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Associations among medication regimen complexity, medical specialty, and medication possession ratio in newly diagnosed hypertensive patients

A population-based study

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Abstract

The aim of this study was to explore the associations among the medication regimen complexity index (MRCI), medical specialty, and medication possession ratio (MPR) in newly diagnosed hypertensive patients.

Data from 19,859 newly diagnosed hypertensive patients were collected from 2,000,000 random samples of the National Health Insurance Research Database in Taiwan. All study participants were followed for 1 year after the first diagnosis of hypertension. MPR was defined as total days of antihypertensive drugs supplied/365 days. MRCI was calculated on the basis of the type of dosage forms, dosing frequency, and additional directions for use of antihypertensive drugs. Patients were further restricted to those who visited the same medical specialty to examine specialty-specific variations in the MRCI and MPR.

The mean MPR was 54.83%, and the sample sizes for the low-, medium-, and high-MPR groups were 9806 (49.38%), 4619 (23.26%), and 5434 (27.36%), respectively. More than 50% of the patients visited the same medical specialty during the 1-year follow-up. The mean MRCI was 3.64; the cardiology specialty had the highest MRCI, and the family medicine specialty had the lowest. Multiple linear regression analyses showed that MRCI was negatively associated with MPR (β = −7.75, P ≤ .01) whether or not the patients visited the same medical specialty. For the patients who visited the same medical specialty, those treated by endocrinology and metabolism specialists had a significantly higher MPR (β = 9.87, P ≤ .01) than that of those treated by family medicine specialists.

MRCI and medical specialty were both significantly associated with the MPR of newly diagnosed hypertensive patients.

Abbreviations: ACEIs = angiotensin-converting enzyme inhibitors, ANOVA = the analysis of variance, ARBs = angiotensin receptor blockers, ATC = Anatomical Therapeutic Chemical, BP = blood pressure, CCBs = calcium channel blocks, Clinical Modification, Dec = December, HTN = hypertension, HWSAC = the Health and Welfare Statistics Application Center, ICD-9-CM = the International Classification of Diseases, 9th revision, Jan = January, MPR = medication possession ratio, MRCI = medication regimen complexity index, NHI = National Health Insurance, NHIRD = NHI Research Database, SDs = standard deviations.

Keywords: hypertension, medical specialties, medication possession ratio, medication regimen complexity, newly diagnosed

1. Introduction

Adequate blood pressure (BP) control is important in hypertensive patients to prevent development of cardiovascular disease, stroke, diabetes, chronic kidney disease, and even death.[1–3] In Taiwan, hypertension is among the 10 leading causes of death, and the prevalence and mortality rates in 2013 were 25.0% and 21.6%, respectively.[4] In 2010, Taiwan's National Health Insurance (NHI) estimated the cost for overall medications to be US$ 4.5 billion, of which the cost for antihypertensive medications was US$ 0.7 billion.[5] In the United States, the

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estimated direct and indirect costs of hypertension for 2010 totaled US$ 46.4 billion, of which the costs for antihypertensive medication totaled US$ 20 billion.[6] Thus, hypertension is one of the most important public health issues worldwide.

Some evidence has indicated that approximately 50% of hypertensive patients took their antihypertensive medications regularly, and 50% to 60% of these patients receiving medications controlled their BP.[7–10] The medication possession ratio (MPR) represents the ratio of medication possession for hypertensive patients and accounts for the medical specialties visited by the patients and prescriptions for hypertension.[11,12] Therefore, the MPR of antihypertensive medications is important for achieving BP goals (140/90 mm Hg) and reducing health care expenditures in hypertensive patients.[11–13] Taiwan's NHI was implemented in 1995; it is a mandatory nationwide health insurance, and the overall coverage rate continues to rise (from 92.4% in 1995 to 99.9% in 2014).[14,15] According to previous studies using Taiwan's NHI Research Database (NHIRD), the overall MPRs for hypertensive patients varied from 36% to 79% in Taiwan during the period of 2000 to 2011.[11,16,17]

