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MEDICAL ABSTRACTS

Chronic inflammatory demyelinating nephropathy and concurrent nephrotic syndrome: the association with Paranodal antibodies

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Abstract:

There has been a suggested association between demyelinating polyneuropathies and nephrotic syndrome. Chronic inflammatory demyelinating neuropathy and membranous nephropathy are both immune mediated conditions of unclear aetiology. No clear pathophysiological relationship between the conditions has been identified. This clinical case report highlights the importance of testing for paranodal antibodies for both diagnostic and therapeutic purposes and supports evidence of a potential association between the two.

We report a rare case of a 76-year-old gentleman who presented after a fall at home. He had a past medical history of well controlled Type 2 diabetes, peripheral vascular disease and established CKD3. He reported leg weakness and recent weight loss. Examination revealed a motor and sensory peripheral neuropathy. He was also noted to have severe peripheral oedema. Investigations revealed nephrotic-range proteinuria. Renal biopsy confirmed a diagnosis of presumed secondary membranous glomerulonephritis with electron microscopy showing many irregular outward projections of the basement membrane associated with numerous subepithelial electron-dense deposits. Immunoperoxidase staining for PLA2R protein was negative as was serum anti-PLA2 receptor antibody testing.

Subsequent nerve conduction studies demonstrated a demyelinating polyneuropathy with secondary axonal loss, consistent with CIDP. He was later found to be paranodal antibody positive, of the CNTN1 IgG4 subset. Treatment was initiated with high dose corticosteroids and later rituximab. Despite treatment ongoing disease progression was demonstrated with a deterioration in his Modified Rankin Scale and IV immunoglobulins were commenced.

This case prompts multiple important discussion points, including the potential association between CNTN1 IgG4 antibodies and a presentation of concurrent glomerulonephritis and demyelinating polyneuropathy. A knowledge of this association will prompt early testing of paranodal antibody status, assist with identifying disease aetiology and may influence the decision to commence immunotherapy.

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Epidemiology of bloodstream infections in a Scottish haemodialysis population with focus on vascular access method.

Dr Kirsty Crowe

Background

Infection is the second highest cause of mortality amongst patients with end-stage renal disease. Vascular access-related infections (VARI) account for a significant proportion of infection-associated hospitalisations, and the rates differ by the access modality in use – arteriovenous fistulas (AVF) exhibiting the lowest rates, followed by arteriovenous grafts (AVG), and central venous catheters (CVC) the highest rates.

Bloodstream infection (BSI) surveillance in the HD population has traditionally centred on *Staphylococcus aureus* VARIs, but there is increasing recognition of the burden of Gram-negative BSIs which are often associated with non-VARI sources. Additionally, the increasing prevalence of multi-drug resistance (MDR) is of growing concern in the HD population, for which effective antimicrobial stewardship is required. There is a relative paucity of UK contemporary work which summarises the all-source profile of HD BSI organisms, their AMR and their relationship to vascular access.

Aim

The rate and anti-microbial resistance (AMR) of all-source bloodstream infections (BSIs) in a Scottish haemodialysis (HD) cohort is reported by vascular access type.

Methods

Retrospective analysis was undertaken of prospectively recorded Strathclyde Electronic Renal Patient Record data from 2017 on adult patients across seven HD units in NHS Greater Glasgow & Clyde and NHS Forth Valley. Total HD days for each vascular access type were calculated. BSIs were analysed with rates expressed per 1000 HD days. AMR patterns were verified using health board microbiology databases.

Findings

There was an overall BSI rate of 0.68/1000 HD days. The highest all-source and access-related BSI rates per 1000 HD days were in the non-tunnelled central venous catheter (CVC) group (3.11 and 2.07 respectively), followed by tunnelled CVC (1.26 and 0.68), arteriovenous graft (0.55 and 0.31) and finally arteriovenous fistula (AVF) (0.39 and 0.02). The non-VAI source BSI rates were lowest in the AVG group.

Staphylococci comprised the majority of events, with *Staphylococcus aureus* implicated in 24.5% of BSIs. Gram-negative BSIs were prevalent, particularly in CVC groups, and associated with higher mortality. MDR *S. aureus* and carbapenem-resistance were relatively low whereas MDR Gram-negatives were high compared with the Scottish population.

Conclusions: AVF access is confirmed as having lowest all-source and VAI BSI rates, and AVG access lowest non-VAI BSI rates. Staphylococci remain the prevailing genus, however the associated mortality of Gram-negative BSIs and the representation in CVC access BSIs is notable. Empirical vancomycin and gentamicin remain appropriate for this HD cohort given representation of pathogens and their AMR.

The Assessment of Renal Tissue Oxygenation (R2*) in Kidney Transplants Post Operation Using BOLD MRI

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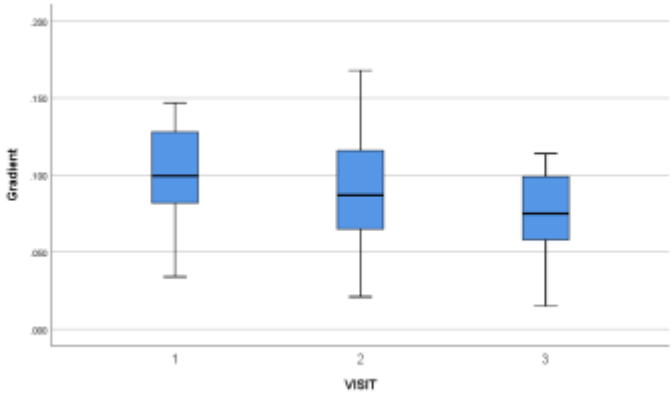
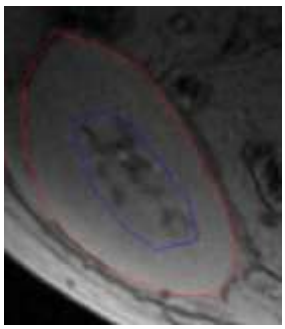
Background. Kidney transplantation (KT) is the optimal form of treatment in end stage kidney disease. Renal functional MRI may provide a non-invasive means of evaluating KT pathology. Blood oxygen level dependent (BOLD) magnetic resonance imaging (MRI) is a measure of tissue deoxygenation and can augment risk stratification in chronic kidney disease (1). Its role in KT is uncertain.

Methods. Renal MRI was undertaken at 2, 6 and 12 months post transplantation. Creatinine, estimated glomerular filtration rate (eGFR), and various MRI parameters were measured at each visit. T2* measurements were analysed using the twelve layered concentric object (TLCO) technique (2). Images were analysed with MATLAB R2020a and statistical analysis was performed with SPSS and Microsoft Excel. This creates an image highlighting 12 layers of the kidney. After this, a graph was plotted to show R2* against percentage depth within the kidney. Minimum and maximum R2* values were used to create a gradient of the BOLD signal in the kidney, theoretically representative of tissue oxygenation.

Results. 20 patients were studied. Mean creatinine at 2 months post kidney transplantation was 146micmol/L and this improved to 140micmol/L at six months. Over the similar period gradient of R2* decreased in parallel with evolution of kidney function with significant difference in R2* between 2 months and 6 months (paired t-test visit 1 vs visit 3, p=0.025) See figure below with contour of MRI of kidney.

