International Journal of Gerontology 14 (2020) 28–32
https://doi.org/10.6890/IJGE.202002_14(1).0006

International Journal of Gerontology

journal homepage: http://www.sgecm.org.tw/ijge/

Original Article

Impact of Different Incident Dialysis Modalities on the Cardiac Structure and Function of Elderly Uremic Patients

Dong-hua Jin [a,b], Yu-xian Xie [b], Hong Qiu [b], Miao Jia [b], Li-hua Lin [b], Sheng Feng [c], Zhou-bing Zhan [c], Guo-yuan Lu [a *]

[a] *Department of Nephrology, The First Affiliated Hospital of Soochow University, Suzhou City, Jiangsu Province, China;* [b] *Department of Nephrology, The People's Hospital of Suzhou National Hi-Tech District, Suzhou City, Jiangsu Province, China;* [c] *Department of Nephrology, The Second Affiliated Hospital of Soochow University, Suzhou City, Jiangsu Province, China.*

ARTICLE INFO

Accepted 31 July 2019

Keywords:
elderly,
hemodialysis,
hemodiafiltration,
hemoperfusion,
cardiac structure and function

SUMMARY

Background: To observe the impact of different incident dialysis modalities on the cardiac structure and function of elderly uremic patients.
Methods: After screening, 79 elderly dialysis patients were included, including 29 hemodialysis (HD) patients, 26 HD plus hemodiafiltration (HD+HDF) patients, and 24 HD plus hemoperfusion (HD+HP) patients. The β2-microglobulin (β2-MG) and intact parathyroid hormone (iPTH) levels were measured before the initial dialysis and 6 months afterward; at the same time, cardiac structure and function were documented by echocardiography.
Results: There were significant differences in the levels of plasma β2-MG and iPTH 6 months later in the HDF and HP groups (all $p < 0.05$). After 6 months of treatment, the left ventricular end-diastolic volume (LVEDV) and left ventricular end-systolic volume (LVESV) decreased in the HP group, while the ejection fraction (EF) increased significantly in both the HP and HDF groups (all $p < 0.05$). The EFs in the HP and HDF groups were significantly higher than that in the HD group, while the LVESV and LVEDV in the HP group were significantly lower than those in the HD group (all $p < 0.05$). The differences in LVEDV, E/A, and EF in the HP and HDF groups were greater than those in the HD group (all $p < 0.05$).
Conclusion: HP and HDF can clear β2-MG and iPTH, and improve the cardiac structure and functional efficiency in elderly uremic patients.

1. Introduction

End-stage renal disease affects millions of people worldwide, and the prevalence of patients requiring hemodialysis has continuously increased over recent decades.[1,2] Cardiovascular diseases are common and substantially contribute to increased morbidity and mortality among patients on hemodialysis.[3–5] A variety of studies carried out using either human subjects or laboratory animals suggest that β2-microglobulin (β2-MG) and intact parathyroid hormone (iPTH) carry out important activity in the cardiovascular system.[6–8] In addition to the increasing aging population in recent years, the emergence of elderly uremic patients has become evident in China,[2] the physiology of elderly uremic patients is different from that of the general population, with various related complications, for instance, refractory heart failure is among the most commonly complications and severely affects the elderly uremic patient's quality of life and long-term survival.[9,10] Hemodialysis (HD), especially high-flux HD, is currently the most commonly used blood purification method in the world, however, in China and other developing countries, given the low level of economic development, low-flux dialysis is the primary means of blood purification therapy, which can hardly remove middle-molecule uremic toxins given the changes in the patient's cardiac structure and function.[10,11] By contrast, hemodiafiltration (HDF) can remove middle molecular substances via the principles of diffusion and convection,[11,12] thus resulting in hemoperfusion (HP), which is achieved via the principle of absorption.[12,13] To compensate for the deficiencies associated with HD, many Chinese hospitals have adopted a combined HD with HDF (HD+HDF) or HD with HP (HD+HP) treatment regimen.

