NEPHROLOGY - ORIGINAL PAPER



Achievement of guideline targets in elderly patients on hemodialysis: a multicenter study

Nada Dimković^{1,2} · Ljubica Djukanović¹ · Jelena Marinković¹ · Živka Djurić² · Violeta Knežević³ · Tatjana Lazarević⁴ · Stanimir Ljubenović⁵ · Rodoljub Marković⁶ · Violeta Rabrenović⁷

Received: 21 April 2015 / Accepted: 6 July 2015 / Published online: 30 July 2015 © Springer Science+Business Media Dordrecht 2015

Abstract

Objectives Advanced age is associated with shorter survival on dialysis. The aim of the present study was to compare the adherence with KDOQI guideline targets and the association between mortality and satisfying the guidelines targets between hemodialysis patients aged 65 years and over and those younger than 65 years.

Methods Data were collected using a questionnaire sent to all 46 HD centers in Serbia with totally 3868 HD patients. The 24 centers responded and sent the data on all patients aged 18 years or older that were on regular HD for more than 3 months (2153 patients, 1320 males, aged 18–90 years). Data are presented in two groups: a group of patients younger than 65 years (1438, 66.8 %) and a group of patients aged 65 years and over (715, 33.2 %). The percentage of patients whose values failed to meet the targets recommended by

KDOQI Clinical Practice Guidelines was calculated for dialysis dose (spKt/V), hemoglobin, serum phosphorus, serum calcium and plasma iPTH (150–300 pg/mL). Patients were followed from enrollment until their death, kidney transplantation, departure from the center or the end of the study.

Results Elderly patients were more likely to have hypertension, significantly lower systolic and diastolic blood pressure and smaller dialysis vintage than younger patients. They were less frequently treated with highflux membranes and hemodiafiltration and they had significantly lower number of dialysis hours per week and significantly lower interdialytic weight gain. They used ESA and phosphate binders less frequently than younger patients (p < 0.001 and p = 0.002). Older patients had similar Kt/V as younger ones but they had significantly more frequent Hb level outside the target range than younger patients. During the year follow-up period, by using a Cox proportional hazards model it has been confirmed that age, dialysis vintage, weekly dialysis time and target values for Kt/V were significant independent predictors of time to death for younger patients and gender, dialysis vintage and iPTH were independent predictor of time to death for older patients.

Conclusion Despite less favorable dialysis prescription, older patients had similar Kt/V and less frequent deviations from the target values proposed by KDOQI for serum phosphorus and iPTH but more frequent deviation for Hb value as compared with younger patients. Risk factors for mortality differ between older and younger patients; out of five KDOQI targets, only Kt/V proved to be a significant risk factor for mortality for younger and iPTH for older patients.

Keywords Elderly on hemodialysis · KDOQI targets · Survival



Nada Dimković dim@eunet.rs

School of Medicine, University of Belgrade, Belgrade, Serbia

² Clinical Department for Renal Diseases, Zvezdara University Medical Center, D. Tucovica 161, Belgrade 11 000, Serbia

Nephrology Department, Clinical Center Novi Sad, Novi Sad, Serbia

⁴ Nephrology Department, Clinical Center Kragujevac, Kragujevac, Serbia

Nephrology Department, Clinical Center Nis, Nis, Serbia

Nephrology Department, Clinical Center Zemun, Zemun, Sorbia

Nephrology Department, Military Medical Academy, Belgrade, Serbia

Introduction

As elderly population continues to grow, diagnosis and treatment of renal diseases in elderly becomes the challenge of everyday nephrology practice. Patients over the age of 75 have higher incidence rates of end-stage renal disease (ESRD) than younger patients and constitute the fastest growing segment of the ESRD population worldwide [1]. Up to one-third of elderly patients with ESRD have four or more chronic health conditions when they reach ESRD [2] and many are not considered candidates for kidney transplantation. Thus, the vast majority of elderly patients with ESRD face the prospect of dialysis therapy for the remainder of their lives. HD does not always substantially prolong life among older adults. For example, in two studies, median survival was similar among geriatric patients receiving nondialytic management when compared with elderly patients who started HD after emergency referral or who had coexisting ischemic heart disease [3, 4]. Therefore it is of great importance to identify the factors that may have an impact on survival of elderly dialysis patients.

Survival is an important parameter of successful treatment of elderly ESRD patients and as expected, advanced age is associated with shorter survival on dialysis. Integrated prognostic models may take into account a number of factors to establish a risk profile for older patients undergoing dialysis. In addition to patient demographic information and laboratories, the instruments may include comorbidities, changes in comorbidity score over time, functional status/frailty, health-related quality of life (HRQOL) and either the patient's or clinician's prediction of survival [5-9]. The elderly have many comorbid conditions and most of them die of diseases that were present at the start of dialysis [10]. Independent predictors of poor survival among old patients were older age, poor nutritional status, inactivity, late referral for dialysis and significant comorbidity [11].

Numerous guidelines defined standards of dialysis with the aim to improve results of HD treatment and patient outcomes. The publication of these guidelines was followed by a number of studies on the levels of guideline adherence [12–16]. However, information on the achievement of targeted guidance relating to the aging population lacking. At the same time, it is not clear if achieving of the current guidelines affect the survival of elderly dialysis patients. Therefore, the aim of the preset study was to compare the adherence with KDOQI guideline targets and the association between mortality and satisfying the guidelines targets between hemodialysis patients aged 65 years and over and those younger than 65 years.



