Analyzing clinical characteristics of patients with different cumulative hemodialysis durations: a cross-sectional study

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ABSTRACT

Background. The objective of this study was to examine the clinical characteristics of patients with different cumulative hemodialysis (HD) durations, so as to improve their survival rate.

Methods. In this cross-sectional study, we extracted background information and relevant clinical data from 145 patients who were undergoing maintenance HD three times a week at the Affiliated Hospital of Nantong University between January 1998 and January 2019. The study subjects were divided into four groups according to the duration of their HD: <5 years, 5–10 years, 10–15 years, and >15 years of HD. We collected the medical history and relevant clinical parameters for each subject, and measured the urea reduction ratio (URR), hemoglobin (Hb), serum calcium, phosphorus, parathyroid hormone (iPTH), and serum albumin (ALB) levels for each group.

Results. The average patient age was 52.06 ± 11.93 years old. The average patient age in the 10–15 years and >15 years groups was significantly lower than in the <5 years and 5–10 years groups ($P = 0.002$, $P < 0.001$, $P = 0.012$, and $P = 0.0025$, respectively). The most common cause of end-stage renal disease (ESRD) was chronic glomerulonephritis. We found no significant differences in URR, Hb, serum calcium, serum phosphorus, iPTH, and ALB levels.

Conclusion. A prolonged HD duration was related to a younger mean age at the start of HD treatment. The leading cause of ESRD was chronic glomerulonephritis. We predominantly found diabetic nephropathy in the group with a duration of <5 years cumulative HD. Most of the indexes related to hemodialysis almost satisfied the recommended values in these patients.

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INTRODUCTION

Despite the continuously improving health care system in China, the number of patients undergoing maintenance hemodialysis (HD) is rapidly growing and the number of kidney transplant donors remains limited (*Eckardt et al., 2013*). HD, a relatively safe treatment for end-stage renal disease (ESRD) patients, is still widely used, and advanced technology

and therapeutic strategies have improved the survival rate of HD patients (*Tattersall et al., 2007*; *Slinin et al., 2015*). Potential strategies that can reduce complications and incidence while improving prognosis and long-term survival rates in patients undergoing maintenance HD are gaining increased attention. The survival rates of patients undergoing maintenance HD depend on adequate HD performance. Inadequate HD is independently associated with increased morbidity and mortality (*Chandrashekar, Ramakrishnan & Rangarajan, 2014*). Following the establishment of the Kidney Disease Improving Global Outcomes (KDIGO) national and regional guidelines (*European Best Practice Guidelines Expert Group on Hemodialysis ERA , 2002*; *Andrassy, 2013*; *National Kidney F, 2015*; *Adequate Hemodialysis Work Group of the Chinese Medical Doctor Association, 2015*), *Port et al. (2004)* suggested that adhering to and improving certain guidelines could further prolong patient life expectancy. Specifically, adequate HD, mineral-bone metabolism, improved anemia, improved nutritional status, controlled weight gain during HD, and less frequent application of catheters for vascular access have been associated with prolonged survival (*Port et al., 2004*). Several studies have reported on the negative correlation between hemoglobin (Hb) levels and poor survival (*Collins, 2002*; *Avram et al., 2003*). Moreover, Owen, et al. (*1993*) found a 6.7-fold increase in mortality when serum albumin (ALB) levels were < 30 g/L (*Owen Jr et al., 1993*; *Dwyer et al., 2005*). However, no studies have grouped patients according to different HD durations and analyzed the clinical characteristics of each group and related HD treatment indices. This exploratory study explores the causes of ESRD and the clinical characteristics of patients undergoing maintenance HD across different cumulative durations. We hypothesized that the main cause of ESRD was chronic glomerulonephritis and that the group with a longer cumulative HD duration would adhere more to clinically relevant HD treatment target parameters.

The current study aimed to: (1) compare demographic clinical characteristics; (2) explore ESRD etiology and the incidence of concomitant diseases; and (3) investigate clinically relevant HD treatment parameters of adequacy, anemia, nutritional status, and metabolic bone disease across four groups with different HD durations (< 5 years, 5–10 years, 10–15 years, and >15 years).

MATERIALS AND METHODS

This was a cross-sectional study performed at the Affiliated Hospital of Nantong University's HD center. The study was approved by the ethics committee of the Affiliated Hospital of Nantong University, Nantong, Jiangsu, China (#2020-K009). All patients underwent maintenance HD between January 1998 and January 2019. We obtained information from standardized forms filled out by providers when the patients started HD and confirmed their accuracy using the patient's previous outpatient and inpatient medical history information. The inclusion criteria were: (1) age > 18 years; (2) regular HD treatment longer than three months, three times a week, and 4 h each session; and (3) signed informed consent. The following patients were excluded: (1) patients who had undergone kidney transplantation, and (2) patients who had undergone peritoneal dialysis.