The purpose of this study was to compare the capabilities of HD, HD+HDF, and HD+HP in terms of their ability to clear the middle molecule toxins, and subsequently alter the cardiac structure and function of elderly uremic patients.

2. Materials and methods

2.1. Patients

In China, older adults are those who greater than 60 years of age, according to the Law of the People's Republic of China on the protection of the rights and interests of the elderly (2018 amendment).[14] After screening, 79 older adult patients from the Dialysis Center at the Second Affiliated Hospital of Soochow University were included in September 2017, including 29 cases in the HD group, 26 cases in the HDF group, and 24 cases in the HP group. In addition, all included patients had gone through conventional HD (thrice weekly)

* Corresponding author. 188 Shizi Street, District of Gusu, City of Suzhou, Jiangshu Province, China.
E-mail address: dhjin18@hotmail.com (G.-y. Lu)

for 6–60 months, none had severe heart and liver diseases, severe chronic diseases, or serious complicating infections. The most common primary diseases were chronic glomerulonephritis, diabetic nephropathy, and hypertensive nephropathy (Table 1).

2.2. Methods

2.2.1. Basic treatment

The daily sodium intake of all patients was controlled at 2.0–3.0 g and was adjusted according to the serum sodium level. The phosphorus intake was < 600–800 mg·d^{-1}. The protein intake exceeded 1.2 g·kg^{-1}·d^{-1}. The daily caloric intake was 35–40 kcal/kg. Patients received intravenous erythropoietin and oral iron therapy to maintain hemoglobin levels at 110–130 g/L. Patients with serum iPTH levels > 300 ng/L were all given oral calcitriol capsules at night at a daily dose of 0.25 μg since the start of dialysis. No patients were treated with intravenously administered vitamin D3. The patients' medication information was collected and analyzed.

2.2.2. Dialysis treatment

In the HD group, conventional HD was performed thrice weekly. All patients used a MEDICA SMARTFLUX LFP140 hollow fiber dialyzer (MEDICA International, Inc., Abu Dhabi, United Arab Emirates) for dialysis; the membrane area was 1.3 m^2 and the ultrafiltration coefficient was 10 mL·h^{-1}·mm Hg^{-1}. The calcium concentration in the dialysate was 1.5 mmol/L, the dialysate flow was 500 mL/minute, the dialysis blood flow was 230–250 mL/minute. For the HDF group, one HDF was performed every week (TS-1.6U hemofilter; Toray Medical Co., Shizuoka, Japan), based on twice-weekly conventional HD. The blood-filtration replacement volume after each session was diluted to 40–50 L. Each treatment session was 4 hours. For the HP group, the patients received HD alone twice a week, as well as HD+HP once a week. Those in the HP group were treated with a neutral macroporous resin apparatus (HA-130; ZhuhaiLiZhu Group, Biological Material Co., Ltd., Zhuhai, Guangdong, China). The apparatus was compounded in series with the dialyzer (Figure 1). Two steps were involved during the HD+HP treatment. The first step was HD+HP treatment for 2 hours; then, when the HP apparatus became saturated, it was removed (during this process, the blood flow rate was between 180–200 mL/minute). For the next 2 hours, the blood went through the dialyzer alone (this time, the blood flow rate returned to 230–250 mL/minute).

2.2.3. Measurements of the β2-MG and iPTH levels

Changes in the levels of serum β2-MG and iPTH were measured according to the radioimmunoassay method before the initial dialysis, as well as 6 months later. The kits used to detect serum β2-MG and iPTH levels were obtained from the American Biosource Company (San Diego, CA, USA). During these periods, the Kt/V was also calculated in each group.

Table 1
Etiology of the study population.