The current study analyzed data of 2153 patients on regular HD in 24 centers which accounts for about 56 % of all hemodialysis population in Serbia. Data were collected using a questionnaire sent to all 46 HD centers in Serbia with totally 3868 HD patients. The 24 centers responded and sent the data on all patients aged 18 years or older that were on regular HD for more than 3 months on January 1 2010. Out of 2281 patients whose data were obtained 2153 (1320 males, aged 18–90 years) with complete data were included in the study. The study was approved by The Ethics Committee of Zvezdara University Medical Center and appropriate patient consent was obtained at all study centers.

For comparison, the data are presented in two groups, a group of patients younger than 65 years (1438, 66.8 %) and a group of patients aged 65 years and over (715, 33.2 %). Data on patient demographic characteristics, medical history, HD treatment and laboratory data were obtained from medical records at the onset of the study. Based on these data the percentage of patients whose values failed to meet the targets recommended by KDOQI Clinical Practice Guidelines was calculated in the following areas: dialysis dose (spKt/V > 1.2), anemia (hemoglobin >110 g/L), serum phosphorus (1.1–1.8 mmol/l), serum calcium (2.1–2.4 mmol/l) and plasma iPTH (150–300 pg/mL) [17]. We selected KDOQI guidelines for analysis since it was mainly used up to 2012 when KDIGO guidelines became accepted.

Hemoglobin, serum levels of urea, phosphorus calcium, albumin were measured by routine laboratory tests and iPTH by (Diagnostic Product Corporation, USA). Measured calcium was corrected for level of serum albumin with the following formula: Corrected total calcium (mmol/L) = TCa (mmol/L) + 0.8 [40 (g/L) – albumin (g/L)]. Dialysis dose (spKt/V) was calculated from values of blood urea nitrogen pre- and post-dialysis, body weight and dialysis duration using the second generation Daugirdas formula [18]. Patients were followed from enrollment until their death, kidney transplantation, departure from the center or the end of the study on December 31, 2012.

Descriptive statistics were presented as mean values and standard deviation (SD) for the continuous variables, or as frequencies for categorical variables. Pearson correlation coefficients were used to detect correlation among variables. Univariate Cox proportional hazards analysis was used to select variables significantly associated with the risk of time to death. As independent variables patient age, gender, primary kidney disease, dialysis modality (HD/hemodiafiltration), duration of HD treatment (years), HD hours/week, Kt/V, hemoglobin, serum calcium, phosphorus, iPTH, systolic blood pressure, interdialytic weight gain, iron therapy,



Table 1 Characteristics of patients and hemodialysis treatment at the onset of the study

| | Total (No, %) | <65 years (No, %) | ≥65 years (No, %) | p^{a} |
|------------------------------------|-----------------|-------------------|-------------------|---------|
| Number pt | 2153 | 1438 (66.8) | 715 (33.2) | |
| Gender | | | | |
| Males | 1320 (61.3) | 898 (62.5) | 422 (59.0) | 0.122 |
| Age, years—range | 18-90 | 18-64 | 65-90 | |
| Mean \pm SD | 59.0 ± 12.5 | 52.3 ± 9.3 | 72.4 ± 4.9 | 0.000 |
| Etiology of ESRA | | | | |
| Glomerulonephritis | 370 (17.3) | 329 (22.9) | 41 (5.7) | 0.000 |
| TIN (without Balkan nephropathy) | 118 (5.4) | 69 (4.8) | 48 (6.7) | |
| Balkan nephropathy | 90 (4.2) | 38 (2.6) | 52 (7.3) | |
| Hypertensive nephropathy | 540 (25.1) | 335 (23.2) | 205 (28.7) | |
| Diabetic nephropathy | 276 (12.8) | 204 (14.3) | 73 (10.2) | |
| Polycystic kidney disease | 168 (7.8) | 116 (8.1) | 52 (7.3) | |
| Other | 396 (18.4) | 245 (17.1) | 151 (21.1) | |
| Unknown | 195 (9.0) | 102 (7.0) | 93 (13.0) | |
| Blood pressure, mmHg mean \pm SD | | | | |
| Systolic | 136 ± 21 | 137 ± 21 | 134 ± 20 | 0.011 |
| Diastolic | 77 ± 10 | 78 ± 10 | 76 ± 10 | 0.000 |
| Dialysis vintage, years | | | | |
| Range | 0.5-35 | 0.5-35 | 0.5-25 | |
| Mean \pm SD | 5.3 ± 5.3 | 5.7 ± 5.7 | 4.1 ± 4.2 | 0.000 |
| Dialysis modality | | | | |
| Low flux | 956 (44.4) | 488 (34.0) | 467 (65.3) | 0.000 |
| High flux | 858 (39.8) | 643 (44.7) | 215 (30.1) | |
| Hemodiafiltration | 339 (15.8) | 307 (21.3) | 33 (4.6) | |
| Dialysis, number/week | 2.9 ± 0.3 | 2.9 ± 0.3 | 2.8 ± 0.4 | 0.000 |
| Dialysis, hours/week | 11.8 (1.9) | 11.9 ± 1.8 | 11.4 ± 1.9 | 0.000 |
| <9 h/week | 213 (9.9) | 107 (7.7) | 106 (15.7) | 0.000 |
| 9–12 h/week | 1608 (78.2) | 1104 (79.9) | 504 (74.7) | |
| >12 h/week | 235 (10.9) | 170 (12.3) | 65 (9.6) | |
| Missing data | 97 | 57 | 40 | |
| ID weight gain, kg | | | | |
| Range | 0–9 | 0–9 | 0.3-6 | |
| Mean \pm SD | 2.8 ± 1.1 | 2.9 ± 1.2 | 2.6 ± 0.9 | 0.000 |

