

Congress Service

45th Congress of the ERA-EDTA

Mai 10-13, 2008, Stockholm, Sweden



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Selected Abstracts of the
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Christina Lage, MD
Ilona Weber-Fürsicht

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1. Anemia

Time Outside Hb-target Ranges in Respect of Old and New K/DOQI Guidelines for Anemia Management

Hans-Joachim Müller¹, Patrick Biggar², Jan Galle³, Lars-Christian Rump⁴, Matthias Girndt⁵, Hans-Gernot Asmus⁶, Roland Winkler⁷, Johann Braun⁸, Johannes Mann⁹, Christoph Wanner¹⁰, Frank Dellanna¹¹

¹ Dept. of Nephrology, Klinikum Fulda, Germany

² KfH Nierenzentrum Coburg, Germany

³ Dept. of Nephrology, Klinikum Lüdenscheid, Germany

⁴ Dept. of Nephrology, University of Düsseldorf, Germany

⁵ Dept. of Nephrology, University of Homburg, Germany

⁶ KfH Nierenzentrum Berlin, Germany

⁷ Dialysegemeinschaftspraxis Rostock, Germany

⁸ KfH Nierenzentrum Nürnberg, Germany

⁹ Dept. of Nephrology, Klinikum München-Schwabing, Germany

¹⁰ Dept. of Nephrology, University of Würzburg, Germany

¹¹ Dialysegemeinschaftspraxis Düsseldorf, Germany

Introduction and Aims: Quality management is an important fact in dialysis centers and guideline fulfillment is one important part of it. Recently guidelines for anemia management have been changed and thus distribution of patients below, in and above target ranges may also have changed. Thus we analyzed in this study the changes in distribution of patients in the three different strata for old (11-13 g/dl) and new (10-12 g/dl) guidelines.

Methods: We performed a multi-center (n = 26) retrospective study with data from the German AENEAS-database. All patients (n = 901; age = 65.3±14.2 years; m = 512; diabetes = 402) with 12 months Hb (2006) and ESA data with at least one Hb per month have been included. To calculate time outside target ranges all Hb consecutive values have been connected lineary and the intersection points with the lines representing the upper and lower limits

have been calculated. Thus the time between two intersections represented the time below, inside or above target ranges. Time inside the three different groups have been compared for old and new guideline fulfillment.

Results: The mean observation period has been 343±6.7 days. The mean Hb value during the observation period was 11.76±0.85 g/dl (normally distributed). The median time for the different guidelines below target ranges has been 19% and 0% (p<0.001), in target ranges 62%, 50% (n.s.) and above 6%, 40% (p<0.001) respectively (F-Test).

Conclusions: In this quite well managed patient cohort the change of guidelines in anemia management would shift the time below targets significantly towards time above target without a significant increase of time in target. Thus no gain in fulfillment of guideline recommendations could be seen.

Changes Between 1999 and 2005 in the Risk of Death with High or Low Haemoglobins in UK Haemodialysis Patients: Data from 32,500 Patient Years Observation

Eight Best Abstracts

David Ansell¹, Dan Ford¹,
Donald Richardson²

¹ UK Renal Registry, Bristol, United Kingdom

² Renal Unit, York District Hospital, York, United Kingdom

Introduction and Aims: There has been considerable interest in the new guidelines recommending that haemoglobin should be kept within a new upper limit target of under 13 g/dl (12.5 g/dl in the UK). This has been generated from concerns in randomised trials showing increased risk of thrombosis in patients with higher Hbs. This upper limit raises concerns, as the distribution of patient Hbs within a given renal unit are normally distributed and it is very difficult to narrow that distribution with a smaller 'tail' at both the top 'high Hb' and bottom 'low Hb' ends.

The risk of this new strategy is that it may generate an increase in the number of patients with a haemoglobin below 10 g/dl. Are the risks of a low haemoglobin equal to those of having a high haemoglobin?

Methods: The UK Renal Registry has been collecting quarterly Hb data since its outset, although patient numbers were small in 1997 and 1998 so we have only included data from 1999 to 2005. The data is collected via automated software data extraction process from hospital renal IT systems.

All prevalent patients on HD within each of the sequential years were included. In 2005 cohort there

were 8,500 prevalent patients included. The 4 quarterly Hb results for the year were meaned and relative risk of death in the following year (compared with an Hb 10.0-10.9 g/dl) was calculated adjusted for age, primary diagnosis and length of time on RRT.

Results: The relative risk of death for the different Hb groups appears to be consistent over the 7 year period. There is a lower risk of death with Hb > 10 g/dl.

Conclusions: This stability in relative risk of death, is seen despite a large shift of patients from low Hbs to higher Hbs over this time period and this could indicate that it is related to achievement of Hb rather than a patient factor. Within the UK, average Hb in HD patients has continued to improve year on year. In 1999 there were 36% with Hb <10 and compared with 13% in 2005. Similarly in 1999 only 11% had an Hb >13 g/dl, compared with 22% in 2005.

This is observational data (not a randomised control trial) but it is not demonstrating a higher risk of death with achieving a higher Hb compared with the higher risk seen with a low Hb. Implementing an upper Hb limit may result in more patients having an Hb under 10 g/dl which is known to be related to an increased risk of death.

Does Routine Blood Sampling Contribute to the Iron Requirements of Renal Patients? A Comparison of a Haemodialysis and Peritoneal Dialysis Population

Best Abstracts Presented by Young Authors

William Herrington, Ramesh Naik,
Mobin Mohteshamzadeh,
Emma Vaux, Lindsey Barker.

Renal Unit, Royal Berkshire Hospital,
Reading, Berkshire, United Kingdom

Introduction and Aims: All dialysis patients have routine blood tests to monitor anaemia, electrolyte balance, blood borne viruses and dialysis adequacy. Phlebotomy in our unit utilises the Vacutainer® system which removes a pre-specified volume of blood for each test. HD patients require more frequent iron administration than PD patients. HD patients have more frequent blood tests than PD patients.

The aim was to calculate the volume of blood and estimate the iron removed for routine blood samples from a population of peritoneal dialysis (PD) and haemodialysis (HD) patients in a single renal unit.

Methods: All dialysis patients (of at least 90 days) in a single renal unit from 01/01/2006 to 31/12/2006 were analysed. Data were collected retrospectively from a clinical computer database on patient demographics; number of blood tests; plasma haemoglobin (Hb) and ferritin levels; Erythropoiesis-stimulating agent (ESA) and intravenous (IV) iron dose and blood transfusion. From the data, annual volume of blood and iron removed were estimated.

Results: 224 HD and 118 PD patients were eligible for analysis, equivalent to 191 and 93 treatment years. Demographics showed 72% Caucasian, 63% male, 30% diabetic and HD patients were older than PD 63 v 58 years ($p < 0.01$, paired t-test). The proportion on warfarin was similar (14%). Results are shown in the table.

Conclusions: HD patients achieve a lower Hb with a higher ESA and IV iron requirement than PD patients. Routine blood sampling removes a significant amount of iron, twice as much in HD patients. This is more than would be required for standard unit monitoring but is small compared with the amount of IV iron received (6% HD and 35% PD). It is recognised that HD patients lose iron in the dialysis process but this is unlikely to account for all the difference and would not apply to PD patients. Other sources of iron loss such as occult gastrointestinal bleeding must be considered. A policy to reduce blood sampling to standard levels would not impact hugely on the IV iron requirement of HD patients.

Table: Results

	HD n=224	PD n=118	
Annual blood sample volume	365 mls (291-508)	172 mls (125-247)	$p < 0.0001$
Min unit requirement	216 mls	90 mls	
Annual Iron removed	141 mg [116-185]	72 mg [50-95]	$p < 0.0001$
Annual IV iron given	2000 mg [950-2950]	200 mg [0-600]	$p < 0.0001$
Iron from transfusion	225 mg	4.7 mg	
Plasma ferritin	607 ug/l [456-756]	463 ug/l [375-602]	$p < 0.0001$
Weekly Epo dose	7000U [5000-10000]	4000U [2000-6000]	$p < 0.0001$
Haemoglobin	11.5 g/dl [10.7-12]	11.9 [10.9-12.6]	$p < 0.0001$

[all median +IQR, Mann-Witney U test]

2. Bone Disease and Mineral Metabolism

Is Centre Performance for Achievement of the Phosphate Clinical Practice Guideline in Hemodialysis Patients a Stable Characteristic over Time? Data from 7,900 Patients in 50 Centres

Alexandra Hodsman¹, Julie Gilg¹, Yoav Ben-Shlomo², Paul Roderick³, David Ansell¹, Charlie Tomson¹

¹ UK Renal Registry, Southmead Hospital, Bristol, United Kingdom

² Social Medicine, University of Bristol, Bristol, United Kingdom

³ Public Health Sciences, University of Southampton, Southampton, United Kingdom

Introduction and Aims: The UK Renal Registry is unique in collecting sequential biochemical data which are audited against national (Renal Association) clinical practice guidelines. This study, using phosphate as an example, shows the benefit of combining longitudinal and cross sectional analysis to audit dialysis centre performance.

Methods: The 2005 HD cohort were analysed. Patients were excluded if they had <3 PO₄ values in 2005. % of patients in each centre with PO₄<1.8mmol/L (current national guideline) were calculated using both the value for the last quarter of 2005 (Q4) and mean annual value (MAV). As the mean value included the Q4 value, Bland-Altman plots were derived to compare: difference between MAV and Q4 vs average of MAV and Q4. For each unit, % of PO₄<1.8mmol/L by quarter were plotted on statistical process control charts which are used to analyse performance longitudinally. Data were plotted both before and after 2005 as at least 7 consecutive data points are required to detect a significant change in process over time. These data were compared with the Bland-Altman plots for 2005 data.

Results: The analysis included 7,912 HD patients in 50 dia-

lysis centres. There was a strong correlation between % with PO₄<1.8mmol/L using Q4 value and MAV ($r^2=0.87$ $p<0.0001$). The Bland-Altman plot showed a mean difference of 1.79% (CI = 0.68-2.9) when the difference between Q4 and MAV was plotted against the average value by centre (figure 1). 2 units lay outside of the limits of agreement (+/- 2SD). Statistical process control charts explain these data. For most units lying within the limits of agreement the % of patients with PO₄<1.8mmol/L is stable over 4 quarters and therefore Q4 value is a good measure of annual performance. For centres lying outside the limits of agreement, 2005 data points are part of an 'unstable process' on the statistical process control chart indicating a significant change in outcome over time. For these centres, Q4 data alone is not a good measure of performance.

Conclusions: The stability of centre performance over time is an important factor in understanding inter centre variability in outcomes. Statistical process control charts enable early identification of improvement/deterioration in performance and allow clinicians to track the effects of new clinical processes designed to improve performance.

