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Outcomes in Incident Hemodialysis Patients in One Center: Results from 15 Years Cohort Study

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Abstract

Aim: While mortality among hemodialysis patients has been well researched in Western countries, only few systematic studies have been reported from China. The aim of this study was explore outcome in chronic hemodialysis patients in an academic Chinese hospital.

Methods: We extracted data from consecutive incident patients who initiated hemodialysis and survived at least 90 days between 1/1/1998 and 31/12/2012 in the Renji hospital, Shanghai, China. The follow-up period ended on 30/6/2014. We used Kaplan Meier and Cox proportional hazards analysis to explore survival characteristics and associated covariates.

Results: Out of 646 patients who started dialysis, 522 patients had a documented survival beyond 90 days. Their median age at dialysis initiation was 55.3 years (range 15.4-89.6), 322 patients (61.7%) were males. By 30/6/2014, 172 patients (33%) had died, 253 (48.5%) were alive on hemodialysis, 60 patients (11.5%) were transplanted, 35 (6.7%) transferred to another center, and 1 patient each switched to peritoneal dialysis and recovered kidney function. Five-year and ten-year survival rates were 74.2% and 53.6%, respectively. Age at dialysis initiation (hazard ratio 1.053, 95% CI [1.039, 1.266], p<0.001) and diabetic nephropathy (HR 1.73, 95% CI [1.046, 2.081], p<0.033) were associated with increased mortality.

Conclusion: Our findings indicated a comparably low 5- and 10-year mortality in patients who had a documented survival beyond the first 90 days. This finding may in part be due to the lower age at dialysis initiation and the low prevalence of diabetes in the study population.

Keywords: Age; Diabetic nephropathy; ESRD; Chronic hemodialysis; Mortality

Introduction

While hemodialysis has seen major technical advances over the last decades and is a life-sustaining therapy in patients with end stage of renal disease (ESRD) patients, the mortality in chronic dialysis patients is still poor in most parts of the world. The crude death rate per 1000 patient-years was 183 in US (2012) [1], 127 in Australia (2012) [2], 146 in New Zealand (2012) [2], and 98 in Japan (2010) [3]. While mortality among hemodialysis patients has been well researched in Western countries, only few systematic studies have been reported from China. In fact, only two studies, one each from Shanghai and Beijing, respectively, have reported crude mortality rates [4,5]. These mortality rates were comparably low and ranged from 47.8 to 77.3 per 1000 patient years. The aim of this study was to increase the body of knowledge concerning outcomes in Chinese chronic hemodialysis patients.

Subjects and Methods

Data source

We conducted a single-center retrospective cohort study in chronic hemodialysis patients who were accepted for hemodialysis between 1/1/1998 and 31/12/2012 at the Renji Hospital, Shanghai, China, and who survived at least 90 days of dialysis. Patient follow-up ended on 30/6/2014. The Renji Hospital is an urban academic tertiary referral center with a catchment zone of around 5 million people. Data were extracted from paper records until 2006 and thereafter from electronic health records. We analyzed patient demographics (sex, age at dialysis start), primary kidney disease resulting in ESRD, pre-hemodialysis treatment modalities (peritoneal dialysis, renal transplantation), and cause of death.

Statistics analysis

Descriptive statistics and survival analyses were conducted in the entire population and in tertiles of age at dialysis initiation (<=55 years, 55-77 years, and >77 years). Summary statistics of continuous variables are reported as means, standard deviations, median and range, as appropriate; categorical variables are presented as percentages. Distributions were compared by chi-square test (dichotomous and categorical variables), and unpaired t-tests (continuous variables). Survival probabilities were estimated using Kaplan-Meier analysis and strata were compared using log-rank test. Cox proportional hazard models were constructed for multivariate survival analyses. Patients were censored when transferred to other dialysis facilities, recovery of renal function; change of renal replacement therapy modality, and at the end of the follow-up period. SAS version 9.3 (Cary, NC, USA) was used for statistical analysis. A two-tailed type 1 error (p-value) < 0.05 was considered statistically significant.