ESRD end-stage renal disease, ID interdialytic

blood transfusion, use of phosphate binders and calcitriol were used. Variables number of HD weekly, erythropoietin stimulating agents (ESA) dose/week, duration of ESA treatment (years), product of calcium and phosphorus were not included in analysis due to colinearity. Significant variables in univariate analysis (p < 0.10) were tested in a multivariate Cox models using the backward stepwise method. The p values of <0.05 were considered as statistically significant. Models were adjusted for patient age, gender and duration of HD treatment (years).

All analyses were performed using the SPSS statistical software package (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp).

Results

The study involved 2153 patients with mean age of 59 years. Characteristics of patients and HD treatment at the onset of the study are presented in Table 1. Elderly patients were more likely to have hypertension than younger patients who had more frequently glomerulonephritis as a primary renal disease. Also, older patients had significantly lower systolic and diastolic blood pressure and they had smaller dialysis vintage than younger patients. Dialyzers with synthetic membranes were used in all patients included in the study and 340 (15.7%) of patients were on hemodiafiltration. Older patients were less frequently treated with high-flux membranes and



^a According to Chi-square, t or Mann–Whitney test where appropriate

Table 2 Treatment of anemia and mineral metabolism disorders

| Treatment | Total (No, %) | <65 years (No, %) | ≥65 years (No, %) | p |
|---|--------------------------|-------------------|-------------------|-------|
| Total number of patients | 2153 | 1438 | 715 | |
| Iron use, No (%) | 994 (46.2) | 689 (48.0) | 304 (42.5) | |
| Oral | 247 (11.5) | 173 (12.4) | 74 (10.4) | 0.242 |
| Intravenous | 747 (34.7) | 516 (35.6) | 230 (32.2) | 0.082 |
| ESA use, No (%) | 1402 ^a (65.1) | 965(67.2) | 436 (61.0) | 0.000 |
| ESA dosage, U/week (mean \pm SD) ^a | 3574 ± 2601 | 3543 ± 2528 | 3623 ± 2745 | 0.664 |
| Transfusion, No (%) | 269 (16.8) | 163 (15.3) | 106 (19.9) | 0.565 |
| Units/year | 0.72 ± 2.44 | 0.61 ± 2.18 | 0.93 ± 2.88 | 0.027 |
| Phosphate binders use, No(%) | 1446 (67.2) | 981 (68.3) | 465 (65.0) | |
| CaCO ₃ | 1354 (63.0) | 912 (63.5) | 442 (61.8) | 0.002 |
| Other | 92 (4.2) | 69 (4.8) | 23 (3.2) | |
| Vit. D3 metabolites use, No (%) | 827 (38.4) | 549 (76.8) | 278 (38.9) | |
| 1 alpha D_3 | 525 (24.4) | 339 (47.4) | 186 (26.0) | 0.334 |
| 1,25 D ₃ | 302 (14.0) | 210 (29.4) | 92 (12.9) | |

^a 378 of patients were treated with darbepoetin alfa and the others used epoetin. Dose of darbepoetin was multiplies by 200 before calculation of mean value

Table 3 Mean values (\pm SD) of variables whose adherence to guideline target was examined

| | Total (No, %) | <65 years (No, %) | ≥65 years (No, %) | p |
|-----------------------------|-------------------|----------------------|-------------------|-------|
| Single pool Kt/V, No | 1736 | 1176 | 560 | |
| Mean \pm SD | 1.24 ± 0.31 | 1.25 ± 0.32 | 1.23 ± 0.27 | 0.083 |
| Hemoglobin, g/L, No | 1812 | 1219 | 591 | |
| Mean \pm SD | 102 ± 17 | 103 ± 17 | 99 ± 16 | 0.000 |
| S-phosphorus, mmol/L, No | 1781 | 1203 | 576 | |
| Mean \pm SD | 1.58 ± 0.56 | 1.64 ± 0.57 | 1.45 ± 0.49 | 0.000 |
| S-calcium, mmol/L, No | 1772 | 1198 | 572 | |
| Mean \pm SD | 2.31 ± 0.29 | 2.30 ± 0.29 | 2.31 ± 0.25 | 0.231 |
| S-iPTH, pg/mL No | ., 1292 | 872 | 420 | |
| $\text{Mean} \pm \text{SD}$ | 407.8 ± 512.4 | 440.5 ± 533.5 | 337.5 ± 457.2 | 0.001 |

hemodiafiltration and they had significantly lower number of dialysis hours per week and significantly lower interdialytic weight gain compared to younger patients.

