Original Article

Association of cardiovascular disease with 30-day hospital readmission in Chinese patients receiving maintenance dialysis

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Background: Previous studies have shown cardiovascular disease (CVD) to be a risk factor in the prediction of 30-day hospital readmission among patients receiving dialysis. However, studies of Asian populations are limited. In the present study, we examined the association between CVD and 30-day hospital readmission in Chinese patients receiving maintenance dialysis.

Methods: Patients receiving maintenance dialysis were identified by searching a national claims database, the China Health Insurance Research Association (CHIRA) database, using the International Classification of Diseases revision 10 (ICD-10) and items of medical service claims. Patients aged ≥18 years who were discharged after index hospitalization between January 2015 and December 2015 were included in our retrospective analysis. CVD-related diagnoses were divided into three categories: coronary heart disease (CHD), heart failure (HF), and stroke. Thirty-day hospital readmission was defined as any hospital readmission within the 30 days following discharge. Logistic regression models adjusted for logit of propensity scores (PS) were used to assess the association of CVD with 30-day hospital readmission.

Results: Of 4,700 patients receiving dialysis, the 30-day hospital readmission rate was 10.4%. Compared with patients without CVD, there was an increased risk of 30-day hospital readmission among maintenance dialysis patients with total CVD [odds ratio (OR): 1.33, 95% confidence interval (CI): 1.06–1.66]. Patients with HF (OR: 1.77, CI: 1.27–2.47) and stroke (OR: 2.14, 95% CI: 1.53–2.98) had a greater risk of 30-day hospital readmission. The fully adjusted OR of CHD for the risk of 30-day hospital readmission was 1.22 (95% CI: 0.97–1.55).

Conclusions: CVDs, especially stroke and HF, are independent predictors of 30-day hospital readmission in Chinese patients receiving dialysis, and could help to guide interventions to improve the quality of care for these patients.

Keywords: Cardiovascular disease (CVD); dialysis; 30-day hospital readmission; China

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Introduction

High hospital readmission rates are increasingly viewed as an unnecessary drain on social and financial resources (1). The hospital readmission rate at 30 days is an important measure of care quality, and it can also be used to predict subsequent morbidity and mortality among patients with end-stage kidney disease (ESKD) (1-6). Reducing 30-day hospital readmission rates is becoming a major focus for health systems (7). The Healthcare Cost and Utilization Project Statistical Brief indicates that the 30-day readmission rate for general inpatients is 13.9% (8). Compared with other patients, those with ESKD have a higher rate of hospital readmission within 30 days (5,9,10). Data from the United States Renal Data System (USRDS) showed that the 30-day readmission rate of ESKD patients and patients receiving hemodialysis (HD) was 34.6% and 36.6%, respectively (5). In 2015, 23.2% of dialysis patients in China were readmitted within 30 days (10). Data from the urban basic health insurance (UBHI) scheme showed that HD and PD patients accounted for only 0.16% and 0.02% of the population covered by UBHI, respectively; however, their medical costs accounted for 2.08% and 0.34% of the total UBMI expenditures, respectively (5,10). The 30-day readmission rate in China, although lower than that in the USA, is still high, placing a considerable burden on patients and society (5,9).

Cardiovascular disease (CVD), a leading cause of hospitalization and death, is common among patients receiving maintenance dialysis (5,10). Accumulating evidence on dialysis patients suggests that CVD increases the risk of hospital readmission (11-14). Previous studies on HD patients have suggested that heart failure (HF) increases the risk of hospital readmission (11). Studies have shown that ischemic heart disease (IHD) and HF are associated with higher rates of hospital readmission among patients receiving peritoneal dialysis (PD) (12,13). Another study found that hospital readmission rates were higher among HD and PD patients with CVD (14). However, studies on the risk of 30-day hospital readmission in Asian populations are limited. Therefore, in the present study, we examined the association between CVD and 30-day hospital readmission in Chinese patients receiving maintenance dialysis. We present the following article in accordance with the STROBE reporting checklist (available at http://dx.doi.org/10.21037/atm-20-2367).

