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Short Commentary

Mortality and Low Serum Bicarbonate Level in Patients on Hemodiafiltration versus Peritoneal Dialysis

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Abstract

Background: Mortality is substantially elevated in patients on chronic kidney disease in comparison to general population. In this study, we observed the mortality rate in relation to risk factors including low serum bicarbonate level, coronary artery disease and dialysis modality in patients on dialysis during a median follow up time of 60 months.

Methods: We studied 96 dialysis patients, 62 males and 34 females, on mean age 62.1±14.27 years old. The treatment modalities which were applied were: predilution haemodiafiltration (HDF, n=76) and Peritoneal Dialysis (PD, n=20). We performed Kaplan-Meier curves and a Cox regression analysis to investigate significant risk factors for mortality including hypertension, diabetes mellitus, smoking, bone disease defined by i-PTH, serum albumin, and serum bicarbonate levels less or more than 22mEq/L, dialysis modality and the existence of Coronary Artery Disease (CAD).

Results: Cox-regression analysis revealed significant impact of serum bicarbonate levels less than 22mEq/L on mortality in combination to dialysis modality and CAD. The prevalence of CAD on mortality was found significant (log-rank=5.507, p=0.02). Also, the impact of dialysis modality on mortality was shown significant (log-rank=22.4, p=0.001), noting that during the first 28-30 months from the treatment initiation, the survival was better for peritoneal dialysis, but then the mortality was significantly increased comparatively to hemodiafiltration.

Conclusion: Uncorrected metabolic acidosis and coronary artery disease were shown as independent significant predictors for mortality in patients on renal replacement therapy. Peritoneal dialysis may provide worse survival after 2-2.5 years of treatment initiation than hemodiafiltration.

Keywords

Coronary artery disease; Hemodiafiltration; Metabolic acidosis; Peritoneal dialysis; Survival

Introduction

Mortality is potentially elevated in patients on Chronic Kidney Disease (CKD) in comparison to general population. Previously, it has been showed that patients in CKD stages 4 and 5 approached a rate of threefold and sixfold higher mortality risk respectively, than patients with GFR>60ml/min/1.73m^2 [1,2].

Dialysis mortality was showed as an eightfold higher age-stardardised mortality compared to general population unseparated to dialysis modality [3]. However, it has been reported that mortality may differ between dialysis modality. Comparative studies between patients treated with Peritoneal

Dialysis (PD) and HemoDialysis (HD) have frequently shown conflicting results [4]. It has been showed that PD patients have a higher survival rate depended on dialysis vintage for younger and non-diabetic patients than HD patients, despite in some studies HD displayed better survival [5]. Controversially, previous study from a single Chinese Center showed that dialysis modality itself has no effect on the survival rate of dialysis patients [6].

The cardiovascular disease is recognized as the main reason for the increased mortality in dialysis patients [7]. Recently, it has been suggested that the unfavorable effects of metabolic acidosis including malnutrition, inflammation and oxidative stress can contribute to elevated mortality in dialysis patients [8,9].

In this study, we observed the mortality rate in relation to risk factors including low serum bicarbonate level, coronary artery disease and dialysis modality in patients on dialysis during a median follow up time of 60 months.

Methods

Patients

This is a retrospective study of a cohort of 96 dialysis patients, 62 males and 34 females, on mean age 62.1±14.27 years old. The data collection became during a time of 60 months, from the 1st of January of 2007 until the end of December of 2011.

The treatment modalities which were applied were: on-line-predilution hemodiafiltration (on-l HDF, n=76) and peritoneal dialysis (PD, n=20).The median time on hemodialysis was 5.0± interquartile range 3-10 years and the mean time on peritoneal dialysis was 2.8±1.61 years before the starting of our study. In our data, 13 patients were initiared dialysis treatment after the starting of this study and 83 patients were already in permanent dialysis therapy.