There are several reasons for a poor MPR, such as inadequate treatment regimens, cost of therapy, medical specialties, presence of comorbidities, treatment complexity, and polypharmacy.[11,13,16–19] Nevertheless, treatment complexity and polypharmacy are major contributory causes of poor MPR.[11,13,16] For measuring treatment complexity, the medication regimen complexity index (MRCI) is a valuable tool.[19,20] The MRCI has been calculated for different dosage forms, dosing frequencies, and with additional directions.[20–22] The MRCI has been shown to be a factor that affects the MPR of patients.[23] Clinically, the MRCI of antihypertensive drugs may be influenced by medical specialties because the guidelines of hypertension state that pharmacotherapy can differ among medical specialties.[2,3,24–28] Furthermore, patients who visit different medical specialties tend to have different patient characteristics, such as comorbidities. Previous studies have been less likely to consider medical specialties as a factor in investigations of the association between the MPR and MRCI.[11,13,16–23]

The aim of this study was to explore the relationship between the MPR and MRCI for different medical specialties among newly diagnosed hypertensive patients in Taiwan.

2. Materials and methods

2.1. Study population

A retrospective cohort study was conducted to examine the association between the MPR and MRCI for medical specialties in hypertensive patients treated with antihypertensive drugs. Hypertensive patients were identified by using the NHIRD in Taiwan. The NHIRD contains claims data on ambulatory care, inpatients, and contracted pharmacy records and demographics data on enrolled beneficiaries. We obtained data on 2,000,000 beneficiaries randomly sampled from the Registry of NHIRD between January 2008 and December 2010 that was provided by the Health and Welfare Statistics Application Center, Ministry of Health and Welfare, Taiwan. The diagnosis of hypertension was determined according to the International Classification of Diseases, 9th revision, Clinical Modification (ICD-9-CM) codes 401.x–405.xx.[29] We included newly diagnosed hypertensive patients from January 2009 to December 2009 as a 1-year washout period (January 2008–December 2008) for excluding prevalent patients.[30] The inclusion criteria were 18 to 80 years

of age, had at least 3 diagnoses of hypertension, and (3) taking ≥1 antihypertensive medication.[30] Patients who had ≥2 diagnoses of cancer (ICD-9-CM codes 140.x–208.xx) during the study period were excluded.[31] A total of 28,286 newly diagnosed hypertensive patients were selected. To evaluate the relationships between MPR and MRCI for different medical specialties, the patients were followed up for 1 year after their index date, which was the first date on which medications were prescribed for hypertension.

Seven types of antihypertensive drugs were classified by using the NHI Pharmaceutical Subsidy Anatomical Therapeutic Chemical (ATC) classification system.[32] Antihypertensive drug records were classified into 7 types: angiotensin receptor blockers (ARBs, ATC code: C09CA), angiotensin-converting enzyme inhibitors (ATC code: C09AA), calcium channel blockers (CCBs, ATC codes: C08CA, C08DA, and C08DB), diuretics (ATC code: C03), β-blockers (ATC codes: C07AA and C07AB), α-blockers (ATC code: C02CA), and others (ATC codes: C02A-B, C02CC, C02D, C02K, C02L, C07A-F, C08C-G, C09B-X, G04CA).[11,32,33] The study protocol was approved by the Research Ethics Committee of the Buddhist Tzu-Chi General Hospital in Hualien, Taiwan, and met all criteria for protection of human individuals.

