Clinical Outcomes and Healthcare Costs in Hypertensive Patients Treated With a Fixed-Dose Combination of Amlodipine/Valsartan

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This retrospective claims database analysis compared two strategies of hypertension treatment in outpatient, emergency, and inpatient departments: a fixed-dose combination (FDC) of amlodipine/valsartan vs free combinations of angiotensin receptor blockers (ARBs) and calcium channel blockers (CCBs) (ARB+CCB group). After a mean follow-up of 15.2 months, the FDC group had significantly lower total healthcare costs (US $1844 vs US $2158; *P*<.001) and hospitalization rates (14.57% vs 18.43%; *P*<.001), a higher proportion of days covered (80.35% vs 72.57%; *P*<.001), and better persistence (266 vs 225 days; *P*<.001) compared with the ARB+CCB group. The FDC group also had a better major adverse cardiovascular event (MACE)–free survival (hazard ratio, 0.83; 95% confidence interval, 0.73–0.94; *P*=.003) and decreased rates of heart failure (2.12% vs 3.26%; *P*<.001), malignant dysrhythmia (0.18% vs 0.42%; *P*=.021), and percutaneous coronary intervention (0.76% vs 1.26%; *P*=.015). Compared with free combinations of ARB+CCB, an FDC of amlodipine/valsartan improved MACE-free survival and medication compliance and decreased total healthcare costs and hospitalization rates in hypertensive patients. *J Clin Hypertens (Greenwich).* 2015;17:51–58. © 2014 Wiley Periodicals, Inc.

Hypertension is recognized as one of the most important risk factors for cardiovascular disease, with a substantial impact on morbidity and mortality.[1] The worldwide prevalence of hypertension was reported to be around 26% in 2000, and is expected to increase to 29% by 2025.[2] Blood pressure (BP) reduction has been reported to effectively protect against complications such as myocardial infarction, heart failure, stroke, and renal function impairment.[3–5] However, despite enormous advances in antihypertensive drug therapy, the BP control rate remains low.[6] In the United States, about 50% of patients with hypertension achieve BP control.[6] In the Taiwanese Survey on Hypertension, Hyperglycemia, and Hyperlipidemia conducted between 1993 and 2002, 50.4% of hypertensive patients were treated with antihypertensive drugs, only 24.5% of whom had good BP control.[7]

In addition to a low treatment rate, nonadherence and lack of persistence are two of the main reasons for inadequate BP control.[8,9] Adherence and persistence rates with antihypertensive drugs are often low, ranging from 24% to 51% and 29% to 58% in the United States, respectively.[10] Given that the majority of patients with hypertension require two or more medications to maintain BP control,[11,12] the complexity of treatment regimens has been assumed to be responsible for the low adherence and persistence.[13] Among the strategies to improve medication adherence and persistence, fixed-dose combination (FDC) medications are commonly used. FDC medications combining two active agents in a single pill and therefore simplifying drug regimens have been demonstrated to improve compliance.[13,14] Prior meta-analyses have reported improved adherence and lower healthcare costs associated with FDC medications compared with free-drug combinations of the same classes in treating patients with chronic illnesses or hypertension.[13–15] However, data on the impact of FDCs on major adverse cardiovascular events (MACEs) are sparse. The most frequently prescribed FDC of a renin-angiotensin system inhibitor and a calcium channel blocker (CCB) in Taiwan is amlodipine/valsartan (Exforge; Novartis Pharmaceutical, Basel, Switzerland). In the present study, we aimed to compare the clinical outcomes and heathcare costs of hypertension treatment with an FDC of amlodipine/valsartan vs free-drug combinations of angiotensin receptor blockers (ARBs) and CCBs.

METHODS

Data Sources

We obtained data from the National Health Insurance Research Database (NHIRD) of Taiwan. The National Health Insurance (NHI) program, a state-operated, universal health insurance program implemented in March 1995, covers approximately 99% of the entire population of Taiwan. The database contains inpatient registries from all medical facilities

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contracted with the NHI Administration, and provides information regarding all admissions, including new-onset MACEs in inpatients with one principal and four secondary *International Classification of Diseases, 9th Revision, Clinical Modification* (*ICD-9-CM*) diagnosis codes. All personal identifiers are encrypted by the Bureau of the NHI before release to researchers. Confidentiality assurances were addressed by following the data regulations of the Bureau of the NHI, and institutional review board approval was waived.