We excluded patients <18 years of age at initiation of dialysis and patients that had less than 6 months of follow-up. Patients without regular vascular hemodialysis access and who had dialysis catheter and those with autoimmune diseases, infections or malignancy were excluded from our study. Particularly for the enrolled patients on PD, those who had been on hemodialysis or received a kidney transplant before the initiation of PD and patients that started PD for other reasons, such as congestive heart failure or acute renal failure, were excluded from the study.

The hemodialysis treatment was performed 3-times weekly with a dialysis time of 3.5-4 hrs per session, a filter of 1.5-2m^2 surface area by high-flux synthetic membrane, defined by a ultrafiltration coefficient >20ml/h [10] and a blood flow of 350-400ml/min. A bicarbonate-based ultrapure buffer dialysis solution was used with a dialysate flow rate of 500-600ml/min, a calcium concentration of 1.50-1.75mmol/L, a sodium concentration of 138-145mmol/L and low molecular weight heparin as anticoagulant therapy. The final concentration of bicarbonate in dialysate was 32mEq/L. Dialysis dose defined by Kt/V/day for urea, which was calculated according to the formula of Daugirdas [11]. Patients were excluded if they had Kt/V for urea <1.2.

The included PD patients were following continuous ambulatory peritoneal dialysis (CAPD) with 4 changes per day using a combination of 2 changes of 2L of hypertonic glucose-based solution (3.86% glucose; Baxter Healthcare) and 2 changes of 2L of semi-hypertonic glucose solution (2.5% glucose; Ariti; Bieffe Medital S.p.A.). All patients underwent urea kitenic analysis including residual renal function every three months of PD initiation. Dialysis dose defined according to the formula of Daugirdas by total Kt/V/week for urea including peritoneal Kt/V urea and residual GFR (ml/min/1.73m^2).The patients, who had Kt/V/week for urea <1.7 were excluded from our study. We used peritoneal liquids in dual backs with a final concentration of bicarbonate equal to 37.5 mEq /L.

The enrolled patients were in a good status, they did not have interdialytic peripheral oedema, high blood pressure, interdialytic orthostatic hypotension or other characteristics of an inaccurate dry body weight. However, patients with pre-dialysis blood pressure ≥140/90 (n=40, a ratio of 41.7%) were considered hypertensive, or if they were receiving anti-hypertensive drugs.21 of the studied patients were current smokers (a ratio of 21.9%).

At start of study, the existence of coronary syndrome (n=30, a ratio of 31.3%) was documented by history of myocardial infarction, coronary artery angioplasty or bypass surgery, or clinical signs of angina pectoris. Also, the first and the current cardiovascular events during the study were written down as one event for the coronary artery disease manifestation.

20 hemodialysis patients and 15 peritoneal dialysis patients excreted up to 100 ml of urine per day. Calcium channel blockers, beta-blockers or inhibitors of angiotensin II receptors were included in the receiving medications by our patients. Some of the enrolled patients were receiving statin, folic acid and only calcium-free phosphate binders were prescribed. All of the studied patients were on erythropoetin-an or-β therapy.

The underlying renal diseases were hypertensive nephrosclerosis (n=31), chronic glomerulonephritis (n=28), polycystic kidney disease (n=12), diabetic nephropathy (n=11), and other/unknown (n=14).

Approval and Consent

The study was approved by the ethics committee of the Hospitals "Laiko, University General Hospital of Athens" and Renal Unit of "Diagnostic and Therapeutic Center of Athens Hygeia SA". Written informed consent was obtained from all subjects.

Blood collection

Blood samples were obtained by venipuncture in the peritoneal dialysis patients in a twelve hours fasting state during a regular appointment in our Peritoneal Unit. In hemodialysis patients blood was drawn just before the start of the mean weekly dialysis session also in a twelve hours fasting state from the vascular access. In the end of the treatment the blood pump speed was reduced to <80ml/min and blood samples was obtained at 2 min post-dialysis from the arterial dialysis tubing for the calculation of the adequacy of dialysis by Kt/V for urea.