3. Data collection

3.1. Baseline characteristics

Baseline information, such as demographic information (age and sex), comorbidity, and variables related to medication, were recorded. Baseline information for each patient was collected during the 6 months before the index date. This information included age at hypertension onset, sex, and comorbidities [diabetes (ICD9 CM code: 250.xx), hyperlipidemia (ICD9 CM code: 272.x), chronic kidney disease (ICD9 CM code: 580.xx–589.x), stroke (ICD9 CM code: 430–438.xx), and cardiovascular disease (ICD9 CM code: 390–398.xx, 410.xx–414.xx, 420.xx–429.xx, 440.xx] and whether they had inpatient or outpatient diagnoses at baseline.[29] These coexisting diseases were considered because a patient's comorbid conditions could influence health-seeking behaviors. During the 1-year follow-up, we obtained information on medical specialties visited, including the type of medical specialties and number of medical specialties. The spectrum of visiting patients in each subspecialty clinic in Taiwan is different from the United States. It is common for patients to sort themselves into various subspecialty clinics according to their symptoms. The highest proportion of patients with hypertension, diabetes, or hyperlipidemia are managed by family medicine doctors because the bulk of government sponsored screening for metabolic syndrome among adults 40 years or older are contracted to them by the Health Promotion Administration of Taiwan. Many patients are managed by the same doctor who explains the meaning of the screening results to them. Nearly all endocrinologists manage diabetes, hypertension, and hyperlipidemia together. It is also very common for neurologists and cardiologists to manage hypertension because dizziness and chest tightness are common symptoms to suggest visits to these 2 subspecialties. Hence, medical specialties were classified into 5 types: family medicine, cardiology, endocrinology and metabolism, neurology, and others. For each type of antihypertensive drug, the number of medications, number of prescriptions, and cumulative days of prescription were collected.

3.2. MPR

The primary outcome variable, MPR, was defined as total days of antihypertensive drugs supplied/365 days, during the 1-year follow-up.[11,16–19] For patients treated with ≥1 type of antihypertensive medication, MPR was calculated for each type of antihypertensive drug, and the average MPR of multiple antihypertensive medications was obtained as the overall MPR.[34] To eliminate the source of bias, we further excluded patients with poor-MPR medication, that is, MPR of any antihypertensive drug < 10%. Most of these patients received a short period of drug therapy because they were replaced by other regimens. It was supported by the fact that these patients continued to have drug prescription records during the 1-year follow-up. Finally, a total of 19,859 newly diagnosed hypertensive patients were selected (Fig. 1). All patients were further categorized into 3 groups: high (MPR ≥80%), medium (50% < MPR < 80%), and low (MPR <50%) groups.[11,17,19]

3.3. MRCI

The MRCI was defined as the sum of weighted scores of dosage forms, dosing frequency, and additional directions for antihypertensive medications.[20–22] Prespecified weighted scores for each domain followed the instructions given in a previous report.[20] Similarly, the MRCI was calculated for each type of antihypertensive drug as a mean MRCI among multiple antihypertensive medications for patients treated with more than a single drug during the 1-year follow-up.

