Lowered Cancer Risk With ACE Inhibitors/ARBs: A Population-Based Cohort Study

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There are conflicting reports on cancer risk associated with angiotensin-converting enzyme (ACE) inhibitors/angiotensin receptor blockers (ARBs). This retrospective cohort study was conducted to analyze the risk of cancer development in patients who received ACE inhibitors/ARBs as treatment for essential hypertension. Using the Taiwan National Health Insurance Research Database, 297,688 eligible study patients with essential hypertension were identified. According to their antihypertensive prescriptions, the study patients were stratified into an ACE inhibitor group, an ARB group, or a control group. After matching, participants were observed for the occurrence of cancer. In the ACE inhibitor group compared with the control group, the hazard ratio was 0.51 (95% confidence interval, 0.39–0.68). In the ARB group compared with the control group, the hazard ratio was 0.8 (95% confidence interval, 0.65–0.97). Regular use of ACE inhibitors/ARBs was not associated with an increased risk of cancer development and was actually found to decrease overall cancer risk in this study. *J Clin Hypertens (Greenwich).* 2014;16:27–33. ©2013 Wiley Periodicals, Inc.

Angiotensin-converting enzyme (ACE) inhibitors have been found to have protective effects against cancer development.[1] Although two meta-analyses failed to show clinical significance,[2,3] the majority of studies have found that the use of ACE inhibitors is associated with a decreased risk of cancer development.[4–7]

Patients who use angiotensin II receptor blockers (ARBs) have been shown to be at higher risk of cancer development in some clinical studies.[3,8] However, those studies were meta-analyses based on data from studies not originally designed to explore the risk of cancer. The nature of meta-analyses or collaborative studies carries a considerable risk of bias regarding cancer occurrence.[9] For example, one meta-analysis found similar overall risk of cancer development comparing patients treated with ACE inhibitors/ARBs with those treated without ACE inhibitors/ARBs. However, when the meta-analysis was restricted to cohort and nested case-control studies, the effect of ACE inhibitors/ARBs on cancer development became protective.[10] The clinical impact of ARBs on the risk of developing cancer became an issue under debate.[11,12]

This study was designed to compare the incidence of cancer development between patients with essential hypertension who received ACE inhibitors or ARBs with those who received other antihypertensive medications.

METHODS

Data Source

This retrospective cohort study was designed to investigate the relationship between antihypertensive medications and cancer risk. Study patients were selected from the Taiwan National Health Insurance Research Database (NHIRD), which is maintained by the Bureau of National Health Insurance (NHI). The NHI system is a universal, obligatory health insurance system in Taiwan operated by the Department of Health. At the end of 2009, a total of 23,026,000 people, representing more than 99.59% of the population in Taiwan, were enrolled in the NHI program. In this study, we used a randomly sampled longitudinal health insurance data subset issued by the NHI with a total coverage of 1,868,128 beneficiaries. There are no statistical differences in the distribution of age, sex, or premium-based monthly salary of the beneficiaries between individuals in the subset and those in the original NHI registration dataset.

Study Participants

The population of interest comprised patients with newly diagnosed essential hypertension (*International Statistical Classification of Diseases* [ICD] 401) that was diagnosed during the period from 2000 to 2008. All ICD codes used in this study complied with ICD, *Ninth Revision, Clinical Modification* (ICD-9-CM). Patients 20 years or older who had at least 3 outpatient visits coded with essential hypertension in a certain year from 2000 to 2008 were included. Patients with a history of hypertension-related diseases prior to inclusion, including hypertensive diseases (ICD 401–405), iatrogenic hypertension (ICD 997.91), pregnancy-related hypertension (ICD 642), or hypertension-related illness such

as elevated blood pressure without a diagnosis of hypertension (*ICD* 796.2), hypertension retinopathy (*ICD* 362.11), blood vessel diseases (*ICD* 440–449), chronic obstructive pulmonary diseases (*ICD* 490–496), and chronic pulmonary heart diseases (*ICD* 416) were excluded. In addition, patients with Bureau of NHI-defined catastrophic illnesses (including cancers) occurring in the year of inclusion or in the year prior to inclusion were excluded.