Methods

Study population

Hospitalization records of patients receiving maintenance dialysis who were discharged from hospital during 2015 were identified within the China Health Insurance Research Association (CHIRA) database using International Classification of Disease revision 10 (ICD-10) codes (i.e., N18.000, N18.001, and N18.900) and items of medical service claim, including hemodialyzer and PD fluid (15). The CHIRA database is a repository of claims from individuals covered by UBHI. It uses a two-stage sampling design to create a national sample of claims. It contains inpatient and outpatient whole-year medical records, and includes data on patient demographics, medical events, operation procedures, prescription drugs, and detailed medical expenditure. The CHIRA database has been described in detail previously (10).

All eligible patients included in the study were aged >18 years and were discharged after index hospitalization between January 1st, 2015 and December 31st, 2015. Patients with maintenance HD and maintenance PD were defined as having maintenance dialysis. All patients who did not receive dialysis were excluded. We also excluded patients with acute kidney failure and those with a history of kidney transplantation. Patients hospitalized without a recorded admission or discharge date, those with a length of stay >1 but <3 days, or >180 days were also excluded (14). The flow chart of patient selection is shown in *Figure 1*. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of Peking University First Hospital (approval number: 2018-25), and informed consent from patients was not required due to the secondary use of deidentified patient data and identifiable personal information not being used. The procedure was performed in accordance with all relevant guidelines and regulations.

Identification of CVD

CVD was defined using information from claims records (Tables S1-S3). This information included diagnosis, ICD-10 codes, the International Classification of Diseases, 9th revision, Clinical Modification (ICD-9-CM) procedure codes, and prescription drugs. CVD was categorized into three types: coronary heart disease (CHD), HF, and stroke.