3.4. Statistical analysis

Descriptive statistics, including percentages and frequencies, were used for categorical variables, and means and standard deviations (SDs) were used for continuous variables. The Chi-square test and analysis of variance (ANOVA) were performed for comparisons of demographic variables, antihypertensive drug classes, and MRCIs among low-, medium-, and high-MPR groups. Multiple regression analysis was used to examine the correlation between the MPR and MRCI while controlling for potential confounding factors, such as age, sex, medical specialties, and comorbidities. We performed a subgroup analysis to examine possible effects of medical specialties in relation to the MPR and MRCI. In other words, the subgroup consisted of patients who visited the same medical specialty during the study period. Data were analyzed by using SAS 9.4 statistical analysis software (SAS Institute Inc, Cary, NC). The significance level was set at 0.05, and all tests were 2-tailed.
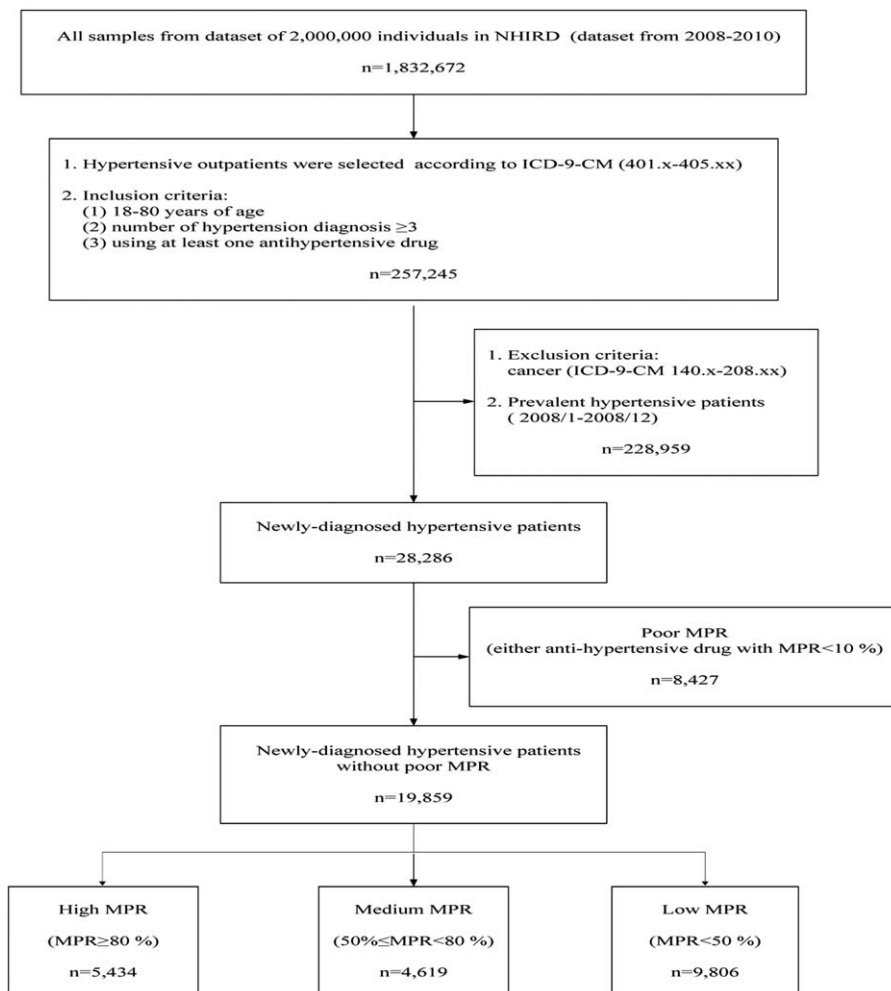

Figure 1. Selection of newly diagnosed hypertensive patients.

4. Results

4.1. Patient characteristics by MPR groups

Among 19,859 newly diagnosed hypertensive patients, the mean (SD) age was 56.0 (12.28) years, and there were more males (54.21%) than females (45.79%) (Table 1). For medical specialties at the first diagnosis of hypertension, either the family medicine or cardiology specialty accounted for 46.04% of newly diagnosed patients. Approximately 44.15% of our samples had ≥1 comorbid disease. The most prevalent comorbidities were hyperlipidemia (19.76%) and diabetes (19.04%). On average, there were 1.7 types of antihypertensive drugs treated during the 1-year follow-up. CCBs (62.72%), β-blockers (29.24%), and

ARBs (21.60%) were the top 3 commonly prescribed antihypertensive drugs. The mean MPR was 54.83%; thus, the low-MPR group (n=9806, 49.38%) accounted for the most subjects followed by the high-MPR group (n=5434, 27.36%) and the medium-MPR group (n=4619, 23.26%). There were significant differences in age, sex, medical specialties, comorbidities, number of prescriptions for hypertension, and antihypertensive drug types among the 3 MPR groups. In the high-MPR group, the patients had more comorbid diseases, and >50% of them visited the same medical specialty during the 1-year follow-up. The number of prescriptions for hypertension was larger in the high-MPR group than in the low-MPR group. In addition, the patients used fewer antihypertensive drugs and had lower dosing