The steps of data processing are shown in Figure 1. A total of 297,688 individuals with newly diagnosed essential hypertension that had been diagnosed from 2000 to 2008 were identified. According to their antihypertensive prescription patterns, the individuals were assigned into one of the following three groups: the ACE inhibitor group, comprising patients who received ACE inhibitors (ATC C09A and C09B) for at least 80% of the days every year (which was 292 days) during observation and who never received ARBs (ATC C09C, C09DA, C09DB, C09DX01, and C09DX03); the ARB group, comprising patients who received ARBs for at least 80% of the 365 days annually since the year after inclusion until the end of the study and who had never received ACE inhibitors; and the control group, comprising patients who took other antihypertensive medications (ATC C02, C03, C07, and C08 excluding combinations containing ACE inhibitors/ARBs) for at least 80% of the days every year during observation. Threshold of compliance was set as medication available during ≥80% of the observation period according

to Caro's classification.[13] ACE inhibitors included benazepril, captopril, cilazapril, enalapril, fosinopril, imidapril, lisinopril, perindopril, quinapril, and ramipril. ARBs included candesartan, eprosartan, irbesartan, losartan, olmesartan, telmisartan, and valsartan. Renin inhibitors were not administrated during the study period.

Study Process

The ACE inhibitor group comprised 4988 individuals, the ARB group comprised 6960 individuals, and the control group comprised 143,887 individuals. Using propensity score matching, the ACE inhibitor and ARB groups were then respectively matched at a ratio of 1:5 to form their control groups. Individual characteristics used for matching included demographic information (sex and age), socioeconomic status (premium-based salary), and environmental factors (urbanization level of residence).[14] By tracing from the year of inclusion back to 1997, cerebrovascular diseases (*ICD* 430–438), heart diseases including ischemic heart diseases and heart failure (*ICD* 398.91, 402.01, 402.11, 402.91, 404.01, 404.11, 404.91, 404.03, 404.13, 404.93, 410–414, and 428), chronic liver diseases (*ICD* 456.0–456.2, 571, and 572.2–572.8), diabetes mellitus (*ICD* 250), chronic renal diseases (*ICD* 403–404 and 585–586), chronic obstructive pulmonary diseases (*ICD* 490–496), and metabolic syndrome-related diagnoses (*ICD* 272.0–272.4, 274, 278, and 277.7) were considered to represent initial health status and were also matched. The above diseases were admitted only if coded in at least 3 outpatient visits from 1997 to the year of inclusion.

After matching, the ACE inhibitor group comprised 4971 individuals and its corresponding control group comprised 24,855 participants. Likewise, the ARB group comprised 6639 individuals and its corresponding control group comprised 33,195 participants. Patients in each group were observed for cancer occurrence of any type, according to the official registry of Catastrophic Illness Dataset of the Bureau of NHI, since the year after inclusion until the end point. The end point was defined as the end of 2009, the year of cancer occurrence, or the last year in which the participants complied with the grouping criteria. The diseases representing initial health status coded in at least 3 outpatient visits during observation were taken into consideration as comorbidities in subsequent analyses.

Statistical Analysis

We used chi-square test to measure differences in categorical data, including groupings of antihypertensive prescription pattern, sex, age, premium-based salary, level of urbanization, and the presence or absence of diseases. Parametric data, including age and duration of observation, were examined using Student *t* test. The Cox proportional hazards model adjusted for sex, age, premium-based salary, level of urbanization, and comorbidities was employed to calculate the hazard ratios (HRs) and 95% confidence
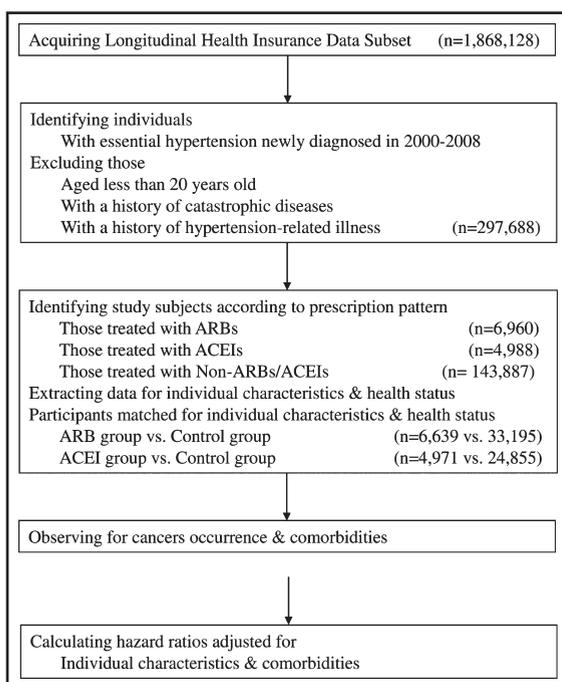

