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Hospitalizations of Chronic Dialysis Patients: A National Study in China

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Keywords
Hospitalizations · Dialysis patients · Cause of hospitalizations

Abstract

Background: Patients receiving chronic dialysis are usually with multiple comorbidities and at high risk for hospitalization, which lead to tremendous health care resource utilization. This study aims to explore the characteristics of hospitalizations among chronic dialysis patients in China. ***Methods:*** Hospital admissions from January 2013 to December 2015 were extracted from a national inpatient database in China. Chronic dialysis, including hemodialysis and peritoneal dialysis, was identified according to inpatient discharge records and International Classification of Diseases-10 (ICD-10) codes. The primary kidney disease, causes of admissions, modalities of dialysis, and comorbidities were analyzed. Multivariable logistic regression model was used to assess the association of patient characteristics with multiple hospitalizations per year. ***Results:*** Altogether, 266,636 hospitalizations from 124,721 chronic dialysis patients were included in the study. The mean age was 54.46 ± 15.63 years and 78.29% of them were receiving hemodialysis. The leading cause of hospitalizations was dialysis access-related, including dialysis access creation (25.06%) and complications of access (21.09%). The following causes were nonaccess surgery (1.89%), cardiovascular disease (1.66%), and infectious diseases (1.43%). One-fourth of the patients were hospitalized more than once per year. Multivariate logistic regression models indicated that the primary kidney disease of diabetic kidney disease (odds ratio [OR]: 1.16, 95% confidence interval [CI]: 1.11–1.22) or hypertensive nephropathy (OR: 1.33, 95% CI: 1.27–1.40), coronary heart disease (OR: 1.09, 95% CI: 1.05–1.14), cancer (OR: 1.21, 95% CI: 1.13–1.30), or modality of peritoneal dialysis (OR: 2.67, 95% CI: 2.59–2.75) was risk factors for multiple hospitalizations. ***Conclusion:*** Our study described characteristics and revealed the burden of hospitalizations of chronic dialysis patients in China. These findings highlight the importance of effective and efficient management strategies to reduce the high burden of hospitalization in dialysis population.

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Introduction

Patients receiving chronic dialysis for end-stage kidney disease (ESKD) are usually with multiple comorbidities and at high risk of death [1–3]. Compared with the general population, chronic dialysis patients tend to have a higher risk of hospitalization, longer length of stay, and increased rate of readmission [2, 4]. Consequently, dialysis patients consume disproportionately tremendous health care resources. For example, ESKD patients with kidney replacement therapy, including dialysis and kidney transplantation, comprise about 0.15% of the global population, but they absorb 2–4% of the healthcare budget in some countries [5]. Furthermore, the inpatient spending accounted for approximately 32.5% of total Medicare fee-for-service expenditures for beneficiaries with ESKD in the USA [6]. The population of worldwide patients receiving kidney replacement therapy was projected to grow more than double from 2010 to 2030, with the most growth in Asia [7]. In China, the total number of dialysis patients was estimated to be 346,178 in 2013 and was predicted to rise to 874,373 in 2025 [8], which could lead to a growing health care burden of disease.

Hospitalizations among ESKD patients receiving kidney replacement therapy were tracked in the USA for many years via the US Renal Data System (USRDS). The 2020 USRDS Annual Data Report (ADR) demonstrated that the rates of hospitalization for ESKD patients decreased from 1.82 per person-per year (PPPY) in 2009 to 1.58 PPPY in 2018 [6]. A Dialysis Outcomes and Practice Patterns Study (DOPPS) of five European countries observed an overall hospitalization rate of 1.08 PPPY using data collected from 1998 and 2000 [9]. Data from the ADR generated by the China Kidney Disease Network reported that hospitalization rates of dialysis patients in China were 1.78 PPPY in 2015 and 2.67 PPPY in 2016 [10, 11]. However, detailed characteristics of hospitalization among dialysis patients in China are still unknown, constituting an obstacle to develop effective and efficient management strategies. Therefore, this study aims to explore the characteristics of hospitalizations among chronic dialysis patients in China.

