

Dipyridamole decreases dialysis risk and improves survival in patients with pre-dialysis advanced chronic kidney disease

SUPPLEMENTARY MATERIALS

Supplementary Table 1: The formula of propensity scores in logistic model

	coefficient	Standard error	Odds ratio	95% lower confidence interval	95% upper confidence interval	P value
Age, y	-0.00305	0.0011	0.997	0.995	0.999	0.0056
Male vs. female	-0.039	0.0279	0.962	0.911	1.016	0.1621
Comorbid condition with in the 3 preceding the index date						
Diabetes	0.112	0.0336	1.119	1.047	1.195	0.0009
MI	-0.1343	0.0325	0.874	0.82	0.932	<.0001
Stroke	0.0421	0.0376	1.043	0.969	1.123	0.2629
Cancer	0.2743	0.0503	1.316	1.192	1.452	<.0001
CCI score	-0.0435	0.0074	0.957	0.944	0.971	<.0001
Nephrologist visits within the 3 y preceding the index date						
0	1	1	1	-	-	
1–6	0.0635	0.0399	1.066	0.985	1.152	0.1115
> 6	0.0734	0.0361	1.076	1.003	1.155	0.0418
Anti-hypertensive agents used						
ACEI	-0.2652	0.0326	0.767	0.72	0.818	<.0001
ARB	0.093	0.0287	1.097	1.037	1.161	0.0012
Beta-blockers	-0.0219	0.0326	0.978	0.918	1.043	0.5004
Calcium channel blockers	0.0553	0.0283	1.057	1	1.117	0.0504
Diuretics	-0.0239	0.0326	0.976	0.916	1.041	0.464
Pentoxifylline	0.2839	0.0394	1.328	1.23	1.435	<.0001
Insulin	0.2212	0.0368	1.248	1.161	1.341	<.0001
Statin	-0.0232	0.0378	0.977	0.907	1.052	0.5402
Aspirin	0.0184	0.0358	1.019	0.949	1.093	0.6077
Acetaminophen	0.0147	0.0284	1.015	0.96	1.073	0.6043
NSAIDs						
COX-2 inhibitors	-0.1039	0.0298	0.901	0.85	0.956	0.0005
Non-COX-2 inhibitors	-0.0428	0.0636	0.958	0.846	1.085	0.501
Geographic location						
Northern	1	1	1	-	-	
Middle	-0.274	0.0346	0.76	0.71	0.814	<.0001
Southern	0.1503	0.0323	1.162	1.091	1.238	<.0001
Eastern or other islands	0.405	0.109	1.499	1.211	1.856	0.0002

ACEI = angiotensin converting enzyme inhibitor. ARB = angiotensin II receptor blocker. CCI = Charlson comorbidity index. COX-2 = cyclooxygenase -2. MI = myocardial infarction. NSAID = non-steroidal anti-inflammatory drug.

Supplementary Table 2: Risks of long-term dialysis and death in pre-dialysis stage 5 CKD patients with dipyridamole exposure within 30 days and observation period beginning 30 days after the index date

