE programme, with 1 run occurring each quarter, is 2 for successful pairs. However the average numbers of runs for all patients listed is 4 (range 1 -28 runs).

Conclusion: PKE remains an option for incompatible donor-recipient pairs which should be explored prior to desensitization and can offer patients who are highly sensitized the option of a living donor transplant. Current success rates for Irish patients are approximately 18.4% with a trend toward lower success rates in the highly sensitized group.

Abstract 28

Altruistic Kidney Donation in Northern Ireland: Allocation and Motivations

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Background: Non-directed altruistic kidney donors (NDAD) are an increasing proportion of living donors. Since 2012 UK donors have had the choice to enter a pooled donation scheme (initiating a chain of transplants) or to donate directly to the national waiting list. There is currently no legislation permitting altruistic kidney donation in the Republic of Ireland, despite increasing public interest. This study focuses on outcomes for all NDAD in Northern Ireland from 2011-14.

Methods: From a retrospective review of a prospectively kept database, donor demographics, serum creatinine, kidney allocation and motivating reasons for donation were evaluated.

Results: There were 20 NDAD, 12 (60%) were female. Mean age was 55 years (27-71 yr.). One patient was from the Republic of Ireland. 6 (30%) donors chose to enter the pooled scheme and 4 (20%) actually donated this way. The remainder donated directly to the national waiting list. Three (15%) kidneys were matched locally. Underlying motivation included the desire to help another person in 10 (50%), strong faith was a contributing factor in 10 (50%), 11 (65%) had a family member or friend with chronic illness and 18 (90%) participated in other altruistic acts such as blood donation. A smaller cohort identified donation with the need to rectify feelings of guilt and injustice.

Discussion: NDAD make a valuable contribution to kidney donation but entry into the UK pooled scheme should be encouraged to maximize the full potential of such gifts. Consideration should be given to permissive legislation for NDAD in the Republic of Ireland.

Abstract 29

The impact of donor and recipient weight incompatibility on outcomes in renal transplantation

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Background: Kidney transplantation has been proposed as an accelerated model of nephron reduction resulting from the accumulation of repeated insults, both immunologic and non immunologic events. The direct impact of matching the donor weight (Dw) to the recipient weight (Rw) has been assessed in both deceased and living kidney donations; however conflicting results have been produced. The aim of this retrospective study was to directly evaluate the impact of Dw/Rw ratio on allograft function in the Irish population.

Methods: Between January 2006 and June 2013, 1043 deceased kidney transplants were performed. Of these, 942 recipients were selected after exclusion of recipients with multiple-organ transplantation and en bloc dual kidney transplant. Patients were divided into quartiles (Q) depending on the ratio of Dw/Rw: Q1 (<0.89), Q2 (0.89-1.01), Q3 (1.02-1.22) and Q4 (>1.22). Recipient and donor characteristics were obtained from the National Kidney Transplant Centre database.

Results: Patient profiles varied between quartiles with 77% males in Q1 compared to 76%, 67% and 40% in Q2-Q4 respectively (p<0.001). Ages were higher in the lower quartiles with mean ages (SD) ranging from 50.0 (13.2) in Q1 to 41.0 (18.8) in Q4 (p<0.001). Patients in Q4 had a higher level of eGFR at one year post transplant (median 65.8ml/min, IQR 48.5 -85.5) compared to Q1-Q3 which had median eGFRs of 54.4, 54.8 and 55.3 ml/min respectively (p<0.001). There were no significant differences in 1-year and 5-year allograft survival between the groups, however at five years post transplant, there were significant differences in the eGFR across four quartiles Q1-4 (median eGFR of 56.8, 61.3, 60.8 and 62.7ml/min respectively, p=0.02).

Conclusion: In the setting of cadaveric renal transplantation, mismatching of the allograft size to the recipient size does not impact significantly on patient or graft survival however recipients that were lighter and received kidneys from larger donors had higher eGFR at 5 year compared to heavier recipients.

Abstract 30

Vaccinations in Renal Transplant Patients

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Background: Adverse outcomes of influenza & pneumococcal infections in solid organ transplant recipients have been well documented. Vaccinations are therefore recommended. Despite emerging evidence of the safety &effectiveness among immunosuppressed patients, most vaccines are still underutilized, we conducted a survey among the renal transplant patients in Beaumont Hospital to determine the awareness & if vaccinations are up to date

Methods: Questionnaires were handed to patients during a clinic visit over a span of 2 weeks, it addressed various aspects including the awareness of importance of vaccinations, source of information, if they were up to date with the vaccines & where did they receive it?

Results: A total of 65 patients participated in the survey, 57% male & 43% female patients, it was the 1st transplant for 71%,2nd for 15% and 3rd for 3% patients ,11% patients left this question blank,94% of the patients admitted awareness of the importance of the vaccinations whereas 6% admitted otherwise.46% patients got the information from consultant,35% patients from the gp,11% from both Consultant and GP & 8% from other source.78% patients had received the influenza vaccine, 20% had not and 2% did not know, 80% received the vaccination at GP 2% in Beaumont Hospital and 18% in other locations. 49% patients had received Pneumococcal vaccine, 34% had not,15% of the patients did not know & 2% left the question blank, 97% patients received it at GP and 3% at other locations.

Conclusions: We can conclude that the majority of the patients are aware of the importance of vaccinations, however there is still a significant percentage who are not up to date, especially with pneumococcal vaccine, steps should be taken to ensure that transplant patients are routinely reminded about receiving their vaccinations during clinic & GP visit and periodic reminders should be sent out in post.

Abstract 31

Kidney Transplant Outcome in Familial C3 Glomerulopathy

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Background: C3 glomerulopathy has recently been proposed as a new entity to describe glomerular abnormalities associated with dysregulation of the alternative complement pathway. An Irish family was first reported with autosomal dominant C3 glomerulopathy and linkage to the regulators of complement activation locus. A novel hybrid CFHR3-1 gene was subsequently identified encoding an abnormal CFHR3-1 protein in affected family members over three generations. Here, we describe the outcome of kidney transplantation in this family.

Methods: A retrospective review of patients' medical records and kidney biopsies was performed.

Results: Table 1 outlines the characteristics of all five affected family members who underwent kidney transplantation (status of kidney transplant: NF, non functioning; F, functioning)

Conclusions: Post transplant recurrence is common in all forms of C3 glomerulopathy. In this family cohort, 4 out of the 8 kidney transplantations had evidence of recurrence.

Case index	**1**	**2**	**3**	**4**	**5**
Age of diagnosis (years)	25	51	28	4	21
No. of kidney transplantation	2	1	1	3	1
Age at 1st tx (year)	51	59	34	11	31
Status of 1st tx	NF	F	F	NF	F
Age at 2nd tx (years)	72	-	-	24	-
Status of 2nd tx	F	-	-	NF	-
Age at 3rd tx (years)	-	-	-	41	-
Status of 3rd tx	-	-	-	F	-
1st graft survival (months)	116	127 (follow up)	103 (follow up)	79	47 (follow up)
2nd graft survival (months)	8 (follow up)	-	-	170	-
3rd graft survival (months)	-	-	-	5 (follow up)	-
Recurrence in graft (biopsy-proven)	Yes	-	Yes	Yes	-
Time to recurrence (months)	101	-	93	0.5	-
Creatinine (µmol/L)	90	137	105	115	74
UPCR (mg/mmol)	39	10	179	-	13

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Abstract 32

Abatacept in the treatment of recurrent primary focal segmental glomerulosclerosis post kidney transplantation

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Background: Abatacept is a cytotoxic T lymphocyte associated antigen 4 immunoglobulin fusion protein (CTLA-4-Ig). It is a costimulatory inhibitor that targets B7-1, which is a transmembrane protein normally expressed on antigen presenting B cells where it interacts with CD28 on CD4+ T cells. B7-1 is induced in podocytes in some animal models of proteinuric kidney disease and it has been reported in biopsy specimens of patients with recurrent focal segmental glomerulosclerosis (FSGS). We describe three patients treated with Abatacept for recurrent primary FSGS post-transplantation.

Methods: A retrospective review of patients' medical records and kidney biopsies was performed.

Results:

Variable	Patient 1	Patient 2	Patient 3
Age at first presentation (years)and Sex	33, female	11, male	40, male
Interval from initial diagnosis to development ESKD (years)	11	3	3
Kidney Donor	Deceased donor; earlier transplant from a deceased donor failed owing to recurrent FSGS (despite plasma exchange, Rituximab and steroid tx) over 5 years	Deceased donor	Deceased donor
Treatment for FSGS before Abatacept therapy	Recurrence at day 7	Recurrence at day 1 (treated with plasma exchange 8 weeks and Rituximab 375mg/m2 x2 doses)	Recurrence at day 14
Abatacept therapy	10mg/kg x 2 doses	10mg/kg x 5 doses	10mg/kg x 2 doses
Clinical response	Clinical remission	No clinical response	No clinical response
UPCR (mg/mmol) at presentation	2873	287	736
UPCR (mg/mmol) post tx	245	1511	1136

Conclusions: These three cases highlight the varied clinical response to treatment with Abatacept. It is likely that the underlying mechanisms of disease are divergent in subtypes of FSGS. The durability of the response in the patient 1 remains to be determined.

Abstract 33

The association of Vitamin D with Persistent Secondary Hyperparathyroidism after Renal Transplantation

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Background: The prevalence of Vitamin D deficiency and its relationship with persistent secondary hyperparathyroidism post successful renal transplantation is unclear.

Methods: This was a cross-sectional observational study. Patients attending for routine post transplant follow-up were included. Data on eGFR, PTH, 25OH Vitamin D, ionized and serum calcium was collected. Clinical characteristics and medication history was abstracted from the medical record. Results are given as mean (sd) or median (Intra-Quartile Range [IQR]) as appropriate.

Results: 104 patients (>18years) were included. Mean (sd) age was 51.6 (14.7) years, 57.5% were male. Median transplant duration was 6.3 [3.0-9.3] years and mean eGFR was 57.5(19.9)ml/min/1.73m^2. The majority (84%) received a deceased donor renal transplant, 10% had a Living Donor allograft and 5% had dual organ transplants (Liver and Kidney). 9 patients were receiving Vitamin D analogs, 3 were on Cinacalcet and 13 were taking combined calcium/Vitamin D supplements. Median PTH was 74.6 [55.5-117.3], 60.6% had elevated PTH (>65ng/ml). Median 25-OH Vitamin D was 46.7 [27.9-63.2]. Overall, 57.6% of patients had sub-optimal 25-OH Vitamin D levels (<50nmol/L). 8.7% of patients had Total Calcium >2.6mmol/L. There was no significant association between eGFR and PTH or 25-OH Vitamin D. There was a significant inverse association between PTH and 25-OH Vitamin D, $r = -0.533$, $p<0.001$.

Conclusion: Vitamin D deficiency/insufficiency is common after renal transplantation, despite excellent allograft function and is associated with persistent secondary hyperparathyroidism. Few patients received Vitamin D supplementation, which may be beneficial in this population.

Abstract 34

Significant prevalence of respiratory disability in renal transplant recipients.

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Introduction & Aims: Renal transplant patients are frequently afflicted with varying degrees of breathlessness and have not had formal Respiratory Medicine assessment. The aim of this study, was to systematically quantify the prevalence of respiratory disablilty in this population.

Methods: 103 renal transplant recipients, currently under follow up at this Institution had screening tests of their respiratory function status. Following recording of key patient demographics, all were assessed using a validated Dyspnea Score and spirometry. Those displaying respiratory impairment proceeded to lab-based pulmonary function testing and had a formal consultation with a Respiratory Physician.

Results: The patients evaluated had a mean age of 50 years and mean time elapsed since transplantion of 113 months. 44% had a forced expiratory volume in one second(FEV1) less than 90% predicted, with 36% having a Medical Research Council (MRC) Dyspnea Score of ≥2. Of the cohort, 17% were current smokers and 34% ex-smokers.

Conclusion: A significant number of transplant patients displayed evidence of co-morbid respiratory disability as demonstrated by reduced FEV1 and high MRC Dyspnea Scores. Respiratory diability may be commoner in this population that currently anticipated. Formal evaluation of respiratory function should be considered in all patients both before and after renal transplantation.

Abstract 35

The total costs of ESKD-specific medications progressively decline following renal transplantation despite the apparent high cost of immunosuppressant medications

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Health care provision for ESKD patients is complex and resource intensive. Transplantation, once established, is the optimal treatment, associated with the lowest attributable costs. Traditional cost-analysis of transplant vs. dialysis often does not accommodate for medication changes that occur pre- and post-transplant, erroneously viewing transplant-specific medications as 'new/additional' costs. We evaluated the changed usage patterns and costs of ESKD-specific medications used pre- and post-transplantation.

KDCPMS and other clinical records of 103 patients from the South West Ireland ESKD Register were interrogated to analyse patterns of usage and costs of selected medications (erythropoietics, CKD-MBD agents, transplant immunosuppressants & anti-virals). 57 dialysis patients, added to the Transplant Wait List over the last 2 years, were compared with 46 patients transplanted, for at least one year, within the last 3 years. Drug dose, frequency and cost were evaluated at 3, 6, 12 and 24-month intervals. Pharmacoeconomic evaluation utilised a Hospital Pharmacy pricing regimen. Key outcome measures were differences in medication costs and usage patterns within and between pre and post-transplant recipients.