Materials and Methods

Data Source

Patients receiving chronic dialysis were identified from a national inpatient database, Hospital Quality Monitoring System (HQMS), under the authority of the National Health Commission (NHC) of the People's Republic of China and the World Health Organization (WHO). Details of the HQMS were described elsewhere [10–13]. Briefly, the NHC requires that all tertiary hospitals in China submit inpatient discharge summaries to HQMS in a standardized electronic format on a daily basis [10–12]. The HQMS database contains 346 patient-level variables including demographic characteristics, discharge diagnoses, procedures, and medical expenses. The discharge diagnoses were coded using International Classification of Diseases-10 (ICD-10) coding system and the procedures were coded using the International Classification of Diseases-9, Clinical Modification Volume 3 (ICD-9-CM-3).

Study Population

Hospitalization records of chronic dialysis patients between January 1, 2013, and December 31, 2015, were extracted from the HQMS, and details of search strategy and conduction were described previously [13]. In brief, we enrolled hospitalization records of chronic dialysis patients identified by ICD-10 and ICD-9-CM-3 codes, which were provided in online supplementary Table S1 (for all online suppl. material, see www.karger.com/doi/10.1159/000530069), and excluded records of patients: (1) without identification number and therefore multiple hospitalizations could not be identified; (2) aged <18 years and >100 years; (3) died during the index hospitalization; (4) diagnosed as acute kidney injury, chronic kidney disease stage G1-4, with history of kidney transplantation. The ICD codes of AKI, CKD stages G1-4, and kidney transplantation were provided in online supplementary Table S2. Patients were divided into single hospitalization group and multiple hospitalization group according to whether they had more than one hospitalization record a year. However, if patients suffered two hospitalizations in a year, but with one admission caused by dialysis access creation, were also enrolled in single hospitalization group. The flowchart of patient selection is shown in Figure 1. The Ethics Committee of the Peking University First Hospital has approved the study.

Causes of Hospitalizations and Comorbidities

Causes of hospitalizations were identified by the medical procedures, dialysis access creation, and complications of access, as well as principal diagnoses of medical records consecutively. Hospitalizations with both of the following features were included in the group of nonspecific causes: (1) none of coding information referred to medical procedures, dialysis access creation, and complications of access was found in medical records; (2) the principal diagnoses were CKD G5, ESKD, the causes of ESKD, or those that accounted for less than 0.05% of all hospitalizations in this database. Comorbidities were extracted from all 11 diagnoses of medical records. The coding information of medical procedures and diseases is shown in online supplementary Table S3a and S3b.

Statistical Analyses

Characteristics of chronic dialysis patients were assessed using descriptive statistics. Data were reported as proportions (%) for categorical variables and the mean ± standard deviation (SD) for continuous variables. Multivariable logistic regression model was used to assess the association between different characteristics (age, gender, modality of dialysis, cause of ESKD, and common comorbidity) and multiple hospitalizations per year among dialysis patients, which was presented as adjusted odds ratio (OR) and 95% confidence interval (CI). Statistical significance of tests was

