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44th Congress of the ERA-EDTA
June 21–24, 2007, Barcelona, Spain



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1. Basic Science

The Role of Gene Polymorphisms in the Progression of Chronic Kidney Diseases

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Introduction and Aims: We investigated gene polymorphisms – nitric oxide synthase (eNOS) T-786C; methylene-tetrahydrofolate reductase (MTHFR) C677T; paraoxonase 1 (PON1) Q192R, M55L; endothelin-1 (ET-1) G5727T; angiotensin converting enzyme (ACE) I/D; angiotensinogen (AGT) M235T and angiotensin II type 1 receptor (AT II 1R) A1166C gene-polymorphisms – that are in connection with endothelial functions and may influence the development of end-stage renal disease (ESRD) in three patient groups.

Methods: The study population (n = 530) consisted of 266 adult patients suffering from ESRD on maintenance hemodialysis (HD), 64 kidney patients without HD (GFR = 15–90 ml/min), and 200 healthy, age matched controls. All patients were Caucasians of Hungarian origin.

The etiologies of kidney diseases were: primary glomerulonephritis, interstitial nephritis, nephrosclerosis caused primarily by hypertension, diabetic nephropathy, hereditary diseases, others unknown or other diseases.

Gene polymorphisms were measured with real time PCR (Light Cycler) technique using melting-point analysis, allele-specific amplification and gel electrophoretic method.

Statistic analysis was carried out with chi-squared test with Yates' correction.

Results: Analysing the T-786C eNOS polymorphism, significant decrease of normal TT genotype was only detected in interstitial nephritic patients on HD and in nephrosclerotic patients without HD. The increase of TC+CC genotypes in these groups did not reach the significance level.

The frequency of MTHFR C677T genotypes and the PON1 Q192R did not differ significantly in HD patients and healthy controls. A difference in the frequency of the PON1 M55L polymorphism was found in 17 patients in the nephrosclerotic group without HD,

therefore more patient analyses are required.

The nephrosclerosis affected HD patients' endothelin gene G5727T GG genotype proved significantly less, the GT+TT genotypes significantly more than in the controls and the patients without HD.

Significantly more ACE DD genotypes were found in HD groups compared to controls and patients without HD. It was the primary glomerulonephritis and the interstitial nephritis within the HD group where most of the ACE DD polymorphism could be found. At the same time, significantly less I/D heterozygote frequency was detected only in the glomerulonephritic group.

No significant differences have been determined in the frequency of AGT M235T and AT-II 1R A1166C polymorphisms between the kidney patients and controls.

Conclusions: Certain gene polymorphisms might have relevance to progression in chronic renal failure. In our study it is the ESRD patient group where the most differences were found regarding the investigated gene polymorphisms.

Among the non end-stage kidney patients, the group with nephrosclerosis caused primarily by hypertension showed the only significant difference compared to the control group.

These findings have confirmed the correlation between the endothelial dysfunction and the severity and etiology of kidney diseases.

Mesenchymal Stem Cells Prevent Progressive Experimental Renal Failure but Maldifferentiate into Glomerular Adipocytes

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Introduction and Aims: We recently demonstrated that intrarenal injection of mesenchymal stem cells (MSC) could accelerate glomerular healing in a rat model of mesangioproliferative nephritis (Kunter et al. JASN 17:2202-2212, 2006). We asked whether MSC can preserve renal function in a progressive rat model of GN as well.

Methods: Normally, anti-Thy 1.1 nephritis in rats follows a self-limited course. In order to enhance the relevance of the model for progressive renal disease in humans, we induced progressive renal failure by prior uninephrectomy. Fluorescently labeled MSC were injected into the left renal artery 2 days after disease induction (n = 10). Control rats received medium injections (n = 10). Living biopsies were performed on day 10. Follow-up included measurements of blood pressure, proteinuria, S-BUN and S-creatinine. Kidneys were evaluated by immunohistochemistry for collagens and alpha-smooth muscle actin and glomerulosclerosis scores.

Results: Early in GN, MSC labeled with PKH26 localized to more than 70% of glomeruli, led to amelioration of transient acute renal failure and reduced glomerular adhesions. At day 60, proteinuria had progressed in controls to 40 ± 25 mg/d but stayed low in MSC treated animals (13 ± 4 mg/d; $p < 0.01$). Renal function in the MSC group was better than in controls (S-BUN 12.4 ± 1.4 mmol/l in MSC vs. 14.0 ± 1.3 mmol/l in controls; $p < 0.05$). Renal morphology in the MSC group as compared to controls on day 60 was remarkable for a 11% higher number of glomeruli per 1mm^2 of renal cortex, but also significantly higher glomerular accumulation of collagen types I, III and IV, and alpha-smooth muscle actin. About 20% of the glomeruli of MSC treated

rats contained single or clusters of large adipocytes with a pronounced fibrotic response surrounding them. Adipocytes exhibited PKH26 fluorescence in their cytoplasm and/or intracellular lipid droplets. Lipid composition in these adipocytes *in vivo* was similar to that of MSC undergoing adipogenic differentiation *in vitro*. We found no evidence of fat cell formation in biopsies of day 10, using both oil red O stainings and electron microscopy. mRNA analyses of cell cultures prior to and after fat cell induction showed a significant difference in expression of typical fat cell markers, i.e. adiponectin (2500 fold upregulation in cultures under adipogenic differentiation conditions).

Conclusions: In our GN model the early beneficial effect of MSC of preserving damaged glomeruli and maintaining renal function was offset by a long-term partial maldifferentiation of intraglomerular MSC into adipocytes accompanied by glomerular sclerosis. Given the results, a contamination of the injected MSC by adipocytes is highly unlikely. Our data therefore raise a major safety concern for a potential clinical application of mesenchymal stem cells in renal disease.

2. Clinical Nephrology

Progression of Coronary Artery Calcification (CAC) in Hemodialysis Patients Despite Excellent Control of LDL Cholesterol: The Calcium Acetate Renegel Evaluation-2 (CARE-2) Study

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Introduction and Aims: Some, but not all studies in the general population, have reported that treatment of hypercholesterolemia with statins is associated with attenuation or even regression of CAC. CARE-2 is a prospective, multicenter, randomized trial designed to test the hypothesis that, if LDL is lowered by statins to equal levels in calcium acetate (CaA) and sevelamer (SV)-treated patients, there will be no difference in the progression of CAC.

Methods: HD patients with serum phosphorus (P) > 5.5 mg/dL, LDL > 80, and EBCT CAC scores (CACS) of 30 to 7000 Units were randomized to either CaA or SV for 1 year. Atorvastatin was added to achieve LDL < 70 mg/dL in both groups. Primary endpoint is percent change in CACS at 1 year. Secondary endpoints: serum P, Ca, Ca X P product, PTH, HCO₃, and LDL levels. 203 patients randomized (103 CaA, 100 SV). EBCT was done at baseline, day 180, and 360 EBCT data.

Results: Achieved LDL levels are 68 and 58 mg/dl in CaA and SV respectively. Median CACS increased 28% in CaA group and 32% in SV group (p = 0.7). Geometric mean values increased 30% in the CaA group and 40% in the SV group (p = 0.4) (Table). There was significant within group progression of CAC and aorta calcification in CaA- and SV-treated patients, but no between group difference in progression of CACS and aorta calcium scores.

Conclusions: Our data showed that despite excellent control of LDL cholesterol, there was significant within group progression of CAC in CaA- and SV-treated patients, suggesting that factors other than LDL play a key role in progression of CAC in ESRD patients. The data also suggest that calcium absorbed from use of CaA does not contribute to progression of calcification.

	Time Point	Calcium Acetate		Sevelamer		P-Value
		N	EBCT	N	EBCT	
Geometric Mean	Day 0	99	489.2	99	411.4	
	Day 360	54	746.7	64	574.6	
	Day 360/Day 0 Ratio	54	1.3	64	1.4	0.3544
Ratio of Geometric Mean % Change i.07 (CI 0.92-1.25)						
Median	Day 0	103	468.0	100	439.0	
	Day 360	59	681.7	67	528.5	
	Change from Day 0	59	121.3	67	96.0	0.2132
	% Change from Day 0	54	27.5%	64	32.3%	0.7129

Relation Between Serum Calcium, Phosphate, Parathyroid Hormone and 'non-dipper' Circadian Variability Profile in Hypertensives with Normal Renal Function

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Introduction and Aims: In patients with renal disease, an association between an abnormal circadian blood pressure profile and abnormalities in bone and mineral metabolism, including vascular calcifications are well known. However, such a link has not yet been reported in hypertensive patients with normal renal function. We aimed to evaluate whether higher serum phosphate, calcium, parathyroid hormone (PTH) level and calcium x phosphate (CaxP) product would be associated with a non-dipper hypertension, in patients with normal renal function and without any parathyroid hormone disorder.

