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World Congress of Nephrology
May 22–26, 2009, Milan, Italy




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1. Anemia

Target Level of Hemoglobin Correction and the Influence on Renal Function for Chronic Kidney Disease (CKD) Patients not on Dialysis

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Introduction and Aims: Erythropoiesis stimulating agent (ESA) is widely used for the correction of anemia in CKD patients, but therapeutic hemoglobin (Hb) target in CKD patients not on dialysis is still under debate and clinical evidences are few. We previously reported that in a one year randomized controlled trial (RCT) in which we divided CKD patients not on dialysis into two different Hb target groups, improvement in QOL and left ventricular hypertrophy in the higher targeted Hb group was observed. Furthermore, there was no cause of concern in safety. In order to evaluate the correlation of high Hb level and renal function, further studies are required. So we conducted an additional two-year follow-up study for patients who completed the study reported above.

Methods: In this RCT, we enrolled CKD patients not on dialysis who had Hb levels under 10g/dL and serum creatinine levels above 2 mg/dL to under 6 mg/dL. We assigned two groups, patients receiving darbepoetin alfa targeted to achieve Hb level of 11.0 to 13.0 g/dL (high Hb group) and those receiving recombinant human erythropoietin to achieve Hb level of 9.0 to 11.0 g/dL (low Hb group). The primary endpoints were cumulative renal survival rate (a

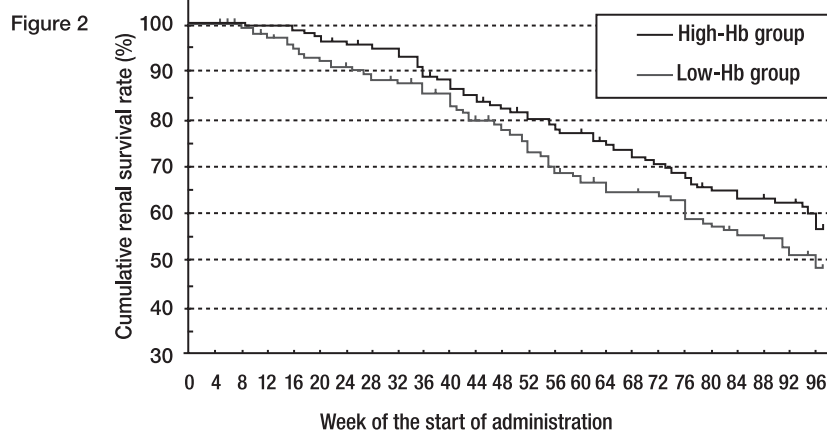
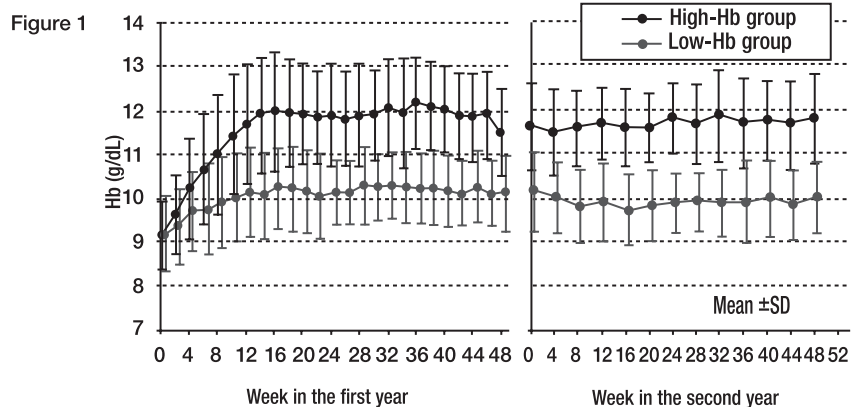
composite of death, doubling of serum creatinine, infusion of renal replacement therapy and renal transplantation) and safety. In this report we present the two-year intermediate result.

Results: A total of 321 patients were randomly assigned to high Hb and low Hb group. There was no significant difference in the mean Hb and serum creatinine at baseline between the two groups. Hb level transition was maintained at target range in both groups throughout the two years (Figure 1). The cumulative renal survival rate evaluated by Kaplan-Meier in year one was 81.4% in high Hb group and 77.9% in low Hb group ($p=0.361$). Additionally, the result of year two was 56.6% and 48.0% respectively ($p=0.103$) and although

there was no significant difference, renal survival rate was higher in the high Hb group (Figure 2).

The serious adverse events that occurred were 42.9% in the high Hb group and 48.8% in the low Hb group. Those associated to cardiovascular were 34.2% and 36.3% respectively and there was no significant difference.

Conclusions: High Hb group had better outcomes in cumulative renal survival rate although it was not significant. The difference between the two groups is expanding with time and further results of the study are expected. For safety, there was no significant difference between the two groups. These results suggest that 11.0 to 13.0 g/dL is the appropriate Hb target for CKD patients not on dialysis.



Haemoglobin Variability is not an Independent Predictor of Mortality in a European Haemodialysis Population: Results from the ARO Study

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Introduction and Aims: Haemoglobin (Hb) variability is a common phenomenon in haemodialysis (HD) patients, but it remains unclear whether this impacts on future clinical outcomes. The aim of this study was to evaluate the association between Hb variability and mortality in a large European HD population.

Methods: In an open-cohort design, 11,153 patients were randomly selected from 172 Fresenius Medical Care facilities between

Jan 2005 and Dec 2006 (n=7,037 prevalent, n=4,116 incident) and met study inclusion criteria. Hb variability was measured using standard methods: standard deviation (SD), time spent in target (11–12 g/dL), and categories as previously defined by Ebben et al. (table). We also applied a novel method which takes into account both amplitude and duration of excursion of each Hb cycle in a quantitative index which measures the area under the curve (AUC). Hazard ratios for all-cause and cardiovascular disease (CVD)-related mortality were derived using multivariable Cox regression, adjusting for demographics, medical history, dialysis parameters, medications, laboratory tests, markers of inflammation, hospitalisation, change in vascular access and ESA use. Assessment of the at-risk population started after 6 months of Hb measurements were collected. Subsequently, patients were followed for up to 18 months until death, transplantation, lost to follow-up or study completion. Patients with bleeding episodes or blood transfusions during the 6-month exposure period were excluded.

Results: A total of 4,988 patients with at least 6 continuous monthly Hb measurements were included in these analyses. Multivariable Cox regression showed that SD (Q4 v Q1: HR=1.10, 95%CI=0.84–1.43), time spent in target (Q4 v Q1: HR=0.76, 95%CI=0.56–1.03) and AUC (Q4 v Q1: HR=0.98, 95%CI=0.75–1.27) were not predictive of increased mortality. Likewise, patients who were consistently high (CH) (HR=1.82, 95%CI=0.85–3.88), LAH (HR=1.40, 95%CI=0.77–2.57), LAL (HR=1.75, 95%CI=1.00–3.04), and HA (HR=1.52, 95%CI=0.88–2.64) did not experience an increased risk. However, patients with consistently low (CL) levels of Hb (<11 g/dL) had over twice the risk of death (HR=2.36, 95%CI=1.25–4.45) compared to patients consistently on target (CT). Results for CVD-related mortality were concordant with those for all-cause mortality.

Conclusions: Hb variability is not an independent predictor of mortality in this European HD population. This is in contrast to previous findings which were derived mainly from HD populations in the United States.

Definitions of Ebben Categories (Ebben et al., Clin JASN 1:1205, 2006)

CT consistently on target (Hb levels consistently between 11–12.5 g/dl)

CL consistently low (Hb<11 g/dl)

CH consistently high (Hb>12.5 g/dl)

LAH low-amplitude fluctuation with Hb levels > 11 g/dl

LAL low-amplitude fluctuation with Hb levels < 12.5 g/dl

HA high-amplitude fluctuation (Hb ≤ 11 to ≥ 12 g/dl)

Hemodialysis Patients who Maintain Higher Hemoglobin Concentration without ESA Treatment: Prevalence, Characterization, and Mortality, in the DOPPS

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Introduction and Aims: The optimal target haemoglobin (Hb) for patients undergoing HD remains unclear. Practice guidelines and instructions from ESA manufacturers caution against Hb > 12 g/dL. However, a subset of patients maintain higher Hb in the absence of ESA prescription. This study characterizes these patients and their mortality rate.

Methods: Analyses included 33,959 patients from the Dialysis Outcomes and Practice Patterns Study (DOPPS), an observational study of HD patients in Australia/New Zealand (ANZ), Belgium, Canada, France, Germany, Italy, Japan, Spain, Sweden, UK, and US. Data were collected from 1996–2008, with median follow-up of 1.7 years. Patients who entered the study with 2 consecutive 4-month periods of no prescribed ESA and Hb \geq 12 g/dL were defined as 'Endogenous Epo patients' and were compared to all Others (patients receiving ESA exogenously or Hb < 12 g/dL). Cox models were used to assess the relative risk (RR) of mortality. Models were adjusted for age, sex, race, vintage, hemoaccess type, 14 comorbidities, Kt/V, PTH, and cause of ESRD, and were stratified by region and phase of study.

Results: Approximately 2–3% of HD patients maintain Hb \geq 12 g/

dL without ESA. The prevalences were highest in Germany and Italy (4–5%) and lowest in the US (1–2%). Differences in patient characteristics are shown in table 1.

Death rates were 12.1/100 patient-year for Endogenous EPO; 15.8 for Other. Unadjusted RR of mortality for Endogenous Epo vs Other patients = 0.80 (P<0.01). After adjusting (see Methods), RR=0.95 (P=0.55). Adjusted RR comparing Endogenous Epo patients with only Others whose Hb was 10–12 g/dL = 0.96 (P=0.69). Adjusted mortality risk is significantly lower among Endogenous Epo patients with Hb \geq 14 g/dL vs Hb 12–13 g/dL (RR=0.56, P=0.04) (Table 2).

Conclusions: Endogenous Epo patients comprise 2–3% of HD patients and tend to be younger, male and have fewer comorbidities. Underlying cystic disease is over-represented, but present in only a minority. There is no evidence that Hb >12 g/dL is associated with higher mortality risk in Endogenous Epo patients. In fact the unadjusted RR is lower among the Endogenous Epo group than the Others, but this is likely due to better overall health. Within the Endogenous Epo group, the adjusted mortality risk for those with Hb \geq 14 g/dL vs Hb 12–13 g/dL was significantly lower.

