

# ABSTRACT OF SOCIETIES

## Scottish Cardiac Society

Annual Meeting of the Scottish Cardiac Society, held in Turnberry Hotel in November 2005

### Measurement and Treatment of Lipids in the over 80s with Coronary Heart Disease (CHD)

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Quality markers for CHD in the new General Medical Services contract (nGMS) include the recommendation that 90% of patients should have cholesterol measured and that 60% should have serum cholesterol less than 5 mmol/l. The very elderly are not automatically excluded from this recommendation. Against this background we conducted a survey of the impact of the nGMS on the measurement of lipids and prescription of statins in octogenarians with CHD in south west Scotland. All 119 GPs currently in post responded to our questionnaire, the results of which are shown in the table.

Most of those who said they were more likely to measure cholesterol in this age group were also more likely to prescribe statins. One practice with a list size of 3750, 214 (5.7%) patients aged 80 and over, 63 (29.4%) of whom had CHD

More likely to measure cholesterol*	77 (65%)
Less likely to measure cholesterol*	2 (1%)
About as likely to measure cholesterol*	40 (34%)
More likely to treat with statins*	71 (60%)
Less likely to treat with statins*	2 (1%)
About as likely to treat with statins*	46 (39%)
*as a result of nGMS	

(G3 Reid code) reported an increase in cholesterol measurement from 49.2% to 90.5% and in statin prescription from 33.8% to 61.9% in this age group.

Our results suggest that the nGMS contract has had a profound influence on the measurement of lipids and prescribing of statins in the over 80s, a group for whom the evidence of benefit is limited.

### 11 $\beta$ HSD1 -/- Mice Have Enhanced Angiogenic Response and Improved Myocardial Function Following Coronary Artery Ligation

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**Introduction:** Glucocorticoids affect cardiovascular disease by influencing systemic risk factors, inhibiting inflammation in the vessel wall, and inhibiting angiogenesis. We have shown that regeneration of active glucocorticoids from 11-keto metabolites by 11 $\beta$ -hydroxysteroid dehydrogenase type 1 (11HSD1) in the mouse arterial wall inhibits angiogenesis both in vitro and in vivo. Here we explore the influence of glucocorticoid regeneration on myocardial angiogenesis following infarction. **Hypothesis:** Generation of active glucocorticoids by 11HSD 1 in the heart inhibits the angiogenic response to ischaemia and thus influences the severity of myocardial infarction. **Methods:** Ligation of the anterior descending coronary artery or sham surgery was performed in male C57Bl6 wild type control and 11HSD1 -/- knockout mice. Seven days following ligation, cardiac function was measured by echocardiography. Transverse sections of hearts were stained with an anti-von Willebrand factor antibody and vessels counted. **Results:** Seven days following ligation, vessel density was greater in infarcted myocardium from 11HSD1 -/- (116.4  $\pm$  8.0 vessels/mm<sup>2</sup>, n=10) than in wild-type (79.74  $\pm$  1.3 vessels/mm<sup>2</sup>; n=11; p<0.001) or in sham operated mice (35.33  $\pm$  0.9 vessels/mm<sup>2</sup>; n=6). Left ventricular ejection fraction (sham 58.24  $\pm$  3%; n=7) was preserved in 11HSD1 -/- (38.1  $\pm$  3%, n=10) compared with controls (27.9  $\pm$  3 %, n=9; p<0.01). **Conclusions** These findings confirm the role of 11HSD1 in attenuating the angiogenic response to ischaemia. Enhanced collateral reperfusion in 11HSD1 -/- mice may explain their improved cardiac function following coronary artery ligation. These data raise the possibility that 11HSD1 inhibition in vessels and heart might enhance cardiac function after myocardial infarction.

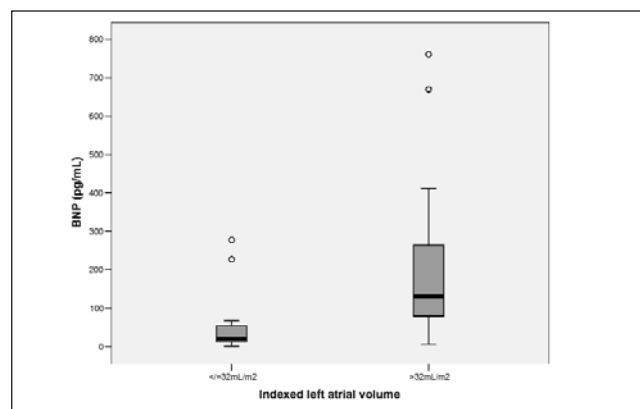
### Left Atrial Volume is the Best Echocardiographic Correlate of BNP in Patients with Chronic Heart Failure

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**Introduction** B-type natriuretic peptide (BNP) is released from ventricular myocardium in response to myocyte stretch. Elevated levels are correlated with raised pulmonary capillary wedge pressure (PCWP) and independently predict outcome in patients with heart failure. A number of echocardiographic markers of elevated left ventricular (LV) filling pressure have also been identified. The ratio of early transmitral flow velocity to early mitral annulus velocity (E/e') is the best echocardiographic correlate of PCWP. Likewise, left atrial volume indexed to body surface area (LAVi) appears to be an indicator of chronic LV filling pressures. The current study assessed the relationship between BNP and echocardiographic indices of LV filling. **Methods** Sixty-three patients with stable chronic heart failure in sinus rhythm underwent echocardiography with detailed assessment of systolic and diastolic function. BNP collected at the time of echocardiography was measured using the Bayer ADVIA Centaur immunoassay. Assessment of systolic function included determination of cardiac index, wall motion score index and ejection fraction using Simpson's biplane method. Diastolic function parameters included transmitral flow velocities, mitral deceleration time, LAVi by the area-length method and E/e' ratio. **Results** The best echocardiographic correlate of BNP was LAVi, r=0.68, p<0.001; table. Patients with LAVi >32mL/m<sup>2</sup> (>2 SD above normal) had a

	LVEF	WMSI	Cardiac index	LAVi	E/e' (lateral)	E/e' (septal)	Mitral DT
BNP r	-0.31	0.35	-0.05	0.68	0.30	0.41	-0.06
P	0.02	0.02	0.72	<0.001	0.02	0.001	0.66



mean BNP of 192pg/mL ( $\pm$ 166) vs 49pg/mL ( $\pm$ 72) in patients with LAVi <=32mL/m<sup>2</sup>, p<0.001; figure [median and quartiles]. **Conclusion** LAVi is the best echocardiographic correlate of BNP in patients with stable chronic heart failure. In this setting, BNP is rarely elevated in patients with normal LAVi.