Methods: 190 hypertensive subjects with the following inclusion criteria were enrolled: 1) normal phosphate and PTH levels, 2) glomerular filtration rate (GFR) > 60 ml/min, 3) no history of calcium, phosphate, vitamin D medication and hyperparathyroidism.

Results: Of the total population, 76 patients (40%) were classified as dippers and 114 (60%) as non-

dippers. Non-dipper patients had higher levels of phosphate (3.70 ± 0.61 vs. 3.35 ± 0.44 mg/dL, $p = 0.001$), CaxP product (35.4 ± 6.5 vs. 31.5 ± 5.0 , $p = 0.001$) and PTH (75.7 ± 28.8 vs. 46.6 ± 17.1 pg/ml, $p = 0.000$), compared to dipper patients. Independent predictors (multiple regression) for non-dipper hypertension were PTH ($\beta = 0.43$, $p = 0.001$) and phosphate ($\beta = 0.9$, $p = 0.03$). To assess the ability of PTH to predict non-dipping patients, a ROC curve was constructed and the area under the curve was calculated – AUC = 0.83, $p = 0.0001$. When the cut-off point for PTH was selected as 54.5 the sensitivity was 80.6% and the specificity was 74.5%.

Conclusions: We demonstrated a graded independent relation between higher levels of phosphate, parathyroid hormone, calcium x phosphate product and the risk of non-dipping, in hypertensive patients with a GFR > 60 ml/min and normal mineral metabolism.

The Association Between Hyperphosphataemia and Loss of Residual Renal Function in Haemodialysis and Peritoneal Dialysis Patients

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Introduction and Aims: Preserving residual renal function (RRF) is of primary importance, even after initiation of dialysis treatment. Compared to well-known effects of high blood pressure or proteinuria, disorders of the mineral metabolism have not attracted much attention as influencing factors in the decline of RRF. Therefore, the aim of this study was to assess the associations between plasma phosphorus concentrations and loss of RRF in incident haemodialysis (HD) and peritoneal dialysis (PD) patients.

Methods: As part of NECOSAD, a large prospective cohort study in the Netherlands, we included 1,434 patients who started HD or PD treatment between 1997 and 2004 and who were not anuric at the time of dialysis initiation. Total loss of RRF was defined as anuria (urine production < 200 mL/24 hours). The analyses evaluated the relative risk (RR) of total loss of RRF during the first 2 years of dialysis therapy utilizing time-dependent Cox regression models, stratified for treatment modality, and controlling for age, sex, comorbid conditions, systolic and diastolic blood pressure, albumin, calcium, intact PTH, and urinary protein loss. Each plasma phosphorus concentration was used to predict loss of RRF in the following 6 months. The reference category was plasma phosphorus between 3.5 – 5.5 mg/dL (K/DOQI target range).

Results: Mean age of the patients was 59 ± 15 years, 62% were men, and 61% were treated with HD. Three months after start of dialysis, 39% of HD patients and 51% of PD patients had plasma phosphorus concentrations in the target range. Hyperphosphataemia (phosphorus > 5.5 mg/dL) was present in 54% of HD and 40% of PD patients. Mean urine production at baseline was 927 ± 619 mL/24h in HD and 1229 ± 769 mL/24h in PD patients ($p < 0.0001$). During follow-up, 708 HD patients (81%) and 407 PD patients (73%) became anuric

and the median time until loss of RRF was 9 months in the HD group and 15 months in the PD group. In HD patients, disordered plasma phosphorus concentrations were not statistically significantly associated with loss of RRF (RR: 1.1; 95%CI: 0.9 to 1.3; $p = 0.40$). PD patients with a plasma phosphorus concentration > 5.5 mg/dL had a 50% higher risk of total loss of RRF than PD patients with normal plasma phosphorus concentrations (RR: 1.5; 95%CI: 1.2 to 1.9; $p = 0.002$).

Conclusions: The relative risk of loss of RRF was significantly higher in PD patients with hyperphosphataemia when compared to PD patients with normal plasma phosphorus levels. This finding implies that control of phosphorus levels might contribute to the preservation of RRF in PD patients.

Importance of Strict Volume Control on Blood Pressure Level and Kidney Disease Progression in Patients with Advanced Chronic Kidney Disease (CKD)

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could contribute to a faster kidney disease progression in these patients. The aim of our study was to analyse the effect of strict volume control on BP values and CKD progression among patients with stage 4–5 CKD followed in our pre-dialysis outpatient unit, where strict hyponatremic diet is prescribed and high doses of loop diuretics are employed for strict volume control.

Methods: We compared the individual rates of decline in renal function and BP control for the 2 years before and after referral to our pre-dialysis unit in 66 new referrals with stage 4–5 CKD (CCr at referral: 20 ± 6 mL/min). BP values, number of antihypertensive drugs, use of ACE inhibitors, use and dose of diuretics, proteinuria, hemoglobin (Hb) and serum C-reactive protein (CRP) levels were compared before and after referral. For each period, an average value of all clinical and biochemical data was calculated in every patient and this value was included in the database. The decline in renal function (measured as final minus basal CCr/months of follow-up) was also compared between the two periods. In addition, a logistic regression analysis was used for determine the factors influencing on a faster progression of CKD during the pre-dialysis period.

Results: Systolic BP fell in the post-referral period (151 ± 16 to 137 ± 12 mmHg; $p < 0.001$) despite a similar number of anti-

hypertensive drugs ($p = 0.1$) employed in the two periods. However, the proportion of patients with loop-diuretics as well as the mean dose of diuretics received, were higher in the post-referral period ($p < 0.001$). There was a trend to lower proteinuria in the post-referral period (1.8 ± 1.8 to 1.4 ± 1.6 g/d; $p = 0.06$) despite a lower proportion of patients with ACE inhibitors (42% vs 83%; $p < 0.001$) following referral. There were no differences in Hb or CRP values between the two periods. The median decline in renal function slowed after referral (0.4 to 0.04 mL/min/month; $p < 0.001$). During the pre-dialysis period, 28 patients (42%) showed stabilization of renal function and 16 patients were in the higher quartile group (faster progressors) showing a decline in CCr > 0.2 mL/min/month. Logistic regression analysis showed that only younger age and lower time under nephrological care were predictors of a faster progression whereas BP values were not independently associated with a faster decline in renal function.

Conclusions: Retarding the progression of CKD is possible even in patients with advanced renal failure. Strict volume control is necessary to achieve adequate BP control in these patients. However, our results suggest that once BP is well controlled, it seems that time under nephrological care is the key factor influencing on CKD progression.

Introduction and Aims: Interventional studies have shown the effectiveness of blood pressure (BP) control in slowing CKD progression even in advanced stages of CKD. However, adequate BP control is very difficult to achieve in renal patients. We tested the hypothesis that fluid overload could be an underestimated cause of poor hypertension control among patients with CKD and therefore,

When to Measure Blood Pressure on the Beginning of Haemodiafiltration Session?

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(> 90 days) on-line haemodiafiltration (HDF) treatment using Fresenius 5008 machine, 3 times a week. The baseline BP (BP1) was taken before HDF, after 10 min. of bed rest and using upper arm cuff of F5008's automatic BP equipment. Then the standard procedure of starting HDF was performed and the second BP (BP2) measurement was taken not exceeding a maximum up to 10 min. time from the beginning of treatment. The study lasted one month and BP measurements of all consecutive HDF sessions were entered. The statistical evaluation was performed by paired t-test evaluating the whole group and comparing diabetic (DM) vs. non-diabetic (nonDM) patients, respectively.

Results: The mean age was 67.3 years, female gender was predominant (56%), the mean time of RRT was 32.2 months, 28% of patients with diabetic nephropathy. Altogether 320 BP measurements were performed with a mean of 12.6 HDF sessions/patient. 44% patients were on antihypertensive treatment with a mean of 1.4 agents.

Mean BP1 was 136.8 ± 17.5 / 65.4 ± 13.0 mmHg and pulse BP1, i.e. difference between systolic (s) and diastolic (d) BP1, was 71.4 ± 19.1 mmHg, whereas mean BP2 was 131.2 ± 14.4 / 64.3 ± 11.7 mmHg and pulse BP2 was 67.0 ± 18.1 mmHg.

Mean difference (D) of systolic BP, i.e. difference between sBP1 and sBP2, was 5.6 ± 16.3 mmHg

which was highly significant ($p = 0.00001$). Rise of sBP was observed in 31.3% of measurements. Mean D of diastolic BP was 1.2 ± 10.8 mmHg (not significant) and with BP increase in 37.5%. Mean D of pulse BP was 4.4 ± 17.5 mmHg and highly significant ($p = 0.0001$) as well.