Phosphorus Burden is Higher in Peritoneal Dialysis than in Hemodialysis

Pieter Evenepoel¹, Björn Meijers¹, Bert Bammens¹, Kathleen Claes¹, Dirk Kuypers¹, Dirk Vanderschueren², Yves Vanrenterghem¹

¹ University Hospital Gasthuisberg, Nephrology, Dialysis and Transplantation, Leuven, Belgium
² University Hospital Gasthuisberg Endocrinology, Leuven, Belgium

Introduction and Aims: The phosphorus burden is generally considered to be higher in hemodialysis (HD) as compared to peritoneal dialysis (PD). Predialysis phosphorus concentrations are misleading as a measure of phosphorus exposure in HD as these neglect significant intra- and interdialytic variations in serum phosphorus concentration. The major aim of the present study was to compare the phosphorus homeostasis between two unselected cohorts of PD and HD patients. The secondary aim was to identify determinants of FGF-23 in maintenance dialysis patients.

Methods: Parameters of mineral metabolism including calcidiol, bioactive PTH, and FGF-23 were determined in 79 HD and 61 PD patients. In PD phosphorus levels were determined mid-day. In HD, time-averaged phosphorus concentrations were modeled from measurements before and after the midweek dialysis session. Weekly renal, dialytic and total phosphorus clearances as well as mass removal were calculated from urine and dialysate collections.

Results: Time-averaged serum phosphorus concentrations in HD (3.5 ± 1.0 mg/dL) were significantly

lower than the mid-day concentrations in PD (5.0 ± 1.4 mg/dL, $p < 0.0001$). In contrast, predialysis phosphorus concentrations (4.6 ± 1.4 mg/dL) were not different from PD. biPTH (119 vs. 82 ng/L, $p < 0.05$) and FGF-23 (10334 vs. 5075 ng/L, $p = 0.008$) were higher in PD. Despite higher residual renal function, total phosphorus clearance was significantly lower in PD ($p < 0.0001$). Phosphorus mass removal, conversely, was significantly higher in PD ($p < 0.05$).

In multivariate analysis, time-averaged P concentration, serum calcium level, residual glomerular filtration rate, age, active vitamin D usage and total mass removal of urea nitrogen were found to be independently associated with FGF-23. These variables explain 57 % of the variation of FGF-23 ($p < 0.0001$).

Conclusions: Opposite to prevailing thoughts, our data indicate that the phosphorus burden in patients treated with PD is higher as compared to patients treated with HD. Both a higher dietary phosphorus intake and a lower phosphorus clearance contribute to this increased burden. Serum phosphorus targets should be adjusted downwards in PD patients.

Influence of Using a Low-Calcium Dialysate on Achieving the Target Parameters of Calcium-Phosphorus Metabolism in a Population of Hemodialysis Patients

Best Abstracts Presented By Young Authors

Adrian Dorin Zugravu¹,
 Simona Hildegard Stancu¹,
 Roxana Martinescu², Christian Klein²,
 Gabriel Mircescu¹

¹ Dr. Carol Davila Clinical Hospital of Nephrol; Carol Davila Univ of Medicine and Pharmacy, Bucharest, Romania

² Carol Davila Fresenius NephroCare Dialysis Center, Bucharest, Romania

Introduction and Aims: Dialysis patients have an increased cardiovascular morbidity and mortality, which are associated with the presence of vascular calcifications and abnormalities of the calcium-phosphorus metabolism. The study aims to assess the influence of using a low-calcium dialysate (AF13–1.25mEq/l calcium – Fresenius Medical Care, Germany) on the parameters of the mineral metabolism in a cohort of hemodialysis patients.

Methods: Corrected serum calcium, serum phosphate, calcium-phosphorus product and PTH were followed up in a cohort of 172 stable chronic hemodialysis patients for 9 months before and after starting using low-calcium dialysate. Low-calcium dialysate was used in patients with already high values of serum calcium, in which it is impossible to use vitamin D derivatives like calcitriol or to further increase the dose of calcium-based phosphate binder, because of resulting hypercalcemia.

Results: The study cohort comprises younger patients with a long dialysis vintage, more often with hypoparathyroidism, less often treated with vitamin D derivatives. Compared to the data available in the literature, there was a higher

percentage of normocalcemic and a lower percentage of hypercalcemic patients. The percentage of normophosphatemic patients is marginally higher. Caution should be exerted, as hypocalcemia can develop in these patients and lead to hyperparathyroidism and further hypercalcemia.

Conclusions: Employing a low-calcium dialysate is useful in the attempt to reach the goals for the calcium-phosphorus metabolism parameters recommended by the guidelines. Nevertheless, other measures (non-calcium based phosphate binders, non-hypercalcemic vitamin D products, calcimimetics) are also needed in order to achieve the targets.

Reference: Kovcsdy CP et al. Clin J Am Soc Nephrol, doi: 10.2215/CJN.03850907

Table 1:

Baseline characteristics	
Male (%)	56.4%
Mean age (years)	55.1±12.6
Hemodialysis vintage (years)	10.7±9.6
Vitamin D therapy	18.6%
Hypoparathyroidism (%)	46%

Table 2: Parameters of mineral metabolism before and after using low-calcium dialysate

	Before AF13	After AF13	p
8.4<serum Ca<9.5mg/dl*	61%	76.2%	<0.05
Serum Ca<9.5mg/dl	13.4%	7%	<0.05
3.5<serum P _i <5.5mg/dl*	24.4%	32.6%	<0.05
Ca X P <55 (mg/dl) ² *	53.5%	53.5%	<0.05
3 normal parameters*	14%	26%	<0.05

*According to K/DOQI Guidelines

Serum Fetuin-A Forms Precipitable Complex with Calcium, Magnesium and Phosphate under Extra-Osseous Calcification Stress

Isao Matsui, Takayuki Hamano,
Satoshi Mikami, Kodo Tomida,
Hirofumi Tanaka, Yoshitaka Isaka,
Takahito Ito, Enyu Imai.

Nephrology, Osaka University
Graduate School of Medicine, Suita,
Osaka, Japan

Introduction and Aims: Vascular calcification is the most common type of extra-osseous calcification in human chronic kidney diseases. In patients on dialysis, serum concentrations of fetuin-A, a potent inhibitor of calcium phosphate precipitation, have been revealed to be negatively associated with high cardiovascular mortality. However, the preventative mechanism of fetuin-A to calcification is not well understood. To elucidate this subject, we performed the following animal experiments.

Methods: We made an adenine-induced renal failure model and analyzed it with usual laboratory technique including real time PCR, immunoblot analysis and mass spectrometry.

Results: In liver, fetuin-A mRNA was down-regulated in adenine rats in comparison with normal rats. Immunoblot analysis showed that protein levels of fetuin-A in liver almost disappeared in adenine rats although serum concentration was not much different. This discrepancy may be partly attributable to extra-hepatic production of

fetuin-A, because we found that fetuin-A mRNA was upregulated in testis of adenine rats. We also found that physical characteristic of serum fetuin-A was quite different between control and adenine rats. Serum from adenine rats but not control rats formed precipitation after centrifugation at room temperature at 16,000 g for 2 hours. SDS-PAGE followed by Coomassie-stain revealed a clear 59 kDa band containing fetuin-A, which was confirmed by mass spectrometry. The precipitate contained calcium, magnesium and phosphate, and the addition of EDTA to serum prior to centrifugation eliminated the precipitate formation. In addition, both the precipitate formation and the vascular calcification of adenine rats disappeared by weekly subcutaneous administration of alendronate.

Conclusions: Our data suggest that fetuin-A mineral complex plays a role in the extra-osseous calcification and that the detection of this complex may be useful for the evaluation of calcification risk.

3. Cardiovascular Diseases

When is the Best Screening Time for Coronary Heart Disease in Hemodialysis Patients Who have no Significant Coronary Artery Disease at the Initiation of Dialysis Therapy?

Nobuhiko Joki¹, Yuri Tanaka¹, Hisao Hara², Masao Moroi², Hiroshi Fukuda², Igor G. Nikolov⁴, Yoshitsugu Iwakura¹, Haruka Masuda¹, Hiroyasu Ishikawa¹, Yoji Inishi¹, Sonoo Mizuiri³, Hiroki Hase¹

¹ Division of Nephrology, Toho University Ohashi Medical Center, Tokyo, Japan

² Division of Cardiovascular Medicine, Toho University Ohashi Medical Center, Tokyo, Japan

³ Division of Nephrology, Toho University Omori Medical Center, Tokyo, Japan

⁴ Inserm Unit 845, Necker Hospital, Paris, France

Introduction and Aims: Screening for coronary artery disease (CAD) at the initiation of dialysis therapy is an actual K/DOQI guideline recommendation. It remains controversial when is the optimal second screening time for CAD in dialysis patients without significant CAD at the initiation of dialysis. The purpose of this work was to study 1) the survival of hemodialysis (HD) patients without CAD at HD initiation, 2) the major predictors of cardiac events and 3) to propose the best second CAD screening time point after HD initiation.

Methods: In order to know the survival of de novo major adverse cardiac events (MACE) in hemodialysis (HD) patients without CAD, we prospectively followed the HD patients with normal imaging by screening tests for CAD at the initiation of HD. To detect CAD, 177 of 305 new HD patients underwent coronary angiography and/or pharmacologic stress thallium-201 single photon emission computed tomography (SPECT) within 1 month after start of HD. From 177 patients, 100 were without significant CAD and were followed for a median of 24 months.

Results: Five MACE were observed in follow-up period, but no MACE was observed within 1 year after initiation of HD. All 5 events occurred in the second year of HD initiation. Two of 5 MACE occurred immediately after the first year of HD initiation. Increased C-reactive protein (CRP) was the only independent predictor of MACE (hazard ratio: 1.39; 95% confidence interval: 1.03 to 1.78, $p=0.008$) using Cox regression analysis. The best cutoff point of CRP to predict MACE was determined as 3.5 mg/L. MACE-free rates (99% vs. 79%, $p=0.0008$) at 2 years were significantly higher in patients with $CRP < 3.5$ mg/L than with $CRP > 3.5$ mg/L.

Conclusions: In conclusion, one year after the initiation of HD could be the best optimal second screening time point for CAD in patients without CAD at HD initiation. If serum CRP concentration is less than 3.5 mg/dL at the initiation of HD, postpone of second screening for CAD should be considered.

Comparison of Progression Rates of Coronary Artery Calcification in Eight-Hour and Four-Hour thrice Weekly Hemodialysis

Soner Duman¹, Gulay Asci¹,
Ebru S. Gunay¹, Mumtaz Yilmaz¹,
Mehmet Ozkahya¹, Alfert Sagdic²,
Siddik M. Adam², Sihli Caliskan²,
Hakan Kaplan², Ercan Ok.¹

¹ Nephrology, Ege University School
of Medicine, Izmir, Turkey
² FMC Turkey Clinics

Introduction and Aims: In this prospective-controlled study, we compared progression rate of coronary artery calcification (CAC) in patients on 8-hour and 4-hour thrice weekly HD treatment in a prospective manner.

Methods: Eighty-nine patients undergoing 4-hour (n= 46) or 8-hour (n= 43) thrice weekly HD treatment for at least 6 months were enrolled in the study. CAC was measured twice with an interval of 10 months by multi-slice computerized tomography and scored by Agatston method by the same radiologist. Demographical, clinical and time-averaged laboratory data were assessed.

For statistical assessments student's t-test, Wilcoxon rank sum test, Pearson and Spearman correlation analysis, and logistic regression analysis were used.