Table 1: Patient Characteristics

	Europe ANZ		Japan		North America	
	Endogenous EPO	Other	Endogenous EPO	Other	Endogenous EPO	Other
Characteristics						
Sample Size	410	14,101	132	6,419	196	12,701
Age (years)	60.9	62.8	56.9*	61.0	55.1*	61.4
Male (%)	77.1*	57.9	84.1*	61.2	75.5*	54.3
Black (%)	0.2*	1.6	–	–	28.6	31.8
Vintage (years)	6.7*	3.7	10.2	6.5	5.0*	2.4
Catheter (%)	6.3*	21.7	0.0*	1.9	23.2*	37.5
Comorbidities (%)						
CAD	42.0	42.7	25.8	27.3	55.1	53.8
CHF	26.1*	30.8	12.9	16.6	40.3	44.4
Other Cardiac	40.2	36.7	32.6	27.6	29.1	32.3
Cerebrovascular	15.4	15.6	9.8	13.3	15.8	18.0
PVD	30.2	26.5	15.9	12.9	27.6	26.9
Hypertension	70.0*	78.4	37.9*	66.0	82.1	85.8
Diabetes	20.2*	29.1	22.0*	31.1	39.3*	50.9
Cause of ESRD (%)						
Diabetes	11.5*	19.2	18.9*	27.2	33.2*	37.6
Hypertension	7.6*	14.9	0.0*	3.6	20.4*	26.6
GN	21.2*	19.1	58.3*	49.3	12.2*	11.0
Cystic	33.7*	7.2	6.8*	3.8	12.8*	2.8
Urologic	2.0*	2.2	0.0*	0.3	2.6*	1.0
Other	23.6*	37.4	16.0*	15.8	18.8*	21.0

*p < 0.05 vs. other patients within region

Table 2: Mortality Risk among Endogenous EPO Patients by Hemoglobin Levels (n = 729)

Baseline Hemoglobin (g/dl)	% Patients	Unadjusted RR (p-value)	Adjusted RR (p-value)
12–13	42.5	1.00 (ref)	1.00 (ref)
13–14	29.6	0.97 (0.90)	1.18 (0.48)
>14	27.9	0.81 (0.34)	0.56 (0.04)

Vitamin C Improves Hemoglobin Levels and Reduces EPO Resistance in Hemodialysis (HD) Patients with Functional Iron Deficiency (FID). A Randomized, Open Label, Controlled, Multicentric Trial

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Introduction and Aims: Erythropoietin (EPO) hyporesponsive anemia in HD patients is usually associated to FID. Chronic inflammation and oxidative stress could lead to this situation but pathogenesis is still poorly understood. We hypothesized that Vitamin C, an antioxidant and cofactor for iron mobilization process could improve hemoglobin (Hb) levels and reduce EPO resistance, increasing iron availability to red cells.

Methods: We conducted a randomized, open label, controlled, multicentric trial in 3 dialysis units in Buenos Aires. Patients with at least 90 days on HD, anemia (defined as Hb < 11 g/dl or < 12.5 g/dl and EPO requirement) and FID (defined as ferritin > 500 ng/ml, TSAT < 20%) were included. Patients with non renal anemia, acute infection, malignancies, hospitalizations, active bleeding or who received transfusions during three months prior study start were excluded.

Patients were randomized between two groups; Group 1: Standard anemia care + Vitamin C 300 mg IV three times per week, during 90 days and Group 2: Standard anemia care during 90 days.

EPO and iron dosing for anemia treatment were defined in a protocol in order to avoid bias. A large set of laboratory values and EPO resistance index (ERI) was recorded at baseline and after 90 days. ERI was defined as EPO dose (IU/kg/wk) divided by Hb (g/dl). To be able to detect a change of 1 g/dl in Hb (alpha 0.05, beta 0.8, single side), sample size was estimated in 34 patients. Means were compared using paired samples t-test. Linear regression was used to predict association controlling for covariates.

Results: From 35 patients who met inclusion criteria, 7 were excluded during the study (1 death, 1 bleeding, 2 hospitalizations, 3 lost to follow-up). From 28

patients ending the study (Group 1: 13 – Group 2: 15) mean age was 55.9 ± 14.8 years, males 46.4%, vintage 60.7 ± 42.2 months, diabetics 21.4%. There was no difference between groups at baseline in age, vintage, gender, diabetes, vascular access (VA), Hb, transferrin, TSAT, ferritin, eKt/V, albumin, ERI and iron dose. Hb increased in group 1 from 10.8 ± 1.17 to 12.9 ± 0.83 g/dl (p < 0.0001, CI 1.24 – 2.86) while there was no change in group 2 (10.99 ± 1.14 vs 10.83 ± 0.87). ERI decreased from 12.59 ± 5.14 to 9.49 ± 4.38 IU/kg/wk/g/dl in group 1 (p 0.007) and rose from 9.01 ± 3.12 to 11.48 ± 4.64 IU/kg/wk/g/dl in group 2 (p 0.005). Adverse reactions were not observed in both groups.

After controlling for age, vintage, gender, diabetes, VA, dialysis center, iron profile, eKt/V, albumin, PCR, iPTH, ERI and iron dose at baseline Vitamin C administration still maintained an independent effect on Hb levels (model R 0.962, p 0.004).

Conclusions: Vitamin C improves Hb levels in HD patients with renal anemia and FID independently. It also modifies EPO requirements, reducing EPO resistance. Those effects could be related to antioxidant and anti-inflammatory effects of Vitamin C. Large double blinded randomized controlled trials are needed to support these findings.

2. Bone Disease and Mineral Metabolism

Phosphate – The Silent Stealthy Cardiorenal Culprit in All Stages of Chronic Kidney Disease: A Systematic Review

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Introduction and Aims: The increasing recognition and acceptance of a link between hyperphosphataemia and cardiovascular disease, mediated through vascular calcification in patients on dialysis, of necessity then prompts a question 'At what stage of CKD does this relationship between elevated phosphate, vascular calcification and increased cardiovascular mortality begin?' The purpose of the current study was therefore to critically review the current literature.

Methods: We performed a systematic search of the National Library of Medicine and the Cochrane Library databases from January 1985 to February 2008 to identify clinical studies examining the effects of plasma phosphate on adverse cardiovascular outcome, mortality, and progression of kidney disease in subjects with and without CKD but not yet on dialysis. The primary outcome measure was the development of

cardiovascular disease, mortality and progression of kidney disease.

Results: Twelve clinical trials investigated the role of serum phosphate level and adverse outcome [9 studies examining cardiovascular disease outcomes and 3 examining progression of kidney disease]. After adjustment for risk factors for mortality, adverse cardiovascular outcome and progression of kidney disease, all studies found a graded independent significant association between phosphate and death, development of cardiovascular disease and progression of kidney disease. There was no such association with plasma calcium levels.

Conclusions: There is a graded independent association between serum phosphate level and mortality, mainly through cardiovascular disease and the progression of renal disease in subjects with and without definable CKD.

The Relation between Parathyroid Hormone and Mortality in Dialysis Patients is Modified by Protein-Energy Wasting

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Introduction and Aims: High parathyroid hormone (PTH) levels are associated with poor outcome in the general population. The issue of an independent association between PTH and mortality in dialysis patients is controversial, however. We hypothesized that protein-energy wasting (PEW), as a common condition related to adynamic bone disease, modifies the association of PTH with mortality and cardiovascular events, respectively.

Methods: We analyzed data from 1,255 hemodialysis patients with type 2 diabetes mellitus, participating in the German Diabetes and Dialysis Study (4D Study). Patients were stratified for the presence / absence of PEW (albumin ≤ 3.8 vs albumin >3.8 g/dl) and divided into tertiles according to their PTH levels at baseline. They were followed for 4 years. In both groups of patients with and patients without PEW, hazard ratios (HR) for the risk of PTH on 1) all-cause mortality and 2) cardiovascular events (CVE) were determined using Cox regression analyses. Adjustments were made for age, sex, atorvastatin treatment, duration of dialysis, comorbidity, HbA1c, phosphate, calcium, blood pressure and hemoglobin. Additional analyses were performed using a BMI ≤ 23 kg/m² for the classification of PEW.

Results: Patients had a mean age of 66 ± 8 years, 54% were male, and 53% had protein-energy wasting (PEW) as defined by

albumin levels ≤ 3.8 g/dl. Median PTH levels were lower in patients with PEW (64.4 pg/mL; IQR 31.7–117.7 pg/mL) as compared to those without PEW (78.8 pg/mL; IQR 38.5–144.0 pg/mL). In the latter group of patients without PEW, high PTH levels were strongly associated with poor outcome: patients in the highest PTH tertile had a 73% higher risk of death (HR_{adj} 1.73, 95%CI 1.23–2.38, $p=0.001$) and a 49% higher risk of CVE (HR_{adj} 1.49, 95%CI 1.05–2.11, $p=0.026$) than patients in the lowest PTH tertile. Accordingly, in analyses using PTH as a continuous variable, all-cause mortality rose by 23% ($p=0.001$) and the risk of CVE by 19% ($p=0.013$) per unit increase in log PTH. Similar results were found when a BMI > 23 kg/m² was used to define the absence of PEW: both mortality and the risk of CVE significantly rose by 14% per unit increase in log PTH. In contrast, no association of PTH with mortality or CVE was seen in patients with PEW.

Conclusions: In conclusion, protein energy wasting modifies the association of PTH with adverse outcomes in dialysis patients. High levels of PTH were associated with increased mortality and cardiovascular events in patients without protein energy wasting (PEW), but not in patients with PEW. High levels of PTH are of concern in dialysis patients without PEW, while the effect of PTH on mortality is nullified in patients with PEW.

Short-Term Mortality Risk Factors in a Large French Cohort of Hemodialysis Patients: Importance of Nutritional Parameters

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Introduction and Aims: Phosphorus and calcium disturbances and nutritional abnormalities are common in patients with ESRD but their impact on clinical outcomes, and specifically on the survival rate is still poorly understood. There are no randomized clinical studies that determined

the optimal levels of phosphorus and calcium parameters to improve outcome of dialysis patients. Marked differences exist among CKD-MBD patterns and clinical practices across countries.

Methods: The French Phosphorus and Calcium Photo-Graph observational study is the largest prospective cohort aiming to describe clinical practices and to identify factors predictive of survival in dialysis patients in France. More than 7,000 patients entered into the cohort in June 2007 and will be followed for up to 3 years. Here we report the results of an intermediate survival analysis at 12 months. Mineral metabolism parameters were evaluated in reference to K/DOQI practice guidelines, whereas serum albumin and

hemoglobin were analyzed as continuous variables.

Results: At 12 months, age, male sex, history of CV disease and diabetes were significant predictors of relative risk of death. In our model, BMI, low serum phosphorus, high serum calcium, hemoglobin and albumin were the only modifiable factors that affected one-year survival. All-cause mortality was not associated with serum PTH levels.

Conclusions: The Photo-Graph cohort study shows the predictive value of nutritional factors (low serum phosphate and albumin, low BMI) for short-term survival in dialysis patients. The impact on survival of hyperphosphatemia, hypocalcemia and other factors may become significant only after longer follow-up.