Study Cohorts

Two study cohorts of patients with the diagnosis of hypertension (*ICD-9-CM*: 401.x) were generated from the NHIRD. The first included patients receiving an FDC of amlodipine/valsartan, and the second included those receiving ARB+CCB combination therapy.

The patients who received an FDC of amlodipine/valsartan between April 1, 2008, and December 31, 2010, were identified and classified as the FDC cohort. The date of the first prescription of this regimen during this period was identified as the index date, and the 6-month period prior to the index date was defined as the baseline period. The patients were followed for 12 months after the index date (defined as the follow-up period), and the patients with hypertension and/or high costs were identified. The inclusion criteria were at least two filled prescriptions for an FDC of amlodipine/valsartan (including the index prescription) during the follow-up period with a total supply of 90 days or more, continuous enrollment with pharmacy and medical claims in both the baseline and follow-up periods, and an age of 18 years or older at the index date.

The patients who received free-dose ARB+CCB combination therapy between April 1, 2008, and December 31, 2010 were identified and classified as the ARB+CCB cohort. The date of the first prescription for ARB+CCB combination therapy during this period was identified as the index date, and the 6-month period prior to the index date was defined as the baseline period. The patients were followed for 12 months after the index date (defined as the follow-up period). The inclusion criteria were at least two filled prescriptions for ARB+CCB (including the index prescription) during the follow-up period with a total supply of 90 days or more, continuous enrollment with pharmacy and medical claims in both the baseline and follow-up periods, and an age of 18 years or older at the index date.

To evaluate the effectiveness of treatment and patient compliance between the two cohorts, we measured the proportion of days covered (PDC) and discontinuation (persistence) with claims for the medications.[16]

To identify an appropriate control group, propensity score matching[17] was deemed to be a valid method for the real-world data obtained from NHIRD. A propensity score, which is the probability an individual will be assigned to a group based on conditions that exist at the time of the group assignment, was calculated to correct for potential sample selection bias caused by nonrandom assignment. In this study, the variables used for the matching process in the propensity score model included the baseline variables age, sex, coronary heart disease (*ICD-9-CM*: 410–414), myocardial infarction (*ICD-9-CM*: 410), peripheral vascular disease (*ICD-9-CM*: 443), stroke (*ICD-9-CM*: 434.91), congestive heart failure (*ICD-9-CM*: 428), dyslipidemia (*ICD-9-CM*: 272), diabetes mellitus (*ICD-9-CM*: 250), obesity (*ICD-9-CM*: 278), chronic kidney disease (*ICD-9-CM*: 585), medical costs, and overall pill burden. The overall pill burden was defined as the total number of pills prescribed in the baseline period. The control group was matched at a ratio of 4:1 to the FDC group.

MACEs included any of the following: (1) myocardial infarction (*ICD-9-CM* codes 410–410.9); (2) heart failure (*ICD-9-CM* codes 428.0–428.10); (3) percutaneous coronary intervention (*ICD-9-CM* codes 36.0–36.03 and 36.05–36.09); (4) coronary artery bypass surgery (*ICD-9-CM* codes 36.1–36.99 and V45.81); (5) stroke (*ICD-9-CM* codes 430–437); (6) thrombolysis therapy (*ICD-9-CM* codes 36.0–36.99); (7) malignant dysrhythmia (*ICD-9-CM* codes 426.0, 426.12–426.13, 426.51–426.52, 426.54, 427.1, 427.4, 427.41–427.42, and 427.5); and (8) cardiogenic shock (*ICD-9-CM* code 785.51). Mortality related to a MACE was identified using death certificate data files with any diagnosis code, which also indicated the cause of death related to the cardiovascular event.