Table 1

Baseline characteristics of newly diagnosed hypertensive patients by MPR groups[*].

| | | **MPR groups** | | | |
Characteristics	All n = 19,859	High n = 5434	Medium n = 4619	Low n = 9806	P
Baseline					
Age, y	56.0 (12.28)	56.8 (11.68)	56.0 (11.95)	55.6 (12.72)	<.01
					.01
<60	12,377 (62.32)	3294 (60.62)	2891 (62.59)	6192 (63.15)	
≥60	7482 (37.68)	2140 (39.38)	1728 (37.41)	3614 (36.85)	
Sex					<.01
Male	10,766 (54.21)	2955 (54.38)	2631 (56.97)	5254 (53.58)	
Female	9093 (45.79)	2479 (45.62)	1988 (43.03)	4552 (46.42)	
Medical specialties at the first diagnosis					
Family medicine	6048 (30.45)	1630 (29.99)	1369 (29.63)	3049 (31.09)	<.01
Cardiology	3096 (15.59)	960 (17.66)	825 (17.87)	1311 (13.37)	
Endocrinology and metabolism	807 (4.06)	387 (7.12)	199 (4.32)	221 (2.25)	
Neurology	888 (4.47)	278 (5.13)	222 (4.80)	388 (3.95)	
Others	9020 (45.42)	2179 (40.10)	2004 (43.39)	4837 (49.33)	
Comorbidities					
Diabetes	3782 (19.04)	1288 (23.70)	919 (19.90)	1575 (16.06)	<.01
Hyperlipidemia	3924 (19.76)	1189 (21.88)	971 (21.02)	1764 (17.99)	<.01
Chronic kidney disease	545 (2.74)	157 (2.89)	145 (3.14)	243 (2.48)	.06
Stroke	1277 (6.43)	416 (7.66)	313 (6.78)	548 (5.59)	<.01
Cardiovascular disease	3139 (15.81)	912 (16.78)	795 (17.21)	1432 (14.60)	<.01
No. of comorbidities					<.01
0	11,090 (55.84)	2774 (51.05)	2461 (53.28)	5855 (59.71)	
1	5537 (27.88)	1598 (29.41)	1341 (29.03)	2598 (26.49)	
≥2	3232 (16.27)	1062 (19.54)	817 (17.69)	1353 (13.80)	
During 1-year follow-up					
MPR score	54.83 (29.81)	94.51 (6.35)	64.10 (8.33)	28.48 (11.74)	<.01
No. of medical specialties					<.01
1	11,248 (56.64)	2769 (50.96)	2411 (52.20)	6068 (61.88)	
≥2	8611 (43.36)	2665 (49.04)	2208 (47.80)	3738 (38.12)	
No. of prescriptions for HTN	13.8 (11.07)	20.9 (11.74)	18.8 (10.65)	7.4 (6.16)	<.01
No. of HTN medications	1.7 (0.90)	1.5 (0.70)	2.1 (0.99)	1.7 (0.90)	<.01
Antihypertensive drug types					
ARBs	4290 (21.60)	1104 (20.32)	1314 (28.45)	1872 (19.09)	<.01
ACEIs	3541 (17.83)	740 (13.62)	980 (21.22)	1821 (18.57)	<.01
CCBs	12,455 (62.72)	3173 (58.39)	3205 (69.39)	6077 (61.97)	<.01
Diuretics	2735 (13.77)	582 (10.71)	875 (18.94)	1278 (13.03)	<.01
β-blockers	5806 (29.24)	1450 (26.68)	1645 (35.61)	2711 (27.65)	<.01
α-blockers	499 (2.51)	103 (1.90)	167 (3.62)	229 (2.34)	<.01
Others	4796 (24.15)	1026 (18.88)	1368 (29.62)	2402 (24.50)	<.01
MRCI score[†]	3.39 (1.67)	3.13 (1.39)	3.90 (1.89)	3.29 (1.65)	<.01
Dosing frequency	1.86 (1.12)	1.64 (0.91)	2.24 (1.27)	1.80 (1.10)	<.01
Additional directions	0.53 (0.92)	0.49 (0.80)	0.67 (1.05)	0.50 (0.90)	<.01

ACEIs = angiotensin-converting enzyme inhibitors, ARBs = angiotensin receptor blockers, CCBs = calcium channel blocks, HTN = hypertension, MPR = medication possession ratio, MRCI = medication regimen complexity index, SDs = standard deviations.