We divided the study subjects into four groups according to their HD duration: < 5 years, 5–10 years, 10–15 years, and >15 years. Medical histories and relevant biochemical

examination parameters, including current age, gender, age at the beginning of HD, causes of ESRD, and concomitant diseases, were collected from all patients. We calculated the urea reduction ratio (URR), which is an index of HD adequacy, as the difference between pre-dialysis blood urea nitrogen (BUN) and post-dialysis BUN, divided by pre-dialysis BUN (*Liang, Zhang & Palevsky, 2019*). Blood routine test, serum phosphorus, serum calcium, parathyroid hormone (iPTH), and serum ALB levels were used to evaluate the patients' anemia management, bone mineral metabolism, and nutritional status. We compared the background information and relevant indicators of each group. The recommended values were taken from the Chinese clinical guidelines for adequate HD treatment (*Adequate Hemodialysis Work Group of the Chinese Medical Doctor Association, 2015*).

We used SPSS 19.0 (IBM, Armonk, NY, USA) statistical software for data processing. Measurement data with normal distribution were shown as mean $\pm$ standard deviation (SD). The multiple-group comparison was performed using an ANOVA test, while the two groups were compared using a t-test. Measurement data with non-normal distributions were shown as the median (M) (25th–75th interquartile range). We used a Pearson chi test to compare the categorical data between groups. A P-value less than 0.05 was considered statistically significant.

RESULTS

Background information of maintenance HD patients

A total of 145 maintenance HD patients were enrolled in this study: 87 males and 58 females, with a 1.5:1 male to female ratio. The ages ranged from 26 to 86 years, with an average age of 52.06 $\pm$ 11.93 years. Patients were divided into four groups according to the duration of their HD treatment. There were 43 cases in the < 5 years group, 52 cases in the 5–10 years group, 38 cases in the 10–15 years group, and 12 cases in the > 15 years group. The statistical results of the patient baseline data from each group are shown in Table 1. There were no significant gender differences across the four groups. The average HD duration for the four groups was 3.93 $\pm$ 0.83 years, 7.32 $\pm$ 1.41 years, 11.54 $\pm$ 1.17 years, and 18.36 $\pm$ 1.71 years, respectively (all p <0.05). The average age of patients with an HD duration > 15 years was relatively young (49.82 $\pm$ 12.26), but it was not statistically significant. When compared with patients in the < 5 years and 5–10 year group, the 10–15 years and >15-years group had significantly lower average ages at the start of HD (all p <0.05). As the HD duration increased, the average age at the beginning of HD was significantly lower, as shown in Fig. 1. The ages at which patients from each group started HD are shown in percentages in Table 2 and Fig. 2. Patients undergoing HD > 15 years were between 26 and 47 years old at the beginning of their HD treatment.

Comparing ESRD etiology and the incidence of concomitant diseases across the different groups

The main cause of ESRD across all groups was chronic glomerulonephritis. Diabetic nephropathy was the second most common cause of ESRD in the < 5 years and 5–10 years groups. The <5 year group had an 19.05% incidence of diabetic nephropathy, the >15 years

Table 1 Comparison of background information, the etiology of ESRD and incidence of concomitant diseases.

	Duration of hemodialysis (years)			
	<5 (n = 43)	5–10 (n = 52)	10–15 (n = 38)	>15 (n = 12)
Male n (%)	29(67.44)	28(53.85)	22(57.89)	8(66.67)
Duration of hemodialysis (years)	3.93 ± 0.83	7.32 ± 1.41[a]	11.54 ±1.17 [a]	18.36 ± 1.71[a]
Age	54.74 ± 14.48	53.04 ± 13.21	50.63 ± 7.75	49.82 ± 12.26
Age at initiation of hemodialysis	50.83 ± 14.43	45.72 ± 13.57	38.5 ± 12.57[b]	34.26 ± 7.16[b]
Cause of ESRD n (%)				
Diabetic nephropathy	8(18.6)	5(9.6)	1(2.6)	0[c]
Chronic glomerulonephritis	29(67.4)	41(78.8)	30(78.9)	11(91.7)
Polycystic kidney disease	3(7.1)	3(5.8)	3(7.9)	1(8.3)
Lupus nephritis	0	2(3.8)	2(5.3)	0
RPGN	1(2.3)	0	0	0
Uric acid nephropathy	1(2.3)	0	2(5.3)	0
Multiple myeloma related kidney disease	0	1(2.0)	0	0
Other	1(2.3)	0	0	0
Comorbidity n (%)				
Diabetes	10(23.3)	8(15.4)	1(2.6)	0[d]
Hypertension	36(83.7)	41(78.9)	31(81.6)	8(66.7)
Chronic heart failure	8(18.6)	7(13.5)	3(7.9)	1(8.3)
Cerebrovascular disease	0	1(1.9)	2(5.3)	0
Thyroid disorder	1(2.3)	0	1(2.6)	1(8.3)

Notes.