Conclusions. Changes in renal function as transplanted kidneys recover from acute tubular injury of transplantation are accompanied by changes in MRI imaging signal which have been associated with kidney oxygenation. Further work is required to establish the functional significance of these imaging findings and whether this can differentiate acute tubular necrosis from other pathologies





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Is there any role for prophylaxis in patients receiving intravenous contrast for contrast-enhanced CT scanning? A systematic review and meta-analysis.

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Background: Contrast-induced nephropathy (CIN) is a controversial entity for which a number of prophylaxis measures have been used in clinical practice. The American College of Radiologists have recently published guidance that intravenous (IV) saline should only be used routinely as prophylaxis in patients with an eGFR of less than 30ml/min/m^2. Other forms of contrast prophylaxis are currently not recommended.

Aim: To perform a systematic review of the current literature to determine whether there is any role for either fluid prophylaxis or other forms of prophylaxis in reducing the rates of CIN, as well as the longer term impacts of CIN and side effects of prophylaxis methods

Methods: A systematic review was carried out to identify studies examining patients undergoing CT scanning with IV contrast who received treatment for contrast prophylaxis as part of a randomised controlled trial or as part of a case-control or observational study. Studies were subdivided into those comparing IV volume expansion alone to no IV volume expansion and those comparing forms of prophylaxis against control (IV fluid, oral fluid or no fluid)

Meta-analyses were performed to examine the pooled effect of prophylactic treatments on the prevention of CIN. Meta-regression was used to determine if baseline characteristics of the study participants had any relationship with the effectiveness of prophylactic treatments. Risk-of-bias assessments were carried out in keeping with PRISMA guidance.

Results: 20 papers were identified which met the search criteria of which19 were included in the meta-analysis. The majority of studies assessed a single intervention against a control group receiving IV saline, with the exception of 3 studies, 2 used no hydration and 1 non-specific hydration. The majority of studies included studied the use of N-Acetylcysteine (NAC) followed by sodium bicarbonate. No papers compared IV hydration with saline against no IV hydration.

Meta-analysis demonstrated that prophylactic treatments were associated with reduced incidence of CIN (OR=0.49, 95% CI 0.37-0.69, p<0.001). This was true of both NAC (OR=0.54, 95% CI 0.27-0.79, p<0.001) and sodium bicarbonate (OR=0.44, 95 CI 0.25-0.77, p=0.016). No significant improvement in change in mean creatinine was observed with prophylactic treatment (-0.61mg/dl, 95% CI -1.24-0.02, I^2=96%). Other outcomes (mortality, need for renal replacement therapy, fluid overload and persistent renal impairment) were sparsely reported and prophylaxis was not demonstrated to have a statistically significant impact on these outcomes.

Conclusion:

Prophylaxis with NAC and sodium bicarbonate appear to reduce the incidence of CIN. However, there is no standardised definition of CIN currently in use and definitions used in the included studies differ from KDIGO AKI definitions meaning extrapolation that reducing incidence of CIN would impact longer term outcomes is not possible. There is currently little evidence to currently support their use.

There is an alarming lack of evidence to support the use of IV volume expansion to prevent CIN and further investigation is needed.

Impact of COVID-19 pandemic on the incidence of nephrotic syndrome in patients with minimal change disease and primary focal segmental glomerulosclerosis.

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Background.
Previous studies have identified an association between viral infection and relapse of nephrotic syndrome (NS) in patients with minimal change disease (MCD) and primary focal segmental glomerulosclerosis (FSGS)

Aim
The aim of this study was to determine if the incidence of NS relapse in patients with MCD and FSGS changed during the three month peak of the COVID-19 pandemic (01/March/2020 – 31/May/2020) compared to the same months in the preceding 4 calendar years.

Methods
All prevalent adults alive and attending the Glasgow Renal and Transplant Unit with known MCD or primary FSGS not on renal replacement therapy on 1st March of each of the years between 2016 and 2020 were identified from the electronic patient record (EPR). Age, sex, time since diagnosis, last serum creatinine, last urine protein:creatinine ratio (uPCR), prescribed immunosuppression at 1st March each year were extracted.The first measure of urine protein:creatinine ratio >300mg/mmol , urine albumin:creatinine ratio >200mg/mmol or new prescription of high dose prednisolone (>20mg per day) in the 3 month study periods were identified as 'possible relapse'. The record was then viewed in detail to determine if this was a confirmed relapse of NS.

Results
The number of prevalent patients with known MCD or primary FSGS on 1st March in each of the 5 years 2016-2020 ranged from 182 to 210. The mean age, proportion of male:female, median years since diagnosis, proportion on maintenance immunosuppression, mean serum creatinine and median urine protein:creatinine ratio in each of the prevalent cohorts was similar. In 72,787 days of follow up during March-May the prevalent cohorts for 2016-2019 experienced 36 confirmed relapses of nephrotic syndrome compared with 9 relapses in 17737 days follow up in the 2020 cohort. This equates to 18.1 v 18.5 relapses per 100 patient years of follow up ($p>0.05$). The results were the same when MCD and primary FSGS were considered separately and when new cases of MCD or FSGS with nephrotic syndrome diagnosed during the study periods were added.

Conclusion
The incidence of nephrotic syndrome relapse in patients with known MCD or primary FSGS did not change during the peak of the COVID-19 pandemic.

Sinus tachycardia, bacterial infection, and thrombosis - complications in cases of COVID-19-associated AKI requiring RRT

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Introduction: In this case report we describe University Hospital Monklands renal unit's experience of managing three cases of acute kidney injury (AKI) requiring renal replacement therapy (RRT) in patients who also required mechanical ventilation for COVID-19, and the infective and thrombotic complications these patients experienced.

Case A: Patient A is a 33 year old woman with a background of polycystic ovary syndrome and obesity. She presented to hospital with dyspnoea, cough, and fever, and a nasopharyngeal swab was positive for SARS-CoV2 by polymerase chain reaction (PCR). She was in type 1 respiratory failure and was admitted to ICU, intubated, and ventilated. She developed oliguric AKI, and was started on continuous veno-venous haemofiltration (CVVHF) on day 3. On discharge to our hospital's renal unit on day 8, she had a persistent sinus tachycardia of 120bpm, and remained RRT-dependent. Her fluid balance was 431ml positive, which was an effective negative fluid balance when insensitive losses were considered. Her tachycardia did not improve with IV crystalloid. She was investigated with a CT pulmonary angiogram and an echocardiogram, which revealed a non-occlusive middle lobe pulmonary artery thrombus and a mass adjacent to the tip of the haemodialysis line in her right atrium, respectively. The echocardiogram changes resolved with anticoagulation, and serial blood cultures did not grow any organisms. She was discharged on day 28 with a plan to continue RRT via a tunnelled dialysis line, but recovered native function and became RRT-independent within a week of discharge.
Case B: Patient B is a 41 year old male with a history of Type 2 diabetes mellitus and hypertension. He presented with dyspnoea and had Type 1 respiratory failure, which led to admission to ICU, intubation, and ventilation. While initially nasopharyngeal swabs tested negative for SARS-CoV2, endotracheal secretions were positive for the virus on day 6. He developed AKI and was started on CVVH on day 4. On discharge to the renal unit on day 16, he remained RRT-dependent. He had a sinus tachycardia with a rate of 132bpm. His fluid balance was 8167ml negative at this point. Blood cultures were performed in the context of a rising CRP, and yielded a growth of Enterococcus faecalis. This was managed with IV Co-amoxiclav. An echocardiogram showed no vegetations. He had his last dialysis session on day 23 and subsequently recovered native renal function. He was discharged on day 29 independent of RRT.
Case C: Patient C is a 51 year old woman with a background of CKD3 resulting from a nephrectomy, hypertension, and obesity. She was readmitted to our hospital having previously tested positive for SARS-CoV2, and intubated and ventilated in ICU. By day 2, she had developed oliguric AKI, which prompted the start of CVVH. RRT continued until day 14, and on discharge to the renal unit on day 17, her creatinine was static at 564µmol/L. On arrival at our unit, she had a marked sinus tachycardia at a rate of 140bpm and was febrile. Her fluid balance was 9853ml positive. We noted a line tip culture from day 14, which had yielded a growth of Staphylococcus epidermidis and Candida albicans – on this basis she was treated for line sepsis with IV Amoxicillin, Temocillin, Metronidazole, and Fluconazole. Her excretory function continued to recover and she was discharged on day 38, independent of RRT.

