

A1. The prevalence and patterns of cardiovascular risk factors in European children receiving renal replacement therapy

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Background. Cardiovascular disease is a major cause of morbidity and mortality in paediatric patients with end stage renal disease. We aimed to describe the prevalence of hypertension, anaemia, dyslipidaemia, overweight/obesity, and underweight as key cardiovascular risk factors (CVRFs) and their combination in European children receiving renal replacement therapy (RRT).

Methods. To estimate prevalence of the CVRFs we included patients from the ESPN/ERA-EDTA Registry for whom at least one measurement of one CVRF was available. Dyslipidaemia was defined by the presence of hypertriglyceridaemia (triglycerides >1.13mmol/l) (0–9 years of age) or triglycerides >1.47 mmol/l (10–19 years of age) or low high density cholesterol (HDL) (<1.03 mmol/l) or high non-HDL cholesterol (>3.75 mmol/l). Hypertension was defined as systolic and/or diastolic blood pressure ≥95th percentile for sex, age, and height or prescription of antihypertensive medication. Anaemia was defined as haemoglobin < 10.5 or 11.0 g/dL for children younger than 2 and older than 2 years, respectively. Body mass index (BMI) was used to define underweight, overweight, and obesity. For 0–1 year old children BMI was categorized according to age- and sex specific criteria of the World Health Organization. BMI for children older than 2 years old was categorised based on cut-off values defined by the International Obesity Task Force. The prevalence of single CVRFs was calculated using weighted averages of repeated measurements. The prevalence of multiple CVRFs was estimated in patients who had at least one measurement of all CVRFs during the entire follow-up period.

Results. In total 7845 (65%) patients with one or more CVRF measurements out of 12140 patients in the Registry were included in the current study. Mean age was 9.5 (SE 0.06) years, 58.9% were boys, the most common cause of renal failure was congenital anomalies of kidney and urinary tract (40.8%), and 45.6% of children received one or more kidney transplants during follow-up. The overall prevalence of CVRFs in the study population was 84.9% for dyslipidaemia, 76.9% for hypertension, 34.8% for anaemia, 28.4% for overweight/obesity and 4.5% for underweight. Among the 1294 children with at least one measurement of all CVRFs only 0.7% did not have any risk factors and almost 80% had two or three CVRFs. The patterns of combinations of CVRFs are shown in Venn diagrams (Figure 1, 2).

Figure 1. Venn diagram of multiple risk factors (dyslipidaemia, hypertension, overweight/obesity and anaemia)

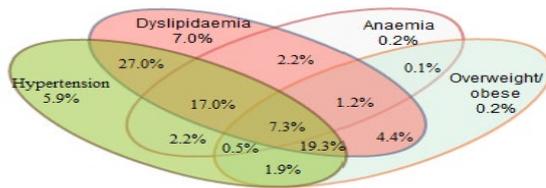
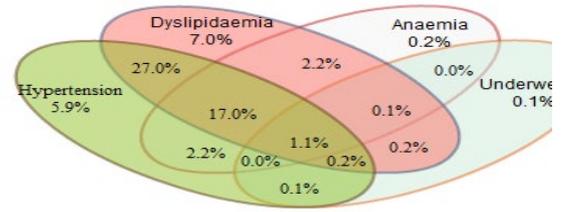


Figure 2. Venn diagram of multiple risk factors (dyslipidaemia, hypertension, underweight and anaemia)



Conclusion. Prevalence of dyslipidaemia and hypertension in European paediatric RRT patients was high. Dyslipidaemia and hypertension commonly exist in association with overweight/obesity and anaemia. **The source of funding of the work-** European Renal Association- European Dialysis and Transplant Association (ERA-EDTA) short- term fellowship. **Conflict of interest-**no

A2. Risk of major complications with percutaneous ultrasound-guided nephrologist-performed native renal biopsy

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Introduction and Aim: Bleeding is a well-recognised complication of percutaneous renal biopsy. Antiplatelet and anticoagulant therapies are commonly prescribed, and many centres discontinue these due to perceived higher risk (or greater severity) of post-procedure bleeding. This study was designed to examine the rate of complications after percutaneous renal biopsy where aspirin is not routinely discontinued.