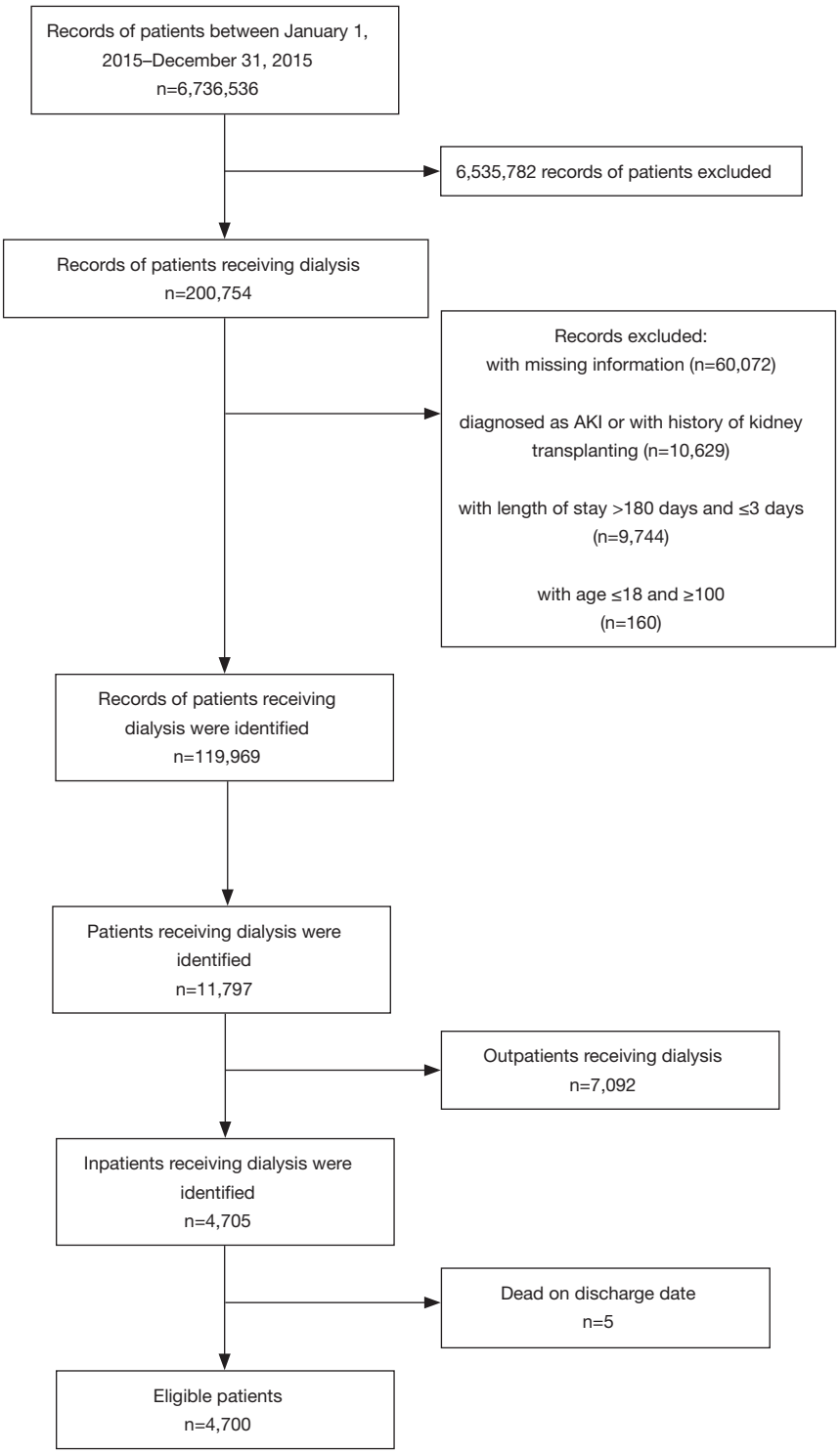

Figure 1 Selection of patients. Records represent detailed information of the medical process. Outpatients represent patients with outpatient records only. Inpatients represent patients with more than one hospitalization record.

Other covariates

Covariates included demographic characteristics (sex and age), geographic region, type of health insurance, length of stay, hospital grade, dialysis modality, weekend discharge, season of hospital admission, comorbidities (diabetes mellitus, hypertension, infection, malignant tumor, immunosuppression, airway disease, and dyslipidemia), the need for critical care, the use of proton-pump inhibitors (PPIs), the use of anticoagulant drugs, and the use of Chinese traditional medicine. Causes of index hospitalizations were identified and categorized as CVD, infectious disease, and vascular access events.

Definition of index hospital admission and 30-day hospital readmission

Hospital admission was defined as the index admission of patients with only 1 hospitalization. If a patient had ≥2 hospital admissions, the index admission used was a single admission randomly selected from the set of available admissions (15,16). This measure was used to reduce the effect on the study of dependent observations. Thirty-day hospital readmission was defined as any readmission within the 30 days following discharge.

Statistical analysis

We employed covariate adjustment using propensity scores (PS). PS are the estimated probability of having CVD based on all relevant confounding variables using a logistic regression model (17). To balance the effect of comorbidities and reduce the degrees of freedom, we reduced each of the comorbidities associated with CVD to a PS to adjust for the effect of related covariates (18). For each patient, we calculated the PS for comorbidities with a logistic regression model using the variables listed in *Table 1*. Variables were selected using previous studies of plausible associations between comorbidities and outcome. PS were used to adjust for potential confounders in the multivariable models that assessed the association between CVDs and 30-day hospital readmission.

Characteristics of dialysis patients were exemplified using descriptive statistics. Continuous variables were expressed as means (± standard deviations) or medians (25^{th} and 75^{th} percentiles), and categorical variables as proportions (%). To compare the distribution of groups, the *t*-test, analysis of variance, or the Wilcoxon rank-sum test was used for continuous variables, and the χ^2-test was used for categorical variables.