Results: There was no difference between 4-h and 8-h HD groups regarding age (48±13 and 51±10 years), dialysis vintage (63±56 and

64±49 months), and frequency of diabetes (20% and 16%); there was male predominance in 8-h HD group (69% and 56%). Mean duration of HD sessions and mean blood flow rates were 241±24 and 267±24 ml/min in 4-h group and 405±46 and 238±18 ml/min in patients in 8-h group.

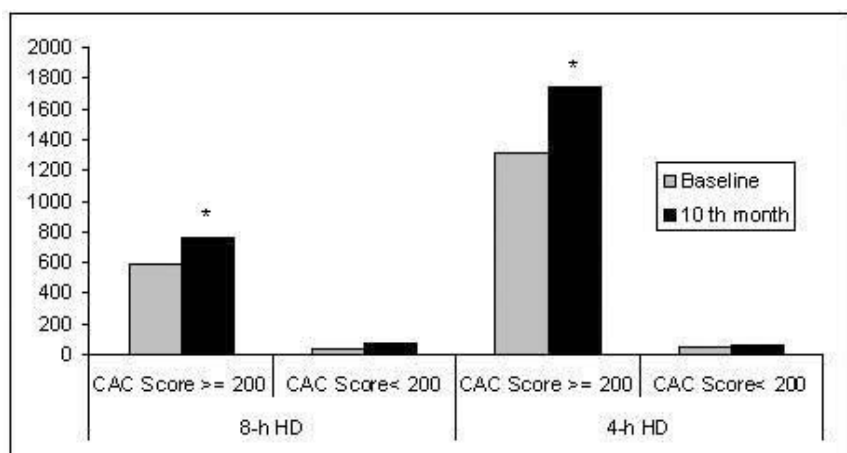
Serum phosphate level (4.0±0.9 and 4.9±1.1 mg/dl, p<0.001) and CaxP product (36±11 and 43±11 mg²/dl², p<0.01) were significantly lower in 8-h HD compared to 4-h HD, although needed phosphate binder dosage was lower in 8-h HD than 4-h HD treatment (534±440 and 2563±1788 mg/day, p<0.001).

Baseline CACs was lower in patients treated by 8-h HD for at least six months compared to conventional HD patients but difference did not reach significance (median CACs 312 and 468). CACs significantly increased during follow-up in both groups; progres-

sion rates were not different (ΔCACs 116 and 127 in 8-h and 4-h group). In patients with baseline CACs higher than 200, progression rate was significantly lower in 8-h HD group than 4-h HD group (median ΔCACs 141 (67-291) and 372 (142-695), p<0.001). ΔCACs was positively correlated with pre- and post-dialysis urea (r= 0.42 and r= 0.43) and creatinine (r= 0.33 and r= 0.39), phosphate (r= 0.42), CaxP product (r= 0.41), phosphate-binder dosage (r= 0.46) and inversely correlated with serum bicarbonate (r= -0.34), Kt/V (r= -0.39), and duration of HD session (r= -0.35). In multivariate analysis, serum phosphate level was independent predictor for the progression of CACs.

Conclusions: Longer hemodialysis sessions reduce progression of coronary artery calcification in patients with CACs higher than 200, possibly related to better phosphate control.

CAC Progression Rates



Comparison of Arterial Compliance in Patients Treated with Hemodialysis and Peritoneal Dialysis in the Early and Late Years of Renal Replacement Therapy

Grzegorz Wystrychowski,
Ewa Zukowska-Szczechowska

Department of Internal Medicine,
Diabetology and Nephrology, Medical
University of Silesia, Zabrze, Poland

Introduction and Aims: A survival advantage of peritoneal dialysis (PD) over hemodialysis (HD) in the initial years of renal replacement therapy (RRT) and an opposite trend in the later years of RRT have been reported in numerous studies. The origin of these observations is not entirely clear.

We aimed to assess whether arterial stiffness - an independent predictor/risk factor of cardiovascular mortality - differs between HD and PD patients in the first two or in the subsequent years of RRT. If present, such variations might explain/contribute to the observed differences in mortality between the two populations.

Methods: All the center's 100 eligible end stage renal disease patients treated with hemodialysis

or peritoneal dialysis for at least 3 months have been studied. Exclusion criteria included acute clinical conditions, severe heart failure, arrhythmia, valve abnormalities, and switches between RRT modalities. The study group consisted of 31 HD and 18 PD patients dialysed for ≤ 2 years (15 M/16 F, aged 61.3 ± 12.4 years and 11M/7F, aged 50.6 ± 15.3 years, respectively), as well as 32 HD and 19 PD patients dialysed for >2 years (15 M/17 F, aged 55.7 ± 12.1 years and 13M/6F, aged 58.4 ± 14.1 years, respectively).

Large (C1) and small artery (C2) compliance indices were estimated non-invasively with use of modified Windkessel model analysis of pulse waveform (HDI/Pulse Wave CR-2000 Research Cardiovascular Profiling System) before HD procedure or with dialysate in the peritoneal cavity in PD patients. Blood pressures and pulse rate were recorded, and major laboratory parameters were assessed.

C1 and C2 were compared between HD and PD patients of ≤ 2

or >2 years of RRT with univariate test, as well as by means of analysis of covariance with adjustment for independent correlates of arterial compliance, dissected in a cohort of 226 patients with stage 2-5 chronic kidney disease, as reported previously (WCN 2007). These included age, mean blood pressure, body surface area, as well as heart rate and use of angiotensin-inhibiting agent (C1) or serum CRP and diabetes duration >16 years (C2).

Results: There were no significant differences in the crude or adjusted values of C1 and C2 between both dialysis modalities in the first two or later years of RRT (table).

Conclusions: Arterial compliance does not differ between patients treated with hemodialysis or peritoneal dialysis in the early, nor in the later years of renal replacement therapy. Variation in survival between both populations contingent on the duration of dialysis therapy seems not determined by arterial stiffness.

Table: Arterial Compliance

	Dialysis ≤ 2 years			Dialysis > 2 years		
	HD	PD	P	HD	PD	P
C1 /crude/ [ml/mmHg*10]	8.1 \pm 3.5	9.5 \pm 3.2	0.16*	11.7 \pm 4.8	10.9 \pm 3.8	0.55*
C1 /adjusted/	8.3	9.3	0.23^	10.8	11.7	0.37^
C2 /crude/ [ml/mmHg*100]	2.9 \pm 2.2	3.2 \pm 1.4	0.10#	3.8 \pm 1.9	3.6 \pm 1.4	0.89#
lnC2 /adjusted/	0.92	1.07	0.30^	1.21	1.24	0.81^

*t-test; # Mann-Whitney U test; ^ANCOVA

Haemodialysis Induced Myocardial Dysfunction is Associated with Increased Incidence of Intradialytic Ventricular Ectopy

James Burton¹, Shvan Korsheed¹, Ben Grundy², Christopher McIntyre^{1,3}

¹ Department of Renal Medicine, Derby City General Hospital, Derby, United Kingdom;

² Department of Clinical Measurement, Derby City General Hospital, Derby, United Kingdom;

³ School of Graduate Entry Medicine and Health, University of Nottingham, Nottingham, United Kingdom

HD session. Frequency of isolated ectopy was classified as a percentage of the total beats on the Holter monitor record during each time period. Ventricular arrhythmias were stratified according to the Lown classification. Classes 3 and above were taken as complex ventricular arrhythmias (CVAs). Patients also underwent baseline and intradialytic echocardiography to assess the development of concurrent RWMAs. Blood was taken pre- and post-dialysis for biochemical testing.

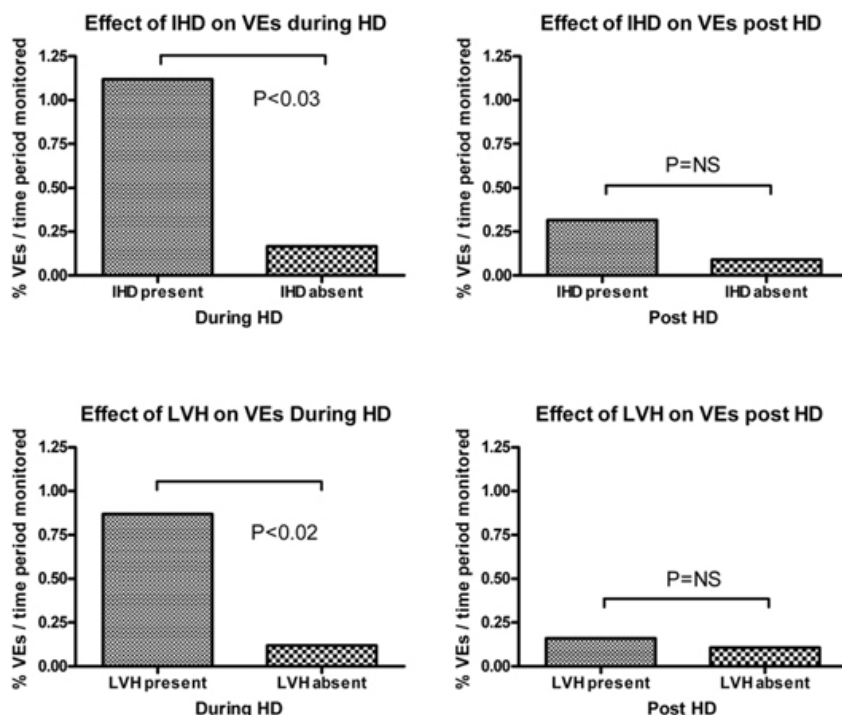
Results: Premature ventricular ectopics (VEs) were detected in 63% of patients and classed as frequent (>1% total) in 25%. More ectopics occurred during HD than

in the monitored period thereafter ($P<0.01$) and 53% were classified as CVAs. Patients who developed RWMAs had significantly more VEs during HD than afterwards ($P<0.0001$). Patients with ischaemic heart disease (IHD) and left ventricular hypertrophy (LVH) both had a higher frequency of VEs during HD than those without ($P<0.03$ and $P<0.02$ respectively, see figure).

Conclusions: Cardiac arrhythmias are common in HD patients. The frequency of VEs is significantly higher during HD in patients who develop RWMAs and may be related to factors associated with demand ischaemia.

Introduction and Aims: Conventional haemodialysis (HD) results in intradialytic cardiac ischaemia in a significant proportion of patients. Segmental myocardial ischaemia results in the development of left ventricular regional wall motion abnormalities (RWMAs). Sudden death is the most common cause of mortality in HD patients. This study aimed to examine any association between the development of left ventricular RWMAs and cardiac arrhythmias.