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Results

Patient demographics

A total of 646 patients started dialysis between 1/1/1998 and 31/12/2012. Out of these patients 522 (80.8%) had a documented survival beyond 90 days; these patients resembled the analytical cohort and all results reported subsequently refer to that group. No further information is available about the 124 patients who have no documented survival beyond 90 days, because they left the hospital. The majority of patients were male (61.7%), mean age at hemodialysis initiation was 55.5 ± 15.7 years (median age was 55.3 year (range 15.4-89.6)). Chronic glomerulonephritis was the primary disease of ESRD in 189 patients (36.2%), followed by diabetic nephropathy (11.3%), and hypertensive nephrosclerosis (9.2%). Other primary causes of ESRD included autosomal dominant polycystic kidney disease in 28 (5.4%) patients, lupus nephritis in 25 (4.8%) patients, interstitial nephritis in 12 (2.3%) patients, obstructive nephropathy in 10 (1.9%) patients, vasculitis in 10 (1.9%) patients, gouty nephropathy in 7 (1.3%) patients, surgery for kidney cancer in 5 (0.9%) patients, amyloidosis in 3 (0.6%) patients, neurogenic cystitis in 3 (0.6%) patients, rapidly progressive glomerulonephritis (RPGN) in 3 (0.6%) patients, non-recovery for acute kidney injury (AKI) in 2 (0.4%) patients, HBV-associated glomerulonephritis in 2 (0.4%) patients, light-chain deposition disease in 2 (0.4%) patients, multiple myeloma in 1 (0.2%) patient, and nephrocalcinosis due to primary hyperparathyroidism 1 (0.2%) patient. The cause of ESRD was unknown in 112 (21.5%) patients.

Patient outcomes (Figure 1)

The median hemodialysis vintage was 5.8 years (range 0.3-16y). By 30/6/2014, 172 patients (33%) had died, 253 (48.5%) were alive on hemodialysis. During follow-up 60 patients (11.5%) received a kidney transplant, 35 patients (6.7%) were transferred to other dialysis centers, 1 patient switched to peritoneal dialysis, and 1 patients experienced recovery of kidney function. The crude mortality rate in the study cohort was 57.8 per 1000 patient years. Stroke was the leading cause of death (32.6%), followed by cardiovascular (20.3%) and infectious causes (17.4%). Other causes of death included malignancy in 16 (9.3%) patients, malnutrition in 16 (9.3%) patients, withdrawal from dialysis for economic reason in 2 (1.2%) patients, and in 1 patient (0.6%) each gastrointestinal hemorrhage, intestinal obstruction, and renal cyst bleeding. The cause of death was unknown in 14 (8.1%) patients.

Survival rate

In the total population 5-year and 10-year survival rates were 74.2% and 53.6%, respectively (Figure 2A). Mortality did not differ between males and females (log-rank test: p=0.9553) (Figure 2B). Younger patients (≤55.3 years of age) had better survival compared to older patients (>55.3 years of age), with 5-year survival rates of 82.1% and 68.2% (p<0.0001), respectively (Figure 2C). Compared with non-diabetic patients, 5-year survival was lower in diabetic patients (60.4% vs 76.6%, p=0.0006) (Figure 2D).

Comparison between survivors and non-survivors

Univariate analysis of baseline characteristics indicated that survivors were younger, had more frequently chronic glomerulonephritis and less frequently diabetic or hypertensive nephropathy as primary kidney diseases. Multiple Cox proportional hazard analysis indicated that age at dialysis initiation (hazard ratio (HR) 1.05 (95% confidence interval (CI): 1.039-1.066; p<0.0001) and diabetic nephropathy (HR 1.73, 95% CI: 1.046-2.861; p<0.05) as significant predictors of mortality.

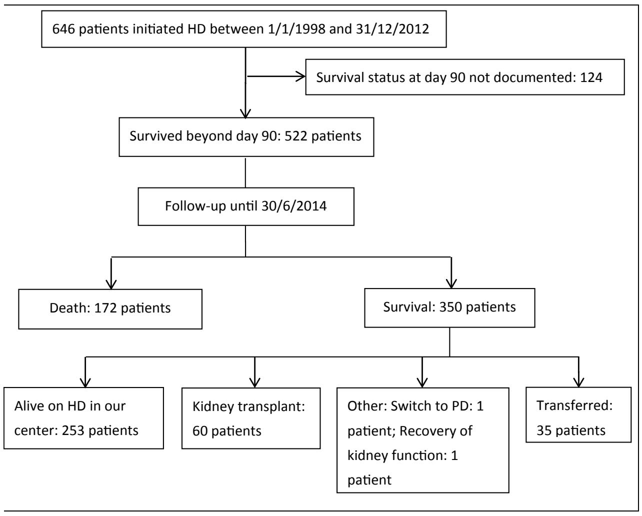

Figure 1: Patients flow chart.

