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Association of Statin Use With Mortality After Dialysis-Requiring Acute Kidney Injury: A Population-Based Cohort Study

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Abstract

Objective: To investigate the association between statin use and mortality in patients with dialysis-requiring acute kidney injury (AKI-D).

Patients and Methods: This nationwide, population-based, retrospective cohort study included 6091 hospitalized patients with AKI-D (1271 statin users and 4820 statin nonusers) retrieved from the National Health Insurance Research Database of Taiwan between January 1, 2000, and December 31, 2012. All the patients were followed up until December 31, 2013. Primary and secondary outcomes were 1-year and in-hospital mortality, respectively. All the primary analyses were performed using the intention-to-treat approach.

Results: During 1-year follow-up, 492 of 1271 statin users (38.7%) and 2365 of 4820 statin nonusers (49.1%) died. After propensity score matching, statin use was independently associated with lower risks of 1-year all-cause mortality (hazard ratio [HR], 0.79; 95% CI, 0.69-0.9; $P<.001$) and in-hospital all-cause mortality (HR, 0.84; 95% CI, 0.71-0.99; $P=.04$). The survival benefit of statin treatment was dose-dependent and consistent across subgroups based on sensitivity analyses.

Conclusion: Statin use was independently associated with reduced risks of 1-year and in-hospital mortality in patients with AKI-D. Statin therapy may be beneficial in this patient group. However, further clinical trials should be performed to confirm the findings.

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Acute kidney injury (AKI) is a severe condition characterized by a rapid decline in renal function, and it has become an increasing global health concern.[1] Acute kidney injury can be diagnosed in outpatient settings, emergency departments, or hospitals and is associated with high in-hospital and postdischarge mortality rates.[2,3] Moreover, AKI survivors have higher risks of developing chronic kidney disease (CKD) and other morbidities, such as cardiovascular diseases (CVDs),[4] severe sepsis,[5] and upper gastrointestinal bleeding,[6] causing a substantial economic burden to society.

Statins are effective in reducing low-density lipoprotein cholesterol levels.[7] Moreover, these drugs reduce mortality in both primary and secondary prevention.[8,9] Currently, statins are used as first-line treatment for the prevention of CVDs in high-risk individuals, such as patients with previous CVD, diabetes mellitus, and CKD.[10,11]

Data on whether statin use improves the survival of patients with AKI are limited. Its use may be associated with recovery from AKI after a major surgery, and it may also have a beneficial effect on long-term survival.[12] A recent meta-analysis also reported that statin use may prevent AKI and reduce the risk of mortality in patients undergoing cardiac surgery.[13] However, Murugan et al[14] reported that statin use was not associated with a lower risk of 1-year mortality in patients with community-acquired pneumonia and AKI. The effect of statins on the mortality of patients with AKI has not been validated. Furthermore, the association between statin use and the risk

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of mortality in patients with dialysis-requiring AKI (AKI-D), who are at the highest risk of death during hospital admission or after discharge, has not been examined.[15] Thus, we conducted a nationwide observational cohort study to assess the effect of statin use on the mortality of patients with AKI-D.

PATIENTS AND METHODS

Data Source

This study included patient information from the National Health Insurance Research Database (NHIRD) of Taiwan, which includes the health care data of more than 99% of the Taiwanese population. One million patients were randomly selected from the NHIRD. Deidentified and encrypted data were obtained on demographic characteristics, geographic distribution, outpatient visits, emergency department visits and hospital admissions, diagnostic codes based on the *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)*, drug prescriptions, and medical procedures, and these data were longitudinally linked from 1996 through 2013. This study was exempted from full ethical review and was approved by the institutional review board of Changhua Christian Hospital.

Study Design and Participants

From January 1, 2000, through December 31, 2012, we identified 9374 patients who were diagnosed as having AKI (*ICD-9-CM* codes 584.x, 634.3, 635.3, 636.3, 637.3, 638.3, 639.3, 669.3, and 958.5) and underwent dialysis during hospitalization, and these patients were monitored until December 31, 2013, to ensure follow-up of at least 1 year for each patient. We excluded 3283 patients (35%) who were younger than 18 years or older than 100 years, who underwent dialysis because of CKD or kidney transplant, who experienced events of AKI, and who had prolonged hospitalization (>365 days) and those with missing demographic or inpatient information. The remaining 6091 patients (65%) who experienced AKI-D for the first time were selected for further analysis. Among them, those who received statins within 90 days before their index hospitalization because of AKI-D were considered statin users, and the remaining patients were considered statin nonusers

TABLE 1. Baseline Characteristics of the Study Population Stratified by Statin Use[a,b]

Characteristic	Statin nonusers (n = 4820)	Statin users (n = 1271)	*P* value[c]
Demographic features			
Age (y), mean ± SD	65.5±16.1	66.3±13.0	.10
Male sex (No. [%])	2749 (57.0)	656 (51.6)	.001
Monthly income (NTD), mean ± SD	12,091.7±12,196.7	11,768.6±11,824.5	.40
Geographic location (No. [%])			
Northern Taiwan	2184 (45.3)	594 (46.7)	.38
Central Taiwan	894 (18.6)	211 (16.6)	.12
Southern Taiwan	1598 (33.2)	438 (34.5)	.41
Eastern Taiwan and islands	144 (3.0)	28 (2.2)	.16
Preexisting comorbidities (No. [%])			
Hypertension	3401 (70.6)	1132 (89.1)	<.001
Hyperlipidemia	615 (12.8)	714 (56.2)	<.001
Diabetes mellitus	2052 (42.6)	993 (78.1)	<.001
CAD	1170 (24.3)	598 (47.1)	<.001
CHF	1292 (26.8)	525 (41.3)	<.001
Stroke	889 (18.4)	290 (22.8)	<.001
PAOD	150 (3.1)	75 (5.9)	<.001
CKD	2617 (54.3)	913 (71.8)	<.001
Advanced CKD[d]	1202 (24.9)	345 (27.1)	.11
COPD	968 (20.1)	231 (18.2)	.13
Malignancy	627 (13.0)	91 (7.2)	<.001
CCIS, mean ± SD	4.1±2.7	5.2±2.4	<.001
In-hospital acute comorbidities (No. [%])			
Radiographic contrast media exposure	1188 (24.7)	220 (17.3)	<.001
Cardiac catheterization	169 (3.5)	179 (14.1)	<.001
ICU admission	2800 (58.1)	723 (56.9)	.44
CRRT use	744 (15.4)	178 (14.0)	.21
Acute organ dysfunction			
Acute respiratory organ dysfunction	425 (8.8)	90 (7.1)	.048
Acute cardiovascular organ dysfunction	68 (1.4)	15 (1.2)	.53
Acute hepatic organ dysfunction	25 (0.5)	4 (0.3)	.35
Acute hematologic organ dysfunction	4 (0.1)	0	.30
Acute neurologic organ dysfunction	19 (0.4)	3 (0.2)	.40
Acute metabolic dysfunction	10 (0.2)	1 (0.1)	.34
Operation categories			
Cardiothoracic	320 (6.6)	128 (10.1)	<.001
Hepatobiliary	106 (2.2)	9 (0.7)	.001
Upper gastrointestinal	170 (3.5)	18 (1.4)	<.001
Lower gastrointestinal	82 (1.7)	12 (0.9)	.05
Medications (No. [%])			
Antidiabetic agents	1750 (36.3)	915 (72.0)	<.001
Antihypertensive drugs	3469 (72.0)	1175 (92.5)	<.001

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