Etiology of ESRD	HD Group (n = 29)	HDF Group (n = 26)	HP Group (n = 24)
Chronic glomerulonephritis	16	12	13
Diabetic nephropathy	5	4	5
Hypertensive nephropathy	4	4	3
Adult polycystic kidney disease	1	0	2
Obstructive nephropathy	0	2	0
Gouty nephropathy	1	1	0
Unknown	2	3	1

2.2.4. Echocardiography

All patients underwent detailed echocardiographic analysis and the corresponding images were reviewed by a consultant cardiologist. Transthoracic echocardiography was performed using a Vevo 660 system (VisualSonics, Toronto, ON, Canada) equipped with a 30 MHz transducer, according to the operation instructions. The left ventricular ejection fraction (EF), end-systolic volume (LVESV), end-diastolic volume (LVEDV), and wall thickness (IVST) were assessed before the initial dialysis and 6 months later. The diastolic function parameter, the ratio of peak early (E) and late (A) mitral inflow velocities (E/A) was measured accordingly. Three cycles were measured for each assessment and the average values were obtained.

2.3. Statistical analysis

Statistical analysis was performed with SSPS version 17.0 software (IBM Corporation, Armonk, NY, USA). The measurement data were presented as means ± standard deviations ($\bar{x} \pm s$) and were analyzed with analysis of variance (ANOVA). Comparisons between two groups were performed with *t*-tests. Comparative analyses of multiple groups were performed with the single-factor ANOVA. Comparisons of factors before and after dialysis were performed with the paired *t*-test, and the count data were examined with the χ^2 test. If the data were not normally distributed, the Satterthwaite approximate *t*-test was used. The significance level was as follows: two-tailed alpha = 0.05. The study protocol was approved by the ethics committee at our institution.

3. Results

3.1. Comparison of the clinical characteristics and Kt/V in each group

Before the initial dialysis, a comparison of the clinical parameters, including the patients' age, creatinine (Cr), albumin (Alb), and other variables revealed no significant differences (all $p > 0.05$). The Kt/V reached 1.4 in all three groups before the initial dialysis and 6 months later; each group achieved adequate dialysis. A comparison of the mean arterial blood pressure (MAP) and fasting glucose levels revealed no differences either before the initial dialysis or 6 months later (all $p > 0.05$). There were also no differences in the number of patients who were taking the primary specialized drugs, or in the dosage of calcitriol being taken (all $p > 0.05$; Table 2).

3.2. Serum β2-MG and iPTH level changes

Before the initial dialysis, the β2-MG and iPTH levels in all three groups were not significantly different (all $p > 0.05$). After 6 months of dialysis, the β2-MG level in the HD group changed from 17.87 ± 4.67 mg/L to 19.23 ± 5.09 mg/L ($t = -0.106$; $p = 0.298$); the iPTH level changed from 465.44 ± 214.45 ng/L to 472.34 ± 256.29 ng/L ($t = -0.111$; $p = 0.912$). In the HDF group, the β2-MG level decreased from 16.91 ± 5.32 mg/L to 13.54 ± 3.85 mg/L ($t = 2.612$; $p = 0.015$);

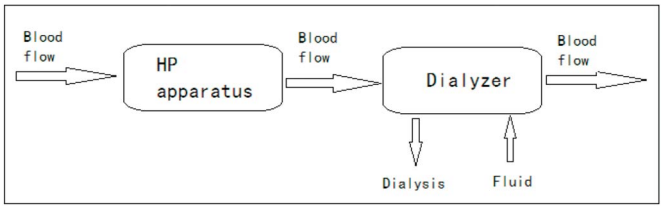

Figure 1. Flow chart detail for HD+HP.

Table 2
Clinical characteristics and medications of the three groups.