Samples were centrifuged immediately; serum was separated and processed for various assays.

In each subject, three sequences of samples (every month within 3 months) were received for the serum bicarbonate measurements, and their average was used for statistical analysis.

Laboratory measurements

Albumin, high density lipoproteins (HDL) and low density lipoproteins (LDL) were measured by biochemical analysis and the ratio of LDL / HDL was calculated.

High sensitivity C-reactive protein (hsCRP) and oxidized LDL (ox-LDL) serum concentrations were measured using enzyme linked immunoabsorbed assays (ELISA, Immundiagnostik AG., Germany and Immundiagnostik AG. Stubenwald-Allee, Bensheim respectively) is according to manufacturer's specifications.

The concentrations of intact-parathormone (i-PTH) and beta2-microglobulin (beta2M) were measured by radioimmunoassays (CIS bio international/France and Immunotech by Beckman, Czech Republic respectively).

Insulin levels were measured using a immunoradiometric assay (BioSource Europe S.A., Belgium) with a reported interassay coefficient of variation 6.1%.

Insulin resistance was calculated using the homeostasis model assessment of insulin resistance (HOMA-IR) [12].

Metabolic acidosis was defined by serum bicarbonate concentrations less than 22.0mEq/L, which were measured in gas machine (Roche, combas b 121) taking care of the blood specimens [13]. The low serum bicarbonate level was considered in combination to low arterial pH (acidemia) and decreased PCO_2, thus the decreased serum bicarbonate concentrations to reflect metabolic acidosis rather than respiratory alkalosis. Respiratory alkalosis is another clinical condition that causes decreased bicarbonate level in the end stage of renal disease patients, due to the loss of buffering capacity by the kidney in these patients.

Normalized Protein Catabolic Rate for dry body mass (nPCR) was calculated from the urea generation rate [14]. Body Mass Index (BMI) was obtained from height and post-dialysis body weight.

Haemodynamic measurements

Predialysis peripheral Systolic and Diastolic Blood Pressures (SBP and DBP respectively) in enrolled patients were calculated as the mean of 10 measurements during a treatment month using an automatic sphygmomanometer OMRON M4-I (Co Ltd Kyoto Japan). Mean peripheral pre-dialysis BP (MBP) was calculated as: MBP = DBP+1/3 (SBP-DBP).

Electrocardiographical analysis and M-mode echocardiography were performed the day after dialysis with a Hewlett Packard SONOS 2500 using a 2.25MHz transducer to estimate the ejection fraction and the ischaemic findings according to the recommendations of the American Society of Echocardiography [15].

Arterial stiffness was measured as carotid-femoral pulse wave velocity (c-f PWV) and carotid augmentation index (AIx) using the SphygmoCor system® (AtCor Medical Pty. Ltd, Sydney, Australia).In each subject two sequences of measurements were performed, and their mean was used for statistical analysis. We recorded the carotido-femoral PWV by positioning one sensor over the right femoral artery and a second sensor over the left carotid artery. The distance between the two sensors was measured with a measuring tape, and three recordings of both pulse waveforms were performed (8-10 heart beats for each recording).The Complior software automatically detected the foot of each pulse waveform from the two arterial sites and then measured the mean distance between the two feet as being the travel time of the wave. PWV was then computed using the formula: PWV=travel distance/travel time, as previously validated [16].

Central Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Mean Blood Pressure (MBP), PP, and the time of return of the reflected wave (Tr) were derived. Pressure and time of first peak (P1 and T1) and second peak (P2 and T2), and central augmented pressure (AP) were obtained. Central augmentation index (AIx) was computed (AP= P2-P1; AIx = (AP/PP) x 100) and corrected for a heart rate of 75 beats/minute.