Significant anticipated changes in medication usage occurred. Mean annual patient medication costs pre-transplant were €5,494, progressively decreasing from €6880 to €4264 depending on number of years post transplant (Table). Targets for procurement-led cost reductions were identified in both groups.

Timepoint	PreTransplant Medications (mean cost/year)	PostTransplant Medications (mean cost/year)	Difference
(0-6mths)		*€4039*	
(7-12mths)		*€2840*	
1 year	€5,494	€6,880	+€1,386
2 year	€5,494	€4,569	-€925
3 year+	€5,494	€4,264	-€1,230

Mean dosage and costs of post-transplant medications decline from 3 to 24 months post-transplantation. Pre-transplant medications are more costly when compared with the patient transplanted for more than one year. ESA's offer the most immediate target for procurement-led cost reductions.

Abstract 36

Screening for cervical neoplasm in kidney transplant recipients: a snapshot of current practice

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Background: The increased risk and incidence of malignancy in kidney transplant recipients (KTRs) is described, particularly in association with viral infections. Screening for neoplasm is routine post transplantation. The standard incidence ratio recently calculated for cervical cancer post transplantation was 3.85 based on US and Australian data. KDIGO recommends patients undergo screening as per local guidelines. Some guidelines recommend yearly screening in the form of a papanicolaou test.

Methods: A phone survey of female KTRs of our unit was performed. The date and result of their most recent cervical smear along with where the smear was undertaken was recorded.

Results: 84 of 99 female KTRs were surveyed. The median age of those surveyed was 49. Two patients were exempt given their history of previous total hysterectomy. 34 patients (40%) satisfied AVOG guidelines. 58 patients met KDIGO guidelines (69%). 28.6% and 17.8% did not have smear in the past 3 and 5 years, respectively. 78 (92.8%) had cervical smear performed by their primary care physician. Six were performed by a gynaecological service. Six patients had abnormal smears (7%); two required treatment (One LLETZ procedure and one Chemoradiotherapy) for cervical cancer.

Conclusion: 69% of our patients satisfied KDIGO guidelines regarding cervical screening. Further research is required as to why 28.6% of our kidney transplant patients have failed to have a cervical smear within the past 3 years. There is a role for strengthening the relationship between the renal unit and our colleagues in primary care to provide optimal care for our female kidney transplant recipients.

Abstract 37

Outcomes of renal transplantation in patients with Bipolar disorder and Schizophrenia

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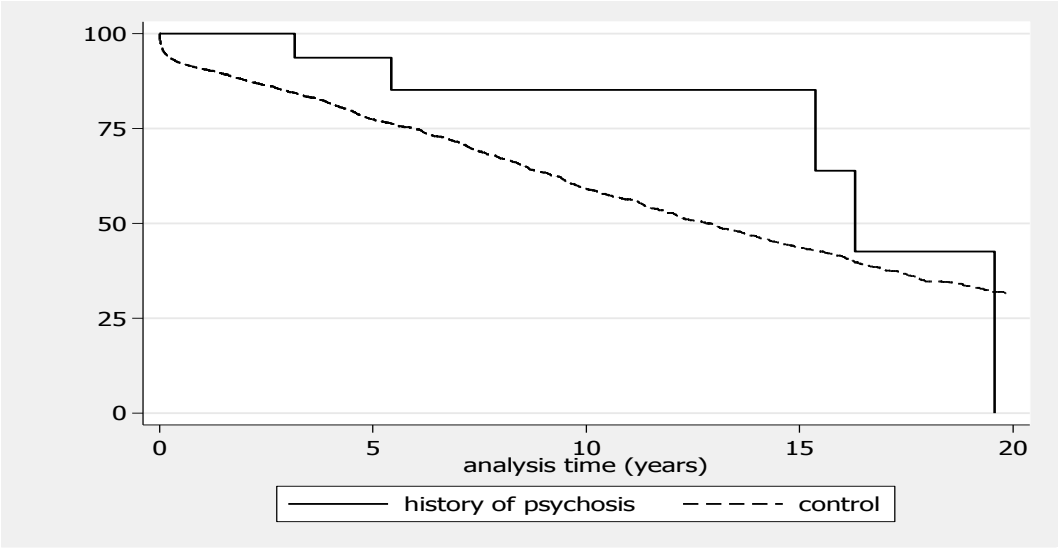
Background: There is paucity of literature concerning renal transplant outcomes in psychiatric patients with Bipolar Affective Disorder (BPAD) or Schizophrenia. Presumed future lack of compliance to anti rejection medications and their potential interactions with psychotropic medications has been a major concern and an important factor to preclude their activation on solid organ transplant recipient pool in most centres.

Aims: Our aim was to describe the patient and graft survival in Ireland in this cohort as compared to general renal transplant population.

Methods: Renal data base from national renal transplant centre was used to identify patients with BPAD or Schizophrenia who had kidney transplantation between January 1984 and December 2013. Clinical notes were reviewed retrospectively for data collection.

Results: Total of 3241 patients received kidney transplants between January 1984 and December 2013. Twenty one (0.65%) recipients had underlying BPAD or Schizophrenia. Eleven (52.43%) patients were male. Mean age at transplant was 51 years (range 13-71). One patient received living related donation. Mean follow up time was 99.25 months (range 12-354). Only 1 recipient died. Graft survival was 100% at 1 year, 94% at 5 years and 85% at 10 & 15 years follow up. Total of 8 acute allograft rejection episodes (T cell mediated = 6, Antibody mediated = 2) noted.



Conclusion: Patient and graft survival outcomes in renal transplant recipients with BPAD or Schizophrenia are favourably comparable to overall renal transplant population therefore history of psychiatric illness should not negatively impact consideration for renal transplantation.

Abstract 38

Practice patterns in blood pressure management and targets among non-dialysis chronic kidney disease patients: results of a multi-centre audit and national survey.

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Background: The aim of this study was to describe the burden of hypertension and treatment patterns at nephrology clinics in Ireland and correlate with opinions of Irish nephrologists.

Methods: A multi-centre cross-sectional study was conducted across 18 specialist nephrology clinics (n=530 patients) in Ireland during 2012-2013. The study was accompanied by a national survey that captured attitudes and opinions of nephrologists on treatment strategies and practices.

Results: Average age was 57.1(18.3) years and 56 % were male. Mean systolic BP was 137.7 (19.6), diastolic BP 77.5(13.3) mmHg. BP control of < 140/90 mmHg and < 130/80 mmHg was achieved in less than 50% and in 29% of patients respectively. Overall, 49% received anti-hypertensive treatment. 41% of patients received either an ACE or ARB, and significant differences were present across centres (range 26.2% to 54.3%, P<0.001). Only 25% overall were given advice on exercise (range 0-66.7%), 26% on salt restriction (range 7.1-66.7%), and a mere 3.2 % (range 0-9.3%) on diet and weight reduction. In contrast, the survey questionnaire (response rate 86%), found that 92% nephrologists accepted BP < 140/90 or 130/80 mmHg as the desired target. 94% and 96% of nephrologists respectively claimed to write and review medication lists at visits. 98% and 80% reported providing advice on exercise and salt restriction.

Conclusions: Blood pressure management falls short of acceptable standards with substantial variability across specialist nephrology centres in Ireland. This study found discrepancies between "*what is said and what is actually achieved*" in routine clinical practice. Greater understanding of the barriers to effective implementation of CKD guidelines for hypertension is warranted.

Abstract 39

ACEi/ARB prescription is lower in diabetic and non-diabetic patients with CKD-5/ESRD compared to earlier stages of CKD

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Introduction: Renin angiotensin system (RAS) blockade with ACE-inhibitor (ACEi) or Angiotensin-II Receptor Blocker (ARB) reduces GFR loss and is considered standard-of-care for diabetic nephropathy (DN) and other proteinuric causes of CKD.

Methods: Clinical data were analysed for clinically-stable adults with CKD 1-5 or ESRD receiving chronic haemodialysis (cHD) enrolled in a bio-sampling study at a single centre between 05/14 and 03/15. Relevant clinical indices were entered into a database and included eGFR/CKD stage, cause of CKD, presence/type of diabetes mellitus (DM), current medication classes and occurrence of hyperkalaemia (>5.5mEq/L).

Results: 187 enrolled subjects had clinical data, including medication prescription and laboratory details, available for analysis. This cohort included 35 (18.5%) KTx recipients who were assigned to CKD stage based on eGFR at enrolment. 45/187 (23.7%) had co-morbid DM (7 Type 1 and 38 Type 2). In total, 104/187 (57%) subjects were currently prescribed an ACEi or ARB. The frequency of ACEi/ARB prescription was compared across CKD stage for DM and non-DM subjects (see Table). For this analysis CKD stages 1/2 and CKD stage 5/cHD were combined. For DM subjects not prescribed ACEi/ARB, the frequency of hyperkalaemia in the preceding year was not significantly greater than for those prescribed ACEi/ARB (50.0% vs. 42.3%, p=0.6 by χ^2).

	DM (n=44)	**Non-DM (n=143)**	**Total (n=187)**
All	26/44 (59.1%)	78/143 (54.5%)	104/187 (55.6%)
CKD ½	3/5 (60.0%)	14/32 (43.8%)	17/37 (45.9%)
CKD 3	6/9 (66.7%)	43/54 (79.6%)	49/63 (77.8%)
CKD 4	12/17 (70.6%)	18/28 (64.3%)	30/45 (66.7%)
CKD 5/cHD	5/13 (38.5%)	3/29 (12.5%)	8/42 (19.0%)
CKD1-4 vs. CKD5/cHD (p value by χ^2)	*0.071*	*<0.001*	*<0.001*

Conclusions: 1. For CKD stages 1-4, ACEi/ARB prescription was frequent in both DM and non-DM subjects. 2. For CKD-5/cHD, ACEi/ARB prescription fell below 40% in DM and below 15% in non-DM subjects. 3. Factors contributing to drop-off in RAS blockade in advanced CKD require further attention.

Abstract 40

Title: Pre-operative Ultrasound Vessel Assessment: Charting a Path Towards Improved AVF Outcomes

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Background: Although the native arteriovenous fistula (AVF) is the gold standard of vascular access, reported rates of failure to mature (FTM) are 20-50%. Pre-operative ultrasound vessel mapping has been associated with improvements in outcomes[1]. We report our results following the establishment of a nephrologist-led vascular access clinic (VAC) in July 2011.

Methods: Patients who had pre-operative ultrasound vessel mapping carried out between July 2011 and December 2014, and whose native AVF had a functional outcome by March 2015 were included (n=150). These patients were compared to a retrospective cohort who had AVF created in 2009 and 2010, and whose AVF had a functional outcome by March 2015 (n=230). Outcomes were defined as below:

Functional patency: 2-needle use on haemodialysis for at least 6 sessions following creation.

Failure of maturation: Defined either by clinical examination or failure to sustain 2-needle dialysis.

Results: Compared to the historic cohort, functional patency rates improved from 57% to 68 % following establishment of the VAC and FTM rates have decreased from 44% to 32%.In the cohort that had VAC pre-operative mapping, female gender and vein size diameter <2.5 mm were associated with higher FTM rates.

Conclusions:A nephrologist-led VAC combined with a multi-disciplinary team predialysis pathway has improved patient outcomes. It provides timely assessment, enhances our surgical-medical interface and provides a mechanism to expedite patients through the predialysis pathways if they are progress rapidly.

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Abstract 41

Predicting AVF Outcomes in a Northern Irish CKD Cohort

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Background: AVF reported failure to mature (FTM) rates of 20-50% potentially lead to a significant waste of resources and contribute to patients starting dialysis with a line. Lok et al[1] devised a pre-operative clinical prediction score for AVF FTM based on 4 factors: age ≥65, presence of peripheral vascular disease or cardiovascular disease, and race. This model has not been validated in a European cohort.

Methods: All patients who had an AVF created from January 2009 to December 2014 and had a functional outcome by March 2015 were included (n=525). Analysis was then restricted to first AVF created during study time frame (n=384). Data was collected from hospital vascular access audit information and from the prospective regional database EMED. Functional outcome was defined as below:

Functional patency: 2-needle use on haemodialysis for at least 6 sessions following creation.

Failure of maturation: Defined either by clinical examination or failure to sustain 2-needle dialysis.

Results: Functional patency occurred in 57% (n=218) of the patients. The over-all FTM rate was 43% during this period (n=166).

Conclusions: In this Northern Irish cohort, the Lok FTM model did not predict AVF failure of maturation. Further studies are required to identify contributing factors to FTM in our population to optimise AVF outcomes.

