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Epidemiologic features and long-term outcome of dialysis patients with infective endocarditis in Taiwan

Ming-Ting Chou [a,b,1], Jhi-Joung Wang [c,1], Wen-Shiann Wu [a,b,1], Shih-Feng Weng [c,d], Chung-Han Ho [c,d], Zhe-Zhong Lin [a], Tain-Junn Cheng [e,f], Chih-Chiang Chien [g,h,*]

[a] Department of Cardiology, Chi-Mei Medical Center, Tainan, Taiwan
[b] The Center of General Education, Chia-Nan University of Pharmacy and Science, Tainan, Taiwan
[c] Department of Medical Research, Chi-Mei Medical Center, Tainan, Taiwan
[d] Department of Hospital and Health Care Administration, Chia Nan University of Pharmacy and Science, Tainan, Taiwan
[e] Department of Neurology, Occupational Medicine, Medical Information Management, Chi Mei Medical Center, Tainan, Taiwan
[f] Department of Occupational Safety and Health, Institute of Industrial Safety and Disaster Prevention, College of Sustainable Environment, Chia-Nan University of Pharmacy and Science, Tainan, Taiwan
[g] Department of Nephrology, Chi-Mei Medical Center, Tainan, Taiwan
[h] Department of Food Nutrition, Chung Hwa University of Medical Technology, Tainan, Taiwan

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ABSTRACT

Background: The incidence of infective endocarditis (IE) is high in dialysis patients. Limited data are available on the risk factors for IE and long-term outcome after IE in dialysis patients, especially in Asian populations.
Methods: We used Taiwan National Health Insurance Research Database to design a longitudinal cohort study. 68,426 ESRD patients who began dialysis between 1999 and 2007 were included. The follow-up period was from the start of dialysis to death, end of dialysis, or end of 2008. Cox proportional hazards models were used to identify the risk factors for IE.
Results: IE was diagnosed in 502 patients during follow-up (201.4 per 100,000 person-years). Diabetes mellitus (DM), congestive heart failure (CHF), cerebro-vascular accident (CVA), and rheumatic heart disease (RHD) (HR: 3.07, 95% CI: 1.99–4.75) were associated with an increasing risk of development of IE. The cumulative incidence rate of IE in patients with RHD was 1.4, 2.2, and 3.9% at 1, 3, and 5 years. In-hospital mortality was 23.5%. Cumulative survival rates post-IE were 54.3% at 1 year and only 35.3% at 5 years.
Conclusion: Dialysis patients had a higher risk of IE. Those who were older and had DM, CHF, CVA, or especially RHD were at a greater risk. Dialysis patients with IE also had high mortality.

1. Introduction

The incidence of mortality and morbidity in dialysis patients is a major global concern because their effect on public health is greater than previously thought [1]. The trend of hospitalization due to infection increases in recent years [1]. Infection is second only to cardiovascular disease as the leading cause of death in patients with end-stage renal disease (ESRD); it occurs in approximately 12–22% of patients [2]. Infective endocarditis (IE) is one of the infectious diseases that always has a high mortality rate unless it is appropriately treated [3].

Chronic rheumatic heart disease (RHD), which was a prime risk factor for IE in the pre-antibiotic era, is now rare in industrialized countries [4]. However, it continues to be a disease with high prevalence in some developing countries [5]. Even in more industrialized places, namely, Hong Kong and Thailand, RHD was found in 18% and 12%, respectively, of cases of IE [6]. Therefore, RHD probably has a different effect on the occurrence of IE in ESRD patients in Asia and western countries. The cumulative incidence of IE in dialysis patients has been estimated [7] to be approximately 267 cases/100,000 person-years which is much higher than that in the general population. In a study using the United States Renal Data System (USRDS) database, the in-hospital mortality rate was 23.5% and 1-year mortality was 61.6% [8].

The incidence and prevalence rates of patients with ESRD on dialysis are high in Taiwan [9]. In addition, RHD is still an ongoing problem in Asia [6]. However, limited data are available on the risk factors for IE and long-term outcome after IE in ESRD dialysis patients, especially in the Asian population. The purpose of this study was to determine the long-term outcome of dialysis patients hospitalized for IE in Taiwan.

* Corresponding author at: Department of Nephrology, Chi-Mei Medical Center, and Department of Food Nutrition, Chung Hwa University of Medical Technology, 901 Jung-Hua Road, Yung Kang District, Tainan City 710, Taiwan.
E-mail address: ccchien58@yahoo.com.tw (C.-C. Chien).
[1] Ming-Ting Chou, Jhi-Joung Wang and Wen-Shiann Wu contributed equally and are also first authors for this article.

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Using data from 1999 to 2007 in the Taiwan National Health Insurance Research Database (NHIRD) database, we investigated the epidemiologic features and outcome of IE in dialysis patients.

2. Research design and methods

2.1. Database

Taiwan's National Health Insurance (NHI) program has provided compulsory universal health insurance since 1995. With the exception of prison inmates, all citizens are enrolled in the program. All contracted medical institutions must submit standard computerized claim documents for medical expenses. Patients with ESRD are eligible for any type of renal replacement therapy free of any charge. All patients on chronic dialysis are covered by NHI.

Data were obtained from the NHIRD (Bureau of National Health Insurance; www.doh.gov.tw/statistic/index.htm [in Chinese]; http://www.doh.gov.tw/EN2006/ index_EN.aspx [in English]) and released for research by the Taiwan National Health Research Institute. The NHIRD covers nearly all (99%) inpatient and outpatient medical benefit claims for Taiwan's 23.3 million residents, is one of the largest and most comprehensive databases in the world, and has been used extensively in various studies [10–14]. Patient identification numbers, gender, birthdate, dates of admission and discharge, medical institutions providing the services, the ICD-9-CM diagnostic and procedure codes (up to five each), and outcomes are encrypted. This study tapped the NHIRD for ambulatory care claims, all inpatient claims, and the updated registry for beneficiaries from 1998 to 2008 for this study. All data sets can be interlinked.