Clinical parameters	HD Group (n = 29)	HDF Group (n = 26)	HP Group (n = 24)	*p*-value
Clinical characteristics				
Age (years)	68.25 ± 11.38	66.96 ± 10.42	67.52 ± 8.85	0.895
Male (%)	44.83% (13/29)	42.31% (11/26)	50.00% (12/24)	0.857
Dialysis vintage (months)	48.27 ± 16.32	49.39 ± 13.25	46.87 ± 15.27	0.840
Hb (g/L)	107.55 ± 8.31	110.22 ± 17.37	104.91 ± 15.28	0.410
Alb (g/dL)	34.88 ± 8.04	37.44 ± 9.28	36.07 ± 6.98	0.514
MAP^{+} (mmHg)	105.35 ± 9.77	108.19 ± 8.04	102.36 ± 9.55	0.445
MAP^{++} (mmHg)	107.28 ± 8.65	102.74 ± 7.24	105.43 ± 7.58	0.109
BMI (kg/m^2)	22.87 ± 5.34	23.78 ± 6.54	21.77 ± 6.73	0.520
Scr (μmol/L)	887.23 ± 178.96	957.32 ± 237.87	985.66 ± 214.58	0.216
P^{3+} (mg/dL)	6.18 ± 1.61	5.67 ± 1.87	6.02 ± 1.91	0.566
DM (%)	17.24% (5/29)	23.08% (6/26)	20.83% (5/24)	0.862
EF (%)	48.27 ± 8.34	50.69 ± 11.12	47.74 ± 10.27	0.526
SI (μmol/L)	11.94 ± 3.67	12.67 ± 4.69	12.83 ± 5.23	0.742
HR (time/min)	88.34 ± 18.21	79.77 ± 20.19	83.65 ± 19.57	0.262
nPCR (g/kg/d)	0.92 ± 0.38	0.87 ± 0.43	0.85 ± 0.25	0.796
CRP (mg/L)*	4.9 (3.2, 9.1)	4.7 (3.4, 7.3)	5.4 (3.7, 9.5)	0.578
Ca^{2+} (mg/dL)	8.34 ± 1.13	9.01 ± 1.27	8.77 ± 0.94	0.137
$spKt/V^{+}$	1.56 ± 0.55	1.49 ± 0.36	1.47 ± 0.29	0.714
$spKt/V^{++}$	1.52 ± 0.48	1.48 ± 0.40	1.46 ± 0.33	0.863
Glu^{+}(mmol/L)	5.73 ± 0.87	5.49 ± 1.23	6.01 ± 1.13	0.241
Glu^{++}(mmol/L)	5.29 ± 0.86	5.85 ± 1.17	5.48 ± 1.05	0.132
Medications				
ACEI or ARB	41.38% (12/29)	38.46% (10/26)	33.33% (8/24)	0.833
β-Blocker	24.14% (7/29)	19.23% (5/26)	25.00% (6/24)	0.868
CCB	51.17% (15/29)	50.00% (13/26)	54.42% (13/24)	0.957
Statins	17.24% (5/29)	26.92% (7/26)	16.67% (4/24)	0.585
$CaCO_3$	55.17% (16/29)	65.38% (17/26)	62.50% (15/24)	0.725
Sevelamer	20.69% (6/29)	15.38% (4/26)	20.83% (5/24)	0.849
Diuretics	37.93% (11/29)	46.15% (12/26)	33.33% (8/24)	0.640
Aspirin	31.03% (9/29)	23.08% (6/26)	29.17% (7/24)	0.794
VitD3 use	44.83% (13/29)	42.31% (11/26)	54.17% (13/24)	0.677

Hb = hemoglobin; Alb = serum albumin; MAP = mean arterial pressure; BMI = weight/height^2; Scr = serum creatinine; P^{3+} = serum phosphorus; DM = diabetes mellitus; EF = ejection fraction; SI = serum iron; HR = heart rate; nPCR = normalized protein catabolic rate; CRP = C-reactive protein; Ca^{2+} = serum calcium; spKt/V = -Ln(R – 0.008 × T) + (4 – 3.5 × R) × UF/BW; * Expressed as the median (interquartile range), $^{+}$ Expressed as before the initial dialysis, $^{++}$ Expressed as 6 months later; Glu = fasting glucose; ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor antagonists; CCB = calcium channel blockers; $CaCO_3$ = calcium carbonate; VitD3 = calcitriol.