FIGURE 1. Steps of data processing using the National Health Insurance Research Database of Taiwan. ACEI indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker.

intervals (CIs) for cancer occurrence. For all analyses, a *P* value <.05 was considered to represent statistical significance. All statistical analyses were conducted using SAS (version 9.2, SAS Institute, Cary, NC).

RESULTS
Individual characteristics and initial health status before and after matching in the ACE inhibitor group,

the ARB group, and their control groups are shown in Table I and Table II, respectively. After matching, there was no significant difference in individual characteristics and initial health status between the groups.

The duration of observation ranged from 1 to 9 years for all of the groups. The mean duration of observation was 2.36±1.81 years in the ACE inhibitor group and

TABLE I. Individual Characteristics and Initial Health Status in the ACE Inhibitor Group and Control Group Among Patients With Newly Diagnosed Essential Hypertension in Taiwan in 2000 to 2008

| Variables | Before Matching | | | After 1:5 Matching | | |
	ACE Inhibitor (4988) No. (%)	Control (143,887) No. (%)	*P* Value	ACE Inhibitor (4971) No. (%)	Control (24,855) No. (%)	*P* Value
Sex						
Women	1996 (40.0)	69,173 (48.1)	<.001	1996 (40.2)	10,103 (40.7)	.52
Men	2992 (60.0)	74,714 (51.9)		2975 (59.9)	14,752 (59.4)	
Age, mean (SD), y						
	58.88 (13.19)	55.21 (14.51)	<.001	58.85 (13.20)	59.21 (13.37)	.084
≤39	301 (6.0)	19,286 (13.4)	<.001	301 (6.1)	1417 (5.7)	.54
40–49	986 (19.8)	33,320 (23.2)		958 (19.8)	4866 (19.6)	
50–59	1365 (27.4)	37,981 (26.4)		1364 (27.4)	6683 (26.9)	
60–69	1145 (23.0)	27,222 (18.9)		1137 (22.9)	5816 (23.4)	
70–79	890 (17.8)	18,449 (12.8)		883 (17.7)	4425 (17.8)	
≥80	301 (6.0)	7629 (5.3)		301 (6.1)	1648 (6.6)	
Premium-based salary (NT$)						
Dependents	1567 (31.4)	37,171 (25.8)	<.001	1559 (31.4)	7848 (31.6)	.91
≤17,280	1039 (20.8)	28,678 (19.9)		1033 (20.8)	5295 (21.3)	
17,281–22,800	1655 (33.2)	53,290 (37.0)		1653 (33.3)	8257 (33.2)	
22,801–28,800	166 (3.3)	5508 (3.8)		166 (3.3)	795 (3.2)	
28,801–36,300	157 (3.2)	5367 (3.7)		156 (3.1)	797 (3.1)	
36,301–45,800	187 (3.8)	6784 (4.7)		187 (3.8)	843 (3.4)	
45,801–57,800	113 (2.3)	3728 (2.6)		113 (2.3)	555 (2.2)	
≥57,801	104 (2.1)	3361 (2.3)		104 (2.1)	495 (2.0)	
Level of urbanization						
1 (most)	1344 (26.9)	39,653 (27.6)	<.001	1335 (26.9)	6732 (27.1)	.90
2 or 3	2422 (48.6)	65,125 (45.3)		2414 (48.6)	12,037 (48.4)	
4 or 5	796 (16.0)	25,753 (17.9)		796 (16.0)	4027 (16.2)	
6 or 7 (least)	426 (8.5)	13,356 (9.3)		426 (8.6)	2059 (8.3)	
Cerebrovascular diseases						
No	4550 (91.2)	137,103 (95.3)	<.001	4540 (91.3)	22,843 (91.9)	.177
Yes	438 (8.8)	6784 (4.7)		431 (8.7)	2012 (8.1)	
Heart diseases						
No	4181 (83.8)	132,089 (91.8)	<.001	4181 (84.1)	20,905 (84.1)	1.00
Yes	807 (16.2)	11,798 (8.2)		790 (15.9)	3950 (15.9)	
Liver diseases						
No	4377 (87.8)	128,151 (89.1)	.004	4360 (87.7)	21,882 (88.0)	.51
Yes	611 (12.3)	15,736 (10.9)		611 (12.3)	2973 (12.0)	
Diabetes mellitus						
No	3467 (69.5)	131,824 (91.6)	<.001	3467 (69.7)	14,344 (69.8)	.96
Yes	1521 (30.5)	12,063 (8.4)		1504 (30.3)	7511 (30.2)	
Renal diseases						
No	4777 (95.8)	140,610 (97.7)	<.001	4762 (95.8)	23,893 (96.1)	.27
Yes	211 (4.2)	3277 (2.3)		2,09 (4.2)	962 (3.9)	
Metabolic syndrome						
No	3670 (73.6)	120,314 (83.6)	<.001	3668 (73.8)	18,435 (74.2)	.57
Yes	1318 (26.4)	23,573 (16.4)		1303 (26.2)	6420 (25.8)	