Methods: Consecutive adult patients undergoing native renal biopsy in the Glasgow Renal and Transplant unit between 2000 and 2014 were included. Data relating to biopsy indication and complications were prospectively recorded using the electronic patient record. Biopsies were performed by more than 50 operators on the ward using real time USS guidance and 16G spring loaded Bard Max Core biopsy guns. To minimise the risk of bleeding the following pre-biopsy parameters are used as a guide: INR ≤ 1.3 ; platelets ≥ 100 and blood pressure controlled where possible. Bleeding times are not checked and DDAVP is not administered. Aspirin is routinely continued but clopidogrel and warfarin stopped. Data were extracted electronically from the Electronic Renal Patient Record (SERPR) for biopsy indication, pre-biopsy haemoglobin, platelet count, prothrombin time, estimated glomerular filtration rate, serum creatinine, urinary protein creatinine ratio, use of antiplatelets or anticoagulants and diagnosis. Major complications post biopsy were need for blood transfusion, surgical or radiological intervention, or death. Binary logistic regression analysis was used to assess factors associated with increased risk of major complication. Analyses were carried out using SPSS software (version 22).

Results: 2619 patients underwent renal biopsy (1536 elective, 1083 emergency). 57.3% were male, average age 57 (SD 17) years. 508 were conducted as day case procedures. The overall major complication rate was 2.1%. 47 patients required transfusion (1.8%), 10 patients underwent embolisation (0.4%), no patients required nephrectomy and 3 patients died post biopsy. Major complications were more common in those undergoing emergency compared with elective renal biopsy (3.4% versus 1.2% respectively, $p < 0.001$). Aspirin was being taken at time of biopsy in 342 of 1564 patients with no significant increased risk of bleeding ($p = 0.93$). Pre-biopsy platelet count, PT and blood pressure were not associated with risk of bleeding. Increased age and decreased estimated glomerular filtration rate were associated with increased risk of major complication (HR 1.025 (1.007–1.043), $p = 0.006$; 1.034 (1.05-1.018), $p < 0.001$ respectively). Complications were more common in patients diagnosed with vasculitis but numbers were small.

Conclusions: The risk of major bleeding following native renal biopsy in the modern era is low. Few modern 'real world' case series are available for comparison. Biopsies in our centre are largely done by nephrology trainees under supervision, without stopping aspirin and commonly in a day case setting.

A3. Hip fracture in chronic kidney disease: incidence and mortality

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Introduction: Chronic kidney disease (CKD) has many complications. For those on renal replacement therapy (RRT) there is an increase in the risk of fracture. The evidence regarding those with less advanced CKD is not so clear.

Aim: To understand the association between CKD and (i) hip-fracture related admissions; and (ii) mortality after hip-fracture.

Methods: The Grampian Laboratory Outcomes Mortality and Morbidity Study (GLOMMS-II) cohort was used, in particular, ~20,000 Grampian residents in 2003 who had evidence of CKD and ~20,000 with normal eGFR. Data-linkage to hospital episode data and National Records of Scotland allowed ascertainment of comorbidities, hip fracture and mortality events up until 2009. The incidence of hip fracture in those with CKD and those with normal eGFR in 2003 was calculated and the incidence rate ratios (IRR), unadjusted and adjusted for potential confounders. To estimate the risk of hip fracture attributable to CKD, the population attributable risk (PAR) and fraction (PAF) were calculated. To investigate whether mortality after a hip fracture differed between those with CKD and normal eGFR, the mortality rates in those who had suffered a hip fracture was calculated and the mortality rate ratio (MRR) calculated (unadjusted and adjusted).

Results: There were 19,537 persons with CKD in 2003 and a 19,748 sample with normal eGFR, the incidence of hip fracture was 10.01 and 1.45 per 1000 patient-years (py) respectively. Unadjusted IRRs for stage 3a, 3b, 4 and 5 were 5.61, 9.74, 10.96 and 2.27 [6.90 (CI 5.83, 8.15) overall for stage 3-5 CKD]. When adjusted for age and sex the overall IRR for stage 3-5 CKD was 1.56 (CI 1.31, 1.86). In the population of Grampian as a whole in 2003 49% of fractures (18% after adjusting for confounders) could be attributed to CKD. From the time of fracture the mortality rates in those with CKD and normal eGFR were 488.04 and 308.86 per 1000py respectively. The unadjusted MRRs for those with stage 3a, 3b, 4 and 5 CKD were 1.36, 1.75, 2.87 and 2.47 [1.58 (CI 1.26, 1.98) overall for stage 3-5 CKD]. When adjusted for age and sex, the overall MRR for stage 3-5 CKD was 1.11 (CI 0.88, 1.41).

Conclusion: Amongst those with CKD there is a higher rate of hip fracture than in those without, this represents a significant proportion of those who suffer hip fractures within the region, even adjusting for confounders. Although the mortality rates after a fracture are not significantly different between those with CKD and those with a normal eGFR, reducing the incidence of fractures would reduce the number of fracture related deaths in CKD. Prospective management of future fracture risk in those with CKD is warranted.