Data analysis

Data were analyzed using SPSS 15.0 statistical package for Windows (SPSS Inc, Chicago, Illinois) and expressed as mean±standard deviation or as median value (interquartile range) for data that showed skewed distribution; Differences between mean values were assessed by using unpaired *t*-test for two groups and data that showed skewed distributions were compared with Mann-Whitney *U*- test.

Correlations between variables were defined by Pearson and Spearman coefficient and p values less than 0.05 were considered significant. Correlations between categorical variables were defined by log-rank tests with Kaplan-Meier

analysis during our median follow up time of 60 months. The total dialysis vintage, determined from the starting of dialysis treatment until the end of the follow up of 60 months of our study, was used for the definition of mortality rate in our data by life table and also for the prevalence of dialysis modality on mortality by Kaplan-Meier curve.We performed a Cox regression analysis to investigate significant risk factors for mortality including traditional and specific confounders for these patients, such as hypertension, diabetes mellitus, smoking, bone disease defined by i-PTH, serum albumin, serum bicarbonate levels less or more than 22mEq/L, dialysis modality and the existence of coronary artery disease.

Results

Demographical characteristics of the studied population at the time of inclusion are listed in Table 1.

Characteristic	Valid percent
Sex (males=62/females=34)	66.4/35.4
Diabetes mellitus (yes=11/no=85)	11.5/ 8.5
Hypertension (yes=40/no=56)	41.7/58.3
Current Smoking (yes=21/no=75)	21.9/78.1
Coronary artery disease (yes=30/no=66)	31.3/68.8
Hemodiafiltration / peritoneal dialysis (n=76/n=20)	79.2/20.8
Serum bicarbonate >(n=36) or <(n=60) than 22mEq/L	33.3/66.7
Mortality rate during total dialysis vintage (alive=66/died=30)	68.8/31.3
Reasons of death (cardiovascular events/sepsis/other)	73.3/16.7/10

Table 1: Demographical characteristics of studied patients, n=96.

In this study 30 patients died from the starting of treatment vintage until the end of our follow up time of 60 months (a mortality rate equal to 31.2%, survival function in Figure 1).The main reasons of death were cardiovascular events (n=22, a ratio of 73.3%), sepsis (n=5, a ratio of 16.7%) and other (n=3, a ratio of 10%).

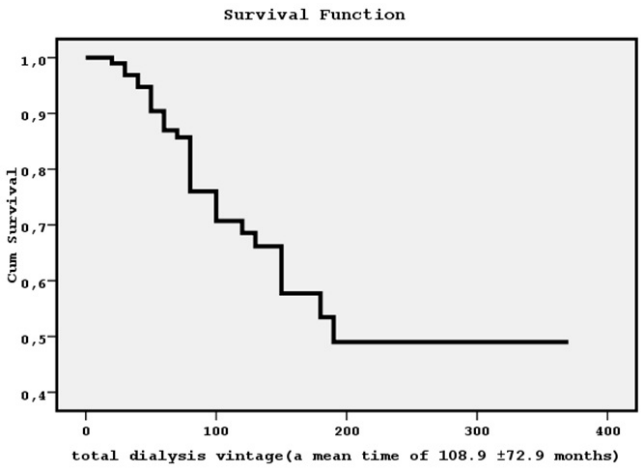

Figure 1: The survival function for 96 dialysis patients from the treatment initiation until the end of our follow up of 60 months (a mean time of 108.9±72.9 months) showed a mortality rate equal to 31.2%.

Kaplan-Meier analysis for the prevalence of CAD on mortality was found significant (log-rank=5.507, p=0.02, hazard function in figure 2). Also, the impact of dialysis modality on mortality was shown significant (log-rank=22.4, p=0.001, hazard function in figure 3) using the total dialysis time for our data, so since the starting of treatment vintage until the end of our follow up time of 60 months. Particularly, we noted that during the first 28 -30 months from treatment initiation, the survival was better for peritoneal dialysis, but then the mortality was significantly increased comparatively to the patients on hemodiafiltration However, the relationship between dialysis modality and the existence of CAD by Kaplan-Meier analysis was found non-significant. The impact of serum bicarbonate levels less or more than 22mEq/L on mortality was found non-significant. Additionally, the relationship between serum bicarbonate levels less or more than 22mEq/L and both, existence of CAD or dialysis modality was found non-significant.