Methods: Forty established HD patients had 24-hour, 12 lead Holter monitor recordings which commenced immediately before a



Prediction of Sudden Cardiac Death in Patients on Hemodialysis by Assessment of the Cardiac Autonomic Nervous Activity

Masato Nishimura¹, Toshiko Tokoro², Masaya Nishida³, Tetsuya Hashimoto³, Hiroyuki Kobayashi³, Satoru Yamazaki³, Ryo Imai⁴, Koji Okino⁵, Hakuo Takahashi⁶, Toshihiko Ono³

¹ Cardiovascular Division, Toujinkai Hospital, Kyoto, Japan;

² Division of Nephrology, Toujinkai Hospital, Kyoto, Japan;

³ Division of Urology, Toujinkai Hospital, Kyoto, Japan;

⁴ Division of Orthopedics, Toujinkai Hospital, Kyoto, Japan;

⁵ Division of Surgery, Toujinkai Hospital, Kyoto, Japan;

⁶ Department of Clinical Sciences and Laboratory Medicine, Kansai Medical University, Hirakata, Osaka, Japan

Introduction and Aims: Cardiac sudden death is one of the important causes of death in patients on chronic hemodialysis. Although obstructive coronary artery disease is an important contributor to sudden death, arrhythmic mechanisms are likely to contribute to sudden cardiac death in hemodialysis patients. In this study, we investigated whether cardiac autonomic imbalance, which may induce fatal arrhythmias, is associated with the occurrence of sudden cardiac death among this population.

Methods: We prospectively enrolled 175 asymptomatic patients on chronic hemodialysis, who had undergone twenty-four hour Holter electrocardiography between dialysis sessions (male/female, 105/70; mean age, 66±12 years; mean dialysis duration, 90.5 months). Patients who had a clinical history of myocardial infarction and/or coronary revascularization were excluded from the study. Time- and frequency-domain analyses of the heart rate variability were carried out. We calculated the percentage of differences between adjacent NN intervals more than

50 msec (pNN50) and high frequency component (HF, 0.15-0.40 Hz) as parameters of the cardiac parasympathetic activity, and the ratio of low frequency component (0.04-0.15 Hz)/HF (LF/HF) as a parameter of the sympathetic activity.

Results: During a 4.5±1.9-year follow-up, sudden cardiac death was recognized in 23 patients. In stepwise Cox hazard analysis, sudden cardiac death was associated positively with age or the LF/HF ratio, and tended to be inversely associated with pNN50 (Table). Kaplan-Meier analysis showed that the sudden cardiac death-free survival rates at 5 years were 29.4% and 98.1% in patients with the LF/HF ratio of 1.9 or more and below 1.9, respectively.

Conclusions: Cardiac sympathetic overactivity with impaired parasympathetic activity is likely to be involved in sudden cardiac death in patients on maintenance hemodialysis. Assessment of imbalance in the cardiac autonomic system using the heart rate variability may be useful for identifying the high-risk group of sudden cardiac death in hemodialysis patients.

Table: Stepwise Cox hazard analysis of sudden cardiac death

	Hazard ratio	95% CI	P
Age (1 year)	1.064	1.014-1.116	0.011
LF/HF ratio	1.422	1.216-1.662	0.0001
pNN50 (1%)	0.692	0.459-1.044	0.079

Dynamics of Systolic Blood Pressure Predicts Mortality in Incident Hemodialysis Patients – Application of a Markov Model

Peter Kotanko, Len Usvyat,
Stephan Thijssen, Nathan W. Levin

Renal Research Institute, New York,
NY, USA

Introduction and Aims: Pre-dialysis systolic blood pressure (SBP) below 120 mmHg is associated with poor survival in chronic hemodialysis (HD) patients. This study aimed to test the hypothesis that in addition to low SBP the change of SBP is a predictor of mortality.

Methods: We studied all incident Renal Research Institute and New York Dialysis Services (RRI and NYDS) in-center maintenance hemodialysis patients with their first dialysis date (FDD) between 10/1/2002 and 12/31/2006. Pre-dialysis sitting SBP (pre-sSBP) was collected for every in-center treatment and averaged for each month of the study period. Only the patients who were alive for at least 240 days from FDD were included in the analysis. A Markov model with two absorbing states (death; censoring for reasons outlined below) was developed based on the median pre-sSBP of months 6 to 8 from FDD (initial state matrix). Patients were divided into three groups of pre-sSBP, <120, 120-160, and >160 mmHg. Survival status was recorded in each patient, and the Markov transition matrix was com-

puted based on the outcomes during months 9 to 11 from FDD. Patients were censored for transfer to another unit, kidney transplant, discharge from the dialysis center for other reasons, or end of study period. For comparison with the Markov model, a Kaplan Meier (KM) survival curve was constructed for the same cohort.

Results: We studied 4,494 incident HD patients (55% females, mean age \pm SD 63.8 \pm 15.5 years, 49% with diabetes mellitus). The group allocation in the initial state matrix was 6.4% (<120 mmHg), 62.7% (120-160), and 30.9% (> 160 mmHg). The transition matrix is shown in the table.

Conclusions: Survival in incident HD patients can be accurately

predicted for up to 2.5 years by means of a Markov model based on pre-sSBP. We hypothesize that a low and/or falling pre-sSBP may represent the common terminal pathway or different pathological processes, such as cardio-vascular disease, chronic inflammation, infection, and poor nutrition. Since the pattern changes after 2.5 years, it may be necessary to apply time-dependent transition matrices. In addition, Markov models stratified by race, gender, age, and diabetes mellitus status may prove to be insightful. Further evaluation of this concept could result in a useful indicator of mortality.

Up to 30 months, the Markov model accurately predicted survival (Figure).

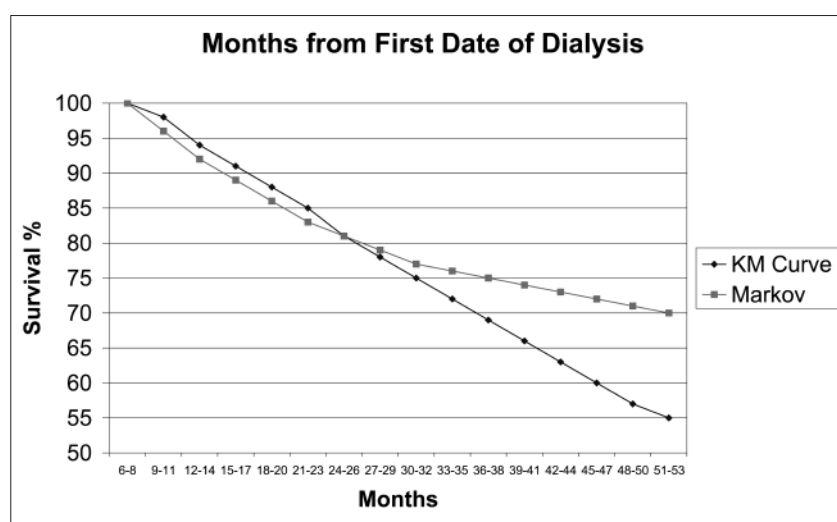


Table: Transition matrix. The elements of the matrix describe the probability of being in a particular group

	< 120	120-160	> 160	Died	Censored
Current Stage					
< 120	0.52	0.27	0.01	0.13	0.08
120-160	0.04	0.71	0.12	0.04	0.09
> 160	0.00	0.26	0.64	0.03	0.07
Died	0.00	0.00	0.00	1.00	0.00
Censored	0.00	0.00	0.00	0.00	1.00

4. Dialysis

OnLine Haemodiafiltration Reduces the Risk of Hospitalization Among Incident End-Stage Renal Disease (ESRD) Patients

Ana Natario, Jose Vinhas, Alvaro Vaz, Carlos Barreto, Jose Assuncao.

Kidney Center, Fresenius Medical Care, Setubal, Portugal

Introduction and Aims: High-flux haemodialysis (HD) and other conventional diffusion-based dialysis modalities are limited in their capacity to clear uremic toxins and are associated with a relatively high incidence of morbidity and mortality. Online haemodiafiltration (online HDF) combining the use of high convective fluid exchange, high flux membrane dialyser and ultrapure dialysis fluid removes more effectively small molecules, and presents an increased clearance of middle molecules (MM) and other, mainly protein bound, uremic toxins. Results from observational studies suggest that online HDF is associated with a reduced mortality and morbidity. This study eval-

uates the impact of online HDF on the rate of hospitalization.

Methods: We studied all the incident patients treated in a single centre over a 28 month-period. In this historical cohort study, 136 incident patients with ESRD on dialysis were studied: 75 patients on high-flux haemodialysis, and 61 patients on haemodiafiltration.

Descriptive statistics characterised the study population. In survival analysis we assessed differences in time to first hospitalisation using the Kaplan-Meier method based on dialysis modality. A Cox proportional hazards regression model was used to generate adjusted hazard ratios and 95% confidence intervals for the association between baseline characteristics and hospitalisation. The full model was adjusted for eight covariates.

Results: The mean age of all patients was 66.5±14.3 (21-90) years, 52.2% were male and 26.5% diabetics. The mean substitution fluid volume of the HDF group was 13.3±2.3 (8.2-18.9) liters. The presence of myocardial infarction, stroke, and amputation was similar in both treatment groups.

The cumulative incidence of hospital admission-free at 26 months was 60.6% among patients who were on HDF compared with 21.9% among HD patients (Log Rank 6.112; p=0.013).

By Cox proportional hazards model, after adjustment for age, gender, dialysis dose, CRP and albumin levels, patients on HDF had a 50.0% lower risk of hospitalization as compared with patients on HD (HR 0.500; 95% CI 0.277 to 0.901). Patients with diabetes (HR 1.994; 95% CI 1.109 to 3.584) had an increased risk of hospitalization. Lower haemoglobin levels were associated with an increased risk of hospitalization (HR 0.754; 95% CI 0.612 to 0.930).

Conclusions: In conclusion these data suggest that HDF may decrease the risk of hospitalization independently of patient characteristics. However, at present it is unclear whether long-term treatment with HDF ultimately results in an improved clinical outcome. The potential benefits of HDF must be confirmed by randomized clinical trials before recommendations can be made for clinical practice.

Table: Patient characteristics

Characteristics at baseline	HD	HDF	p-value
Age	68.9±12.7	63.7±15.6	0.034
Male gender	54.7%	49.2%	ns
Diabetes	24.0%	29.5%	ns
Time on RRT	12.8±8.2	11.2±7.2	ns
Kt/V	1.60±0.35	1.56±0.35	ns
S Haemoglobin (g/dL)	9.9±1.5	9.9±1.4	ns
S CRP (mg/dL)	2.4±2.7	2.1±2.7	ns
S Albumin (g/dL)	3.5±0.5	3.6±0.7	ns

The Effect of On-Line Hemodiafiltration on Heart Rate Variability in End-Stage Renal Disease: 2-Year Prospective Study

Soo-young Yoon¹, Sang Cheol Lee¹,
Tae Woon Park¹, Sung Ja Yang²

¹ Internal Medicine, College of
Medicine, Kwandong University,
Goyang, Republic of Korea
² Dialysis Room, Myongji Hospital,
Goyang, Republic of Korea

Introduction and Aims: The autonomic nervous system plays a central role in the maintenance of hemodynamic stability. Cardiac autonomic dysfunction may result in serious complications, such as sudden cardiac death. Heart rate variability (HRV) is significantly reduced in patients undergoing chronic hemodialysis, even in the absence of cardiovascular dis-

ease. The adequacy of hemodialysis is a predictor of improvement of cardiac autonomic nervous function in chronic uremia.