Source of funding: The analysis for this work was done with funding from NHS Grampian Endowments fund (14/30), however the set-up the cohort was funded by a CSO grant (CZH/4/656).

Conflict of Interests statement: None of the authors have any conflicting interests.

A4. Women and Chronic Kidney Disease: Exploring gender differences in prevalence and outcomes

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Introduction: Much current literature reports a higher prevalence of chronic kidney disease (CKD) amongst women than men. Amongst patients that initiate renal replacement therapy (RRT) there is a preponderance of men. The reasons for this gender discrepancy are poorly reported.

Aim: To investigate gender differences in CKD prevalence and outcomes in a large Grampian cohort, focussing specifically on RRT initiation.

Methods: All creatinine values measured in the Grampian region from mid-1999 to 2009 were available. All individuals who had an eGFR of less than 60ml/min/1.73m² in 2003 that could be demonstrated to be present for at least three months were defined to have CKD in 2003. These individuals' records (as part of the Grampian Laboratory Morbidity and Mortality Study II (GLOMMS-II)) were linked to hospital episode data (SMR01), local and national renal registry data and the National Records for comorbidity, RRT and mortality information.

The prevalence of stage 3-5 CKD in Grampian in 2003 was calculated. Univariate analysis identified potential confounding factors between men and women with stage 3-5 CKD and those who did and did not initiate RRT during six years of follow-up. The rate of RRT initiation by gender was calculated. Gender rate ratios were calculated using poisson regression, adjusting for age, CKD stage, proteinuria and significant co-morbidities. Gender rate ratios were also stratified by age.

Results: There were 19635 individuals who had stage 3-5 CKD in Grampian in 2003 (64.9% women). Grampian women in 2003 had a higher prevalence of CKD than men, at 5.7% (95%CI 5.6, 5.8) vs 3.2% (95%CI 3.1, 3.3). Men with CKD had a 3.4-fold (95%CI 2.6, 4.4) increase in RRT initiation compared to women. This relationship between gender and RRT initiation persisted, after adjustment for potential confounders. However, gender rate ratios stratified by age showed age to be an important effect modifier – the highest gender rate ratio was seen in those aged 75+ years, where men had a 5.13-fold (95%CI 2.8, 9.5) increase in RRT initiation rate compared to women. The lower rates of women initiating RRT is unlikely to be due to death coming before RRT initiation since although 64.9% of the cohort at baseline were women, at the end of follow-up 67.0% of those still alive and not on RRT were women.

Conclusion: In Grampian, women had a higher prevalence of CKD than men. However, men with CKD initiated RRT at a faster rate than women. This imbalance was not explained by available confounders including, CKD stage comorbidity or baseline level of renal function but effect modification by age was shown to be important. Future research is required to investigate other explanations for this effect not explored here, including differences in interaction with health care.

Source of funding: The analysis for this work was done as part of a BMedSci intercalated degree, however a CSO grant (CZH/4/656) funded cohort set-up.

Conflict of Interests statement: None of the authors have any conflicting interests.

A5. Rituximab is non-inferior to cyclophosphamide for the treatment of ANCA-associated vasculitis and achieves good clinical outcomes in older patients

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Background

Cyclophosphamide (CYC) and glucocorticoids is the standard treatment for induction of remission in antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV). This treatment is associated with increased risk of infection, particularly in the elderly. Recent studies have shown that rituximab (RTX, a B cell depleting monoclonal antibody) has equivalent efficacy for remission induction. We performed a retrospective analysis of clinical outcomes in a cohort of AAV patients who received rituximab for remission induction and compared this to the contemporaneous cohort receiving conventional cyclophosphamide induction.

Methods

We performed a retrospective analysis of all patients treated for AAV in the vasculitis service over the 5-year period between January 2010 and January 2015. We recorded demographic data, co-morbidities, organ involvement and laboratory results at diagnosis for each patient. The time taken for induction of remission and the relapse-free survival were analysed by the Kaplan-Meier method with logrank test. Remission was defined as the absence of symptoms of disease activity and maintenance prednisolone dose ≤ 10 mg per day. Relapse included major and minor relapse, and was defined as disease recurrence requiring restarting immunosuppressive treatment. Numbers of adverse events in the year following treatment were recorded.