Abbreviations: ACE, angiotensin-converting enzyme; NT$, New Taiwan dollar; SD, standard deviation.

TABLE II. Individual Characteristics and Initial Health Status in the ARB Group and Control Group Among Patients With Newly Diagnosed Essential Hypertension in Taiwan in 2000 to 2008

	Before Matching			After 1:5 Matching		
	ARB (6960)	Control (143,887)		ARB (6629)	Control (33,195)	
Variables	No. (%)	No. (%)	P Value	No. (%)	No. (%)	P Value
Sex						
Women	3179 (45.7)	69,173 (48.1)	<.001	3052 (46.0)	15,019 (45.2)	.28
Men	3781 (54.3)	74,714 (51.9)		3587 (54.0)	18,176 (54.8)	
Age, mean (SD), y						
	59.68 (13.18	55.21 (14.51)	<.001	59.57 (13.17)	59.56 (13.42)	.99
≤39	398 (5.7)	19,286 (13.4)	<.001	398 (6.0)	1950 (5.9)	.99
40–49	1203 (17.3)	33,320 (23.2)		1195 (18.0)	5932 (17.9)	
50–59	1864 (26.8)	37,981 (26.4)		1808 (27.2)	9042 (27.2)	
60–69	1644 (23.6)	27,222 (18.9)		1556 (23.4)	7736 (23.3)	
70–79	1373 (19.7)	18,449 (12.8)		1244 (18.7)	6276 (18.9)	
≥80	478 (6.9)	7629 (5.3)		2259 (6.8)	438 (6.6)	
Premium-based salary (NT$)						
Dependents	2283 (32.8)	37,171 (25.8)	<.001	2134 (32.1)	10,648 (32.1)	.84
≤17,280	1358 (19.5)	28,678 (19.9)		1278 (19.3)	6491 (19.6)	
17,281–22,800	2118 (30.4)	53,290 (37.0)		2070 (31.2)	10,177 (30.7)	
22,801–28,800	205 (3.0)	5508 (3.8)		202 (3.0)	1016 (3.1)	
28,801–36,300	252 (3.6)	5367 (3.7)		245 (3.7)	1164 (3.5)	
36,301–45,800	331 (4.8)	6784 (4.7)		322 (4.9)	1637 (4.9)	
45,801–57,800	195 (2.8)	3728 (2.6)		180 (2.7)	902 (2.7)	
≥57,801	218 (3.1)	3361 (2.3)		208 (3.1)	1160 (3.5)	
Level of urbanization						
1 (most)	2338 (33.6)	39,653 (27.6)	<.001	2196 (33.1)	11,096 (33.4)	.85
2 or 3	3160 (45.4)	65,125 (45.3)		3018 (45.5)	15,115 (45.5)	
4 or 5	976 (14.0)	25,753 (17.9)		948 (14.3)	4680 (14.1)	
6 or 7 (least)	486 (7.0)	13,356 (9.3)		477 (7.2)	2304 (6.9)	
Cerebrovascular diseases						
No	6209 (89.2)	137,103 (95.3)	<.001	5996 (90.3)	30,201 (91.0)	.086
Yes	751 (10.8)	6784 (4.7)		643 (9.7)	2994 (9.0)	
Heart diseases						
No	5565 (80.0)	132,089 (91.8)	<.001	5494 (82.8)	27,507 (82.9)	.83
Yes	195 (20.0)	11,798 (8.2)		1145 (17.3)	5688 (17.1)	
Liver diseases						
No	5950 (85.5)	128,151 (89.1)	<.001	5697 (85.8)	28,571 (86.1)	.58
Yes	1010 (14.5)	15,736 (10.9)		942 (14.2)	4624 (13.9)	
Diabetes mellitus						
No	4947 (71.1)	131,824 (91.6)	<.001	4947 (74.5)	24,737 (74.5)	.99
Yes	2013 (28.9)	12,063 (8.4)		1692 (25.5)	8458 (25.5)	
Renal diseases						
No	6534 (93.9)	140,610 (97.7)	<.001	6312 (95.1)	31,738 (95.6)	.054
Yes	426 (6.1)	3277 (2.3)		327 (4.9)	1457 (4.4)	
Metabolic syndrome						
No	4791 (68.8)	120,314 (83.6)	<.001	4734 (71.3)	23,884 (72.0)	.29
Yes	2169 (31.2)	23,573 (16.4)		1905 (28.7)	9311 (28.1)	