The aim of this study is to evaluate the effect of on-line HDF on the autonomic nervous system in chronic hemodialysis patients.

Methods: We prospectively studied 11 chronic hemodialysis patients. Participants were 55% male, aged 56.5±16.0 (31-80) years, 18% diabetic, with 3-120 months of dialysis, and on high-flux hemodialysis thrice a week. We analyzed time- and frequency-domain measures of 24-h HRV during the inter-dialytic period before post-dilution on-line HDF and thereafter six monthly for 24 months. Also, blood samples were drawn for routine laboratory assessments including hemoglobin, BUN, creatinine, calcium, phosphate, albumin, total cholesterol, triglyceride, uric acid, cystatin C,

high sensitivity C-reactive protein (hsCRP), intact parathyroid hormone (i-PTH), and 2-microglobulin (2-MG).

Results: After 24 months of on-line HDF, hemoglobin (8.8±1.5 to 10.9±1.2 g/dl, p<0.05), albumin (3.5±0.3 to 3.7±0.3 g/dl, p<0.05), and HDL cholesterol increased (28.3±3.8 to 33.2±7.6 mg/dl, p<0.05). Triglyceride (185.7±105.6 to 119.0±17.8 mg/dl, p<0.05) and 2-MG decreased (42.1±10.5 to 25.3±3.5 mg/l, p<0.05). Frequency-domain HRV parameters increased significantly compared with baseline (HF, 49.8±19.3 vs. 3.5±3.9 ms²; LF, 95.5±34.2 vs. 20.7±7.7 ms²; VLF, 558.5±50.3 vs. 75.4±79.9 ms²; and LF/HF, 2.76±1.52 vs. 1.55±0.58 ms²).

Conclusions: This study shows that on-line HDF can improve autonomic nervous system dysfunction in chronic hemodialysis patients.

Table: Changes of HRV parameters

Time-domain measures	Baseline	12 Months	24 Months	p-Value
Mean NN (ms)	818.4±171.2	842.5±136.7	835.1±116.3	NS
SDNN (ms)	98.6±29.8	94.8±30.3	96.2±28.2	NS
Frequency-domain measures				
HF power (ms ²)	3.5±3.9	39.4±17.3	49.8±19.3	<0.05
LF power (ms ²)	20.7±7.7	82.6±44.5	95.5±34.2	<0.05
VLF power (ms ²)	75.4±79.9	429.5±80.3	558.5±50.3	<0.05
LF/HF (ms ²)	1.55±0.58	2.54±1.60	2.76±1.52	<0.05

NN, normal-to-normal R-R intervals; SDNN, the standard deviation of normal-to-normal R-R intervals during 24 h; HF, high frequency; LF, low frequency; VLF, very-low frequency; NS, not significant

Hydration Status of Patients Treated by Either Hemodialysis or Peritoneal Dialysis: A Cross-Sectional Comparative Study

Bertram Schmitt, Kay Herbrig,
Frank Pistrosch, Jens Passauer.

Nephrology, Department of Medicine,
University Hospital Carl-Gustav-Carus,
Dresden, Germany

Introduction and Aims: Overhydration is regarded as an important factor contributing to hypertension and increased cardiovascular mortality in patients with end stage renal disease. Estimation of dry weight is therefore crucial in both hemodialysis (HD) and peritoneal dialysis (PD). At least during the first two years of treatment both dialysis modalities are considered to be equivalent. However, with decreasing residual diuresis tight volume control becomes more difficult in PD. The aim of this study was to assess the fluid status in a representative number of HD- and PD-patients in whom dry weight prescription was solely based on clinical grounds.

Methods: In 77 PD patients from 8 dialysis centres overhydration (OH) was measured by a newly developed bioimpedance spectroscopy (BIS) device containing a validated body composition model (Body Composition Monitor, Fresenius Medical Care). In addition blood pressure (BP), residual diuresis,

number of antihypertensives and time on dialysis were recorded. Results were compared with data from 370 HD patients from 5 centres. In HD patients OH was measured just before a midweek session and time-averaged fluid overload (TAFO) was calculated ($[\text{pre-dialytic OH} - \text{post-dialytic OH}]/2$) assuming a linear increase in fluid overload during the dialysis-free interval.

Results: TAFO was slightly but significantly higher in PD than in HD (1.4 ± 2.2 vs. 0.9 ± 0.7 L, $p < 0.05$) showing a higher degree of variability in PD. Systolic BP was comparable in both groups while diastolic BP was significantly higher in PD than in HD (83 ± 13 vs. 75 ± 13 mmHg, $p < 0.001$). In PD significantly more anti-hypertensive drugs were prescribed.

Conclusions: In this study PD was inferior to HD with respect to volume control and use of antihypertensive drugs. BIS devices may help to determine the optimal time for a switch from PD to HD.

Optimal Fluid Status Assessed with Bioimpedance Spectroscopy Reduces Intradialytic Morbid Events (IMES) and Hospitalisation in Hemodialysis Patients

Machek Petr¹, Jirka Tomas¹,
Moissl Ulrich², Wabel Peter²,
Chamney Paul²

¹ Fresenius Medical Care Czech,
Prag, Czech Republic;

² Fresenius Medical Care D GmbH,
Bad Homburg, Germany

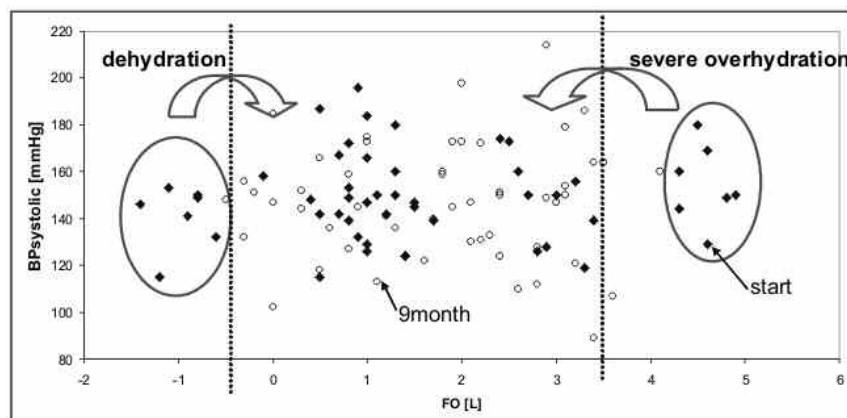
Introduction and Aims: The assessment of fluid status in patients on haemodialysis is one of the basic prerequisites for successful dialysis treatment. Long lasting fluid overload and high blood pressure (BP) in haemodialysis patients contribute significantly to the development of left ventricular hypertrophy (LVH), diastolic dysfunction and gradual heart failure, increasing hospitalization time. The other extreme, dehydration (as compared to a matched healthy subject), increases the risk of hypotensive events during dialysis. It was the aim of this study to first-

ly assess whether extreme fluid status can be identified and corrected, and secondly whether this reduction has an effect on hospitalisation and the number of morbid events.

Methods: To assess the degree of fluid overload we studied 60 HD patients with the Body Composition Monitor (BCM, Fresenius Medical Care) over an average time of nine months. The patients were measured before the dialysis treatment and fluid overload was provided by the BCM in litres (zero litres indicating normal hydration). Measurements were performed at least once a month, more frequent measurements were initiated if the dry weight had to be adjusted. Dry weight was gradually reduced in "severely overhydrated" patients who presented more than 3.5 L of fluid overload. On the contrary the dry weight was gradually increased in patients with "significant dehydration" (fluid overload pre-dialysis less than -0.5 litres).

Results: 30% of all patients were either severely over- or dehydrated at initiation of the study. At the end of the study 50% of these patients had been returned to a normal hydration status. The fluid overload -distribution of all patients was reduced by more than 1 L (2 SD). In the interval of the intervention period no emergency dialysis because of pulmonary edema had to be performed, no heart attacks were observed and the number of intra-dialytic complications such as hypotension or spasms was reduced.

Conclusions: It is too early to assess the influence on the overall mortality after one year of monitoring. In our study we managed to prove that achieving a normal fluid status, avoiding severe over- or dehydration helps to improve the treatment quality with less IMEs and emergency dialysis. The target provided by the BCM is an invaluable help in the assessment of the fluid status of HD patients.



Assessment and Reduction of Fluid Overload Using the BCM – Body Composition Monitor

Pedro Ponce¹, Petr Taborsky²,
Jiri Vlasak³, Tomas Jirka⁴,
Peter Wabel⁵, Ralf Wojke⁶

¹ Centro Medical National S.A. FME,
Miratejo, Portugal;

² Dialyzacni Stredisko FME-DS,
Praha, Czech Republic;

³ Dialyzacni Stredisko FME-DS,
Sokolov, Czech Republic;

⁴ FME-DS, Praha, Czech Republic;

⁵ Research & Development FME,
Bad Homburg, Germany;

⁶ Clinical Research FME,
Bad Homburg, Germany

Introduction and Aims: In patients with chronic renal failure the assessment and reduction of fluid overload is a major clinical problem [Charra *Hemodial Int* 2007]. Non-invasive bioimpedance spectroscopy with a body composition model is a validated method to assess fluid volumes (e.g. total body water [Moissl *Physiol Meas* 2006], fluid overload [Chamney *Am J Clin Nutr* 2007]). This study investigates whether the new bed-side BCM-Body Composition Monitor (Fresenius Medical

Care) can help the physician in determining and reducing fluid overload in a normal clinical setting.

Methods: The study consisted of two phases: fluid overload was assessed once in 139 HD patients (cross-sectional study), in a sub-population (N=34) fluid overload was measured repeatedly and reduced following the target defined by BCM (longitudinal study).

Results: The patients were grouped on the basis of the pre-dialytic fluid overload in quartiles from I (low fluid overload) to IV (high fluid overload), see table 1. Mean fluid overload was 1.81±1.83 L, with >9 L at maximum. fluid overload was found predominantly in men. Patients with larger amounts of fluid overload (group III-IV) had the highest incidence of hypertension and the highest ultrafiltration (UF) volumes. Patients with high body mass index (BMI) were less likely fluid overloaded.

Patients from all groups (I-IV) were followed up for 6 months (mean

5.9±1.7) in the longitudinal study, mean fluid overload was significantly reduced by 0.6L from study start to study end, see table 2.

The patients were categorized according to pre-dialytic fluid overload (high: fluid overload >1.1 L) and pre-dialytic systolic blood pressure (BP) (high: BP>140 mmHg).

The subpopulation with high BP and fluid overload had a pre-dialytic BP of 165±18 / 77±13 mmHg, a post-dialytic BP of 145±19 / 69±14 mmHg, and a UF volume of 2.5±1.0 L at study start. At study end, the UF volume was higher (2.8±0.9 L, p=0.044), fluid overload was reduced. A trend to lower BP was seen, pre-dialytic BP: 157±26 / 73±11 mmHg (p=0.140 / p=0.286), post-dialytic BP: 132±20 / 64±13 mmHg (p=0.035 / p=0.132).

Conclusions: The BCM allows to detect fluid overload easily and provides the target for reduction of fluid overload, which could be successfully achieved in this study.