ESRD, end stage renal disease; RPGN, rapidly progressive glomerulonephritis.

[a] $p = 0.045$ <5 versus 5–10 $p = 0.038$ 5–10 versus 10–15 $p = 0.027$ 10–15 versus >15.

[b] $p = 0.002$ <5 versus 10–15 $p < 0.001$ <5 versus > 15 $p = 0.012$ 5–10 versus 10–15 $p = 0.0025$ 5–10 versus >15.

[c] $p = 0.027$ <5 versus >15.

[d] $p = 0.0031$ <5 versus >15.

group had an incidence of 0% ($p = 0.027$). The incidence of other etiologies, such as polycystic kidney disease, lupus nephritis, and rapidly progressive glomerulonephritis (RPGN), was not significantly different across the groups. Hypertension ranked first among the main concomitant diseases in each group, but its incidence was not statistically significant. Diabetes ranked second among all concomitant diseases in the <5 years and 5–10 years groups. The <5 year group had a 23.3% incidence of concomitant diabetes, the >15 years group had an incidence of 0/% ($p = 0.0031$). The incidence of other concomitant diseases, such as chronic heart failure, cerebrovascular disease, and thyroid dysfunction, was not significantly different across the four groups (Table 1).

Comparing relevant HD treatment parameters across different groups

The URR, Hb, serum calcium, and ALB levels across the groups were consistent with the recommended guidelines (*Adequate Hemodialysis Work Group of the Chinese Medical Doctor Association, 2015*). The <5 years group and the 10–15 years group had iPTH values that were within the recommended values, while the 5–10 years group and the >15 years group had iPTH values that were higher than the recommended values. The serum phosphorus values across the groups were also higher than the recommended values. The
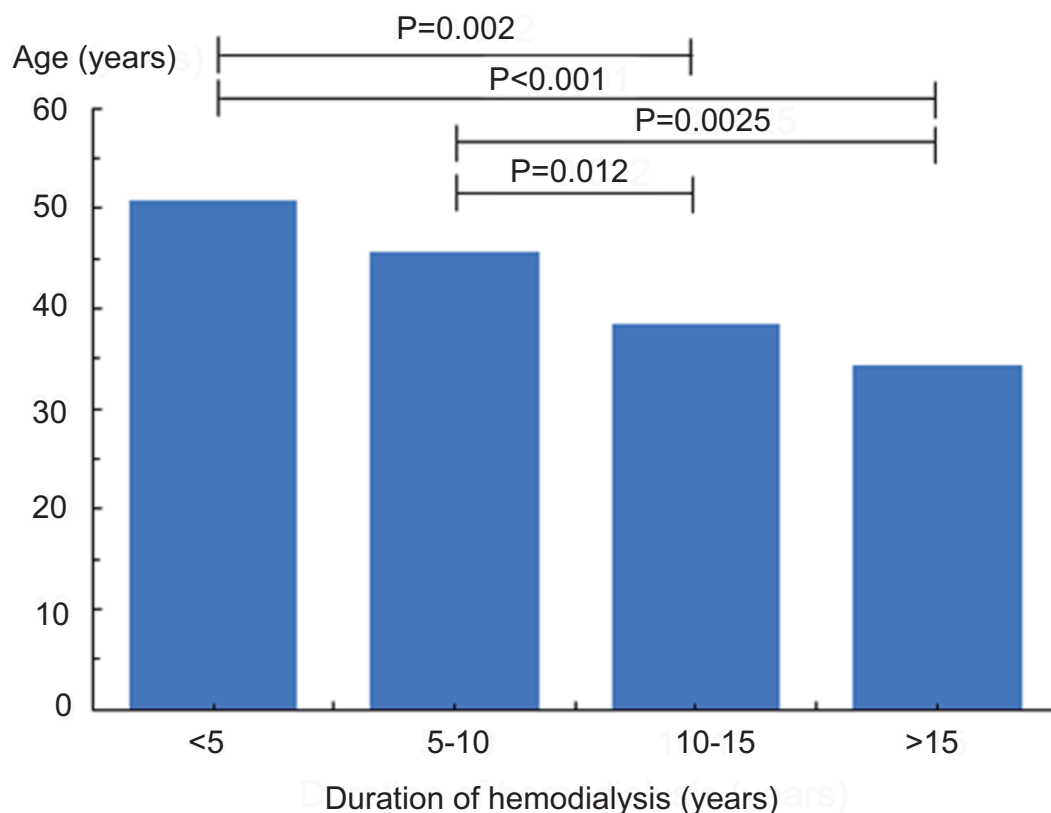
Figure 1 Comparison of the average age among patients starting hemodialysis in each group. As the duration of hemodialysis became longer, the average age at the beginning of hemodialysis became significantly smaller. $p = 0.002$ <5 versus 10–15, $p < 0.001$ <5 versus >15, $p = 0.012$ 5–10 versus 10–15, $p = 0.0025$ 5–10 versus >15.