Discussion/Conclusion: All three patients eventually became RRT-independent, although patients A and B did not return to their baseline glomerular filtration rate. While biopsies were not performed, the observation that patient C, treated with a more liberal fluid regimen, recovered more quickly and to baseline native function, highlights the relevance of cautious fluid balance in this disease. All patients were in sinus tachycardia that took several days to settle. This was in the context of restrictive IV fluid therapy while intubated and ventilated, bacterial secondary infection, and a thromboembolic event in one case. While tachycardia seems common in the recovering COVID-19 patient, this should still prompt a consideration of alternative pathologies that would require treatment, rather than being considered a feature of the disease. We also noted despite reports of thromboembolic events in COVID-19, as seen in case A, none of our patients experienced haemodialysis access loss due to clot formation.

Prevalence of Pain among the Chronic Kidney Disease Population: a systematic review and meta-analysis

Emilie Lambourg

BACKGROUND: Pain is one of the commonest symptoms in chronic kidney disease (CKD) patients, resulting in a further reduction in quality of life, a higher use of other medical resources and major healthcare costs. The precise prevalence of pain in the CKD population is a current research gap. However, it is known to be much higher than in the general population and thought to range between 40 and 60%, with a very high heterogeneity between studies (20 to 90%).
There is clear evidence for a lack of recognition and undertreatment of pain in the CKD population. Potential underlying reasons include the complexity of managing late-stage CKD patients, often affected by multiple concomitant symptoms and comorbidities, and the fragmentation of care issue, only worsened by a poor communication between patients and renal providers.
A systematic review and meta-analysis was conducted in accordance with the PRISMA guidelines, in order to determine up-to-date and reliable estimates of the prevalence of different types of pain among CKD patients. The aim was to better understand the epidemiology and characteristics of pain profiles in the CKD population and explore the heterogeneity in prevalence measurements reported by previous studies.

METHODS: Four databases (MEDLINE, Embase, CINAHL, CENTRAL) and the grey literature were searched. All studies that reported a prevalence of pain in adult participants, with an estimated glomerular filtration rate (eGFR) less than 60mL/min/1.73m^2 for over three months, were included.
Relevant studies were then assessed for external and internal validity by two independent reviewers. Generalised Linear Mixed Models were implemented to conduct random-effect meta-analyses grouped by pain types and stratified by CKD management strategy (CKD non-dialysis, dialysis, kidney transplantation, palliative care). Meta-regression were conducted with the following covariates: age, gender, ethnicity, diabetes, hypertension and body mass index (BMI).

RESULTS: 110 studies conducted in more than 30 different countries were included. Meta-analyses yielded an overall prevalence of: 60% (95% CI 56-64) for recent pain, 49% (95% CI 43-56) for chronic pain and 10% (95% CI 6-16) for neuropathic pain. Studies conducted in Africa/Middle-East displayed the highest levels of pain compared with other geographic areas.
Stratification by CKD management strategy revealed that pain prevalence was significantly lower among kidney transplant recipients (KTR) (48%, 95% CI 39-57%) compared with CKD non-dialysis (64%, 95% CI 58-70%) and dialysis patients (63%, 95% CI 57-68%).
Meta-regression showed that samples with a higher percentage of patients of black ethnicity were significantly associated with a higher prevalence of pain ($p=0.04$). Likewise, neuropathic pain was more frequent in samples containing a high proportion of patients affected by hypertension and in samples where participants were characterised by a higher mean BMI ($p=0.002$ and $p<0.0001$).
Investigating pain affecting various specific body sites enabled to identify different pain profiles according to patients' CKD management strategies: if bone/joint pain appeared to be the most common pain symptom overall (52%, 95% CI 42-62%) and among dialysis patients (52%, CI 41-64%), abdominal pain was predominant among KTR (41%, 95% CI 21-65%).
Finally, a substantial prevalence of fibromyalgia was observed in the CKD population overall (10%, 95% CI 8-14), superior to what is usually observed in the general population.

CONCLUSION: All subgroups of patients with CKD suffer from a high burden of pain. However, the prevalence was found especially high among dialysis and CKD non-dialysis patients, suggesting a clear benefit of kidney transplantation on quality of life.
By providing quantitative and qualitative information on pain profiles, these findings bring crucial evidence to inform service delivery and potentially reduce the burden of pain in the CKD population.

An Exploration of Clinicians' Views on Weight Management in Renal Transplant Candidates and Recipients.

Authors: Robert McLaren, Bernadine Chau, Margaret MacDougall, Gillian Walker, Tineke Rennie and Paul Phelan

Introduction: Weight management both pre- and post-transplant is an important issue in renal transplantation and access to these services is often limited .We aimed to ascertain which weight management approaches clinicians currently use and how they view them, explore what barriers they feel prevent them from delivering effective weight management and finally gauge their thoughts towards utilising bariatric surgery in this population.

Methods: We designed a survey which explored respondents' views toward the aforementioned topics. This online survey was accessible by a web link, which was shared via email to renal transplant dieticians and co-ordinators across NHS Scotland. It was also shared directly with renal transplant physicians and surgeons working in both transplant centres. Finally the web link was shared on twitter by the Scottish Renal Association (@Scottishrenal) and a transplant physician (@paulphel).

Results: There were 55 responses to the survey, the cohort composed of 22 transplant physicians, 4 transplant surgeons, 8 specialist trainees, 10 dieticians and 11 nurses (inc. transplant co-ordinators). 78.2% of subjects measured obesity solely with body mass index (BMI) and most felt there should not be a BMI 'cut-off' to access the transplant list. Respondents utilised the weight management approaches of exercise and dietary modification equally. 75-84.3% of clinicians delivered their chosen intervention exclusively as 'advice' rather than as a prescriptive regimen over the pre- and post-transplant periods. They often used multiple methods of communicating such information, however verbal instruction was used by 95% of respondents. Written patient literature was the second most common method of delivery, being utilised by 17% and 20% of clinicians in the pre- and post-transplant respectively. Respondents were generally unhappy with the current resources. More than 80% rated the 'accessibility' and 'effectiveness' of them as 'okay' or 'poor'. Most respondents would like access to bariatric surgery, with 71.4% suggesting so in pre-transplant period and 54.5% for post-transplant patients.

Conclusions: It is clear that clinicians remain open to transplanting obese patients and that obesity is measured uniformly across the health care system using BMI. However clinicians feel weight management resources are lacking and clinicians would especially like to have more access to bariatric surgery. Patient views' towards weight management should also be explored given the frequency that 'a lack of patient engagement' was reported.