2.2. Patient selection and definition

This longitudinal cohort study selected all adult (≥18 years old) patients with ESRD on maintenance dialysis who began renal replacement therapy between January 1, 1999 and December 31, 2007. Maintenance dialysis was defined as having undergone dialysis for more than 90 days. Patients were followed-up from the first reported date of dialysis to the date of death, end of dialysis, or December 31, 2008.

The inpatient claims include the records of all hospitalizations and provide a substantial amount of information. We linked the study subjects to the inpatient claim data to identify the first episode of IE (ICD-9 codes 421.0, 421.1, and 421.9) after the initiation of dialysis. During the follow-up period, 502 patients were diagnosed with IE.

2.3. Determining the demographic and comorbid variables

We linked to the diagnostic codes through the inpatient and outpatient claim databases of the NHI. We included not only survival status, but also date of death, patient demographics, and baseline comorbidities. Baseline comorbidities – listed by ICD-9 code — diabetes mellitus (DM) (250, 357.2, 362.0X, 366.41), congestive heart failure (CHF) (428, 398.91, 422, 425, 402.X1, 404.X1, 404.X3), coronary artery disease (CAD) (410–414), cerebrovascular accident (CVA) (430–438), other cardiac diseases (420–421; 423–424; 429; 785.0–785.3), valvular heart disease (424.0–424.3), rheumatic heart disease (391, 392.0, 393–398) – are important factors affecting episodes of IE and were assessed at the start of dialysis. Which comorbidities the patients had was determined by whether they fit one of the following two definitions: (1) diagnostic codes from outpatient visits if the patient had an initial diagnosis at any time in the 1 year before the start of dialysis and then had one or more additional diagnoses within the subsequent 12 months. The first and the last outpatient visit within 1 year had to have been >30 days apart to avoid accidental inclusion of miscoded patients; (2) diagnostic codes in hospitalization databases at least once in 1 year before the start of dialysis. The accuracy of the diagnoses of major disease in the NHIRD has been validated [15,16]. In addition, the methods of identifying these comorbidities have been extensively employed in various studies using the Taiwan NHIRD as a data source, and many articles based on these studies have been published [10–14].

2.4. Statistical analysis

The incidence of newly diagnosed IE is expressed as the number of cases of IE per 100,000 person-years. A parametric Pearson's χ^2 test was used to compare each variable in the groups of patients with and without IE. Age was entered as a categorical variable (18–44, 45–64, and ≥65 years). Significance was set at $p < 0.05$. The cumulative proportions of patients with IE and of survivors after IE were calculated using the Kaplan–Meier method. The log rank test was used to analyze significance. Cox proportional hazards models were used to identify the risk factors of IE. Hazard ratios (HRs) and 95% confidence intervals (CIs) were derived from Cox proportional hazards models, which met the assumption of the proportionality of risks. SPSS 17.0 for Windows (SPSS Inc; Chicago, IL, USA) was used for all statistical analyses.

3. Results

3.1. Demographics and clinical characteristics

We enrolled 68,426 adult patients with incident dialysis. During the 9-year follow-up, 502 (0.73%) patients developed IE (men: 236 [0.7%]; women: 266 [0.8%]; p = 0.486) (Table 1). The incidence rate of IE was 201.4/100,000 person-years. There incidence rate of IE increased over the study period (range: 158.81/100,000 person-years [between 1999

Table 1
Patient characteristics and association with (n = 502) and without (n = 67,924) infective endocarditis in end-stage renal disease dialysis patients.

	Without IE (n = 67,924)		With IE (n = 502)		p
	n	(%)	n	(%)	
Gender					0.486
Female	34,933	(51.4)	266	(53.0)	
Male	32,991	(48.6)	236	(47.0)	
Age (years) mean ± SD	60.11 ± 14.06		62.12 ± 13.09		0.007
Age (years)					<0.001
18–44	9689	(14.3)	42	(8.4)	
45–64	29,604	(43.6)	216	(43.0)	
≥65	28,631	(42.2)	244	(48.6)	
Dialysis modality					0.003
PD	5078	(7.5)	20	(4.0)	
HD	62,846	(92.5)	482	(96.0)	
Diabetic mellitus					<0.001
No	33,955	(50.0)	204	(40.6)	
Yes	33,969	(50.0)	298	(59.4)	
Congestive heart failure					<0.001
No	50,907	(74.9)	330	(65.7)	
Yes	17,017	(25.1)	172	(34.3)	
Coronary artery disease					<0.001
No	52,325	(77.0)	352	(90.1)	
Yes	15,599	(23.0)	150	(29.9)	
Cerebrovascular disease					0.023
No	59,519	(87.6)	423	(84.3)	
Yes	8405	(12.4)	79	(15.7)	
Other cardiac diseases[a]					<0.001
No	61,975	(91.2)	434	(86.5)	
Yes	5949	(8.8)	68	(13.5)	
Valvular heart disease					0.001
No	66,669	(98.2)	483	(96.2)	
Yes	1255	(1.8)	19	(3.8)	
Rheumatic heart disease					<0.001
No	67,130	(98.8)	480	(95.6)	
Yes	794	(1.2)	22	(4.4)	

IE, infective endocarditis; HD, hemodialysis; PD, peritoneal dialysis; SD, standard deviation.

[a] Includes pericarditis, endocarditis, myocarditis, other complications of heart disease, heart transplant, heart valve replacement, and cardiac devices.