Table 1: Cross-sectional Study Data (N=139)

	I	II	III	IV	p	Comparison
Fluid overload (L)	-0.14±1.4	1.12±0.22	2.12±0.35	4.13±1.50	<0.01	all
Male gender (%)	43	35	54	77	<0.01	I-IV*
Hypertension (%)	82.4	76.5	85.7	94.1	<0.05	II-IV*
UF volume (L)	3.0±0.9	2.6±0.8	2.7±1.0	3.1±0.8	<0.05	II-IV, III-IV*
BMI (kg/m ²)	27.8±4.5	26.3±5.3	24.2±4.5	25.0±4.3	<0.01	I-III, I-IV*

*other differences not significant: p>0.05 (Mann-Whitney)

Table 2: Longitudinal Study (N=34), Fluid Overload at Start and End of the Study

	N	Fluid overload _{start} (L)	Fluid overload _{end} (L)	p
All patients	34	2.32±1.82	1.71±1.61	0.001
Patients with high FO	24	3.14±1.42	2.33±1.40	0.001
Patients with high BP	19	2.37±2.09	1.70±1.80	0.018
Patients with high BP and FO	14	3.19±1.68	2.32±1.61	0.013

N = Number of patients p = Probability (Wilcoxon); FO = Fluid Overload; BP = Blood Pressure

Comparison of Eight-Hour and Four-Hour Thrice Weekly Hemodialysis

Best Abstracts Presented by Young Authors

Ercan Ok^{1,2}, Soner Duman¹,
Gulay Asci¹, Murat Tumuklu¹,
Ozen O. Sertoz¹, Meral Kayikcioglu¹,
Huseyin Toz¹, Siddik M. Adam²,
Mehmet Ozkahya¹,

¹ Ege University, Department of
Nephrology & Cardiology, Izmir,
Turkey;

² FMC Turkey Clinics

Introduction and Aims: Mortality rate in hemodialysis (HD) patients remains unacceptably high. Longer HD regimen seems promising in retrospective, uncontrolled studies. In this prospective, controlled study, we compared the effects of 8-h and 4-h thrice weekly HD.

Methods: We assigned 224 prevalent conventional HD patients to thrice weekly 8-h in-center nocturnal HD and 224 age-, sex-, diabetes status-, and HD vintage-matched control cases to 4-h HD for a year (mean age 45±13 years, dialysis vintage 59±44 months, female 32%, diabetes 20%). Over-

all mortality (primary outcome), changes in clinical and laboratory parameters were evaluated. Cardiac structure and functions determined by echocardiography and quality of life, cognitive functions, and depression burden were assessed at baseline and after 12 months.

Results: Mean follow-up was 12.4±5.0 months. Mean duration of HD sessions were 462±18 and 236±7 min, blood flow rates 241±47 and 291±35 ml/min in 8-h and 4-h arms, respectively. Overall mortality rates were 1.29 and 6.03 per 100 patient-year in 8-h and 4-h HD groups, respectively (p<0.01). Adjusted RR for death was 0.22 in 8-h group (95% CI 0.06-0.76; p<0.05).

URR increased from 0.75±0.07 to 0.82±0.06, eKt/V from 1.48±34 to 2.62±89 in 8-h HD group (p<0.001). Post-dialysis body weight increased from 64.9±14.6 to 66.7±14.9 kg in 8-h group (p<0.001). Mean blood pressure and hemoglobin were similar in both groups during follow-up; use of anti-hypertensive medication and erythropoietin declined in 8-h group (from 24 to 8% and from 57 to 25%, respectively; p<0.01). Intradialytic hypotension episodes were significantly less in 8-h arm (19 and 85/1000 HD session, p<0.001).

Albumin levels increased in 8-h HD group (from 3.95±0.29 to 4.10±0.30 g/dL, p<0.001). Despite reduction in use of phosphate-

binder from 81 to 22% in 8-h arm, phosphate level decreased from 4.59±1.31 to 3.82±1.19 mg/dl (p<0.001); it rose from 4.82±1.27 to 5.03±1.12 mg/dl in 4-h group (p<0.001).

In 8-h HD group, left ventricular mass index regressed from 141±45 to 120±34 g/m² (p<0.01), left atrial diameter from 4.03±0.58 to 3.73±0.53 cm (p<0.001), left ventricular ejection fraction increased from 62±10 to 66±11% (p<0.001) in 8-h HD group.

Cognitive functions, reflected by immediate and delayed recall scores, improved in 8-h HD group (p<0.05). Depression and anxiety scores did not change in both groups. Quality of life scores (mental health, vitality and bodily pain perceptions) deteriorated in 4-h HD group (p<0.05). If otherwise indicated no change was observed in group not mentioned.

Conclusions: These data point out that 8-h thrice weekly HD regimen provides a clear benefit on morbidity and mortality compared to conventional 4-h HD.

10 Years Experience with Short Daily Haemodialysis

Jules Traeger¹, Roula Galland²,
Nguen Koa Man²

¹ Association Utilisation du Rein
Artificiel Lyon (AURAL), Lyon,
France

² Centre Associatif de Dialyse
(Calydial), Lyon, France

Introduction and Aims: We report our experience with 61 patients treated during the last 10 years with short daily haemodialysis (sDHD) since 1997. Most of patients were converted from standard haemodialysis (SHD) to sDHD, thus, we compared the clinical and biological results in the two periods.

Methods: 61 patients 49 male / 12 female, mean age 44.5±14.3 years, mean time on standard

haemodialysis (SHD) 53.4±77.7 months (0-333), mean times on sDHD is 34.9±23.2 months (6-131), 16 patients were treated at home, 35 in self-care units and 10 patients in-centre. Observational period was 137 patient-years. 59 patients dialysed with native arterio-venous fistula, only 2 patients with central venous catheter. Sessions frequency was 5.9±0.4 times / week (5 - 6), treatment time was 138.9±19.5 min (120 -180). Outcome of these patients 28 continue sDHD, 15 were transplanted, 11 returned to the standard strategy and 7 patients died. The causes of death were cancer in 3 cases, 1 accident , 1 stroke, 1 cirrhosis and 1 pulmonary graft rejection. The mean annual gross mortality was 5%. sDHD indication indications were: cardiovascular instability (9), uncontrolled hypertension (8), malnutrition (7), important interdialytic weight gain (13), improved patient

well-being (5), socio-professional reason (14), and 5 patients for pregnancy.

Results: Clinical results are given in the table, tolerance of dialysis sessions was excellent.

Urea Kinetics in sDHD: Urea RR: 49.3±3 % (38.5–56.7), urea TAC: 12.45±2.3 mmol/L (17.8–9.4), urea TAD: 2.39±0.79 mmol/L (2.1-2.5), spKt/V / session = 0.8±0.12 (0.56-1.1), eKt/V = 0.54±0.08 (0.37-0.75), std(Kt/V) / week = 2.5±0.3 (1.91-3.24), Ultrafiltration rate (UF): 1.34±0.3 litres (0.4-2.8).

Conclusions: These 10 years experience with sDHD is highly positive, the cardiovascular improvement allowed renal graft in patients previously postponed on the waiting list. The clinical improvement was obtained even with a dialysis dose as low with Kt/V = 0.37/ session showing that frequency is most important factor of adequate dialysis.

Table: Clinical Results in sDHD and SHD

	sDHD	SHD	p
MBP (mmHg)	93.9±12.9	103±13.9	<0.005
LVMI (g/m ²)	129±33	180±65	<0.01
Hb (g/l)*	115±35	113±24	n.s.
BMI (k/m ²)	21.2±2.3	20.4±2.3	<0.01
Alb (g/l)	42.0±3.1	39±2.6	<0.01
pre Alb (g/l)	0.41±0.05	0.36±0.04	<0.05
nPNA	1.3±0.3	1.1±0.2	n.s.
Quality of life			
Physical Score Component (%)	72	82	<0.05
Mental Score Component (%)	63	72	<0.05

*with reduction in EPO dose from 4,000 to 2,118 IU/week

Relationship of Predialysis Body Temperature to Survival in Hemodialysis Patients

Len Usvyat¹, John Rogus²,
Eduardo Lacson, Jr²,
Stephan Thijssen¹, Nathan W. Levin¹,
Peter Kotanko¹,

¹ Renal Research Institute, New York,
NY, USA

² Fresenius Medical Care, Waltham,
MA, USA

Introduction and Aims: The relationship of body temperature over time to survival of dialysis patients has not been systematically studied. We hypothesized that increased temperature (due to inflammation and/or infection) would be associated with increased mortality.

Methods: A retrospective record review involving white (40%) and black (60%) patients undergoing three times weekly in-center dialysis between January 1st 2002 and

June 30th 2002 was performed. The mean pre-dialysis temperature (done prior to each dialysis session by oral thermometer), urea distribution volume (V; derived from urea kinetic modeling), and patient's age were recorded. Patients were stratified by race, tertiles of V, tertiles of body temperature, and age (<60, and >60 years). Patient survival was followed over five years (July 1st 2002 to December 31st 2006) and expressed as deaths per 1000 patient-years.

Results: In the 1,782 Black patients (51% males) mean (\pm SD) V was 39.8 \pm 7.9 L and mean temperature was 36.58 \pm 0.26 °C. In Whites (N=1,177; 58% males) V was 37.6 \pm 7.6 L and mean temperature 36.33 \pm 0.35 °C.

In all patients combined, death rates increase with advancing age, lower tertiles of V, and lower tertiles of temperature (Table). The effect of temperature on survival appears to be independent of age and V.

Conclusions: Our initial hypothesis is rejected. The reasons for a favorable effect of higher temperatures and/or the unfavorable effect of low temperature are unclear. Possible hypothesis include a "low T3 syndrome", as observed in earlier studies (Zoccali et al, J Am Soc Nephrol. 2005;16:2789) and decreased oxidative stress in the presence of uncoupled oxidative phosphorylation. The higher temperature in Black is compatible with increased muscle mass.

	Black Patients					
	Temp. Tertile 1 (to 36.51 °C) V Tertiles (L)			Temp. Tertile 3 (to 37.54 °C) V Tertiles (L)		
	to 35.6	to 42.6	to 60	to 35.6	to 42.6	to 60
Age < 60	116.1	92.7	69.7	90.6	90.5	82.3
Age > 60	226.1	183.5	181.3	190.0	160.8	167.9

	White Patients					
	Temp. Tertile 1 (to 36.25 °C) V Tertiles (L)			Temp. Tertile 3 (to 37.16 °C) V Tertiles (L)		
	to 33.6	to 40.5	to 59.0	to 33.6	to 40.5	to 59.0
Age < 60	143.5	186.4	115.5	110.1	108.5	77.3
Age > 60	267.1	239.0	282.4	215.5	222.8	190.1

	All Patients					
	Temp. Tertile 1 Volume Tertiles			Temp. Tertile 3 Volume Tertiles		
	1	2	3	1	2	3
Age < 60	125.0	108.5	82.1	98.1	96.3	80.3
Age > 60	243.0	209.0	233.8	200.1	187.4	179.6

5. Epidemiology and Outcome in Chronic Kidney Disease

Anti-Hypertensive Agents (AHAS) and Clinical Outcomes Among Incident Hemodialysis Patients: The Dialysis Outcomes and Practice Patterns Study (DOPPS)

J.L. Bragg-Gresham¹, R.L. Pisoni¹, B.W. Gillespie², D.A. Goodkin¹, S.P.B. Ramirez¹, H. Morgenstern², V. Andreucci³, S. Jacobsen⁴, S. Fukuhara⁵, T. Akizawa⁶, B.M. Robinson¹

¹ Arbor Research, Ann Arbor, MI, USA;

² U of M, Ann Arbor, MI, USA;

³ Universita Federico II di Napoli, Napoli, Italy;

⁴ Danderyd Hospital, Stockholm, Sweden;

⁵ Kyoto University, Kyoto, Japan;

⁶ Showa University School of Medicine, Shinagawa, Japan

Introduction and Aims: Use of angiotensin receptor blockers (ARBs) and beta blockers (BBs) has been associated with lower mortality in recent studies of prevalent HD patients, but there is concern that their use may hasten loss of residual renal function (RRF) among incident HD patients.