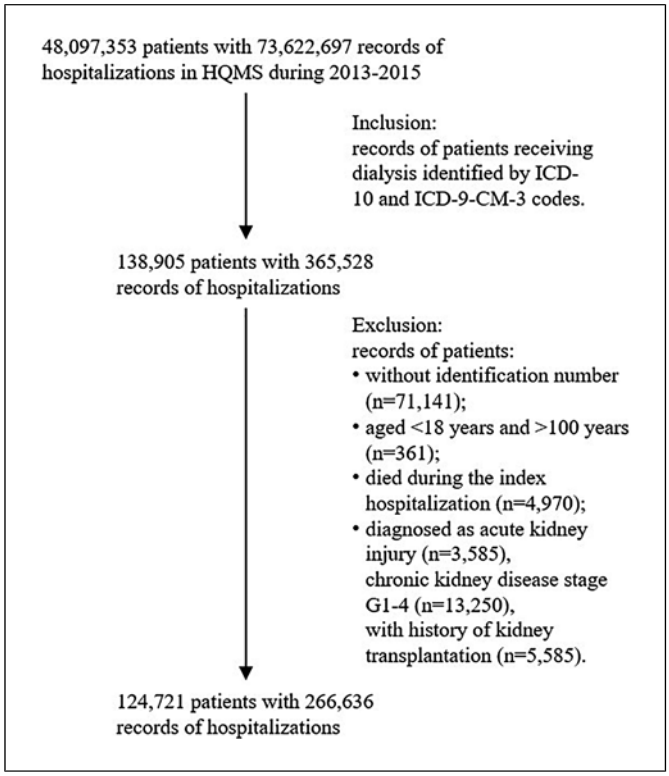

Fig. 1. Procedure of study population selection. HQMS, Hospital Quality Monitoring System; ICD-9-CM-3, International Classification of Diseases-9, Clinical Modification Volume 3; ICD-10, International Classification of Diseases-10.

required as two-tailed p value <0.05. All analyses were done using the STATA 15.0 software.

Results

General Characteristics of the Study Population

Altogether, there were 48,097,353 patients with 73,622,697 records of hospitalizations in HQMS during 2013–2015, in which 124,721 patients receiving chronic dialysis (0.26%) with 266,636 hospitalizations (0.36%) were included in this study. Hospitalizations among chronic dialysis patients increased from 0.26% of all records in HQMS in 2013–0.44% in 2015. Overall, 79.8% of hospitalizations were in nephrology wards, 4.82% in surgical wards, and 3.27% in emergency departments or intensive care units.

Characteristics of chronic dialysis patients are described in Table 1. The mean age was 54.46 ± 15.63 years, 58.38% of them were women, and 78.29% received hemodialysis. The average length of stay in the hospital was 11 (6–9) days. The average inpatient spending was 10,736.90 (5,887.89–18,514.00) RMB. The leading cause of ESKD was glomerulonephritis (16.51%), followed by diabetic kidney disease (14.27%) and hypertensive nephropathy (12.35%).

Common Causes and Comorbidities of Hospitalizations

The common causes and comorbidities of hospitalizations among chronic dialysis patients are listed in Table 2. The leading specific cause of hospitalizations was dialysis access-related infection at around 46.15%, including dialysis access creation (25.06%) and complications of access (21.09%). Access-related infection was enrolled in the group of access complications. The following causes of admissions were surgery (1.89%) and infectious diseases (1.43%). In the group of infectious diseases, pneumonia/chronic obstructive pulmonary disease was present in 0.93% of hospitalizations and other infectious diseases in 0.50%. On the other hand, admissions for cardiovascular disease (CVD), a combination of coronary heart disease (0.85%), stroke (0.53%), and heart failure (0.28%) were also common at around 1.66%.

The most common comorbidity of hospitalizations was hypertension (69.99%), followed by diabetes (19.62%) and infectious diseases (19.02%). The group of infectious diseases included pneumonia/COPD (13.62%), urinary tract infection (2.26%), and gastrointestinal infection (1.11%). Similarly, on the other hand, CVD comorbidity was present in 27.12% of hospitalizations.

Additionally, cancer was the seventh common cause of hospitalizations at around 0.8% and 12th common comorbidity at around 2.99%. Admissions for cancer were more frequent in hemodialysis subgroup (1.03%) than that in peritoneal dialysis one (0.26%), probably because hemodialysis was the preferred long-term dialysis modality for cancer patients. As a common cause of hospitalizations, gastrointestinal hemorrhage was ranked 11th in the total records, hemodialysis, and peritoneal dialysis subgroup, accounting for 0.17%, 0.19%, and 0.10% correspondingly. The comorbidity of gastrointestinal hemorrhage was present in 1.84% of hospitalizations.