Table: Short-term All-Cause Mortality Risk Associated with Parameters Assessed in Photo-Graph Cohort

	Hazard Ratio	95% CI	P
Age (yr)	1.04	1.04 – 1.05	< 0.0001
Gender F/M	0.78	0.65 – 0.94	0.010
CV history	1.57	1.28 – 1.93	< 0.0001
Diabetes	1.23	1.00 – 1.50	0.048
BMI (kg/m ²)	0.96	0.94 – 0.98	< 0.0001
Low serum P	1.27	1.03 – 1.57	0.029
High serum P	1.05	0.84 – 1.32	0.668
Low serum PTH	1.08	0.86 – 1.34	0.512
High serum PTH	1.11	0.89 – 1.38	0.369
Low serum Ca	0.95	0.77 – 1.18	0.656
High serum Ca	1.37	1.08 – 1.74	0.009
Hemoglobin (g/L)	0.88	0.82 – 0.94	< 0.0001
Albumin (g/L)	0.92	0.91 – 0.94	< 0.0001

N = 4,937. Models were adjusted for age, sex, BMI, diabetes, history of CV disease, serum albumin, hemoglobin, and baseline serum levels of total calcium, phosphorus and PTH. Patients with recent parathyroidectomy (less than 6 months) were excluded from the analysis.

Prevalence of Parathyroidectomy (PTX) in the European Hemodialysis Population. Results from COSMOS

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Introduction and Aims: COSMOS is a multicenter study aiming to survey Chronic Kidney Disease related Mineral and Bone Disorders (CKD-MBD) in hemodialysis patients as well as the current clinical practice for the prevention, diagnosis and treatment of this condition. The aim of this analysis was to assess the prevalence and characteristics of the parathyroidectomized population in COSMOS.

Methods: COSMOS (Current Management Of Secondary Hyperparathyroidism – a Multicenter Observational Study) is a 3-year, multicenter, open-label, prospective study collecting data from 4,500 hemodialysis patients at 227 centers in 20 European countries. Facilities and patients were identified using a stratified, random selection methodology. The number of patients was selected according to the hemodialysis population of each country. At enrolment, patient data were collected by site investigators and entered into a web-based data entry system including demographics, medical history (including PTX), routinely collected laboratory parameters during the previous 6 months, and concomitant treatments. Data from baseline analysis are presented in this report.

Results: The prevalence of PTX was 6.6% and increased with time on hemodialysis (0.7%, 2.9% and 17.4% in patients on hemodialysis for <1, 1 to 5 and ≥5 years respectively, $p<0.001$). PTX was more fre-

quent in female patients (7.7% vs 6.0%, $p<0.001$) and in young patients (11.9, 9.4, 5.8 and 2.6% in patients aged <45, 45–64, 65–74 and ≥75 years respectively). The percentage of patients with hypocalcemia (calcium corrected by albumin lower than 8.4 mg/dL) was higher in patients with PTX (23.0% vs 9.9%, $p<0.001$). More than half of the patients with PTX (58.8%) showed PTH levels <150 pg/mL, a percentage significantly higher than those without PTX (34.9%, $p<0.001$). Overall, 86.4% of COSMOS patients were on phosphate binders and no differences were found between patients with PTX and patients without PTX (88.0% and 86.4% respectively, $p=0.42$). The percentage of patients receiving more than one phosphate binder was higher in patients with PTX (32.4% vs 22.8%, $p<0.001$). Interestingly, patients with PTX showed higher levels of hemoglobin (Hb). In fact, 43.9% of patients with PTX showed Hb levels ≥ 12 g/dL, whereas only 34.8% of patients without PTX achieved the same levels ($p<0.001$) despite the fact that in the latter the percentage of patients receiving erythropoietin was higher (90.7% vs 84.0% respectively, $p<0.001$).

Conclusions: The prevalence of PTX was high, particularly in patients ≥ 5 years on hemodialysis and younger than 65 years. PTX patients had a higher rate of hypocalcemia, lower PTH levels and higher Hb levels than those without PTX.

3. Cardiovascular Complications

Effect of Rosuvastatin versus Placebo on Cardiovascular Outcomes in Patients with End-Stage Renal Disease on Hemodialysis - Results of the AURORA Study

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Introduction and Aims: Most patients with end-stage renal disease (ESRD) on hemodialysis (HD) have atherogenic lipid abnormalities, but do not have raised cholesterol. The benefits of statin therapy, irrespective of baseline levels, on cardiovascular (CV) outcomes in ESRD patients are uncertain. AURORA (NCT00240331) is a large-scale, international, double-blind, placebo-controlled study to assess the effect of rosuvastatin on CV morbidity and mortality in patients with ESRD on HD.

Methods: Patients aged 50–80 years with ESRD who had been receiving HD for at least 3 months were enrolled in 281 centers in 25 countries. Patients were randomized 1:1 to rosuvastatin (RSV) 10 mg daily or to placebo. The primary endpoint was time to CV death, non-fatal myocardial infarction, or non-fatal stroke; secondary endpoints included all-cause mortality, CV event-free survival, CV death, non-CV death, and thrombosis of HD vascular access.

Results: Overall, 2,776 patients were randomized into the study. At baseline, mean age was 64.2 ± 8.7 years, BMI was 25.4 ± 4.9 kg/m², and systolic and diastolic blood pressure were 136.9 ± 24.5 and 75.8 ± 12.7 mmHg, respectively. A total of 51% of patients had a history of CV disease (CVD) or CVD risk equivalent, diabetes, angina, and peripheral arterial disease being the most common. Mean baseline levels (mg/dL) of total cholesterol, LDL-cholesterol, triglyceride, and HDL-cholesterol were 175 ± 42, 99 ± 34, 155 ± 93 and 45 ± 15, respectively. Mean hemoglobin levels were 11.68 ± 1.60 g/dL. Median time on renal replacement therapy was 32 months, with 92% on HD and the remainder on hemofiltration. There was a prompt 43% reduction in LDL-cholesterol by 3 months in the RSV arm. Hs-CRP was elevated at baseline, but was reduced by 11% in the RSV group ($p < 0.001$). There was no

beneficial effect of RSV upon the primary composite endpoint cardiac death, non-fatal myocardial infarction or non-fatal stroke, or in any of the secondary endpoints or pre-specified sub-populations that were analyzed. Adverse events were similar in both groups.

We are currently assessing associations of baseline and on-treatment LDL-cholesterol and hsCRP levels with clinical outcomes in the AURORA population.

Conclusions: Baseline data confirm that the AURORA study population is representative of patients with ESRD on chronic HD. Despite a reduction in LDL-C of 43% and a reduction by 11% in CRP, no beneficial treatment effects on primary or secondary CV endpoints were observed confirming the lack of benefit of statins in the ESRD population seen with atorvastatin in the 4D trial. Rosuvastatin therapy was well tolerated in this patient population. We hope to report on any associations of baseline and on-treatment LDL-cholesterol and hsCRP levels with clinical outcomes.

Effect of Rosuvastatin on Cardiovascular Outcomes in Diabetic Patients Receiving Hemodialysis – Results from the AURORA Study

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Introduction and Aims: The 4D study which recruited type 2 diabetes hemodialysis patients, showed no beneficial effect of atorvastatin therapy on a primary composite cardiovascular endpoint. However, the predefined combined secondary cardiac endpoints indicated a protective effect of statin therapy. The primary cardiovascular endpoint in AURORA (NCT00240331) was negative in diabetic patients. However, we examined the effects of rosuvastatin therapy in diabetic patients in the trial for a pre-defined specific atherosclerotic cardiac endpoint.

Methods: Patients aged 50–80 years with ESRD who had been receiving hemodialysis for at least 3 months and had a diagnosis of diabetes at enrollment were analyzed. Patients were randomized 1:1 to rosuvastatin 10 mg daily or to placebo. The secondary atherosclerotic cardiac endpoint was time to fatal or non-fatal myocardial infarction.

Results: Of the 731 diabetic patients, 343 were randomized to placebo and 388 to rosuvastatin. The groups were well matched. At

inclusion, mean age was 65.0±8.3 years, 65.5% were males and body mass index was 26.7±5.3 kg/m². Systolic and diastolic blood pressures were 140.8±25.2 and 75.1±12.4 mmHg, respectively. Mean baseline levels (mmol/L) of total-cholesterol were 4.5±1.2 and 4.4±1.1, LDL-cholesterol 2.5±0.9 and 2.4±0.9, triglycerides 1.9±1.3 and 1.9±1.1, HDL-cholesterol 1.1±0.4 and 1.1±0.4 respectively in the rosuvastatin and the placebo arm.

There was a 25.2% reduction in total cholesterol and a 39.1% reduction in LDL-cholesterol by 3 months in the rosuvastatin arm. Adverse events were similar in both groups.

Diabetic patients randomized to rosuvastatin had a 32% reduction in atherosclerotic cardiac events (HR 0.68, CI 0.51–0.90, p= 0.0079).

Conclusions: For diabetic patients receiving hemodialysis in the AURORA trial rosuvastatin was well tolerated with an effective reduction of LDL-cholesterol and was associated with a reduced rate of atherosclerotic cardiac events.

Blood Pressure Lowering Reduces Cardiovascular Events and Mortality in Dialysis Patients: A Systematic Review of Randomised Controlled Trials

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Introduction and Aims: Patients receiving dialysis have a markedly increased cardiovascular risk. Although blood pressure (BP) lowering trials have clearly demonstrated cardiovascular benefit in the general population, the efficacy and safety of BP lowering in dialysis patients are uncertain. We systematically reviewed all available randomised trials of BP lowering in dialysis patients.

Methods: MEDLINE, EMBASE and the Cochrane Library database were searched for trials reported between 1950 and November 2008, without language restriction. We extracted a standardised dataset from randomised controlled trials that employed any form of BP lowering in dialysis patients and reported cardiovascular outcomes.

Results: Eight trials involving 1,679 patients and 495 cardiovascular events were included. In actively treated patients, weighted average systolic and diastolic BP levels were -4.5 mmHg and -2.3 mmHg lower, respectively. BP lowering was associated with a

29% (95% (CI) 8–45%, $p=0.009$) lower risk of cardiovascular events, a 20% (CI 4–34%, $p=0.014$) lower risk for all-cause mortality and a 29% (CI 1–50%, $p=0.044$) lower risk for cardiovascular mortality as compared with control regimens. Heterogeneity ($I^2=67.5\%$ $p=0.003$) in the magnitude of the effect was observed for the outcome of all cardiovascular events, but not for all-cause mortality. The magnitude of risk reduction was similar for the different classes of BP lowering agents. Furthermore, the effects appear to be consistent irrespective of the presence or absence of hypertension or other co-morbidities.

Conclusions: BP lowering agents significantly reduce the risk of cardiovascular events, all cause mortality and cardiovascular mortality in patients undergoing dialysis. These data suggest that administration of BP lowering agents should be considered routinely for individuals undergoing dialysis to reduce the very high cardiovascular morbidity and mortality rate in this population.