the iPTH level decreased from 434.97 ± 196.53 mg/L to 302.38 ± 177.23 mg/L (t = 2.555; p = 0.017). In the HP group, the β2-MG level decreased from 18.06 ± 4.53 mg/L to 12.29 ± 3.64 mg/L (t = 4.864; p = 0.000); the iPTH level decreased from 445.71 ± 223.17 mg/L to 289.65 ± 161.35 mg/L (t = 2.776; p = 0.011). Further, after 6 months of dialysis, the β2-MG and iPTH levels in the HDF and HP groups were both significantly lower than those in the HD group (both $p < 0.05$; Table 3). The β2-MG and iPTH levels in the HP group and HDF group were both not significantly different (both $p > 0.05$) 6 months following dialysis, but the differences in the β2-MG and iPTH levels before and after treatment in the HP group were both significantly greater than that in the HDF group (both $p < 0.05$; Table 4).

3.3 Comparison of cardiac structure and function indexes

Before the initial dialysis, the EF, LVESV, LVEDV, IVST, and E/A of the three groups were not significantly different (all $p > 0.05$). When compared with the levels before the initial dialysis, the EF, LVESV, and LVEDV in the HD group all increased, while the IVST and E/A were on the contrary, but the changes were all not significant (all $p > 0.05$). After 6 months of dialysis, the LVEDV and LVESV values decreased in the HP group, while the EF value increased in HP and HDF groups (all $p < 0.05$); the E/A ratios in the HP and HDF groups were higher than before, but the changes were not significant (both $p > 0.05$); the EF values in the HP and HDF groups were significantly higher than those in the HD group, while the LVESV and LVEDV values

Table 4
Comparison of the difference in the β2-MG or iPTH levels ($\bar{x} \pm s$).

	HDF	HP	*p*
β2-MG	3.98 ± 1.25	5.64 ± 1.65	0.001
iPTH	130.92 ± 52.17	158.23 ± 38.28	0.047

Table 3
Comparison of the serum β2-MG and iPTH levels ($\bar{x} \pm s$).

Group	n	β2-MG (mg/L)		iPTH (ng/L)	
		Before the initial dialysis	After 6 months of dialysis	Before the initial dialysis	After 6 months of dialysis
HD	29	17.87 ± 4.67	19.23 ± 5.09	465.44 ± 214.45	472.34 ± 256.29
HDF	26	16.91 ± 5.32	13.54 ± 3.85*	434.97 ± 196.53	302.38 ± 177.23*
HP	24	18.06 ± 4.53	12.29 ± 3.64**	445.71 ± 223.17	289.65 ± 161.35*

Compared with the same group before the initial dialysis: * $p < 0.05$, ** $p < 0.01$; 6 months after the initial dialysis, as compared with the HD group, * $p < 0.01$, ** $p < 0.01$.

in the HP group were lower than those in the HD group (all $p < 0.05$; Table 5). The differences before and after treatment in the LVEDV, E/A, and EF values in the HP and HDF groups were all greater than those in the HD group (all $p < 0.05$). The differences in the LVEDV and EF values in the HP group were greater than those in the HDF group (both $p < 0.05$). There were no significant differences in the remaining indexes (all $p > 0.05$; Table 6).

4. Discussion

The accumulation of middle-molecule toxins such as β2-MG and iPTH has been shown to cluster with a variety of cardiovascular and metabolic disorders, including hypertension, congestive heart failure, insulin resistance and peripheral vascular disease.[10,15,16] Although the association between heart function and iPTH or β2-MG levels has been recognized for many years,[6,8] the precise pathophysiologic mechanisms remain unclear. Green et al.[17] showed that continuous elevation of serum iPTH levels in humans is associated with cardiovascular disease risk. There are potential mechanisms that support a role for iPTH in the underlying pathology that negatively affects cardiac structure and function. Specifically, serum iPTH may serve as a mediator of calcium overload in cardiomyocytes and mitochondria. Increased intracellular calcium may induce electrical and mechanical abnormalities in cardiac tissues, which might affect the cardiac structure and function overall.[18] Other possible effects of iPTH may include its direct effects on cardiomyocytes, which can induce cardiac hypertrophy.[19] It has been shown that the β2-MG content in cardiac tissues increases with the duration of dialysis, and β2-MG is a major component of dialysis-associated amyloidosis.[20,21] Cardiac amyloidosis is an underlying cause of heart failure.[22] Furthermore, Xie J et al.[23] showed that β2-MG can suppress the activation of the Raf/MEK/ERK signal transduction cascade, which is a vital mediator of cardiac cellular fate, including cell growth, proliferation, differentiation, and survival.