The Impact of Obesity and Post-Transplant Weight Gain on Renal Transplant Outcomes.

Authors: Robert McLaren, Tineke Rennie, Bernadine Chau, Margaret MacDougall, Paul Phelan

Introduction: The proportion of patients being waitlisted for kidney transplantation who are overweight or obese is rising. However there is evidence of inferior renal transplant outcomes in these patients, leading to uncertainty regarding timing of waitlisting and if weight cut-offs should be used. Many patients' also gain considerable weight after transplantation, which may add to the risk of complications. We aimed to examine the associations between recipients' pre-transplant body mass index (BMI) as well as post transplant weight gain on several transplant outcomes

Methods: We carried out a single centre, retrospective cohort study of 205 consecutive patients transplanted in 2015 and 2016 .We assessed the following outcomes: surgical complications, serious infection, delayed graft function, length of index hospital stay, re-admission rate within 90 days, new onset diabetes after transplant (NODAT), graft function, graft failure and death. The follow up period of subjects ranged from 37 to 61 months post-transplantation.

Results: Mean age at transplant was 49.2 years and 59% of the cohort was male. Distribution of subjects across the BMI classifications at transplant were as follows: under weight (<20kg/m^2) 4.3%, healthy weight (20-24.99 kg/m^2) 38.8%, overweight (25-29.99 kg/m^2) 40.4% and obese (>30 kg/m^2) 16.5%. Pre-Transplant obesity was associated with new onset diabetes at 1 year post-transplant (p=0.018). There was also a correlation between higher patient BMI at transplant and lower eGFR at 1 and 2 years post-transplant (p<0.001 and p<0.001 respectively), in unadjusted analysis. There was no association between patient BMI and surgical complications, infectious complications, length of index hospital stay, re-admission within 90 days, delayed graft function, graft failure or death.

Post-transplant weight gain was especially prevalent in the first 12 months with mean weight gain being 3.0kg, resulting in 35.5% of healthy weight patients becoming overweight and 30.6% of overweight patients becoming obese. Weight gain slowed between 12 and 36 months post-transplant, with a mean change of +0.833kg. There was no association between recipients' relative weight gain over the first 2 years post-transplant and their graft function (eGFR), glucose intolerance, NODAT or graft failure.

Conclusions: Our results suggest that higher BMI is associated with NODAT within the first 12 months of their transplant. Most patients gain weight post-transplant but this may not be associated with short term complications. Our future work will investigate any association with graft dysfunction.

Renal and Cardiovascular Effects of SGLT2 inhibition in combination with loop diuretics in patients with Type 2 Diabetes and Chronic Heart Failure: The RECEDE-CHF Trial

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Background Sodium-Glucose Co-Transporter-2 (SGLT2) inhibitors improve heart failure (HF) associated-outcomes in patients with type 2 diabetes (T2D). In patients with HF, SGLT2 inhibitors will likely be co-prescribed with a loop diuretic, but this combined effect is not well-defined. Our aim was to assess the diuretic and natriuretic effect of empagliflozin in combination with loop diuretics.

Methods The RECEDE-CHF trial (NCT03226457) was a randomized, double-blind, placebo-controlled, cross-over trial of patients with T2D and HF with reduced ejection fraction taking regular loop diuretic who were randomized to empagliflozin 25 mg once daily or placebo for 6 weeks with a 2-week washout period. The primary outcome was change in 24-hour urinary volume from baseline at week 6.

Results Twenty-three participants (mean age 69.8 years, 73.9% male, mean furosemide dose of 49.6±31.3mg/day, mean HbA1c 7.9±3.8%) were recruited. Compared to placebo, empagliflozin caused a significant increase in 24-hour urinary volume at both day 3 (mean difference 535 ml, 95% CI 133 to 936, p =0.005) and week 6, (mean difference 545 ml, 95% CI 136 to 954 p = 0.005) after adjustment for treatment order, baseline 24-hour urine volume and percentage change in loop diuretic dose. At 6 weeks empagliflozin did not cause a significant change in 24-hour urinary sodium (mean difference -7.85 mmol/L, 95% CI -2.43 to 6.73, p = 0.57). Empagliflozin caused a non-significant increase in fractional excretion of sodium at day 3 which was absent at week 6 (mean difference day 3: 0.30%, 95% CI -0.03 to 0.63, p=0.09; week 6 0.11%, 95% CI -0.22 to 0.44, p > 0.99) and a significant increase in electrolyte-free water clearance at week 6 (mean difference 312 ml, 95% CI 26 to 598, p=0.026) compared to placebo. Empagliflozin also caused significant reductions in body weight and serum urate at week 6.

Conclusions Empagliflozin caused a significant increase in 24-hour urine volume without a significant increase in urinary sodium when used in combination with loop diuretic. Empagliflozin also caused a significant increase in electrolyte-free water clearance, significant weight loss and reduced loop diuretic requirement. These findings provide further insight into the mechanism of the diuretic effect of empagliflozin and suggest that the combination of loop diuretic and SGLT2 inhibition could have a beneficial role in HF patients.

Comparison of two prophylaxis strategies to reduce Cytomegalovirus infection post kidney transplantation in Scotland

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Background: Cytomegalovirus (CMV) infection is the most common opportunistic infection following kidney transplantation. Antiviral prophylaxis is effective in reducing the risk of infection in high risk (CMV D+/R-) recipients, however, the best strategy to prevent CMV is not defined for intermediate risk (CMV R+) recipients.

Methods: Prospective cohort study describing Scottish experience of two CMV prophylaxis strategies in kidney transplant recipients; 1) up to 900mg/day Valganciclovir (VGCV900) in high risk and intermediate risk recipients, and 2) prophylaxis with up to 450mg VGCV in high risk recipients only. Kaplan Meier survival analysis was used to compare efficacy in reducing CMV infection (including CMV viraemia, syndrome and disease), leukopenia (WCC<$3.5*10^3$) and graft survival. Statistical analyses were performed in SPSS.

Results: Included were 482 kidney transplant recipients (2015 – 2016 in Scotland); 285 were male (59%), mean age was 49 (SD±13) and mean follow up 3.7 (SD±1.2) years. One hundred four were D+/R- (22%) and 251 (52%) were R+. Ninety-six patients (20%) developed CMV infection; of which 75% were in year 1. High and intermediate risk groups developed more CMV infection (40% and 20%) than low risk groups (3%, p<0.001). Disease rates were 29% in D+/R- and 6% in R+ recipients. Prophylaxis in R+ patients reduced early CMV infection compared to non-prophylaxis strategies (6% vs 21% at 9 months), as well as late infection (12% vs 25% at 2 years [p=0.001]), but did not improve CMV disease risk (1% vs 8% and 5% vs 9% at 9 months and 2 years respectively, p=0.199).
Higher dose VGCV did not reduce CMV infection risk in R+ or D+/R- recipients (17% at 2 year for both VGVC900 and VGCV450 [p=0.751]). The risk of leukopenia at 9 months was increased in patients on prophylaxis (64% vs 21%, p<0.001), regardless of the dose of VGCV. Risk of leukopenia within 6 months was 80% in patients receiving VGCV and enhanced induction, 54% in those on VGCV and standard induction and 20% in those without prophylaxis on standard induction (p<0.001). CMV infection was associated with impaired transplant function (eGFR 48 vs 57 mL/min/$1.73m^2$, p<0.001), but not with graft loss.