### Invasive Management in Acute Coronary Syndrome (ACS): Why Might Women Benefit Less Than Men?

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**Background** Recent trials have demonstrated that interventional management reduces the risk of recurrent ischaemia in men with an acute coronary syndrome (ACS). The benefit of this approach in women is less certain. We studied whether prognostically-important gender differences in ACS patients might in part explain the different outcomes in men (M) and women (W). **Methods** All patients with a suspected ACS referred for catheter laboratory management (31-07-03 to 30-07-04) were studied. **Results** Of 1558 ACS admissions, 455 (29%) underwent invasive management. ST-elevation myocardial infarction (MI), non-ST elevation MI or unstable angina occurred in 74 (17%), 193 (46%) and 188 (41%) patients, respectively. Their outcomes were: 48% medical therapy, 38% PCI, 14% CABG, 1% PCI+CABG. W (n=147, 32%) were older than M (mean (SD) age (yrs): 64(12) vs. 59(12); P<0.00001). 75 (51%) W and

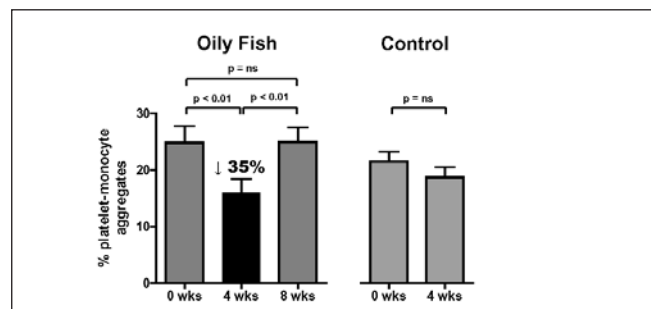
95 (31%) M were 365 years ( $P < 0.0001$ ). Fewer W had previous coronary revascularisation (15 (10%) vs. 62 (20%);  $P = 0.006$ ). Mean (SD) GFR (mL/min/1.73m<sup>2</sup>) was lower in W than in M (60 (17) vs. (70 (18);  $P < 0.00001$ ). Anaemia on admission tended to be more common in W ( $< 12$  g/dL; n(%): 53 (37)) than in M (Hb  $< 13$  g/dL; 94 (31%);  $P = 0.1$ ). The proportions of W and M who were troponin positive (60%), or who were low (33% both), intermediate (44 vs. 47%), or high (23 vs. 19%) risk, according to the TIMI-NSTEMI score, were similar ( $P = 0.6$ ). Secondary prevention therapy use was also similar. 25% of W and 14% of M had minor disease  $< 50\%$ . Obstructive disease (coronary stenosis  $\geq 75\%$ ) occurred less often in W than in M (single vessel: 31 vs. 37%; double vessel: 16 vs. 25%; triple vessel: 18 vs. 18%;  $P = 0.002$ ). PCI or CABG occurred in 171 (n=50 (30%) W) and 65 (n=20 (30%) patients, respectively. A similar proportion of W and M underwent PCI (35 vs. 40%;  $P = 0.3$ ) or CABG (14% both). The target vessel diameter was similar in W (3.04 [0.38] mm) and in M (3.11 [0.44] mm) who underwent PCI ( $P = 0.2$ ). Multivessel PCI was less common in W (18% vs. 32%;  $P = 0.07$ ). Admission duration (days) tended to be longer in W compared to in M (11 (13) vs. 9 (11);  $P = 0.09$ ). Of those who died in hospital (n=9), 6 (67%) were W ( $P = 0.033$ ). Female gender did not predict admission duration or in-hospital mortality after correction for age, renal function and revascularisation history.

**Conclusions** Some adverse prognostic attributes were more common in W (increased age and renal dysfunction). Coronary artery disease was less severe and multivessel PCI less common in W. The influence of gender on outcome can be partly explained by gender-related differences in prognostically important attributes.

### Dietary Supplementation With Oily Fish Reduces Platelet-Monocyte Aggregation

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**Objective** High dietary intake of oily fish is associated with a reduction in cardiovascular events. The mechanisms for this are uncertain. Platelet-leukocyte aggregates (PMA) are sensitive markers of platelet activation and may contribute to the initiation and progression of atherothrombosis. This study assessed the effect of dietary supplementation with oily fish on PMA. **Methods** Fourteen healthy male volunteers had their diet supplemented with 500g smoked mackerel a week (equivalent to 1.5g of EPA+DHA per day) for 4 weeks. A control group of 14 healthy males received no dietary intervention over a 4 week period. Peripheral venous blood sampling was performed before and after dietary supplementation with oily fish as well as 4 weeks following cessation of fish supplementation. PMA was assessed by 2-colour flow cytometry. **Results** PMA was reduced by 35% following dietary supplementation with oily fish ( $24.8 \pm 2.9\%$  vs.  $16.0 \pm 2.4\%$ ,  $p < 0.01$ ). PMA had returned to previous levels four weeks after discontinuation of supplementation ( $24.8 \pm 2.9\%$  vs.  $23.6 \pm 2.9\%$ ,  $p = ns$ ). There was no significant change in PMA over 4 weeks in the control group ( $21.5 \pm 1.8\%$  vs.  $18.7 \pm 1.8\%$ ,  $p = ns$ ). **Conclusion** Dietary supplementation with fish rich in omega-3 fatty acids reduces PMA, an effect that is fully reversed 4 weeks following cessation of supplementation. This may represent an important and previously unreported mechanism by which intake of oily fish reduces cardiovascular events.

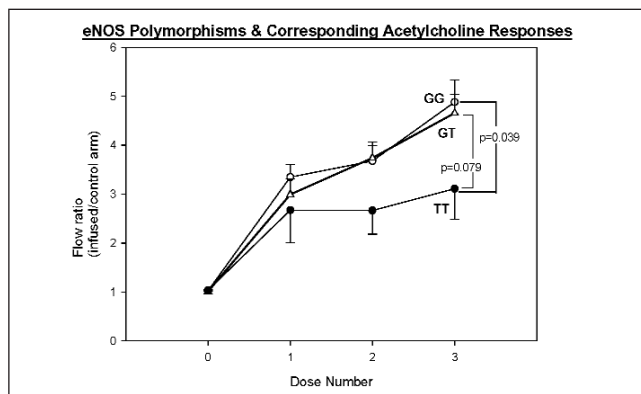


### Glu298Asp Polymorphism of the eNOS Gene is Associated with a Blunted Response in Endothelial Dependent Vasodilatation in Healthy Subjects

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**Aims and Background** The Glu298Asp polymorphism of the endothelial nitric oxide synthase (eNOS) gene has been linked to coronary artery disease, hypertension and acute myocardial infarction. However, the functional consequences of this polymorphism have not been fully defined. Therefore, our aim was to investigate if the Glu298Asp polymorphism of the eNOS gene is functionally relevant in healthy humans by having an effect on endothelial-dependent vasodilatation. **Methods** Endothelial function was assessed in 68 normal volunteers (aged 18-44y) by bilateral forearm venous occlusion plethysmography with intra-arterial infusions of increasing doses of acetylcholine for endothelial dependent vasodilatation (25, 50 and 100 nmol/mL), sodium nitroprusside (4.2, 12.6, 37.8nmol/mL) and verapamil (10, 20, 40 nmol/mL) for endothelial independent vasodilatation. Blood was collected at the screening visit for genotyping. The genotype of the Glu298Asp polymorphism of the eNOS gene was determined from genomic DNA by Polymerase Chain Reaction and *BanII* digestion. **Results** There were 3 different genotypes: Homozygous for the Glu298 variant (GG), homozygous



for the Asp298 variant (TT) and heterozygous (GT). The TT genotype's vasodilatory response to the endothelial-dependent vasodilator acetylcholine was lower than the GG variant ( $p = 0.039$ ) and GT variant ( $p = 0.079$ ) (Fig). No differences were found between the GG and GT groups ( $p = 1.000$ ). There was also no effect of eNOS genotype on the response to the endothelial-independent vasodilators sodium nitroprusside or verapamil. **Conclusions** The Asp298 variant of the eNOS gene is associated with a blunted endothelial-dependent vasodilatation in healthy subjects. These findings may provide an important insight into the pathophysiology of endothelial dysfunction in cardiovascular diseases.