HD has been in development for nearly 70 years with a rich background of accumulated experience. But in China and other developing countries, low-flux dialysis is still the main means, and it can hardly remove the middle molecule uremic toxins.[11] HDF can remove middle-molecular and macromolecular substances via the principles of diffusion and convection,[11,12] and thus HP operates via the principle of absorption.[12,13] Our previous clinical study observed that pruritus in patients was relieved after the application of HDF or HP.[10,12] Currently, many hospitals in China adopt a combination treatment of HD+HDF or HD+HP to compensate for the deficiency of HD. As iPTH is a short-living peptide secreted from the parathyroid, calcitriol therapy can suppress iPTH levels. Nevertheless, it seems that dialysis treatment also directly influences iPTH levels, as iPTH levels decrease in the first year after starting dialysis.[24]

In this study, we applied three different dialysis modalities to elderly uremic patients and found that there were significant differences in the levels of plasma β2-MG and iPTH 6 months later in the HDF and HP groups (all $p < 0.05$). After 6 months of treatment, the LVEDV and LVESV decreased in the HP group, while the EF increased significantly in both the HP and HDF groups (all $p < 0.05$). The EFs in the HP and HDF groups were significantly higher than that in the HD group, while the LVESV and LVEDV in the HP group were significantly lower than those in the HD group (all $p < 0.05$). The differences in LVEDV, E/A, and EF in the HP and HDF groups were greater than those in the HD group (all $p < 0.05$). The results of this study suggest that HP and HDF can partially remove middle-molecule toxins such as serum β2-MG and iPTH in uremic patients, thus improving cardiac structure and function; conversely, HD demonstrates a worse performance in terms of middle-molecule toxin clearance, and cardiac structure and function improvements.

Although several previous studies have found an association between the reduction of β2-MG and iPTH with heart function improvement,[6,15,16] this study focused on elderly uremic patients who received different incident dialysis modalities, in accordance with the findings of our literature search, few related studies in this population have been reported to date; therefore, this study presents novel findings.

5. Conclusion

In order to improve the cardiac structure and function in elderly uremic patients, HP or HDF treatment would be a better choice in China and other developing countries, because low-flux HD will not be so effective.

6. Limitations

The underlying mechanism for the changes in cardiac structure and function in elderly uremic patients is complex. In addition to middle-molecule toxins such as β2-MG and iPTH, cardiac structure and function can also be associated with many factors, such as persistent volume overload, coexisting hypertension, inflammation, anemia, lipid status, diabetes mellitus, protein-bound uremic toxins, oxidative stress, and myriad additional elements.[5,25,26] Prior to the initial dialysis in this study, a comparison of some of these aforementioned factors was performed for all three groups. The findings

Table 5
Comparison of the cardiac structure and functional indexes ($\bar{x} \pm s$).

Index	HD (n = 29)	HDF (n = 26)	HP (n = 24)	*p*-value
EF^{+}	48.27 ± 8.34	49.12 ± 11.12*	47.74 ± 10.27*	0.883
EF^{++}	49.34 ± 10.54$^{\#}$	56.98 ± 14.38**	55.46 ± 11.22**	0.052
LVESV^{+}	39.12 ± 8.67	40.03 ± 12.23	38.44 ± 9.61*	0.859
LVESV^{++}	39.94 ± 10.07$^{\#}$	35.34 ± 11.79	32.32 ± 8.76**	0.029
LVEDV^{+}	51.26 ± 13.06	54.25 ± 12.04	55.66 ± 14.63*	0.464
LVEDV^{++}	53.87 ± 11.56$^{\#}$	48.46 ± 9.91	46.34 ± 14.44**	0.066
IVST^{+}	12.02 ± 1.53	10.94 ± 1.86	11.36 ± 1.77	0.131
IVST^{++}	11.08 ± 2.23	10.12 ± 2.03	10.49 ± 1.84	0.222
E/A^{+}	0.97 ± 0.37	0.89 ± 0.30	0.90 ± 0.32	0.625
E/A^{++}	0.89 ± 0.23	0.93 ± 0.41	0.98 ± 0.46	0.683