	Before Matching				After Matching		
	N of events	Incidence rate (100 person-years)	Crude HR (95% CI)	Adjusted HR (95% CI)	N of events	Incidence rate (100 person-years)	Adjusted HR (95% CI)
Long-term dialysis							
Dipyridamole nonuser	19,622	79.94	1.0 (reference)	1.0 (reference)	14,160	77.62	1.0 (reference)
Dipyridamole user	7,685	76.12	0.97 (0.94–0.99)*	0.99 (0.96–1.01)	7,511	76.60	0.98 (0.96–1.01)
< 140 DDD	4,086	83.83	1.06 (1.02–1.10)*	1.10 (1.06–1.14)*	3,995	84.53	1.10 (1.06–1.14)*
≥ 140 DDD	3,599	68.93	0.88 (0.85–0.91)*	0.88 (0.85–0.92)*	3,516	69.22	0.88 (0.85–0.91)*
< 75 mg/day	3,908	84.98	1.08 (1.04–1.11)*	1.11 (1.07–1.15)*	3,819	85.75	1.11 (1.07–1.15)*
≥ 75 mg/day	3,777	68.71	0.87 (0.84–0.90)*	0.88 (0.85–0.92)*	3,692	68.99	0.88 (0.85–0.91)*
Death							
Dipyridamole nonuser	5,327	21.70	1.0 (reference)	1.0 (reference)	4,039	22.14	1.0 (reference)
Dipyridamole user	1,992	19.73	0.91 (0.86–0.96)*	0.89 (0.84–0.93)*	1,941	19.80	0.89 (0.84–0.94)*
< 140 DDD	1,160	23.80	1.10 (1.04–1.18)*	1.04 (0.97–1.10)	1,128	23.87	1.04 (0.97–1.11)
≥ 140 DDD	832	15.93	0.73 (0.68–0.78)*	0.74 (0.69–0.79)*	813	16.01	0.74 (0.69–0.80)*
< 75 mg/day	1,101	23.94	1.11 (1.04–1.19)*	1.04 (0.97–1.11)	1,071	24.05	1.04 (0.97–1.11)
≥ 75 mg/day	891	16.21	0.74 (0.69–0.79)*	0.75 (0.70–0.81)*	870	16.26	0.76 (0.70–0.81)*

Abbreviations: CI, confidence interval; CKD, chronic kidney disease; DDD, defined daily doses; HR, hazard ratio

A multivariate analysis was adjusted for all of the variables listed in Table 1.

* $P < 0.05$ compared with dipyridamole nonusers.

Supplementary Table 3: Risks of long term dialysis and death in pre-dialysis stage 5 CKD patients with dipyridamole exposure within 60 days and observation period beginning 60 days after the index date

	Before Matching				After Matching		
	N of events	Incidence rate (100 person-years)	Crude HR (95% CI)	Adjusted HR (95% CI)	N of events	Incidence rate (100 person-years)	Adjusted HR (95% CI)
Long-term dialysis							
Dipyridamole nonuser	16,804	77.01	1.0 (reference)	1.0 (reference)	12,199	75.69	1.0 (reference)
Dipyridamole user	6,614	72.82	0.96 (0.94–0.99)*	0.98 (0.95–1.01)	6,459	73.26	0.97 (0.94–1.00)*
< 140 DDD	3,329	77.61	1.01 (0.98–1.05)	1.06 (1.02–1.10)*	3,254	78.46	1.05 (1.01–1.09)
≥ 140 DDD	3,285	68.53	0.91 (0.87–0.94)*	0.91 (0.88–0.95)*	3,205	68.63	0.89 (0.86–0.93)*
< 75 mg/day	3,169	78.46	1.03 (0.99–1.07)	1.07 (1.03–1.11)*	3,096	79.39	1.06 (1.02–1.11)
≥ 75 mg/day	3,445	68.30	0.90 (0.87–0.93)*	0.91 (0.88–0.95)*	3,363	68.39	0.89 (0.86–0.93)*
Death							
Dipyridamole nonuser	4,679	21.44	1.0 (reference)	1.0 (reference)	3,571	22.16	1.0 (reference)
Dipyridamole user	1,787	19.68	0.92 (0.87–0.97)*	0.90 (0.85–0.95)*	1,739	19.72	0.89 (0.84–0.94)*
< 140 DDD	979	22.83	1.07 (1.00–1.14)	0.99 (0.93–1.07)	948	22.86	0.98 (0.91–1.05)
≥ 140 DDD	808	16.86	0.78 (0.73–0.84)*	0.80 (0.75–0.87)*	791	16.94	0.80 (0.74–0.86)*
< 75 mg/day	926	22.93	1.07 (1.00–1.15)*	0.99 (0.92–1.07)	897	23.00	0.98 (0.91–1.04)
≥ 75 mg/day	861	17.07	0.79 (0.74–0.85)*	0.82 (0.76–0.88)*	842	17.12	0.81 (0.75–0.87)*

Abbreviations: CI, confidence interval; CKD, chronic kidney disease; DDD, defined daily doses; HR, hazard ratio

A multivariate analysis was adjusted for all of the variables listed in Table 1.