Abbreviations: ARB, angiotensin receptor blocker; NT$, New Taiwan dollar; SD, standard deviation.

2.38±1.77 years in the ARB group. During the observation period, 53 of 4971 (1.07%) patients in the ACE inhibitor group developed cancer compared with 911 of 24,855 (3.67%) in the control group (*P*<.001). In the ARB group, 112 of 6639 (1.69%) patients developed cancer compared with 1226 of 33,195 (3.69%) in the control group (*P*<.001).

The Cox proportional hazards model was employed to adjust for individual characteristics, comorbidities, and duration of observation. As shown in Table III, the adjusted HR was 0.51 (95%, CI 0.39–0.68; *P*<.001) for the ACE inhibitor group and was 0.8 (95% CI, 0.65–0.97; *P*=.023) for the ARB group. The accumulative probabilities of cancer occurrence and the duration of

TABLE III. Cancer Risk Adjusted for Individual Characteristics and Comorbidities Among Patients With Newly Diagnosed Essential Hypertension in Taiwan in 2000 to 2008

Variables	ARB vs Control			ACE Inhibitor vs Control		
	Adjusted HR	95% CI	P Value	Adjusted HR	95% CI	P Value
ACE inhibitor/control	–	–		0.51	0.39–0.68	<.001
ARB/control	0.80	0.65–0.97	.023	-	–	
Men/women	1.52	1.50–1.70	<.001	1.55	1.35–1.79	<.001
Age, y						
≤39	1			1		
40–49	2.12	1.30–3.45	.002	2.78	1.40–5.54	.004
50–59	3.52	2.20–5.62	<.001	5.04	2.58–9.87	<.001
60–69	6.40	4.00–10.22	<.001	8.22	4.19–16.10	<.001
70–79	8.15	5.09–13.05	<.001	13.51	6.89–26.47	<.001
≥80	7.99	4.88–13.07	<.001	11.70	5.84–23.45	<.001
Premium-based salary (NT$)						
Dependents	1			1		
≤17,280	0.99	0.86–1.15	.96	0.83	0.69–0.98	.029
17,281–22,800	1.04	0.90–1.21	.57	0.94	0.79–1.11	.44
22,801–28,800	0.91	0.61–1.37	.66	0.72	0.42–1.21	.21
28,801–36,300	0.82	0.54–1.25	.36	0.77	0.46–1.32	.35
36,301–45,800	0.86	0.61–1.21	.39	0.72	0.42–1.23	.23
45,801–57,800	0.45	0.25–0.82	.010	0.53	0.26–1.09	.084
≥57,801	0.59	0.37–0.93	.023	0.64	0.33–1.26	.20
Level of urbanization						
1 (most)	1			1		
2 or 3	1.02	0.90–1.15	.81	1.06	0.91–1.24	.43
4 or 5	0.91	0.76–1.09	.90	0.93	0.75–1.15	.50
6 or7 (least)	0.92	0.73–1.16	.47	0.89	0.68–1.16	.39
Comorbidities						
Cerebrovascular diseases	0.67	0.57–0.78	<.001	0.65	0.54–0.78	<.001
Heart diseases	0.92	0.81–1.04	.190	0.90	0.77–1.05	.170
Liver diseases	1.93	1.69–2.20	<.001	1.96	1.68–2.30	<.001
Diabetes mellitus	1.00	0.89–1.13	.95	1.02	0.89–1.17	.81
Renal diseases	1.34	1.03–1.75	.030	1.34	0.98–1.82	.062
Lung diseases	1.03	0.91–1.17	.65	1.01	0.86–1.17	.96
Metabolic syndrome	0.78	0.69–0.88	<.001	0.84	0.73–0.96	.012

Abbreviations: ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; CI, confidence interval; HR, hazard ratio; NT$, New Taiwan dollar.