Comparisons of Dialysis Patients with Single and Multiple Hospitalizations

Comparisons of chronic dialysis patients with single and multiple hospitalizations per year are shown in Table 1, and the logistic regression analysis of characteristics for multiple hospitalizations is shown in Table 3. Approximately, one-fourth of the patients were

Table 1. Characteristics of chronic dialysis patients with single versus multiple hospitalizations per year in China, 2013–2015

	Total patients (*N* = 124,721)	Single hospitalization (*N* = 92,762)	Multiple hospitalizations (*N* = 31,959)
Number of hospitalizations	266,636	118,317	148,319
Age, mean±SD, years	54.46±15.63	54.21±15.57	55.16±15.78
Gender, *N* (%)			
Men	51,815	38,541 (74.38)	13,274 (25.62)
Women	72,666	54,066 (74.40)	18,600 (25.60)
Health insurance, *N* (%)			
Yes	107,746	79,387 (73.68)	28,359 (26.32)
No	16,975	13,375 (78.79)	3,600 (21.21)
Modality of dialysis, *N* (%)			
Hemodialysis	93,393	73,663 (78.87)	19,730 (21.13)
Peritoneal dialysis	25,893	15,291 (59.05)	10,602 (40.95)
Cause of ESKD, *N* (%)			
Diabetic kidney disease	17,801	13,115 (73.68)	4,686 (26.32)
Hypertensive nephropathy	15,403	10,970 (71.22)	4,433 (28.78)
Glomerulonephritis	20,596	15,623 (75.85)	4,973 (24.15)
Common comorbidity, *N* (%)			
Pneumonia/COPD	20,678	16,104 (77.88)	4,574 (22.12)
CHD	13,273	9,586 (72.22)	3,687 (27.78)
Other infectious disease*	12,048	9,231 (76.62)	2,817 (23.38)
Heart failure	10,689	8,042 (75.24)	2,647 (24.76)
Stroke	9,588	7,024 (73.26)	2,564 (26.74)
Cancer	4,867	3,698 (75.98)	1,169 (24.02)

CHD, coronary heart disease; COPD, chronic obstructive pulmonary disease; ESKD, end-stage kidney disease; *N*, number of dialysis patients; SD, standard deviation. *The group of other infectious diseases excluded pneumonia/COPD, tuberculosis, or sexually transmitted disease.

Table 2. Top ten most common causes and comorbidities of hospitalizations among dialysis patients in China, 2013–2015

Rank	Admission cause (total, *n* = 266,636)	%	Admission cause (HD, *n* = 183,157)	%	Admission cause (PD, *n* = 68,273)	%	Comorbidity (total, *n* = 266,636)	%
1	Dialysis access		Dialysis access		Dialysis access		Hypertension	69.99
	Creation	25.06	Creation	31.78	Creation	13.09		
	Complications[a]	21.09	Complications[a]	25.79	Complications[a]	12.58		
2	Surgery[b]	1.89	Surgery[b]	1.93	Surgery[b]	1.95	Diabetes mellitus	19.62
3	Infectious diseases[c]	1.43	Infectious diseases[c]	1.54	Hypertension	1.43	Infectious diseases[c]	19.02
4	Hypertension	1.25	Hypertension	1.18	Infectious diseases[c]	1.14	CHD	10.94
5	CHD	0.85	Cancer[b, d]	1.03	Diabetes mellitus	0.84	Heart failure	8.18
6	Diabetes mellitus	0.80	CHD	0.99	CHD	0.49	Stroke	8.00
7	Cancer[b, d]	0.80	Diabetes mellitus	0.79	Stroke	0.37	Hyperparathyroidism	7.81
8	Stroke	0.53	Stroke	0.60	Hyperparathyroidism	0.31	Gastrointestinal diseases	5.42
9	Hyperparathyroidism	0.29	Heart failure	0.31	Cancer[b, d]	0.26	Liver diseases	5.35
10	Heart failure	0.28	hyperparathyroidism	0.23	Heart failure	0.22	Gout/hyperuricemia	5.05
	Nonspecific causes	45.24	Nonspecific causes	33.28	Nonspecific causes	66.88		

CHD, coronary heart disease; COPD, chronic obstructive pulmonary disease; HD, hemodialysis; PD, peritoneal dialysis; *n*, number of hospitalizations of dialysis patients. [a]Access-related infections were enrolled in access complications group. [b]The group of surgery excluded cancer-related surgeries, which were enrolled in the cancer group. [c]The group of infectious diseases excluded tuberculosis or sexually transmitted disease. [d]The group of cancer excluded thyroid carcinoma.