Table 2 Comparison of the distribution of the percentages of patients with different HD durations within each age group.

Age at initiation of hemodialysis	Duration of hemodialysis (years)			
	<5 n(%)	5–10 n(%)	10–15 n(%)	>15 n(%)
9–19	0	0	4(10.53)	0
20–29	3(6.98)	6(11.54)	4(10.53)	3(25.00)
30–39	6(13.95)	12(23.08)	12(31.58)	6(50.00)
40–49	14(32.56)	14(26.92)	9(23.68)	3(25.00)
50–59	6(13.95)	12(23.08)	7(18.42)	0
60–69	10(23.26)	4(7.69)	2(5.26)	0
70–79	2(4.65)	4(7.69)	0	0
80–89	2(4.65)	0	0	0

URR, Hb, serum calcium, serum phosphorus, iPTH, and ALB levels were not significantly different across the four groups (Table 3).
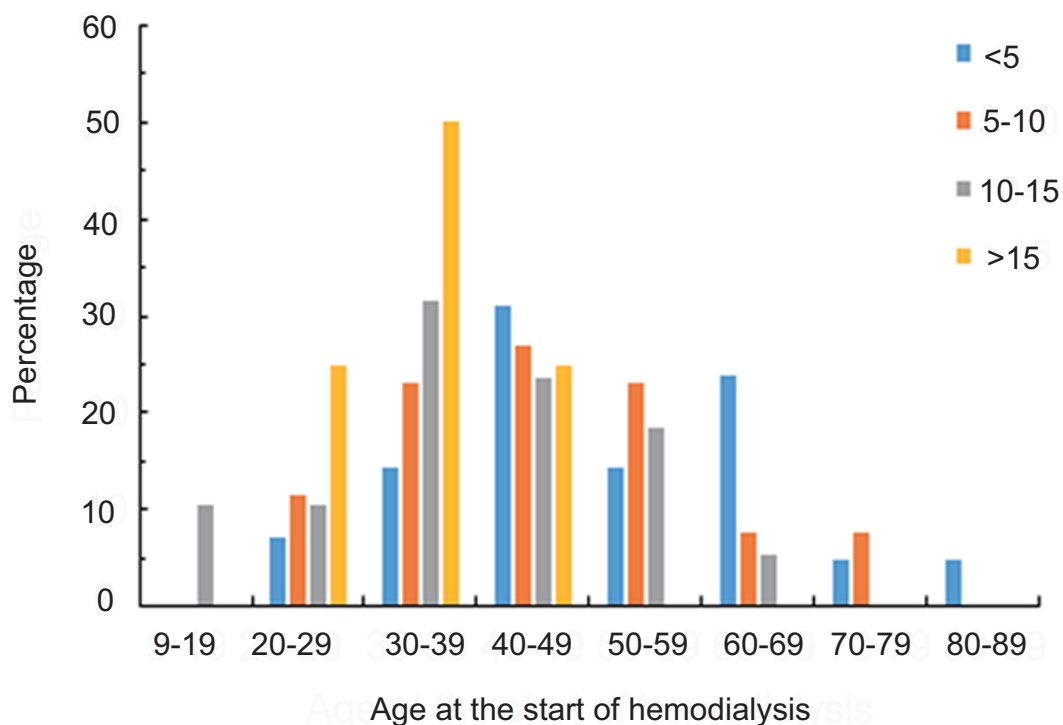
Figure 2 **The distribution of the percentages of patients with different hemodialysis durations within each age group.** Patients with hemodialysis <5 years were 25 to 82 years old at the beginning of hemodialysis. Patients with hemodialysis 5–10 years were 21 to 74 years old at the beginning of hemodialysis. Patients with hemodialysis 10–15 years were 14 to 67 years old at the beginning of hemodialysis. Patients with hemodialysis >15 years were 26 to 47 years old at the beginning of hemodialysis.