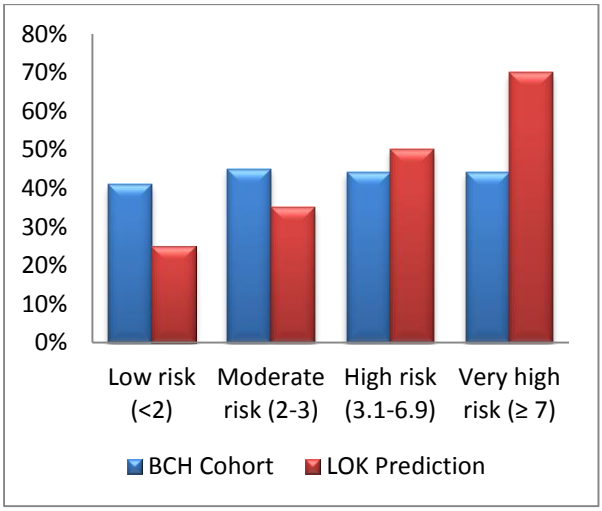

Figure 1: Comparison of Lok Risk predicted FTM percentage per risk category versus NI AVF FTM outcomes (y-axis Percentage (%), x-axis= Lok FTM risk categories)

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Abstract 42

End stage Kidney Disease (ESKD) Mineral & Bone Disorder Management: An Audit of Haemodialysis (HD) Patients in a Dublin Renal Unit

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Background: Secondary hyperthyroidism (SHPT) is common in chronic kidney disease (CKD). Elevated phosphate ($P0^{4-}$), Calcium (Ca^{2+}) and parathyroid hormone (iPTH) are risk factors for mortality, increased hospital admissions and decreased quality of life.

Methods: Monthly pre dialysis PO^{4-}, Ca^{2+} and iPTH levels were averaged for 2014 for all haemodialysis patients and relevant medications documented. Numbers meeting KDIGO and agreed local targets for Ca^{2+}, PO^{4-}, and iPTH were recorded.

Results: Data was collected on 82 patients. 26 patients (32%) had all 3 parameters within local target levels. Seventy-two patients required phosphate binders. The majority (45, 62%) were prescribed calcium based binders. Aluminium hydroxide was the second most common binder (18, 25%). Ten patients (14%) were on multiple binders. Hypercalcaemia was noted in 5% of patients taking calcium based binders. Fifty-two patients were prescribed medication for SHPT, 36 alfacalcidol (2 with cinacalcet) and16 paricalcitol (6 with cinacalcet).

Table 1: Percentage of patients meeting target ranges for PO^{4-}, Ca^{2+} and iPTH

	iPTH		PO4-		Ca2+	
Targets	Local 150-500	KDIGO 130-585 (2-9 times upper normal limit)	Local 0.8-1.6	KDIGO 0.8-1.4	Local 2.2-2.5	KDIGO 2.15-2.55
Below	25%	20%	0%	0%	19%	10%
In range	61%	72%	60%	34%	71%	81%
Above	9%	9%	40%	66%	11%	10%

Conclusions: Five percent of patients prescribed calcium based binders were hypercalcaemic highlighting the need for improved serum calcium control. Frequent use of aluminium hydroxide prompted a review of its use and current serum aluminium monitoring practices. Annual auditing of PO^{4-}, Ca^{2+} and iPTH levels by the renal dietitian is central to the management of mineral bone health.

Abstract 43

Clinical Manifestations of Prune Belly Syndrome

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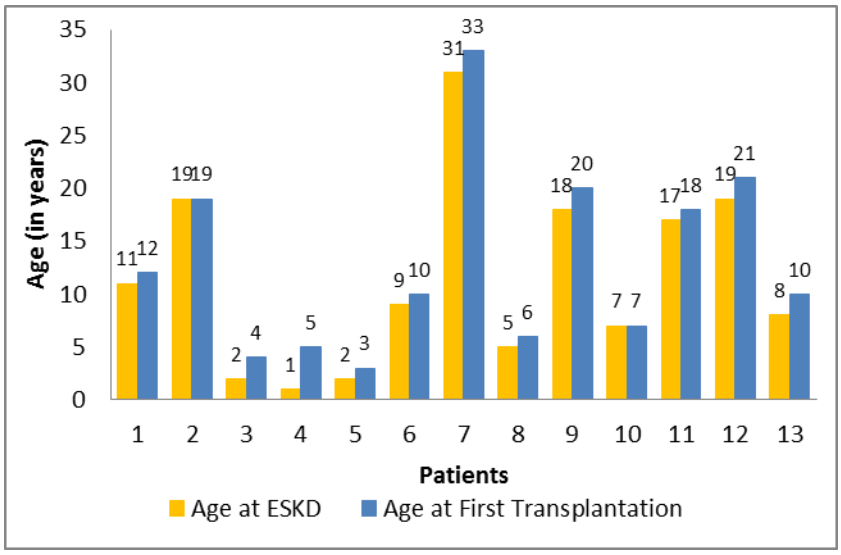
Background: Prune belly syndrome (PBS) is a rare congenital syndrome, characterised by deficient abdominal wall musculature, urinary tract malformations and bilateral cryptorchidism. It occurs in 1 in 50,000 live births. We reviewed a cohort of 13 patients with PBS in our centres and analysed their clinical characteristics, diagnostics, treatment, complications and long term clinical outcome including renal transplantation.

Method: All clinical records of patients with PBS, treated or followed up in Beaumont hospital, Temple Street hospital and Crumlin Children's hospital between 1968 and 2015 were reviewed retrospectively.

Results: In our centre, most patients were diagnosed at birth (84.6%). Cryptorchidism was present in 7 patients (53.8), lax abdominal wall was present in 3 patients (23%). All patients had genitourinary abnormalities, obstruction being the predominant anomaly, present in 53.8%. All patients developed end stage kidney disease (ESKD), at a mean age of 11.4 years. All patients with ESKD were transplanted. Mean age at first transplant was 12.9 years. One patient received a pre-emptive transplant at age 10. 3 patients (23%) required a second transplant. 11 patients (84.6%) of 13 are alive. 2 patients (15.3%) are deceased due to unrelated causes. 10 of the 11 patients (90.9%) who are alive, have a functioning transplant.



Conclusion: PBS is a complex disorder associated with variable severity and clinical manifestations. We demonstrate that successful treatment is possible even in cases of complex anomalies. We have collected DNA on familial trios and are embarking on a whole exon sequence study to try and identify underlying molecular mechanisms.

Abstract 44

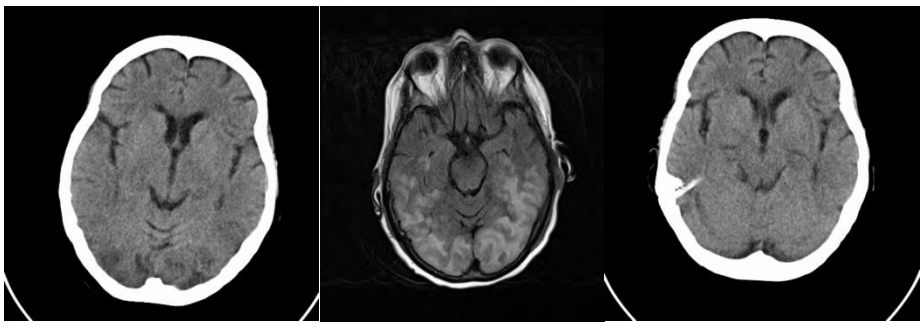
A Case of Posterior Reversible Encephalopathy Syndrome

Chhabra R, Magee C

Beaumont Hospital

Background: Posterior Reversible Encephalopathy Syndrome (PRES) is a clinical radiological syndrome characterised by headache, confusion, visual disturbance and seizures associated with typical neuroimaging findings of posterior cerebral white matter oedema.

Case: We report a case of a 74 year old lady who was electively admitted for initiation of haemodialysis for symptomatic volume overload. Her background history was significant for ESKD and nephrotic syndrome secondary to membranous nephropathy, for which she was recently treated with cyclophosphamide and steroids, hypertension, dyslipidaemia and recent herpes zoster ophthalmicus. She had 3 sessions of uneventful dialysis over 3 consecutive days. However, subsequent development of malignant hypertension was noted post dialysis . She subsequently developed tonic clonic seizures associated with a drop in GCS to 9 and a low grade temperature. Broad spectrum antimicrobial cover was initiated given her immunosuppressed state. An urgent CT brain revealed findings suspicious of PRES. MRI Brain showed bilateral cortical and subcortical white matter symmetric signal abnormality in the occipital, parietal and superior frontal lobes, confirming a diagnosis of PRES. Labetalol infusion was commenced to achieve a slow reduction in blood pressure (BP) to a target of <140/90 mmHg. She made a remarkable recovery with good BP control. A repeat CT Brain in 2/52 showed a significant improvement.



CT Brain (PRES) | MRI Brain (PRES) | CT Brain (Resolution)

Conclusion: PRES is a rare entity. It should be considered in a hypertensive patient who develops headache, visual disturbance or confusion. Most cases are fully reversible with BP control and treating the underlying cause.

Abstract 45

A Case of Post-transplant Parvovirus B19 Infection with Persistent Viremia Despite Resolution of Anaemia Following IVIG Therapy

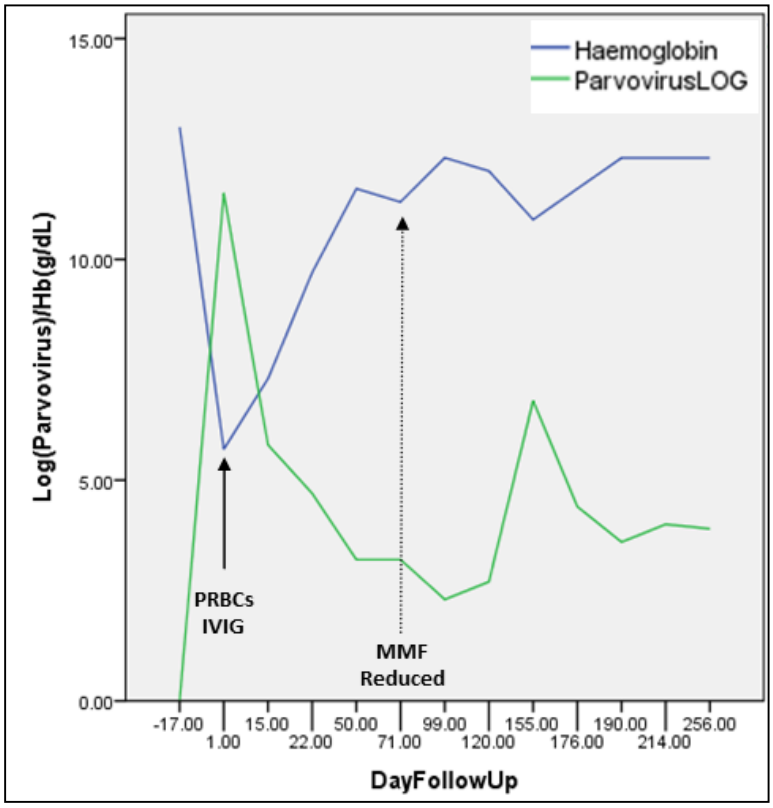
Cormican S*, O'Connor S, Calpin P, Gurney M, Brennan R, Tarmey T, McDonnell T, O'Regan JA, Gleeson J, Giblin L, Reddan D, Griffin MD, Lappin D, Kieran N.

Nephrology Services, Saolta University Healthcare Group and School of Medicine, National University of Ireland, Galway

Background: Parvovirus B19 (PvB19) is an uncommon cause of aplastic anaemia (a.a.) in transplant recipients. We encountered a case of PvB19-associated a.a. in a 20yr.-old woman post-deceased donor kidney transplantation.

Methods: Clinical and laboratory details, including serial PvB19 qPCR assays, were collated from the medical records from 2 weeks prior to presentation to 8 months afterwards.

Results: The patient had an uncomplicated course before presenting with fatigue and headache 6-weeks post-transplant. Medications consisted of tacrolimus, MMF (750 mg bd), prednisolone, co-trimoxazole and ranitidine. She was afebrile and haemodynamically stable with noticeable pallor. Laboratory testing revealed haemoglobin (Hb) 5.8g/dL (from >12.0g/dL 2wks. previously) and low reticulocyte count (5/µL). Hb fell to 5.1 g/dL and she received blood transfusion. Subsequently, serological testing was positive for anti-PvB19 IgM, qPCR assay revealed PvB19 titre of $31.5x10^{10}$IU/µL and IVIG 400mg/kg/day was given for 10 days. Following this, reticulocyte count increased (265/µL day 6 of treatment) and Hb improved slowly to normal range accompanied by steady decline PvB19 titre to <200IU/µL over the following 3 months (Figure). Because of slow viremia response MMF dose was eventually reduced to 250 mg bd. Despite this, PvB19 titres subsequently rose to $7.0x10^{6}$IU/µL at 5 months post-discharge with mild, self-resolving anaemia. At most recent follow-up she remained well with stable graft function and Hb >12g/dL despite persistent low-grade viremia ($7.6x10^{3}$IU/µL).



Conclusions: 1. Profound post-transplant anaemia was associated with high-level PvB19 viremia and resolved slowly following 10-day course of IVIG. 2. Viremia recurred despite MMF reduction but with minimal clinical impact.