### Reversal of Endothelial Dysfunction in Healthy Offspring of Parents with Type 2 Diabetes Mellitus

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**Background** Endothelial function is impaired in healthy subjects at risk of type 2 diabetes mellitus (DM) by virtue of having one or both parents with type 2 DM. Whether endothelial dysfunction can be normalised by statin therapy in this potentially pre-disposed population is unknown. **Methods** We investigated flow-mediated dilation (FMD; endothelium-dependent) and nitroglycerin-induced dilation (endothelium-independent) in 56 (26 men and 30 women, mean age  $26 \pm 4$  years) normotensive first-degree relatives (FDRs) of type 2 DM patients with normal glucose tolerance and in 20 age-, sex- and body-mass index (BMI)-matched control subjects with no family history of DM. Other measurements included insulin resistance index using homeostatic model assessment (HOMA IR), plasma lipids and plasma markers of inflammation. The FDRs were then randomised and treated with atorvastatin (80 mg) or placebo daily in a 4-week prospective randomised, double-blind, placebo

controlled clinical trial. **Results** FMD was significantly impaired in FDRs ( $4.4 \pm 8.1\%$  vs  $13.0 \pm 4.2\%$ ;  $P < 0.001$ ). Compared to controls, FDRs had higher HOMA IR ( $1.72 \pm 1.45$  vs  $1.25 \pm 0.43$ ;  $P = 0.002$ ) and higher levels of plasma markers of inflammation (highly sensitive C-reactive protein (hsCRP),  $2.6 \pm 3.8$  mg/L vs  $0.7 \pm 1.0$  mg/L;  $P = 0.06$ ; interleukin (IL)-6,  $0.07 \pm 0.13$  ng/ml vs  $0.03 \pm 0.01$  ng/ml;  $P < 0.001$ , and soluble intercellular adhesion molecule (sICAM)-1,  $267.7 \pm 30.7$  ng/ml vs  $238.2 \pm 20.4$  ng/ml;  $P < 0.001$ ). FMD improved in the atorvastatin treated subjects when compared to the placebo treated subjects (atorvastatin, from  $3.7 \pm 8.5\%$  to  $9.8 \pm 7.3\%$ ; placebo, from  $3.9 \pm 5.6\%$  to  $4.7 \pm 4.2\%$ ;  $P = 0.001$ ). No changes were observed in nitroglycerin-induced dilation in either group. In the atorvastatin treated subjects, there were reductions in the levels of IL-6 ( $0.08 \pm 0.02$  ng/ml vs  $0.04 \pm 0.01$  ng/ml;  $P < 0.001$ ) and hsCRP ( $3.0 \pm 3.9$  mg/L vs  $1.0 \pm 1.3$  mg/L;  $P = 0.006$ ). **Conclusion** In healthy offspring of patients with type 2 DM, treatment with atorvastatin markedly improved endothelial function and decreased plasma levels of inflammatory markers.

### Intervention in Acute Coronary Syndrome in Scotland 2002-4; Impact on Readmission and Mortality

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Hospital admissions > 500 angina /AMI 2002-2004 Facility	% PCI/CABG	% re-admitted for PCI/CABG	Total
Angiography + PCI	16.6	5.2	21.8
Angiography only	5.5	5.8	11.3
No Angiography facility	6.5	6.3	12.8
Hospital admissions > 500 angina /AMI 2002-2004 Facility	Emergency admission at 1 month %	Death at 1 month %	Death at 1 year %
Angiography + PCI	3.2	7	15.6
Angiography only	4.9	8	17.5
No Angiography facility	4.0	8.5	17.0

The management of acute coronary syndrome is evolving from primarily medical management, with intervention based on on-going symptoms, to that of more active intervention with almost routine angiography and intervention. While certain clinical trials support this strategy, data from registries do not. Scotland has a well developed and validated ability to track admissions and outcomes. We used data provided by the Information and Statistics Division of the Scottish Health Service to look at outcomes for patients discharged with a diagnosis of angina/acute myocardial infarction for the period 2002-4 from all Scottish Hospitals. The main analysis was restricted to those hospitals with more than 500 such discharges. There were 14221 admissions to hospitals equipped to do angiography and intervention, 8549 to angiography only and 21047 to the remainder "transfer hospitals". The % undergoing angiography on the index admission was 19.5, 7.2 and 7.5 respectively; a subsequent 9, 11 and 13% were readmitted for angiography. The median time to intervention (PCI/CABG)-ranged from 2-7, 14-38 and 10-60 days respectively. Summary, unadjusted mortality showed a 1.5% significant absolute 30 day mortality benefit for patients treated in hospital with angiography facilities and scope for acute intervention. Late mortality showed this benefit to be maintained but not improved on. One year mortality suggests that higher intervention rates in this unselected population results in only modest benefit.

### Radial Versus Femoral Arterial Access for Coronary Angiography and Percutaneous Coronary Intervention

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**Background** Coronary angiography and percutaneous coronary intervention performed via the femoral artery are associated with access site complication rates of 6 - 11%. There is growing evidence that coronary angiography and percutaneous coronary intervention performed via the radial artery are associated with similar rates of success, a lower incidence of access site complications and shorter in-hospital stay. **Methods** We compared outcome, procedure time, radiation dose, complication rates and duration of hospital stay in 286 patients undergoing coronary angiography or percutaneous coronary intervention via the femoral or radial artery. **Results** One hundred and forty five procedures were performed via the femoral artery and 141 procedures via the radial route (Table 1). There were no differences in mean age, body mass index or the ratio of

elective/emergency procedures between the femoral and radial groups. Procedural success was achieved in 97.9% of femoral and 95.7% of radial cases ( $p = 0.3$ ). There were no differences in complication rates (6 [5 haematomas, 1 vasovagal] versus 5 [2 vasovagal, 3 self-limiting vascular complications];  $p = 1.0$ ),

	Femoral	Radial	*P
All Cases	145	141	
Age (years) [range]	63 [37-83]	63 [38-93]	0.8
Body Mass Index (kg/m <sup>2</sup> )	28.7±0.4	32.0±2.1	0.1
Elective/Emergency Cases (n)	103/42	107/34	0.9
Coronary angiography/PCI (n)	72/73	94/45	0.003
Procedural Success (%)	97.9	95.7	0.3
Access Site Complications (n)	6	5	1.0
Procedure Time (min)	26±1	25±1	0.6
Radiation Dose (mSv)	3582±246	4104±301	0.2
Hospital Stay (days)	2.8±0.3	2.9±0.4	0.7
Elective PCI (n)	73	29	
Procedure Time (min)	36±2	41±3	0.2
Radiation Dose (mSv)	4817±488	7291±743	0.005
Hospital Stay (days)	2.7±0.3	1.5±0.5	0.01

Data are presented as mean ± SEM or as indicated. \*P femoral versus radial, unpaired t-test or chi-squared where applicable. PCI, percutaneous coronary intervention.

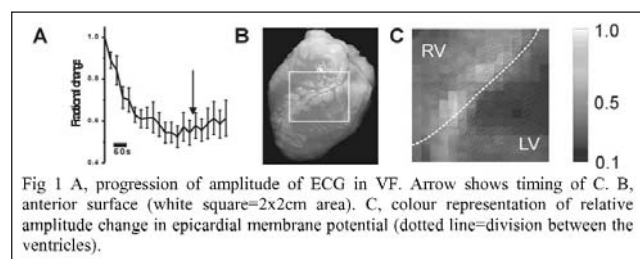
procedure time, radiation dose or length of hospital stay between the femoral and radial groups. In patients undergoing elective percutaneous coronary intervention, procedure time was similar ( $41 \pm 3$  versus  $36 \pm 2$  min,  $p = 0.2$ ), radiation dose greater ( $7291 \pm 743$  versus  $4817 \pm 488$ ,  $p = 0.005$ ) but hospital stay shorter ( $1.5 \pm 0.5$  versus  $2.8 \pm 0.3$ ,  $p = 0.01$ ) when performed via the radial compared to femoral approach respectively. **Conclusions** Our findings confirm that coronary angiography or percutaneous coronary intervention can be performed safely and successfully via the radial artery. In addition, our data suggest that elective percutaneous coronary intervention performed via the trans-radial route may be associated with a shorter in-hospital stay.