$^{+}$ Expressed as before the initial dialysis. $^{++}$ Expressed as 6 months later.
** Compared with * before treatment, $p < 0.05$. ** Compared with $^{\#}$ after treatment, $p < 0.05$.

Table 6
Comparison of the difference in cardiac structure and function indexes ($\bar{x} \pm s$).

Group	n	EF	LVESV	LVEDV	IVST	E/A
HD	29	1.18 ± 0.82	1.20 ± 0.75	3.01 ± 1.08	0.78 ± 0.34	0.11 ± 0.21
HDF	26	6.21 ± 2.16*	5.37 ± 1.68*	6.72 ± 2.78*	0.86 ± 0.42	0.10 ± 0.23
HP	24	7.84 ± 3.01*$^{\#}$	6.39 ± 2.34*	8.78 ± 2.45*$^{\#}$	1.12 ± 0.36**	0.12 ± 0.47

Compared with the HD group (Satterthwait approximate *t*-test): * $p < 0.05$, *$^{\#}$ $p < 0.05$; compared with the HD group (*t*-test): ** $p < 0.05$; compared with the HDF group (*t*-test): ** $p < 0.05$; *$^{\#}$ $p < 0.05$.

revealed no significant differences between groups (all $p > 0.05$). However, due to the small sample size in this study, we could not carry out univariate and multivariate analyses to examine the association in these three small sample's groups. Therefore, further in-depth studies are warranted in the future. In addition, this study had certain limitations. For example, patient inclusion was not randomized, the observation time was short, and only elderly uremic patients from a single institution were studied. All of these factors will be continuously be explored and improved in future studies.

Acknowledgments

This work was supported by Jiangsu University Clinical Medical Science and Technology Development Fund Project, Suzhou, China (Grant No. JLY20180169); The Key Project of Scientific Innovation Fund of The People's Hospital of SND, Suzhou, China (Grant No. SGY2018C05).