Results

83 patients were treated for AAV in the study period. 51 patients were treated with IV pulsed cyclophosphamide (10-15 mg/Kg x 6 over 3 months) and 16 with rituximab (1 g x 2 over 2 weeks). 16 patients were treated with alternative agents and were not included in the analysis. The patients in the rituximab group were significantly older than those in the cyclophosphamide group (median age RTX 74 and CYC 59 years old). The co-morbidities in the two groups were similar. At 90 days, 44 % patients in the RTX group and 39 % in the CYC group had entered remission; at 180 days remission was achieved in 69 % (RTX) and 88 % (CYC). The time taken to achieve disease remission did not differ significantly between the two groups ($p > 0.05$ by logrank test). Patients with serum antibodies to proteinase 3 (PR3) took longer to enter remission with rituximab than with cyclophosphamide. This difference was not observed in patients with serum antibodies to myeloperoxidase (MPO). 2 years after entering remission, 13 % in the RTX group and 16 % in the CYC group had experienced a disease relapse. There was no significant difference between groups in the time to first relapse ($p > 0.05$ by logrank test). In the first year of treatment patients in the RTX group were more likely to have a major infection, although this didn't reach statistical significance (25 % patients in RTX group, 8 % in CYC; $p = 0.085$ by Fisher's exact test).

Conclusions

Rituximab use was favoured in the elderly. It was non-inferior for the induction of remission and duration of relapse-free survival compared to a younger cohort treated with IV CYC. The perceived lower adverse event profile and less frequent hospital attendance with rituximab influenced its use in older patients. Despite this, there was a slightly higher rate of serious infections in the rituximab group. Thus, rituximab has equivalent efficacy to cyclophosphamide in AAV in a non-trial clinical setting.

No funding or conflict of interest to declare

A6. Routine anticoagulation in primary nephrotic syndrome – is the risk of venous thromboembolism high enough to justify it?

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Introduction: Venous thromboembolism [VTE] has been reported to occur in 25-30% of adult patients with nephrotic syndrome (NS). The risk appears highest in patients with membranous nephropathy and those with a serum albumin below 20g/l. This has led some to suggest prophylactic anticoagulation, which comes with an associated bleeding risk. We aimed to assess whether this reported incidence of VTE is applicable to our population.

Methods: All adult patients undergoing native renal biopsy for NS between 2008 and 2013 in the Glasgow Renal & Transplant Unit were identified. This unit serves a population of 1.5 million. Baseline serum albumin, proteinuria, eGFR and histological diagnosis were recorded. Using the prospectively completed electronic patient record, which includes all radiological reports and clinical correspondence, incidence of VTE at any site was determined. Patients were not prospectively screened for VTE but investigated on the basis of clinical suspicion. Follow-up and time to first remission (2 consecutive uPCR <300mg/mmol and serum albumin >30g/L) were calculated.

Results: 291 patients underwent first renal biopsy for NS during the 6 year period. In 85 patients, NS was secondary to systemic disease (diabetes, lupus or amyloidosis) and these patients were excluded from further analyses. Of the remaining 206 patients, 59.7% were male, mean age at biopsy was 55 years (SD 19), mean eGFR 72ml/min/1.73m² (SD 40), median uPCR 812 mmol/mol (IQR 535-1200) and mean serum albumin 19.1 g/l (SD 7.1). Histological diagnoses were membranous nephropathy (MN) (39%, n=80), focal segmental glomerulosclerosis (FSGS) (18%, n=37), minimal change nephropathy (MCN) (25%, n=53), IgA nephropathy (IgAN) (11%, n=22) and mesangiocapillary GN or post-infectious (MCGN) (7%, n=14). Median follow-up was 3.1 years (IQR 1.8-4.7). Fifteen (7.2%) patients suffered a VTE (8 MGN, 1 IgAN, 1 FSGS, 5 MCN). Mean age was 55 years and a third were male. The site of VTE was pulmonary (n=9), leg deep vein (n=2), renal vein (n=2) and other (n=2). Median time to diagnosis of VTE from renal biopsy was 24 days (IQR -22 to 195). Excluding VTE pre-biopsy (n=7), median time to VTE was 177 days. There was no significant difference in the mean age (p=0.9), serum albumin at diagnosis (p=0.5) or median uPCR (p=0.9) between those who suffered a VTE and those who did not. 149 patients entered remission during follow-up and overall median duration of nephrosis was 2.03 years. 506 patient years of nephrosis post-biopsy were observed, during which time there were 8 VTEs, which routine anticoagulation may have prevented, resulting in a 1.6% risk per year of nephrosis.

Conclusions: In this cohort, the incidence of VTE at 7.2% is lower than quoted in the literature. The risk appears highest early in the course of nephrotic syndrome, is higher in MGN and MCN, but does not appear to be associated with the severity of nephrotic syndrome. Overall post-biopsy VTE risk is low at 1.6% per year, suggesting that routine anticoagulation of nephrotic patients may not be justified.