### Electrophysiological Characteristics of Isolated Perfused Rabbit Heart During Ventricular Fibrillation

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Clinical studies of VF show that as the heart becomes ischaemic, ECG amplitude decreases and survival diminishes. We studied the amplitude changes using ECG, optical mapping and floating microelectrode. Hearts were perfused at 40ml/min, stained with RH237 dye and illuminated. Fluorescence, representing membrane voltage, was recorded by 16x16 photodiode array from 2x2cm area of the anterior surface. VF was induced by burst pacing (50Hz, 8s). Peak-to-peak amplitude was determined for the ECG and each pixel. As shown in Fig 1A, the amplitude of the ECG decreased to ~50% of initial value during VF. The reduction was more pronounced in the left ventricle (LV) than the right (RV). Examining the RV and LV separately using 3x3 sites indicated that the mean relative amplitude was greater in the RV than the LV (RV  $0.6 \pm 0.2$ , LV  $0.3 \pm 0.1$ ,  $p < 0.0001$ ). Separate experiments, using floating glass microelectrodes, verified the reduction of LV action potential amplitude. This latter result indicates the reduction in the amplitude of the ECG is not due to asynchronous global activity, but rather a reduction of the amplitude of the underlying signals. This reduction was more pronounced in the LV than the RV.



## Auto-Titrating Continuous Positive Airway Pressure in Patients With Obstructive Sleep Apnoea And Chronic Heart Failure: a Randomised Placebo Controlled Trial

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**Introduction** Obstructive sleep apnoea (OSA) is highly prevalent in patients with chronic heart failure (CHF). OSA may contribute to CHF progression by causing nocturnal hypoxia, increased sympathetic nervous system activity and adverse cardiac haemodynamics. This study aimed to determine whether treatment of OSA by regular nocturnal continuous positive airway pressure (CPAP) would improve symptoms, functional capacity and objective measures of CHF severity. **Methods** Twenty-six patients (age  $61 \pm 8$  [mean  $\pm$  sd] years) with stable symptomatic CHF (left ventricular ejection fraction [LVEF]  $29 \pm 10\%$ ) and OSA (apnoea/hypopnoea index  $36 \pm 23$  events/hour slept) were randomised to nocturnal auto-titrating CPAP (AutoSet Spirit; ResMed, Sydney, Australia) and sham CPAP for 6 weeks each in a cross-over design with a 1 week washout period. Investigators were blinded to treatment modality. Study endpoints were changes in LVEF, peak VO<sub>2</sub>, VEVC0<sub>2</sub> slope, 6 minute walk distance (6MW) and quality of life (Epworth Sleepiness Scale [ESS], SF-36, Minnesota Living with Heart Failure) measures. **Results** Twenty-three patients completed the study. Mean nightly CPAP and sham CPAP usage were  $3.5 \pm 2.5$  and  $3.3 \pm 2.2$  hours/night respectively ( $p=0.31$ ). Mean CPAP pressure was  $7 \pm 2$  cm H<sub>2</sub>O. CPAP treatment was associated with improvements in daytime sleepiness (ESS  $3 \pm 3$  vs  $2 \pm 3$ ,  $p=0.05$ ) but not in other quality of life measures. There were no significant changes in LVEF, peak VO<sub>2</sub>, VEVC0<sub>2</sub> slope, or 6MW (Table 1). **Conclusions** This first randomised placebo controlled trial of CPAP in patients with OSA and CHF demonstrates improvement in daytime sleepiness but not in other quality of life measures, exercise capacity or LV systolic function. These data suggest that symptomatic benefit in this patient group is achieved by alleviation of OSA rather than by improvement in cardiac function. **Funded by** British Heart Foundation.

	Baseline	CPAP	Sham	p value*
LVEF, %	29 $\pm$ 10	31 $\pm$ 10	30 $\pm$ 10	0.22
Peak VO <sub>2</sub> , ml/kg/min	15 $\pm$ 4	14 $\pm$ 4	15 $\pm$ 4	0.44
VEVC0 <sub>2</sub> slope	31 $\pm$ 6	32 $\pm$ 8	32 $\pm$ 7	0.73
6MW distance, m	551 $\pm$ 118	546 $\pm$ 120	553 $\pm$ 117	0.98
ESS	10 $\pm$ 5	7 $\pm$ 4	8 $\pm$ 5	0.05

\*Comparison between CPAP and Sham limbs.

## ABSTRACT OF SOCIETIES

### Scottish Renal Association

Meeting of the Scottish Renal Association held in Inverness in March 2006

#### Vascular Access, Bacteraemia and Mortality in a Cohort of Haemodialysis Patients - Is There a Link?

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**Introduction and Aims** Bacteraemia and the development of sepsis syndrome are amongst the leading causes of death in patients on renal replacement therapy. The objectives of the study were to determine which laboratory and clinical variables were independently associated with the development of bacteraemia and death in a cohort of haemodialysis patients. **Methods** We performed a retrospective analysis of all prevalent haemodialysis patients within our renal unit at the beginning of January 2004 recording baseline clinical, demographic and laboratory variables for each patient. Outcomes were analysed over an 18-month period of follow up to record the development of clinically significant bacteraemia and death. Univariate analysis was performed on all variables with significant associations being put forward for inclusion in a formal multivariate analysis using a Cox proportional hazards model. **Results** A total of 265 patients were identified with median age of 66.7 years (range 16.3-88.9) and median time on renal replacement therapy of 1076 days (range 7-12,829). At baseline 206/265 (77.7%) were dialysing via a native

arteriovenous fistula, 31/265 (11.7%) were dialysing via a tunnelled central venous catheter, 26/265 (9.8%) were dialysing via a non-tunnelled central venous catheter and 2/265 (0.8%) were dialysing via a synthetic vascular graft. Over the 18-month period 45/263 (17.1%) patients developed at least one episode of bacteraemia and 65/263 (24.7%) died. Univariate analysis demonstrated significant association between use of vascular access catheters, low serum albumin, low dialysis blood flow and elevated C-reactive protein and the development of bacteraemia. Vascular access catheters, low haemoglobin, elevated neutrophil count, low lymphocyte count, low albumin, low calcium phosphate product, elevated alkaline phosphatase, elevated C-reactive protein, diabetes and previous bacteraemia were all significantly associated with mortality. Cox regression identified vascular access catheters as the main factor in the development of bacteraemia and death with hazard ratios of 5.4 ( $p<0.001$ ) and 2.9 ( $p=0.009$ ) for tunnelled catheters and 3.1 ( $p=0.01$ ) and 3.3 ( $p=0.001$ ) for non-tunnelled catheters respectively. Elevated C-reactive protein was also independently associated with bacteraemia (hazard ratio=1.5,  $p=0.006$ ). Low baseline serum albumin (hazard ratio=0.92,  $p=0.005$ ), elevated alkaline phosphatase (hazard ratio=1.002,  $p=0.023$ ) and increasing age (hazard ratio=1.05,  $p<0.001$ ) all had a significant association with mortality. Finally, there was a trend towards an association between bacteraemia and death but this failed to reach significance ( $p=0.06$ ). **Conclusions** Our data suggests that the use of synthetic vascular access catheters has an independent association with bacteraemia and death that is stronger than any other traditional clinical or laboratory risk factor variable. Additionally our data suggest that an increased baseline inflammatory state may be independently linked with adverse outcome. **Declarations** There are no conflicts of interest. This study was entirely funded by the Glasgow Royal Infirmary Renal Unit Research Fund.