Comparing DM (87 measurements of BP) vs nonDM patients (233 measurements), the following results were found: 1) sBP differed significantly in both groups: mean D in DM was 4.0 ± 2.0 mmHg ($p = 0.048$) and mean D in nonDM was 6.2 ± 15.3 mmHg ($p = 0.0001$); 2) dBP differed significantly only in nonDM patients with mean D of 2.5 ± 9.5 mmHg ($p = 0.0008$); 3) pulse BP changed significantly in both groups as well: mean D in DM was 6.5 ± 22.5 mmHg ($p = 0.001$) and mean D in nonDM was 3.7 ± 15.2 mmHg ($p = 0.0003$).

Conclusions: We confirmed significant changes in BP values measured before vs after the beginning of on-line haemodiafiltration sessions. Reasons for that could be speculated, because of no volume changes in the beginning of HDF the emotional stress could play a role. Therefore, only the BP measurement performed before the HDF session should be taken as baseline value. It is of interest that the BP increased in a relative high percentage of patients. Surprisingly, the BP changes were more pronounced in nonDM patients

Introduction and Aims: A lot of controversies exist concerning the correct time of blood pressure (BP) measurement while starting the dialysis session. We tested a hypothesis whether there is any difference in taking the BP before or after starting the haemodiafiltration session.

Methods: 25 end-stage renal disease patients were enrolled in the study. All patients were on chronic

Asymmetrical Dimethyl Arginine (ADMA) and Mortality in Patients with End-Stage Renal Disease: A Long-Term, Multicenter, Prospective Study

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Introduction and Aims: The nitric-oxide synthase inhibitor ADMA induces endothelial dysfunction and atherosclerosis in experimental models and high plasma ADMA levels predicts death and adverse cardiovascular (CV) outcomes in the general population and in patients with CV diseases. In ESRD only two cohort studies totalling 443 patients tested the prediction power for death

of this methylarginine. Because external validation of observational studies in diverse populations is important to confirm the link between purported risk factors and adverse outcomes, we set out a prospective study in a large prevalent-incident cohort of hemodialysis patients.

Methods: The relation between plasma ADMA concentration (by liquid chromatography tandem mass spectrometry) and mortality was tested in 288 patients on chronic dialysis, 163 males and 125 females, 42 of whom (15%) were diabetics. Mean age at enrolment was 58 ± 16 years; 270 were being treated by hemodialysis and a small minority ($n = 18$) by peritoneal dialysis. The follow-up was 56 ± 28 months (range 1–91).

Results: Mean plasma ADMA concentration was 1.15 ± 0.34 $\mu\text{Mol/L}$ in ESRD and in 109 patients (37.8%) it exceeded the upper limit (1.17 $\mu\text{Mol/L}$) of the normal range (500 subjects in the general population). During the follow-up, 140 patients died, 70 (50%) by cardiovascular causes. On univariate analysis, plasma ADMA con-

centration was weakly related to age ($r = 0.14$, $p < 0.02$) and to plasma arginine ($r = 0.27$, $p < 0.001$) and Symmetrical Dimethyl Arginine (SDMA, $r = 0.27$, $p < 0.001$) concentrations. On univariate Cox regression analysis, overall mortality was directly related with age, diabetes, previous CV events (all $p < 0.001$), plasma ADMA [hazard ratio (HR) (0.5 $\mu\text{Mol/L}$ increase): 1.44, 95% CI: 1.14–1.81, $p = 0.002$] and inversely related with albumin [HR (1 g/dL increase): 0.52, 95% CI: 0.37–0.72, $p < 0.001$]. Results of the multivariate Cox model (including all univariate predictors of death) are shown in the table.

Conclusions: These data confirm that circulating ADMA is a strong and independent predictor of overall mortality in ESRD patients. Given the exceedingly high risk for death of this population, clinical studies aimed at reducing the high levels of ADMA in this population are a research priority in order to see whether such an intervention may increase survival and limit morbidities in ESRD patients.

Table: Multivariate Cox Model for Predictors of Death

	Unit of increase	HR 95% IC	p
Diabetes	0 = no; 1 = yes	2.04 (1.36–3.07)	< 0.001
Albumin level	1 g/dL	0.52 (0.37–0.75)	< 0.001
Age	1 year	1.04 (1.02–1.05)	< 0.001
Treatment modality	0 = HD; 1 = CAPD	2.62 (1.41–4.85)	0.002
ADMA	0.5 $\mu\text{Mol/L}$	1.37 (1.08–1.74)	0.01
Previous CV events	0 = no; 1 = yes	1.37 (0.90–2.08)	0.14

Improvement of Dialysis Quality According to Legally Advised Benchmarking in Germany

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Introduction and Aims: In Germany all private dialysis units are legally obliged to follow guidelines on quality outcome starting from June 2006. Each unit has to prove the quality delivered to their patients by participating in a benchmarking system and regularly providing the local *Kassenärztliche Vereinigungen* with key data on dialysis treatment. 4 key indicators on dialysis adequacy and anaemia have to be provided on a quarterly basis. Defined targets of $\text{spKt/V} \geq 1.2$, treatment time ≥ 240 min, frequency ≥ 3

sess/wk and $\text{Hb} \geq 10$ g/dL have to be achieved in 85% of patients. In 2003 some units already started with the benchmarking system EuCliD voluntarily. This study investigated the effect of benchmarking on quality improvements in those German units.

Methods: The 4 key indicators were selected as quality markers. Data were collected prospectively in 40 German units using the database EuCliD. 4400 prevalent HD patients on dialysis for more than 90 days from Dec 2000 to Nov 2006 were followed for 4 years. Indicators were evaluated by quarterly means (\pm SD) starting with the 1st quarter (Q1) after implementation of benchmarking. Significance ($p < 0.01$) was tested by one-way ANOVA (SPSS 14).

Results: Mean age at admission to the units was 63.4 ± 15.1 yrs (males: 56.6%), time on dialysis 3.7 ± 2.7 years. With an incremental percentage of obese patients (BMI $M > 27.8$; $F > 27.3$ kg/m²: 34.7 vs 38.1%) dry body weight and BMI increased from 74.6 ± 15.4 to 75.4 ± 17.4 kg and 26 ± 5 to 27 ± 6 kg/m², resp.

(BMI $p < 0.01$). Mean prescribed time was longer in Q8, Q12 and Q16 ($p < 0.01$) than in Q1. The increase was accompanied by a growing proportion of patients treated ≥ 4 h and a higher proportion on ≥ 3 sess/wk. Significantly higher spKt/V values were reached in Q8, Q12 and Q16 ($p < 0.001$). At the same time a higher proportion of patients achieved the $\text{spKt/V} \geq 1.2$. There was a significant increase in Hb over the observation period with a nonsignificant increase of the number of patients with $\text{Hb} \geq 10$ g/dL.

Conclusions: 1 year after implementation of the benchmarking system EuCliD first improvements were observed. After 4 years the threshold of 85% of patients was achieved for all 4 indicators. Despite the increasing trend in body weight and BMI the Kt/V target was reached. As EuCliD evaluates more than 4 key indicators, it delivers an even more sophisticated analysis for assessment of dialysis quality than required by German regulations. Benchmarking is able to support further improvements in quality of dialysis.

Quarters	Q1	Q4	Q8	Q12	Q16
Treatment time (min)	255 \pm 36	255 \pm 44	256 \pm 34	263 \pm 37	265 \pm 2
Patients on ≥ 240 min/sess.	88.2%	83.7%	88.5%	92.8%	94.7%
No. of sess/week	2.91 \pm 0.49	3.01 \pm 0.48	2.98 \pm 0.18	3.02 \pm 0.29	3.02 \pm 0.53
Patients on ≥ 3 sess/wk	92%	94%	97%	98%	94%
Mean spKt/V	1.34 \pm 0.37	1.32 \pm 0.38	1.36 \pm 0.36	1.42 \pm 0.39	1.49 \pm 0.53
Kt/V of ≥ 1.2	66.2%	63.2%	72.1%	78.7%	84.6%
Mean Hb (g/dL)	11.5 \pm 1.32	11.6 \pm 1.38	11.6 \pm 1.32	11.7 \pm 1.32	11.5 \pm 1.38
Hb ≥ 10 g/dL	88.8%	87.3%	88.7%	90.2%	87.9%

Standardising Estimated Glomerular Filtration Rates (eGFR): Do Laboratory Methods Really Matter in Practice?

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Introduction and Aims: Chronic kidney disease (CKD) guidelines have focused on the utility of the modified 4-variable MDRD equation (traceable by isotope dilution mass spectrometry IDMS). This formula accounts for variance in creatinine measured by an analyser different to that used when the original MDRD equation was devised.

To assess theoretically and in practice the effect sizes of IDMS correction over the 4-variable MDRD equation in eGFR calculation with a range of UK creatinine methods and the subsequent impact of this on CKD prevalence.