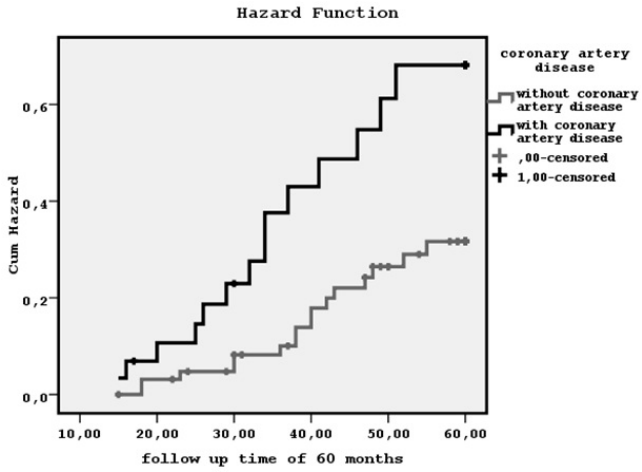

Figure 2: The prevalence of the existence of coronary artery disease on mortality during a follow up time of 60 months by Kaplan-Meier curve (log-rank=5.507, p=0.02).

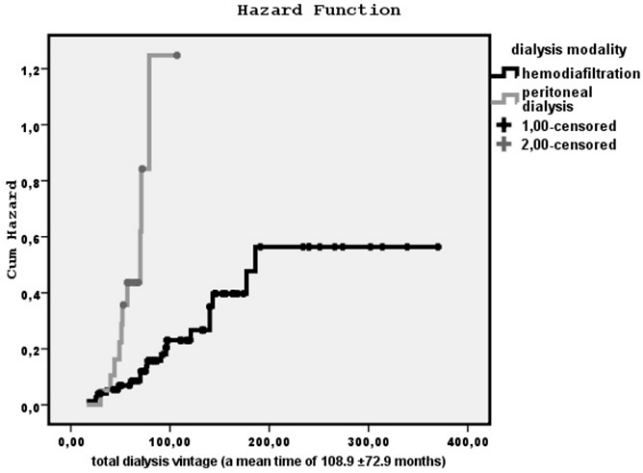

Figure 3: The impact of dialysis modality on mortality from the treatment initiation until the end of our follow up of 60 months (a mean time of 108.9±72.9 months) by Kaplan-Meier curve (log-rank=22.4, p=0.001).

Nevertheless, Cox-regression analysis revealed significant impact of serum bicarbonate levels less or more than 22mEq/L on mortality in combination to dialysis modality and CAD

(Table 2) adjusting for hypertension, diabetes mellitus, smoking, bone disease defined by i-PTH and serum albumin.

	p-value	Odds ratio	Confidence interval
Hypertension	0.09	2.32	0.87-6.2
Diabetes mellitus	0.7	0.8	0.2-3.2
Smoking	0.3	1.8	0.5-5.9
i-PTH	0.8	1.0	0.99-1.0
Albumin	0.8	0.85	0.2-4.1
Serum bicarbonate > or < than 22mEq/L	0.009	8.4	1.7-40.9
Dialysis modality	0.02	6.8	1.22-37.96
Coronary artery disease	0.009	3.8	1.4-10.2

Table 2: Cox-regression analysis for the prediction of mortality in 96 patients on renal replacement therapy.

In Table 3, the differences between the groups of patients with CAD manifestation or without CAD are shown. We observed that the patients with CAD had higher age, beta2M, i-PTH, c-fPWV, PP, AIx, oxLDL and hsCRP, but lower serum bicarbonate concentrations, BMI and albumin than the patients without manifested CAD.