Survival Outcomes in Patients of Different Age-Groups. Comparison of Two Different Time Periods

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Introduction and Aims: Annual acceptance rate for RRT in UK is rising steadily from 20 pmp in the 1980s to 103 pmp in 2004¹: The fastest growing group of patients with ESRD are those over 75 years old².

The aim of the present study was to compare the survival outcomes of the different patients' age groups in two different time-periods.

Methods: The present study is a retrospective computer based study with data extracted from the renal patients' database. The studied patients initiating RRT were divided in two groups according to the time of initiation RRT (group 1 : 813 patients (517 M –296 F) initiating RRT from 1/1/1996 to 31/12/2000 and group 2 : 894 patients (543 M –351 F) initiating RRT from 1/1/2001 to 31/12/2005). Each group was divided into 3 sub-groups according to the age of each patient initiating RRT <65 years old, 65–74 years old and ≥ 75 years old. All subjects were followed up until the point of assessment (10/12/2008) or the time of death.

Results: 90-days and 1-year survival: There were no significant differences in 90-days and one-year survival when we compared the total of the two time periods and the different age groups in the three periods.

Long-term survival: There was no significant difference in 5-years estimated survival for the 2001–2005 when we compared it against the 1996–2000 group. Six-years survival was significantly higher in the latest time period compared to the earlier one (Pearson Chi-Square 4.531, df 1, P=0.033). Five years survival was also significantly higher in the 2001–2005 group in the age group over 75 years old (Pearson Chi-Square 4,340, df 1, P=0.037). There was no significant difference concerning the five years survival of the under 65 years old age group and the 65–74 age group between the periods 1996–2000 and 2001–2005. Six years survival was also significantly higher in the 2001–2005 group in the ages under 65 years old (Pearson Chi-Square 5,713, df 1, P=0.017) in the 65-74 years old group (Pearson Chi-Square 3,814, df 1, P=0.05) and the over 75 years old group (Pearson Chi-Square 5,116, df 1, P=0.024).

Conclusions: The improvements in the RRT therapy have led to improvements in the long term (6-year) survival of the patients. Short term survival has remained unchanged during the last 15 years and further studies are needed to address this issue.

¹ Ansell D et al. UK Renal Registry Report 2005. Bristol, UK

² Farrington K. et al. UK Renal Registry Report 2006

Prediction of Sudden Cardiac Death in Hemodialysis Patients

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Introduction and Aims: Sudden cardiac death constitutes a major cause of death in maintenance dialysis patients. In order to provide appropriate intervention and to evaluate new treatments for its prevention, it is important to identify patients at high risk of sudden death.

Methods: We analyzed data from 1,255 diabetic hemodialysis patients, who participated in the German Diabetes and Dialysis study (4D study) and were followed for a median of 4 years (mean age 66 years, 54% male). We first established a prediction model based on patient history, and investigated whether the addition of 1) routine laboratory markers measured at baseline (incl. albumin, hemoglobin, calcium, phosphate, cholesterol, creatinine, HbA1c) and 2) selective biomarkers (NTproBNP, troponin T, CRP and adiponectin) further improved risk stratification for sudden death. Discriminative abilities were calculated with Harrells C-statistics.

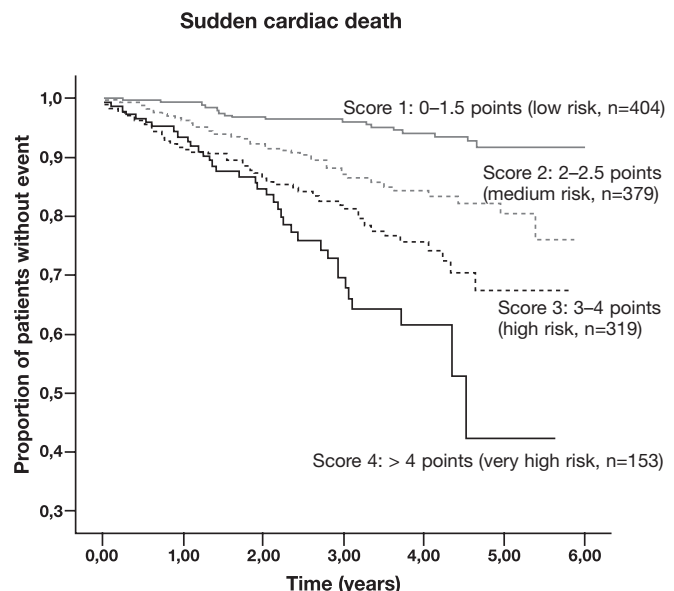
With a score being developed and applied to each patient, groups of patients at high and low risk were formed and compared using Kaplan Meier analyses.

Results: During follow-up, 160 participants died of sudden death. In Cox regression analyses, the presence of CAD, PVD, arrhythmia, CHF, catheter use and BMI were strong and independent predictors of sudden death (model 1). The C-statistic of this model on patient history (corresponding to an area under the ROC curve) was 0.68. From routine laboratory markers, albumin and HbA1c were the strongest predictors of sudden death. When added to model 1, the discriminative power as assessed by the C-statistic increased to 0.70 (model 2). Among the biomarkers, which were all significantly associated with sudden death, NTproBNP proved to have the strongest predictive value. When incorporated

into model 2, the C statistic further increased to 0.72 (model 3). Categorization of patients into groups of low, medium, high and very high risk according to a score developed from model 2 showed good discrimination in Kaplan-Meier analyses. NTproBNP was very useful in specifying risks among the medium scoring category, enabling further stratification of this group into patients at high and low risk.

Conclusions: We provide a prognostic score based on easily obtainable anamnestic and routine laboratory markers, which allows for a good identification of diabetic hemodialysis patients at high vs. low risk of sudden cardiac death. We furthermore suggest that NTproBNP can be helpful in borderline cases, providing additional prognostic information to be used for the further distinction of those patients into groups of high and low risk.

Figure
Kaplan Meier curves for the time to sudden cardiac death in patients grouped according to the score developed from prediction model 2



Effect of Folic Acid on Oxidative Stress and Nitric Oxide Activity in Patients with Metabolic Syndrome

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Introduction and Aims: Alterations in microvascular function play an important role for the development of diabetic nephropathy and retinopathy. Experimental data suggest increased vascular production of superoxide and of nitric oxide (NO), both subsequently reacting to highly toxic peroxynitrite. We hypothesized that folic acid treatment may reduce oxidative stress and microvascular NO activity in subjects at high risk for diabetes.

Methods: Male subjects with metabolic syndrome (n=49) and controls with similar body mass index (BMI) (n=26) were included in a randomized, double-blind, crossover designed trial. After treatment with placebo or folic acid (5 mg/day) for four weeks, oxidative stress was determined as reduced glutathione to oxidized glutathione levels in erythrocytes (GSH/GSSG ratio). Renal and retinal NO activities were assessed *in vivo* as renal plasma flow (clearance-technique)

and retinal blood flow (laser doppler scanning flowmetry) responses to NO synthase inhibition with N(G)-monomethyl-L-Arginine (L-NMMA).

Results: BMI was similarly elevated in subjects with and without metabolic syndrome (34 ± 4 vs 32 ± 3 kg/m², n.s.). In all subjects, GSH/GSSG ratio increased from 42 ± 80 to 100 ± 198 (p=0.04). Only in subjects with metabolic syndrome, folic acid reduced the responses of renal plasma and retinal blood flow to L-NMMA compared to placebo (-48 ± 40 vs -66 ± 48 ml/min/1.73m², p=0.03; and -9 ± 35 vs -27 ± 44 U, p=0.04).

Conclusions: Folic acid reduces oxidative stress in obese subjects, and reduces NO activity in renal and retinal circulations in those with metabolic syndrome.

We hypothesize that folic acid treatment may be useful in this setting to prevent microvascular damage, e.g. via reduced generation of peroxynitrite.

4. Elderly CKD Patients

The Prevalence and Significance of Chronic Kidney Disease in the Elderly Population

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Introduction and Aims: Elderly patients with reduced estimated glomerular filtration rate (eGFR) are now one of the commonest indications for referral to nephrology clinics. The MDRD-4 formula and the new classification of CKD are now being routinely used to screen patients for renal disease in the community. We investigated eGFR values and the prevalence of renal dysfunction in an elderly Scottish population.

Methods: We analysed eGFR (MDRD-4 UK NEQAS) values in 1,043 patients from a population of primary care attenders (age > 64 years). The anonymised eGFR and creatinine results were part of routine blood tests analysed by the biochemistry laboratory for general practitioners. Follow-up bloods were assessed 12 months later. Normal renal function was defined as eGFR > 60 ml/min/1.73m². Statistical analysis was performed using SPSS software. Patients were stratified into 3 age groups.

Results: We investigated 1,043 patients, 432 male and 611 female patients, age range 65 to 99 years. The mean eGFR for each age group was: 65–74 years, eGFR = 67.2; 75–84 years, eGFR = 60.0; and > 84 years, eGFR = 50.7. Multivariate analysis showed a significant association between 10-year increments in age and eGFR (OR 2.3). After 12 months the mean eGFR's for each group were 70.2 (p<0.001), 62.2 (p<0.001) and 51.4 (ns), respec-

tively. eGFR improved in two age groups and was unchanged in the third. There were 464 patients (44.5%) diagnosed with an eGFR < 60 ml/min/1.73m². From these patients, 255 (24.4%) were classified as Stage 3A and 167 (16.0%) as Stage 3B. There were 42 patients (4.0%) with an eGFR < 30 ml/min/1.73m². From these patients, 37 (3.5%) had Stage 4 CKD and 5 (0.5%) had Stage 5 CKD. Mean eGFR values in Stage 3A were 52.5 at baseline and 55.5 at 12 months (p<0.001); Stage 3B, 38.2 and 40.7 (p<0.001); Stage 4, 24.8 and 30.8 (p<0.01); Stage 5, 11.8 and 12.9 (ns), respectively. eGFR values improved or were unchanged after 12 months.

Conclusions: Around 45% of our elderly population had eGFR < 60 ml/min/1.73m² and this was significantly associated with increasing age. The introduction of eGFR reporting has led to a rising number of elderly patients being referred to the renal service for further investigation. The majority (40%) had Stage 3 CKD. Monitoring these elderly patients for 12 months showed no evidence of progressive renal disease. Do these patients have clinically significant treatable disease or are we simply seeing the effect of the normal ageing process? More clinical guidelines for management of CKD in this elderly age group are required. The sub-classification of Stage 3 CKD may assist in appropriate investigations and treatment of elderly patients.

Advanced Age is not a Barrier to Creating a Functional Arteriovenous Fistula

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Introduction and Aims: An AV fistula is the recommended vascular access for hemodialysis patients irrespective of age because of increased patency and lower risk of complications compared to central venous catheters. The elderly are the fastest growing group of patients on dialysis. Previous studies evaluating fistula outcomes in elderly subjects have yielded mixed results and controversy still exists as to the best choice of hemodialysis access in the very elderly.