Methods: MATLAB was used to generate a range of creatinine data (30–300 $\mu\text{mol/l}$) for male and female patients aged 20–100 years. The maximum differences between the IDMS and MDRD equations for all 14 UK laboratory techniques were explored with an averaged (IDMS + MDRD)-eGFR less than 60 ml/min and also 30 ml/min. Similar procedures were applied to 712,540 samples (reflecting 5 creatinine methods in Northern Ireland), belonging to patients 18 years+, to explore graphically maximum differences in techniques. CKD prevalence using both estimation equations was compared.

Results: Simulated creatinine data indicate that the majority of creatinine procedures in the UK demonstrate small differences between the IDMS and MDRD methods in

stages 4 and 5 CKD (where the averaged maximum difference for all laboratory methods was 1.27 ml/min for females and 1.59 ml/min for males). The MDRD equation deviated furthest from the IDMS results for the Endpoint Jaffe method: the maximum difference of 9.93 ml/min for females and 5.42 ml/min for males occurred at extreme ages and in those with eGFR reflecting stage 3 or higher disease. The real data graphically agreed with the theoretical results.

Using existing data 93,870 patients yielded a first MDRD eGFR < 60 ml/min in 2001. 66,429 (71%) had a second test > 3 months later of which 47,093 (71%) continued to have an eGFR < 60 ml/min. This resulted in an estimated crude prevalence of 3.97% for laboratory detected CKD in adults using the MDRD equation which reduced to 3.69% when applying the IDMS equation. Over 95% of this difference in prevalence was explained by older females with stage 3 CKD with data close to the stage 2 interface reemphasizing the need for further research into the sub-categorisation of stage 3 CKD.

Conclusions: Improved accuracy of eGFR is obtainable by using IDMS corrected eGFR especially in early stage CKD; however our data suggests this will have little practical impact on stages 4–5 considering the current referral guidelines.

3. Outcome and Mortality in Dialysis Patients

Factors Associated with Mortality in the First Year After Initiating Hemodialysis: Results from a Multicenter, Prospective, Observational Cohort Study (ANSWER)

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Introduction and Aims: The ANSWER observational study was designed to identify risk factors associated with morbi-mortality in incident haemodialysis (HD) patients.

Methods: From October 2003 through September 2004, 2,341 evaluable patients across Spain were enrolled in this 24-months,

multicenter, prospective, observational cohort study. Using bivariate and multivariate model analyses, baseline characteristics of the patients who died during the first year of follow-up were compared with patients still alive.

Results: Twelve months after HD initiation, 267 patients (11%) had died; CV disease was the main cause of mortality (42%). Patients who died within the first year of HD initiation were significantly older, with lower mean Karnofsky score and higher mean Charlson score than those still alive. Other factors that were significantly

associated with 1-year mortality included previous history of diabetes, malnutrition, ≤ 6 months of follow-up by a nephrologist, use of a catheter for vascular access and anemia (table 1).

Using a multivariate model (table 2), malnutrition and use of a catheter for vascular access were statistically significant with almost double the risk of mortality.

Conclusions: Mortality of incident HD patients in the first year was influenced primarily by baseline general health status, malnutrition and type of vascular access used in HD patients.

Table 1: Comparison of demographic and clinical characteristics between the two populations

	Pts alive at 12 months (N)	Mean (SD) (%)	Pts dead within 12 months (N)	Mean (SD) (%)	p-value	Effect size	CL 95 min	CL 95 max
Baseline characteristics								
Age (Yrs)	2,069	64.3(14.7)	267	72.5 (9.9)	< 0.001	-8.149	-9.5	-6.8
BMI, kg/m ²	1,826	26.7 (5.2)	224	25.6 (5.9)	<0.001	1.142	0.33	1.95
Charlson Score	1,988	4 (1.8)	261	5 (2.1)	<0.001	-1.009	-1.3	-0.77
Karnofsky Score	1,916	76.9 (15.1)	245	61.2 (16.5)	<0.001	15.732	13.7	17.8
Diabetes Mellitus	2,022	34.6%	263	46.8%	<0.001	-12.1%	-19	-6
Diabetic Nephropathy (main reason for CKD)	2,018	25.0%	262	35.1%	0.001	-10.1%	-16	-4
Anemia (Hb<11g/dL)	1,981	56.6%	252	66.3%	0.004	-9.6%	-16	-3
Malnutrition	1,988	9.4%	258	24.8%	<0.001	-15.4%	-21	-10
Previous CV Events	2,074	47.5%	267	64.4%	<0.001	-16.9%	-23	-11
HD Intolerance	1,743	4.6%	227	12.3%	<0.001	-7.7%	-13	-4
Nephrologist follow-up (≥ 6 months)	1,957	76.1%	255	62.7%	<0.001	13.4%	7	20
Vascular Access (Catheter)	1,878	43.6%	246	69.1%	<0.001	-25.5%	-31	-19

Mean (SD) for quantitative variables and % for qualitative variables. If not otherwise stated, in qualitative variables the category shown is 'Presence'

Table 2: Significant variables influencing one-year mortality identified by a multivariate analysis

	B	S.E.	Wald	df	Sig.	Exp (B)	95 CI for Exp.(B)	
							Lower	Upper
Age	0.30	0.007	17.63	1	0.000	1.031	1.016	1.046
Karnofsky Score	-0.048	0.005	85.836	1	0.000	0.953	0.943	0.963
Vascular Access: Catheter vs. AVF	0.822	0.183	20.156	1	0.000	2.275	1.589	3.257
Malnutrition: yes/no	0.687	0.347	3.915	1	0.048	1.987	1.006	3.922
Vascular Access Type by Malnutrition	-0.247	0.410	0.364	1	0.546	0.781	0.350	1.744

B = Beta coefficient – indicates the sense of the association between the dependent and the corresponding independent variable; SE = Standard error; Wald= Wald Statistical Test – it is used to determine the coefficient signification; df = degrees of freedom – associated to the Wald statistical test; p-value = significance – if $p < 0.05$ the variable has statistical significance with a 95% confidence; Exp (B) = exp (B coefficient) – gives the effect size of the variable and is equivalent to the odds ratio (OR); 95%CI = for Exp (B) – 95% Confidence Intervall for effect size (if they contain the 1, variable's effect is not significant)

Malnutrition, Inflammation and Cardiovascular Diseases Interact and Strongly Predict 7-Years Mortality in a Prospective Cohort of Dialysis Patients

Best Abstracts Presented by Young Authors

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Introduction and Aims: Malnutrition, inflammation and cardiovascular diseases (CVD) are highly prevalent comorbid conditions and clearly contribute to the high mortality in dialysis patients. A pathophysiologic association between these three conditions has been proposed, which has

been referred to as the malnutrition, inflammation and atherosclerosis (MIA) syndrome. The aim of this study was to examine the biologic interaction between these three components of the MIA syndrome in the association with mortality.

Methods: In a prospective multi-centre cohort study all incident dialysis patients ≥ 18 years had been included between 1997 and 2005 in The Netherlands (NECOSAD). Data were collected at three months after the start of dialysis (baseline) and subsequently every six months until a maximum of 7 years of follow-up. The presence of malnutrition was defined as a score of 1–5 on the 7-points SGA scale. The presence of inflammation was defined as CRP ≥ 10 mg/L. Cardiovascular comorbidity at baseline had been reported by the patients' nephrologists. The MIA syndrome was defined as the concurrent presence of malnutrition, inflammation and CVD at the baseline of the study. Patients were categorised based on having no, one, any combination of two or all three MIA components. With Cox regression analysis, hazard ratios (HR) were calculated for 7-years all-cause mortality and adjusted for age, gender and treatment modality. The presence of biologic interaction between components was determined, based on additivity of effects.

Results: In total, 817 patients had complete data on SGA, CRP and

CVD at baseline (age: 59 ± 15 years, 60% male, 65% HD). Of all patients, 38% had no MIA components, 35% had one (11% inflammation, 10% malnutrition and 14% CVD), 21% had any combination of two components. Only 6% of the patients had all three MIA components. Overall, the 7-years all-cause mortality was 66%. Compared to no components, patients with either inflammation (HR: 1.6, 95%-CI: 1.1–2.5), malnutrition (HR: 1.9, 95%-CI: 1.2–2.8) or CVD (HR: 2.2, 95%-CI: 1.6–3.2) had an increased mortality risk. Having two components showed only moderate biologic interaction. Patients with all three complications had a HR of 5.3 (95%-CI: 3.5–8.1; expected HR = 3.7), indicating that 31% of deaths among patients with MIA was attributable to the interaction of the three components.

Conclusions: A low proportion of patients suffered from three components of the MIA syndrome at the start of dialysis. Patients with one or two components had an increased mortality risk. Interestingly, the presence of all three components increased the mortality risk strikingly more than expected based on the single components of the MIA syndrome. The clinical implications of this research are that it provides prospective evidence for existence of the MIA syndrome in dialysis patients, and that dialysis patients at especially high risk can be identified.