Table 3 **Comparison of hemodialysis-related parameters in patients undergoing maintenance hemodialysis for different years.**

Clinical parameters	Duration of hemodialysis (years)				*p*-value	Recommended values[a]
	<5	5–10	10–15	>15		
URR(%)	66.23 ± 6.68	68.33 ± 6.05	69.1 ± 4.81	66.4 ± 7.16	0.68	≥ 65
Hb(g/L)	102.29 ± 12.58	100.81 ± 10.32	104.42 ± 19.6	108.38 ± 10.72	0.72	≥100
Calcium (mmol/L)	2.17 ± 0.25	2.29 ± 0.42	2.32 ± 0.23	2.18 ± 0.32	0.56	2.1-2.75
Phosphorus(mmol/L)	1.81 ± 0.43	1.97 ± 0.51	1.92 ± 0.58	2.01 ± 0.52	0.22	1.13-1.78
iPTH(pg/ml)	291.29 ± 466.92	304.13 ± 463.76	299.66 ± 482.95	311.74 ± 413.7	0.43	150-300
ALB(g/L)	40.76 ± 2.61	40.53 ± 2.18	40.62 ± 1.84	39.74 ± 1.72	0.65	≥35

Notes.
[a]Recommendation values were followed by Chinese clinical guidelines for adequacy of hemodialysis.
URR, Urea reduction ratio; Hb, Hemoglobin; iPTH, intact parathyroid hormone; ALB, Albumin;1g/L = 0.1 g/dL; Calcium (1 mmol/L = 4.008 mg/dL); Phosphorus(1 mmol/L = 3.0969 mg/dL).

DISCUSSION

For over 50 years, HD has continued to improve, making it a very popular and commonly-used treatment. In the past, HD was generally connected to poor prognosis (*Zazzeroni et al., 2017*), which is why the long-term survival rate of HD did not receive much attention

from the scientific community. Few studies have reported on the factors that can increase the survival rate for HD patients. In this study, we examined the clinical characteristics of patients undergoing maintenance HD for <5-years, 5–10 years, 10–15 years, and >15 years, and we found a correlation between a significantly younger age at the beginning of HD and a relatively longer HD duration. The leading cause of ESRD was chronic glomerulonephritis. In order to improve the prognosis of patients with diabetic nephropathy, compliance with HD standards during maintenance HD treatment should be emphasized.

Our results showed that a longer cumulative HD duration was related to a younger mean age at the start of HD treatment. Patients undergoing maintenance HD for over 15 years had an average starting age of 34.26 ± 7.16 years, suggesting that patients who started HD at a younger age underwent longer maintenance HD treatment, which is consistent with previous reports (*Heaf, Nielsen & Hansen, 2012*). The age at which HD was initiated may be a prognosis factor for patients undergoing maintenance HD for over 15 years. Additionally, patients who started HD at a younger age will remain on HD for a longer duration unless they die prematurely. This may also explain why the group with a longer cumulative HD duration had more cases of chronic glomerulonephritis, as chronic glomerulonephritis tends to present in younger age groups and lead to rapid ESRD. Diabetes mellitus type 2 (DM2) tends to cause ESRD only after being present for many years in older patients. In this study, the leading cause of ESRD in HD patients was chronic glomerulonephritis. The percentage of patients with chronic glomerulonephritis across the groups was 66.67%, 79.25%, 78.95%, and 91.67%, respectively. Diabetic nephropathy was the second most common cause in the <5 years and 5–10 years groups. Notably, the incidence of diabetic nephropathy causing chronic renal failure was 0% in the >15 years group, which suggests that there were no diabetic patients in this group. This was in line with the results reported by *Otsubo et al. (2007)*, who found that the prognosis of renal failure secondary to diabetes was worse than other ESRD causes. The prognosis for patients with diabetic nephropathy needs to be examined and improved.