[*]Categorical variables used percentages and frequencies. Continuous variables used means and standard deviations (SDs). [†]MRCI = dosage forms + (dosing frequency × number of HTN medications) + (additional directions × number of HTN medications). The scores of dosage forms for all participants were = 1.

Table 2

Baseline characteristics, MPRs, and MRCIs for patients who visited the same sample medical specialty[*].

Characteristics	All (n = 11,248)	Family medicine (n = 3236)	Cardiology (n = 1881)	Endocrinology and metabolism (n = 588)	Neurology (n = 572)	Others (n = 4971)	P
Baseline							
Age, yr	55.8 (12.60)	55.9 (11.99)	54.7 (12.69)	55.3 (12.90)	60.0 (12.07)	55.9 (12.34)	<.01
							<.01
<60	7082 (62.96)	2029 (62.70)	1258 (66.88)	378 (64.29)	278 (48.60)	3139 (63.15)	
≥60	4166 (37.04)	1207 (37.30)	623 (33.12)	210 (35.71)	294 (51.40)	1832 (36.85)	
Sex							.12
Male	6336 (56.33)	1718 (53.09)	1089 (57.89)	335 (56.97)	330 (57.69)	2864 (57.61)	
Female	4912 (43.67)	1518 (46.91)	792 (42.11)	253 (43.03)	242 (42.31)	2107 (42.39)	
Comorbidities							
Diabetes	2252 (20.02)	579 (17.89)	223 (11.86)	462 (78.57)	103 (18.01)	885 (17.80)	<.01
Hyperlipidemia	2167 (19.27)	567 (17.52)	398 (21.16)	259 (44.05)	105 (18.36)	838 (16.86)	<.01
Chronic kidney disease	319 (2.84)	31 (0.96)	35 (1.86)	15 (2.55)	9 (1.57)	229 (4.61)	<.01
Stroke	747 (6.64)	101 (3.12)	71 (3.77)	26 (4.42)	257 (44.93)	292 (5.87)	<.01
Cardiovascular disease	1752 (15.58)	250 (7.73)	799 (42.48)	43 (7.31)	57 (9.97)	603 (12.13)	<.01
No. of comorbidities							<.01
0	6171 (54.86)	2110 (65.20)	805 (42.80)	87 (14.80)	226 (39.51)	2943 (59.20)	<.01
1	3269 (29.06)	767 (23.70)	712 (37.85)	237 (40.31)	193 (33.74)	1360 (27.36)	
≥2	1808 (16.07)	359 (11.09)	364 (19.35)	264 (44.90)	153 (26.75)	668 (13.44)	
During 1-year follow-up							
No. of prescriptions for HTN	12.4 (9.84)	10.64 (7.98)	15.10 (11.70)	13.42 (9.07)	13.40 (10.63)	12.20 (9.90)	<.01
No. of HTN medications	1.7 (0.87)	1.56 (0.76)	1.92 (0.96)	1.60 (0.83)	1.71 (0.89)	1.66 (0.87)	<.01
Antihypertensive drug types							
ARBs	2250 (20.00)	485 (14.99)	520 (27.64)	244 (41.42)	166 (29.02)	835 (16.79)	<.01
ACEIs	2333 (20.74)	701 (21.65)	366 (19.45)	145 (24.61)	113 (19.73)	1008 (20.28)	<.01
CCBs	7022 (62.43)	2063 (66.16)	1054 (56.03)	258 (43.82)	321 (56.07)	3326 (66.91)	<.01
Diuretics	1751 (15.57)	535 (16.53)	288 (15.30)	68 (11.64)	73 (12.68)	787 (15.83)	<.01
β-blockers	3519 (31.29)	887 (27.40)	882 (46.90)	124 (21.01)	167 (29.11)	1459 (29.36)	<.01
α-blockers	267 (2.37)	61 (1.90)	47 (2.51)	9 (1.56)	14 (2.41)	136 (2.73)	<.01
Others	2818 (25.05)	714 (22.07)	544 (28.91)	174 (29.65)	178 (31.16)	1208 (24.30)	<.01
MPR score	51.72 (29.45)	50.19 (28.95)	53.47 (30.73)	63.37 (29.39)	53.07 (30.37)	50.53 (28.84)	<.01
MPR groups							<.01
High	2769 (24.62)	736 (22.74)	506 (26.90)	228 (38.78)	150 (26.22)	1149 (23.11)	
Medium	2411 (21.43)	682 (21.08)	435 (23.13)	135 (22.96)	126 (22.03)	1033 (20.78)	
Low	6068 (53.95)	1818 (56.18)	940 (49.97)	225 (38.27)	296 (51.75)	2789 (56.11)	
MRCI score	3.64 (1.91)	2.98 (1.33)	4.10 (1.92)	3.56 (1.66)	3.75 (1.88)	3.43 (1.74)	<.01