Logistic regression models were used to assess the associations between types of CVDs and 30-day hospital readmission, and the adjusted odds ratios (ORs) and 95% confidence intervals (CIs) were calculated. Covariates included in the model included age (years, continuous; years: 18–44, 45–64, 65–74, ≥75, categorical), sex (male or female), geographic distribution (northern China or southern China), hospital grade (primary, secondary, or tertiary hospital), types of health insurance (employee insurance or resident insurance), season (spring, summer, autumn, or winter), weekend hospital discharge (yes or no), length of stay (continuous), dialysis modality (HD or PD), and PS (continuous). Statistical significance in all tests was defined as a two-tailed P value of <0.05. All analyses were undertaken using SAS version 9.4 (SAS Institute, Cary, NC, USA) and R version 3.6.0.

Results

Patient characteristics

From an initial cohort of 11,797 dialysis patients, 4,700 (39.8%) eligible patients receiving maintenance dialysis were identified. Characteristics of the dialysis patients are given in *Table 1*. The 30-day hospital readmission rates for the 4,700 dialysis patients were 10.4% at the patient level and 23% at the admission level. The patients had a mean age of 56.4±15.6 years, and 44.8% were female. A total of 3,980 (84.7%) patients were receiving maintenance HD. The number of patients receiving maintenance HD with CVD was 955 (20.3%). Compared with patients without CVD, those with CHD, HF, or stroke were more likely to be aged over 45 years old (P<0.001), to be from northern China (P<0.001), and to have multiple comorbidities, including hypertension (P<0.001 *vs.* P=0.107 *vs.* P<0.001, respectively), diabetes (P<0.001 *vs.* P=0.016 *vs.* P<0.001, respectively), airway disease (P<0.001 *vs.* P=0.025 *vs.* P<0.001, respectively), and dyslipidemia (P<0.001 *vs.* P=0.001 *vs.* P<0.001, respectively). Compared to patients without CVD, those with CHD, HF, or stroke were more likely to receive PPI therapy (P<0.001 *vs.* P=0.041 *vs.* P<0.001, respectively). Patients with CVD were also more likely to be rehospitalized for CVD than for other reasons.

Comparison among patients with different types of CVDs

The rates of hospital readmission within 30 days are shown in *Table 2*. Readmission within 30 days occurred more