	Patients with coronary artery disease (n=30)	Patients without coronary artery disease (n=66)
Age (years)	68.9±10.3*	59.0±14.7
BMI (Kg/m^2)	24.9 ± 2.6	25.1 ± 4.3
LDL/HDL	2.1 ± 0.8	2.5±0.9
HOMA-IR (mmol/L)	5.5±4.5	6.0±7.4
Beta2-microglobulin (mg/L)	40.2±34.9	29.5±23.6
Serum bicarbonate (mEq /L)	19.7±2.7	20.9 ± 2.5
i-PTH (pg/ml)	245.9±203.9	196.7±229.2
hsCRP (mg /L)	10.3±6.1*	7.9±5.7
oxLDL (ng/ml)	165.0±240.9*	89.1±87.0
Albumin (gr/dl)	3.7±0.6	3.93±0.3
MBP (mmHg)	99.0 ± 14.4	97.2±13.7
c-fPWV (m/s)	12.2±1.7*	10.8±1.7
AIx	25.06±1.9*	23.7 ± 2.4
PP (mmHg)	64.1±21.8*	54.01±19.3

*: p<0.05

Table 3: Differences between groups of patients according to the existence of coronary artery disease.

In Table 4, the differences between the groups of patients according to dialysis modality are shown. We noted that the patients on hemodiafiltration had lower i-PTH, serum bicarbonate levels, hsCRP, insulin resistance defined by HOMA-IR, but higher albumin, oxLDL and beta2M than the patients on peritoneal dialysis.

In Table 5, the differences between the patients with serum bicarbonate levels less or more than 22mEq/L are shown. We observed that the patients with serum bicarbonate levels less than 22mEq/L were older, they had higher beta2M, HOMA-IR, i-PTH, hsCRP, oxLDL, c-fPWV, PP and AIx, but lower albumin level and lower urine volume in comparison to the patients with serum bicarbonate levels more than 22mEq/L.

	Patients on hemodiafiltration (n=76)	Patients on peritoneal dialysis (n=20)
Age (years)	62.2 ± 15.0	61.6±11.3
BMI (Kg/m^2)	24.4±3.0*	27.4±5.5
Urine volume (ml/day)	229.3±153.8*	517.8±384.6
Serum bicarbonate (mEq/L)	20.09±2.2*	22.08±2.8
i-PTH (pg/ml)	180.4±189.2*	332.2±292.1
HOMA-IR (mmol/L)	5.3±5.1	7.7±10.7
Beta2-microglobulin (mg/L)	33.9±31.1	28.7±7.6
Albumin (gr/dl)	3.9±0.4*	3.5±0.4
hsCRP (mg/L)	7,9±5.8*	11.2±5.8
oxLDL (ng/ml)	129.7±170.6*	48.4±18.1
MBP (mmHg)	98.4±12.6	95.2±18.08
c-fPWV (m/s)	11.3±1.8	11.2±2.0
AIx	24.1±2.1	24.1±2.9
PP (mmHg)	58.2±19.2	53.2±24.9

*: p<0.05

Table 4: Differences between groups of patients according to dialysis modality.

	Patients with serum bicarbonate less than 22 mEq/L (n=60)	Patients with serum bicarbonate more than 22 mEq /L (n=36)
Age (years)	61.5 ± 13.8*	53.9 ± 14.5
BMI (Kg/m^2)	25.2±4.3	25.3±3.8
Urine volume (ml/day)	308.8±223.7	436.15±406.0
Serum bicarbonate (mEq/L)	19.2±1.9	23.3±1.2
HOMA-IR (mmol/L)	6.9±8.7	4.9±3.5
Beta2-microglobulin (mg/L)	29.9±22.3	26.1±9.5
i-PTH (pg/ml)	262.9±280.1*	166.1±132.7
Albumin (gr/dl)	3.8±0.3	3.9±0.4
LDL/HDL	2.4±1.04	2.5±0.7
hsCRP (mg /L)	9.5±5.8*	6.6±5.9
oxLDL (ng/ml)	127.5±175.6	84.1±85.8
MBP (mmHg)	96.3±12.6	94.6±15.9
c-fPWV (m/s)	11.5±1.8*	10.3±1.9
AIx	24.6±2.3*	23.0±2.7
PP (mmHg)	55.9±21.1	49.9±18.9