Conclusion: In intermediate risk recipients, prophylaxis with VGCV reduces CMV infection, but not disease. A reduction in CMV infection post-transplantation with VGCV prophylaxis comes at the price of an increased leukopenia risk, particularly when combined with enhanced immunosuppression.

Effects of haemodialysis arteriovenous fistula creation on cardiac structure and function

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Background and objectives

Arteriovenous fistula (AVF) is considered the preferred type of access for maintenance haemodialysis. The creation of an AVF may contribute to maladaptive cardiovascular remodelling. The degree of maladaptive remodelling depends on AVF blood flow. We conducted a study to evaluate the effect of AVF creation on cardiac structure and function in patients with end-stage renal disease (ESRD).

Methods

In this prospective cohort study, patients with ESRD listed for AVF creation underwent cardiac magnetic resonance (CMR) imaging at baseline and at 6 weeks. All participants had ultrasound measurements of AVF blood flow at 6 weeks. The primary outcome was the change in left ventricular (LV) mass. Secondary outcomes included changes in LV volumes, LV ejection fraction, N-terminal-pro B-type natriuretic peptide (NT-proBNP) levels, cardiac output/index, and LV global longitudinal strain.

Results

A total of 55 patients were enrolled, of whom 40 had AVF creation and completed both scans. Patients were divided into 2 groups based on AVF blood flows: 22 in the high flow group (≥ 600mL/min) and 18 in the low flow group (< 600mL/min). On the second CMR scan, a mean increase of 7.4 g (95% CI, 1.1–13.7, P=0.02) was observed in LV mass; in the high flow group the mean increase was 15.5 g (95% CI, 7.3–23.8) compared with a small decrease of 2.5 g (95% CI, −10.6 to 5.6) in the low flow group (P=0.003). Significant increases in LV end-diastolic volumes, cardiac output, and cardiac index were also seen after AVF creation (P<0.04). No significant changes were observed in LV end-systolic volumes (P=0.12), LV ejection fraction (P=0.52), NT-proBNP (P=0.08), and LV global longitudinal strain (P=0.21).

Conclusions

Creation of AVF for haemodialysis in adults with ESRD resulted in significant increase of LV myocardial mass within weeks after surgery, which was more pronounced in high flow AVF.

An unexpected case of Anti-GBM disease and Membranous glomerulonephritis

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Queen Elizabeth University Hospital, Glasgow

Case Study: A previously fit 60 year-old man had a partial nephrectomy for clear cell renal carcinoma. At the time of surgery, his kidney function was normal with serum Creatinine 85 umol/L, including post-operatively. He did however have an inflammatory response with CRP >200. He developed acute kidney injury (AKI) five weeks later with serum creatinine 1942 umol/L. A CT scan of abdomen and pelvis showed only normal post-operative changes. A specialist renal pathologist reviewed slides of the renal parenchyma adjacent to the resected tumour.

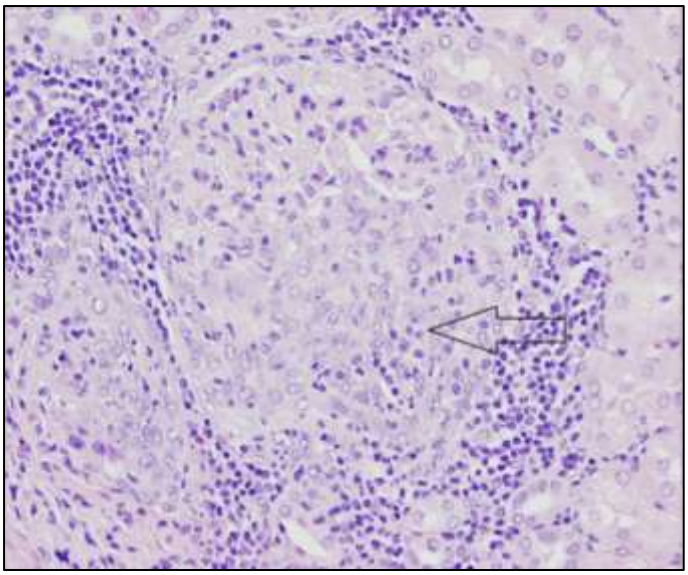

Figure 1. Light

Histological examination of the nephrectomy specimen revealed:

- Light microscopy: dense interstitial inflammatory cell infiltrate and a glomerulus with a cellular crescent (figure 1, arrow)
- Silver stain: craters in the outer aspect of the glomerular capillary wall basement membrane (figure 2)
- Electron Microscopy: subepithelial electron dense deposits (figure 3, arrows)
- Immunofluorescence: weak granular glomerular capillary wall IgG staining

Blood tests showed an unrecordably high anti-GBM antibody level of greater than 680 U/ml (normal <7). No immunology or urine biochemistry samples were available from before the presentation with AKI.

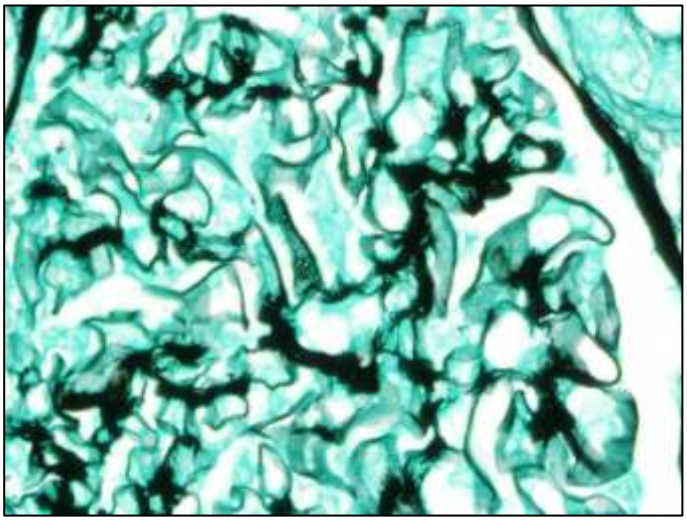

Figure 2. Silver

Membranous Glomerulonephritis (MN) was diagnosed and is likely to be secondary to the renal cell carcinoma. The diagnosis of anti-GBM disease was made based on clinical findings, strongly positive anti-GBM antibody test and the presence of glomerular crescents. Immunofluorescence features of anti-GBM glomerulonephritis were not apparent, perhaps because the immunofluorescence was carried out on paraffin sections. It is also possible the anti-GBM disease developed after the MN.

Immunosuppression was not given initially on the basis that with renal-limited disease, prolonged anuria and recent cancer resection, the likelihood of recovery of kidney function was low. Subsequently the patient developed acute pulmonary haemorrhage and for this indication received seven sessions of plasma exchange, high dose corticosteroids and three months of oral cyclophosphamide. Kidney function did not improve and the patient remains dialysis-dependent. He will be considered for kidney transplantation three to five years after the excision of renal cell carcinonma.