Receiving adequate HD treatment is a key factor in the overall management of HD patients. In this study, we observed similar URRs across all groups. All groups successfully achieved the limits recommended by the guidelines, which indicated that all subjects underwent adequate HD treatments. In order to decrease morbidity and mortality, the following factors should be properly managed in populations that are dependent on maintenance HD: anemia, bone-mineral metabolism, and nutritional status (*Port et al., 2004*). The National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (KDOQI) and other relevant Chinese guidelines all recommend that HD patients should maintain Hb levels of 100 g/L, and iron-deficient patients should use iron and erythropoietin to achieve this level (*National Kidney F, 2015*; *Adequate Hemodialysis Work Group of the Chinese Medical Doctor Association, 2015*). Some retrospective studies recommended a serum Hb level of 10 g/dL to 11 g/dL (*Mikhail et al., 2017*; *Tanaka, Komaba & Fukagawa, 2018*). Serum Alb levels are an effective and clinically useful indicator of protein-energy nutritional status in patients undergoing maintenance HD (*Sabatino et al., 2018*). We observed a strong negative correlation between HD patients' mortality and serum Alb levels (*Roach et al., 2017*), which should be maintained at 35 g/L (*National Kidney F,*

2015; *Adequate Hemodialysis Work Group of the Chinese Medical Doctor Association, 2015*). Patients with serum Alb concentrations below 35 g/L have a 1.5 times higher risk of death (*Roach et al., 2017*).

In this study, serum Alb levels were a satisfactory indicator of the patients' nutritional status, and each group met the recommended standards. In ESRD patients, changes in bone-mineral metabolism generally lead to soft tissue and blood vessel calcification (*Neves et al., 2017*). According to *Young et al.(2005)*, *Block et al. (2004)*, these changes may lead to blood vessel occlusion in the coronary arteries and peripheral and cerebral circulation, which can ultimately increase morbidity and mortality rates. Although KDIGO recommends that the target iPTH levels in HD patients should be two to nine times greater than the upper limit of the standard reference value, multiple clinical studies have shown that patients with iPTH levels between 150 and 300 pg/ml have lower mortality rates (*Floege et al., 2011*; *Naves-Diaz et al., 2011*; *Kalantar-Zadeh et al., 2010*). In this study, the patients had standard serum calcium levels. However, the iPTH levels were higher than the recommended values in the 5–10 years and >15 years groups, and the serum phosphorus levels exceeded the recommended values in each group. A previous study found a correlation between the mortality of HD patients and their serum phosphorus concentrations (*Ma, Zhao & Li, 2017*). Additionally, the mortality rate of patients with low phosphorus concentrations also increased, which may have been due to nutritional deficiencies (*Ma & Zhao, 2017*). Patients with increased serum phosphorus levels should therefore have stricter dietary guidance, properly adjusted drug regimens and HD programs, and improved monitoring.

There were some limitations in this study. First, this was a single-center cross-sectional study with a small sample size. Second, when measuring the adequacy of the HD treatment, we did not measure single pool Kt/V (spKt/V) values, which is a more accurate method. Third, we failed to investigate which dialysis techniques and membranes could most impact survival. Future studies should expand the sample size, focus on patients undergoing HD for more than 15 (or even as long as 30) years, conduct multivariate analyses with more parameters, and more comprehensively assess the patients' quality of life.

CONCLUSION

In this study, we investigated the clinical characteristics of patients with different cumulative HD durations and emphasized the importance of adherence to clinical guidelines for these patients. Chronic glomerulonephritis was the leading cause of ESRD, followed by diabetes mellitus. As HD durations increased, the percentage of renal failure caused by diabetic nephropathy decreased. There were no patients with diabetic nephropathy in the > 15 years group, suggesting that patients with diabetic nephropathy either survived for shorter periods on HD or that patients had an increased mortality rate because they started HD at a later age. It is essential to improve the prognosis of diabetic nephropathy patients who develop ESRD. Most of the patients satisfied the recommended values for the HD treatment indices, with the exception of phosphorus and iPTH levels. This suggests that greater attention should be paid to managing patient metabolic bone disease parameters, regardless of their cumulative HD duration.

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Competing Interests

The authors declare there are no competing interests.

Author Contributions

- Xu Chen conceived and designed the experiments, performed the experiments, analyzed the data, prepared figures and/or tables, and approved the final draft.
- Li Yuan performed the experiments, prepared figures and/or tables, and approved the final draft.
- Yuan Zhang performed the experiments, analyzed the data, prepared figures and/or tables, and approved the final draft.
- Houyong Dai and Yaping Fan analyzed the data, authored or reviewed drafts of the paper, and approved the final draft.
- Xiaolan Chen conceived and designed the experiments, authored or reviewed drafts of the paper, and approved the final draft.

Human Ethics

The following information was supplied relating to ethical approvals (i.e., approving body and any reference numbers):

The study was approved by the ethics committee of the Affiliated Hospital of Nantong University, Nantong, Jiangsu, China (#2020-K009).