The following *ICD-9-CM* codes were not used to define MACEs unless they were accompanied with a diagnosis code of cerebral infarction or cerebral hemorrhage: occlusion or stenosis of extracranial arteries without infarction (*ICD-9-CM* codes 430.00, 431.00, 433.20, 433.30, 433.80, 43.390, 434.90, 434.00, 434.10, and 434.90); basilar, vertebral, and subclavian artery syndrome (*ICD-9-CM* codes 435.0–435.3); hypertensive encephalopathy (*ICD-9-CM* code 437.2); cerebral aneurysm, nonruptured (*ICD-9-CM* code 437.3); cerebral arteritis (*ICD-9-CM* code 437.4); and moyamoya disease (*ICD-9-CM* code 437.5).

Statistics

Continuous variables were compared using Student *t* test, and categorical variables were compared by chi-square test. Data are presented as means, standard deviations, medians, or percentages. A linear regression model was used for the variable of cost, logistic regression for binary outcome, and a Cox proportional hazard model for time to event analysis. All analyses were conducted using SAS statistical software, version 9.3 (SAS Institute Inc, Cary, NC) and R statistical software, version 3.0.1 (R Foundation for Statistical Computing). A P value $<.05$ was considered to be statistically significant.

RESULTS

Using propensity score matching, 3301 patients taking an FDC of amlodipine/valsartan, and 13,204 patients

TABLE I. Patient Demographic Characteristics

	FDC (n=3301)	ARB+CCB (n=13204)	*P* Value
Age, mean±SD, y	60.30±12.53	60.37±13.09	.767
Male, %	1724 (52.23)	6861 (51.96)	.785
Duration of follow-up, mo	15.23±3.93	15.27±4.11	.627
Baseline comorbid conditions, %			
Coronary heart disease	590 (17.87)	2280 (17.27)	.411
Peripheral vascular disease	38 (1.15)	132 (1.00)	.441
Congestive heart failure	24 (0.73)	81 (0.61)	.463
Dyslipidemia	1097 (33.23)	4478 (33.91)	.459
Diabetes	1101 (33.35)	4434 (33.58)	.805
Obesity	24 (0.73)	104 (0.79)	.723
Chronic kidney disease	117 (3.54)	428 (3.24)	.384
Baseline concomitant medications, %			
ACE inhibitor-mono	550 (16.66)	3381 (25.61)	<.001
ACE inhibitor-combo	249 (7.54)	285 (2.16)	<.001
Angiotensin receptor blocker	605 (18.33)	4034 (30.55)	<.001
β-Blockers	1331 (40.32)	5209 (39.45)	.360
Calcium channel blocker	2146 (65.01)	9307 (70.49)	<.001
Diuretics	580 (17.57)	2781 (21.06)	<.001
Other antihypertensive agents	321 (9.72)	1213 (9.19)	.341
Antidiabetic agents	1037 (31.42)	3985 (30.18)	.168
Overall pill burden	419.31±478.83	427.17±477.35	.398

Abbreviations: ACE inhibitor-combo, angiotensin-converting enzyme inhibitor in combination with other antihypertensive agents in a single pill; ACE inhibitor-mono, angiotensin-converting enzyme inhibitor only in a pill; ARB+CCB, free combinations of angiotensin receptor blockers and calcium channel blockers; FDC, fixed-dose combination of amlodipine/valsartan; SD, standard deviation.

taking free combinations of ARB+CCB were enrolled between April 1, 2008, and December 31, 2010. The demographic and clinical characteristics of the two groups are shown in Table I. The mean follow-up duration was 15.2 months. No significant differences were found between the two groups in terms of age, sex,