Table 2 shows that 65.1 % of patients were treated with erythropoietin stimulating agents (ESA), most of them with epoetin and 378 (17.6 %) with darbepoetin alpha. Older patients used ESA less frequently than younger patients (p < 0.001). Intravenous iron was used by 34.7 % and oral iron by 11.5 % of all patients with no significant difference between age groups. The number of patients who received blood transfusions did not differ

significantly between groups but older patients received significantly more units of blood per year than younger patients. Phosphate binders were used more frequently by younger patients (p = 0.002, mainly calcium carbonate). There was no difference in the use of vitamin D metabolites among the age groups.

Results presented in Table 3 show the mean values of Kt/V, hemoglobin, serum phosphorus, calcium and iPTH levels among the groups. There were no difference between the groups in hemoglobin and serum calcium level. The number/percentage of patients outside the target range are presented in Figs. 1 and 2. Substantial percentage of patients was outside the target ranges. Older patients had similar Kt/V as younger ones but they had significantly more frequent deviation for Hb level (Fig. 1), serum phosphorus and iPTH (Fig. 2) outside the target range than younger patients. Namely, elderly had iPTH and serum phosphorus below the lower limit of normal more frequently than younger patients.

During the year follow-up period, 576 (26.7 %) patients died, 44 (2 %) were transplanted, 69 (3.2 %) were lost from the follow-up and 1464 remained on regular HD. We used a Cox proportional hazards model to investigate the association between mortality and satisfying the guidelines targets. When targets for Kt/V, hemoglobin, serum phosphorus, calcium and iPTH were included in multivariate Cox model, age, dialysis vintage, weekly dialysis time and target values for Kt/V were found to be the significant independent predictors of time to death for younger patients and gender, dialysis vintage and iPTH were independent predictor of time to death for older patients (Table 4).



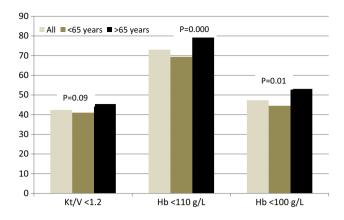


Fig. 1 Proportion of patients within or outside guidelines targets for Kt/V and hemoglobin level at the outset of the study

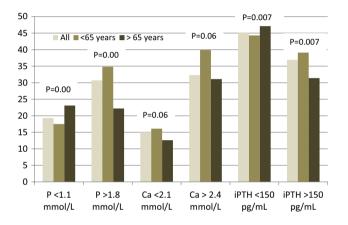


Fig. 2 Proportion of patients within or outside guidelines targets for serum phosphorus, calcium and iPTH at the outset of the study

Discussion

Although elderly patients account for an increasing fraction of patients on renal replacement therapy worldwide, it is not clear whether dialysis prescription for the elderly should be different than that of younger ones. At the same time, it is not clear if risk factor for mortality on dialysis differ regard to patients' age. Numerous national and international studies were undertaken to find out the proportion of patients failing to meet guidelines targets as well as the association of guidelines compliance and patients' outcome [14, 15, 19, 20]. The most of these studies were carried out in developed countries. In recent years, the number of papers presenting epidemiological data on RRT in developing countries increased, but papers on the results of HD treatment and compliance with guidelines in developing countries are scarce, particularly for elderly population [21, 22].

This multicenter study compared 1438 patients younger than 65 years with 715 patients 65 years old and above in their adherence with KDOQI guidelines targets in five crucial HD practice areas: dialysis dose, anemia, serum phosphorus, serum calcium and iPTH. We selected KDOQI guidelines for comparative analysis since they were traditionally used by HD centers until 2012 when KDIGO guidelines started to be adopted as a daily practice.

Older patients had shorter dialysis sessions, lower interdialytic weight gain and used low-flux membranes more frequently than younger patients. Nevertheless, the older patients had similar Kt/V as younger patients, significantly lower phosphorus and iPTH and less frequent deviations from the target values proposed by KDOQI for serum phosphorus and iPTH than younger patients. However, the

Table 4 Multivariate Cox proportional hazard model included guidelines target values as independent variables and confounders