Table 3. Association of risk factors with multiple hospitalizations per year among dialysis patients in China, 2013–2015

Variable	OR	95% CI	*p* value
Age (per 10 years)	1.06	1.05–1.07	<0.001
Gender			
Women	0.97	0.95–1.00	0.024
Men	Reference		
Modality of dialysis			
Hemodialysis	Reference		
Peritoneal dialysis	2.67	2.59–2.75	<0.001
Cause of ESKD			
Diabetic kidney disease	1.16	1.11–1.22	<0.001
Hypertensive nephropathy	1.33	1.27–1.40	<0.001
Glomerulonephritis	Reference		
Common comorbidity			
Pneumonia/COPD	0.84	0.81–0.87	<0.001
CHD	1.09	1.05–1.14	<0.001
Other infectious disease*	0.92	0.88–0.96	<0.001
Heart failure	0.97	0.93–1.02	0.245
Stroke	1.04	0.99–1.09	0.154
Cancer	1.21	1.13–1.30	<0.001

CHD, coronary heart disease; CI, confidence interval; COPD, chronic obstructive pulmonary disease; ESKD, end-stage kidney disease; OR, odds ratio. *The group of other infectious diseases excluded pneumonia/COPD, tuberculosis, or sexually transmitted disease.

hospitalized more than once per year. The proportion of peritoneal dialysis patients with multiple hospitalizations was higher than hemodialysis patients (40.95% vs. 21.13%). Multivariate logistic regression models also indicated that patients with peritoneal dialysis were more likely to have multiple hospitalizations compared to hemodialysis (OR: 2.67, 95% CI: 2.59–2.75). In comparison with glomerulonephritis, patients with diabetic kidney disease (OR: 1.16, 95% CI: 1.11–1.22) or hypertensive nephropathy (OR: 1.33, 95% CI: 1.27–1.40) presented excess risk of multiple hospitalizations. In terms of comorbidities, coronary heart disease (OR: 1.09, 95% CI: 1.05–1.14) or cancer (OR: 1.21, 95% CI: 1.13–1.30) was risk factors for multiple hospitalizations.

Discussion

To the best of our knowledge, this is the first study to investigate the characteristics of hospitalizations among chronic dialysis patients in China using a large nationwide database. The mean age of these inpatients was 54.46 ± 15.63 years; the most common primary kidney disease was glomerulonephritis, and the leading specific cause of admissions was dialysis access-related infection. One-fourth of the patients were hospitalized more than once per year. The primary kidney disease of diabetic kidney disease or hypertensive nephropathy, comorbidity of coronary heart disease or cancer, or modality of peritoneal dialysis was risk factors for multiple hospitalizations per year.

In this study, the most common cause of hospitalizations was dialysis access creation (25.06%)/complications (21.09%), which was only presented in 9.2% reported by USRDS 2016 [14]. The report from a Swedish study showed that the leading cause of hospital admission was access-related infections (26%) in PD patients, whereas this cause was infrequent (1%) in HD group, and in view of overall dialysis population, it only accounted for 9.7% [15]. Dialysis access creation was not listed as the common cause of hospitalization in either the USA or Sweden. Among the top ten most common clinical conditions for hospitalizations in the USA, the leading one was septicemia (9.3%). In terms of cardiovascular conditions, the percentage of hospital admissions for hypertension (8.2%), heart failure (4.4%), and CHD (2.6%) were much higher in the USA compared to only 1.25%, 0.28%, and 0.85% in China, respectively. Admissions for diabetes were also very high in the USA (5.1% vs. 0.8%) [14]. Similarly, cardiovascular conditions-related hospitalizations accounted for 19.8% and diabetes for 6.4% in Sweden [15].