Data Availability

Raw measurements are available as a Supplementary File.

Supplemental Information

Supplemental information for this article can be found online at http://dx.doi.org/10.7717/peerj.10852#supplemental-information.

REFERENCES

Adequate Hemodialysis Work Group of the Chinese Medical Doctor Association. 2015. Chinese clinical guidelines for adequacy of hemodialysis. *Zhonghua Yi Xue Za Zhi* **95**:2748–2753.

Andrassy KM. 2013. Comments on 'KDIGO 2012 Clinical practice guideline for the evaluation and management of chronic kidney disease'. *Kidney International Supplements* **84**:622–623.

Avram MM, Blaustein D, Fein PA, Goel N, Chattopadhyay J, Mittman N. 2003. Hemoglobin predicts long-term survival in dialysis patients: a 15-year single-center longitudinal study and a correlation trend between prealbumin and hemoglobin. *Kidney International Supplements* **64**:S6–S11.

Block GA, Klassen PS, Lazarus JM, Ofsthun N, Lowrie EG, Chertow GM. 2004. Mineral metabolism mortality and morbidity in maintenance hemodialysis. *Journal of the American Society of Nephrology* **15**:2208–2218 DOI 10.1097/01.ASN.0000133041.27682.A2.

Chandrashekar A, Ramakrishnan S, Rangarajan D. 2014. Survival analysis of patients on maintenance hemodialysis. *Indian Journal of Nephrology* **24**:206–213 DOI 10.4103/0971-4065.132985.

Collins AJ. 2002. Influence of target hemoglobin in dialysis patients on morbidity and mortality. *Kidney International Supplements* **61**:44–48.

Dwyer JT, Larive B, Leung J, Rocco MV, Greene T, Burrowes J, Chertow GM, Cockram DB, Chumlea WC, Daugirdas J, Frydrych A, Kusek JW, Group HS. 2005. Are nutritional status indicators associated with mortality in the Hemodialysis (HEMO) Study? *Kidney International Supplements* **68**:1766–1776 DOI 10.1111/j.1523-1755.2005.00593.x.

Eckardt KU, Coresh J, Devuyst O, Johnson RJ, Kottgen A, Levey AS, Levin A. 2013. Evolving importance of kidney disease: from subspecialty to global health burden. *Lancet* **382**:158–169 DOI 10.1016/S0140-6736(13)60439-0.

European Best Practice Guidelines Expert Group on Hemodialysis ERA. 2002. Section I. Measurement of renal function, when to refer and when to start dialysis. *Nephrology, Dialysis, Transplantation* **17**(Suppl 7):7–15.

Floege J, Kim J, Irel E, Chazot C, Drueke T, De Francisco A, Kronenberg F, Marcelli D, Passlick-Deetjen J, Schernthaner G, Fouqueray B, Wheeler DC, Investigators ARO. 2011. Serum iPTH calcium phosphate and the risk of mortality in a European haemodialysis population. *Nephrology Dialysis Transplantation* **26**:1948–1955 DOI 10.1093/ndt/gfq219.

Heaf J, Nielsen AH, Hansen HP. 2012. Long-term haemodialysis survival. *Clinical Kidney Journal* **5**:168–169 DOI 10.1093/ckj/sfs011.

Kalantar-Zadeh K, Shah A, Duong U, Hechter RC, Dukkipati R, Kovesdy CP. 2010. Kidney bone disease and mortality in CKD: revisiting the role of vitamin D, calcimimetics, alkaline phosphatase, and minerals. *Kidney International Supplements* **78**:S10–S21.

Liang KV, Zhang JH, Palevsky PM. 2019. Urea reduction ratio may be a simpler approach for measurement of adequacy of intermittent hemodialysis in acute kidney injury. *BMC Nephrology* **20**:82 DOI 10.1186/s12882-019-1272-7.

Ma L, Zhao S. 2017. Risk factors for mortality in patients undergoing hemodialysis: a systematic review and meta-analysis. *International Journal of Cardiology* **238**:151–158 DOI 10.1016/j.ijcard.2017.02.095.

Ma L, Zhao S, Li Z. 2017. Effects of parathyroidectomy on bone metabolism in haemodialysis patients with secondary hyperparathyroidism. *Scandinavian Journal of Clinical and Laboratory Investigation* **77**:527–534 DOI 10.1080/00365513.2017.1354256.