Methods: We studied 8,176 patients entering the DOPPS I and II studies within 30 days of starting HD. This sample included >400 facilities in 12 countries. Patients were classified as taking one or

more AHAs by class at study entry: BB, renin angiotensin system [RAS] inhibitors (ARB or ACE inhibitor), calcium channel blocker (CCB), peripheral blocker/vasodilator (PB/V), central antagonist (CA), diuretics. Mortality and time to loss of RRF (defined as >200 ml urine/24 hours) were examined using Cox models adjusted for each AHA class concurrently as well as for age, sex, race, 14 summary comorbid conditions; stratified by country and phase. Mortality models also adjusted for SBP, RRF, and albumin. Treatment was characterized at the patient level (Y/N) and facility level (% of incident HD patients prescribed each AHA class at the facility, adjusted for case mix).

Results: Use of BB, RAS, and diuretics increased significantly between DOPPS I and DOPPS II ($p < 0.05$), from 27% to 33%, 28% to 37%, and 32% to 43%, respectively. Use of CCB significantly decreased over the same period from 52% to 47%. Only 21% of this sample was not taking any type of AHA. The majority of patients were taking more than

one AHA. The most common combinations were BB/CCB, BB/RAS, and RAS/CCB. In Cox models, RAS inhibitors were associated with significantly lower mortality in patient- and facility-based models and with RRF preservation in the patient-based model, with $p = 0.10$ in the facility-based model. Associations with mortality and RRF did not vary according to type of RAS inhibitor (ACEI or ARB). Diuretics were associated with preservation of RRF, but this may be because RRF is an indication for diuretic use and diuretics may maintain urine output without preserving renal clearance.

Conclusions: Among incident HD patients, use of RAS (ACEIs and ARBs) was associated with improved survival and possibly with preservation of RRF, accounting for baseline SBP. These data generally support the use of these agents and are inconsistent with the concern that their use may hasten loss of RRF among incident HD patients. No other AHA classes were associated with a survival benefit or loss of RRF in both patient- and facility-based models.

AHA Medication	All-Cause Mortality (n=8,176)				Loss of RRF (n=1,254)			
	Patient based (Med vs No)		Facility Based (per 10% more)		Patient based (Med vs No)		Facility Based (per 10% more)	
	HR	p	HR	p	HR	p	HR	p
Beta Blockers	0.89	0.06	1.02	0.45	0.96	0.67	1.03	0.42
RAS Inhibitors	0.87	0.05	0.95	0.01	0.76	0.004	0.95	0.10
Ca Channel Blocker	0.88	0.04	1.02	0.55	1.04	0.62	0.97	0.45
Peripheral Blocker/Vaso	0.93	0.34	1.02	0.66	0.99	0.92	0.95	0.26
Central Antagonist	0.91	0.31	0.99	0.85	1.04	0.78	0.91	0.06
Diuretic (RRF adjusted)	0.94	0.37	0.98	0.22	0.86	0.06	0.95	0.003
Diuretic (no RRF adjust)	0.94	0.25	0.96	0.02				

*Among patients with RRF at baseline

An Epidemiological Study of Haemodialysis Patients Based on the European Fresenius Medical Care (FMC) Haemodialysis Network: The ARO Research Initiative

Alm DeFrancisco¹, P. Aljama², J. Kim³, D. Marcelli⁴

¹ Hospital Marques de Valdecilla de Santander, Santander, Spain;

² Servicio de Nefrología, Córdoba, Spain;

³ Amgen Ltd, London, United Kingdom;

⁴ Fresenius Medical Care, Bad Homburg, Germany

Introduction and Aims: The ARO (Analysing data, Recognizing excellence, Optimizing outcomes) Chronic Kidney Disease Research Initiative was formed to characterize more fully practice patterns and clinical outcomes to support the informed use of therapies in European haemodialysis (HD) patients.

Methods: In an open-cohort design, patients were randomly selected from 172 participating FMC centres (approximately 25 sites/country; 50 patients/site). Altogether 11,114 patients (n=7,105 prevalent, n=4,009 incident) were followed for up to 2 years between Jan 2005 and Dec 2006 (>15,000 person-years). Incident patients received HD ≤6 months prior to follow-up. Data were collected for demographics, medical history, labs (by date), and medications (by date). Outcomes are available for cause-specific mortality and hospitalisations (ICD-10 codes available).

Results: Demographic and clinical characteristics vary across participating ARO countries (see Table). Prevalent patients (64% of ARO population) received HD for a

mean (±SD) of 4.9 ± 4.7 years prior to the study. Most patients (69%) had fistula placement. The most common etiologies of chronic kidney disease were glomerular disease (15%), hypertension (12%), diabetic nephropathy (12%), cystic tubulo-interstitial disease (10%), kidney disease (5%), and other/unknown (46%). There is wide variation in the distribution of comorbid disease across ARO countries.

Conclusions: Using granular real-life data obtained from FMC centres located across Europe, ARO is consistent with and complements other large epidemiological studies (DOPPS, COSMOS) designed to capture practice patterns in the European HD patient population.

Table: Baseline Characteristics of Patients Treated at FMC Centres in Participating ARO Countries

Baseline variables*	Spain	Turkey	Portugal	Hungary	Italy	CEE†	France	UK	Total
Total subjects N(%)	1879 (17)	1752 (16)	1495 (13)	1414 (13)	1248 (11)	1208 (11)	1100 (10)	1018 (9)	11114 (100)
Age Mean (SD)	66 (15)	56 (15)	64 (15)	62 (14)	66 (14)	62 (14)	61 (17)	62 (16)	62 (15)
Female N(%)	702 (37)	772 (44)	607 (41)	715 (51)	521 (42)	534 (44)	421 (38)	382 (38)	4654 (42)
BMI ‡ Mean (SD)	25.2 (4.6)	24.8 (4.4)	25.0 (4.3)	25.3 (5.6)	25.3 (4.7)	26.3 (5.3)	24.8 (5.1)	26.0 (5.6)	25.3 (5.0)
Prevalent N(%)	1028 (55)	1181 (67)	1063 (71)	834 (59)	890 (71)	763 (63)	686 (62)	660 (65)	7105 (64)
Dialysis vintage for Prevalent pts yrs Mean (SD)	5.0 (5.1)	4.6 (3.7)	5.1 (4.3)	4.4 (3.8)	6.3 (6.1)	4.3 (4.3)	4.6 (5.5)	4.5 (4.8)	4.9 (4.7)
Follow-up yrs Mean (SD)									
Incident	0.9 (0.6)	0.6 (0.6)	1.0 (0.7)	1.0 (0.7)	1.0 (0.7)	1.0 (0.6)	1.1 (0.7)	1.0 (0.6)	0.9 (0.7)
Prevalent	1.5 (0.6)	1.5 (0.6)	1.8 (0.5)	1.5 (0.6)	1.7 (0.6)	1.7 (0.6)	1.6 (0.6)	1.6 (0.6)	1.6 (0.6)
Fistula N(%)									
Incident	548 (69)	401 (70)	261 (62)	353 (61)	292 (82)	289 (73)	158 (89)	175 (50)	2477 (68)
Prevalent	692 (68)	1054 (89)	690 (65)	624 (76)	782 (88)	592 (82)	411 (94)	457 (70)	5302 (78)
Smoker N(%)	514 (37)	567 (33)	243 (18)	105 (10)	472 (42)	393 (35)	145 (25)	280 (30)	2719 (30)
Diabetes N(%)	239 (13)	398 (23)	320 (21)	218 (15)	251 (20)	376 (31)	132 (12)	92 (9)	2026 (18)
CVD § N(%)	806 (43)	650 (37)	673 (45)	546 (39)	440 (35)	821 (68)	335 (30)	162 (16)	4433 (40)

*Missing data were omitted from the calculations

†CEE: Central Eastern European countries (Slovakia, Slovenia, Czech Republic, and Poland)

‡BMI: Body Mass Index

§ CVD: Cardiovascular disease is defined as the presence of hypertension, myocardial infarction, angina, coronary artery disease, transient ischaemic attack, stroke, congestive heart failure, or peripheral vascular disease

High Body Mass Index (BMI) is not Associated with Improved Longterm Survival in Patients Using Peritoneal or Haemodialysis (Hd) for Established Renal Failure (ERF)

Arthur Doyle¹, Roslyn Simms², Keith Simpson¹

¹ Renal Unit, Glasgow Royal Infirmary, Glasgow, United Kingdom;

² Renal Unit, Freeman Hospital, Newcastle-upon-Tyne, United Kingdom

Introduction and Aims: Obesity (BMI >30) is a traditional cardiovascular risk factor in the general population. It is associated with increased all cause mortality. In patients using HD for ERF however longer survival with high BMI has been reported. This apparent reverse relationship has led to uncertainty on how best to manage overweight patients with chronic kidney disease approaching renal replacement therapy.

Methods: Data were obtained from comprehensive electronic records of patients incident to renal replacement therapy (RRT) at one centre between 1987 and 2006. All patients established on

HD or PD for >90 days for whom a BMI result was available were included. Patients were grouped by WHO BMI categories (<18.5, 18.5-24.9, 25-29.9 and >30). The association between BMI, change in BMI, age and comorbidity (by modified Charleston score) with survival, were evaluated in both the short (2 years) and long (15 years) terms. Kaplan-Meier, log rank testing and Cox proportional hazard regression (CoxR) tests were used in analyses.

Results: 1287 patients commenced dialysis (942 HD and 345 PD) of whom 948 (718 HD, 230 PD) had data available. The median age was 60 years (Interquartile range 46-70) and BMI was 24.6 Kg/m² (Interquartile range 21.7-28.0). There was a non significant trend towards longer 2-year survival in obese patients, but this was not apparent in the longer term. Stable BMI in the first month

of RRT was associated with an improved 2-year survival (81%), compared to individuals whose BMI rose (77%) or fell (72%) by more than 2% (log rank 8.59, p=0.014). Comorbidity and increasing age were associated with shorter survival (CoxR 1.153, p<0.001 and 1.032, p<0.001 respectively).