Abstract 46

Bilateral renal vein thrombosis - a potentially devastating cause of acute kidney injury

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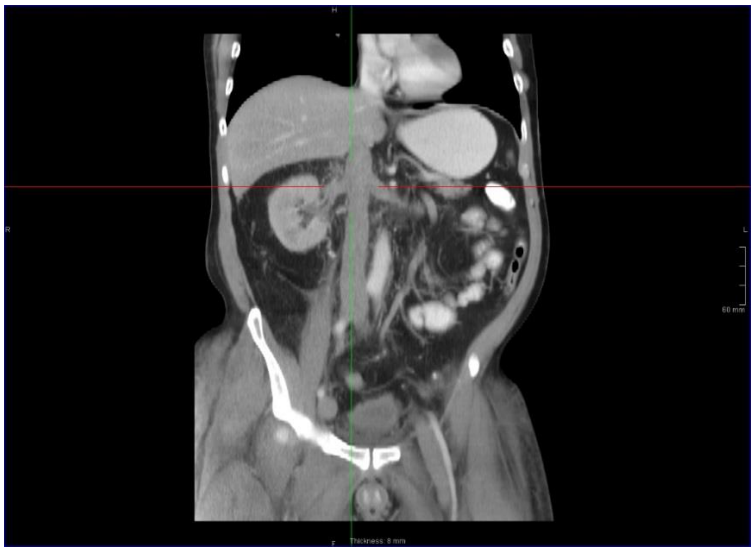
Background: Renal vein thrombosis (RVT) is a rare thrombotic entity outside of severe nephrotic syndrome or malignancy. It may occur with systemic hypercoagulable states, trauma, infection or with use of oral contraceptive pill. It can be diagnosed by Doppler ultrasound (US), commuted tomography (CT) or magnetic resonance imaging (MRI). Chronic RVT is often asymptomatic but acute RVT can present dramatically as we will outline in this case.

Case Description: A 47-year-old gentleman presented with a 10-day history of abdominal pain and distension. Laboratory tests showed severe acute kidney injury (AKI) with peak creatinine 684umol/L. He had microscopic haematuria and no proteinuria. He also had a persistent thrombocytosis with platelet levels of 1059 $X10^9$/L. A contrast-enhanced CT scan revealed extensive thrombus in the inferior vena cava and bilateral renal vein thrombosis (*Figure 1*). He had evidence of acute appendicitis with a small walled off tip perforation. He was commenced on unfractionated heparin and intravenous antibiotics. He required intermittent haemodialysis for 2 months then made an excellent renal recovery. The patient was subsequently diagnosed with a JAK2 positive myeloproliferative disorder and is now maintained on warfarin, hydroxyurea and lifelong aspirin

Figure:



Conclusions: This case illustrates classic symptoms of RVT including flank pain and haematuria. The patient had multiple risk factors for this event including a previously undiagnosed thrombophilia and abdominal sepsis. Bilateral disease can cause a rapidly progressive AKI as in this case. Early diagnosis and prompt management is key as untreated acute RVT has a mortality of greater than 50%.

Abstract 47

The I of the Storm

Gleeson PJ[1], Turnbull L[2], Goodship T[2], Lappin D[1]

[1]Dept of Nephrology UCH, Galway; [2]Northern Molecular Genetics Service, Newcastle, UK

Background: Nephrology is still in the age of discovery, particularly in the field of complement mediated disorders.

Methods: We investigated a young man referred to our Nephrology service with ESKD, microangiopathic haemolysis and low C3 for his underlying cause of renal failure.

Results: A 36 year old man was transferred to our institution with creatinine 1122 µmol/L, urea 39.4 mmol/L, haemoglobin 8.2 g/dL, platelets 83 x 10^9/L and schistocytes on the blood film. His blood pressure was 223/64. He was stabilised and started on intermittent haemodialysis. His past medical history was significant for infection of an intramedullary nail in his humerus 2 years prior. Investigations for renal failure revealed a negative auto-antibody panel and C3 0.71 g/L (0.75-1.86). Renal biopsy showed thrombotic microangiopathy (TMA). Analysis for mutations in *CFH* and *CFI* were initially reported as normal although complement factor I level was low 29 mg/L (35-58). Quantitative molecular analysis using multiplex ligation-dependent probe amplification (MLPA) revealed the patient had a deletion of one of his copies of *CFI*. His father carries the same mutation but has normal renal function.

Conclusion: This is the first report of a heterozygous deletion of the gene encoding complement factor I causing congenital complement mediated TMA. MLPA has been introduced as part of the screening protocol for detection of gene deletions in the complement system at the reference laboratory.

Abstract 48

Biopsy Confirmed Interstitial Nephritis Complicating severe *Plasmodium falciparum* Infection

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[1]Dept of Nephrology, UCH Galway; [2]Dept of Histopathology, UCH Galway; [3]Dept of Infectious Diseases, UCH Galway

Background: When acute renal failure complicates malaria (MARF) the infection is classified as severe and mortality is high. A number of mechanisms have been proposed for MARF including: acute tubular necrosis, acute interstitial nephritis (AIN), post infectious glomerulonephritis and mesangioproliferative glomerulonephritis. Because the majority of cases occur in resource poor settings MARF has not been well characterised by renal biopsy and AIN has only been described in animal models of malaria.

Methods: We routinely investigated acute renal failure in a 44 year old Nigerian man who returned to Ireland with *P. falciparum* infection after visiting family.

Results: The patient presented after being unwell for 5 days with a creatinine of 616 µMol (baseline 89 µMol). He reported taking a single dose of ibuprofen on the day of presentation and otherwise had taken paracetamol for fevers. He was non-oliguric and urinalysis revealed 4+ protein, 3+ blood. Platelet count was 70x10^9/L and haemoglobin 11.2g/dL with 0.3% parasitaemia. ANA and ANCA were negative, C3 was normal and C4 was low (0.09g/L). Renal ultrasound showed diffusely increased echogenicity. A renal biopsy showed acute interstitial nephritis with eosinophils, particularly at the cortico-medullary junction. He was treated with intravenous artesunate and required three sessions of HD. Renal function improved to a baseline creatinine of 122µMol at one year with persistent proteinuria (PCR 172 mg/mmol).

Conclusion: The drug history and histology are not consistent with NSAID induced AIN. This is the first reported case of biopsy proven AIN as a result of severe *P. falciparum* infection.

Abstract 49

Acute Oxalate Nephropathy as a Consequence of Recurrent Gallstone Pancreatitis

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Department of Nephrology, UCH Galway

Background: Gastrointestinal conditions causing fat malabsorption lead to increased oxalate uptake from the gut because calcium is sequestered by fat when it would otherwise bind to oxalate.

Methods: We investigated an 86 year old lady for precipitous decline in renal function. Tests included faecal elastase, urine and serum oxalate levels and renal biopsy. Intensive haemodialysis was instituted in an effort to reverse renal failure.

Results: A multiparous octogenarian was referred by her GP with a creatinine of 333 µMol/L. Background history included DM II and multiple episodes of gallstone pancreatitis with an atrophic pancreas on MRCP. She was euvolaemic at presentation and denied taking any nephrotoxic medications. An immunology screen was negative; renal ultrasound showed bright renal cortices. Faecal elastase was undetectable, urine oxalate (0.39mmol/24hours) and plasma oxalate (30 µMol/L) were elevated. A renal biopsy was performed which showed acute oxalate nephropathy. Creatinine rose to 452 µMol/L over the course of her admission. Enzyme supplementation, oral calcium acetate and a low oxalate diet were instituted. One week of intense haemodialysis using a large ($1.8m^2$) high-flux dialyser daily for 4 hours was trialled however pre-dialysis creatinines did not improve. The oxalate reduction ratio using a high-flux was no better than with a low-flux membrane.

Figure:

Dialysis Delivered	Pre-Plasma Oxalate	Post-Plasma Oxalate	Oxalate Reduction Ratio
Lo15 x 4 hours x Qb 350	30	8	73.3%
Hi18 x 4 hours x Qb 300	22	8	63.6%

Conclusion: Secondary hyperoxaluria from atrophic pancreatitis is a rare cause of renal failure but should be considered in patients with a history of recurrent pancreatitis. End stage kidney disease can be avoided in these patients with appropriate enzyme supplementation and dietary advice.

Abstract 50

The Rotten Problem

Management of Acute Sepsis in an Irish Hospital Setting

Murray, S. L., Sin Yan Too J., McClelland G., Cotter C., O'Brien, B. Lynch, O.

Background: Sepsis is a major cause of morbidity and mortality. It is also a major cause of acute kidney injury. 19% of patients with moderate sepsis and 23% with severe sepsis develop acute kidney injury. The most important interventions when managing sepsis are prompt recognition and early antibiotic initiation. However, recent high profile cases have highlighted that Irish hospitals do not always meet the appropriate standard of care.

Methods: We prospectively reviewed all acute medical admissions to a peripheral Irish hospital, with a suspected diagnosis of sepsis, over a 28 day period. We assessed for the presence or absence of acute kidney injury, the completion of all steps of *The Sepsis Six*, as laid out in "*Surviving Sepsis: International Guidelines for Management of Severe Sepsis and Septic Shock: 2012",* and measured time from presentation to first dose of antibiotic.

Results: 110 patients were reviewed. 33 did not meet the criteria for sepsis. Only 6% of patients had all steps of the *Sepsis Six* completed. 66% of patients had <50% of the steps completed. The median time to first dose of antibiotics was 160 minutes.

Conclusions: Despite education, management of sepsis and prompt delivery of antibiotics remains sub-optimal. In particular, monitoring of urine output remains one of the most poorly recorded metrics.

Table: Percentage patients in which the steps of the Sepsis six were performed (n=77)

Blood Cultures	34 (44%)
Serum Lactate	35 (45%)
FBC	77 (100%)
Urine Output Measurement	21 (27%)
Oxygen	29 (38%)
IV Fluids	51 (66%)
Antibiotics	73 (95%)

Abstract 51

The Screening, Diagnosis and Management of Osteoporosis in a Haemodialysis Population

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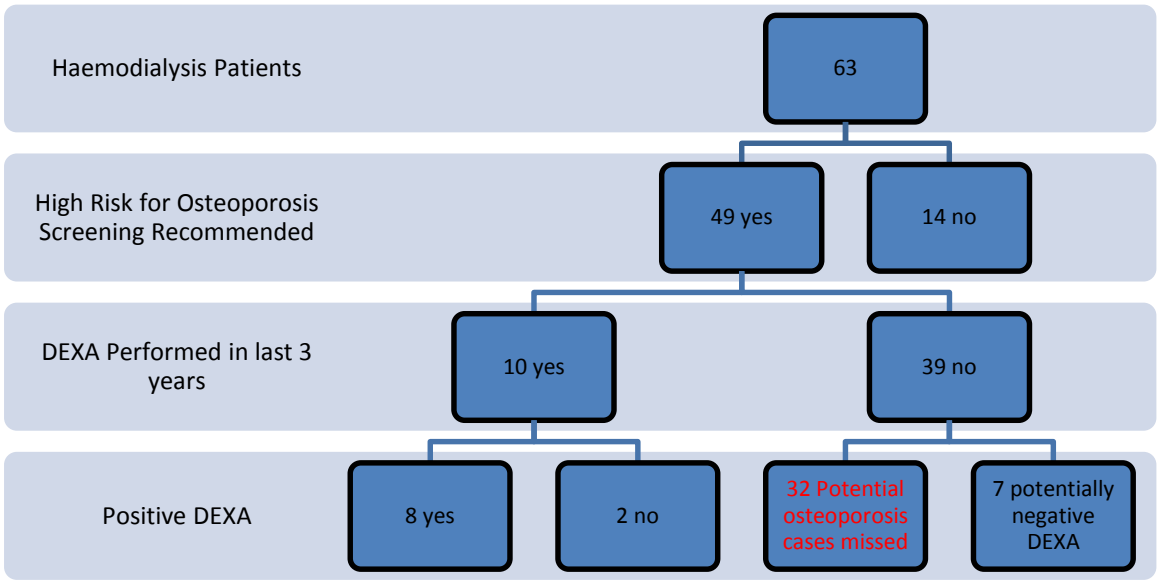
Backround: Osteoporosis is common in chronic kidney disease (CKD) patients especially in those with end stage kidney disease, due to their high number of risk factors. However, diagnosis is not straightforward, as Renal Bone disease can cause reduced bone mineral density. The aim of this research project was to evaluate our existing practice and to develop local guidelines for the screening, diagnosis and management of osteoporosis in a haemodialysis population.

Methods: We examined the medical records of all haemodialysis patients in our unit. We examined which patients fulfilled the recommended criteria for screening for osteoporosis. We then evaluated our screening and treatment practice in relation to osteoporosis.

Results: 49 of 63 haemodialysis patients were classified at high risk for osteoporosis (78%). Only 10/49 high risk patients had been screened with DEXA prior to this study. Following screening only 25% patients with diagnostic criteria for osteoporosis were receiving appropriate treatment. Fracture risk was assessed using the FRAX tool. All confirmed osteoporosis patients had a >20% 10 year fracture risk.

Figure:



Conclusions: Despite the fact that over 78% of our haemodialysis patients were classified as at high risk for developing osteoporosis only 20% had been screened. Length of time on haemodialysis is an additional risk factor for osteoporosis which is often overlooked. A large number of potential osteoporosis cases are being missed through under screening. We concluded that all patients on haemodialysis for >18 months should be screened every 2 years by DEXA scan.

Abstract 52

Risk of ischaemic stroke for incident patients treated with peritoneal dialysis versus haemodialysis

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[1]Department of Nephrology, University Hospital Limerick; [2]Graduate Entry Medical School, University of Limerick; [3]Health Research Institute (HRI), University of Limerick.