#### Modifications to Advanced Life Support in Renal Failure

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**Purpose** Resuscitation practice in renal units is highly variable and few units have a specific resuscitation policy. Our main aim is to improve the delivery of resuscitation to patients with renal failure. **Background** In patients with established renal failure (ERF), cardiopulmonary arrest accounts for 47% of all cardiac deaths and a further 13% of deaths has been attributed to arrhythmias in the USRDS. Fluid and electrolyte abnormalities and a high prevalence of cardiovascular disease are important contributing factors. Patients with ERF undoubtedly pose a challenge to Advanced Life Support (ALS) providers who may seek expert advice. However, nephrologists and renal nurses also receive no specific training as there are currently no specific guidelines or training programs offered by the Resuscitation Council or Renal Association in the UK. **Renal Resuscitation Course** Given the complex medical issues arising from renal failure, it is expected that there may be some modifications to the resuscitation attempt in such patients. Based on the standard ALS approach, the outcome of cardiopulmonary resuscitation has been reported to be worse in patients with renal failure compared with those without renal failure. However, the possibility that this increased mortality may be partly attributed to a sub-optimal and highly variable treatment strategy has not previously been explored. We have designed a full-day training program for ALS or Immediate Life Support (ILS) certified staff responsible for the care of patients with renal failure. The main focus is on practical teaching led by a multidisciplinary team of ALS instructors and renal staff. This program complements the standard UK Resuscitation Council guidelines and highlights the environmental hazards in the setting of a dialysis unit, vascular access in dialysis patients and the role of a renal expert on the cardiac arrest team. The ALS algorithm has been modified to highlight the common reversible causes of cardiac arrest in renal failure with an emphasis on the management of hyperkalaemia. Safety concerns regarding defibrillation of patients who suffer cardiac arrest whilst undergoing haemodialysis are also addressed. **Summary** The Renal Resuscitation Course is the first training program to address the special circumstance of cardiac arrest in renal failure. Standardised teaching and management of cardiopulmonary arrest in patients with renal failure may dispel some myths and improve patient survival. **Funding** This course is supported by the Scottish Renal Association. **Accreditation** This course is accredited by the Royal Colleges of Physicians in the United Kingdom for Continued Professional Development and by Glasgow Caledonian University for nursing education. **Conflict of Interest** None.

#### Are there any correlations between "normal range" albuminuria, vascular and metabolic function in type 1 diabetes?

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Studies in type 1 diabetes have suggested that factors comprising the metabolic syndrome phenotype may promote the development of nephropathy. Furthermore

there is evidence that cardiovascular and renal risk are associated with elevations of urinary albumin excretion below the current threshold for the diagnosis of microalbuminuria. We hypothesised that insulin resistance and endothelial dysfunction may be common pathophysiological features leading to albuminuria, metabolic and vascular dysfunction in type 1 diabetes. We studied 25 type 1 diabetic subjects who had no hypertension, microalbuminuria or hypercholesterolaemia. Mean BMI and BP were 25.8 and 121/67 respectively. The mean albumin: creatinine ratio (ACR) was 0.94. Patients had assessments of insulin mediated glucose uptake and vascular function. Lipoprotein subfractions were analysed. Low level urine albumin was measured from early morning samples by high sensitivity Radioimmunoassay. Results were analysed as a continuous group to observe correlations among factors. The group was also divided into two, above and below the median ACR of 0.84. This yielded two groups with a mean ACR of 1.27 and 0.56 respectively. In the whole group, a correlation was observed between ACR and Insulin Resistance, (R.Sq 25.7%, p=0.01). Those above and below the median ACR had significantly different insulin-mediated glucose uptake. (7.54 vs. 4.8mg/kg/hr respectively, p=0.006). A correlation was also observed between the level of soluble-VCAM and ACR (R.Sq 32%, p=0.003). Those above and below the median ACR had significantly different soluble-VCAM. (269 and 221 respectively, p=0.006). There was a trend to correlations between ACR and Augmentation index, lipoproteins and oxLDL, but these were not statistically significant. No associations were observed between ACR and insulin resistance, age, duration of diabetes, HbA1c or blood pressure. Our results demonstrate an association between insulin sensitivity and very low level albuminuria in healthy type 1 diabetic subjects. The relationship between albuminuria and cardio-renal risk may be a continuum that extends below the conventional definition of microalbuminuria.

### Benefits of managing diabetic nephropathy within the scope of a Joint Renal and Diabetes clinic: An audit of the Royal Infirmary of Edinburgh Joint Clinic November 2003-October 2005

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**Background** Diabetes remains the commonest identifiable cause of established renal failure in the UK accounting for 17.9% of new patients starting renal replacement therapy. Clinical trials support early intervention in many aspects of diabetic management such BP control, reduction of HbA1c, proteinuria and cholesterol, as well as general lifestyle modification. Current national clinical guidelines for type 2 diabetes recommend referral for nephrological specialist opinion if serum creatinine is greater than 150umol/L. In most UK centres this is managed within general nephrology clinics. Alternatively there is an argument that joint renal diabetic clinics allow for a more targeted approach in managing such patients. We present results from an audit carried out in the recently established Joint Renal and Diabetic clinic in the Royal Infirmary of Edinburgh. **Design** This was an observational study of 115 patients referred to the combined renal diabetic clinic over a 24 month period. **Methods** Data was collected prospectively at time of clinic visit and from electronic patient records. **Results** 80% of patients referred were stage IIIb or greater with a mean MDRD of 30.4+/-14.3ml/min/1.73m2. Demographics at first visit showed that patients had a mean blood pressure of 149/74, HbA1c 8.1%+/-1.8% and serum cholesterol of 4.5+/-1.0 mmol/L. At the end of the first 2 years the percentage of patients with BP =130/80 rose from 47% to 64%. Mean arterial pressure fell from 97.7mmHg to 95.4mmHg. The mean rate of decline in renal function of slowed from 0.35ml/min/mth to 0.21ml/min/mth thus almost halving the rate of progression. Mean cholesterol fell slightly from 4.5mmol/l to 4.2 mmol/l. Diabetic control as assessed by HbA1c and body mass index (BMI) remained unchanged. **Discussion** Early data from our study finds that in some aspects of management such as BP control and rate of decline in renal function there has been significant improvement supporting a beneficial role in the care of patients attending the Joint Renal and Diabetic clinic. However management in these areas along with control of diabetes and hyperlipidaemia remains suboptimal. The clinic is currently labour intensive and there is only space to review patients on average 6 monthly. The audit raises the question as to whether some of these patients would be better managed in respect of renoprotection in a protocol driven pharmacist led clinic with the patients being seen as often as required to achieve targets.