ACEIs = angiotensin-converting enzyme inhibitors, ARBs = angiotensin receptor blockers, CCBs = calcium channel blocks, HTN = hypertension, MPR = medication possession ratio, MRCI = medication regimen complexity index, SDs = standard deviations.

[*]Categorical variables used percentages and frequencies. Continuous variables used means and standard deviations (SDs).

frequencies for prescription drugs in the high-MPR group than in the low-MPR group. MRCI was significantly different among the 3 groups of MPR. Bonferroni test indicated that pairwise mean MRCI comparisons were significant ($P < .05$). For the high-MPR group, the overall mean MRCI was 3.13 (1.39), which was less complicated than those of the medium- and low-MPR groups.

4.2. MPR and MRCI for patients who visited the sample medical specialty

Taking into account different guidelines of prescriptions for antihypertensive drugs among the medical specialties, we further examined the relationship of MPR and MRCI regarding patients who visited the same medical specialty during follow-up (n = 11,248). For the 5 types of medical specialties, the most visited specialty was family medicine (28.77%) followed by cardiology (16.72%). The oldest patients (60.0 years old) were treated by neurology specialists. The majority (65.20%) of patients treated by family medicine specialists did not have any comorbidities. Interestingly, 85.21% of the patients who visited the endocrinology and metabolism specialty had ≥1 comorbid disease, such as diabetes (78.57%) and hyperlipidemia (44.05%). CCBs,

β-blockers, and ARBs were the top 3 antihypertensive drugs except for the endocrinology and metabolism specialty. There were significant differences in age, comorbidities, and antihypertensive drug types among the 5 groups of medical specialties. The mean MPR was 51.72%, with 2769 (24.62%), 2411 (21.43%), and 6068 (53.95%) patients in the high-, medium-, and low-MPR groups, respectively (Table 2). MPR and MRCI were significantly different among the 5 types of medical specialties. The endocrinology and metabolism specialty had the highest MPR (63.37%, with 38.78% in the high-MPR group). The overall mean MRCI was 3.64 (1.91), and the highest MRCI of 4.10 (1.92) was in the cardiology specialty and the lowest MRCI of 2.98 (1.33) was in the family medicine specialty.

4.3. Factors correlated with MPR

The MPR was greater for males than for females (Table 3). The MRCI was negatively associated with MPR ($\beta = -7.75$, $P \leq .01$). The MPR was greater for patients who visited the same medical specialty than for those who visited different medical specialties. The MPR of patients was significantly increased by combining diabetes, hyperlipidemia, stroke, and/or cardiovascular disease.