Choice of Initial Modality of Chronic Dialysis Treatment and Effect on Survival

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Introduction and Aims: Several studies investigated the factors related to the chronic dialysis (CD) modality choice and the outcomes of patients starting with hemodialysis (HD), hemodiafiltration (HDF) and peritoneal dialysis (PD). However, few studies were performed using data derived from an area-based registry. The aim of the study is to evaluate the factors influencing the CD modality choice and the effect of first type of dialysis on patients survival.

Methods: Prospective cohort study of 8,122 patients undergoing chronic dialysis notified to Lazio Dialysis Registry (Italy) from 1-1-1995 to 31-12-2005. We performed a multinomial logistic regression to estimate determinants of choice of initial modality of CD, and a multiple Cox model to estimate mortality hazard ratios (HR).

Results: We observed 90.4% HD, 2.2% HDF, 7.3% PD as first dialysis modality; an older mean age in HD patients (64.2 ± 15.8 years), compared to HDF (55.6 ± 17.4 years) and PD (58.5 ± 18.6 years). A higher probability of initiation with HD compared both HDF and PD was found for: age > 64 years (OR 3.50; 95%CI 2.40–5.11 and OR 1.52; 95%CI 1.25–1.85), cancer (OR 2.59; 95%CI 0.94–7.13 and OR 1.88; 95%CI 1.17–3.04). A higher probability of initiation with HD compared to PD was found for vasculopathy (OR 1.40; 95%CI 1.04–1.88) and compared to HDF for women (OR 1.68;

95%CI 1.17–2.43). A higher probability of initiation with HDF compared to HD was found for coronary heart disease (OR 1.54; 95%CI 1.02–2.33) and congestive heart failure (OR 1.71; 95%CI 1.03–2.84) and compared to PD for HCV positive subjects (OR 2.16; 95%CI 1.14–4.09). A higher probability of initiation with PD compared both HD and HDF was found for patients with self-sufficiency (OR 2.12; 95%CI 1.67–2.69 and OR 2.09; 95%CI 1.33–3.29). A higher probability of initiation with PD compared to HD was found for coronary heart disease (OR 1.36; 95%CI 1.06–1.73) and hypertension (OR 1.47; 95%CI 1.22–1.76) and compared to HDF for women (OR 1.85; 95%CI 1.24–2.77) and age > 64 years (OR 2.30; 95%CI 1.52–3.49). No difference in survival was found between patients starting with HD or HDF (HR 1.04; 95%CI 0.78–1.38) and PD (HR 1.10; 95%CI 0.94–1.29).

Conclusions: Our findings seem to suggest that evaluation of clinical condition and patient's autonomy are determinants of choice of initial modality of CD treatment. However, as we confirm no association between long-term survival and first dialysis modality, the preference of the patients should have more relevance in the choice of first type of CD treatment.

Patient Survival in Haemodialysis and Peritoneal Dialysis: Influence of the Actual Treatment Received

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Introduction and Aims: The relative advantages of haemodialysis and peritoneal dialysis on mortality remain unclear. Our objective was to compare patient survival in haemodialysis and peritoneal dialysis.

Methods: A cohort of all patients starting renal replacement therapy between 1991 and 2002 in five Spanish regions (Andalusia, Asturias, Basque Country, Cantabria, and Valencian Community) reporting to their regional renal registries was gathered (MIRCA study). Information was collected on primary renal disease (diabetes, glomerulonephritis, hypertension/renal vascular disease, and others), date of commencement of renal replacement therapy, and dates of changes in therapy modalities. Statistical analysis of time from therapy commencement to death was done using proportional hazard regression models (Cox models) adjusted for gender, age, calendar year, region, and primary renal disease. Two analyses are presented: analysis of first treatment received, ignoring subsequent events until death, and analysis of actual treatment received, in which treatment modalities were included in the models as time-dependent covariates so that every patient contributed for each modality during the time he or she received it.

Results: Among 23,237 patients (mean age 58.4 ± 16.5 years, 60% male, 16% diabetes, 18% glomerulonephritis, 16% hyper-

tension/renal vascular disease), with median follow-up 2.9 years (interquartile range, 1.2–5.5 years), 9,429 died (9.67 deaths per 100 person-years). In the analysis as first treatment received, the adjusted hazard ratio for death (HR) in haemodialysis compared with kidney transplant was 2.06 (95% CI: 1.66, 2.30) and in peritoneal dialysis 2.22 (1.77, 2.48). The adjusted HR of peritoneal dialysis compared to haemodialysis was 1.07 (1.00–1.11). In the analysis of actual treatment received, compared with transplant, the adjusted HR were 6.97 (5.23–9.29) for haemodialysis and 7.12 (5.36–9.45) for peritoneal dialysis. The adjusted HR of peritoneal dialysis compared with haemodialysis was 1.05 (0.75–1.47).

Conclusions: Whereas patient survival seems to be slightly better for haemodialysis than for peritoneal dialysis when only the first dialysis treatment received is considered, once the actual dialysis modalities received in time are taken into account there is not much difference between them although it remains some uncertainty. On the other hand, the benefit of transplant over dialysis is far more remarkable when analysed according to the actual received treatment for chronic kidney disease, independently of other major prognostic factors such as age, gender and primary renal disease.

4. Technical Aspects of Dialysis

The Impact of the Quality of Hemodialysis Water on Chronic Inflammation and its Consequences

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Introduction and Aims: Chronic inflammation is encountered in 50–75% of HD patients and is one of the non-traditional risk factors with proven impact on cardiovascular morbidity and mortality of this population.

If endogenous sources of inflammation are difficult to control, the exogenous ones – related to the HD procedure (e.g. membrane biocompatibility, hemodialysis water) – seem to be more easily influenceable.

We evaluated the impact of improved quality of HD water on inflammation, anemia control and serum albumin level.

Methods: The water treatment and distribution system of our center (microfilters, activated carbon filters, softeners, reverse osmosis and the tubing system) were replaced and Diasafe filters were centrally put in place, in May 2005.

Mean values of inflammation markers (serum CRP), anemia control parameters (hemoglobin level, EPO dose, iv iron dose) and serum albumin level in two periods of three months, before changing the water treatment system and six months thereafter, were compared in 180 chronic, stable HD patients.

Results: Baseline patient characteristics: 56% men, age 52.3 ± 13 years; no one with diabetic nephropathy. The mean HD duration was 8.3 ± 6.8 years (1–26 yrs.); 30% of patients were on HD for more than 10 years and 9% for more than 20 years.

High-flux biocompatible membranes (polysulphone) and bicarbonate solution were used for HD, both before and after the change of the water station. The HD parameters were stable: blood flow 200–300 mL/min, dialysate flow 500 mL/min, three 4.5-hours HD sessions/week and the mean eKt/V was unchanged (1.4 ± 0.3 vs. 1.3 ± 0.4).

Before the change of water treatment system, the analysis of the

water for dialysis constantly revealed low microbial contamination – mean 18 colonies/mm³ (2–50 colonies/mm³), but was germ-free thereafter.

CRP levels were less than 10 mg/L in 80% of patients at both times analysed. The use of germ-free water doubled the proportion of patients with lower than 3 mg/dL CRP levels (57 vs. 27%) and significantly increased the proportion of those with undetectable CRP (17 vs. 0%).

The national Hb targets (10.5 g/dL) were reached by 72% of patients before changing the water treatment system, while the proportion increased to 83% six months thereafter. The mean EPO dose decreased significantly by 16%, from 77.3 ± 41.3 to 66.5 ± 50.9 IU/kg per week, without variation in iron requirements (126.9 ± 105 vs. 131.6 ± 114 mg/patient per month). Mean serum albumin level was significantly higher (3.98 ± 0.3 vs. 3.86 ± 0.3 g/dL) and fewer patients had a serum albumin level below 4 g/dl (44.3 vs. 59.6%).

Conclusions: Improving the quality of HD water could significantly reduce the proportion of patients with chronic inflammation, resulting in a significant increase in serum albumin levels and in the percentage of patients reaching the Hb targets, despite of a decrease in erythropoietin requirement.

A Novel Highly Efficient Bio-Assay to Monitor Microbiological Purity of Dialysis Fluids

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Introduction and Aims: Microbial contamination of the dialysis fluid has a pro-inflammatory potential. The increased application of high-flux hemodialysis and on-line hemodiafiltration has made the need for ultrapure dialysis water even more stringent. Classical test methods for bacteriological contamination, such as bacteriological cultures or the Limulus Amebocyte Lysate (LAL)-test, fail to detect a substantial number of contaminants with intact lipopolysaccharide (LPS) as the only exception.