### Statins and Fusidic Acid - A Bad Combination in Diabetic Nephropathy

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**Introduction and Aims** The benefits of therapy with HMG Co A reductase inhibitors (statins) is well established for a diabetic population although less clear once renal replacement therapy is required. Statins can induce myopathy although life-threatening rhabdomyolysis is rare. There are reports of a fusidic acid-statin

interaction predisposing to myopathy however the precise mechanism is unclear. We describe three cases of such an interaction resulting in severe rhabdomyolysis, associating with significant weakness, in diabetic patients with advanced renal disease presenting to our unit over a six-month period. **Results** Two males and one female aged between 46-65 years developed rhabdomyolysis (mean CK 99487) between 23 and 32 days after commencing fusidic acid for osteomyelitis or septic arthritis. The mean duration of treatment was 25 days. All were taking either simvastatin (20/40mg) or atorvastatin (40mg) for an average of 5 years and were insulin-dependant diabetics (average 13 years) with neuropathy and nephropathy. Two were already dialysis dependant. The third required renal replacement for 11 days before recovering baseline function (creatinine 145micromol/l). All suffered weakness, principally proximal myopathy (grade 2-3/5) and required prolonged rehabilitation. All eventually recovered power. Average hospital stay was 71 days. Weakness was present up to 6 days prior to the finding of elevated CK. In one case statin toxicity was felt not to fully account for the loss of power and IV immunoglobulin was administered. In retrospect no additional diagnosis was found. Pain was a feature in only one case. Nerve conduction studies were performed in two patients acutely to investigate weakness and during recovery. Both demonstrated conduction abnormalities in keeping with diabetic neuropathy with demyelinating and multifocal features. In addition needle EMG studies were consistent with rhabdomyolysis and these features resolved on repeat examination when power had improved. **Conclusions** Rhabdomyolysis should be considered in diabetic patients taking statins who present with profound weakness. We confirm that fusidic acid can interact with statins to potentiate their toxicity. This is especially relevant in a population where neuropathy predisposes to osteomyelitis. These three cases illustrate the hazards of combining fusidic acid with a statin in patients with diabetes, chronic renal failure and neuropathy. It resulted in significant patient morbidity and prolonged hospital stay in each case.

### Nephropathy in systemic IgG4 disease

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Lymphoplasmacytic sclerosing pancreatitis (SP) is the commonest manifestation of an unusual corticosteroid-sensitive systemic fibrosclerotic disease that is associated with high plasma immunoglobulin G4 (IgG4) and tissue infiltration with IgG4-secreting plasma cells. Whilst pancreatic, hepatic and biliary manifestations of this condition are well-reported, there is only one case report of renal involvement - a lymphoplasmacytic tubulointerstitial nephritis. We report here a case of initially unrecognised SP associated with subsequent concurrent membranous nephropathy and a distinctive pattern of lymphoplasmacytic tubulointerstitial nephritis. The patient presented with hypertension, a raised serum creatinine, proteinuria, elevated serum IgG4 and eosinophilia. Immunolabelling of renal tissue demonstrated numerous IgG4 positive plasma cells with patchy peritubular and interstitial IgG4 deposition coincident with areas of inflammation. Membranous nephropathy was confirmed with immunofluorescence and electron microscopy. On steroid therapy there was normalisation of serum IgG4 and the eosinophilia, with improvement in symptomatic wheeze, dry eyes, serum creatinine and liver function tests. This case extends the spectrum of systemic IgG4-associated fibroinflammatory diseases, highlights a morphologically distinctive and potentially treatable form of interstitial nephritis, and provides circumstantial evidence to support the notion that dysregulated IgG4 can facilitate the development of membranous nephropathy.

### Estimated GFR poor predictor of CKD Stages 1 and 2

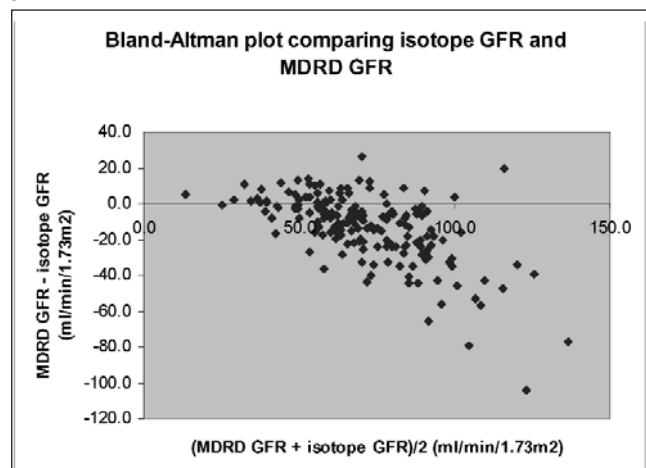
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**Introduction** The routine reporting of creatinine based estimations of glomerular filtration rate (eGFR) will form the basis of screening for and management of chronic kidney disease (CKD) in primary and secondary care. While the MDRD calculation for eGFR has been validated in CKD, its precision in estimating higher levels of GFR is less good and therefore, the level at which quantification of eGFR ceases to be clinically useful requires clarification. This study examined the relationship of calculated and measured GFR in an attempt to do this. **Methods**

GFR	n	Bland-Altman (ml/min/1.73m <sup>2</sup> )		Accuracy within (% of patients)		Correct CKD stage (% of patients)
		Bias	Precision	15%	30%	
<60	43	3	7.12	67.4%	86%	79.1%
60-90	80	-10	10	52.5%	93.8%	58.8%
>90	55	-31	21	16.4%	63.6%	12.7%

Patients undergoing  $^{51}\text{Cr}$ -EDTA measurement of GFR had simultaneous serum sampling to allow calculation of eGFR using the MDRD 4 and 7 equations. The relationship between estimated and measured values was examined using a 2 tailed Pearson correlation and Bland-Altman Plot from which bias (mean difference between measured and estimated) and precision (1 SD of bias), were derived for different levels of function. **Results** 178 adult patients, (58 male, 3 non-caucasian, mean age  $56.8 \pm 14.3$ ), underwent measurement and estimation of GFR between 14/3/05 and 09/12/05 in a single nuclear medicine and biochemistry department. Median measured GFR was 74.2 (range 10.7-175.3). GFR was  $<60$  ml/min/1.73m<sup>2</sup> in 43 patients, between 60-90 ml/min/1.73m<sup>2</sup> in 80 patients and  $>90$  ml/min/1.73m<sup>2</sup> in 55 patients. MDRD 4 did not differ significantly from MDRD 7 in its level of correlation with measured GFR, and MDRD 7 is subsequently quoted. The level of correlation declined with increasing GFR ( $r^2$  value of 0.661 in GFR  $<60$  ml/min/1.73m<sup>2</sup>,  $r^2$  of 0.255 in GFR between 60-90 ml/min/1.73m<sup>2</sup> and  $r^2$  of 0.068 in GFR  $>90$  ml/min/1.73m<sup>2</sup>) eGFR was progressively underestimated with increasing GFR. (Bland-Altman Plot)



**Conclusion** While eGFR provides a valuable tool in the management of CKD, we suggest the level of imprecision in estimating values greater than 60ml/min/1.73m<sup>2</sup> make the clinical value of quantification above this level limited. The level of underestimation of GFR, as much as 30ml/min/1.73m<sup>2</sup> using the MDRD formula could lead to inappropriate K/DOQI CKD staging and put an unnecessary increasing burden to the nephrology service as a whole.