Table 5: Differences between groups of patients according to lower or higher than 22 mEq/L serum bicarbonate level.

Discussion

In this study we observed that the patients with manifested CAD had greater mortality rate than the patients without CAD and the existence of CAD was found such as a significant independent predictor for mortality adjusting for potentially multiple confounding covariates. Also, the patients with manifested CAD had higher c-fPWV, AIx and PP comparatively to the patients without CAD.

Increased pulse wave velocity and augmentation index are integrated indexes of vascular function and structure. They estimate the arterial stiffness, which is a strong predictor of cardiovascular mortality in general population and in dialysis patients [17]. Also, elevated PP is one another consequence of arterial stiffening and vascular calcification. Previously, it has been shown the positive relationship between the extent of vascular calcification and arterial stiffness and it may explain the increased cardiovascular events seen in dialysis patients [18].

Additionally, it has been already established that end-stage renal disease (ESRD) results in accelerated atherosclerosis and increased morbitity and mortality [7]. Even when the patients are undergoing renal replacement therapy, the mortality remains high, mainly for cardiovascular causes due either to uremia-related risk factors (such as anemia, hyperparathyroidism, inflammation, oxidative stress and malnutrition) [19,20] or to traditional ones (age, male gender, diabetes, obesity, hypertension, smoking, dyslipidemia) [21,22]. Indeed, in present study the patients with manifested CAD were older and they had higher i-PTH, hsCRP, oxLDL, beta2M and worse status of metabolic acidosis in combination to lower albumin and BMI, which are some of the malnutrition characteristics, than the patients without CAD.

Interestingly, in our study even though Cox-regression analysis revealed significant impact of low serum bicarbonate levels on mortality adjusting for potentially multiple confounders, Kaplan-Meier analysis did not show significant prevalence of low serum bicarbonate levels on mortality rate, neither on the existence of CAD. These findings may suggest that metabolic acidosis defined by low serum bicarbonate level may be an independent predictor for mortality in relation to confounders in dialysis patients.

In addition, in this study we observed that the patients with low bicarbonate level (less than 22mEq/L) had higher c-fPWV, AIx, PP, beta2M, insulin resistance defined by increased HOMA-IR, i-PTH, hsCRP, oxLDL, but lower albumin level and lower urine volume as an indicator of decreased residual renal function, than the patients with serum bicarbonate levels more than 22mEq/L.

These findings support that metabolic acidosis results in detrimental effects and patients with low bicarbonate level should be treated properly even though they are receiving dialysis therapy.Previously, it has already been reported the role of metabolic acidosis on vascular calcification, as the mineral metabolism disturbances act through the existing metabolic acidosis in dialysis patients [23].The influence of acidosis on vascular calcification is complicated, acting as a stimulator of the solubility of Ca x P deposits and as a blocker of phosphate uptake by the arterial smooth muscle cells, so acidosis may attenuate vascular calcification [23]. But, on the other hand acidosis promotes inflammation of the arterial wall, releasing cytokines that may induce vascular calcification [24]. Additionally, preliminary evidence suggested that metabolic acidosis may play a role in the accumulation of beta2-microglobulin, which serves as a surrogate marker of middle-molecules uraemic toxins, and in the hypertriglyceridemia seen in haemodialyzed patients [25,26]. Previously, it has been already demonstrated the role of beta2-microglobulin on mortality in haemodialyzed patients, independently haemodialysis duration, diabetes, and malnutrition [27], due mainly to vascular inflammation and amyloid formation in the vessel wall resulting in vessels damage [28].