The presence or absence of glomerulonephritis or hypertensive nephropathy did not affect 5-year mortality (Table 1). These results were corroborated in a multivariate analysis with patients stratified by median population age (55.3 years). Of note, diabetic nephropathy and age of dialysis initiation were stronger predictors of survival in patients below the median age (HR 4.21, 95% CI: 1.62-10.93; P=0.003 and HR 1.05, 95% CI: 1.01-1.09; p=0.008) (Table 1). In patients older than 55.3 years diabetic nephropathy was not associated with mortality, while age was retained as a significant predictor (HR 1.09, 95% CI 1.060-1.117, p<0.0001,) (Table 1).

In a subsequent analysis we stratified patients without diabetic nephropathy into age tertiles <=55 years, 55-77 years, and >77 years. Patients in 55-77 years group had 2-folds higher mortality than those in <=55 years group (HR 2.03, 95% CI 1.337-3.068, p=0.0009). Those older than 77 years had 5.4 folds higher mortality than those younger than 55 years (HR 5.42, 95% CI 3.59-8.18, p<0.0001). These results were in essence comparable to those in patients with diabetic nephropathy. Patients younger than 55 years with diabetic nephropathy had 5.2 folds higher mortality than those in the same age stratum but without diabetic nephropathy (HR 5.20, 95% CI 2.177-12.409, p=0.0002). Those in 55-77 years group with diabetic nephropathy had 2.7 folds higher mortality than those younger than 55 years without diabetic nephropathy (HR 2.73, 95% CI 1.357-5.471, p=0.0048). Patients older than 77 years with diabetic nephropathy had 6.1 folds higher mortality than those younger than 55 years without diabetic nephropathy (HR 6.08, 95% CI 2.991-12.37, p<0.0001) (Figure 3).

Discussion

This study is the third report of survival outcomes in chronic hemodialysis patients from China. Our main finding is a comparable low mortality rate in patients who have a documented survival beyond day 90 after dialysis initiation. The results of this analysis add to the well documented variability of dialysis outcomes across countries [5-8]. Geographical disparities in dialysis mortality have been documented for more than 20 years. Held et al. reported that the 5-year mortality between 1982 and 1987 was 15% in US hemodialysis patients compared to patients treated in Europe, and 33% higher compared to patients in

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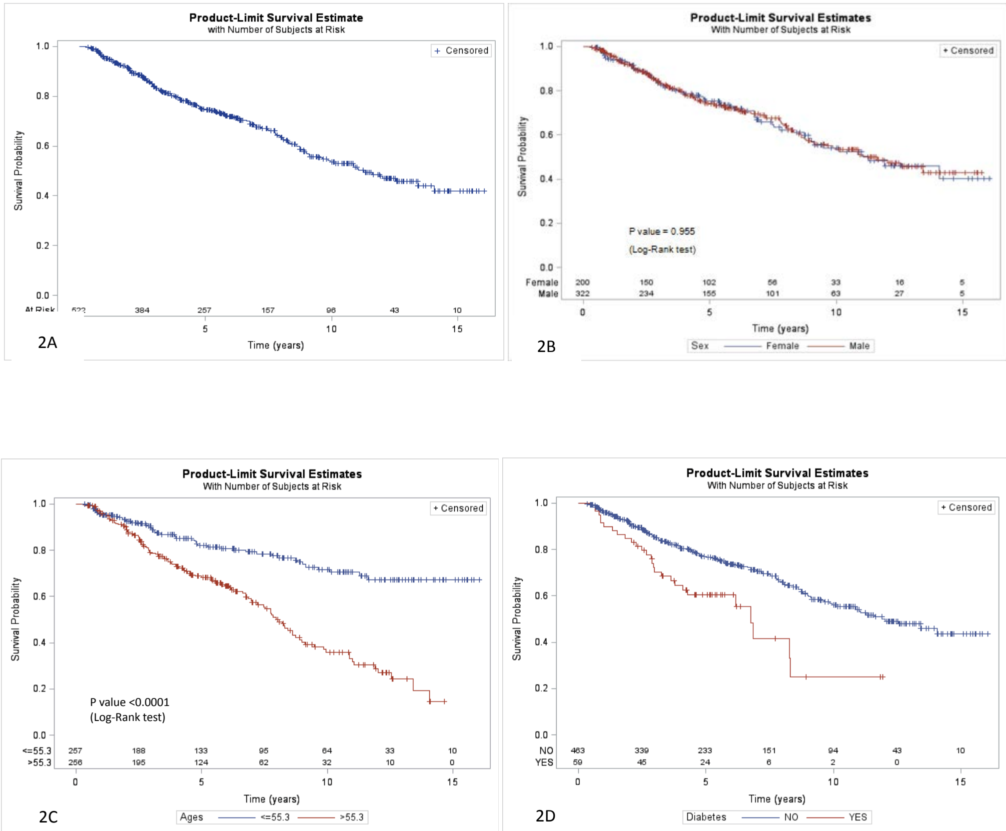

