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Comparison of the risk of de novo cardiovascular disease between hemodialysis and peritoneal dialysis in patients with end-stage renal disease

I-Kuan Wang [a,b,c], Chi-Yu Lu [d], Cheng-Li Lin [e], Chih-Chia Liang [c], Tzung-Hai Yen [f,g], Yao-Lung Liu [c], Fung-Chang Sung [a,e,*]

[a] Graduate Institute of Clinical Medical Science, China Medical University College of Medicine, Taichung, Taiwan
[b] Department of Internal Medicine, China Medical University College of Medicine, Taichung, Taiwan
[c] Division of Nephrology, China Medical University Hospital, Taichung, Taiwan
[d] Department of Biochemistry, College of Medicine Kaohsiung Medical University, Kaohsiung, Taiwan
[e] Management Office for Health Data, China Medical University Hospital, Taichung, Taiwan
[f] Division of Nephrology, Chang Gung Memorial Hospital, Taipei, Taiwan
[g] Chang Gung University College of Medicine, Taoyuan, Taiwan

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ABSTRACT

Background: The purpose of the study was to compare the risk of de novo cardiovascular disease (CVD) between hemodialysis (HD) and peritoneal dialysis (PD) in patients with incident end-stage renal disease (ESRD).
Methods: From a Taiwanese universal insurance claims database, we identified 45309 incident ESRD patients without preexisting CVD from 2000 to 2010. Using the propensity score matching method, we included 6516 patients in HD and PD groups, respectively. All patients were followed up until the end of 2011. The Cox proportional hazards regression model was employed to calculate the impact of dialysis modality on the risk of new onset cardiovascular events including ischemic heart disease, and congestive heart failure (CHF).
Results: No difference was observed in the overall risk of de novo ischemic heart disease between the propensity score-matched HD and PD groups (HD versus PD, adjusted hazard ratio [HR]: 1.03, 95% confidence interval [CI]: 0.86–1.22). However, HD was associated with a higher risk of de novo CHF (adjusted HR: 1.29, 95% CI: 1.13–1.47) than PD was. The risk of de novo CHF was particularly high in the first year under dialysis treatment for propensity score-matched HD patients, compared to PD patients.
Conclusions: No difference was observed in the overall risk of de novo major ischemic heart events between HD and PD patients. However, HD was associated with a higher risk of de novo CHF than PD in the first year under dialysis treatment.

1. Introduction

Cardiovascular disease (CVD) is the leading cause of mortality in patients with end-stage renal disease (ESRD), accounting for 40%–50% of all deaths [1,2]. Patients receiving long-term dialysis are at a 10–20 times higher risk of CVD-related mortality than the general population [3]. Traditional cardiovascular risk factors, such as diabetes mellitus, hypertension, and dyslipidemia, are highly prevalent in long-term dialysis patients. In addition, nontraditional unique risk factors associated with uremic environment and dialysis procedure itself may predispose dialysis patients to CVD [4].

Dialysis modality may affect the outcomes of patients with ESRD [5–13]. Compared with hemodialysis (HD) patients, peritoneal dialysis (PD) patients may have an early survival advantage during the first 1–2 years and a higher risk of death thereafter [13,14]. In addition, however, PD is also associated with an increased risk of death in older patients, and those with comorbidity [5,7–9,12,14]. HD patients may be at a higher risk of CVD because of interdialytic fluid accumulation, greater hemodynamic change and hyperdynamic circulation induced by rapid ultrafiltration and arteriovenous fistula [15,16]. Conversely, PD patients may potentially be at a lower cardiovascular risk because of less shift of fluid and electrolytes, and better preservation of residual renal function [17,18]. However, PD patients receive glucose-based solutions, resulting in higher risk of insulin resistance, dyslipidemia, and metabolic syndrome [19]. Both treatment modalities trigger chronic inflammatory responses, resulting in malnutrition and atherosclerosis [20].

* Corresponding author at: China Medical University College of Medicine, 91 Hsueh Shih Road, Taichung 404, Taiwan.
E-mail address: fcsung1008@yahoo.com (F.-C. Sung).

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Few studies have explored the impact of dialysis modality on the development of CVD [21,22]. Thus, the purpose of the current study was to compare the risk of de novo CVD between PD and HD in patients with incident ESRD by using claims data from the Taiwanese National Health Insurance (NHI) program. We used the propensity score (PS) matching method to reduce potential selection bias.

2. Methods

2.1. Data source

The NHI is a universal insurance program established in 1995 by the Taiwanese Department of Health. This program covers more than 99% of the 23.7 million residents of Taiwan [23]. Diagnoses are based on International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes. The high reliability of the diagnostic codes of this database has been reported [24,25].

2.2. Study population

In this retrospective population-based cohort study, we included patients newly diagnosed with ESRD from 2000 to 2010 and who were on dialysis for 3 months or longer. The date of the first dialysis was defined as the index date to initiate the follow-up process. Patients who were followed-up for less than 90 days were excluded from this study. We also excluded patients who had a history of coronary artery disease (CAD) (ICD-9-CM Codes 410–413, 414.01–414.05, 414.8, and 414.9), congestive heart failure (CHF) (ICD-9-CM Codes 428, 398.91, and 402.x1), or transplantation before the index date.