* $P < 0.05$ compared with dipyridamole nonusers.

Supplementary Table 4: Risks of long term dialysis and death in pre-dialysis stage 5 CKD patients with dipyridamole exposure within 120 days and observation period beginning 120 days after the index date

	Before Matching				After Matching		
	<i>N</i> of events	Incidence rate (100 person- years)	Crude HR (95% CI)	Adjusted HR (95% CI)	<i>N</i> of events	Incidence rate (100 person- years)	Adjusted HR (95% CI)
Long-term dialysis							
Dipyridamole nonuser	12,423	71.29	1.0 (reference)	1.0 (reference)	9,012	68.83	1.0 (reference)
Dipyridamole user	4,990	67.01	0.95 (0.92–0.98)*	0.97 (0.94–1.00)	4,836	67.66	0.98 (0.95–1.01)
< 140 DDD	2,370	69.12	0.97 (0.93–1.01)	1.01 (0.97–1.06)	2,296	70.15	1.03 (0.98–1.08)
≥ 140 DDD	2,620	65.21	0.93 (0.89–0.97)*	0.93 (0.89–0.97)*	2,540	65.56	0.94 (0.90–0.98)*
< 75 mg/day	2,236	69.41	0.98 (0.93–1.02)	1.02 (0.97–1.06)	2,163	70.52	1.04 (0.99–1.09)
≥ 75 mg/day	2,754	65.18	0.92 (0.89–0.96)*	0.93 (0.89–0.97)*	2,673	65.52	0.94 (0.90–0.98)*
Death							
Dipyridamole nonuser	3,579	20.54	1.0 (reference)	1.0 (reference)	2,768	21.14	1.0 (reference)
Dipyridamole user	1,389	18.65	0.90 (0.85–0.96)*	0.89 (0.84–0.95)*	1,343	18.79	0.88 (0.82–0.94)*
< 140 DDD	710	20.71	1.00 (0.93–1.09)	0.94 (0.86–1.02)	681	20.81	0.92 (0.84–1.00)*
≥ 140 DDD	679	16.90	0.81 (0.75–0.88)*	0.85 (0.78–0.93)*	662	17.09	0.85 (0.78–0.92)*
< 75 mg/day	666	20.67	1.00 (0.92–1.09)	0.93 (0.85–1.01)	638	20.80	0.91 (0.83–0.99)*
≥ 75 mg/day	723	17.11	0.83 (0.76–0.89)*	0.86 (0.80–0.94)*	705	17.28	0.86 (0.79–0.93)*

Abbreviations: CI, confidence interval; CKD, chronic kidney disease; DDD, defined daily doses; HR, hazard ratio

A multivariate analysis was adjusted for all of the variables listed in Table 1.

**P* < 0.05 compared with dipyridamole nonusers.

Supplementary Table 5: Risk of bleeding in patients with pre-dialysis stage 5 CKD receiving dipyridamole as compared with dipyridamole nonusers

	Before Matching				After Matching		
	<i>N</i> of event	Incidence rate (100 person- years)	Crude HR (95% CI)	Adjusted HR (95% CI)	<i>N</i> of event	Incidence rate (100 person- years)	Adjusted HR (95% CI)
Bleeding							
dipyridamole nonuser	2,528	1.36	1.0 (reference)	1.0 (reference)	1,884	1.38	1.0 (reference)
dipyridamole user	1,087	1.38	1.03 (0.96–1.11)	0.99 (0.92–1.06)	1,047	1.37	1.00 (0.92–1.08)

Abbreviations: CI, confidence interval; CKD, chronic kidney disease; HR, hazard ratio

A multivariate analysis was adjusted for all variables listed in Table 1.

**P* < 0.05 compared with dipyridamole nonusers.