Figure 2: Survival probability of the different groups' patients. **2A**: Survival probability of the entire study population; **2B**: Survival probabilities of the study population stratified by gender; **2C**: Survival probability of the entire study population stratified by median age of 55.3 years; **2D**: Survival probability of the entire study population stratified by the presence or absence of diabetic nephropathy as the primary cause of ESRD

Japan [6]. These regional disparities have been corroborated by DOPPS [7].

Only few data related to mortality in chronic hemodialysis patients in patient treated in China exist. Cheng et al. reported a crude mortality rate of 76.8 per 1000 patient years in maintenance hemodialysis patients from Beijing, comparable to our data of 57.8 per 1000 patient years [5]. The 5-year survival rate reported by us (74.2%) is comparable to the ones reported from Japan (59.6%), and South Korea (67.4%) [3,9]. The impact of Asian race on outcomes was explored by some studies. Wong et al. suggested that Asian American had had a mortality rate comparable to HD patients in Japan [10]. Asian American patients have better survival than white US patients [1,11]. The reasons underlying the racial / ethnic survival differences remain to be elucidated. A large international registry study in 623,900 HD patients from 26 countries concluded that a substantial portion of the variability in mortality rates observed across dialysis patients worldwide is attributable to the variability in background atherosclerotic mortality rates in the respective general population [8]. While findings indicate that genetic and environmental factors may underlie these differences, further studies are warranted.

It is interesting to compare the causes of death in the Shanghai population to the ones observed in other regions. In our population stroke was with 35% the leading cause of death. In another study from Shanghai, China, cerebrovascular disease was the leading cause of death in dialysis patients, despite the fact that the mortality due to stroke decreased from 24% to 15% in the years between 2000 and 2005 [4]. In Beijing, stroke was the cause of death in 15% of all dialysis patients [5]. In Japanese HD patients the frequency of death caused by stroke has decreased from 14.2% to 8.1% between 1980 and 2010 [3]. These figures as substantially higher than that the stroke death rates observed in the UK (5%) and the US (3.3%) (USRDS) [1,12].

Age and diabetes

Age and diabetes are two important factors to influence mortality. Over past three decades, the number of elderly ESRD patients beginning dialysis has been increasing in many countries. Tamura et al. demonstrated the functional status of elderly ESRD patients had declined after initiation of dialysis [13]. The life expectancy of elder dialysis patients was significantly shorter than younger patients in US, Europe and Japan [14,15]. Another factor is primary disease with diabetes. Diabetic dialysis patients had higher mortality than dialysis patients with no diabetes were reported by US, Europe and Japan renal registry system, respectively [1,3,16]. Our study has demonstrated age and diabetic nephropathy as strong predictors of mortality. Not surprisingly, age was associated with mortality independent of the presence or absence of diabetic nephropathy. Patients with diabetic nephropathy older than 77 years experienced the highest mortality. These findings corroborate previous studies showing the consistent association of age and diabetes with mortality [17-19].