Conflicts of interest: none.

Funding: none

A7. DARE-AKI: Does enhanced Detection, clinical Analytics, Referral and Early therapy improve AKI outcomes in secondary care?

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Acute Kidney Injury AKI occurs in up to 15% of hospital admissionsⁱ, and is associated with an increased risk of deathⁱ: some 40,000 excess deaths/year in England are attributed to AKIⁱⁱ. It is also associated with an increased length of stayⁱⁱ, and the development of chronic kidney diseaseⁱⁱⁱ. This is expensive- one recent economic analysis estimated the associated healthcare costs for England to be over £1bn/yearⁱⁱ. Whilst poor outcomes relate in part to patients' underlying disease states, much of this impact appears causally attributable to AKI itself^{iv}. It may be possible to halt its progression and prevent its clinical sequelae with timely and appropriate intervention^v. Recent drives to reduce 'avoidable harm' in hospitals are underpinned by both early identification of deteriorating patients, and rapid and appropriate intervention. Despite this, the 2009 NCEPOD enquiry reported delays in the recognition of AKI to be commonplace, and care of patients with established AKI to be "good" less than half of the time.

The potential for reduction of patient morbidity, mortality and healthcare costs are thus clear. AKI is a priority workstream in the "reduction of avoidable harm" and "patient safety" domains of the NHS Outcomes Framework, and has been identified as an area of focus for reducing avoidable mortality in the NHS "Five Year Forward View"^{vi}. NHS England have produced an algorithm for the identification and stratification of AKI, mandating that it be incorporated into all hospital Laboratory Information Management Systems by Spring 2015^{vii}. However, this is likely to have minimal impact in its current form; a recent RCT testing the efficacy of simple e-alerting for AKI resulted in no significant differences in patient's peak creatinine, requirement for dialysis or risk of death^{viii}. Specific understanding of organizational management and behaviour change will be required^{ix}.

We have used this algorithm to create a cloud-based AKI detection platform which will detect cases of AKI within milliseconds of creatinine being assayed. This novel platform also uses all other electronically-available information to produce a patient-specific, data-rich report, with a strong emphasis on decision support. This report is automatically sent via secure mobile device to a designated response team, comprised of critical care outreach nurses. Cases in which specialist input is required (e.g. AKI3 or blood tests suggestive of parenchymal kidney disease) are identified and flagged to the on-call nephrology team, automating the referral process for much of the caseload. The report will be used to drive a timely protocol-driven intervention, the individual strands of which map to the principle causes of AKI. Process measures will be gathered and recorded at the bedside.

We believe that this combination of enhanced detection, analytics, automated referral and early therapy will improve outcomes for patients developing AKI in hospital. Feasibility work is now underway; a full pilot study at The Royal Free London NHS trust will then run, data from which will be used in the design of a larger stepped-wedge multi-centre trial. To this end, we have 8 other hospitals in London interested in taking part and providing baseline data, and have formed a collaboration with the local CTU.

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A8. The “Sepsis Six” Bundle of Care May Reduce the Incidence of Severe Acute Kidney Injury in Hospital

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The “Sepsis Six” care bundle uses fixed physiological cutoffs to identify patients at risk of severe sepsis. This bundle specifies six mandatory interventions to be performed within one hour of triggering, and is associated with reduced risk of death. We investigated whether full care bundle compliance was associated with a reduced incidence of Acute Kidney Injury (AKI) at a single NHS Trust.

Retrospective data was collected for 415 consecutive patients triggering for Sepsis Six at The Royal Free Hospital over the course of two and a half years. Primary outcome was presence of AKI (using KDIGO criteria) as defined by peak creatinine in the 10-day period following this trigger. Patients were grouped according to whether they received complete implementation of the sepsis care bundle or not.

Corrective for relevant baseline data, relative risk ratios (RRR) for developing each stage of AKI (versus no AKI) was calculated for patients with complete care bundle implementation: AKI 1 RRR=0.95 (95% CI 0.50-1.79, p=0.87); AKI 2 RRR=1.78 (95%CI 0.87-3.66, p=0.12); AKI 3 RRR=0.28 (95%CI 0.13-0.61, p=0.001).

Sepsis Six triggers identified a cohort with a high incidence of AKI (32%). Full care bundle compliance was associated with a statistically significant reduction in the risk of AKI 3. A non-significant rise in the incidence of AKI 2 suggests potentially severe renal injury may have been converted to moderate injury by complete bundle compliance. These data support the hypothesis that a simple, protocolised intervention, performed early in the course of sepsis, could protect against severe AKI.

No conflict of interest is declared.