Background: Observational studies have shown that the risk of stroke is elevated among patients who undergo dialysis treatment. It is unclear whether treatment modalities, haemodialysis and peritoneal dialysis, contribute selectively to this risk following dialysis initiation.

Methods: This hypothesis was tested on a national cohort of 1,097,747 incident US patients (n=86,168 on PD) who began dialysis between 5/1995 to12/2010 and were followed until 9/2011.Data on first hospitalization from Ischaemic stroke (I-CVA) [ICD 9 codes; 433-435.99] was obtained from the medical evidence, treatment history and mortality files of the US Renal Data System. Multivariate Cox regression compared the hazards ratio [HR] of I-CVA for PD versus HD with a propensity-matched intent-to-treat (ITT) approach and an as-treated analysis.

Results: Overall HRs for stroke using ITT for PD/HD was 1.15 (1.12-1.18). This decreased from 1.20 (1.13-1.27) in the period 1995-1998 to 1.06 (0.97-1.15) in the period 2007-2010. The as-treated model showed a more favourable outcome for PD/HD with an overall HR 0.96 (0.93-0.99), and the HR decreased from 0.99 (0.93-1.05) in the 1995-1998 period to 0.92 (0.85-1.00) in the 2007-2010 period. Patients who had suffered a prior stroke experienced higher hazards of future I-CVA when treated with PD versus HD (P<0.005 for interaction).

	Hazards Ratios (HR) PD/HD of Ischaemic Stroke			
Period	**1995-1998**	**1999-2002**	**2003-2006**	**2007-2010**
Unadjusted	0.99(0.95-1.02)	0.97 (0.93-1.01)	0.89 (0.85-0.93)	0.78 (0.73-0.83)
1. Propensity-based (Intent-to-treat Model)	1.20 (1.13-1.27)	1.14 (1.08-1.20)	1.08(1.02-1.14)	1.06 (0.97-1.15)
2. As-treated Model with Modality Switch				
HD always (referent)	1.00 (referent)	1.00 (referent)	1.00 (referent)	1.00 (referent)
PD always	1.10 (1.03-1.18)	1.04 (0.98-1.11)	0.96 (0.90-1.02)	0.97 (0.88-1.06)
PD>HD	1.41 (1.31-1.52)	1.31 (1.22-1.41)	1.34 (1.24-1.45)	1.56 (1.36-1.80)
HD>PD	1.23 (1.05-1.45)	1.03 (0.89-1.19)	1.04 (0.89-1.22)	1.26 (0.96-1.64)
3. Summary as-treated model	0.99 (0.93-1.05)	0.96 (0.91-1.02)	0.90 (0.85-0.96)	0.92 (0.85-1.00)

Conclusions: The risk of I-CVA was significantly higher for PD than HD patients among incident dialysis patients, and has declined significantly in the period 1995-2010. Patients who switched from PD to HD experienced the highest risk of I-CVA. The reduction in risk over time may be related to better PD therapy and patient selection.

Abstract 53

The impact of symptom burden and other factors on the health-related quality of life of haemodialysis patients: an international study in England and Ireland

Lowney AC[1], Myles H, Bristowe K, Lowney EL, Shepherd K, Murphy M, O' Brien T, Casserly L, McQuillan R, Plant WD, Conlon PJ, Vinen C, Eustace E, Murtagh FEM

[1]*Marymount University Hospital & Hospice, Department of Palliative Medicine, Cork, Ireland*

Background: Nephrologists have a therapeutic relationship with patients that may span decades. Key components of chronic-disease management include symptom control, assessment of health-related quality of life (HRQoL) and advance care planning. This study describes the symptom profile of a large cohort of patients with end-stage renal disease on haemodialysis in England and Ireland and evaluates how symptom burden and other factors influence quality of life scores.

Methods: A prospective cross-sectional observational study of hemodialysis patients conducted in Ireland and England during 2011 and 2012. Two validated clinical tools were used to determine HRQoL and symptom burden. Demographic and clinical data were examined and regression analysis was used to determine associations with HRQoL scores.

Results: 893 patients on hemodialysis (mean (SD) age 64 (16) years) had a high symptom burden and poor HRQoL compared to population norms. Specifically, 64% of patients reported pain (95% CI 61-67%) and 79% reported weakness (95% CI 75-81%). 43% of patients reported between six and ten symptoms in the week preceding the survey. In the final parsimonious multivariate model, HRQoL was significantly and independently associated with poor mobility and pain, and remained significant after adjusting for variations in clinical characteristics. Being listed on a transplant waitlist register was positively associated with HRQoL.

Conclusions: These findings illustrate the high symptom burden and poor HRQoL of the haemodialysis population. The development and application of eevidence based systems for improved palliative and supportive care is urgently needed to improve the health-related experience of haemodialysis patients.

Abstract 54

In Search of the Best Assay for Albumin in End Stage Renal Disease

Gillman B[1], McGing P[2],Galvin C[2], Whelan C[2], Fitzgibbon M[2], O'Meara Y[3].

Departments of [1]Clinical Nutrition and Dietetics, [2]Clinical Chemistry and Diagnostic Endocrinology, and [3]Nephrology.

Background: Serum albumin is an important predictor of mortality and morbidity in patients with ESRD. However, reported albumin values may vary with the analytical method used. The aim of the study was to compare the two albumin assays most commonly used, namely Bromocresol Green (BCG) and Bromocresol Purple (BCP) to a 'gold standard' immunonephelometric (IN) assay.

Methods: Over a ten day period albumin samples requested were measured on Abbott Architect c16000s using BCG and BCP assays (n=3278). A subset of samples were also analysed using a nephelometric assay on Siemens BNII (n=147).

Results: There was a clear difference between methods, with BCG on average reading 5g/L higher than BCP ($p<0.001$). Comparison of BCG and BCP to IN assay is shown in Table 1.

Table 1: Comparison of BCG and BCP methods for albumin versus Immunonephelometric Assay (IN)

Category	n	Difference (BCG-BCP)	Difference (IN-BCP)	Difference (IN-BCG)
Haemodialysis	64	5.2	5.2	0.0
HD (Alb<30)	*11*	*6.4*	*5.0*	*-1.4*
HD (Alb 30-34)	*39*	*5.4*	*5.5*	*+0.2*
HD (Alb>34)	*14*	*3.8*	*4.5*	*+0.7*
Hypo-albuminaemic	23	7.8	1.5	-6.3
'Normals'	60	3.9	2.3	-1.6
Total	147			

Conclusions: This supports other authors' findings that the difference between albumin concentration measured by BCP and BCG is real. Variation in albumin measurements may affect assessment of nutritional status and lead to inaccurate calculation of corrected calcium. Differences in assay methods should be taken into account when performing comparative audit and in determining target levels. In conclusion, BCG appears to be the most accurate assay for patients with ESRD.

Abstract 55

Calcium Measurement in Patients with End Stage Renal Disease (ESRD) – Which Formula to use?

Authors: McGing P[1], Gillman B[2], Galvin C[1], Fitzgibbon M[1], O'Meara Y[3].

Departments of [1]Clinical Chemistry and Diagnostic Endocrinology, [2]Clinical Nutrition and Dietetics, and [3] Nephrology.

Background: Hypercalcaemia is associated with increased mortality and morbidity in patients with ESRD. Many therapeutic decisions on management of mineral bone disease (MBD) are based on corrected calcium levels. This study was undertaken to derive and assess formulae for correcting calcium concentrations with the albumin methods Bromocresol Purple (BCP) and Bromocresol Green (BCG). The aim of our study was to assess the most appropriate formula for use in the hospital and in particular for patients with ESRD.

Methods: Plasma samples (Lithium Heparin; n=3055) were analysed on Abbott Architect c16000s for Calcium (Arsenazo III) and Albumin (BCP and BCG); n=287 renal patient samples (n=20 haemodialysis patients).

Results:
Formulae for calculating corrected calcium in-house were derived from regression analysis of albumin and calcium. Table shows formulae derived and compares mean corrected calcium between in-house and 'standard' correction formula.

Albumin Assay	Source	Formula	Mean CorCa (n=3055)	Mean CorCa HD (n=20)
BCP	In-house	[CaCor] = [Ca] + (0.012*(37 - [Albumin]))	2.37	2.33
BCG	In-house	[CaCor] = [Ca] + (0.015*(42 - [Albumin]))	2.38	2.34
BCP	Textbook	[CaCor] = [Ca] + (0.020*(40 - [Albumin]))	2.46	2.43
BCG	Textbook	[CaCor] = [Ca] + (0.020*(40 - [Albumin]))	2.36	2.32

Applying the 'standard' formula gives a positive bias of 0.09mmol/L versus the specific BCP-derived formula (HD group 0.10mmol/L).

Conclusions: These adjusted calcium formulae are quite different from the 'standard' calculation widely quoted in textbooks and used in on-line calculators. This study illustrates the need for different formulae for BCP albumin versus BCG albumin. In particular, it is very important that where laboratories use BCP albumin the standard on-line formula should not be used to correct patient's calcium.

Abstract 56

Retrospective Cross-Sectional Cohort Study Comparing Erythropoietin Requirements between Patients receiving Haemodialysis and Haemodiafiltration

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Background: Erythropoietin (EPO) is used to increase haemoglobin in dialysis patients however it also increases cardiovascular risk. It has been proposed that EPO resistance might be reduced in patients undergoing haemodiafiltration (HDF) as compared to haemodialysis (HD).

Methods: We retrospectively gathered cross-sectional data for a group of patients receiving HD and a group receiving HDF at different units in February 2015 including haemoglobin (Hb), ferritin, transferrin saturation (TSat), iron dose and EPO dose. Doses of EPO were standardised by converting to equivalent darbapoietin alpha dose per week. EPO responsiveness was defined as the ratio between Hb and weekly EPO dose. Differences in co-morbidities between the two groups were accounted for using the Charlson Index (CI).

Results: There were 56 patients in the HD group and 52 patients in the HDF group. There was no significant difference in mean Hb levels (HD 10.83g/dL, HDF 10.93 g/dL; $p=0.48$) and Hb was above 10g/dL in 77% of HD patients and 79% of HDF patients ($p=0.8$). EPO dose was significantly higher ($p<0.001$) in the HD group (42.1 units/week) compared to the HDF group (16.1 units/week) despite the HDF group having a significantly higher CI ($p<0.001$). Multiple linear regression analysis adjusting for CI and TSat showed a significant association between dialysis modality and responsiveness to EPO with patients receiving HDF more responsive (adj $R^2=0.132$, $t=4.4$, $p<0.001$).

Conclusion: Patients receiving HDF require lower doses of EPO than those receiving HD. Using HDF could indirectly lead to lower costs and lower morbidity through reducing EPO requirements.

Abstract 57

The decline of dialysis in Northern Ireland

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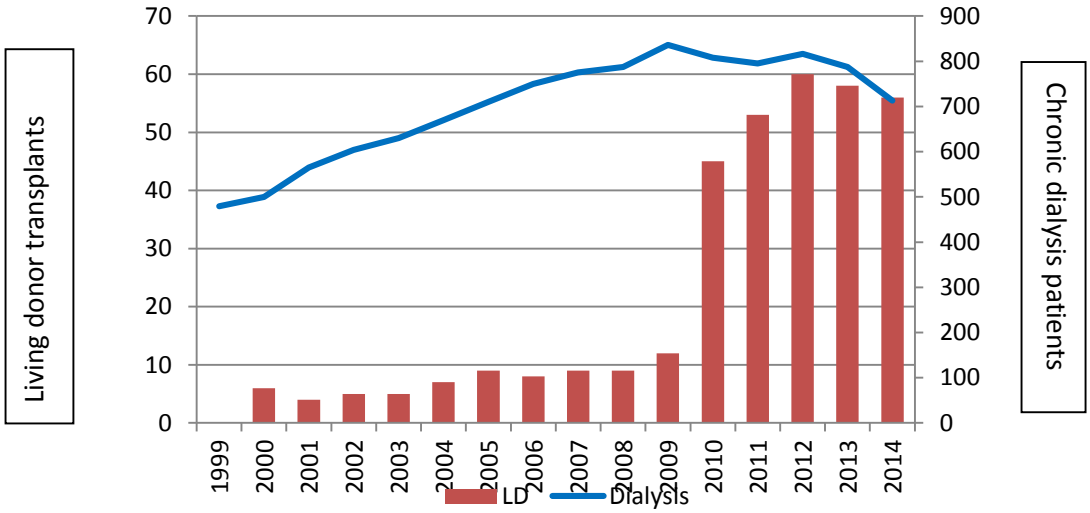
Regional Nephrology Unit, Belfast

Background: The first session of haemodialysis in Northern Ireland (NI) was in 1959 for acute kidney injury. There has been an inexorably rise in the prevalent dialysis population in the province since then, with expansion of dialysis facilities to accommodate ever increasing numbers. However, in addition to inferior outcomes compared to transplantation, there are considerable capital and recurrent costs associated with chronic haemodialysis provision. This study considered the impact of an expansion in the living donor (LD) transplant programme on dialysis in NI.

Methods: The prevalence dialysis population from 1999-2014 (inclusive) data were retrieved retrospectively from collected data. The number of LD transplants in NI patients is prospectively recorded.