Methods: We developed a novel bio-assay for dialysis water contaminants using a monocytic THP-1 cell line. After a 24h rest period, calcitriol (10 nM)-differentiated (72 h) THP-1 cells, were incubated overnight (24 h), in the presence of dialysis fluid samples (1/1) or samples containing potential activating microbiological agents. Secretion of IL-1 β (pg/ml) was detected in the cell culture supernatant as a parameter of biological activity of the dialysis fluid. To validate the sensitivity of this test method to various types of contaminants, response to peptidoglycan (PGN), short bacterial DNA fragments and LPS fragments was compared to the response observed with the LAL-test.

Results: The presence of peptidoglycan (0.1; 1; 5; 10; 50; 100; 500; 1000; 5000 ng/ml) induced IL-1 β secretion from 5 ng/ml on ($p < 0.05$) whereas the classical LAL-test remained unresponsive. Likewise, addition of short bacterial DNA fragments (2006 stimu; 1 μ M and K3; 10 μ M) caused a significant IL-1 β induction but no LAL-response. LPS fragments (MW < 5kD) from *P. aeruginosa* induced no LAL-response, per se, but showed a marked biological activity. Intact LPS induced a significant IL-1 β secretion versus control in a dose dependent manner from a concentration of 0.01 ng/ml on. A comparable evaluation with a biological test based on whole blood emanated in more scattered and/or less sensitive results.

Conclusions: The present data show that this novel bio-assay detects bacteriological derivatives which cannot be found by the classical screening methods. Application of this assay is useful to reveal contaminants which otherwise go undetected aiming at the timely prevention of biofilm formation in the dialysis circuit and micro-inflammation in the hemodialysis patient.

Mortality Risk for Patients Receiving Hemodiafiltration versus Hemodialysis: Results at Two Years from the RISCAVID Study

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Introduction and Aims: RISCAVID (Cardiovascular risk in dialysis) study is an observational and prospective study of the over 800 patients in hemodialysis and peritoneal dialysis of the north-west part of Tuscany. This population is rather peculiar because hemodiafiltration (HDF) is largely used for renal replacement therapy (44%). Characteristics and outcomes at two years were compared for patients receiving HDF versus HD.

Methods: The study followed 757 patients stratified into three groups: standard bicarbonate HD (n = 424), and low- (n = 205) and high-efficiency HDF (n = 128). At the time of the enrolment demographic, clinical and laboratory data of the whole population were registered as well as co-morbidity conditions established by anamnestic and instrumental information. The population was followed up for 24 months reporting overall mortality, CV mortality and CV major non-fatal events (acute myocardial infarction, stroke and ictus). Cox proportional hazards

regression assessed adjusted differences in mortality risk.

Results: Patients receiving standard HD had an higher incidence of diabetes (21.6% vs 16.4% low-efficiency HDF vs 16.0% high-efficiency HDF); patients receiving low and high-efficiency HDF had significantly longer average duration of end-stage renal disease (6.5 and 6.3 versus 5.3 years), patients receiving high-efficiency HDF had significantly more hypertension (60 versus 45% low-efficiency HDF). No significant differences were observed in received single-pool Kt/V (1.40 vs 1.43 vs 1.40). High- and low-efficiency HDF patients had lower crude mortality rates than standard HD patients. After adjustment, high- and low efficiency HDF patients had a significant lower mortality risk than those receiving standard HD (relative risk = 0.78, p = 0.01).

Conclusions: These observational results at two years from the RISCVID study confirm recent findings that HDF may improve patient survival independently of its higher dialysis dose.

Clearance of Urea and Difficult to Remove Uremic Toxins when Modifying Dialysis Time Only

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Introduction and Aims: Several studies already stressed the importance of dialysis time in the clearance of difficult to remove uremic toxins. In those studies, however, the factor time was not the only parameter with a potential impact on adequacy that was modified. Therefore, the present study investigated the isolated effect of the time factor by submitting the same patients to a 4, 6 and 8 hours lasting dialysis session with the Genius[®] system, processing the same blood and dialysate volume.

Methods: Nine stable chronic hemodialysis patients were dialysed on 3 occasions using the Genius[®] single pass batch system (Fresenius MC, Germany) with high-flux FX80 dialyzers. The sessions lasted 4, 6, and 8 hours using blood flows of 350, 250, and 180 mL/min, respectively. For each patient, blood was sampled from the arterial line at 0, 5, 15, 30, 60, 120, 240 min during all sessions, at 360 min during the 6 and 8 h session, and at 480 min during the 8 h session. Dialysate was sampled at the end of dialysis from the ultrafiltrate recipient, of which concentration is representative for total spent dialysate. Samples were analysed for urea, creatinine, phosphorus (P), and beta2-microglobulin (β 2M). Reduction ratios (RR) were calculated at different time points during the

sessions, and Total Solute Removal (TSR) was calculated from spent dialysate concentration and total waste dialysate volume.

Results: RR increased progressively and significantly for urea and creatinine during the entire session, while RR increased slightly for β 2M and remained constant for P from the 120th minute on. At the end of dialysis, no significant differences were found for the RR of all solutes between the different sessions. Mean TSR was found 36,892, 38,561, and 46,320 mg (urea), 934, 1,099, and 1,199 mg creatinine, 621, 753, and 898 mg (P), and 57, 79, and 93 mg (β 2M) for the dialysis session of 4, 6, and 8 hours, respectively. Analysis of variance showed that TSR was significantly larger for protracted dialysis for urea ($p = 0.008$), creatinine ($p < 0.001$), P ($p < 0.001$), and β 2M ($p = 0.006$).

Conclusions: The results indicate that solutes are removed more adequately from the deeper compartments in the patient's body when performing a protracted dialysis, even if blood and dialysate volumes are kept constant. Hence, since solute removal is higher for longer dialysis, the time factor is very important when comparing different dialysis durations, such that care must be taken when using Kt/V_{urea} as parameter to indicate dialysis adequacy.

Crossover Trial of Porous Haemodialysis Membrane Compared to Conventional High-Flux Membrane: Assessment of Middle Molecule Clearance and Nutritional Parameters

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Introduction and Aims: Despite advances in dialysis techniques, uremic toxicity and its detrimental effects on physiological functions remain a major concern. While newer dialysis membranes have been modified making them more biocompatible, reducing the potential for activation of the inflammatory cascade, a further potential modification is to alter the porosity of the membrane to allow greater passage of middle sized molecules. We performed a pilot study to investigate the short-term impact of a more porous dialyser on the clearance of β 2-microglobulin and inflammatory molecules, in addition to monitoring albumin loss.

Methods: The trial was a double-blinded, randomized, cross-over design, in 30 stable haemodialysis patients: 25 male, mean age 59 ± 2.6 years, mean length of dialysis therapy 38 ± 5.0 months, comparing conventional high-flux membranes (FX-60 -polysulfone) with the new porous dialyser (FX-E -polysulfone). Each treatment arm lasted 6 weeks with a 2 week washout period. Other dialysis parameters remained unchanged for the duration of the study. Serum samples were taken at the beginning and end of dialysis and dialysate was collected continuously throughout the dialysis session for albumin concentration.

Results: At the end of treatment the pre-dialysis β 2-microglobulin was 0.07 mg/L lower with the FX-E ($-1.73, 1.59$; $p = 0.93$) which

was not significant, but the post-dialysis β 2-microglobulin was statistically significantly lower with the FX-E by 2.0 mg/L ($-2.54, -1.37$; $p < 0.001$). At the end of the study period the dialysate albumin loss with the FX-E was greater by 25 mg/L at 1 hour ($17.02, 33.40$; $p < 0.001$) and by 10 mg/L at the end of the dialysis session ($7.25, 13.96$; $p < 0.001$). Despite this increased loss, the serum albumin levels were only slightly lower with the FX-E by 0.83 g/L ($-1.60, -0.056$; $p = 0.036$) which is statistically significant, but probably not clinically significant. The pre-albumin levels at the end of treatment were not different, mean difference 26.1 mg/L ($-55.55, 3.35$; $p = 0.08$). There was no significant difference in serum C-reactive protein levels, mean difference 0.22 mg/L ($-4.50, 4.93$; $p = 0.93$).

Conclusions: Our pilot study demonstrates increased clearance of β 2-microglobulin with the more porous FX-E dialyser. Although there is an increased albumin loss in the dialysate, this did not have a large impact on the serum albumin levels and no impact on the serum pre-albumin levels. The FX-E dialyser shows improved middle molecule clearance without causing harmful reduction in albumin levels. A longer trial is needed to ensure these results are maintained over time.

Nocturnal Hemodialysis with the Genius® Dialysis System

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Introduction and Aims: The study investigated the effect of nocturnal hemodialysis (NHD) performed with the Genius® batch dialysis system compared to standard hemodialysis (SHD) on calcium (Ca), phosphorus (P), urea, eKt/V and nPCR. In addition, the impact of nocturnal hemodialysis on the quality of life (QoL) was evaluated.