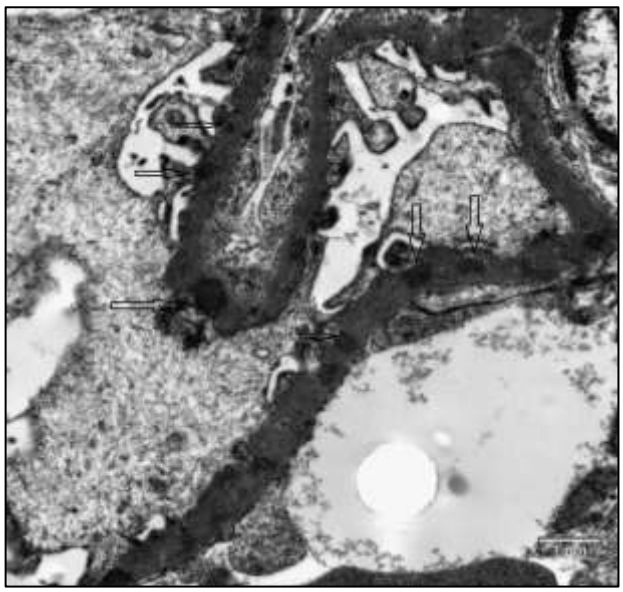

Figure 3. Electron

Learning Points:

1. Several disease processes may present synchronously
2. Healthcare professionals may need to think laterally about where information can be found
3. Events such as biopsies or surgery may trigger disease processes that might otherwise remain inactive

Multimorbidity and the risk of major adverse renal events: findings from the UK Biobank cohort

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Bethany Stanley, Frances S Mair, Patrick B Mark. University of Glasgow

Background

Multimorbidity (the presence of two or more long-term conditions) is associated with a heightened risk of mortality, but little is known about the relationship between multimorbidity and the risk of renal events. Patients with chronic kidney disease (CKD) often have multiple medical conditions, with one study reporting that patients cared for by nephrologists have a mean of 4.2 comorbid conditions, suggesting patients with CKD are likely to be amongst those with the 'greatest degree' of multimorbidity[1].

Method

We studied the associations between multimorbidity and major adverse renal events (MARE) in 68,505 adults in UK Biobank with estimated glomerular filtration rate (eGFR) > 15ml/min/1.73m^2 at baseline. MARE was defined as the need for long-term kidney replacement therapy, doubling of serum creatinine, fall of eGFR to <15 ml/min/1.73 m^2 or 30% decline in eGFR from baseline. Associations between self-reported long-term condition counts and MARE were tested using competing risks analysis.

Results

Over a median follow-up period of 12.0 years, 2,963 participants had MARE. 92.7% of those with MARE had normal kidney function at baseline. There were associations between long-term condition count categories and the risk of MARE (1 long-term condition adjusted subhazard ratio (sHR) 1.29 (95% Confidence Interval 1.15-1.45), 2 long-term conditions sHR 1.74 (1.55-1.96), 3 or more long-term conditions sHR 2.41 (2.14-2.71)). This finding was more pronounced when only cardiometabolic long-term conditions were considered (Figure 1; 1 long-term condition sHR 1.58 (1.45-1.73), 2 long-term conditions sHR 3.17 (2.80-3.59), 3 or more long-term conditions sHR 5.24 (4.34-6.33)).

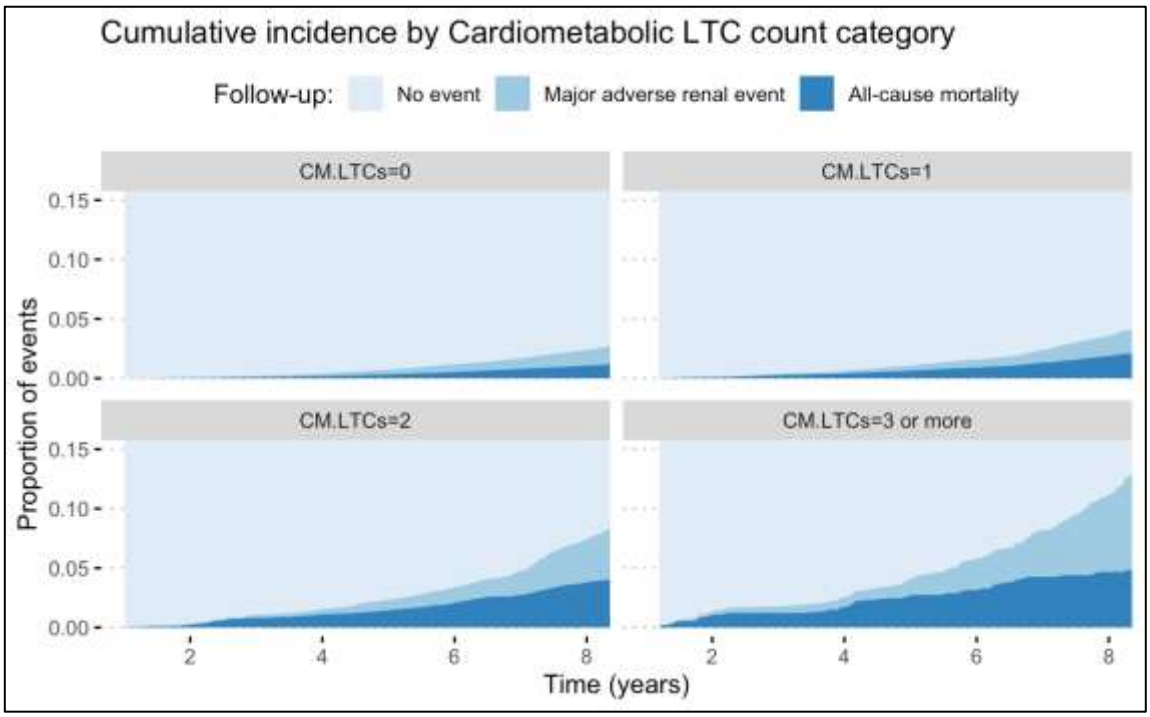


Figure 1. Cumulative incidences of major adverse renal events and all-cause mortality by number of cardiometabolic long term conditions (CM.LTCs: coronary heart disease, hypertension, heart failure, atrial fibrillation, diabetes, peripheral vascular disease, stroke or TIA).

Discussion

Multimorbidity, and in particular cardiometabolic multimorbidity, is a significant risk factor for MARE. The majority of participants with MARE had normal kidney function at baseline, and so it is essential that patients with multimorbidity have their kidney function monitored, regardless of whether they have CKD. Future research should study groups of patients who are at high risk of progressive kidney disease based on the number and type of long-term conditions.

1. Tonelli M, Wiebe N, Manns BJ, et al. Comparison of the Complexity of Patients Seen by Different Medical Subspecialists in a Universal Health Care System. *JAMA Netw open*. 2018;1(7):e184852-e184852. doi:10.1001/jamanetworkopen.2018.4852

NURSING ABSTRACTS

West of Scotland Living Donor Nephrectomy Audit

Ruth Gittins [1], Karen Stevenson [1], Julie Glen [1]
1. Glasgow Renal and Transplant Unit, Queen Elizabeth University Hospital, Glasgow

Background

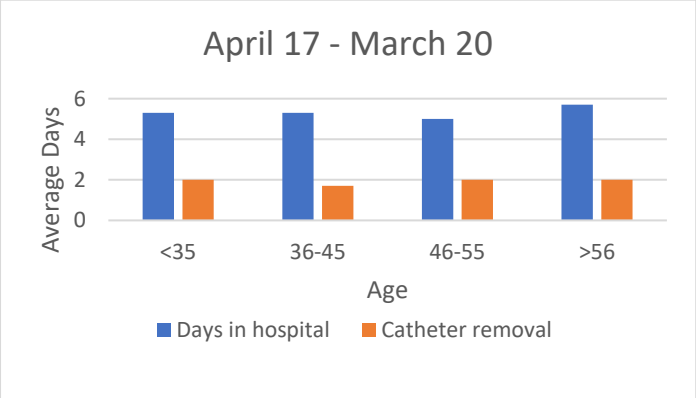
Living Donor Kidney Transplantation has long been recognised as the most effective form of renal replacement therapy. NHS Blood and Transplant published a UK strategy that set very clear goals to increase the number of LDKT's to 26pmp by 2020 matching world class performance in LDKT, with National Service Division (NSD) setting a local target of 60 donors per year. The West of Scotland Transplant Team admit both donor and recipient into ward 4C at the Queen Elizabeth University Hospital, Glasgow, however during the COVID-19 pandemic the Living Donor (LD) Programme stopped completely. An audit was carried out to look at the donors hospital journey to identify areas for optimisation to facilitate recommencement of the LD programme.