Table 1 Characteristics of dialysis patients by type of CVD

Variables	All patients (n=4,700)	Patients without CVD (n=3,745)	Patients with CVD					
			CHD (n=848)		HF (n=250)		Stroke (n=256)	
			N (%)/mean (SD)	P value	N (%)/mean (SD)	P value	N (%)/mean (SD)	P value
Female, n (%)	2,106 (44.8)	1,707 (45.6)	348 (41.0)	0.017	111 (44.4)	0.641	115 (44.9)	0.753
Age (years), mean (SD)	56.4 (15.6)	56.0 (15.9)	58.1 (14.5)	<0.001	58.0 (13.5)	0.753	63.4 (11.9)	0.008
Age group, n (%)				<0.001		0.018		<0.001
18–44	1,105 (23.5)	931 (24.9)	153 (18.0)		42 (16.8)		16 (6.3)	
45–64	2,052 (43.7)	1,596 (42.6)	398 (46.9)		128 (51.2)		118 (46.1)	
65–74	912 (19.4)	719 (19.2)	177 (20.9)		49 (19.6)		75 (29.3)	
≥75	631 (13.4)	499 (13.3)	120 (14.2)		31 (12.4)		47 (18.4)	
Geographic distribution, n (%)				<0.001		<0.001		<0.001
Northern China	1,127 (24.0)	782 (20.9)	317 (37.4)		88 (35.2)		103 (40.2)	
Southern China	3,573 (76.0)	2,963 (79.1)	531 (62.6)		162 (64.8)		153 (59.8)	
Types of health insurance, n (%)				<0.001		0.753		0.015
Employee	3,086 (65.7)	2,350 (62.8)	672 (79.2)		162 (64.8)		181 (70.7)	
Resident	1,614 (34.3)	1,395 (37.2)	176 (20.8)		88 (35.2)		75 (29.3)	
Weekend hospital discharge, n (%)	1,235 (26.3)	990 (26.4)	218 (25.7)	0.809	60 (24.0)	0.667	81 (31.6)	0.577
Length of stay, median [IQR]	13 [7–21]	13 [8–24]	11 [7–17]	<0.001	9 [7–15]	0.152	12 [7–19]	0.318
Dialysis modality, n (%)				<0.001		0.271		0.357
HD	3,980 (84.7)	3,231 (86.3)	656 (77.4)		208 (83.2)		225 (87.9)	
PD	720 (15.3)	514 (13.7)	192 (22.6)		42 (16.8)		31 (12.1)	
Diabetes mellitus, n (%)	1,469 (31.3)	1,098 (29.3)	349 (41.2)	<0.001	79 (31.6)	0.016	123 (48.0)	<0.001
Cancer, n (%)	169 (3.6)	150 (4.0)	16 (1.9)	<0.001	6 (2.4)	0.391	6 (2.3)	0.157
Hypertension, n (%)	3,848 (81.9)	2,947 (78.7)	826 (97.4)	<0.001	221 (88.4)	0.107	242 (94.5)	<0.001
Infection, n (%)	3,334 (70.9)	2,607 (69.6)	668 (78.8)	<0.001	196 (78.4)	0.077	197 (77.0)	0.009
Immunosuppression, n (%)	1,916 (40.8)	1,525 (40.7)	364 (42.9)	0.241	108 (43.2)	0.080	123 (48.0)	0.015
Airway disease, n (%)	928 (19.7)	683 (18.2)	233 (27.5)	<0.001	81 (32.4)	0.025	83 (32.4)	<0.001
Dyslipidemia, n (%)	1,183 (25.2)	809 (21.6)	347 (40.9)	<0.001	98 (39.2)	0.001	125 (48.8)	<0.001
Critical care, n (%)	970 (20.6)	788 (21.0)	171 (20.2)	0.568	50 (20.0)	0.918	98 (38.3)	<0.001
PPI therapy, n (%)	3,170 (67.4)	2,466 (65.9)	648 (76.4)	<0.001	182 (72.8)	0.041	213 (83.2)	<0.001
Use of anticoagulant drugs, n (%)	3,751 (79.8)	2,964 (79.1)	725 (85.5)	<0.001	182 (72.8)	0.876	222 (86.7)	0.005
Chinese traditional medicine therapy, n (%)	4,017 (85.5)	3,120 (83.3)	798 (94.1)	<0.001	246 (98.4)	0.211	240 (93.8)	<0.001
Cause of index hospitalization, n (%)				0.003		0.001		<0.001
CVD	311 (6.6)	204 (5.4)	59 (7.0)		71 (28.4)		93 (36.3)	
Infectious disease	244 (5.2)	219 (5.8)	28 (3.3)		6 (2.4)		13 (5.1)	
Vascular access events	411 (8.7)	357 (9.5)	66 (7.8)		12 (4.8)		17 (6.6)	

Data are presented as n (%) or mean (SD) or median [IQR]. CVD, cardiovascular disease; CHD, coronary heart disease; HF, heart failure; SD, standard deviation; IQR, interquartile range; HD, hemodialysis; PD, peritoneal dialysis; PPI, proton-pump inhibitor.