Conclusions: We have not found a significant association between obesity and survival in patients using HD or PD for ERF. However age, comorbidity and change in body mass in the first month of RRT were associated with shorter survival. Any survival advantage associated with obesity does not appear to persist beyond two years on RRT. Our results do not support a change in current management of obesity in dialysis patients, and suggest that we should continue to treat it as a traditional risk factor.

Table: Cox Proportional Hazard

	Wald	Exp(B)	Sig.
AGE	53.806	1.032	<0.0001
Charleston	23.951	1.153	<0.0001
BMI change	7.176	0.977	0.007
RRT Type	0.955	0.879	0.328
BMI	0.736	0.594	0.391

Obesity is a Risk Factor for Decline of Renal Function After the Start of Dialysis Best Abstracts Presented by Young Authors

Christiane Drechsler¹,
Renée de Mutser¹,
Diana C. Grootendorst¹,
Elisabeth W. Boeschoten²,
Raymond T. Krediet³,
Christoph Wanner⁴, Saskia le Cessie⁵,
Friedo W. Dekker¹

¹ Dept of Clinical Epidemiology,
LUMC, Leiden;

² Hans Mak Institute, Naarden;

³ Dept of Nephrology, AMC,
Amsterdam, Netherlands;

⁴ Div of Nephrology,
Univ. of Wuerzburg, Germany;

⁵ Dept of Medical Statistics, LUMC,
Leiden, Netherlands

Introduction and Aims: Residual renal function (RRF) is beneficial for the survival of dialysis patients, reason why it needs to be preserved. Obesity is a risk factor for loss of renal function in the general population. It is unknown whether it proceeds to affect kidney function once patients already require dialysis. It is furthermore unknown whether underweight, being a risk factor for mortality in dialysis patients, also affects RRF. The aim of this study was to assess the effect of obesity and underweight on the decline of RRF after the start of dialysis.

Methods: A total of 1271 patients with RRF (age 59 ± 15 years, BMI 24.8 ± 4.1 kg/m², GFR 4.7 ± 3.3 ml/min, diuresis $1,055 \pm 702$ ml/day, 57% HD, 62% male) were selected from a prospective multicentre cohort study in incident dialysis patients in the Netherlands (NECOSAD). Patients were divided into 4 categories, based on their BMI at baseline: low (<20 kg/m², $n=112$), normal ($\geq 20-25$ kg/m², $n=620$), overweight ($\geq 25-30$ kg/m², $n=417$) and obese (≥ 30 kg/m², $n=122$) and followed until 18 months after they started dialysis. Every 6 months, GFR was estimated as mean of creatinine and urea clearances, calculated from plasma samples and 24h urine collections. With slope-based analyses using linear mixed models, the decline of GFR was determined for all BMI categories and adjusted for age, sex, primary kidney disease, dialysis modality, smoking, CVD and nPNA. Cox regression analysis was used to calculate hazard ratios (HR)

for the development of anuria, defined as diuresis <200 ml/day.

Results: Baseline GFR was highest (5.8 ml/min) in obese patients, followed by overweight (5.1 ml/min), normal weight (4.6 ml/min) and underweight patients (3.5 ml/min). Patients with normal weight had a mean GFR decline of 1.2 ml/min per year (95% CI: 0.7-1.6). Compared to those, the adjusted loss of GFR was 0.5 (0.02-0.8) ml/min/yr higher for overweight and 1.2 (0.5-1.8) ml/min/yr higher for obese patients. In contrast, the decline of GFR in underweight patients was 0.6 (-0.1-1.3) ml/min/yr lower than in normal weight patients. When the slope-based analyses were performed in strata of baseline GFR, results were similar.

Underweight patients had an increased risk of anuria (crude HR: 1.49, 95% CI: 1.02-2.18) where as obese patients did not (crude HR: 1.11, 0.75-1.64) compared with patients with normal weight. After adjustment for confounders, HRs were 1.39 (0.94-2.05) in underweight and 0.95 (0.63-1.42) in obese patients, and after additional adjustment for baseline diuresis 1.12 (0.76-1.66) and 1.21 (0.81-1.82), respectively.

Conclusions: Obesity is a strong risk factor for the decline of renal function after the start of dialysis. Underweight was associated with a 50% increased risk of anuria, mainly due to baseline diuresis. Whether obese and underweight dialysis patients might benefit from healthy interventions aiming to normalize BMI should be investigated in further studies.

Fluid Overload and Malnutrition Assessed with Bioimpedance Spectroscopy (BIS) are Strong Predictors of Mortality in Hemodialysis Patients

Volker Wizemann¹, Christiane Rode¹, Paul Chamney², Ulrich Moissl², Peter Wabel²

¹ Georg-Haas Dialyse Zentrum, Giessen, Germany;

² Fresenius Medical Care D GmbH, Bad Homburg, Germany

Introduction and Aims: Malnutrition and fluid overload are common problems in hemodialysis (HD) patients. Traditional body-composition assessment methods (e.g. bioimpedance analysis (BIA) and Dual X-Ray Absorptiometry (DEXA)) cannot separate fluid overload from muscle mass. Thus an objective and quantitative assessment of hydration- and nutrition status is currently not possible. A novel high-frequency bioimpedance-spectroscopy device (BCM-Body Composition Monitor, FMC) determines fluid overload and Lean Tissue Index based on a novel body composition model (AJCN 85, 2007). In previous stud-

ies it was shown that the device can be used to assess fluid overload (EDTA 2007) and malnutrition. The aim of this study was to show if protein malnutrition or fluid overload is the major predictor of mortality in HD patients.

Methods: Lean Tissue Index and fluid overload were determined via the BCM in 156 patients. To evaluate Lean Tissue Index and fluid overload, reference ranges were set up on basis of a reference population (RP) of n=1000 normal subjects between 1885 years. To analyse protein malnutrition patients were separated into Lean Tissue Index groups (*low* if Lean Tissue Index < 10th percentile of the RP, *normal* if Lean Tissue Index was > 10th percentile of the RP). Patients were regarded as fluid overloaded, when fluid overload was > 2L at the start of the HD-treatment. Survival analysis was performed using the Gehan-Breslow method, adjusting for age, sex and diabetes. The relative risks were calculated on the basis of the odds ratios.

Results: Mean time on HD before measurement was 3.5 ± 5.7 years, mean age was 67 ± 13 yrs. After 2 yrs, 18% of all patients had died. The *low* Lean Tissue Index group showed a significantly greater mortality (p=0.009) compared to the normal Lean Tissue Index group. Also the *high fluid* overload group showed a significantly increased mortality (p=0.005). After 2 yrs, 27% of patients in the low Lean Tissue Index group had died, while only 12% had died in the normal group. The subgroup of patients with Lean Tissue Index <10% and fluid overload >2L had a 2.4 fold increased risk of dying compared to the subgroup with normal Lean Tissue Index and normal fluid overload.

Conclusions: Malnutrition and fluid overload are both influencing the mortality risk of HD patients. Lean Tissue Index and fluid overload in combination with the reference ranges are key indicators for survival and can be easily obtained in all dialysis patients using the BCM-Body Composition Monitor.

Table: Relative Risk in subgroups

Group	% of Patients	RR
All patients in study	100	1
Low LTI (LTI<10%)	47	1.3
Normal LTI (LTI<10%)	53	0.7
Normal FO (FO<2 L)	64	0.88
High FO (FO>2 L)	36	1.22
Low LTI & high FO (LTI<10%, FO>2.0 L)	25	1.53
Normal LTI & low FO (LTI>10%, FO<2.0 L)	30	0.63

LTI = Lean Tissue Index; FO = Fluid Overload

Excess Mortality in Women with Diabetes may Explain the Equal Survival in Male and Female Dialysis Patients

Renée de Mutsert¹, Jonas Axelsson²,
Juan Jesús Carrero²,
Elisabeth Boeschoten³,
Raymond Krediet⁴, Friedo Dekker.¹

¹ Clinical Epidemiology, Leiden
University Medical Center, Leiden,
Netherlands;

² Renal Medicine and Baxter Novum,
Karolinska Institutet, Stockholm,
Sweden;

³ Hans Mak Institute, Naarden,
Netherlands;

⁴ Nephrology, Academic Medical
Center, Amsterdam, Netherlands

Introduction and Aims: Cardiovascular diseases (CVD) are highly prevalent in end-stage renal disease (ESRD) patients at the start of dialysis, and are the main causes of death on dialysis. In the general population, women have a longer life expectancy partly due to a lower prevalence of CVD. Women in the dialysis population do not have a survival advantage, but the reasons for this are unknown.

We investigated whether male ESRD patients have a different CVD risk profile than female ESRD patients, and whether the effect of CVD and diabetes mellitus (DM) on mortality is different in men and women starting dialysis.

Methods: We conducted an epidemiological study with data from NECOSAD, a prospective observational cohort study in ESRD patients. Patients were followed from the start of dialysis until 5 years of follow-up. First, we calculated male:female odds ratios associated with the baseline presence of cardiovascular risk factors, using logistic regression analysis. Second, with Cox regression analysis we calculated hazard ratios (HR) for male sex and cardiovascular risk factors adjusted for age, dialysis modality, smoking, BMI, cholesterol, use of anti-hypertensive and lipid lowering drugs. Finally, we calculated the relative excess risk due to interaction (RERI) between sex and the cardiovascular risk factors, on the basis of departure from causal additivity of effects.

Results: In total, 1276 dialysis patients were included (61% men, age: 59±15 years, BMI: 24.7±4.1 kg/m²). At baseline, men had more cardiovascular comorbidity (41% vs 26% in women, male: female OR: 2.26 [95%-CI: 1.71, 3.00]) but suffered less from diabetes mellitus (20% vs 26% in women, male: female OR: 0.76 [0.57, 1.01]) than women. During follow-up, 462 patients died, 232 from CVD. Both CVD (HR: 2.09 [1.72, 2.55]) and DM (HR: 2.37 [1.93, 2.91]) were associated with increased risks of mortality. Slightly more men died from CVD than expected, but the

interaction effect between sex and CVD was non-significant (RERI: 0.43 [-0.20-1.05]). Compared with women without DM, men with DM (HR: 2.30 [1.69, 3.11]) had a lower mortality risk than expected (HR in women with DM: 3.17 [2.33, 4.31]). This significant interaction effect between sex and DM (RERI: -1.05 [-1.98, -0.12]) may in part explain the equal survival in men and women (HR men: 0.94 [0.77, 1.14]).

Conclusions: The present study demonstrates that despite a more than two-fold lower prevalence of CVD at baseline, women starting chronic dialysis therapy have the same mortality risk as do men. This may partly be due to the presence of interaction between sex and diabetes, resulting in higher mortality in women with diabetes. To improve survival in the dialysis population, special attention needs to be paid to the treatment of female dialysis patients with diabetes.

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www.fmc-ag.com



Fresenius Medical Care

Fresenius Medical Care Deutschland GmbH · 61346 Bad Homburg v. d. H. · Germany · Phone: +49 (0) 6172-609-0 · Fax: +49 (0) 6172-609-2191
www.fmc-ag.com · Head office: Else-Kröner-Straße 1 · 61352 Bad Homburg v. d. H.