Results: In 1999 there were 479 patients in NI receiving maintenance dialysis treatment. This number increased annually until a zenith of 836 in 2009. There were no living donor transplant procedures in 1999, from 2000-2008 there were between 4 and 9 performed annually. There was an expansion of the LD programme thereafter, and for the past four years there have been between 53-60 LD transplants each year (≥30 donor pmp). This increase has coincided in an initial plateau and then a decline in the prevalent dialysis population (Figure 1).



Conclusion: A proactive approach to living donor transplantation has benefits not only for individual patients but in reducing the prevalent dialysis population and the healthcare costs associated with renal replacement therapy.

Abstract 58

Relationship of glycosylated haemoglobin with death and hospitalisation among diabetic patients undergoing dialysis: a national cohort study

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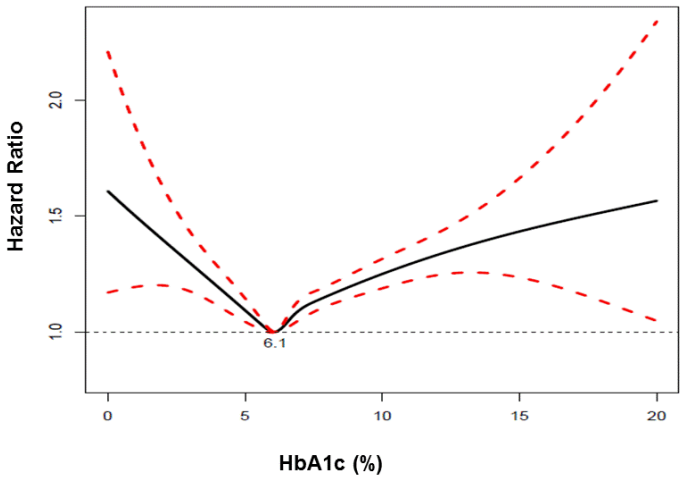
Background: Recommended guidelines suggest that HbA1c levels be maintained below 7% for diabetics in the general population. Due to shortened red cell survival on dialysis and the effects of uraemia on glucose control, it is unclear what relationship exists between HbA1c and mortality in end stage kidney disease (ESKD).

Methods: We identified 48,208 diabetic patients who initiated dialysis from 1995-2008 and were followed until 2010. Data on clinical characteristics were measured at dialysis initiation. The relationship between HbA1c and mortality was explored in quintiles (Q) of HbA1c (Q1 < 5.6 %, Q2 5.6 ≤ HbA1c <6.1, Q3 6.1 ≤ HbA1c < 6.7, Q4 6.7 ≤ HbA1c <7.6, and Q5 > 7.6) with Q2 as referent. Smoothed spline hazard function and multivariable Cox regression models assessed relationships with mortality and hospitalization.

Results: The relationship between HbA1c and mortality followed a U-shaped association. Compared to the referent group (HbA1c 5.6-6.1, HR=1.00), mortality risks were significantly higher for patients with levels < 5.6 (HR 1.12 (1.06-1.08)) and greater than the fourth and fifth quintiles [HR=1.10 (CI 1.04-1.15) and HR=1.20 (CI 1.14-1.26) respectively. The pattern of association was similar for Type 1 and Type 2 diabetes. In secondary analyses, HbA1c levels in the highest quintile were significantly associated with risk of hospitalisation from myocardial infarction, acute coronary syndrome, and stroke.

Conclusions: Among diabetic ESKD patients, the association of HbA1c with mortality is not linear but u-shaped with elevated mortality risks for those with levels greater than 7.6% and less than 5.6%. Values associated with best survival were between 5.6-6.7 %.



Abstract 59

Warfarin use in haemodialysis patients

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Introduction: Haemodialysis patients are prescribed oral anti-coagulants for prevention of thromboembolic stroke, venous thromboembolism and maintenance of dialysis access patency. There is conflicting data in the current literature regarding use of warfarin in this population for atrial fibrillation while its use is unproven for maintenance of dialysis access.This re-audit assesses the indications for warfarin prescription and assesses whether patients knowledge of indications and possible side effects.

Methods: This retrospective analysis included haemodialysis patients who were on warfarin from 01/07/2014-31/12/2014. In all cases indication for anticoagulation, INR values measured and patients' knowledge of complications of warfarin were collected. Data was collected from the medical record, patient interview, warfarin recording notebook and the Laboratory system. Collated data was compared with the previous audit.

Results: 16/95(16.8%) haemodialysis patients were prescribed oral anticoagulants. Six of sixteen (37.5%) were warfarinised for dialysis access patency compared to 29.4% in the previous audit. 87.5% of patients had an INR>4.0 on one or more occasion during the 6-month period, but there was no major bleeding complication reported. Almost all patients recognised the major complication of warfarin therapy as bleeding. All patients included in this study had their target INR documented in their warfarin notebook

Conclusion: A high number of patients were overanticoagulated on at least one occasion; similar to reported literature. However there were no bleeding events reported in this small series. Given the increased risk with use and unclear benefit the decision to use oral anticoagulation needs to be individualised. Patient education about complications and interactions is imperative.

Abstract 60

Adaptation of the National Early Warning Sign to haemodialysis patients in Satellite Dialysis Unit.

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Quality Improvement Tool adaptation of the National Early Warning Sign to haemodialysis patients in Satellite Dialysis Unit.

Ireland adapted the National Early Warning Score (NEWS) in 2013, making Ireland the first country to agree to a NEWS. Patient Safety and quality are central to the delivery of healthcare and improve cost effectiveness across the healthcare services. Using the National Early Warning Score that is locally developed and endorsed is very good practice and would have a positive long lasting impact on quality improvement in satellite haemodialysis unit.

Quality and safety was firmly put on the agenda by the medical director of Beacon Tallaght, National Early Warning Score developed by consultants and healthcare provider to stem line process for managers to focus on patient timely optimum care as per clinical needs and health condition was fully examined, researched and evaluation with the nursing staff.

Adaptation of National Early Warning Score for satellite haemodialysis unit (SHDU) patients , a pilot mode initiated in Beacon Tallaght Dialysis unit in April 2015 will be running for four weeks to evaluate the implantation of EWS_HD, in a bed to optimise patient central care in satellite haemodialysis units, benign the first internationally to recognise the patients' EWS needs in satellite haemodialysis units.

Abstract 61

Determinants of Renal Recovery and Mortality in Patients Undergoing Continuous Renal Replacement Therapy in the ICU

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Background: Continuous Renal Replacement Therapy (CRRT) is commonly used in critically ill patients with acute kidney injury (AKI). Factors which influence outcome in these patients and the optimal way to integrate CRRT into their care needs to be better defined.

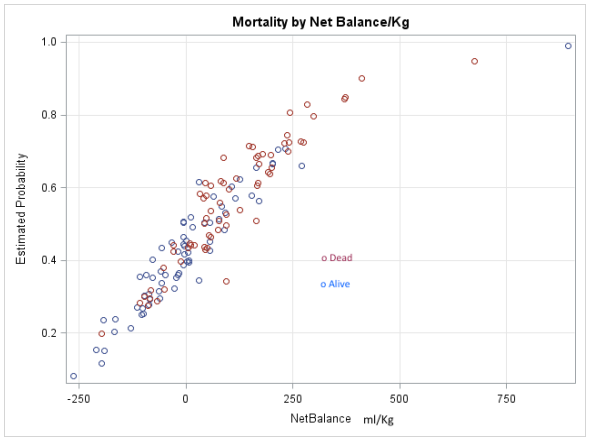
Methods: Electronic medical records of patients requiring CRRT during their stay in our 35-bed medical-surgical ICU (January 2012-December 2013) were reviewed. Binary logistic regression with adjustment for confounders was performed to identify independent variables significantly associated with mortality and renal recovery.

Results: Among the 157 patients treated with CRRT 67 (43%) recovered renal function and 80 (51%) survived. Adjusted predictors of ICU mortality were sepsis (OR 2.5; 95% CI 1.3-4.9 - p=0.008), ARDS (OR 2.1; 1.0-4.4 - p=0.049) and increasing net fluid balance (OR 1.01; 1.00-1.01 - p=<0.001); higher creatinine at start of CRRT was independently associated with lower ICU mortality (OR 0.96; 0.04-0.98 - p=<0.001). Serum urea at start of CRRT was not associated with mortality. Among patients that did not die on CRRT, prior chronic kidney disease (OR 0.38, 0.16-0.91 p=0.03) and increasing ultrafiltration (OR 0.966; 0.94-0.99 - p=0.015) predicted failure to recover renal function. Furosemide dose had no bearing on renal recovery.

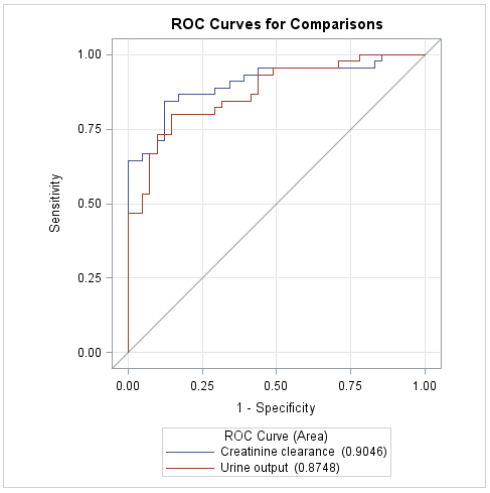
Conclusion: The mortality rate of patients requiring CRRT was high and only a minority of them were independent of RRT after discharge. Higher serum creatinine level at the time of starting CRRT was associated with survival, in keeping with previous studies. Optimising fluid balance for critically ill patients is a key clinical challenge.

Figures:

1. **Relationship between Net Fluid Balance During Period of CRRT and Probability of Death**



2. **ROC for Urine Output and Residual Creatinine Clearance before Stopping CRRT as Predictors of Freedom from RRT**



Abstract 62

ICU continuous renal replacement therapy (CRRT) outcomes in an irish setting – a cohort study

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Background: Despite widespread use there is a paucity of information on the renal outcome for patients receiving Continuous renal replacement therapy (CRRT) in ICU. The primary aim of this study is to determine the renal outcome for ICU patients receiving CRRT. The secondary aim is to assess the factors influencing the outcome.

Methods: We analyzed a retrospective cohort of 176 ICU patients receiving CRRT over a 20 month period. Patients were identified from the ICU Clinical Information System. Age, Gender, APACHE score, AKIN score, presence of co-morbidities, duration of CRRT and duration of ICU admission were recorded. Outcome measures were Hospital Mortality and dialysis dependence on discharge from hospital.

Results: During the study period 577 patients were admitted to ICU of which 176 (32%) required CRRT. Of these, 87 died in hospital (49.4%) and 89 survived to discharge.(50.6%). 16 of the survivors had known ESRD prior to ICU admission and were excluded, leaving 73 for further analysis. 61 of these patients were independent of dialysis at discharge while 11 remained dialysis dependent. The median pre hospital admission creatinine was 92umol/l in the dialysis independence group versus 141umol/l in dialysis dependence. The ICU admission Creatinine was 528 in dialysis dependent group versus 243 in dialysis independence.

Conclusions: 83% of patients receiving CRRT in ICU who did not have ESRD to begin with were dialysis independent on hospital discharge. Dialysis dependent patients had a higher baseline creatinine and a higher creatinine on admission to hospital.

Abstract 63

Acute Kidney Injury: Adding Informatics to Injury - (Electronic Injury Alerts)

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[2] Department of Biochemistry, Altnagelvin Hospital, Glenshane Road, Northern Ireland.

Background: Acute Kidney Injury, (AKI), is common with a variably reported mortality, (15-60%). UK national audit reported that up to 30% of cases were avoidable and that as much as 43-61% of post-admission AKI experienced an unacceptable delay in recognition of insult. There has been a paucity of work with regards to AKI recognition and prevention. National guidelines have recommended the use of electronic alerts (e-alerts) for AKI detection.

Methods: We introduced AKI e-alerts with accompanying electronic guidance in late October 2014 and prospectively collected data on the patients identified with severe AKI. Data collection was carried out for 3 months, (n=110). The demographics of this cohort were compared with a historical cohort of severe AKI (n=89).

Results: Mean age, (72 years vs. 73 years), gender distribution, (M:F: 46% / 54% vs. 47% / 53%), and median time to death, (10 days vs. 9 days), were comparable. Thirty day mortality was similar with regards to hospital acquired AKI, (27.3 % vs. 26.1%). 30 day mortality was significantly lower for community-acquired AKI: (10.7%). Mean and median age was demonstrated to be higher in the group of patient who died, (Mean: 80.1 years vs. 75.7 years), (Median: 82 years vs. 82 years) – negative skew due to outliers.

Conclusion: Although our initial data suggests an electronic AKI alert has no discernable effect on 30 day mortality rate and time to death, we feel that e-alerts with the addition of further Quality Improvement work will eventually result in a steady reduction in AKI mortality.

Abstract 64

Use of a revised nomogram to rationalise dosing of cyclophosphamide for treatment of vasculitis

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Background: Analysis of EUVAS trial data indicates that renal function and age are by far the strongest predictors of treatment-related adverse events. The CYCLOPS dosing regimen includes cyclophosphamide dose adjustments for these parameters; however the cutoffs are arbitrary with possible overdosing in middle-age patients with serum creatinine 150-300umol/l. The adverse event data from the EUVAS trials data was used to generate a dosing model to determine the optimum dose for age and renal function. We have previously reported the outcome using version 1 of the nomogram, which we found to underdose relative to the predicted CYCLOPS protocol. We now report the outcome using an amended version 2 nomogram.