The aim of this study is to compare fistula patency and complication rates in patients <65, 65-75 and >75 years of age in a large, tertiary care, vascular access referral centre.

Methods: This is a retrospective analysis of prospectively collected data. All patients with their first AV fistula created between January 1, 2005 and December 31, 2007 were identified. Patients were excluded if they died, received a transplant or terminated dialysis within three months of fistula creation. Data was collected from January 1, 2005 to December 1, 2008. The primary outcome was

primary patency, evaluated by Kaplan-Meier survival analysis. Secondary outcomes included secondary and functional patency, as well as need for intervention and fistula complications.

Results: A total of 269 patients were eligible for the study and 258 patients met inclusion criteria. The age distribution was as follows: <65, n = 105, mean age 50 ± 10, 65-75, n = 83, mean age 71 ± 3, >75, n = 70, mean age 80 ± 4. The cohort had 64% males, 45% Caucasians, and 33% Asians and no difference was noted among age groups. The >75 age group had more cardiovascular disease versus the <65 age group (61% vs. 38%, n = 0.005). The figure illustrates that primary patency was similar for all age groups.

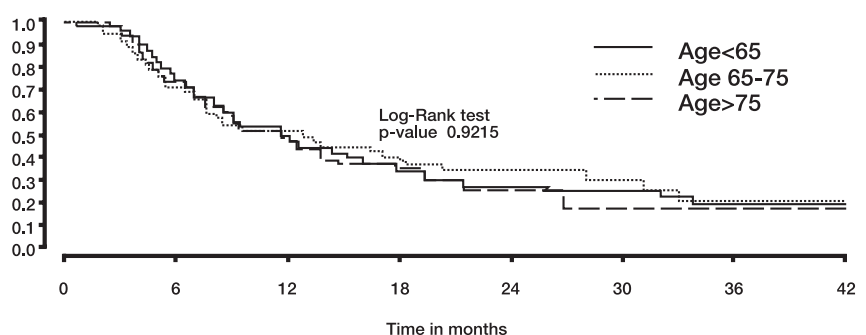
At one year, primary patency was 37% overall. (<65 = 37%, 65-75 = 39%, >75 = 35%). At three years, primary patency was 18% overall and again, there was no difference between the age groups. Importantly, secondary patency and

functional patency were also similar between all age groups at 1,2 and 3 years.

On multivariate analysis, the only variable associated with fistula loss was presence of diabetes HR 1.565 (95% CI 1.089-2.250). AV fistulas created predialysis were associated with increased patency HR 0.550 (95% CI 0.376-0.803). 50% of fistulas needed intervention during the study period (53% = <65, 47% = 65-75, 33% = >75 p=0.61) and 13% had a complication (18% = <65, 7% = 65-75, 11% = >75 p=0.52). Importantly, no differences in number of interventions or complications were noted by age.

Conclusions: There is no difference in AV patency, complications, or need for intervention in older patients when compared to their younger counterparts. Therefore, vascular access decisions, even in the very elderly, should not be made based on concerns of lower patency or high risk of complications.

Figure: Primary Patency of AV Fistulas



Dialysis in Very Elderly (≥ 85 Years Old) Patients with End-Stage Renal Disease

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Introduction and Aims: Advanced age is no longer considered a contraindication to dialysis and in the last decade an increasing number of very elderly (≥ 85 yrs) patients has been admitted to dialysis treatment. Since few data are available in the literature, we aimed to evaluate the impact of treatment modalities, type of dialysis access and various comorbidities on long-term survival in these patients.

Methods: We collected and examined the data of all the ≥ 85 years old patients starting dialysis from Jan 1998 to Dec 2007 in 13 Dialysis Units in the North Milan area (Italy).

Results: We found data regarding 157 patients ≥ 85 years (86 F and 71 M, 3.5 % of all incident patients) with a mean age of 88.0 years (range 85.1–99.4, median 87.25). The most frequent cause of ESRD was renal vascular disease ($n=86$, 54.8%), followed by glomerulonephritis ($n=13$, 8.3%) and diabetes ($n=11$, 7.6%). Treatment was hemodialysis (HD) in 127 (80.9%) and peritoneal dialysis (PD) in 30 patients (19.1%). First access was vascular catheter in 88 patients (56%), AV fistula (AVF) in 38 (24.2%) and peritoneal catheter in 31 (19.7 %).

Among comorbidities, diabetes was present in only 26 patients (16.6%), previous coronary artery disease in 56 (35.7%), peripheral vascular disease in 10 (10.2%), cerebral vascular disease in 30 (19.1%), neoplasia in 24 (15.3%) and liver disease in 5 (3.2%).

Survival rate was 80.3% at 3 months, 62.3% at 12, 46.2% at 24, and 32.6% at 36 months (median 18, interquartile range 5,7–45.5). Excluding patients surviving < 90 days, survival rate was 77.6% at 12 months, 57.5% at 24 and 40.7% at 36 months (median 30.0, interquartile range 13.7–46.6) vs. an average life expectancy of 60.4 months (interquartile range 54–73.5).

Main causes of death were cardiovascular events ($n=47$), cachexia ($n=42$) and infections ($n=14$). Notably, only 2 deaths were due to treatment withdrawal and no fatal events were observed, in the first 90 days, in patients with a functioning AVF. No difference in survival rates was observed between HD and PD treatment. Cox regression analysis (including age, sex, comorbidities, treatment modalities and dialysis access) showed a significantly increased mortality risk for central venous catheter as first access (HR 1.92, CI 1.33–2.80, $P=0.001$) and for the presence of peripheral vascular disease (HR 2.14, CI 1.24–2.70, $P=0.007$). In patients surviving > 90 days, the only significant risk factor for mortality was starting dialysis with a central venous catheter (HR 1.87, CI 1.22–2.86, $P=0.004$).

Conclusions: In very elderly patients, timely decisions on planning treatment and preparing a permanent dialysis access seem to play a more significant role in determining a better outcome than the presence or absence of one or more comorbidities.

Peritoneal Dialysis in the Elderly – Assistance Needed as a Determinant of Unfavourable Outcome

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Introduction and Aims: Consistent recommendations regarding peritoneal dialysis (PD) are difficult to give to elderly patients due to conflicting data published. Therefore, we have analyzed our cohort of PD patients to clarify whether PD is a risk or chance in elderly patients.

Methods: Overall, 98 consecutive patients with PD (58 males, 40 females; mean age 54.2 ± 14.4 ; age ≥ 65 : $n=25$) were prospectively followed for a mean duration of PD of 22.1 ± 19.85 months. All were treated in the same way, i.e. similar catheter implantation technique and similar training. All were started with a standard regimen of 4×2 l, 1.5% glucose exchanges per day of biocompatible PD-solutions, later adapted to the individual's needs. Patients were followed monthly or whenever clinically indicated.

Analyses included descriptive statistics, univariate and multiple Cox regression analyses, cumulative incidence functions of major events and Kaplan-Meier plots regarding mortality in relation to major events.

Results: First analyses revealed that peritonitis was the major event to occur with the highest probability compared to transplantation, transfer to hemodialysis (HD) and death while on PD. Neither age, sex, assistance needed with PD or number of training units had a significant influence on the events. Overall, 43 first peritonitis episodes were seen. In these patients a

higher number of training units indicated a significantly higher risk of a second peritonitis episode ($p<0.001$; $n=9$). Irrespective of age, 25 % of peritonitis were caused by Gram negative bacteria.

Although the frequency of peritonitis episodes was higher in the elderly patients (0.39 episodes/patient year) versus patients <65 years of age (0.29 episodes/patient year) in Cox regression analyses, age had no significant influence on occurrence of peritonitis.

In an intention-to-treat analysis of time until death (at any time) timely transfer to HD ($p=0.035$), transplantation ($p<0.0001$) and no assistance needed with PD ($p=0.03$) were associated with a higher survival probability. Clearly, increasing age is related to shorter survival probability ($p<0.0001$) and was also a risk factor to be transferred to HD. In multiple Cox regression analyses also peritonitis had a significant negative impact on time until death ($p=0.022$).

Conclusions: We conclude that age by itself is not a risk factor and elderly patients may choose PD as their renal replacement therapy. However, the major determinant of a negative outcome is assistance needed with PD. Pre-PD testing to identify those dependent on assistance is warranted. A higher number of training units to learn handling of PD indicates a higher risk of repeated peritonitis episodes in the patients already having had a first episode.

Cost-Benefit Analysis of Supplemented Very Low Protein Diet Versus Dialysis in Elderly CKD5 Patients

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Introduction and Aims: Recent clinical data show that a supplemented very low protein diet (sVLPD) in CKD5 elderly patients allows to postpone the initiation of dialysis of on average 1 year without increasing their risk of death or hospitalization. We aimed to compare benefits and costs of sVLPD vs dialysis (D) in elderly patients.

Methods: A cost-benefit analysis was conducted. Direct medical and non-medical benefits and costs were analysed, from the perspective of the Italian National Health Service (NHS), which is in charge of paying for most of direct costs attributable to renal failure. We quantified cost of dialysis, hospitalizations, drug therapy, blood/instrumental tests, medical visits, reimbursement for transportation to/from hospital and for home dialysis treatment. Prices and tariffs applied in 2007 were used. The net benefit was computed as a difference of benefits and costs estimated in sVLPD vs dialysis group in a time horizon of 3 years, and reported as mean €/pt-year. An annual discount rate of 5% was applied to benefits and costs occurring after the first year. The bootstrap statistic was applied to conduct the analyses.

Results: Data from a subgroup of patients with GFR of 5–7 ml/min/1.73 m² BSA, participating in a randomized controlled trial conducted in 1998–2005 were analysed. Thirty patients were randomized to dialysis (age=77.2 ± 4.6 years): 23 received HD, 7 received PD. Twenty-seven patients were randomized to sVLPD (age=78.6 ± 6.5 years): during the follow-up 19 switched to HD, 2 to PD. The patients were followed for a mean of 3.24 years (dialysis group) and 3.27 years (sVLPD, considering the time on dialysis after shift too). Patients assigned to sVLPD had a mean period on diet of 13 (1–58)

months, receiving during this period 7,160 IU/pt-week of erythropoietin (EPO) on average. Patients assigned to dialysis received 8,104 IU/pt-week of EPO.

No morbidity or mortality increase was detected among patients assigned to sVLPD compared to those assigned to dialysis.

Mean costs for NHS in this 3-year period were 37,595.38 €/pt-year in the dialysis group vs 29,772.54 €/pt-year in the sVLPD group, respectively. In particular, 41,300 € (dialysis) vs 19,860 € (sVLPD) per patient were spent in the 1st year of treatment; 31,600 € (dialysis) vs 26,100 € (sVLPD) in the 2nd year; 28,298 € (dialysis) vs 24,850 € in the 3rd year (sVLPD).