| Variable | <65 years $n = 1436$; 285 dead | | \geq 65 years $n = 715$; 291 dead | | Total stratified by age categories $n = 2151$; 576 dead | |
|------------------------------|---------------------------------|-------|--------------------------------------|-------|--|-------|
| | HR (95 % CI) | p | HR (95 % CI) | p | HR (95 % CI) | p |
| Gender | 0.81 (0.59–1.09) | 0.167 | 0.73 (0.55-0.97) | 0.035 | 0.78 (0.62-0.95) | 0.015 |
| Age, years | 1.03 (1.01-1.05) | 0.000 | 1.02 (0.99-1.05) | 0.063 | 1.03 (1.01-1.04) | 0.000 |
| Dialysis vintage | 0.55 (0.51-0.51) | 0.000 | 0.54 (0.48-0.59) | 0.000 | 0.55 (0.51-0.59) | 0.000 |
| Hours of HD/week | 0.91 (0.83-0.98) | 0.024 | 1.01 (0.92–1.09) | 0.930 | 0.96 (0.91-1.02) | 0.185 |
| Kt/V > 1.2 | 0.61 (0.45-0.81) | 0.001 | 1.06 (0.80-1.40) | 0.670 | 0.81 (0.67-0.99) | 0.041 |
| Hb > 110 g/L | 0.76 (0.55-1.03) | 0.081 | 1.01 (0.72–1.42) | 0.949 | 0.87 (0.69-1.10) | 0.260 |
| S-phosphorus, 1.1–1.8 mmol/L | 0.79 (0.61-1.04) | 0.093 | 1.04 (0.79–1.37) | 0.745 | 0.92 (0.76-1.12) | 0.405 |
| S-calcium, 2.1–2.4 mmol/L | 0.83 (0.63-1.09) | 0.188 | 1.03 (0.79–1.35) | 0.789 | 0.92 (0.76-1.12) | 0.415 |
| iPTH, 150-300, pg/mL | 0.73 (0.44-1.21) | 0.223 | 0.61 (0.37-1.00) | 0.050 | 0.72 (0.51-1.02) | 0.068 |

Bold values indicate significant independent predictors of time to death for younger and for older patients



older patients had significantly lower mean Hb level that was more frequently below targets than younger ones.

Number of patients in Serbia failing to meet Kt/V target significantly decreased during the past decade [16]. According to present analysis, the mean Kt/V in total cohort of hemodialysis patients was 1.24 ± 0.31 and 42.4 % of patients had Kt/V below 1.2 without significant difference between two age groups. It is worth mentioning that more than half of patients in both groups had their Kt/V above 1.2, the minimally adequate dose proposed by KDOOI guidelines. Our data are in agreement with DOPPS study where there were no differences between older and younger patients in delivered dialysis dose as measured by single Kt/V [23]. As in our cohort of patients, they observed that shorter dialysis duration in elderly and maintenance of a satisfactory dialysis dose can be partially explained by the lower dry weight, lower lean body mass and low serum albumin which were common in the elderly group. By using Cox proportional hazards model, we confirmed that target Kt/V was found to be significant independent predictor of time to death but only in younger group of patients. The question arises whether elderly patient may better tolerate uremia than younger patients due to decreased metabolic demand and lower total energy expenditure, physical activity expenditure and lower resting energy expenditure that younger patients [24]. As in all studies based on questionnaire, this one lacks some parameters that may give a better explanation for current Kt/V such as residual renal function, vascular access patency and patients' compliance to dialysis time. The fact that ~45 % of elderly have their Kt/V less than that proposed by guidelines obliges us to find out all the factors that are responsible for it and to correct them for the benefit of patients' outcome.

Percentage of patients who fell within K/DOQI recommended range for serum phosphorus (50 %) and iPTH (18 %) was comparable with those in the DOPPS studies [13-25]. However, serum phosphorus was significantly lower in older than in younger patients and significantly lower percentage of older patients received phosphate binders. Having in mind the similar Kt/V in two groups, we believe that elderly are more compliant with prescribed diet and that they are more prone to malnutrition than younger patients. Similar findings about serum phosphorus and iPTH were published by Yavuz et al., who observed negative correlation between serum phosphorus level and age in patients on chronic peritoneal dialysis. They proposed that it may originate from age-related changes in nutrition and eating habits. Elderly suffer from many comorbid conditions all contributing to malnutrition and low phosphorus level. Indeed, serum phosphorus level positively correlated with serum albumin level. This finding is of great importance since malnutrition is risk factors for morbidity and mortality in dialysis patients and may contribute to low turnover bone disease known to be more frequent in elderly on dialysis. It should be taken into account when prescribing dialysis solution and anti-phosphate drugs for patients with advanced age [26]. Similar data are observed by DOPPS study where authors suggested that low serum albumin and phosphorus were major mortality risk factor [27]. Percentage of patients who achieved targets for serum calcium was similar in both age groups and higher than in DOPPS studies but similar to results presented in some recent studies [14-28]. Special attention should be paid to calcium intake in elderly, as the risk of bone loss is high in the older population [29]. Since dietary calcium intake is generally associated with phosphorus intake, calcium supplements should be prescribed if possible. In our HD population like in many others [14–30] low iPTH level represents twice the bigger problem than severe hyperparathyroidism while the opposite is found in some other countries [31]. By comparing two age groups we confirmed that low parathyroid hormone (<150, g/mL) levels were more common whereas higher parathyroid hormone (>300 pg/mL) was less common in the elderly group. It is well known that apart from numerous factors, older age is a risk factor for low turnover bone disease [32]. There is disagreement about the significance of this finding but according to some data, very few patients with low/normal iPTH had related symptoms (pain and fractures) and their morbidity and mortality did not differ from those patients with a high initial iPTH level [32]. Numerous studies found a significant relationship between serum levels of phosphorus, calcium, PTH and mortality [33-35]. However, several meta-analyses reported conflicting data about increased level of mineral metabolism indices and patients' survival [36–38]. Using multivariate Cox proportional hazard model we found none of three parameters (serum calcium, phosphorus and iPTH) were significant predictors of death in younger patients. In elderly, only being outside target range for iPTH was proved to be significant independent predictor of death.