Methods: We conducted an audit of all vasculitis patients who received cyclophosphamide using the revised nomogram (Table 1) from January 2010 to March 2015 in 2 institutions. We analysed the actual cyclophosphamide dose received and outcome.

Results: We identified 30 patients who were treated with cyclophosphamide during this period. The mean age at first dose was 58.1 years (SD 11.0). 7 (23.3%) patients developed leucopenia (WCC<4X10^9/L). 17 (56.7%) patients were treated for infection. 9 (30%) patients had other adverse events including skin cancer, premature ovarian failure and myopathy. The mean cumulative cyclophosphamide dose over 12 months was 5185.0mg (SD 2451.7). The median dose of cyclophosphamide received was 10.73mg/kg (SD 1.53). The median difference between the prescribed dose and the predicted CYCLOPS dose was -144.77mg (SD 181.63). (-1.85mg/kg).

Figure/table:

	20	*30*	*40*	*50*	*60*	*70*	*80*
10 or dialysis	*11.5*	*11.5*	*11.5*	*10.5*	*9.5*	*8.5*	*7.5*
15	*12.7*	*12.7*	*12.7*	*11.6*	*10.5*	*9.4*	*8.2*
20	*13.3*	*13.3*	*13.3*	*12.2*	*11.0*	*9.8*	*8.7*
30	*14.0*	*14.0*	*14.0*	*12.8*	*11.6*	*10.4*	*9.1*
40	*14.4*	*14.4*	*14.4*	*13.2*	*11.9*	*10.7*	*9.4*
50	*14.7*	*14.7*	*14.7*	*13.4*	*12.1*	*10.8*	*9.6*
60	*14.8*	*14.8*	*14.8*	*13.6*	*12.3*	*11.0*	*9.7*
70	*15.0*	*15.0*	*15.0*	*13.7*	*12.4*	*11.1*	*9.7*
80	*15.0*	*15.0*	*15.0*	*13.7*	*12.4*	*11.1*	*9.8*
90	*15.0*	*15.0*	*15.0*	*13.8*	*12.5*	*11.2*	*9.9*

Proposed cyclophosphamide dose using version 2.

Conclusions: The cyclophosphamide nomogram smoothly adjusts dose for age and GFR. In our study, it resulted in a mean 15% reduction in pulse/dose. Although the incidence of leucopenia was lower than that described in the original CYCLOPS trial, the infection rate remained very high despite the lower intensity of immunosuppression.

Abstract 65

The role of monocyte subsets in ANCA vasculitis

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Background: ANCA vasculitis encompasses several autoimmune conditions characterised by destruction of small vessels, inflammation of the respiratory tract and is the leading cause of rapidly progressive glomerulonephritis. Most patients harbour autoantibodies to myeloperoxidase (MPO) or proteinase 3 (PR3). Clinical and experimental data suggest that pathogenesis is driven by ANCA-mediated activation of neutrophils and monocytes. We investigated a potential role for distinct monocyte subsets.

Methods: Blood obtained from healthy donors, disease controls and remission and acute AAV patients was used to evaluate the subsets of monocytes and the amount of MPO or PR3 being displayed on their surface. Monocytes were treated with monoclonal antibodies (mAb) to MPO and PR3 or patient ANCA and cytokine production measured by ELISA.

Results: The relative proportion of intermediate monocytes is increased in patients versus control individuals, and both MPO and PR3 are preferentially expressed on these cells. We demonstrate that MPO and PR3 are expressed independently of each other on monocytes and that PR3 is not associated with CD177. MPO expression correlates with that of Fc receptor CD16 on intermediate monocytes. Monocyte subsets respond differently to antibodies directed against MPO and PR3, with anti-MPO but not anti-PR3 leading to increased IL-1β, IL-6 and IL-8 production. The intermediate monocytes produced the highest quantity of IL-1β in response to anti-MPO stimulation.

Conclusion: These data suggest that monocytes, specifically, the intermediate subset, may play a role in the severe kidney disease ANCA vasculitis. They also indicate that substantial differences exist between the effect of anti-MPO and anti-PR3 antibodies on these cells.

Abstract 66

Acute TIN: An Initial Recent Retrospective Study from a Dublin Hospital Renal Pathology Department

Authors: Hoolahan, S. Dorman, A.

Sarah Hoolahan, RCSI Research Student, Department of Renal Pathology, Beaumont Hospital.

Background: Tubulointerstitial nephritis (TIN) is a rare but serious condition leading to decreased renal function, which may be irreversible. The most common aetiology is drug-induced TIN, typically attributed in the literature to non-steroidal anti-inflammatory drugs (NSAIDs) and antibiotics. Recently published literature increasingly implicates proton pump inhibitors (PPIs) also. The aim of this study is to examine the incidence, aetiology, demographics and histological features of biopsy-proven TIN in Ireland from 2004-2014 in one major teaching hospital.

Methods: Native kidney biopsies from the last 11 years were assessed, and cases of TIN identified from their pathology reports. These biopsies accounted for approximately 75% of all biopsies performed in Ireland during this time period. Acute and chronic features of all cases were determined

Results: Our investigation showed an average of 7.53% incidence of TIN from all renal biopsies assessed. In 2004 2.75% of biopsies showed TIN, whilst this figure rose to 9.32% in 2014. Almost 25% of cases occurred in the 65-74 age group. Drugs were the suspected aetiology in 81.4% of cases. Granulomatous inflammation, infections, autoimmune conditions, sarcoidosis, familial TIN, neoplastic conditions and tubulointerstitial nephritis and uveitis syndrome (TINU) accounted for the remaining cases.The histological findings are presented in *figure 1* below:

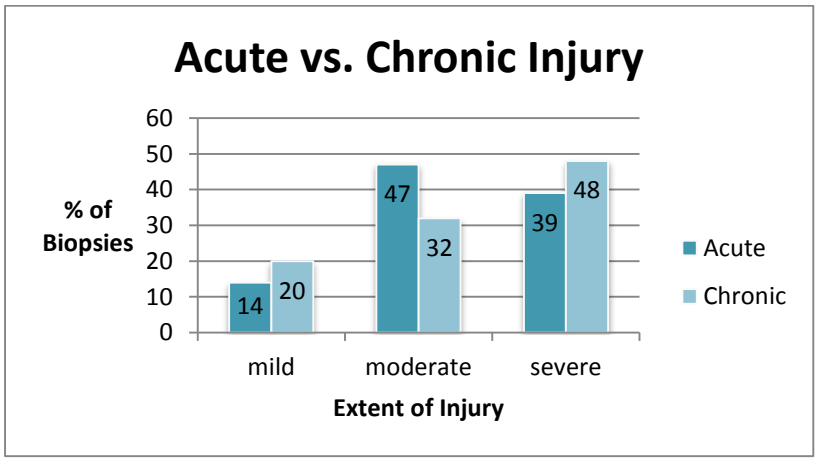

Figure 1

Conclusion: TIN is an increasing problem in Ireland. Drugs are the most commonly implicated cause, with PPIs becoming an emergent cause for concern. Clinicians need to be aware of this growing problem when prescribing medications for patients.

Abstract 67

Familial Interstitial Kidney Disease: a clinical description of tubulo-interstitial kidney disease amongst nineteen Irish families.

H Ryan, DM Connaughton, L Redahan, C Stapleton, J O'Regan, Y Kelly, G Cavalleri, A Dorman, P Lavin, PJ Conlon.

Background: Familial tubulo-interstitial kidney disease is a rare kidney disease with Mendelian patterns of inheritance. We describe a case series of families with tubulo-interstitial nephritis reporting clinical and genetic characteristics.

Methods: Recruitment undertaken using the Irish Kidney Gene Project protocol which aims to identify patients with a positive familial of kidney disease attending renal clinics and dialysis units. Once the diagnosis of tubulo-interstitial kidney disease was established, a detailed family history was obtained and medical records and pathological reports were reviewed.

Results: 19 families with 80 affected individuals were identified with medical records available on 44 individuals. Autosomal dominant inheritance was observed in 16 families; 3 demonstrated an autosomal recessive pattern. Median age of onset of kidney disease was 42 years (range 13-68 years) with median creatinine at presentation of 160 mmol/L. 19 patients developed end stage kidney disease at a median age of 49 years. 34.1% (15/44) of patients received a kidney transplant with no evidence of recurrence. Urine dipstick was available for 70.5% (n=31/44) with 66.7% (21/31) having bland urine sediment at initial presentation. 3 patients demonstrated microscopic haematuria, one with co-existing IgA nephropathy. Additional clinical features reported within families include gout (n=5, 26.3%), uveitis (n=2, 10.5%) and subarachnoid haemorrhage (n=1, 5.3%). To date genotyping has characterised the MUC1 mutation in 2 families and the UMOD mutation in 1 family.

Conclusion: This series provides a clinical description of familial tubulo-interstitial disease in an Irish population. Additional studies are underway to determine the underlying genetic mutations in these families.

Abstract 68

Clinical heterogeneity in familial IgA Nephropathy

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Background: IgA nephropathy is the most common type of primary glomerulonephritis worldwide and a significant cause of end-stage renal disease (ESRD). While most cases of IgA are considered sporadic, there are a small number of reports of familial cases of IgA nephropathy.

Methods: We embarked on a national audit of patients attending renal clinics and dialysis units to identify the presence of a family history amongst patients with kidney disease. We applied this survey to approximately 1500 subjects. As a result of this survey we have identified 20 families involving 56 affected individuals with biopsy-proven IgA nephropathy and one other first or second degree relative with kidney disease. Each family had at least one member with biopsy-proven IgA nephritis and at least one other member with either biopsy-proven IgA nephropathy or ESRD. A detailed family history was obtained from all participating families. Medical records and pathological reports were reviewed where available. All family history and clinical data were recorded and family pedigrees constructed.

Results: Of the 20 families, 15 had two affected family members, while 5 had three or more affected family members. 3 families had more than one member with biopsy proven IgA nephropathy. 6 families demonstrated a clear autosomal dominant mode of inheritance, while 5 demonstrated a clear autosomal recessive mode. In the remaining 9 families, there was evidence of autosomal dominance with incomplete penetrance, but autosomal recessive inheritance could not be excluded. Of the 31 patients with biopsy-proven IgA nephropathy, 20 (65%) were male and 11 (35%) were female. The mean age at diagnosis was 36.4 years (SD 11.6 years; range 17 – 54 years). The mode of this population was 52 years. The mean creatinine at presentation was 222.83 µmol/L (SD 305 µmol/L; range 67 – 1412 µmol/L). 16 (52%) patients had haematuria at presentation, while 22 (70%) had proteinuria. The most common presenting features were Hypertension (n = 11), nausea and vomiting (n=6), gross haematuria (n=5), ankle swelling (n=4), rash (n=1) and acute renal failure (n=1). 6 patients were identified incidentally. 13 (42%) patients had progressed to ESRD by the time of the study. The mean time to progression to ESRD from diagnosis was 4 years (SD 2.94 years; range 1 -10 years). Of these 13 patients, 3 were currently on dialysis while 10 had been transplanted. In those transplanted, recurrence of disease was reported in 6 cases.

Conclusion: These data suggest familial aggregation of IgA nephropathy, with both autosomal dominant and autosomal recessive modes of inheritance. Progression to ESRD and recurrence post renal transplantation were common in individuals affected by IgA nephropathy.

Abstract 69

The Irish National Rare Kidney Disease Registry and Biobank: update on recruitment and activity

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[1]Trinity Health Kidney Centre; [2]Dublin Centre for Clinical Research; [3]Beaumont Hospital; [4]St. Vincent's University Hospital; [5]Cork University Hospital; [6]Tallaght Hospital

Introduction: The RKD Registry and Biobank is a national registry of vasculitis and other rare kidney disease patients, with recording of detailed longitudinal clinical data linked to biological samples. We aim to compile sufficiently large cohorts of patients to address fundamental questions relating to the epidemiology, pathogenesis and pathophysiology of disease as well as facilitating phase II/III interventional studies.

Methods: Blood and urine are collected from patients and controls (disease and healthy). Blood samples are processed for plasma, serum, DNA, peripheral blood mononuclear cells and stabilised RNA. Urine is processed to be suitable for a variety of end-point experiments including metabolomic and proteomic analyses and the extraction of exosomes. Samples are inventoried using Freezerworks software.

Results: Since September 2012, 782 individuals (383 vasculitis patients, 153 healthy controls and 246 disease controls) have been recruited from 6 centres across Ireland (Beaumont, St James's, Tallaght, St Vincent's, Limerick and Cork University Hospitals). Many have contributed biological samples on more than one occasion. Of the 383 vasculitis patients recruited, 183 had samples collected when they had active disease and 131 of these contributed samples at both active and remission disease stages.The RKD Biobank has acted as a platform for collaboration and provided biological samples to both national and international partners, from academic institutions and industry. Collaborators include Agilent Technologies, the European Vasculitis Genetics Consortium, Imperial College London, Duke University, McMaster University, Harvard Medical School and Boston Children's Hospital. These studies have used a range of biological samples to investigate biomarkers of disease, urine metabolomic signatures and genetic linkage of disease.