As the dialysis treatment was the cost driver (70% of total costs), the main benefit to the NHS derived from saving this costs during the sVLPD period.

Conclusions: To our knowledge this is the first study on cost-benefits of initiating sVLPD compared with initiating dialysis in CKD5 elderly patients. sVLPD allows to save on average 1 year of dialysis per patient, without negative consequences on morbidity and mortality, and allows the NHS to save >30,000 €/pt in 3 years from treatment initiation, of which >20,000 € already the 1st year.

5. Dialysis

High spKt/V – Which Dialysis Practice? Results from German EuCliD-Users

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Introduction and Aims: With the implementation of the official guideline on dialysis quality in Germany each individual unit is legally bound to prove the dialysis quality delivered to their patients. The dialysis dose is here one key indicator. A spKt/V ≥ 1.2 has to be achieved in 85% of patients. Whereas this seems to be an easy target for some units, for others it appears to be a struggle.

The current analysis intends to disclose potential centre differences and to identify the rationale behind it. Therefore the centres were grouped according to their achieved mean spKt/V and the impact of patients' characteristics and dialysis prescription was investigated by analysis of variance and Chi², when appropriate.

Methods: 44 centres participating in the EuCliD-Benchmarking System were included. They were categorised in 4 groups according to their mean spKt/V achieved for all point prevalent patients (4,536) on September 30, 2008. The individual centre-groups were characterised by mean spKt/V-values of [1] 1.36 \pm 0.30 [2] 1.46 \pm 0.35 [3] 1.57 \pm 0.32 [4] 1.70 \pm 0.41.

Results: Centres with low spKt/V treated non-significantly less females (41% vs. 46%); their patients were younger (66 \pm 14 vs. 68 \pm 14 yrs $p=0.021$), also at start of dialysis (62 \pm 16 vs 64 \pm 15 yrs $p=0.005$) and longer on dialysis

treatment ($p=0.001$) compared to centres with high Kt/V. Patients in the low-Kt/V centres slightly were heavier than the ones in high-Kt/V centres (77 \pm 18 vs 75 \pm 17 kg, $p<0.05$). Further, native AVF were found less often in centres with low Kt/V (77.9% vs 86.8%, $p=0.001$) as were artificial grafts (8.6% vs 10.5%, $p=0.001$). Low Kt/V-centres achieved lower blood flows but higher dialysate flows (Qb: 278 \pm 53 vs 303 \pm 62 ml/min, $p<0.001$; Qd: 50 \pm 25 vs 478 \pm 89 ml/min, $p<0.001$) and shorter treatment times (253 \pm 28 vs 274 \pm 39 min, $p<0.001$). Accordingly, less total blood volume was processed (70 \pm 16 vs 84 \pm 20L) and less patients achieved the target Kt/V (74% vs 94%) in low-Kt/V centres compared to high-Kt/V centres. The significant differences remained after adjustment for age, gender and time on dialysis.

Conclusions: The analysis confirmed that despite gender and age differences the main factors influencing adequate dialysis are the type of vascular access, sufficient blood flow and treatment time.

Accordingly, it is mandatory to monitor and re-adjust the treatment parameters frequently in order to continuously improve dialysis quality. In this respect, particularly patient's body weight should be taken into account when prescribing treatment times.

The Practice of Prescribing Longer Hemodialysis (HD) Sessions Improves Patient Outcomes: Results from the Dialysis Outcomes and Practice Patterns Study (DOPPS)

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Introduction and Aims: Longer HD sessions have been associated with decreased mortality. However, previous results may be biased by the fact that patients who undergo longer HD sessions are likely more compliant with other therapeutic aspects of their

care, e.g. adherence to medication prescription and dietary restrictions. We postulate that the practice of prescribing longer HD time for all patients in a unit may be associated with improved outcomes, independently of patient characteristics.

Methods: Analyses used DOPPS data from 1996–2008 in 12 countries: Australia/New Zealand (ANZ), Belgium, Canada, France, Germany, Italy, Japan, Spain, Sweden, the UK, and the US (n=929 facilities; with 24,475 patients). The dialysis facility mean prescribed time on HD (treatment time [TT]) was used as predictor, continuously and in categories (<3.5, 3.5–4.0 [ref], and >4.0 hours). Association with laboratory values of hemoglobin, PO₄, K, and pre-dialysis systolic blood pressure (SBP) was assessed by linear mixed models. Cox models assessed the risk of mortality and hospitalization with TT, adjusted for age, sex, race, years on dialysis, 14 comorbidities, BMI, residual renal function, Kt/V, and 5 other

facility practices (catheter use, PO₄, K, hemoglobin, and albumin); stratified by country and phase; accounted for facility clustering.

Results: Great variability in facility TT was observed both within and across countries.

Longer TT was associated with significantly higher hemoglobin (+0.10 g/dl), lower serum phosphorus (–0.12 mg/dl), SBP (–1.19 mmHg), and K (–0.03 mEq/L) per 30 minute longer TT.

Facilities with longer mean TT had the greatest reduction in risk of sudden deaths and composite outcome of sudden death and myocardial infarction (table).

Conclusions: The facility practice of prescribing longer HD sessions was associated with improved anemia, PO₄, SBP, K, and decreased mortality. Operational factors (e.g. limited staffing, number of stations, etc.) and patient reluctance to prolong TT are likely to influence clinicians' ability to prescribe longer TT. Overcoming these barriers may result in better outcomes.

Outcome	Continuous TT (per 30 minutes)		Categorical TT (vs. 3.5–4 hours)			
	RR	CI	TT < 3.5 hrs		TT > 4 hrs	
			RR	CI	RR	CI
Mortality						
All-Cause	0.94*	0.88–1.00	1.17	0.99–1.39	0.89	0.64–1.22
Sudden Death	0.82*	0.70–0.98	1.50	0.95–2.37	0.43	0.18–1.02
Sudden Death/MI	0.90	0.79–1.02	1.35	0.95–1.91	0.70	0.36–1.36
Sudden Death/MI Death or Hospitalization	0.89	0.79–1.01	1.25	0.87–1.80	0.62	0.31–1.26

* p<0.05

Serum Concentrations of Natriuretic Peptides in Hemodialysis Patients. Relationship with Dialytic Technique and Cardiac Impairment

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MHD patients may be affected by the extreme reduction of renal function and by the eventual removal during hemodialysis session. The aim of this study was to investigate serum levels of different natriuretic peptides in MHD patients to assess their removal with diffusive and mixed dialytic techniques, and their relationship with nutritional and inflammatory status and with cardiac function.

Methods: Thirty-two patients (F11), aged 32–88 years were examined. Sixteen patients were treated with diffusive hemodialysis (HD) and 16 with mixed diffusive and convective technologies (HDF). Serum concentrations of C-type natriuretic peptide (CNP), brain natriuretic peptide (BNP) and their precursors NT-proBNP, NT-proCNP, and of the precursor of atrial natriuretic peptide (NT-proANP) were measured immediately before and after a dialytic session. At the same time, dialytic efficiency for small molecules and middle molecules (β 2-microglobulin reduction ratio – β 2M RR), inflammatory status (C reactive protein; interleukin 6 – IL-6), nutritional status (serum albumin concentration) were assessed. Furthermore, body composition and body fluids were evaluated by means of bio-electrical impedance analysis. Echocardiographic parameters were also measured.

Results: A relevant increase in serum concentration of all NP and pro-NP was found in MHD patients: 10 to 20 times the mean

values found in normal subjects. Removal during dialysis: NT-proANP, NT-proBNP, NT-proCNP and BNP decreased significantly after HDF (reduction ratios from 48 to 82%), while their removal was very poor after HD. Similar reduction ratios were found for β 2M (RR was 52% after HDF and 17% after HD). The removal of CNP was very modest with both dialytic techniques.

Relationship with heart function: serum CNP showed a negative correlation with ejection fraction. NT-proANP, NT-proBNP and BNP were positively correlated with left ventricle end-diastolic diameter and left atrium diameter. **Relationship with nutritional and inflammatory status:** NT-proCNP correlated positively with phase angle and with the body cell mass, which are indicators of nutritional status, and negatively with inflammatory markers (IL-6). To the contrary CNP correlated positively with IL-6 and negatively with phase angle. Nt-proBNP correlated negatively with nutritional marker serum albumin, positively with IL-6. No correlation was found between BNP and nutritional and inflammatory status.

Conclusions: In MHD patients a relevant increase in serum concentration of NP is found, which is probably due to the reduced renal clearance of the peptides, and is also dependent from dialytic clearance, cardiac function, inflammation and nutritional status of patients.

Introduction and Aims: Different types of natriuretic peptides (NP) and their precursors (pro-NP) circulate in the serum. An increase in their serum concentrations is indicative for heart failure and/or endothelial dysfunction. In maintenance hemodialysis (MHD) patients an increase in serum concentration of NP could also indicate a body fluid retention. Furthermore, serum levels of NP in

Negligible Transfer of Endotoxins across High-Flux Haemodialysis Membranes Designed for Convective Therapies

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Introduction and Aims: The long-term success of modern dialysis treatment modalities based on convective transport (such as online-haemodiafiltration, OL-HDF) is largely dependent upon the availability of dialysis fluids of high microbiological purity. Bacterial endotoxins are present in the water supply systems of most dialysis units and measures have to be taken to prevent the entry of these pro-inflammatory substances into the blood of dialysis patients.

It is therefore crucial that modern high-flux membranes afford a high degree of safety to the patient by retaining endotoxins from potentially-contaminated fluids.

Objective: We compared the endotoxin retention properties of the new polysulfone-based FX_{HDF}-600 haemodiafilter with the FX60 high-flux dialyser (both Fresenius Medical Care, Germany).

The FX_{HDF}-600 has been specifically designed to meet the requirements of high-efficiency convective treatment modalities (OL-HDF); it allows high exchange volumes as well as having high sieving properties for middle molecules.

Methods: The dialysers were tested in 3 independent experiments in an in-vitro dialysis set-up using isotonic saline spiked with commercially-available purified endotoxin (LPS; lipopolysaccharide) from *Pseudomonas aeruginosa*. Both blood and dialysate compartments of the dialysers were rinsed and filled with pyrogen-free isotonic saline. After a pyrogen-free recirculation phase (60 min), the dialysate compartment was spiked with LPS at a target concentration of 500 EU/mL. Samples for endotoxin determination were drawn from blood and dialysate compartments after 15 and 60 min under diffusive conditions (QB=200mL/min and QD=500mL/min); during a subsequent 60 min filtration phase at QF=50mL/min, and a 60 min filtration phase at QF=100mL/min, samples were drawn from both compartments in each phase again after 15 and 60 min. Endotoxin was quantified

using a kinetic chromogenic limulus amoebocyte lysate (LAL) assay with a detection threshold of 0.005 EU/mL. Adsorption of endotoxin to the membrane of the filters was calculated from the difference in endotoxin concentration in the pool before and after the experiment.