References

1. United States Renal Data System. *Chapter 11: International Comparisons*. In: 2017 Annual Data Report. Volume 2: End-Stage Renal Disease in the United States. Bethesda, MD: National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases; 2017. Available at: https://www.usrds.org/2017/view/v2_11.aspx. Accessed July 6, 2018.
2. Cai GY, Chen XM. Prevention, diagnosis, and treatment of chronic kidney diseases in older adults: Current status and prospective. *J Integr Nephrol Androl*. 2016;3:71–73.
3. Go AS, Chertow GM, Fan D, et al. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. *N Engl J Med*. 2004; 351:1296–1305.
4. Foley RN, Collins AJ. End-stage renal disease in the United States: An update from the United States renal data system. *J Am Soc Nephrol*. 2007; 18:2644–2648.
5. Silberberg JS, Barre PE, Prichard SS, et al. Impact of left ventricular hypertrophy on survival in end-stage renal disease. *Kidney Int*. 1989;36:286–290.
6. Kestenbaum B, Katz R, Boer I, et al. Vitamin D, parathyroid hormone, and cardiovascular events among older adults. *J Am Coll Cardiol*. 2011;58: 1433–1441.
7. Levitskaya E. Renal function markers for long-term cardiovascular prediction in individuals after myocardial revascularization. *Georgian Med News*. 2017;262:43–48.
8. Menaa C, Esser E, Sprague SM. Beta2-microglobulin stimulates osteoclast formation. *Kidney Int*. 2008;73:1275–1281.
9. Tsai MT, Liu HC, Huang TP. The impact of malnutritional status on survival in elderly hemodialysis patients. *J Chin Med Assoc.* 2016;79(6):309–313.
10. Jin DH, Shen HY, Feng S, et al. Treatment effects of different incident dialysis modalities on pruritus in elderly uremic patients. *Int J Gerontol*. 2014;8:223–227.
11. Tsuchida K, Minakuchi J. Effect of large-size dialysis membrane and hemofiltration/hemodiafiltration methods on long-term dialysis patients. *Contrib Nephrol.* 2011;168:179–187.
12. Jin DH, Shi YB, Shen HY, et al. Treatment effect of different dialysis modalities on pruritus in elderly maintenance hemodialysis patients. *Chinese Journal of Geriatrics.* 2012;12:1092–1096.
13. Yantasee W, Fryxell GE, Porter GA, et al. Novel sorbents for removal of gadolinium-based contrast agents in sorbent dialysis and hemoperfusion: Preventive approaches to nephrogenic systemic fibrosis. *Nanomedicine*. 2010;6:1–8.
14. Standing Committee of the National People's Congress. *Law of the People's Republic of China on Protection of the Rights and Interests of the Elderly* (2018 Amendment). Chapter I General Provisions, Article 2.
15. Gejyo F, Homma N, Suzuki Y, et al. Serum levels of beta 2-microglobulin as a new form of amyloid protein in patients undergoing long-term hemodialysis. *N Engl J Med*. 1986;314:585–586.
16. Anderson JL, Vanwoerkom RC, Horne BD, et al. Parathyroid hormone, vitamin D, renal dysfunction, and cardiovascular disease: Dependent or independent risk factors? *Am Heart J*. 2011;162:331–339.
17. Green JJ, Robinson DA, Wilson GE, et al. Calcitriol modulation of cardiac contractile performance via protein kinase C. *J Mol Cell Cardiol*. 2006; 41:350–359.
18. Kolaszko A, Nowalany-Kozielska E, Ceranowicz P, et al. The role of parathyroid hormone and vitamin D serum concentrations in patients with cardiovascular diseases. *Dis Markers*. 2018;2018:5287573.
19. Tastan I, Schreckenberg R, Mufti S, et al. Parathyroid hormone improves contractile performance of adult rat ventricular cardiomyocytes at low concentrations in a non-acute way. *Cardiovasc Res*. 2009;82:77–83.
20. Yamamoto S. Molecular mechanisms underlying uremic toxin-related systemic disorders in chronic kidney disease: Focused on β2-microglobulin-related amyloidosis and indoxyl sulfate-induced atherosclerosis-Oshima Award Address 2016. *Clin Exp Nephrol*. 2019;23:151–157.
21. Stoppini M, Bellotti V. Systemic amyloidosis: Lessons from β2-microglobulin. *J Biol Chem.* 2015;290:9951–9958.
22. Slart RHJA, Glaudemans AWJM, Noordzij W, et al. Time for new imaging and therapeutic approaches in cardiac amyloidosis. *Eur J Nucl Med Mol Imaging*. 2019;46:1402–1406.
23. Xie J, Wang Y, Freeman ME 3rd, et al. β2-microglobulin as a negative regulator of the immune system: High concentrations of the protein inhibit in vitro generation of functional dendritic cells. *Blood*. 2003; 101:4005–4012.
24. Malberti F, Corradi B, Imbasciati E. Effect of CAPD and hemodialysis on parathyroid function. *Adv Perit Dial*. 1996;12:239–244.
25. Curtis BM, Parfrey PS. Congestive heart failure in chronic kidney disease: Disease-specific mechanisms of systolic and diastolic heart failure and management. *Cardiol Clin*. 2005;23:275–284.
26. Kim Y, Matsushita K, Sang Y, et al. Association of high-sensitivity cardiac troponin T and natriuretic peptide with incident ESRD: The Atherosclerosis Risk In Communities (ARIC) study. *Am J Kidney Dis.* 2015;65: 550–558.