Methods: Out of 14 stable patients dialyzed thrice weekly with SHD (4–5 h) with FX 80 (n = 12), Diapes BLS 517G (n = 1) and F10 HPS (n = 1) membranes, 6 patients were switched to NHD (8 hours). A control group of 8 patients remained on SHD. During NHD, patients were dialyzed with the Genius® batch dialysis system (90 L) with an FX 80 membrane, blood flow and dialysate flow were 180 mL/min each. A comparison was made between the values obtained immediately before and 4 weeks after the switch. For the control group identical time points were considered and compared. eKt/V_{urea}, urea reduction rate (URR), nPCR and pre-HD serum levels of P, Ca and urea were assessed. The daily dose of phosphate binders, such as Sevelamer and CaCO₃ were noted. All patients completed SF-36 QoL questionnaires at the two time points.

Results: Pre-HD serum levels of P, Ca, urea and nPCR were similar at the two time points for the patients remaining on SHD. In the patients switched on NHD, urea,

nPCR, eKt/V_{urea} (1.32 ± 0.17 versus 1.35 ± 0.13), and URR (70 ± 4 versus 66 ± 4%) remained unchanged. Ca was 9.2 ± 0.5 and 9.3 ± 0.5 mg/dL (NS) at the two time points respectively. Serum P levels, however fell from 5.6 ± 2.1 mg/dL before to 4.3 ± 0.4 mg/dL after the switch to NHD (p=0.026) and the doses of Sevelamer and CaCO₃ tended to decrease from 2.4 to 1.6 g/day and 5 to 4 g/day respectively. The total score of the QoL questionnaire increased from 65 ± 18 to 82 ± 7 % (p = 0.034) during NHD but remained unchanged in the SHD-group.

Conclusions: Serum phosphate levels were better controlled during NHD with the Genius® allowing patients to lower their phosphate binders. Urea removal and nPCR remained unchanged. The QoL improved during nocturnal dialysis.

Effects of Low Sodium Dialysate in Chronic Hemodialysis Patients with Hypertension

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Introduction and Aims: In a limited number of studies including few hemodialysis patients, it has been shown that lowering the level of dialysate sodium (Na) may drop blood pressure. In this study we investigated the effects of two different dialysate Na compounds based on applicable approaches in hemodialysis patients.

Methods: Twenty-four patients undergoing chronic hemodialysis were included in the study on a prospective, crossover and single blinded basis. In those patients with predialysis plasma Na ≥ 137 mEq/L, a dialysate Na concentration of 137 mEq/L was applied, whereas patients with predialysis plasma Na level approximating or lower than 137 mEq/L were given a dialysate Na concentration of 135 mEq/L according to course in 8 weeks. The patients subsequently underwent a hemodialysis procedure with a standard 140 mEq/L dialysate Na for 4 weeks; clinical evaluations of the patients were then made with standard dialysate Na, lower dialysate Na and again standard Na during the last three-dialysis sessions.

Results: The mean blood pressures were significantly lower with lower dialysate Na and after returning to standard dialysate Na when compared to basal level (respectively 181.42 ± 24.20 / 103.18 ± 12.44 , 148.50 ± 15.68 / 93.10 ± 10.25 , 155.24 ± 16.68 / 93.7 ± 87.19 mmHg; $p < 0.00$). The interdialytic weight gain

(IDWG) dropped after lower dialysate Na (2597.58 ± 673.30 , 1756.79 ± 632.77 gr. $p < 0.001$), whereas it increased after standard Na treatment (2597.58 ± 673.30 , 2602.79 ± 807.50 gr.; $p > 0.1$). There was no statistically significant difference between this value and the initial one (2597.58 ± 673.30 , 2602.79 ± 807.50 gr.; $p > 0.1$). Predialysis Na concentrations of the patients dropped when they were given treatment with lower dialysate Na (136.88 ± 1.48 , 132.96 ± 2.07 mEq/L; $p < 0.001$). After the treatment with standard dialysate Na, predialysis Na concentrations increased compared with the initial values (136.88 ± 1.48 , 140.13 ± 2.86 mEq/L; $p < 0.001$). Feeling for thirst decreased after treatment with lower dialysate Na. However, when the patients were treated with standard Na their feeling of thirst increased, no significant difference was observed compared with initial value. During the course of the study, no significant change was observed in the frequency of intradialytic hypotensive attacks.

Conclusions: Lowering dialysate Na in hemodialysis patients according to predialysis Na concentrations decreased IDWG, feeling of thirst and blood pressure. When the patients were given standard Na dialysate treatment again, this positive affect lasted despite increase of predialysis serum Na.

5. Body Fluid Management

A Comparison of Three Different Therapeutic Options in Prevention of Intradialytic Hypotension

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is ultrafiltration (UF) control by Blood Volume Monitor (BVM) along with zero temperature balance by BTM-Blood Temperature Monitor. (BVM and BTM are trademarks of Fresenius, Bad Homburg, Germany). Among medications, positive effects are reported with administration of midodrine (alpha-1 adrenergic receptor agonist) or sertraline (serotonin uptake inhibitor). Those three therapeutic options have not been compared directly in the same group of patients. The aim of this paper was to show our results of comparison of the efficacy of each that protective-therapeutic manoeuvre in the prevention of IDH.

Methods: Ten (6 female, 4 male) chronic (7.3 ± 4.5 years) HD patients (mean age 59.0 ± 20.5 years; range: 28–82) which were prone to IDH (IDH in more than 40% of HD treatments), after first (monitoring) phase (9 standard HD treatments, during 3 weeks) underwent three therapeutic phases in random order in a blinded fashion: B-phase (biofeedback, controlled UF rate by BVM, with zero temperature balance achieved by BVM), M-phase (midodrine, 10 mg per os, 30 min. prior to HD, during 3 weeks), S-phase (sertraline, 50 mg p.o. daily, during 3 weeks). In every phase, for each patient, blood pressure and pulse were measured in the same time periods of HD, and the number of episodes of IDH was noted.

During the study, all patients had their usual dialysis conditions, and

they were asked not to change significantly their usual interdialysis weight gain, medications and life habits.

Results: In the first phase, during 3 weeks and 90 HD treatments, 80 IDH episodes were registered, or 0.89 ± 0.23 episodes per treatment. Individual critical relative blood volume (crit. RBV) was determined for each patient. Mean value of all crit. RBV was 81.1 ± 3.9 % (range 74–87%). In the second part of the study, during B-phase: 27 IDH episodes (0.30 ± 0.25 episodes IDH per treatment), during M-phase: 57 IDH episodes (0.64 ± 0.23 episodes IDH per treatment), and in S-phase: 63 IDH episodes (0.70 ± 0.25 episodes IDH per treatment).

Conclusions: According to the obtained results, we concluded that all three therapeutic options significantly decrease the number of IDH episodes compared to the first or monitoring phase ($p < 0.01$). „Biofeedback“ (with BVM and BTM) control of HD was a more efficient way to prevent IDH than both other (midodrine or sertraline) options ($p < 0.01$), and there was no significant difference between last two therapeutic options ($p > 0.05$).

Introduction and Aims: In spite of all hemodialysis technology advances and despite of all pharmacological and other preventive interventions, intradialytic hypotension (IDH) remains a very frequent complication of hemodialysis (HD) treatment. Most authors report the presence of IDH in 15–30% of all HD treatments. Among technical devices, most promising

Intradialytic Blood Volume Monitoring and its Effect on Haemodynamic Instability

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Introduction and Aims: Haemodynamic instability with symptomatic hypotension constitutes one of the major intradialytic complications in patients on chronic haemodialysis. This occurs because fluid removal during haemodialysis (HD) exceeds the transfer capacity between compartments. A strategy to reduce hypotensive events is to avoid excessive and fast blood volume reductions.

Methods: The authors retrospectively analysed 17 months haemodialysis treatments of 18 end-stage renal patients with frequent hypotensive episodes. There were 14 women, 5 diabetics, mean age 77.8 ± 2.6 years and on maintenance HD for 57 ± 25.7 months. We used Fresenius 4008H delivery systems with a blood volume monitor module.

The study had 5 phases: one month before blood volume monitoring (BVM) (month -1), one, four, seven and fifteen months with BVM haemodialysis. There were several variables evaluated including net UF/HD session, medium blood pressure (mBP), net mBP/HD session (mBP in the beginning of the session minus mBP in last hour of treatment), symptomatic hypotension episodes, Kt/V, phosphorus, albumin and darbepoietin consume.

Results are presented in mean and standard deviation. Statistical analysis was made using Wilcoxon and t-tests for a significance level of $p < 0.05$.