At the onset of the present study 73 % of patients had hemoglobin level below KDOQI target of 110 g/L and this percentage is lower than in most of developed countries [39–41], but similar or even higher than in developing countries [30, 42, 43]. That unfavorable result is the consequence of local policy since Serbian national health Found restricted target hemoglobin value between 10 and 11 g/dL. However, elderly had significantly lower mean hemoglobin value as compared to younger group of patients: 80 % of them had their Hb value below 110 g/dL and 53 % had Hb value below 100 g/dL—finding significantly unfavorable than in younger patients. Elderly are at higher risk of gastrointestinal disorders including gastritis, ulcer disease, diverticulosis, and carcinoma. Therefore they are of particular risk of bleeding while on hemodialysis



and it may potentially influence their Hb level. Even so, ESA were used less frequently in elderly than in younger patients. Although we have no data about comorbidity, we may speculate that Hb range in elderly was kept in the lower range of target due to more frequent cardiovascular morbidity including vascular access thrombosis. Patients from both groups who received ASE had similar dose of the drug. Unfortunately, body mass index (BMI) was not included in this analysis and ESA dose is difficult to comment between two age groups. We may expect that the elderly have lower BMI and the ESA dose appropriately lower than younger patients with higher BMI. In Europe, ANZ and North America, a higher percentage of elderly patients achieved the hemoglobin target value [23]. Also, elderly patients from that regions had lower erythropoietin resistance index than younger patients [23]. However, data from Japan have shown that patients with lower Hb tended to be older [44]. We did not observe a correlation between hemoglobin values and survival in either group of patients. However, authors from Japan confirmed the difference in the effect of Hb on survival between elderly and nonelderly population. Nonelderly patients had increased risk of death if they had Hb < 10 g/dL, whereas only for the <9 g/dL category among elderly population. The reason why low Hb had a weaker link to poorer survival could be related to the reduced activity in the elderly patients. Also, oxygen consumption in the elderly population is reported to be lower than in the younger as well as exercise capacity [44]. This is something that should be kept in mind when treating elderly patients.

By using Cox proportional hazard model, this study pointed out the difference in mortality risk factors in regard to age. While age, dialysis vintage, weekly dialysis time and target values for Kt/V were found to be the significant independent predictors of time to death for younger patients, gender, dialysis vintage and iPTH target values were proven as significant predictors for elderly patients.

This study should be viewed in light of its shortcomings. First, information on comorbid conditions was not available and adjusting for these conditions in the Cox models was not possible. Vascular access, residual renal function QoL could put more light on quality of treatment in two age groups. Differences in local medical practice prevent adequate comparison between patients from different regions (target Hb value). Age of the patients was different between our data and those of other authors which hampers the mutual comparison.

Conclusion

Despite less favorable dialysis proscription, older patients had similar Kt/V and less frequent deviations from the

target values proposed by KDOQI for serum phosphorus and iPTH but more frequent deviation for Hb value as compared with younger patients. Risk factors for mortality differ between older and younger patients; out of five KDOQI targets, only Kt/V proved to be a significant risk factor for mortality for younger and iPTH for older patients. These findings have to be confirmed in the future to a larger number of patients.

Acknowledgments The authors thank all the colleagues from Serbian hemodialysis centers contributing on the study (in alphabetical order): Branislav Andrić (Kruševac), Jasmina Bogdanović (Valjevo), Ivana Budošan (Novi Sad), Anica Cvetičanin (Sremska Mitrovica), Kosta Djordjev (Vršac), Verica Djordjević (Smederevska Palanka), Branimir Haviža Lilić (Pirot), Nasta Jovanović (Žagubica), Rosa Jelačić (Zrenjanin), Svetislav Kostić (Niš), Ivko Marić(Lazarevac), Srboljub Milenković (Kosovska Mitrovica), Olivera Milićević (Kikinda), Igor Mitić (Novi Sad), Vesna Mićunović (Vrbas), Milena Mišković (Obrenovac), Dragana Pilipović (Bačka Palanka), Steva Plješa (Zemun), Miroslava Radaković (Barajevo), Marina Stojanović Stanojević (Mladenovac), Biserka Tirmenštajn Janković (Zaječar), Goran Vojinović (Pančevo), Kornelija Šefer (Subotica).

Compliance with ethical standards

Conflict of interest None.