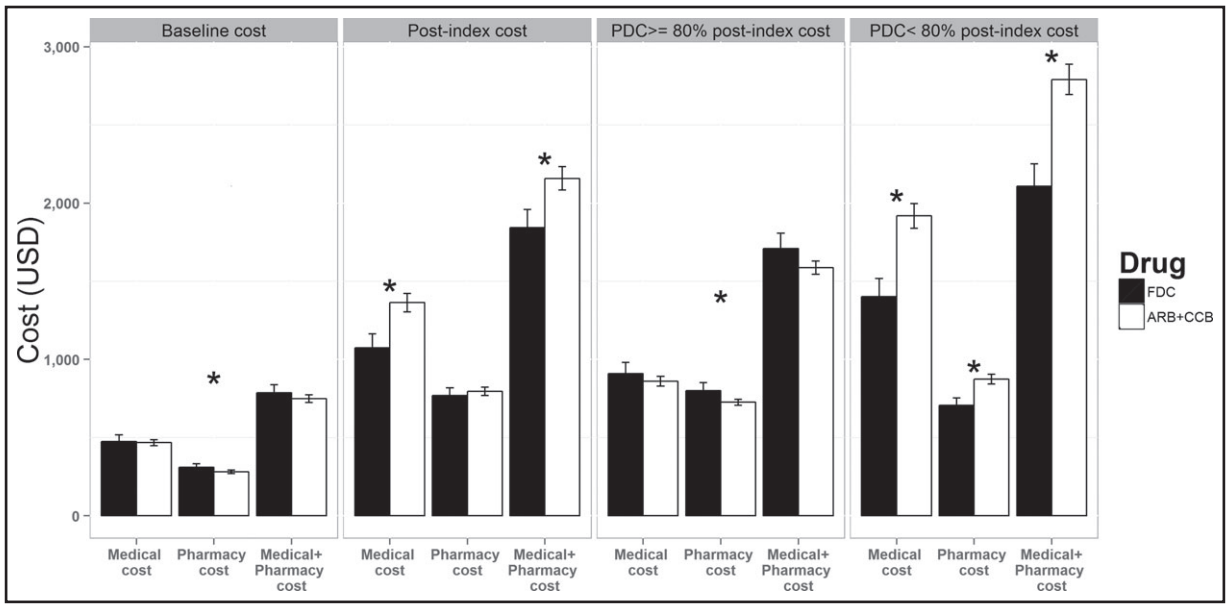

FIGURE 1. Comparison of total healthcare costs. The patients taking a fixed-dose combination of amlodipine/valsartan (FDC) had significantly lower post-index total healthcare costs (medical plus pharmacy costs). ARB+CCB indicates free combinations of angiotensin receptor blockers and calcium channel blockers; PDC, proportion of days covered. *P<.05.
[Correction added after initial online publication on December 5, 2014: Figure 1 has been revised.]

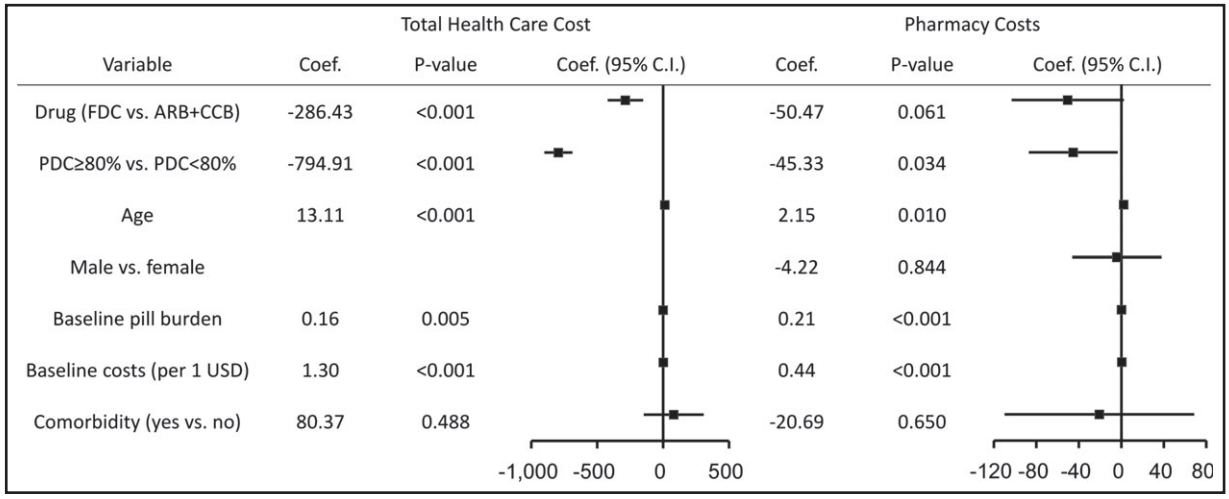

FIGURE 2. Multivariate analysis of total healthcare and pharmacy costs. Proportion of days covered (PDC) ≥80% predicted both lower total healthcare and pharmacy costs. A fixed-dose combination of amlodipine/valsartan (FDC) significantly reduced lower total healthcare costs but not pharmacy costs. Age and baseline pill burden were significantly associated with higher total healthcare and pharmacy costs. ARB+CCB indicates free combinations of angiotensin receptor blockers and calcium channel blockers.