### Granulomatous interstitial nephritis in Glasgow

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Granulomatous interstitial nephritis (GIN) is a rare histological diagnosis. We identified all patients diagnosed with GIN in Glasgow over a 15-year period from electronic patient records. The renal histology was reviewed by a pathologist without prior knowledge of the clinical history at the time of the biopsy or the final diagnosis. This series, which is the largest to date, reports the presenting features, associated conditions, treatment and outcome of patients. Nineteen cases were identified: five cases were associated with sarcoidosis, two with tubulointerstitial nephritis and uveitis, three with medication and nine were idiopathic. The patients presented with advanced renal failure (mean estimated creatinine clearance [ECC] 19 ml/min) and minimal proteinuria (urine albumin to creatinine ratio [ACR] 10.7 mg/mmol). Seventeen patients were treated with prednisolone (mean dose 0.32 mg/kg/day in first 3 months) for a mean of 24 months. Six patients relapsed with a reduction in prednisolone dose (4 had sarcoidosis) and four patients required steroid sparing agents. During the mean follow up of 45 months, renal function improved or stabilised in 18 patients with the rate of improvement most marked in the first year after diagnosis with a gain in function of +1.8 ml/min/month. Throughout the remaining follow up period the rate of improvement slowed to +0.14 ml/min/month and the mean ECC at final visit was 55 ml/min. No patient required long-term renal replacement therapy. The features on biopsy did not help determine the cause of GIN and there was no correlation between the degree of fibrosis or inflammation on biopsy and renal outcome. GIN is a treatable cause of renal failure that highlights the value of renal biopsy in patients with advanced renal failure and minimal proteinuria. In the absence of therapeutic trials our retrospective data suggests treatment with a moderate dose of prednisolone is associated with a good prognosis irrespective of the underlying aetiology and of the degree of fibrosis. No funding and no conflicts of interest.

### Clinical outcomes of patients with stage 4 chronic kidney disease (CKD)

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**Introduction** The widespread introduction of MDRD eGFR is likely to result in increased detection of patients with stage 4 CKD, all of whom should be referred to the nephrology service according to recent guidelines. We sought to determine the outcome of patients with stage 4 CKD referred to the nephrology clinic in order to rationalise the management of this growing population. **Methods** A retrospective analysis of all patients with eGFR 15-29 referred to the Renal Unit of Daisy Hill Hospital and the outreach nephrology clinic at the Western General Hospital, Edinburgh between April 1998 to Dec 2002 inclusive. Baseline characteristics were recorded and renal and patient outcomes determined in Dec 2005. **Results** We identified 200 patients referred with CKD 4 during this time period. Median age was 71yrs, 52.5% were male and median eGFR at referral was 23.4ml/min/1.73m<sup>2</sup>. After a mean follow-up of 5.23yrs, only 48 (24%) progressed to renal replacement therapy (RRT). In a univariate analysis age, baseline eGFR, proteinuria and cholesterol, and the rates of fall in eGFR and proteinuria over the first three clinic attendances predicted renal outcome. In a multivariate analysis only baseline proteinuria (RR:1.33 for every g/24hrs increase; 95%CI:1.18-1.51,  $p < 0.0001$ ), baseline eGFR (RR:0.84 for every ml/min/1.73m<sup>2</sup> increase; 95% CI:0.78-0.91,  $p = 0.01$ ), the rate of fall in eGFR over the 1st three clinic attendances (RR: 1.05 per ml/min/1.73m<sup>2</sup>/yr fall in GFR; 95%CI:1.01-1.09,  $p < 0.0001$ ) were independent predictors of the need for RRT. In the subgroup that did not require RRT the rate of deterioration in renal function was very slow (median: 0.8ml/min/1.73m<sup>2</sup>/yr). During follow-up, 69 patients were discharged from the nephrology clinic to primary care. Reassuringly, the median rate of decline in renal function in those discharged was 0.34ml/min/1.73m<sup>2</sup>/yr and only seven were referred due to a progressive deterioration in renal function. **Conclusion** Approximately 25% of patients with stage 4 CKD referred to the renal service required RRT within five years, and these could be identified by a rapid early decline in eGFR and by elevated baseline proteinuria. Prioritisation of this subgroup for renal education and timely vascular access surgery could help rationalise the pre-dialysis clinic. No funding or conflict of interest declared.

### Validation of an IgA Nephropathy Prediction Algorithm

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Predicting the rate of progression of chronic renal impairment is difficult, even after several years of follow up. In order to address this difficulty, using data held by the Toronto GN registry, a formula to predict rate of decline in eGFR has been devised. It uses mean blood pressure and proteinuria over the first two years of follow up to predict rate of progression in patients with IgAN. Being better able to predict rate of progression may allow targeting of treatment to those most likely to progress and more efficient preparation for renal replacement therapy. In order to test the validity of such an algorithm in a different population, albeit with the same disease, we attempted to compare actual rate of progression with that predicted by the Toronto formula. Patients with biopsy-proven IgAN and at least 2 years of follow up were selected from a single centre in the West of Scotland. Actual rate of progression was calculated from the rate of change in creatinine clearance estimated by the Cockcroft & Gault formula. This was compared to the rate of progression predicted by the Toronto formula. As rate of change in estimated creatinine clearance is a rather abstract concept to explain to patients, an evaluation was also made of the utility of the formula in predicting which patients progressed to ESRD within 10 years. 170 patients (82% male) were studied. They were comparable to the Toronto group in terms of age and blood pressure at presentation, but the Toronto group had heavier proteinuria and more advanced renal disease. Not surprisingly, therefore, the Glasgow group progressed more slowly than the Canadians (3.7 versus 4.8 ml/min/year). When comparing the predicted with the actual rates of progression there was a good correlation ( $r^2 = 21\%$ ,  $p < 0.001$ ). In 75% of the individuals studied the formula predicted the actual rate of progression to within 4 ml/min/year. In predicting those who would require dialysis within 10 years of presentation the formula had a negative predictive value of 92% and a positive predictive value of 52%. Formulae which predict future rate of progression of renal disease may be a useful adjunct in helping to manage patients with progressive chronic renal impairment.

## An Audit of Osteoporosis Protection in Renal Transplant Recipients in the Royal Infirmary of Edinburgh

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Patient and graft survival after kidney transplant continues to improve and therefore the importance of preventing late complications and improving quality of life is paramount. This involves addressing such factors as cardiovascular risk, post-transplant diabetes mellitus, cancer and bone disease. Recipients of renal transplants invariably have abnormal bone architecture at the time of surgery and have accelerated bone loss in the first three months of around 5%. The incidence of vertebral fracture is four times that of the general population. Conventional therapy including bisphosphonates, calcitriol and calcitonin have been shown to increase bone mineral density (BMD) but have so far not been shown to decrease fracture risk. The current RIE protocol advocates a combination of alfacalcidol and calcichew until the GFR is greater than 50ml/min at which stage adcal D3 (calcium 600mg/colecalciferol 10mg) is substituted, and to use parenteral bisphosphonates in high-risk patients. A suspicion that a significant number of patients were not being converted to adcal D3 and subsequent concern regarding calcium load and the potential increased risk of arterial calcification and possibly coronary heart disease lead to this audit. We studied all patients transplanted between 01/01/03 and 31/12/04 in Edinburgh. Data was collected from Proton and included; serum corrected calcium and phosphate at transplant, one, three and six months; bone protection medication at the same time intervals and serum PTH at one point during the six-month period. A GFR was calculated at six months using the MDRD formula. A calcium of  $>2.45\text{mmol/l}$  was considered 'high' and  $>2.60\text{mmol/l}$  as hypercalcaemia. At transplantation 24% had high calcium and 7% were hypercalcaemic. The median calcium was  $2.28\text{mmol/l}$  (IQR 2.06 - 2.39) At six months 60% had high calcium with 33% hypercalcaemic. The median calcium was  $2.55\text{mmol/l}$  (IQR 2.34 - 2.59) Phosphate tended to be high at transplant, with 36%  $>1.6\text{mmol/l}$ , but dropped quickly to only 3.6%  $>1.6\text{mmol/l}$  at six months. The median calcium phosphate product was 3.2 at transplant and this dropped to 2.7 by six months. 49% had no PTH measured in the six-month period. Of those measured 5% had a PTH greater than 320ng/ml and could be considered as secondary hyperparathyroidism. The drugs used varied very little with 67% patients on alfacalcidol, calcichew or both at transplant and six months. The use of adcal D3 increased from 4% to 7% however by six months 60% of patients had a GFR  $>50\text{ml/min}$ . There was no record of any bisphosphonate use. Information relating to bone density and fracture incidence is not currently collected. In conclusion this audit would suggest that, although the majority of renal transplant patients are receiving some form of bone protection, the RIE protocol is not being followed and as a consequence a significant number of patients are becoming hypercalcaemic. It would be useful to know how many patients have BMD assessed and whether this would alter subsequent treatment.