The differences observed could due to differences in the patient populations in terms of demographics (especially age), causes of ESKD, comorbid conditions, and clinical practice. First, elderly represented a different proportion of dialysis populations across countries [16]. In China, the highest proportion of dialysis patients was subgroup 45–64 years of age, accounting for 45%, reported by China Kidney Disease Network ADR 2015, and the mean age of total dialysis patients was 55.0 years, which was younger than that reported from the USA (59.1 years) or Japan (66.6 years) [10, 17, 18]. For inpatients, the mean age was 55 years in this study, which was younger than 65 years reported from Sweden [15]. Elderly dialysis patients could have more age-related comorbidities, such as atherosclerosis and diabetes mellitus, increased levels of frailty and malnutrition, higher risk of cognitive dysfunction, which may contribute to poor physical performance and clinical outcome compared to younger patients [16, 19–24]. Second, glomerulonephritis was the leading cause of ESKD in China, while diabetes and hypertension were more common in the USA, European countries, and some other counties in Asia [6, 10, 11, 14–16, 25]. Previous

studies indicated the high prevalence of diabetic and cardiovascular complications in diabetic dialysis patients [26, 27]. The heart and vascular system could undergo certain structural and functional changes from kidney function declines to kidney replacement therapy is required [28, 29]. Development of cardiac and vascular disease could be rapid in dialysis population, especially for the individuals with cardiovascular risk factors, e.g., diabetes or hypertension. Third, for health care practice of dialysis patients in China, dialysis access creation and complications are more often treated on an inpatient basis, especially in tertiary hospitals, while in the USA they are more often treated in the outpatient setting. Moreover, the hospital admissions for CVDs and infectious diseases in secondary and primary hospitals were more common than those in tertiary hospitals for both hemodialysis and peritoneal dialysis patients in China [10]. Analysis in this study was based on data from tertiary hospitals, which may slightly underestimate the proportions of CVDs or infectious diseases-related hospitalization.

In this study, approximately one-fourth of these patients suffered multiple hospitalizations per year, and peritoneal dialysis patients had a higher risk. Previous studies of hospital readmissions have mainly focused on 30-day readmissions between patients on home-based peritoneal dialysis and in-center hemodialysis therapy. Lin et al. [13] in our group described the higher proportion of the 30-day unplanned readmission in peritoneal dialysis population compared to hemodialysis (21.68% vs. 13.88%). A population-based cohort study of 28,026 dialysis patients in Canada indicated peritoneal dialysis patients were more likely to be readmitted within 30 days compared to hemodialysis patients (adjusted HR, 1.19; 95% CI, 1.08–1.31) [30]. However, some studies yielded conflicting results, which reported absence or small differences in readmission risks between dialysis modalities [15, 31]. Nevertheless, the view was consistent that 30-day readmissions might identify gaps in health care during patient follow-up from the inpatient to outpatient setting. Differences in performance of multiple hospitalizations could be in part due to differences in clinical practice between peritoneal dialysis and hemodialysis therapy. In-center hemodialysis patients usually visit the dialysis unit three times per week and could have earlier and broader medical care by health care staffs. In contrast, peritoneal dialysis patients interact with their health care staff in dialysis unit less frequently, usually once per month. In this study, as much as 66.88% of hospitalizations for peritoneal dialysis patients do not had specific causes of admission, which potentially represented more complex conditions and requirement of comprehensive therapy in these populations. Sanabria et al. [32] demonstrated that the use of remote patient monitoring in home-based automated peritoneal dialysis was associated with lower hospitalization rates and fewer hospitalization days, which highlighted the benefit of increased medical care interaction.