Results: Using a kinetic chromogenic LAL test, no transfer of endotoxins was detectable for the FX60 and for the FX_{HDF}-600 dialysers.

Conclusions: Under the conditions used in these experiments, both the FX60 high-flux dialyser and the new FX_{HDF}-600 haemodiafilter exhibited no detectable endotoxin transfer and high endotoxin adsorption capacities and are therefore safe barriers against endotoxins from potentially contaminated dialysis fluids – even when exposed to extremely high levels of endotoxin contamination. Thus, unlike polyethersulfone/polyarylethersulfone-based membranes which have been shown in the literature to be permeable to endotoxins, Fresenius Polysulfone[®]-based membranes offer an unparalleled safety in terms of reduction of the inflammatory risk.

Table: Transfer of Endotoxins

Dialyser Type	LAL Reactivity	Endotoxin Adsorption per Dialyser (EU)	Surface Area (m ²)	Endotoxin Adsorption (EU/cm ²)
FX60	below detection limit	952,380 ± 249,460	1.4	64.6 ± 19.9
FX _{HDF} -600	below detection limit	1,012,500 ± 178,500	1.5	67.5 ± 11.9

Less Complications During Haemodialysis by Combined Blood Temperature Control and Blood Volume Control

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Introduction and Aims: Intradialytic morbid events (IME, e.g. hypotension, cramps, headache) are the most frequent complications during haemodialysis (HD). A 50% reduction of sessions with IME was obtained in a randomized crossover trial by blood temperature (BT) control (Maggiore et al., Am J Kidney Dis 2002); and a 20% reduction of sessions with IME was observed in a randomized crossover trial due to blood volume (BV) control (Gabrielli et al., J Nephrol, in press).

Methods: Clinical benefit of simultaneous control of both parameters (BT and BV) was investigated in this international study with randomized crossover design: after a screening phase patients with at least 5 sessions with IME in 5 weeks underwent a study phase with standard HD for 5 weeks and a study phase with

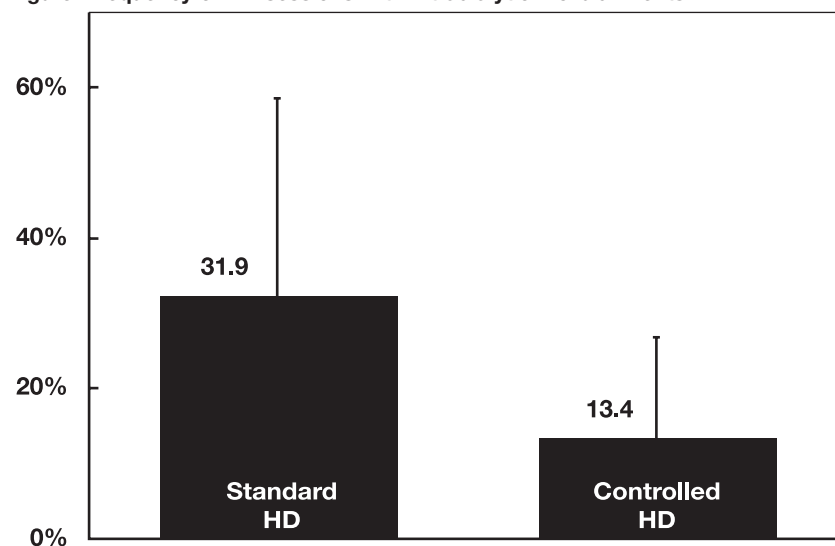
BT- and BV-controlled HD for 5 weeks in randomized sequence. During BT control the individual blood temperature is kept constant during the HD session, during BV control the ultrafiltration rate is adjusted to stay above the individual blood volume limit (automatically by Blood Temperature Monitor BTM and Blood Volume Monitor BVM, Fresenius Medical Care, Germany). IME and other treatment related parameters were recorded.

Results: 43 hypotension-prone patients were recruited, 20 patients could not be included into the analysis population (mainly due to less IME than required by protocol), 23 patients completed the study according to study protocol. Their mean age was 53 ±14 years, they were for 7±4 years on renal replacement therapy, and 39% male. The mean duration of the HD session was 244±17 minutes for both standard and controlled

HD; the mean ultrafiltration during the HD session was 3.4±0.9 L for standard HD, and 3.3±1.0 L for controlled HD (NS). Pre- to post-dialytic changes in both, blood pressure and heart rate, were less pronounced in controlled HD than in standard HD. 131 IME were observed during 344 standard HD sessions and 52 IME during 344 controlled HD sessions; IME occurred in 31.9±26.7 % of the sessions during standard HD, but only in 13.4±13.2 % during controlled HD ($P=0.013$) (see figure).

Conclusions: This prospective randomized trial demonstrates the benefit of an individualized HD treatment with combined blood temperature control and blood volume control. In hypotension-prone HD patients the combination of BT and BV control reduces the percentage of sessions with IME by 58%, more than each control mode alone.

Figure: Frequency of HD sessions with Intradialytic Morbid Events



mean values ± standard deviation; $p = 0.013$

Improving the Efficiency of Short-Term Single-Needle Hemodialysis

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Introduction and Aims: It is widely believed that single-needle (SN) hemodialysis is inferior to conventional double-needle (DN) hemodialysis. The purpose of this study was to compare two SN dialysis regimens using different blood flow rates with conventional DN hemodialysis.

Methods: We studied eight patients (2 women, 6 men) undergoing chronic intermittent DN bicarbonate hemodialysis three times per week on a Cimino-Brescia fistula for at least 3 months. The study had a prospective four-period design and lasted 4 weeks. During weeks 1 and 3 the participants had standard DN hemodialysis sessions with Wallace needles at a blood flow rate of 250–300 ml/min. During week 2 they had single-needle dialysis sessions with a short 15-Gauge stainless-steel needle and an effective blood flow rate of 180 ml/min (360 ml/min for each of the two pumps) and a venous pressure below 200 mmHg. During week 4 they had SN dialysis sessions with a short 15-gauge stainless-steel needle, an effective blood flow rate of 250 ml/min (500 ml/min for each of the two pumps) and a venous pressure below 200 mmHg. The primary outcome measure was ionic dialysance.

Results: The effective blood flow target of 250 ml/min was achieved in six of the eight patients. Ionic dialysance 45 minutes after the beginning of the session differed among the four periods ($p < 0.001$, Friedman test). Ionic dialysance was better during each DN dialysis period than during the 180 ml/min SN period ($p < 0.01$, Dunn's multiple comparison test) but there was no difference with the 250 ml/min SN period. Ionic dialysance 30 minutes before the

end of the dialysis session differed among the four periods ($p < 0.001$, Friedman test). Ionic dialysance was far better during each DN period than during the 180 ml/min SN period ($p < 0.001$, Dunn's multiple comparison test) and slightly better than during the 250 ml/min SN period ($p < 0.05$, Dunn's multiple comparison test). The single-pool Kt/V ratio differed among the four periods ($p < 0.0001$, Friedman test). The Kt/V ratios were far better during each DN period than during the 180 ml/min SN period ($p < 0.001$, Dunn's multiple comparison test) and slightly better than during the 250 ml/min SN period ($p < 0.01$, Dunn's multiple comparison test). The Kt/V provided by the dialysis monitor gave identical results to single pool Kt/V.

Conclusions: We conclude that single-needle dialysis with an effective blood flow rate of 180 ml/min delivers an inadequate dialysis dose, which may be harmful. In contrast, an effective blood flow rate of 250 ml/min appears acceptable for brief periods of single-needle dialysis lasting one or two weeks. Otherwise, an increase in the length of the dialysis session and or use of higher surface membrane and even higher blood flow, is required to obtain the same quality of dialysis as with conventional double-needle hemodialysis. A careful monitoring of dialysis dose delivered is mandatory in single needle dialysis.

Assessment of Fluid Status in Amputees Using Bioimpedance Spectroscopy

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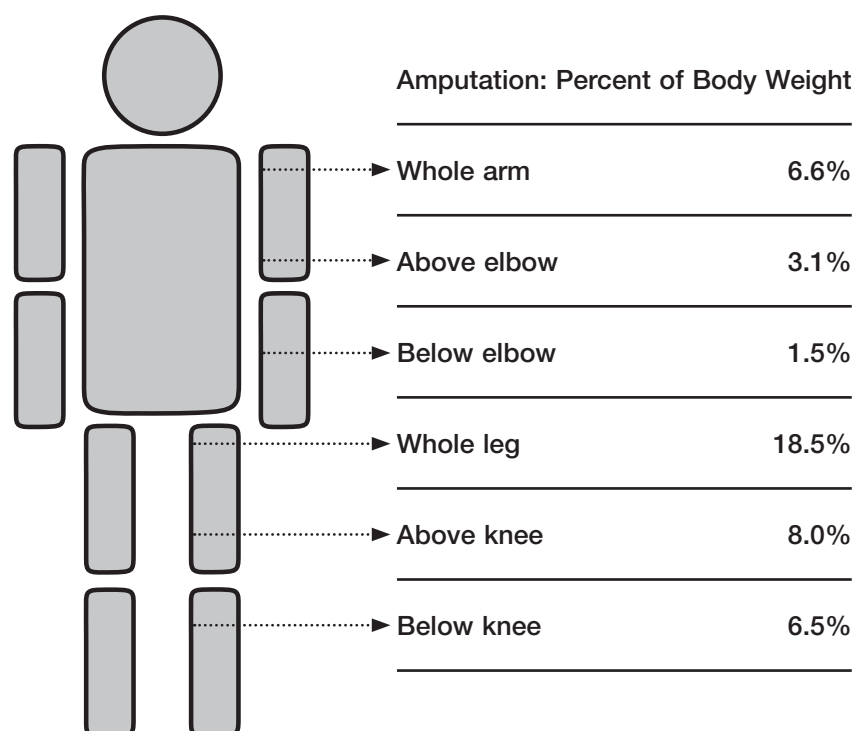
Introduction and Aims: In a recent publication (Am J Clin Nutr 85, 2007) a 3C body composition model was introduced which allows calculating the fluid status of healthy subjects and patients in absolute litres. The model requires extra- and intracellular water volumes as an input, which can be determined sufficiently well using the latest bioimpedance spectroscopy (BIS) techniques. However, these equations cannot be applied in a straight forward way to amputees since they assume a total body measurement, and currently there are no other appropriate equations available for amputees. This work presents a method to correct for missing limbs.

Methods: Correction factors for the most common amputations were determined using dual energy x-ray absorptiometry (DXA) in 151 healthy subjects. 18 dialysis patients with amputations from 3 different centers were analysed. Body weight was corrected to simulate a “full body weight”, impedance measurements were performed (BCM-Body Composition Monitor), and then the resulting body compartments were corrected for the missing limb.