ACE inhibitor and ARB exposure are illustrated in Figure 2 and Figure 3, respectively.

DISCUSSION

Healthcare databases are considered close to the ideal material for pharmacoepidemiologic research.[15] In comparison with ad hoc studies and meta-analyses, healthcare database research often has fewer selection, recall, and reporting biases. In addition, information regarding prescription is relatively clear and contains implicit drug compliance information, which is often lacking in meta-analysis and collaborative studies. High drug compliance has been shown to improve outcome; therefore, this study was designed to magnify the impact of ACE inhibitors/ARBs on cancer risk by requiring a high ACE inhibitor/ARB compliance threshold (over 80% of the days in every year during observation).[13] In the comparison groups, the same criteria for compliance were also required to address the "healthy adherer effect."[16]

In this study, the adjusted HR was 0.51 for the ACE inhibitor/control group. ACE inhibitors exert their protective effect possibly by decreasing the rate of angiotensin I degradation into angiotensin II, which, in turn, decreases the accumulation of angiotensin I.[17] Furthermore, with ACE inhibitors, angiotensin I can be catabolized by endopeptidase into angiotensin (1-7), which has been proven to be anti-carcinogenic.[18]

Two types of angiotensin II receptor have been identified and were found to be counter-regulatory to each other. Type 1 angiotensin II receptor has been shown in some studies to be pro-carcinogenic while type 2 angiotensin II receptor was considered anti-carcinogenic.[4,19,20] ARBs block only type 1 angiotensin II receptor and were therefore considered to be anti-carcinogenic. However, there were opposite opinions on
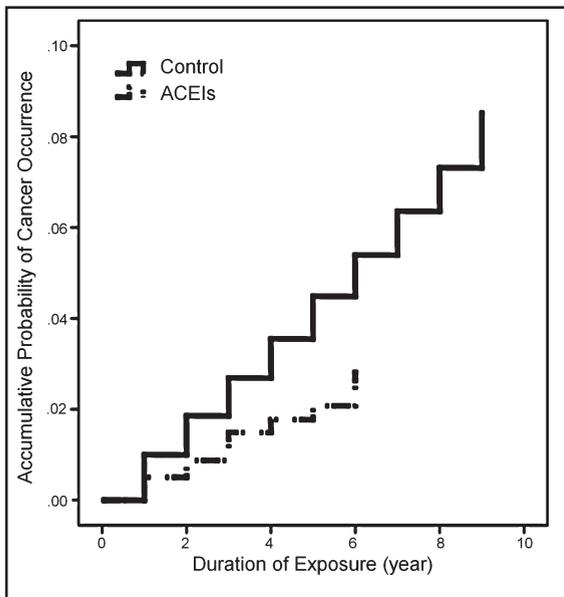
FIGURE 2. Accumulative probability of cancer occurrence and the duration of angiotensin-converting enzyme inhibitor (ACEI) exposure among patients with newly diagnosed essential hypertension in Taiwan in 2000 to 2008. After Cox proportional hazards model analysis adjusted for other variables including sex, age, premium-based salary, level of urbanization, cerebrovascular diseases, heart diseases, liver diseases, diabetes mellitus, renal diseases, and metabolic syndrome–related diagnoses, the adjusted hazard ratio of participants in the ACEI group compared with its control group was 0.51 (95% confidence interval, 0.39–0.68; P<.001).
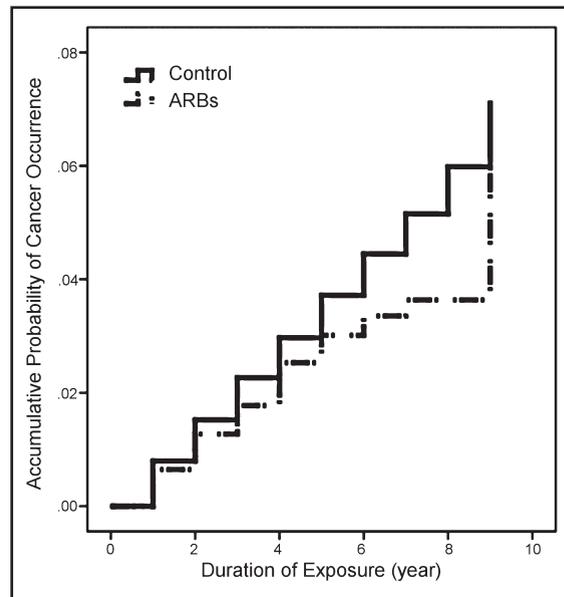
FIGURE 3. Accumulative probability of cancer occurrence and the duration of angiotensin receptor blocker (ARB) exposure among patients with newly diagnosed essential hypertension in Taiwan in 2000 to 2008. After Cox proportional hazards model analysis adjusted for other variables including sex, age, premium-based salary, level of urbanization, cerebrovascular diseases, heart diseases, liver diseases, diabetes mellitus, renal diseases, and metabolic syndrome–related diagnoses, the adjusted hazard ratio of participants in the ARB group compared with its control group was 0.8 (95% confidence interval, 0.65–0.97; P=.023).