In addition, we found the comorbidities of pneumonia/COPD (OR: 0.84, 95% CI: 0.81–0.87) or other infectious disease (OR: 0.92, 95% CI: 0.88–0.96) were associated with lower odds of multiple hospitalizations per year for chronic dialysis patients. We made the following interpretations: (i) Infections are usually acute illnesses. For a patient, they would not always appear in the diagnosis lists of admission records like chronic diseases such as hypertension or diabetes mellitus. Moreover, Jencks et al. [33] reported that among patients admitted for pneumonia and COPD, the cause of readmission is the same as that of the index admission for only 29.1% and 36.2%, respectively, for the general population in the USA. Similarly, Xu et al. [15] reported that 59% of dialysis patients showed discordance between the causes of admission and readmission in Sweden. One of the main discordant transitions was from an infection-related admission to a readmission attributed to other disease. (ii) Infections usually have certain symptoms or could be recognized via regular tests of dialysis patients per month, which could result in early initiation of medical care in dialysis units or the outpatient setting. (iii) The admissions for infectious diseases in secondary and primary hospitals were more common than those in tertiary hospitals for dialysis patients in China [10].

This study analyzed the characteristics of hospitalizations among chronic dialysis patients in China using a large nationwide inpatient database HQMS with strict quality-control processes but also has limitations. First, HQMS summarized inpatient discharge records from all tertiary hospitals and did not include hospitalization information from the primary and secondary hospitals. In the absence of a standard referral system, tertiary hospitals could provide primary, secondary, and tertiary health care service to a nationwide patient population. However, patients in tertiary hospitals tend to have more severe and complex situations, which may cause certain selection bias. Second, we extracted the patients on chronic dialysis based on the diagnosis code of ICD-10 and the procedure code of ICD-9-CM-3, which was a common method to extract patients from an administrative or claims database for observational

study with relatively high specificity. However, this method may ignore those dialysis patients with no records of the dialysis diagnosis or procedure in the hospital discharge records. Third, the identification of hospital admission causes was based on the diagnosis code of ICD-10 and the procedure code of ICD-9-CM-3, but about 45% of records labelled with CKD5, ESKD, or primary causes of ESKD, rather than the information of specific reasons, thereby could impact on the further analysis. Meanwhile, hospitalizations of dialysis patients due to regular assessments could not be identified by ICD-10 or ICD-9-CM-3 codes. For example, admissions of peritoneal dialysis patients for the regular functional assessment of peritoneum by peritoneal equilibration test could not be identified and were usually enrolled in the group of nonspecific causes, which may lead to an overestimation of the proportion of peritoneal dialysis patients admitted for nonspecific reasons and for multiple hospitalizations in this study. Finally, in view of multiple hospitalizations analysis, the study population excluded the records of patients died during the index hospitalization, which may impact on the admission causes and comorbidities analysis. But only small amount of records referred to in-hospital death were identified and excluded (shown in Fig. 1), the impact was limited.

Conclusions

Our study described characteristics and revealed the burden of hospitalizations of chronic dialysis patients in China. These findings highlight the importance of effective and efficient management strategies to reduce the high burden of hospitalization in dialysis population. Moreover, the large number of chronic dialysis patients and the high proportion of hospitalizations show the need to both develop low-cost treatments and implement effective population-based prevention strategies.

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Statement of Ethics

This study was reviewed and approved by the Ethics Committee of Peking University First Hospital, approval number (No. 2015[928]). Acquisition of informed consent was exempted.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Research idea, study design, and the methodology for extracting patients and identifying diseases: H.C. and L.Z.; data analysis and statistical analysis: H.C., C.Y., Y.L., and J.W.; supervision or mentorship: L.Z., G.K., P.L., and M.Z.; manuscript writing: H.C., C.Y., and L.Z. Each author contributed important intellectual content during manuscript drafting and accepts accountability for the overall work by ensuring that questions pertaining to the accuracy or integrity of any portion of the work are appropriately investigated and resolved. All the authors have read and given final approval of the version to be published.

Data Availability Statement

The data that support the findings of this study are available from the Bureau of Medical Administration and Medical Service Supervision, National Health Commission of China but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are, however, available from the authors upon reasonable request and with permission of the Bureau of Medical Administration and Medical Service Supervision, National Health Commission of China.

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