Limitation

Our study has several limitations, first and foremost its retrospective

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Cox proportional hazards regression analysis of mortality predictors			
	HR	**95% CI**	**p**
Gender (female)	1.073	0.787-1.464	0.657
Age at dialysis initiation (per 1 year)	1.053	1.039-1.066	<0.001*
CGN (yes)	Reference		
DN (yes)	1.73	1.046-2.861	0.033*
HTN (yes)	1.505	0.912-2.482	0.11
Others[1](yes)	1.315	0.899-1.923	0.158
Cox proportional hazards regression analysis of mortality predictors in patients stratified by median age of 55.3 years			
	HR	**95% CI**	**P**
Patients ≤ median age			
Gender (female)	1.419	0.797-2.529	0.236
Age at dialysis initiation (per 1 year)	1.055	1.014-1.098	0.008*
CGN (yes)	Reference		
DN(yes)	4.216	1.625-10.936	0.003*
HTN(yes)	2.281	0.89-5.846	0.086
Others[1](yes)	1.02	0.539-1.928	0.952
Patients >median age			
Gender (female)	1.037	0.71-1.514	0.851
Age of start dialysis (per 1 year)	1.088	1.06-1.117	<.0001*
CGN (yes)	Reference		
DN (yes)	1.847	0.998-3.418	0.051
HTN (yes)	1.468	0.796-2.704	0.219
Others[1] (yes)	1.634	0.992-2.693	0.054

HR: Hazard Ratio; CI: Confidence Interval; CGN: Chronic Glomerulonephritis; DN: Diabetic Nephropathy; HTN: Hypertensive Nephrosclerosis.
[1]This category includes autosomal dominant polycystic kidney disease, lupus nephritis, interstitial nephritis, obstructive nephropathy, vasculitis, gouty nephropathy, surgery for kidney cancer, amyloidosis, neurogenic cystitis, rapidly progressive glomerulonephritis (RPGN), non-recovery for AKI, HBV-associated glomerulonephritis, light-chain deposition disease, multiple myeloma, nephrocalcinosis due to primary hyperparathyroidism and unknown.
Table 1: Cox proportional hazards regression analysis of mortality predictors of the entire study population.

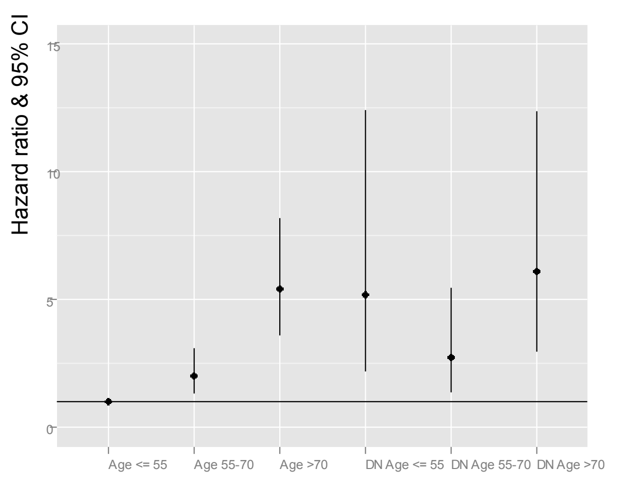

Figure 3: Hazard ratio of mortality in tertiles of age groups with or without diabetic nephropathy.

observational nature. Second, absent data we could not provide comorbidities before dialysis initiation. Third, our data base does not include information concerning the types of vascular access. Finally, the study is limited to a single academic center. In addition, more detailed information on the 124 patients who have no documented survival beyond 90 days after dialysis initiation would have been highly desirable.

Conclusion

Our findings indicated a comparably low 5- and 10-year mortality, in part possibly because of the lower age and the low prevalence of diabetes in the study population. Prospective multi-center studies in different parts of China are required to further explore mortality pattern and their relationship to conventional and non-conventional predictors of survival, including life style, inflammation, body composition, and genetic markers.

Acknowledgement

Conflict of interest statement: Peter Kotanko holds stock in Fresenius Medical Care.

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