Results: The average correction factor (relative to body weight) for a whole leg was 18.5%, for an above-knee amputation 8% and for a below-knee amputation 6.5%. Correction factor for a whole arm was 6.6%, for an above-elbow amputation 3.1% and a below-elbow amputation

1.5% (see Figure). Six patients had an upper-knee amputation, eleven patients a below-knee and one patient a whole arm amputation. Pre-dialysis fluid status of all patients with the original uncorrected equations was 2.5 ± 2.3 L (mean \pm SD); after correction fluid status was 2.0 ± 1.8 L.

Conclusions: Application of DXA-correction factors allows correcting fluid status and body composition determined by whole body BIS for amputations. Using traditional BIS equations in amputees results in an overestimation of body compartment masses of up to 20%, depending on the type of amputation. This work presents a systematic approach to enable accurate BIS-measurements in amputees.



Overhydration in Peritoneal and Dialysis Patients as Measured with Multi-Frequency Bio-Impedance

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Introduction and Aims: Achieving euvoemia is an important goal in patients on renal replacement therapy (RRT). However, evaluation of volume status is hampered by lack of a reliable, clinical tool. Most likely, fluid status is often misqualified and volume overload is still present subclinically. Multi-frequency bio-impedance (MFBI) has been re-introduced to evaluate volume status. It has been demonstrated that overhydration as measured with MFBI is related to mortality. It is often perceived that volume status is worse in peritoneal (PD) versus hemodialysis

(HD) patients. There is, however, evidence that volume status in PD patients is centre dependent. This study evaluates volume status in PD vs HD patients in a single centre, using MFBI.

Methods: Volume status was assessed in clinically stable RRT patients using MFBI (BCM – Body Composition Monitor, FMC, Bad Homburg). In PD patients, measurements were done with full abdomen, in HD patients once just before (HDpre) and 20' after (HDpost) dialysis, according to the instructions of the manufacturer. Overhydration (OH) was defined as a ratio overhydration volume (OHvol) over extracellular water (ECW) >0.15.

Results: 44 HD and 34 PD patients were evaluated, the univariate data (one-way anova) are given in the table.

In the multivariate analysis, overhydration was only related to gender (RR 2.9, $p=0.03$) and status HDpost. After correction for confounders, overhydration was similar in PD as in HDpre, and was only better in HDpost (RR=0.5, $p=0.007$). After multivariate correction, PD patients did not have more fat tissue than HD patients ($p=0.9$).

Conclusions: Overhydration is still quite prevalent in a clinically stable dialysis population. PD patients were more overhydrated than HD patients immediately after dialysis, but not than HD patients before dialysis. Male gender and age were risk factors for overhydration. More attention to fluid status of dialysis patients is needed. BCM – Body Composition Monitor analysis can be a useful tool to routinely assess fluid status.

Table: Univariate Analysis

	HDpre	HDpost	PD	p-value
Age (years)	67.7±13.5		61.2±16.9	0.06
Gender (male)	50		55.9	0.6
Diabetes (%)	36.4		14.7	0.04
Ideal weight (kg)	71.4±18.8		70.0±10.4	0.7
Height (cm)	167±9		164±10	0.2
Systolic RR (mmHg)	144±24	135±30	127±28 ^a	0.02
Diastolic RR (mmHg)	72±12	72±12	76±16	0.2
Albumin (mg/dl)	3.7±0.4		3.6±0.4	0.3
hs CRP (mg/l)	0.5±0.8		1.3±3.2	0.3
Total Body Water (l)	33.7±6.9	31.8±8.1	33.9±6.7	0.3
Extracellular water (l)	16.4±3.9	15.3±4.0	16.8±3.3	0.3
Intracellular water (l)	17.1±6.2	16.5±4.6	17.2±3.9	0.7
ECW/height	9.7±1.9	9.1±2.0 ^b	10.2±1.9	0.05
Lean Tissue Mass (l)	31.1±10.7	31.9±11.0	34.5±10.2	0.2
Fat Tissue Mass (l)	27.5±13.0	27.2±12.2	24.2±8.3	0.2
Overhydration Volume (l)	1.9±1.7	0.6±1.7 ^c	2.1±2.3	0.001
Relative Overhydration	0.11±0.08	0.03±0.09 ^c	0.11±0.11	0.001
Overhydrated (%of patients)	24.1	10 ^c	22.3	0.001

a: $p=0.008$ vs Hdpre; b: $p=0.01$ vs PD; c: $p=0.001$ vs PD and vs HDpre

Influence of Peritoneal Fluid on Measurements of Fluid Overload by Bioimpedance Spectroscopy in Peritoneal Dialysis Patients

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Introduction and Aims: The correct estimation of the patient's volume status is a central problem in dialysis therapies. It is a particular challenge in peritoneal dialysis (PD) because here the patient's response to short-term ultrafiltration can not be quoted for clinical dry weight assessment (as in hemodialysis). Very recently a newly developed bioimpedance spectroscopy (BIS) device (BCM – Body Composition Monitor, FMC, Germany) has attained growing interest in this context. By processing the raw data for extracellular water (ECW) and intracellular water (ICW) by means of a validated body composition model, this device for the first time allows a quantification of the individual fluid overload (FO) compared to a representative healthy population.

In this study we asked whether the presence of peritoneal dialysate has an impact on measurements of FO by BIS in PD patients.

Methods: 42 BIS measurements by the BCM – Body Composition

Monitor device were performed both in the absence (D–) and presence (D+) of peritoneal fluid in 17 stable PD patients. Data for extracellular resistance (RE), intracellular resistance (RI), ECW, ICW and FO (D+; D–) were analyzed by paired t-test and linear regression.

Results: Mean FO was 0.99 ± 1.17 L in D– and 0.94 ± 1.27 in D+ ($p = \text{n.s.}$ paired t-test). Linear regression demonstrated an excellent degree of conformity between FO (D–) and FO (D+) ($r^2 = 0.93$, $\text{SEE} = 0.35$). The very small deviations for FO could be best explained by small deviations in Ri and ICW, respectively.

Conclusions: In conclusion, the presence of peritoneal fluid in PD patients has a negligible influence on measurements of FO by BIS. BIS measurements can be therefore conveniently and reliably performed without emptying the peritoneal cavity which may facilitate the use of BIS in this particular group of patients.

Final Results on the Effects of GDP-Reduced Dialysate (Balance, FMC) for Peritoneal Dialysis on the Epithelial-To-Mesenchymal Transition of Mesothelial Cells *in vivo*

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Introduction and Aims: Ex-vivo culture of PD fluid-derived mesothelial cells (MC) showed phenotype modifications related to an epithelial-to-mesenchymal transition (EMT) during PD. Transdifferentiated MC acquired fibroblast-like phenotype, with the loss of E-cadherin expression and an increased production of VEGF, fibronectin and procollagen, which correlated with altered peritoneal function. We have also demonstrated that lactate containing fluid induces EMT of MC *in vitro* and exacerbates the effect of TGF- β in

transdifferentiation. In contrast, Balance fluids reduce EMT manifestations.

We hypothesized that patients treated with Balance, a GDP-reduced fluid, should show a decrease in the expression of EMT markers in MC taken from fresh peritoneal effluent and grown *ex vivo*, compared to a GDP rich fluid.

Methods: Twenty patients in control group and 13 Balance patients were followed during 24 months to determine EMT markers in MC released into effluent and grown *ex vivo*, every six months. A definition of EMT of MC was based in fibroblastoid phenotype, higher production of VEGF to supernatant (pg/mg of cell protein), higher content of fibronectin in MC cell extract (ELISA) (ng/mg protein) and higher content of procollagen in MC cell extract (ELISA) (ng/mg of cell protein). ICAM-1 expression demonstrated the mesothelial nature of the cells and showed no difference between groups. Lately, we added the determination of IL-8 and TGF- β to explore inflammatory and pro-fibrotic molecules.

Results: There were significant greater levels of VEGF (4-fold), procollagen (2-fold), fibronectin (5-fold) and IL-8 (2-fold) in fibroblastoid phenotype, all samples. Overall, control group showed

greater values of VEGF ($p=0.001$), IL-8 ($p=0.03$), TGF- β ($p=0.01$), procollagen (NS) and fibronectin (NS) than the Balance fluid group.

1. The fibroblastoid phenotype in the control fluid group was significantly more prevalent (91–100%) than in Balance fluid group (27–11%) at mid-term 18–24 months, respectively.

2. VEGF production (pg/ml) into supernatant showed significant lower values in the Balance group ($5,204 \pm 7,190$ and $4,938 \pm 34,635$) than in control group ($36,443 \pm 25,726$ and $46,458 \pm 26,823$), $p=0.001$ and 0.03 at 18 and 24 months, respectively.

3. Fibronectin levels in MC cell extract showed a non-significant increase in both groups at 18 months.

4. Procollagen levels in MC cell extract did not change over time in both groups.

5. IL-8 and TGF- β did not show significant change over time on PD.

Conclusions: Fibroblastoid phenotype and VEGF production to supernatant, as EMT markers, have demonstrated a significant favorable outcome in patients using Balance fluid relative to those using standard fluids. The results confirm the hypothesis that GDP-reduced fluid protects mesothelial cell from the development of EMT in humans.

Comparison Between Different Creatinine-Based Equations for Estimating Total Creatinine Clearance in Peritoneal Dialysis: A Multicentre Study

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Introduction and Aims: It is crucial to assess the adequacy of peritoneal dialysis (PD) situation because of its influence on patient outcome. Collecting dialysate and urine for 24 hours can be rather troublesome, so a simple and inexpensive alternative method for rapidly evaluating adequacy in PD would be very useful. Our study aimed to assess the performance of 12 different creatinine (Cr)-based equations commonly used to estimate GFR in predicting total Cr clearance in PD.

Methods: Four Italian dialysis centres enrolled 355 PD patients with 2,916 fluid collections. To rank the equations, their accuracy (ability to match measured values → % estimates with error <30%), precision (ability to give reproducible estimates → root mean square error, RMSE), and sensitivity/specificity (ability to diagnose inadequacy correctly → area under ROC curves, AUC, where $x = 1 - \text{specifi-$

city and $y = \text{sensitivity}$) were calculated with reference to the measured total Cr clearance.

Results: The Gates, 4-MDRD, and Virga equations showed the best global performance as concerns accuracy (error <30% = 86%, 84%, 78% respectively), precision (RMSE = 13.2, 13.4, 13.3), and sensitivity/specificity (AUC = 0.825, 0.820, 0.826), while the Cockcroft-Gault formula revealed a rather poor reliability. Given the reported 6–9% coefficient of variability for single total Cr clearance measurements in PD, the real predictive power of these equations might well be acceptable for use in clinical practice.

Conclusions: Fluid collection remains the gold standard for assessing PD adequacy, but the most reliable of the Cr-based equations can be used for a more frequent and straightforward monitoring of adequacy at no extra cost.

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