Mikhail A, Brown C, Williams JA, Mathrani V, Shrivastava R, Evans J, Isaac H, Bhandari S. 2017. Renal association clinical practice guideline on Anaemia of Chronic Kidney Disease. *BMC Nephrology* **18**:345 DOI 10.1186/s12882-017-0688-1.

National Kidney F. 2015. KDOQI clinical practice guideline for hemodialysis adequacy: 2015 update. *American Journal of Kidney Diseases* **66**:884–930 DOI 10.1053/j.ajkd.2015.07.015.

Naves-Diaz M, Passlick-Deetjen J, Guinsburg A, Marelli C, Fernandez-Martin JL, Rodriguez-Puyol D, Cannata-Andia JB. 2011. Calcium phosphorus PTH and death rates in a large sample of dialysis patients from Latin America. The CORES Study. *Nephrology, Dialysis, Transplantation* **26**:1938–1947 DOI 10.1093/ndt/gfq304.

Neves PD, Graciolli FG, Oliveira IB, Bridi RA, Moyses RM, Elias RM. 2017. Effect of mineral and bone metabolism on restless legs syndrome in hemodialysis patients. *Journal of Clinical Sleep Medicine* **13**:89–94 DOI 10.5664/jcsm.6396.

Otsubo S, Otsubo K, Sugimoto H, Ueda S, Otsubo Y, Otsubo O, Yajima A, Yagi S, Kataoka H, Iwasaki T, Iwasa Y, Takahashi M, Aoki A, Ino J, Uchida K, Yumura W, Akiba T, Nitta K. 2007. Characteristics of patients on hemodialysis therapy for more than 30 years. *Ther Apher Dial.* **11**:274–279 DOI 10.1111/j.1744-9987.2007.00490.x.

Owen Jr WF, Lew NL, Liu Y, Lowrie EG, Lazarus JM. 1993. The urea reduction ratio and serum albumin concentration as predictors of mortality in patients undergoing hemodialysis. *New England Journal of Medicine* **329**:1001–1016 DOI 10.1056/NEJM199309303291404.

Port FK, Pisoni RL, Bragg-Gresham JL, Satayathum SS, Young EW, Wolfe RA, Held PJ. 2004. DOPPS estimates of patient life years attributable to modifiable hemodialysis practices in the United States. *Blood Purification* **22**:175–180 DOI 10.1159/000074938.

Roach LA, Lambert K, Holt JL, Meyer BJ. 2017. Diet quality in patients with end-stage kidney disease undergoing dialysis. *Journal of Renal Care* **43**:226–234 DOI 10.1111/jorc.12215.

Sabatino A, Piotti G, Cosola C, Gandolfini I, Kooman JP, Fiaccadori E. 2018. Dietary protein and nutritional supplements in conventional hemodialysis. *Seminars in Dialysis* **31**:583–591 DOI 10.1111/sdi.12730.

Slinin Y, Greer N, Ishani A, MacDonald R, Olson C, Rutks I, Wilt TJ. 2015. Timing of dialysis initiation, duration and frequency of hemodialysis sessions, and membrane

flux: a systematic review for a KDOQI clinical practice guideline. *American Journal of Kidney Diseases* **66**:823–836 DOI 10.1053/j.ajkd.2014.11.031.

Tanaka M, Komaba H, Fukagawa M. 2018. Emerging association between parathyroid hormone and anemia in hemodialysis patients. *Therapeutic Apheresis and Dialysis* **22**:242–245 DOI 10.1111/1744-9987.12685.

Tattersall J, Martin-Malo A, Pedrini L, Basci A, Canaud B, Fouque D, Haage P, Konner K, Kooman J, Pizzarelli F, Tordoir J, Vennegoor M, Wanner C, Ter Wee P, Vanholder R. 2007. EBPG guideline on dialysis strategies. *Nephrology, Dialysis, Transplantation* **22**(**Suppl 2**):ii5–ii21 DOI 10.1093/ndt/21.suppl_6.vi5.

Young EW, Albert JM, Satayathum S, Goodkin DA, Pisoni RL, Akiba T, Akizawa T, Kurokawa K, Bommer J, Piera L, Port FK. 2005. Predictors and consequences of altered mineral metabolism: the dialysis outcomes and practice patterns study. *Kidney International Supplements* **67**:1179–1187 DOI 10.1111/j.1523-1755.2005.00185.x.

Zazzeroni L, Pasquinelli G, Nanni E, Cremonini V, Rubbi I. 2017. Comparison of quality of life in patients undergoing hemodialysis and peritoneal dialysis: a systematic review and meta-analysis. *Kidney and Blood Pressure Research* **42**:717–727 DOI 10.1159/000484115.