the activity of the two types of angiotensin II receptors.[21–23] In an in vitro assay, ARBs were found to enhance breast cancer progression by blocking type 1 angiotensin II receptor.[24]

In some clinical studies, ARBs have been shown to increase the incidence of respiratory system tumors.[3,8] However, in other studies, ARBs were found to be protective against cancer occurrence or to improve cancer prognosis.[5–7,10,25] In addition, several studies, including meta-analyses, have shown neutral results regarding the association between ARBs and risk of cancer development.[11,26–30] In this study, the adjusted HR was 0.8 for the ARB/control group. Although it is unlikely that a convincing conclusion on the current debate could be drawn through this single study, the result of this study would make a considerable contribution for literature in this field.

General risk factors for cancer development include smoking, obesity, an unhealthy diet, and physical inactivity.[31] In addition, age, sex, income, alcohol use, unsafe sex, occupational exposure, environmental factors, and health conditions are also related to the risk of developing cancer.[32–36] Some of the risk factors are difficult to qualify or even quantify. One of the limitations of this study is that not all possible risk factors of cancer could be controlled.

It is possible that some of the patients from the control group had indications for treatment with ACE

inhibitors/ARBs but were not given one. However, the reason certain patients might not have received ACE inhibitors or ARBs is beyond the scope of this observational study.

Besides the use of ACE inhibitors/ARBs, we found that sex, age, and premium-based salary also affect cancer incidence. Although some comorbidities such as cerebrovascular diseases, liver diseases, renal diseases, and metabolic syndrome showed significant impact on cancer occurrence, the numbers could be biased because this study was not specifically designed to examine the relation between these comorbidities and cancer risk.

This study was based on secondary data analyses. Patient compliance with medication could only be estimated from prescription records. Additionally, because of the high compliance required for inclusion, any effect of ACE inhibitors/ARBs on cancer development might only appear with regular and long-term use. Because of the high threshold of compliance and other exclusion criteria, only a limited number of patients were included in the final analysis. As a result, cancer developed in only 53 patients in the ACE inhibitor group and in 112 patients in the ARB group. Nevertheless, the case number was large enough to demonstrate a statistical significance.

The study examined the risk of all cancers. The most common cancers in Taiwan involve the liver/intrahepatic

biliary tract, lung/bronchus, breast, colon, prostate (male), cervix uteri (female), rectum, and stomach.[37] However, the effects of ACE inhibitors/ARBs on different cancers lack uniformity.[38] The impact of ACE inhibitors/ARBs could vary among different cancers. Furthermore, different ACE inhibitors or different ARBs may have a different impact on cancer risk.[26] Therefore, further investigations into the effect of specific ACE inhibitors/ARBs on the occurrence of specific cancers may be of value.

CONCLUSIONS
We found that the relative risk of cancer development was lower among patients who received ACE inhibitors/ARBs than among patients who received other types of antihypertensive medications.

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