## Predictors of New Onset Diabetes After Renal Transplantation

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The development of new onset diabetes after transplantation (NODAT) is a serious complication that is associated with an increased risk of cardiovascular morbidity and mortality. Identifying high-risk patients may be beneficial and would allow tailoring of immunosuppression in the hope of improving long-term outcome. All patients who received a renal transplant between 1994 and 2004 and had at least one year of follow up were identified. Age, gender, weight, Carstairs deprivation category, type of immunosuppression, pre and post-transplant random glucose concentrations were collected. Seven hundred and eighty seven transplants were identified. Seventy patients (8.9%) were known to have diabetes pre-transplant, these were excluded from further analyses, and 55 developed NODAT (7%). The patients who developed NODAT were significantly older (49 vs 40 years,  $p=0.001$ ), heavier (78 kg vs 69 kg,  $p=0.001$ ), more likely to live in Carstairs deprivation category 6 and 7 (42.9% vs 28.6%,  $p=0.038$ ) and were more likely to be treated with tacrolimus (25.5% vs 11.8%,  $p=0.006$ ). The mean glucose pre-transplant was significantly higher (6.4 mmol/L vs 5.5 mmol/L,  $p=0.002$ ) and the glucose within the first 24 hours post-transplant was higher (12.8 mmol/L vs 10.5 mmol/L,  $p=0.047$ ) in those who developed NODAT. There was no difference in gender or the use of high dose corticosteroids. By multivariate analyses, the predictors of NODAT were age (HR 1.04, 95% CI 1.008-1.073), weight (HR 1.032, 95% CI 1.006-1.059), mean glucose pre-transplant (HR 1.60, 95% CI 1.18-2.169), glucose within the first 24 hours (HR 1.088, 95% CI 1.015-1.166) and the use of tacrolimus (HR 3.84, 95% CI 1.632-9.046). NODAT developed in 27.3% of patients who were over the age of 50 years, weighed more than 75 kg and had a pre-transplant random blood glucose concentration greater than 5.5 mmol/L. Patients with NODAT had a ten-year survival of 67.1% compared to 81.9% for those who did not develop NODAT. There

was no difference in graft survival at 10 years. In conclusion, patients at high-risk of developing NODAT can be identified by age, weight and pre-transplant glucose concentration. High-risk patients should be considered for tailoring of immunosuppression and anti-hypertensive medication. Reducing the incidence of NODAT may improve long term outcome by reducing death with a functioning graft. No conflicts of interest. This research was partially supported by a National Health & Medical Research Council (NHMRC) Neil Hamilton Fairley Fellowship awarded to Dr Staatz, and by Darlinda's Charity for Renal Research.

## Six-Year Outcome in Renal Allograft Recipients Comparing Ciclosporin (Neoral)-Led With Tacrolimus (FK-506)-Led Therapy

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This single centre retrospective study compared the outcomes over 6 years of consecutive patients treated with Neoral or Tacrolimus-led immunosuppression between June 1995 and June 1998, bridging a change in unit protocol. 63 patients started Neoral (N) and 45 Tacrolimus-led therapy. Donor and recipient demographics and graft matching were comparable between the groups. Outcome measures were graft survival and function, patient survival, number of rejection episodes and incidence of post-transplant diabetes, hypertension, CMV disease and malignancies. Data were collected at 1, 3, 6, 12 months and annually thereafter. Analyses were on an intention-to-treat basis, patients were censored at time of change of calcineurin phosphatase inhibitor (11 patients), loss of graft or death. At 6 years follow-up there were no differences between the 2 groups in terms of graft survival (73% N: 71% T) or patient survival (95% N: 93% T). Estimated GFR (abbreviated MDRD) was consistently higher in the T group at all census points. The rate of decline in GFR from baseline (3 months post-transplant) was not significantly different between the two groups. Biopsy proven rejection was more common in the N group with 44.8% of patients experiencing at least one episode compared with 25.6% in the T group ( $p=0.03$ ). CMV disease was more common in the T group (22.2% T: 10.9% N); skin malignancies were also more common in the T group, but neither reached statistical significance. There was a higher incidence of CMV D+/R- in the T group. There was no difference between the two groups in the incidence of post-transplant diabetes (10.9%N: 6.7% T) or the attained mean arterial BP at each census point. Tacrolimus-led immunosuppression has reduced the incidence of acute rejection and resulted in improved graft function in our unit.

## Living-unrelated spousal kidney transplantation: a review of the East of Scotland programme

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**Introduction** Spousal kidney donation is an attractive method of increasing the kidney donor pool, however with husband-to-wife donation there is a risk of donor-specific antibody (DSA) formation due to sensitisation to donor antigen during pregnancy. We sought to review the East of Scotland spousal donation programme and compare the rates of DSA, rejection and graft outcome between husband-to-wife and wife-to-husband donation. **Methodology** A single-centre retrospective analysis of husband-to-wife (group 1) and wife-to-husband (group 2) kidney donation. **Results** Between 1997 and 2005, there have been 11 husband-to-wife and ten wife-to-husband renal transplants performed in East of Scotland. There were no significant differences in the mean recipient age between the wives and husbands (49.1 v 49.3yrs respectively,  $p=0.98$ ), however there was a trend for the husband donors to be older (53.1 v 45.9yrs,  $p=0.09$ ). The degree of mismatching (MM) was similar between the groups (total MM: 4.1 v 4.0,  $p=0.88$ ; DR MM: 1.4 v 1.6,  $p=0.38$ , for 1 and 2 respectively). Cytotoxic cross-match was negative for all transplants, however T-cell flow cytometric cross-match (FACS) was positive for 4 of group 1 and none of group 2. DSA were present in two of group 1 and none of group 2. The acute rejection rates within 6 weeks of transplantation for group 1 (0.54) and group 2 (0.6) did not differ significantly ( $p=0.76$ ). Four of group 1 and two of group 2 had histological evidence of acute vascular rejection. All four group 1 patients were FACS positive and two had HLA-DSA present pre-operatively. Both patients who had DSA pre-operatively developed C4d positive rejection, one mild responsive to steroids and plasma exchange, the other severe and unresponsive to steroids, plasma exchange, rituximab or conversion to sirolimus. **Conclusion** While rates of rejection were similar between the two groups, there was a greater frequency of more severe rejection for husband-to-wife donation. A pre-operative positive FACS test and presence of DSA could identify high-risk patients. Mechanisms to prevent and treat rejection in high-risk patients remain uncertain. No source of funding or conflict of interest declared.