Methods

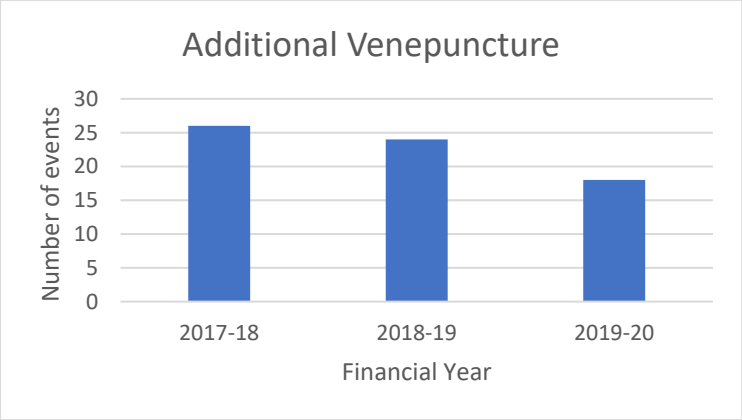
A retrospective audit was carried out identifying all donor nephrectomy patients from 1st of April 2017 to the 31st of March 2020. The audit reviewed preoperative assessment investigations, days in hospital and objective measures of in hospital stay. In-patient hospital notes and electronic patient records were interrogated for data collection.

Results

During this 3 year period 152 donor nephrectomies were performed. Days spent in hospital ranged from 3 to 11 with an average of 5 days. Donor age ranged from 24 to 73 years. Urinary catheters were removed on average on the second post-operative day (SD +/- 1.0)



All donors had pre operative bloods taken approximately 10 days before admission at the same time as a final crossmatch was obtained. 45% of donors had repeat venepuncture carried out on the day of admission despite pre op blood results being available.



Conclusions

This audit highlights areas of care that are repetitive and do not enhance the donor experience. Age does not appear to be a factor in the length of hospital stay despite general fitness. It also highlights inappropriate use of resource. This has improved following education. The additional cost of processing the blood tests taken was calculated at £1851.00, this does not take in to account the staff time (including lab staff), making clinic space unavailable for other donors, etc. and most importantly donor experience. Enhanced Recovery After Surgery (ERAS) is common practice within other specialities and a protocol has now been developed to enhance and optimise donor nephrectomy care and is currently being piloted.

Outcomes for potential living kidney donors- the Glasgow Experience 2017-2020

Julie Glen [1], Rajan K Patel [1]

1. Glasgow Renal and Transplant Unit, Queen Elizabeth University Hospital, Glasgow

Background

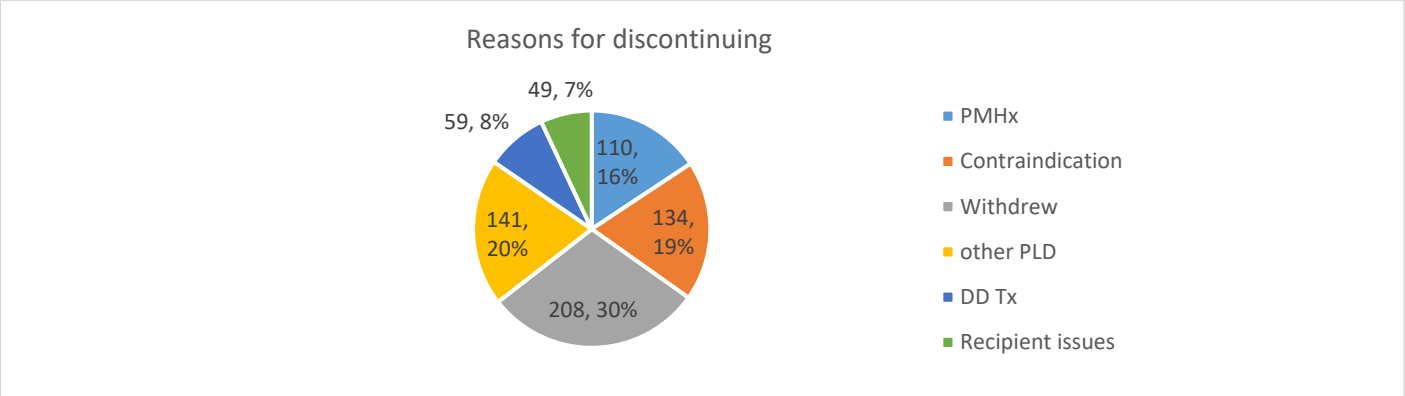
Living Donor Kidney Transplantation has long been recognised as the 'Gold Standard' renal replacement therapy for those patients deemed suitable. NHS Blood and Transplant published a UK strategy that set very clear goals to increase the number of LDKT's to 26pmp by 2020 matching world class performance in LDKT, with National Service Division (NSD) setting a local target of 60 donors per year. Despite numbers increasing each year in Scotland we have failed to achieve this target. This study aimed to identify common themes for donors not progressing to donation in the hope that these donors can be identified early to allow for streamlining of the assessment process and focusing resources on those that are likely to proceed.

Methods

A retrospective patient electronic record search was performed to identify all potential donors who had assessment for living kidney donation discontinued during a 3 year period from 1st of April 2017 to the 31st of March 2020. Potential donors lived within GGC catchment area or were referred to GGC from other UK health boards for assessment or completion of their assessment. The reason for discontinuation was identified and documented along with baseline demographics.

Results

During the 3 year period 945 donor referrals were received, 152 subjects proceeded to donation and 701 donors had their assessment discontinued. 54% of those donors were female. Age ranged from 17 to 84 years. 30% of donors withdrew or were lost to follow up. 20% did not continue as other potential donors were identified as more suitable to continue. 16% were ruled out on their past medical history. Contraindications were found in 19% and reassuringly only 7% of donors were ruled out as their renal function was below the threshold for donation.



Conclusions

This study highlights the volume of foot traffic through the Live Donor programme with 50% of donors withdrawing from the assessment process. It is reassuring that the Health Check questionnaire used to screen donors at the time of registration successfully identifies past medical history that precludes donation reducing the number of hospital appointments. Donors are provided with information, written or online, and are encouraged to read through this prior to their first appointment in the hope that they will be fully informed and committed to the process when they attend. It is difficult to identify the reasons people withdraw from assessment as they often miss appointments or are lost to follow up. However these donors create a substantial work load for a valuable and already over stretched clinical resource. We propose an early education of potential donors using remote resources to ensure they are fully aware of the process and time commitments required.