and comorbid conditions including coronary heart disease, peripheral vascular disease, congestive heart failure, dyslipidemia, diabetes, obesity, and chronic kidney disease. Angiotensin-converting enzyme inhibitors, ARB, CCB, and diuretics were significantly more frequently used in the ARB+CCB group at baseline. No significant differences were noted in the duration of follow-up (15.23 vs 15.27 months; *P*=.63) and overall pill burden (419 vs 427; *P*=.4) between the two groups.

We analyzed the healthcare costs, including medical and pharmacy costs, of the two study groups (Figure 1, Tables S1 and S2). At baseline, there was no significant difference in total healthcare costs between the FDC and ARB+CCB groups ($787 vs $750; *P*=.21), although the pharmacy cost was higher in the FDC group ($311 vs $282; *P*=.019). The post-index total healthcare cost was significantly lower in the FDC group compared with the ARB+CCB group ($1844 vs $2158; *P*<.001). In subgroup analysis, adherence status was divided into two categories: PDC ≥80% and PDC <80%. The patients taking an FDC of amlodipine/valsartan with a PDC ≥80% had insignificantly higher total healthcare costs than those taking ARB+CCB ($1710 vs $1587; *P*=.07). Of the patients with a PDC ≥80%, the total pharmacy cost was higher in the FDC group ($801 vs $726; *P*=.03). Of the patients with a PDC <80%, those taking an FDC of amlodipine/valsartan had a significantly lower total healthcare cost ($2109 vs $2791; *P*<.001).

The factors of total healthcare and pharmacy costs were analyzed using multiple linear regression analysis (Figure 2, Table S3). A PDC ≥80%, compared with a PDC <80%, was associated with both lower total healthcare (coefficient, −25,152; 95% confidence interval [CI], −28,522 to −21,783; *P*<.001) and pharmacy (coefficient, −1434; 95% CI, −2759 to −110; *P*=.034) costs. The FDC group had a significantly lower total healthcare cost (coefficient, −9063; 95% CI, −13,316 to −4811; *P*<.001), and a borderline significant reduction in pharmacy costs (coefficient, −1597; 95% CI, −3269 to 75; *P*=.06). Increased age and baseline pill burden were significantly associated with higher total healthcare and pharmacy costs.

Table II demonstrates medication adherence, persistence, and utilization of healthcare resources in the two groups. The patients in the FDC group had a significantly lower hospitalization rate (14.57% vs 18.43%; *P*<.001). In the patients with a PDC ≥80%, no significant difference in hospitalization rate was detected between the two groups. However, in the patients with a PDC <80%, an FDC of amlodipine/valsartan resulted in a significant reduction in hospitalization rate compared with the ARB+CCB regimen (19.5% vs 25.0%; *P*<.001). The FDC group also had a higher PDC (80.35% vs 72.57%; *P*<.001) and better medication persistence (266 vs 225 days, *P*<.001) than the ARB+CCB group. The improvement in medication compliance remained significant even in the patients with a PDC ≥80% (PDC: 93.42% vs 92.98%, *P*=.002; persistence: 341 vs 335 days, *P*=.001).

The results of multivariate analysis using Cox regression for medication persistence and PDC are presented in Figure 3 and Table S4. An FDC of amlodipine/valsartan and presence of comorbidities were significantly associated with better persistence (hazard ratio [HR], 0.69; 95% CI, 0.66–0.73; *P*<.001) and PDC ≥80% (odds ratio [OR], 1.82; 1.67–1.98; *P*<.001). Baseline pill burden and healthcare costs were negative preditors of persistence and PDC ≥80%.