References

- Collins AJ, Kasiske B, Herzog C et al (2007) Excerpts from the United States renal data system 2006 annual data report. Am J Kidney Dis 49(1 Suppl 1):A6–A7
- Kurella M, Covinsky KE, Collins AJ et al (2007) Octogenarians and nonagenarians starting dialysis in the United States. Ann Intern Med 146:177–183
- Murtagh FE, Marsh JE, Donohoe P et al (2007) Dialysis or not? A comparative survival study of patients over 75 years with chronic kidney disease stage 5. Nephrol Dial Transplant 22:1955–1962
- Carson RC, Juszczak M, Davenport A et al (2009) Is maximum conservative management an equivalent treatment option to dialysis for elderly patients with significant comorbid disease? Clin J Am Soc Nephrol 4:1611–1619
- Chang TI, Paik J, Greene T et al (2010) Updated comorbidity assessments and outcomes in prevalent hemodialysis patients. Hemodial Int 14:478–485
- Miskulin DC, Martin AA, Brown R et al (2004) Predicting 1 year mortality in an outpatient haemodialysis population: a comparison of comorbidity instruments. Nephrol Dial Transplant 19:413–420
- Lopez Revuelta K, Garcia Lopez FJ, de Alvaro Moreno F et al (2004) Perceived mental health at the start of dialysis as a predictor of morbidity and mortality in patients with end-stage renal disease (CALVIDIA Study). Nephrol Dial Transplant 19:2347–2353
- Jhamb M, Argyropoulos C, Steel JL et al (2009) Correlates and outcomes of fatigue among incident dialysis patients. Clin J Am Soc Nephrol 4:1779–1786
- Thong MS, Kaptein AA, Benyamini Y et al (2008) Association between a self-rated health question and mortality in young and old dialysis patients: a cohort study. Am J Kidney Dis 52:111–117



- Issad B, Benevent D, Allonache M, Durand PY, Aguilera D, Milongo R et al (1996) 213 Elderly uremic patients over 75 years of age treated with long-term peritoneal dialysis: a French multicenter study. Perit Dial Int 16(Suppl I):S414–S418
- Joly D, Anglicheau D, Alberti C, Nguyen AT, Touam M, Grunfeld JP, Jungers P (2003) Octogenarians reaching end-stage renal disease: cohort study of decision-making and clinical outcomes. J Am Soc Nephrol 14:1012–1021
- Port FK, Pisoni RL, Bommer J, Locatelli F, Jadoul M, Eknoyan G et al (2006) Improving outcomes for dialysis patients in the international Dialysis Outcomes and Practice Patterns Study. Clin J Am Soc Nephrol 1(2):246–255
- Moret KE, Grootendorst DC, Dekker FW, Boeschoten EW, Krediet RT, Houterman S, NECOSAD Study Group et al (2012) Agreement between different parameters of dialysis dose in achieving treatment targets: results from the NECOSAD study. Nephrol Dial Transplant 27(3):1145–1152
- Lebner AC, Beard KM, Soroka SD, Cournoyer SH, Da Roza GA, Geary DF et al (2011) Interprovincial differences in the achievement of K/DOQI targets of mineral metabolism in Canada. Nephrol Dial Transplant 26(1):156–163
- 15. Piera L, Cruz JM, Braga-Gresham JL, Eichleay MA, Pisoni RL, Port FK (2007) Estimación, según el estudio DOPPS, de los años de vida de pacientes atribuibles a las prácticas de hemodiálisis modificables en España. Nefrologia 27(4):496–504
- Djukanović L, Aksić-Miličević B, Antić M, Baković J, Varga Ž, Gojaković B et al (2012) Epidemiology of end-stage renal disease and hemodialysis treatment in Serbia at the turn of the millennium. Hemodial Int 16(4):517–525
- NKF-KDOQI Guidelines. http://www.kidney.org/professionals/ KDOQI/guideline_upHD_PD_VA/index.htm Accessed 16 Nov 2014
- Daugirdas JT (1993) Second generation logarithmic estimates of single-pool variable volume Kt/V: an analysis of error. J Am Soc Nephrol 4:1205–1213
- Djukanovic N, Djuric Z, Knezevic V, Lazarevic T, Ljubenovic S, Markovic R, Rabrenovic V, Marinkovic J, Dimkovic N (2014) Hemodialysis practice in Serbia and guidelines implementation. 51th ERA-EDTA Congress, May 31–June 3, Amsterdam, MP389
- Dimkovic N, Marinkovic J, Djuric Z, Knezevic V, Lazarevic T, Ljubenovic S, Markovic R, Rabrenovic V, Djukanovic L (2014) Predictors of mortality for patients on regular hemodialysis in Serbia. 51th ERA-EDTA Congress, May 31–June 3, Amsterdam, MP514
- Adas H, Al-Ramahi R, Jaradat N, Badran R (2014) Assessment of adequacy of hemodialysis dose at a Palestinian hospital. Saudi J Kidney Dis Transplant 25(2):38–42
- Suleymanlar G, Utas C, Ecder T, Ates K, Bieber B, Robinson BM et al (2014) The Dialysis Outcomes and Practice Patterns Study (DOPPS) in Turkey: study design and initial comparisons with Turkish registry data. Nephrol Dial Transplant 29(suppl 3):iii516–iii527 MP561
- Canaud B, Tentori F, Akiba T, Karaboyas A, Gillespie B, Akizawa T et al (2011) Clinical practices and outcome in elderly hemodialysis patients: results from the dialysis outcomes and practice patterns study (DOPPS). Clin J Am Soc Nephrol 6(7):1651–1662
- Chandna SM, Da Silva-Gane M, Marshall C, Warwicker P, Greenwood RN, Farrington K (2011) Survival of elderly patients with stage 5 CKD: comparison of conservative management and renal replacement therapy. Nephrol Dial Transplant 26(5):1608– 1614. doi:10.1093/ndt/gfq630
- Al Saran K, Sabry A, Hassan AH, Al Halawany Z (2011) Evaluation of quality of care in a large Saudi Hemodialysis Center