Table 2 Thirty-day readmission rates among dialysis patients by type of CVD

Characteristic	Patients without CVD	Patients with CVD					
		CHD		HF		Stroke	
		N (%)	P value	N (%)	P value	N (%)	P value
All, n (%)	337 (9.0)	123 (14.5)	0.032	50 (20.0)	<0.001	59 (23.0)	<0.001
Sex, n (%)			0.145		0.233		0.373
Male	192 (9.4)	77 (15.4)		30 (21.6)		34 (24.1)	
Female	145 (8.5)	46 (13.2)		20 (18.0)		25 (21.7)	
Age group, n (%)			0.017		0.049		0.031
18–44	70 (7.5)	14 (9.2)		4 (9.5)		1 (6.3)	
45–64	156 (9.8)	64 (16.1)		28 (21.9)		31 (26.3)	
65–74	59 (8.2)	26 (14.7)		12 (24.5)		14 (18.7)	
≥75	52 (10.4)	19 (15.8)		6 (19.4)		13 (27.7)	
Geographic distribution, n (%)			<0.001		<0.001		<0.001
Northern China	68 (8.7)	46 (14.6)		15 (17.0)		17 (16.5)	
Southern China	269 (9.1)	77 (14.5)		35 (21.6)		42 (27.5)	
Dialysis modality, n (%)			0.063		0.047		0.043
HD	302 (9.35)	101 (15.4)		44 (21.2)		55 (24.4)	
PD	35 (6.81)	22 (11.5)		6 (14.3)		4 (12.9)	
Diabetes mellitus, n (%)	148 (13.5)	45 (12.9)	<0.001	12 (15.2)	<0.001	35 (28.4)	<0.001
Cancer, n (%)	53 (35.33)	1 (6.3)	<0.001	3 (50.0)	<0.001	2 (33.3)	<0.001
Hypertension, n (%)	313 (10.6)	122 (14.8)	<0.001	43 (19.5)	<0.001	57 (23.6)	<0.001
Use of anticoagulant drugs, n (%)	307 (10.4)	110 (15.2)	<0.001	33 (18.1)	<0.001	53 (23.9)	<0.001
Chinese traditional medicine therapy, n (%)	317 (10.2)	118 (14.8)	<0.001	49 (19.9)	<0.001	58 (24.2)	<0.001

Data are presented as n (%). CVD, cardiovascular disease; CHD, coronary heart disease; HF, heart failure; HD, hemodialysis; PD, peritoneal dialysis.

often in dialysis patients with CVD than patients without CVD. Patients with two comorbidities (CVD and one other comorbidity, except diabetes) were significantly more likely to be readmitted than those without CVD.

CVD and the risk of 30-day hospital readmission

Table 3 shows the logistic regression analysis of three groups for 30-day hospital readmission. Compared to patients without CVD, maintenance dialysis patients with total CVD were more likely to be readmitted within 30 days (OR: 1.33, 95% CI: 1.06–1.66). Patients with HF (OR: 1.77, CI: 1.27–2.47) or stroke (OR: 2.14, 95% CI: 1.53–2.98) had a higher rate of 30-day hospital readmission. The fully adjusted OR of CHD for 30-day hospital readmission was 1.22 (95% CI: 0.97–1.55).

Discussion

To the best of our knowledge, the present study is the first to investigate the association of 30-day hospital readmission with CVD among Chinese patients receiving maintenance dialysis. Using a nationwide claims database for urban citizens in China, we found the rate of 30-day hospital readmission to be higher for patients with HF and stroke than for patients without CVD. Moreover, HF and stroke

Table 3 Association between CVD and risk of 30-day readmission in patients receiving maintenance dialysis [OR (95% CI)]

Models	Patients without CVD (n=2,221)	All CVD (n=950)	Patients with CVD		
			CHD (n=843)	HF (n=250)	Stroke (n=199)
Crude	Reference	1.78 (1.44–2.20)	1.66 (1.33–2.07)	2.34 (1.69–3.24)	2.82 (2.04–3.89)
Model 1[a]	Reference	1.75 (1.42–2.16)	1.61 (1.31–2.03)	2.31 (1.67–3.20)	2.69 (1.94–3.72)
Model 2[b]	Reference	1.33 (1.06–1.66)	1.22 (0.97–1.55)	1.77 (1.27–2.47)	2.14 (1.53–2.98)