Figure 4 illustrates Kaplan-Meier curves of MACE-free survival. The patient taking an FDC of amlodipine/valsartan had better MACE-free survival than those taking free combinations of ARB+CCB (HR, 0.83; 95%

TABLE II. Medication Adherence, Persistence, and Utilization of Healthcare Resources

	FDC (n=3301)	ARB+CCB (n=13,204)	*P* Value
Baseline			
Length of stay, mean±SD	6.38±6.25	6.72±7.11	.415
Visits			
Patients with ≥1 ED visits, %	506 (15.33)	2154 (16.31)	.169
Patients with ≥1 outpatient visits, %	3248 (98.39)	12,993 (98.40)	.975
Patients with ≥1 inpatient visits, %	300 (9.09)	1091 (8.26)	.127
Post-index, all patient			
Length of stay, mean±SD	7.04±10.08	8.40±13.89	.012
Visits			
Patients with ≥1 ED visits, %	788 (23.87)	3297 (24.97)	.191
Patients with ≥1 outpatient visits, %	3301 (100)	13,204 (100)	–
Patients with ≥1 inpatient visits, %	481 (14.57)	2433 (18.43)	<.001
Adherence-PDC, mean±SD, %	80.35±21.90	72.57±25.95	<.001
Persistence-days, mean±SD	265.75±130.89	224.67±142.60	<.001
Post-index, patients with PDC ≥80%			
Length of stay, mean±SD	6.39±11.72	7.54±18.45	.231
Visits			
Patients with ≥1 ED visits, %	460 (20.98)	1337 (19.27)	.080
Patients with ≥1 outpatient visits, %	2193 (100)	6939 (100)	–
Patients with ≥1 inpatient visits, %	265 (12.08)	869 (12.52)	.586
Adherence-PDC, mean±SD, %	93.42±5.62	92.98±5.77	.002
Persistence-days, mean±SD	340.5±69.04	334.88±78.07	.001
Post-index, patients with PDC <80%			
Length of stay, mean±SD	7.83±7.56	8.87±10.52	.073
Visits			
Patients with ≥1 ED visits, %	328 (29.60)	1960 (31.29)	.265
Patients with ≥1 outpatient visits, %	1108 (100)	6265 (100)	–
Patients with ≥1 inpatient visits, %	216 (19.50)	1564 (24.96)	<.001
Adherence-PDC, mean±SD, %	54.47±18.93	49.96±20.24	<.001
Persistence-days, mean±SD	117.81±93.05	102.57±88.02	<.001

Abbreviations: ARB+CCB, free combinations of angiotensin receptor blockers and calcium channel blockers; ED, emergency department; FDC, fixed-dose combination of amlodipine/valsartan; PDC, proportion of days covered; SD, standard deviation.

CI, 0.73–0.94; *P*=.003). Compared with the ARB+CCB group, the FDC group had significantly decreased rates of heart failure (2.12% vs 3.26%; *P*<.001), malignant dysrhythmia (0.18% vs 0.42%; *P*=.021), and percutaneous coronary intervention (0.76% vs 1.26%; *P*=.015), and a borderline significant decrease in myocardial infarction (0.58% vs 0.92%; *P*=.052) (Table S5).