Conclusions: The Irish National RKD Registry and Biobank has recruited well beyond its target. Each sample set is linked to a detailed clinical record, with recorded sample provenance, in line with the upcoming ISO/TC 276 standard. We have supported numerous national and international studies. Efforts now focus on sustainability and alignment with the Irish national biobank strategy.

Abstract 70

An Audit of Bone Health Parameters in Stage 4 CKD patients

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[1]Department of Clinical Nutrition and Dietetics, [2]Trinity Health Kidney Centre, Tallaght Hospital, Dublin

Background: Secondary hyperthyroidism (SHPT) is very common in chronic kidney disease (CKD). Contributing factors such as elevated phosphate ($P0^{4-}$), Calcium (Ca^{2+}) and parathyroid hormone (iPTH) have all been shown as risk factors for mortality, increased hospital admissions and decreased quality of life.

Methods: Serum Ca^{2+}, $P0^{4-}$, and iPTH levels, and relevant medications, were recorded for patients with stage 4 CKD attending dietetic outpatient appointments in 2014. Numbers of patients meeting target ranges were compared with 2011.

Results: Data was collected on 114 patients. 37 patients (32%) had all 3 parameters (PO^{4-}, Ca^{2+} and iPTH) within recommended levels.

Table 1: Percentage of patients meeting target ranges for PO^{4-}, Ca^{2+} and iPTH

	iPTH (70-110)		PO4- (0.8-1.6)		Ca2+ (2.2-2.6)	
	2011	**2014**	**2011**	**2014**	**2011**	**2014**
Below	17%	22%	1%	4%	7%	7%
In range	21%	33%	98%	94%	91%	90%
Above	62%	45%	1%	2%	2%	3%

Table 2: Medication in the treatment of SHPT according to iPTH level

iPTH level	No. of patients	alfacalcidol	paracalcitol	cinecalcet	none
Over suppressed <70	25	9	1	1	12
On target 70-110	38	13	1	1	18
High>110	51	33	0	4	12
Total	114	55	2	6	42

Conclusion: The percentage of patients achieving target levels of iPTH has improved since 2011. More frequent iPTH monitoring in patients on treatment for SHPT may help prevent oversuppression of iPTH. Annual cholecalciferol levels should be measured to identify and supplement deficiency in earlier stages of CKD and this should be included in future audits.

Abstract 71

Adherence to KDIGO's Anaemia in CKD guidelines in an Irish Tertiary hospital

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Background: Many guidelines for the management of anaemia in CKD have been published. The Kidney Disease: Improving Global Outcomes (KDIGO) Clinical practice guidelines are one such example. Previous multicentre Irish studies have shown a high prevalence and suboptimal management of anaemia in CKD. An audit of practice to assess adherence of the KDIGO guidelines was completed.

Methods: Patient data and serology were extracted from the Kidney Disease Clinical Patient Management System (eMed). All registered patients from 2014 were included. Custom software algorithms were used to assess compliance to KDIGO's Anaemia in CKD guidelines specifically testing for anaemia, Iron status evaluation and use of ESA therapy.

Results: 3192 patients and 20,082 blood results were analysed. 32.93% of patients had anaemia. Total patients with CKD stage 3, 4, 5 were 1262, 427 and 285 respectively. The adherence results are summarised in Table 1.

Table 1 - Results

CKD patients without anaemia – Measure Hb	N	Adherence
CKD 3 – Annually	562	100%
CKD 4 – Twice per year	105	78.10%
CKD 5HD – Every 3 months	17	35.29%
CKD patients with anaemia not being treated with an ESA - Measure Hb		
CKD 3–5ND – Every 3 months	239	24.69%
CKD 5HD – Monthly	140	21.43%
Evaluate iron status (TSAT and ferritin) at least every 3 months during ESA therapy	120	56.67%
Incorrect use of ESAs to maintain Hb concentration above 11.5 g/dl.	120	18.33%

Conclusions: The results show a sub-optimal adherence to KDIGO guidelines. The use of automated software algorithms and pathways could potentially facilitate better guideline adherence.

Abstract 72

Prognostic importance of Urea and Urea: creatinine ratio for mortality as compared to Creatinine concentrations in the General Population

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Background: High Creatinine (Cr) concentrations reflect poor kidney function and are associated with a higher risk of death. It is unclear whether other measures of kidney function such as blood urea nitrogen (BUN) concentration and BUN/creatinine ratio, are better predictors of mortality in the general population.

Methods: A cohort of 15,773 non-pregnant subjects age >20, representative of the U.S. population, were identified from the Third National Health and Nutrition Examination Survey (1988-1994). Vital status was obtained through linkage with the National Death Index through to 2006. Subjects were classified into deciles of Cr, BUN and BUN/Creatinine Ratio (B/Cr). A series of weighted multivariable Cox regression models, compared hazard ratios [HR] and 95% CI for death among the decile groupings for each variable. The prognostic capacity of differing models was compared using Akaike Information Criterion (AIC).

Results: In multivariable analysis, BUN was found to be the most important single predictor of mortality, from the 3 variables with Cr being second best. Further exploration revealed a strong interaction (P< 0.001) between BUN and Cr in their relationships with mortality. This interaction was explored by fitting models comparing the HR for death of Cr level, (referent 70.7<SC<79.6), stratified by BUN level, as shown below.

	Creatinine (mmol/L)						
	<70.7	**70.7-79.6**	**79.6-88.4**	**88.4-97.2**	**97.2-106.1**	**106.1-114.9**	**>=114.9**
Urea (mmol/L)							
< 2.86	1.55(0.75,3.34)	1.00	0.60(0.28,1.20)	0.51(0.16,1.67)	0.21(0.06,0.69)	0.20(0.06,0.62)	0.09(0.02,0.64)
2.86-7.5	1.04(0.81,1.34)	1.00	0.99(0.82,1.20)	1.04(0.87,1.25)	1.04(0.83,1.29)	0.97(0.77,1.23)	1.28(1.00,1.64)
>7.5	0.84(0.31,2.28)	1.00	1.78(0.72,4.40)	1.13(0.55,2.34)	1.49(0.70,3.19)	1.98(0.96,4.09)	2.31(1.15,4.65)

[1] Multivariable models adjusted for: age, sex, race, comorbidities, smoking status and physical activity levels

Conclusions: Both BUN and Cr independently predict death in the general population. Among patients with malnourished states (Low BUN); higher SC were associated with lower mortality. In contrast, among patients with normal-high BUN concentrations, higher Cr was associated with elevated death risk. Prediction models should take BUN levels into consideration when estimating future death risk.

Abstract 73

Use of serum Cystatin C to determine renal function in patients with Cystic Fibrosis.

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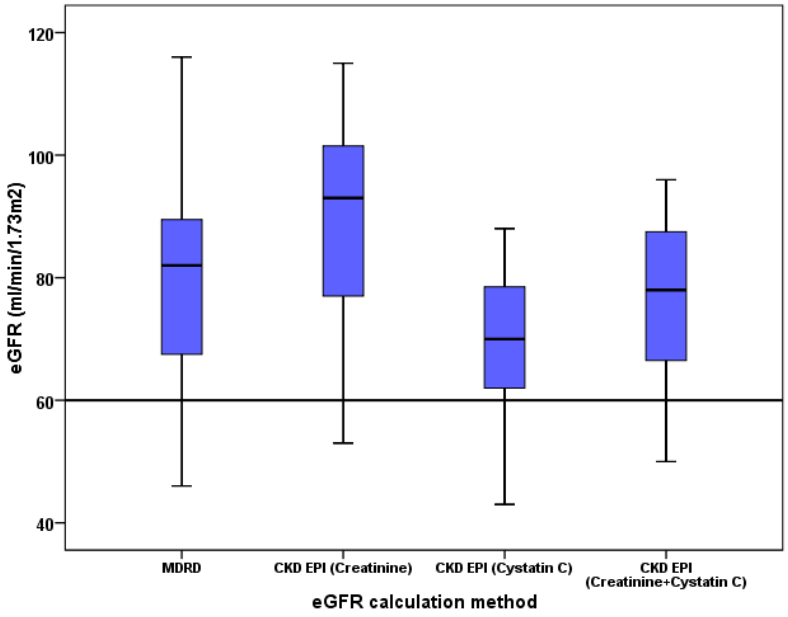
Background: Cystatin-C has received much attention as an alternative filtration marker to creatinine, particularly in patients with co-morbid conditions and reduced muscle mass. We compared Cystatin-C with creatinine based methods in calculating eGFR in patients with Cystic Fibrosis (CF) where renal disease is increasingly prevalent.

Methods: Stable patients with CF (aged >18years) were included. Serum samples for measurement of creatinine and Cystatin-C were collected simultaneously. Creatinine based eGFR was calculated using the 4-variable MDRD and CKD-EPI (2009) equations. Cystatin-C based eGFR was calculated using CKD-EPI Cystatin-C (2012) and CKD-EPI creatinine-Cystatin-C (2012). Mean differences in eGFR were calculated using paired T-Tests. (SPSS V 20).

Results: 24 patients were included, 54% male, mean (sd) age 41.8 years. Mean (sd) MDRD and CKD-EPI eGFR was 85.1(29.6) and 91.2(19.8) ml/min/1.73m^2 respectively. Mean (sd) eGFR calculated using CKD-EPI Cystatin-C (2012) and CKD-EPI Creatinine-Cystatin-C (2012) were 69.9 (13.9) and 78.5 (15.9)ml/min/1.73m^2 respectively. Mean eGFR determined by CKD-EPI Creatinine-Cystatin-C (2012) was significantly lower than that determined by CKD-EPI, 78.5 Vs 91.2ml/min/m^2, p<0.001. This resulted in a higher proportion of patients being classified as CKD-2 using the CKD-EPI Creatinine-Cystatin-C (2012) equation (70.8% Vs 33.3%), compared to CKD-EPI.

Figure 1:



Conclusions: The use of Cystatin-C based equations produced lower estimations of GFR than creatinine based equations in this group of Cystic Fibrosis patients with near normal levels of renal function. Use of Cystatin-C resulted in more patients being classified as CKD-2. Cystatin-C may be useful in detecting early CKD development in patients with Cystic Fibrosis.

Abstract 74

Novel Methods for Record Linkage in the Irish Health System: Applications for merging Laboratory and Mortality records

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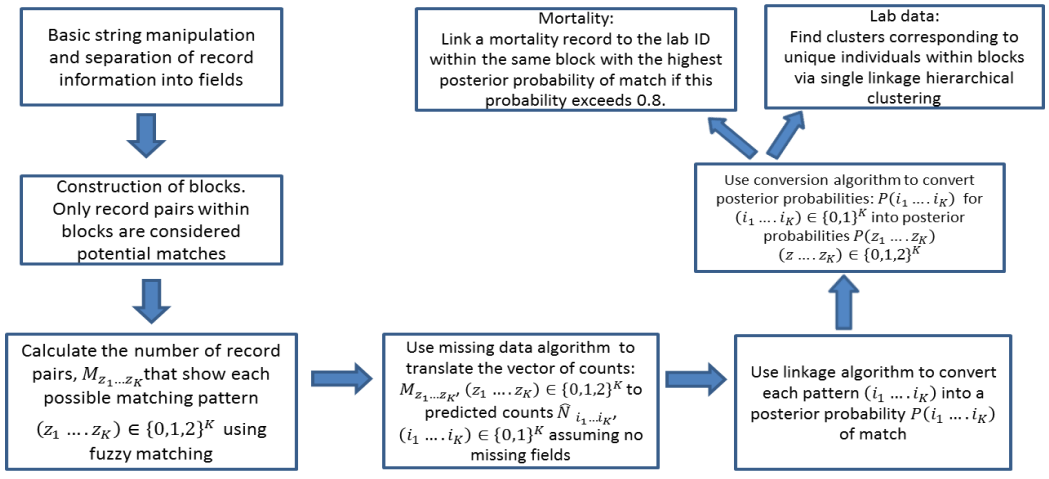
Background: We describe a novel record linkage algorithm designed to link together laboratory and mortality records in the Irish health system. The first task involved linking together laboratory test results corresponding to the same patient, from a combined set of 171,000,000 tests, from two large regional databases in the Midwest and Northwest of Ireland from 1999-2013; the second task was ascertainment of the vital status of these patients during Jan 2007-Dec 2012, via linkage with national mortality records obtained from the Central Statistics Office (CSO). Noisy demographic identifiers needed to be used for this linkage, since no unique identifier was available.

Methods: The algorithm is multi-staged, and Bayesian in nature. Suppose two databases, A and B, are to be linked. Each record pair, one from A and one from B, is converted to a posterior probability of the records being from the same patient. The resulting posterior probability is thresholded to decide which record-pairs constitute matches. A schematic flowchart describing the algorithm is given below.



Results: Using the algorithm, we linked together laboratory data for 784,296 patients in the Irish Health System. A subsequent linkage with 149,548 mortality records over the calendar years 2007-2012 yielded 25,169 matches.

Conclusions: A novel feature of our approach is the utilization of log-linear models to capture arbitrary dependence patterns among variables within each database. Simulations suggest that explicitly modelling these dependences results in more accurate linkage, in comparison with existing approaches.