Results: After initiating BVM, even with similar net UF/HD session during that period (month -1: 2274 ± 527 mL vs 15th month: 2247.87 ± 482.24 mL, $p > 0.05$), there was a 30% reduction in net mBP/HD session (month -1: 20.89 ± 19.08 mmHg vs 15th month: 14.85 ± 16.82 mmHg, $p < 0.0005$). The incidence of symptomatic intradialytic hypotension episodes (IHE) was also considerably lower with BVM haemodialysis (0.78 ± 0.63 IHE/patient at month -1 vs. 0.26 ± 0.52 IHE/patient at 15th month, $p < 4 \times 10^{-14}$).

No statistically significant difference was observed in Kt/V, albumin and darbepoietin dosage before and after the introduction of BVM. Phosphorus level declined between months -1 and 15 ($p < 0.03$).

The subgroup of diabetic patients also benefits with BVM, with better haemodynamic stability and less IDH (month -1: 0.79 ± 0.61 IHE/patient vs 15th month: 0.49 ± 0.70 IHE/patient, $p < 0.0031$).

Conclusions: Utilization of blood volume monitors with on-line control of ultrafiltration reduced 77% of the symptomatic hypotensive episodes, with lower mBP variability and without affecting intradialytic water removal. Maximum benefit was obtained after 4 months of treatment and persisted during the 15 months analysed. In the diabetic subgroup the results weren't different.

Differences in Hydration Status between Healthy, Pre-ESRD, Dx and Tx Subgroups can be Distinguished Clearly with Bioimpedance Spectroscopy

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Introduction and Aims: Although it is well known that changes in renal function alter the volume of fluid accumulated in the body, the majority of traditional bedside methods for assessment of fluid status are subjective. The objective of the current study was to evaluate recent developments in body composition analysis that enable excess fluid to be quantified from bioimpedance spectroscopy (BIS) measurements.

Methods: Intracellular water (ICW) and extracellular water (ECW) were measured using BIS (Moissl et al., *Physiol Meas* 27, 2006) in the subgroups of healthy (A), Pre-ESRD (B), Dialysis (C), Transplanted (D). Each group consisted of 50 subjects. The characteristics of these subjects were:

(A) Male = 20, female = 30, age 49 ± 5 yrs, BMI 26.3 ± 4.6 kg/m²

(B) Male = 29, female = 21, age 50 ± 9 yrs, BMI 27.5 ± 6.6 kg/m²

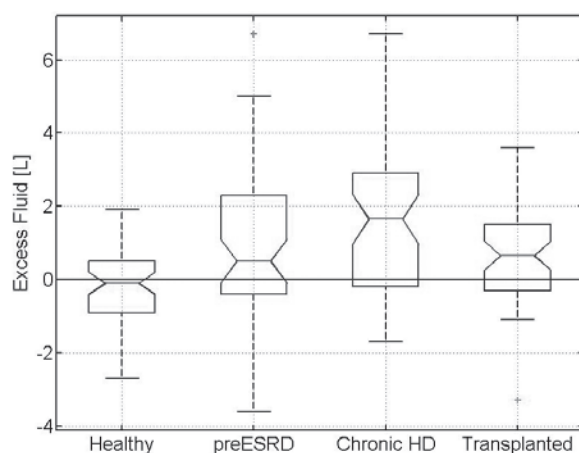
(C) Male = 30, female = 20, age 50 ± 2 yrs, BMI 26.3 ± 5.1 kg/m²

(D) Male = 30, female = 20, age 49 ± 14 yrs, BMI 24.8 ± 3.8 kg/m²

ECW and ICW measurements were combined with body weight information in a model described elsewhere (Chamney et al., *AJCN*, Jan 2007) to calculate the volume of excess fluid (ExF).

Results: The boxplot (Figure) shows the estimation of ExF for the four subgroups. As expected, ExF of healthy subjects is distributed around zero, while ExF in the other groups is significantly greater than zero. There seems to be a trend to increasing ExF from healthy to chronic HD, even if the difference between Pre-ESRD and chronic HD is not significant. ExF of the transplanted group is lower than in chronic HD, but has not reached normal levels.

Conclusions: BIS in combination with an advanced body composition model is an effective method for objective determination of fluid status. Excess fluid is significantly higher in Pre-ESRD and dialysis patients than compared with healthy controls. Transplantation returns fluid status towards the healthy subject range.



Accuracy of Bioimpedance Spectroscopy (BIS) to Detect Fluid Status Changes in Hemodialysis Patients

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Introduction and Aims: BIS is a technique that measures the impedance of body tissues over a wide frequency range and thus allows the accurate assessment of extracellular (ECW) and total body water (TBW) [Moissl et. al., *Physiol. Meas.* 2006]. Based on ECW and TBW the overhydration (OH) of patients can be determined via a fluid and body composition model [Chamney et. al. *Am J Clin Nutr.* 2007]. However, it has yet to be demonstrated how accurately BIS can detect changes in the fluid status. The ultrafiltration volume (UFV) withdrawn from the patient during the hemodialysis (HD) treatment, should be reflected in the change of OH, ECW and TBW, while the intracellular water (ICW), the fat and lean tissue mass (LTM) should remain unchanged.

Methods: 33 hemodialysis patients were measured with BIS before

(T1), at the end (T2), 30 min (T3) and 120 min (T4) after a hemodialysis treatment. The measured UFV was compared for each patient to the measured change in ECW, ICW, TBW, OH, Fat and LTM.

Results: The mean differences in UFV and the measured changes at time T3 are given in the table. Δ OH, Δ ECW were not statistically different to UFV at times T2, T3 and T4. The hypothesis of constancy in ICW, TBW, Fat and LTM was found to be valid at any time greater than 30 min (T3 or T4) after the end of hemodialysis treatment.

Conclusions: The overhydration calculated with the fluid and body composition model accurately reflects changes in the fluid status induced by UFV. BIS measurements should not be performed directly at the end of hemodialysis treatments.

	Mean \pm SD	p-value
UFV	2.5 \pm 0.79 l	
Δ ECW	2.45 \pm 1.12 l*	(p = 0.9p91)
Δ TBW	2.54 \pm 1.40 l*	(p = 0.863)
Δ ICW	-0.09 \pm 0.57 l**	(p = 0.506)
Δ OH	2.44 \pm 1.09 l*	(p = 0.996)
Δ Fat	0.397 \pm 0.90 kg**	(p = 0.506)
Δ LTM	-0.395 \pm 0.95 kg**	(p = 0.174)

* statistically not different from UFV,

** statistically not different from zero

Access Flow Measurement without Injection of Indicator: Reproducibility of the Method

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Introduction and Aims: A new technique to measure access flow without injection of indicator has recently been introduced. The technique is based on measuring the change of extracorporeal temperature or concentration gradients caused by switching the extracorporeal blood line. The technique does not require the injection of indicator. The coefficient of variation of the new technique was evaluated and compared to that of the accepted reference method.

Methods: Access flow was calculated from changes in extracorporeal temperature gradients measured by the blood temperature monitor (BTM, Fresenius Medical Care, Bad Homburg, Germany). Measurements were done during regular hemodialysis treatments using Twister/Combiset blood lines (Fresenius Medical Care, Lexington, MA) which include a switch for the purpose of reversing blood flow without disconnecting the blood lines. In these lines the switch is located between the BTM measuring heads and the dialyzer (in a distal position to the BTM). This is different from the position of the manual switch which is done in a proximal position to the BTM. The change in position has consequences with regard to the temperature changes measured in the extracorporeal circulation and with regard to the calculation of access flow. Therefore, the equation to calculate access flow has to be modified. Access flow (Q_a) was calculated as $Q_a = (T_{ven,x} - T_{art,x}) / (T_{art,n} - T_{ven,x}) \times (Q_b - UFR)$ where T_{art} and T_{ven} refer to arterial and venous line temperatures extrapolated to the level of the access, Q_b and UFR refer to blood and ultrafiltration flows, and where the indices n and x refer to normal and reversed line positions, respectively.

Access flow was measured early in dialysis using the new technique and saline dilution (HDM02, Transonic Systems Inc., Ithaca, NY) as

a reference method. For the duration of access flow measurements, dialysate temperature was set to 35°C. As required by the reference technique blood flow was set to 300 mL/min for the duration of all access flow measurements. Techniques were used alternately within the same treatment and measurements were done in triplicate.

Results: The mean access flow measured in nine studies was 874.6 mL/min (range 540 to 1221 mL/min) with a coefficient of variation of 7.4% for the new temperature gradient technique compared to 947.4 mL/min (range 520 to 1293 mL/min) and a coefficient of variation of 5.1% for the reference method. The mean bias between techniques was -71 mL/min.

Conclusions: The close agreement for average access flow and comparable coefficients of variation for both techniques show that the new approach which does not require the injection of indicator could be an interesting alternative to current access flow technology.

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