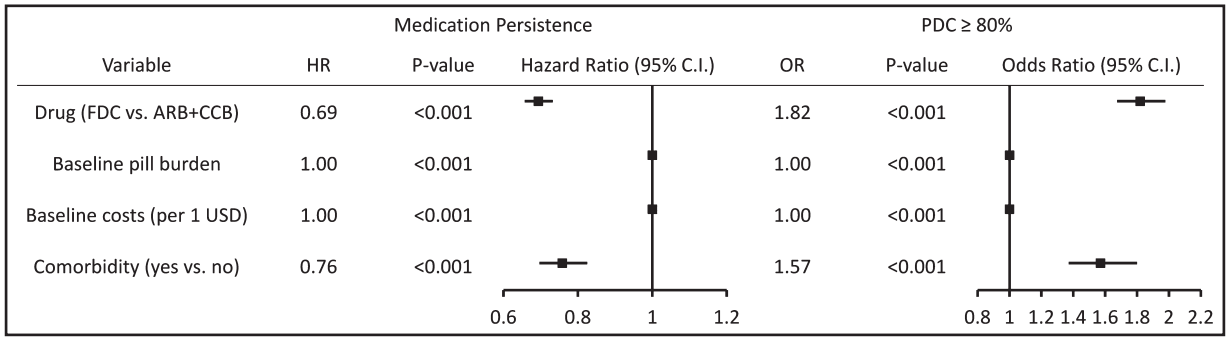

FIGURE 3. Multivariate analysis of persistence and proportion of days covered. A fixed-dose combination of amlodipine/valsartan (FDC) and the presence of comorbidities were significantly associated with better persistence and proportion of days covered (PDC) ≥80%. Baseline pill burden and healthcare costs were negative predictors of persistence and PDC ≥80%. ARB+CCB indicates free combinations of angiotensin receptor blockers and calcium channel blockers; HR: hazard ratio; OR: odds ratio.

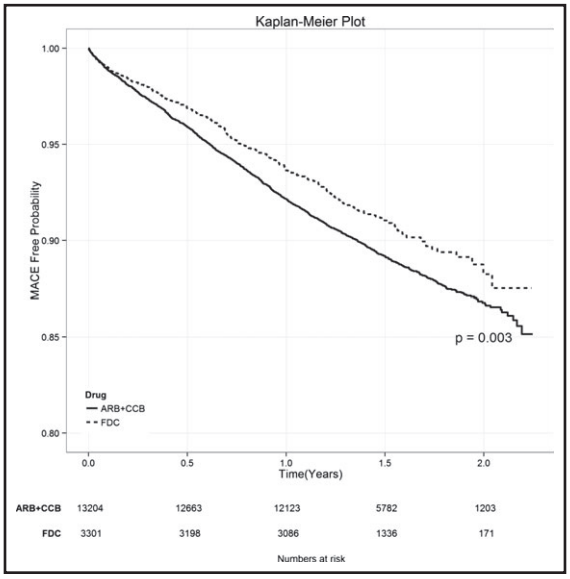

FIGURE 4. Kaplan-Meier survival curves of major adverse cardiovascular events. The patients taking a fixed-dose combination of amlodipine/valsartan (FDC) had better major adverse cardiovascular event (MACE)–free survival than those taking free-combination regimens of angiotensin receptor blockers and calcium channel blockers (ARB+CCB).

DISCUSSION

This retrospective claims database analysis compared two strategies for hypertension treatment: an FDC of amlodipine/valsartan vs free combinations of ARBs and CCBs. After a mean follow-up of 15.2 months, the FDC group had significantly lower total healthcare costs and hospitalization rates, a higher PDC, and better persistence compared with the ARB+CCB group. The FDC group also had better MACE-free survival than the ARB+CCB group.

In this study, total healthcare costs were significantly lower in the patients taking an FDC of amlodipine/valsartan than those in the patients taking ARB+CCB, mainly due to significant cost reduction in the patients with a PDC <80%. This reduction in healthcare costs is consistent with the results of prior reports. In a meta-analysis comparing annual healthcare costs of FDC and free-combination regimens for hypertension treatment, Sherrill and colleagues[15] estimated a $2039 reduction (95% CI, $1030–$3047) in all-cause total costs and a $709 reduction (95% CI, $117–$1302) in hypertension and cardiovascular-related costs in the FDC group. In their analysis of pharmacy costs, patients taking an FDC had an average $605 reduction (95% CI, $376–$835) in annual pharmacy costs compared with those taking free drug combinations. In contrast to their results, we found no significant difference in total pharmacy costs between the two groups (P=.36), which may be the result of relatively lower pharmacy costs and reimbursements from the NHI program in Taiwan. Because of the limitations of data retrieval from the NHIRD, we could not specifically estimate pharmacy costs related to hypertension or cardiovascular disease, and inconsistent results have been reported in previous analyses.[18,19]

By reducing overall pill burden and simplifying medication regimens, FDCs have been shown to improve medication compliance and persistence in numerous studies. We used a PDC ≥80% to define the threshold of adherence. The patients taking an FDC of amlodipine/valsartan had better medication adherence and persistence, regardless of their adherence status. In a meta-analysis of chronic diseases including diabetes mellitus, hypertension, and human immunodeficiency virus, Bangalore and associates[13] reported a 26% reduction in the risk of noncompliance in those taking an FDC compared with those taking a free-drug combination (relative risk, 0.74, 95% CI, 0.69–0.8; P<.0001). In another meta-analysis of hypertension treatment with the use of an FDC, Gupta and colleagues[14] found that an FDC was associated with a 29% increase in compliance and persistence (OR, 1.29; 95% CI, 1.11–1.50).