ESRD patients were classified into HD and PD cohorts on the basis of the dialysis modality at day 90 after the first dialysis session. Additional PD and PS-matched HD cohorts were formed. Logistic regression was used to estimate the probability of the treatment assignment by calculating the PS. Baseline variables for calculating the PS included the year of dialysis initiation, age, sex, medication use including aspirin and clopidogrel, and comorbidities including stroke (ICD-9-CM Codes 430–438), hyperlipidemia (ICD-9-CM Code 272), hypertension (ICD-9-CM Codes 401–405), diabetes (ICD-9-CM Code 250) and peripheral arterial occlusive disease (PAOD) (ICD-9 codes 440.0, 440.2, 440.3, 440.8, 440.9, 443, 444.0, 444.22, 444.8, 447.8, 447.9). All patients with ESRD were followed-up from the date of the first dialysis session to the occurrence of cardiovascular events, renal transplantation, death, withdrawal from the insurance program, or the end of 2011. Patients were not censored as the dialysis modality switched. Cardiovascular events included ischemic heart disease (having acute coronary syndrome [ICD-9-CM Codes 410, 411.1, 411.8], undergoing coronary artery bypass graft surgery, or receiving percutaneous coronary intervention treatment), and CHF (ICD-9-CM Codes 428, 398.91, and 402.x1).

2.3. Independent variables

The comorbidities before the index date were recorded, and the covariates included sex, age, stroke, hyperlipidemia, hypertension, diabetes, and PAOD. In addition, the year of dialysis initiation, baseline aspirin and clopidogrel use were analyzed between the HD and the PD patients.

2.4. Ethics statement

The National Health Research Institutes encrypts the personal information of patients to protect their privacy and provides researchers with anonymous identification numbers associated with relevant claim information. This study was approved by the Institutional Review Board (IRB) of China Medical University (CMU-REC-101-012). Because this study involved retrospective review of existing data, the IRB specifically waived the need for informed consent.

2.5. Statistical analysis

Two statistical methods were used to compare the risk of cardiovascular events (ischemic heart disease, or CHF) between the PD and HD groups. One method employed a non-matching design, and the other method employed a PS-matching design. Hazard ratios (HRs) and 95% confidence intervals (CIs) were calculated using the Cox proportional hazards regression model. Furthermore, we considered death as a competing risk for estimating the risk of cardiovascular events. The multivariate competing-risk regression model was used to estimate the risk of cardiovascular events. Baseline characteristics were compared using the Chi-square test for categorical variables and the *t* test for continuous variables. Incidence rates of cardiovascular events were calculated for both cohorts (per 1000 person-years). The Kaplan–Meier method was used to plot the cumulative proportion of the subjects who experienced cardiovascular events (ischemic heart disease, and CHF) during the follow-up period, and the log-rank test was used to assess the differences between these curves. All statistical analyses were performed using SAS statistical software (Version 9.3 for Windows; SAS Institute, Inc., Cary, NC, USA). The statistical significance was set at a two-tailed *P* value less than 0.05.

3. Results

3.1. Characteristics of the study patients

Table 1 lists the baseline characteristics and comorbidity statuses of the patients in all dialysis patients and the PS-matched cohorts. We identified 45,309 patients with newly diagnosed ESRD and without pre-existing CVD, who underwent initial dialysis between 2000 and 2010 and included them in the non-matched cohorts. Similarly, 6516 patients in the HD group were matched with 6516 PD patients according to the PS. In non-matching cohorts, the mean age in the HD group was 59.3 ± 14.1 years and 49.7 ± 14.2 years in the PD group, respectively. In the PD group, 51.7% of the subjects were ≤49 years of age. Stroke, diabetes, PAOD, aspirin use, and clopidogrel use were more prevalent in the HD group than in the PD group.

In the PS-matched cohorts, the distribution of age was similar, and younger patients were predominant (approximately 77% of patients were aged <60 years). Women were predominant (approximately 55%). No significant differences were observed for age, sex, comorbidity and medication statuses between the PD and the PS-matched HD groups.

3.2. Incidence rate and hazard ratio of cardiovascular events

The overall incidence densities of ischemic heart disease, and CHF were higher in the HD group than in the PD group (13.2 vs. 9.35, and 24.6 vs. 15.7 per 1000 person-years, respectively) (Table 2) in the non-matching cohorts. No statistically significant difference was observed in the overall risk of ischemic heart disease between patients in the HD and PD groups (Tables 2 and 3). The risk of CHF in the HD group was significantly higher by 38% and 29% than that in the PD group using these two methods (95% CI = 1.24–1.53, and 95% CI = 1.13–1.47, respectively) (Table 2). In the competing-risk regression model, the risk of CHF remained significantly higher in the HD cohort (adjusted HR = 1.60, 95% CI = 1.44–1.78) among the non-matching cohorts (Table 3). Similar trends were observed in PS-matched cohorts. Table S1 shows the results of stratification by age, gender, comorbidity, and medicine use in the PS-matched cohorts. Among patients without hypertension, the risk of ischemic heart disease in PS-matched HD patients was 3.13-fold higher than that in the corresponding PD patients (95% CI = 1.00–9.76, $P < 0.05$). The risk of CHF in PS-matched HD patients was significantly higher than that in the PD patients in the age groups of 50–59 and 60–69 years. Compared with the PD group, the adjusted HRs of CHF for women in the PS-matched HD group was 1.48 in