In the mean time, there is no consensus about the optimal bicarbonate levels in ESRD patients. A few studies have addressed this issue and they have conflicting results [29,30]. Previous study showed that serum bicarbonate level >22 mEq/L was associated with lower mortality risk [31] and another study reported that an increased risk was observed in patients with high (>27 mEq/L) or low (<17 mEq/L) bicarbonate levels [32]. In this study, we were considered uncorrected metabolic acidosis in enrolled patients, when serum bicarbonate level was <22 mEq/L combined to low arterial pH and decreased PCO_2. Therefore, the low bicarbonate level may be diagnostic of metabolic acidosis rather than of respiratory alkalosis, another clinical condition that causes decreased bicarbonate level, given the loss of buffering capacity by the kidney in ESRD. However, in our data the mean value of serum bicarbonate concentrations particularly for enrolled patients on hemodiafiltration was lower comparatively to previous reports [32], due may to the different used bicarbonate concentration in dialysis dialysate. Also, we did not exclude from the study the diabetic patients, who may have worse metabolic acidosis state in our baseline measurements.

In agreement to our results, the underlying pathophysiological mechanisms for increased mortality and morbidity in dialysis patients with low serum bicarbonate levels include metabolic disorders, bone disease, chronic inflammation [33] and loss of residual renal function that has been established to be a powerfull predictor of mortality in patients on dialysis [34].

Moreover, in this study the dialysis modality showed significant influence on mortality rate notifying that the patients on peritoneal dialysis presented worse survival than the patients on hemodiafiltration, despite dialysis modality was not significantly associated with the existence of CAD, neither with low bicarbonate level by Kaplan-Meier curves during our follow up time of 60 months. Specifically, during the first 28-30 months from treatment initiation, the survival was better for peritoneal dialysis, but then the mortality was significantly increased comparatively to the patients on hemodiafiltration. Supportingly, Cox-regression analysis showed dialysis modality to be an important predictor for mortality adjusting for confounders. Comparing the patients on hemodiafiltration and on peritoneal dialysis between them, we observed that the patients on hemodiafiltration had lower i-PTH, HOMA-IR, serum bicarbonate concentrations, BMI and hsCRP, but higher

beta2M, albumin and oxLDL than the patients on peritoneal dialysis. According to our findings, despite the continous provision of peritoneal dialysis treatment, the patients on peritoneal dialysis had more metabolic disturbancies, malnutrition, excited inflammation and bone disease, but better metabolic acidosis status, may lower oxidative stress and relatively decreased beta2M serum concentrations than the patients on hemodiafiltration. These factors should be connected to the pathophysiological mechanisms which contribute to the different survival rate between hemodiafiltration and peritoneal dialysis.

Comparative studies between patients treated with peritoneal dialysis and hemodialysis have frequently provided conflicting results, due may to methodological and design differences [31,35]. It has been reported that PD patients have a slightly higher survival rate in the first 1-2 years, in agreement with our findings [36]. Other study found that PD patients had better survival irrespectively to treatment vintage [37]. In contrast, in some studies HD displayed better survival or both dialysis modalities had similar effect on survival rate [5,6].

There are several limitations in the present study. This is an observational study with a relatively small sample size. However, we tried to enroll patients in a good status minimizing the risk of inclusion of more sick patients with excited cardiovascular disease or probably connected to serum bicarbonate <22mEq/L. Also, data representing overall nutritional status assessment, anthropometry and dietary protein intake were not available for the analysis.

Conclusion

Uncorrected metabolic acidosis and coronary artery disease were shown as independent significant predictors for mortality in patients on renal replacement therapy. Peritoneal dialysis may provide worse survival after 2-2.5 years of treatment initiation than hemodiafiltration.

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