Data are presented as ORs (95% CIs). The reference group is patients without CVD. [a], model 1 was adjusted for age and sex; [b], model 2 was further adjusted for age, sex, geographic distribution, hospital grade, types of health insurance, season of admission, weekend hospital discharge, length of stay, dialysis modality, and the probability of the PS using the following covariates: diabetes mellitus, cancer, hypertension, infection, immunosuppression, airway disease, dyslipidemia, critical care, use of PPI therapy, use of anticoagulant drugs, and use of Chinese traditional medicine. CVD, cardiovascular disease; OR, odds ratio; CI, confidence interval; CHD, coronary heart disease; HF, heart failure; PS, propensity score; PPI, proton-pump inhibitor.

could independently predict 30-day hospital readmission. These findings suggest that appropriate treatment of CVD could reduce hospital readmission among dialysis patients.

Previous studies have indicated that CVD is associated with an increased risk of 30-day hospital readmission. Using data from the Nationwide Readmission Database (NRD), Chan *et al.* found that HF leads to an increased risk of 30-day hospital readmission in patients receiving HD (11). However, the NRD only contains data from community hospitals, and information on patients whose initial admission occurred in other states is not captured by this database; therefore, the rate of hospital readmission in HD patients may be underestimated. Data from the USRDS suggests that IHD, cerebrovascular disease, and HF are associated with hospital readmission in PD patients (12). A recent study indicated that CVDs, including arteriosclerotic heart disease, congestive HF, and transient ischemic attack, could predict 30-day hospital readmission among patients receiving dialysis (14). These studies tended to focus on readmissions among patients receiving a single type (HD or PD) of continuous renal replacement therapy (12,14). In their study, Wetmore *et al.* investigated hospital readmission, focusing on patients frequently hospitalized for CVD (14).

However, despite many studies on the association of CVD with 30-day readmission, there are no studies on Chinese populations receiving maintenance dialysis. It is thought that hospital readmission in Asia is significantly different to the rest of the world (5). Therefore, we evaluated the association between CVD and 30-day hospital readmission among HD and PD patients in China. Consistent with previous studies, our study indicated an increased risk of 30-day hospital readmission for HF (1.77 times) and stroke patients (2.14 times) when compared with patients without CVD.

Several potential mechanisms may underlie the correlation observed between CVD and increased risk of 30-day hospital readmission. First, CVD is associated with an increased likelihood of other chronic diseases, such as diabetes, pulmonary circulatory disease, and chronic obstructive pulmonary disease (19), and each disease serves as a potential cause of hospitalization (20). Second, sterile inflammation that occurs after stroke can result in atherosclerosis (21-24), which, as the main factor underlying most CVDs, can result in a new CVD (25). Third, with the progression of HF, anemia can arise due to iron deficiency (26), the use of angiotensin-converting enzyme (ACE) inhibitors (27), and increased hepcidin levels (28). Low hemoglobin levels serve as an independent factor of increased risk of hospital admission among dialysis patients (29). The potential biological mechanism underlying this phenomenon requires further study.

The main strength of the present study is that it evaluated 30-day hospital readmission risk among dialysis patients with control for various potential confounding variables. However, our study also has limitations. First, similar to other studies using administrative databases, claims data may contain potential errors due to the misclassification of patients. Despite this, claims data, being real-world data, are widely-used due to their authenticity. In addition to diagnosis, we used operation procedures, prescription drugs, and detailed medical expenditure to confirm patients' conditions. Second, most patients were HD patients. Third, we did not include laboratory results, dialysis age, vascular access procedures in HD patients, outpatient dialysis unit, PD subtype, severity of

comorbidity, or other unmeasured confounders. Fourth, we did not include information about out-of-hospital deaths, which is a competing risk for hospital readmission. Fifth, we did not validate our conclusion in patients with different CHD types, and differences in the type of CHD may result in variation in prognostic outcomes. Finally, the patients in our study were beneficiaries covered by UBHI. Despite the wide coverage of UBHI in China, this raises the question of how representative our study population is.