Online living donor transplantation learning resource for Renal Nurses and Allied Healthcare Professionals

Jen Lumsdaine[1], L White[2]
[1]Edinburgh Transplant Centre, Royal Infirmary of Edinburgh, UK [2] Organ Donation Policy Team, Scottish Government

Background
The aim over the next five years is to encourage all patients needing a kidney transplant to explore living donation as the default first option. This will require consistent messaging and support from all healthcare professionals caring for patients approaching end stage renal failure. With the evolving changes in living kidney donation it is important that all staff have access to up-to-date information and learning opportunity. We propose to develop a certificated online learning resource on the TURAS platform which all staff can access.

Method
With the support of the Scottish Renal Nurses Strategy Group we circulated a survey via Survey Monkey to ascertain the views of nurses and allied healthcare professionals (AHPs). We asked about current living donation discussion and perceived barriers; how beneficial a learning tool would be and views on content and time.

Results
We have received 171 responses to date, with 89% of the respondents often or sometimes asked about living kidney donation by their patients/clients. Over 70% often or sometimes raised the subject with their patients. Sixty percent did not feel their knowledge was sufficient and 76% felt an online learning resource would be beneficial or very beneficial with 21% stating it would be somewhat beneficial. The majority of respondents worked in dialysis units.

Conclusion
We viewed 171 responses as a positive rate and are very appreciative of the support of the renal community. Wide ranging suggestions were offered for subject matter to be included and this survey has confirmed the acceptability and enthusiasm for this type of resource. We shall now move forward with the development of the learning tool with the support and advice of the participants.

Junior Doctors' Attitudes to Fluid Prescribing in NHS Fife

Marcia McDougall: Fluid Lead, Emily Ridley: Specialist Nurse, Fluid Management

Background:
A programme in NHS Fife, aiming to improve intravenous (IV) fluid prescription and fluid balance charting, began in 2009 with audits examining fluid prescribing in the Queen Margaret Hospital, Dunfermline. It was led by a consultant anaesthetist, renal physician, ortho-geriatrician, general surgeon and pharmacist, who were joined in 2014 by the first Fluid Management Nurse in NHS Scotland. The group developed the NHS Fife Guidance for IV Fluid and Electrolyte Prescription in Adults in 2012 and a new combined fluid prescription and balance chart in 2014 which incorporates the main points of the guidance at the point of care. The guidance follows the NICE Guidelines for IV Fluid Therapy in Adults in Hospital (CG174). Education in the form of a 1 hour workshop for FY1s and an half hour induction talk for all other junior doctors occurs at each medical staff induction. Previous studies have recorded a lack of good teaching, and poor confidence and knowledge on this topic amongst junior doctors in the UK, most of whom are expected to prescribe fluids regularly.

Aims and Objectives
To assess whether education on fluids and the existence of prescribing guidelines is having an effect on the confidence of junior doctors in prescribing fluids; to explore practical issues in fluid prescribing and to find out how education may be improved.

Methods
A questionnaire about fluid prescribing was given to 19 junior doctors, all FY1s in medicine and surgery, at the midpoint of their FY1 year while working in NHS Fife. Free comments were encouraged on the questionnaire.

Results
18/19 doctors prescribe fluids daily and out of hours, up to ten times per day and up to a further ten times out of hours. 19 routinely check U&Es prior to prescribing fluids.
Barriers to carrying out fluid reviews were**:** Time was poor in day shifts, better at night: mentioned by 6 doctors. Fluid balance charts not filled in: 4. Bloods sometimes not done: 2. Not seen as good use of time by seniors, lack of support from senior doctors; often asked to prescribe off hand and not time to fully assess; large number of reviews at weekends means reduced quality.
'Are fluid issues handed over properly at night?' Agreed: 7, neutral: 6, disagreed: 5.
'The fluid charts in Fife provide me with the information I need to safely prescribe fluids': Agreed: 15, disagreed: 1. 'I am confident in calculating a patient's daily fluid and electrolyte requirements': 16 agreed 3 did not answer. 'Do you believe you have had adequate training in fluid prescribing?' Agreed:15 Neutral: 4

Other comments: Encourage ward rounds to consider next 24hrs of fluids, knowing electrolytes in advance of prescribing essential, no issues with current fluid chart, weight rarely on chart, good training and policy generally, not enough support for difficult groups – e.g. decompensated liver disease and AKI, cardiac failure, hyponatraemia, fluid balance charts variable, working in Fife has helped my confidence a lot.

Conclusion: Comments on the level of education and confidence by the FY1s are encouraging and a commitment to a thorough approach to prescribing was evident. However the lack of senior support, inadequate time given for prescribing in daytime shifts and a lack of attention to fluids in ward rounds are concerning; plans to address this include teaching at departmental meetings and encouragement to complete Learnpro training. Future teaching for juniors should include more complex cases.

Fluid prescribing and administration: are we following NHS Fife IV Fluid Guidance?

Emily Ridley Specialist Nurse for Fluid Management, NHS Fife

Background:
A programme in NHS Fife, aiming to improve intravenous (IV) fluid prescription and fluid balance charting, began in 2009 with audits examining fluid prescribing in the Queen Margaret Hospital, Dunfermline. It was led by a consultant anaesthetist, renal physician, ortho-geriatrician, general surgeon and pharmacist, who were joined in 2014 by the first Fluid Management Nurse in NHS Scotland. This is now a permanent post in Fife. The group developed the NHS Fife Guidance for IV Fluid and Electrolyte Prescription in Adults in 2012 and a new combined fluid prescription and balance chart in 2014 which incorporates the main points of the guidance at the point of care. The guidance follows the NICE Guidelines for IV Fluid Therapy in Adults in Hospital (CG174). The guidance led to a significant reduction in the use of 0.9% sodium chloride and associated acidosis, an overall reduction in fluid use, standardisation of fluids stocked within ward areas and a significant cost saving. The focus has been on patient safety, avoiding harm from poor fluid prescribing, and a change in culture around fluids with recognition of their importance in patient care. NHS Fife's changes are now being spread across NHS Scotland in the National IV Fluid Improvement Programme.

Aims and Objectives:
These were to establish if the NHS Fife IV Fluid Guidance is being followed by all prescribers, to identify any areas where improvements may be made and to provide evidence of progress to NHS Fife and to the national fluid programme.

Method

An audit tool was devised to capture detailed information on fluid prescribing: the reason for the prescription, prescribed rate in ml/hr or 'x hourly', fluid used, use of volumetric pumps, type of giving set used, use of hourly infusion monitoring charts, recording of weight on the prescription chart and whether giving sets were flushed after drug administration.
The data were collected over three separate days in August 2019 in the medical and surgical wards of the Victoria Hospital.

Results
A total of 78 infusions were in progress in the wards; 40 were drug infusions and 38 IV fluid infusions. 97% of prescriptions followed the guidelines for recommended fluid use and 92% had prescriptions in ml/hr as recommended (essential as both 500ml and 1000ml bags are now used).

Other findings were that there are too many different giving sets in use and that a guide is needed to ensure the correct set is used and available, with potential cost savings. There were two outdated versions of the infusion monitoring chart in use (since updated). Patient weight was not universally recorded and some drug infusions were not always adequately flushed through, resulting in under-dosing of antibiotics in some cases, one by almost half.

Summary
Intravenous fluids were overwhelmingly prescribed according to the guidance, suggesting that it is firmly embedded into practice in Fife. Continuing education aims to ensure that new prescribers are taught this approach and the national programme will gradually lead to a consistent approach to prescribing across Scotland, reducing variability and patient harm, caused by poor fluid management. Any fluid improvement programme must also address nursing practice with regard to fluid balance and administration, and look at practical issues around stock control and storage of IV fluids.