- (Prince Salman Center for Kidney Diseases, Riyadh, KSA). Ren Fail 33(6):555–561
- Yavuz A, Ersoy F, Passadakis PS, Tam P, Evaggelos DM, Katopodis KP (2008) Phosphorus control in peritoneal dialysis patients 73:S152–S158
- Dialysis Outcomes and Practice Patterns Study. 2009 DOPPS annual report. http://www.dopps.org/annualreport/index.htm. Accessed 13 June 2014
- Block G, Port FK (2003) Calcium phosphate metabolism and cardiovascular disease in patients with chronic kidney disease. Semin Dial 16:140–147
- Blumberg J (1997) Nutritional needs of seniors. J Am Coll Nutr 16:517–523
- Ibrahim S (2010) Quality of care assessment and adherence to the international guidelines considering dialysis, water treatment, and protection against transmission of infections in university hospital-based dialysis units in Cairo, Egypt. Hemodial Int 14(1):61–67. doi:10.1111/j.1542-4758.2009.00398.x
- Lamb EJ, Hodsman A, van Schalkwyk D, Ansell D, Warwick G (2007) Serum calcium, phosphate, parathyroid hormone, albumin, aluminum and cholesterol achievement on replacement therapy (chapter 9). Nephrol Dial Transplant 22(Suppl 7):vii105-vii118
- Dimkovic NB, Bargman J, Vas S, Oreopoulos DG (2002) Normal or low initial PTH levels are not a predictor of morbidity/mortality in patients undergoing chronic peritoneal dialysis. Perit Dial Int 22(2):204–210
- 33. Stevens LA, Djurdjev O, Cardew S, Cameron EC, Levin A (2004) Calcium, phosphate, and parathyroid hormone levels in combination and as a function of dialysis duration predict mortality: evidence for the complexity of the association between mineral metabolism and outcomes. J Am Soc Nephrol 15:770–779
- Young EW, Albert JM, Satayathum S, Goodkin DA, Pisoni RL, Akiba T et al (2005) Predictors and consequences of altered mineral metabolism: the Dialysis Outcomes and Practice Patterns Study. Kidney Int 67:1179–1187
- 35. Covic A, Kothawala P, Bernal M, Robbins S, Chalian A, Gold-smith D (2009) Systematic review of the evidence underlying the association between mineral metabolism disturbances and risk of all-cause mortality, cardiovascular mortality and cardiovascular events in chronic kidney disease. Nephrol Dial Transplant 24:1506–1523
- 36. Palmer SC, Hayen A, Macaskill P, Pellegrini F, Craig JC, Elder GJ et al (2011) Serum levels of phosphorus, parathyroid hormone, and calcium and risks of death and cardiovascular disease in individuals with chronic kidney disease: a systematic review and meta-analysis. JAMA 305:1119–1127
- 37. Natoli JL, Boer R, Nathanson BH, Miller RM, Chiroli S, Goodman WG et al (2013) Is there an association between elevated or low serum levels of phosphorus, parathyroid hormone, and calcium and mortality in patients with end stage renal disease?. A meta-analysis. BMC Nephrol 14:88. doi:10.1186/1471-2369-14-88
- Fukagawa M, Kido R, Komaba H, Onishi Y, Yamaguchi T, Hasegawa T et al (2014) Abnormal mineral metabolism and mortality in hemodialysis patients with secondary hyperparathyroidism: evidence from marginal structural models used to adjust for time-dependent confounding. Am J Kidney Dis 63(6):979–987
- Rath T, Mactier RA, Weinreich T, Scherhag AW, on behalf of the GAIN investigators (2009) Effectiveness and safety of recombinant human erythropoietin beta in maintaining common hemoglobin targets in routine clinical practice in Europe: the GAIN study. Curr Med Res Opin 25:961–970



- 40. Van der Weerd NC, Grooteman MP, Blankestijn PJ, Mazairac AH, van den Dorpel MA, den Hoedt CH CH, CONTRAST Investigators et al (2012) Poor compliance with guidelines on anemia treatment in a cohort of chronic hemodialysis patients. Blood Purif 34(1):19–27
- Wiecek A, Covic A, Locatelli F, MacDougall IC, ORAMA Study Group (2008) Renal anemia: comparing current Eastern and Western European management practice (ORAMA). Ren Fail 30(3):267–276
- McFarlane PA, Pisoni RL, Eichleay MA, Wald R, Port FK, Mendelssohn D (2010) International trends in erythropoietin use and hemoglobin levels in hemodialysis patients. Kidney Int 78(2):215–223
- 43. Locatelli F, Pisoni RL, Combe C, Bommer J, Andreucci VE, Piera L et al (2004) Anemia in haemodialysis patients of five European countries: association with morbidity and mortality in the Dialysis Outcomes and Practice Patterns Study (DOPPS). Nephrol Dial Transplant 19:121–132
- 44. Hanafusa N, Nomura T, Hasegawa T, Nangaku M (2014) Age and anemia management: relationship of hemoglobin levels with mortality might differ between elderly and nonelderly hemodialysis patients. Nephrol Dial Transplant 29(12):2316–2326. doi:10.1093/ndt/gfu272