Conclusions

CVDs, especially stroke and HF, are independent predictors of 30-day hospital readmission in Chinese patients receiving dialysis. Our findings indicate an association between CVD and 30-day hospital readmission, which may prove to be important in guiding interventions to improve quality of care. By improving medical care for CVD, the healthcare system can potentially improve outcomes and significantly reduce healthcare costs. Further intervention studies seeking to improve CVD care quality are required.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at http://dx.doi.org/10.21037/atm-20-2367

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/atm-20-2367). RC, CY, HC, JW, BG, LL, YJ, YL, JW, GK, FW, LZ, and M Zhao report grants from the National Natural Science Foundation of China, Peking University, the Ministry of Science and Technology of the People's Republic of China, the University of Michigan Health System-Peking University Health Science Center Joint Institute for Translational and Clinical Research, and Peking University First Hospital. The other author has no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by The Ethics Committee of Peking University First Hospital (No. 2018-25). Informed consent from patients was not required due to the secondary use of deidentified patient data and identifiable personal information not being used. The procedure was performed in accordance with all relevant guidelines and regulations.

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Supplementary

Table S1 Codes used to identify records of patients with CVD

Index condition	ICD-10-CM diagnosis codes
CHD	I20.001, I20.002, I20.003, I20.004, I20.005, I20.101, I20.801, I20.804, I20.806, I20.807, I21, I22, I23, I24, I25
HF	I50.003, I50.001, I50.005, I50.000x006, I50.100, I50.100, I50.102, I50.103, I50.107, I50.000, I50.907, I50.908, I50.900, I97.100x004, P29.000, I11.001, I11.000, I11.900, I13.000, I13.200, I50.900x017, I97.102, I97.803, I50.103, I50.901, P29.001, I50.900x018, I50.102, J81xx02, O99.417, O99.429, O75.403, O99.423, O99.402, O99.507, O29.102, O74.202, O75.402, O89.102, I50.901, I50.902, I50.903, I50.904, I50.905, I50.900x007, I50.900x008, I50.900x009, I50.900x010, R57.901, J81.x00, R57.000, J96.102
Stroke	I60, I61, I63, I64, I69, H34.1, G45

CVD, cardiovascular disease; CHD, coronary heart disease; HF, heart failure; ICD-10-CM, International Classification of Diseases, 10th revision, Clinical Modification.

Table S2 Operation codes used to identify records of patients with CVD

Index condition	Operation	ICD-9-CM procedure codes	
		Beijing edition	Clinic edition
CHD	CAG	88.55001, 88.56001, 88.57002	88.5500, 88.5500x02, 88.5600, 88.5600x002, 88.5700, 88.5701, 88.5700x003, 88.5900
	PCI	36.06003, 36.06004, 36.07003	36.0600. 36.0601, 36.0602, 36.0700, 36.0700x004, 36.0701
	CABG	36.1101, 36.1201, 36.1301, 36.1401, 36.1501, 36.1601, 36.1701, 36.2001	

CVD, cardiovascular disease; CHD, coronary heart disease; CAG, coronary angiography; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; ICD-9-CM, International Classification of Diseases, 9th revision, Clinical Modification.

Table S3 Prescription drugs categories used to identify records of patients with CVD

Index condition	Drug category
CHD	Organic nitrate esters
HF	Cardiac glycosides, phosphodiesterase inhibitors, adrenergic, and dopaminergic drugs
Stroke	Antihypertensive agents, almitrine-raubasine combination, calcium channel blockers, antimelancholic agents, peripheral vasodilators, antivertigo medication

CVD, cardiovascular disease; CHD, coronary heart disease; HF, heart failure.

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