In the current study, the patients taking an FDC of amlodipine/valsartan had a lower hospitalization rate than those taking ARB+CCB, which was mainly the result of a reduction in hospitalization rates in the patients with a PDC <80%. Moreover, we also observed an improvement in MACE-free survival in the FDC group. It has been well documented that medication compliance is associated with decreased use of medical care services in various clinical diseases[20–24] and improvement in cardiovascular outcomes.[25–28] However, to the best of our knowledge, no meta-analyses or randomized prospective trials have demonstrated the superiority of an FDC over free-combination regimens in MACEs. An observational, multicenter study of 1605 patients in Spain in 2006 reported a decreased cumulative incidence of cerebrovascular events in patients taking single-pill combinations for hypertension control (2.4% in single-pill combinations vs 4.6% in free combinations; P=.041) after 2 years of follow-up.[29] In the meta-analysis conducted by Gupta and colleagues,[14] there was a beneficial trend in the use of an FDC, with a reduction of 4.1 mm Hg in systolic BP (95% CI, −9.8 to 1.5; P=.15) and a 3.1-mm Hg reduction in diastolic BP (95% CI, −7.1 to 0.9; P=.13). The recently published Use of a Multidrug Pill in Reducing Cardiovascular Events (UMPIRE trial) was an open-label, randomized, blinded end-point trial comparing an FDC of aspirin, statin, and two antihypertensive agents with usual care in patients with established cardiovascular disease or at risk for cardiovascular disease.[30] After a median follow-up of 15 months, the FDC group showed a significant improvement in adherence and small but statistically significant reductions in systolic BP (2.6 mm Hg; 95% CI, −4.0 to −1.1 mm Hg; P<.001) and low-density lipoprotein cholesterol (4.2 mg/dL; 95% CI, −6.6 to −1.9 mg/dL; P<.001). However, no significant differences were found between the groups in terms of serious adverse events or cardiovascular events. In contrast to the results of the UMPIRE trial, we found

that patients taking an FDC of amlodipine/valsartan had better MACE-free survival compared with those taking free combinations of ARB+CCB. Given the better compliance in the FDC group in this study, we hypothesized that it was the result of improved compliance with the use of an FDC regimen, not necessarily the pharmacologic effect of it, that may lead to better efficacy in BP control and improvement in clinical outcomes as well.

Study Limitations

There are some limitations to this study. This retrospective cohort analysis was based on a claims database and therefore has inherent limitations. The claims data are collected based on prescription information but not for study purposes. A claim for a refill prescription does not indicate that the medication is actually taken, so the assessment of PDC or persistence may have been overestimated or underestimated. Incorrect coding is also possible in daily clinical practice. Instead of specifically focusing on hypertension or cardiovascular disease, we evaluated healthcare costs and medical service utilization of all causes, which could potentially lead to bias. In addition, the claims database does not contain clinical data such as BP records at baseline or at follow-up visits. Therefore, the efficacy of BP control, an important link between medication compliance and clinical outcomes, could not be evaluated. Prospective randomized control trials are required to evaluate the impact of FDC regimens on major outcomes in treating hypertensive patients.

CONCLUSIONS

This retrospective study presents real-world results of FDC vs free-combination regimens in the treatment of hypertension. We found that the use of an FDC of amlodipine/valsartan improved MACE-free survival and medication adherence and persistence and decreased all-cause healthcare costs and hospitalization rates compared with free combinations of ARBs and CCBs. The reductions in costs and hospitalization rates were more substantial in the nonadherent subgroup. The use of an FDC provides an important opportunity to improve the quality of hypertension treatment.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Table S1. Patient baseline costs and resource use.

Table S2. Patient post-index costs.

Table S3. Multivariate analysis of total health care and pharmacy costs.

Table S4. Multivariate analysis of medication persistence and proportion of days covered.

Table S5. Number of patients with major adverse cardiovascular events.