Table 3

Factors correlated with MPR in multiple regression analysis.

Characteristics	β*	95% CI	P
Model 1[†]: total sample (n = 19,859)			
Age, ref ≤60 y	0.41	−0.22 to 1.04	.20
Sex, ref = female	1.52	0.91–2.13	<.01
MRCI	−7.75	−7.97 to −7.53	<.01
The same medical specialties, ref = yes	−0.83	−1.44 to −0.22	.01
Diabetes, ref = no	4.71	3.91–5.51	<.01
Hyperlipidemia, ref = no	2.43	1.65–3.21	<.01
Chronic kidney disease, ref = no	1.37	−0.45 to 3.19	.14
Stroke, ref = no	1.72	0.50–2.94	.01
Cardiovascular disease, ref = no	0.93	0.11–1.75	.03
No. of prescriptions for HTN	2.24	2.20–2.28	<.01
Model 2[‡]: patients visiting the sample specialty (n = 11,248)			
Age, ref ≤60 y	0.28	−0.21 to 0.77	.27
Sex, ref = female	0.75	0.27–1.22	<.01
MRCI	−6.03	−6.17 to −5.89	<.01
Medical specialty, ref = family medicine providers			
Cardiology	−0.06	−0.80 to 0.68	.88
Endocrinology and metabolism	9.87	8.52–11.22	<.01
Neurology	0.83	−0.35 to 9.51	.16
Others	−2.22	−2.77 to −1.67	<.01
No. of comorbidities	2.52	2.19–2.85	<.01
No. of prescriptions for HTN	2.77	2.75–2.79	<.01

HTN = hypertension, MPR = medication possession ratio, MRCI = medication regimen complexity index.

* β is the regression coefficient.
† R^2_{adj} is 0.49 for MPR.
‡ R^2_{adj} is 0.62 for MPR.

For the patients who visited the same medical specialty, the MRCI remained negatively associated with MPR (β = −6.03, $P \leq .01$). The MPR was significantly higher (β = 9.87, $P \leq .01$) for the patients who visited the endocrinology and metabolism specialty than for those who visited the family medicine specialty. The MPR increased as the number of comorbidities increased.

5. Discussion

In this large-scale study, we found that the overall MPR was approximately 54.83% for newly diagnosed hypertensive patients. This estimate is not similar to that (34%) reported by Baggarly et al [35] for newly diagnosed hypertensive patients. The MPR for newly diagnosed hypertensive patients is expected to be lower than that (42–79%) in previously diagnosed hypertensive patients.[11,17,34,36] The reason for relatively high MPR in our study might be that we excluded newly diagnosed hypertensive patients with poor MPR (MPR < 10%). Our calculated MRCI of 3.39 for antihypertensive medications is greater than the 3.0 reported by Rettig et al.[37] This result might be because our patients used 1.7 types of antihypertensive drugs and had a combination of one or more related hypertension comorbidities (44.15%). According to guidelines for hypertension, the recommended number of drugs ranges from 1 to several.[2,3,24–28] When hypertensive patients have related hypertension comorbidities, the medication regimen for hypertension is more complex.[2,3,24–28] The most prevalent comorbidities for newly diagnosed hypertensive patients are diabetes and hyperlipidemia. CCBs, β-blockers, and ARBs are the top 3 commonly prescribed antihypertensive drugs. It was also consistent with the findings of previous studies.[16,36] We found that the use of CCBs, β-blockers, and ARBs varied significantly among the 3 groups of MPR, a finding that was similar to that of a previous study.[36]

The findings that sex, comorbidities, number of prescriptions for hypertension, and antihypertensive drug types were factors related to MPR are consistent with those of previous reports,[11,16,34–36] but age was not found to be a related factor for MPR in our results. Males had greater MPRs than those of female patients. When hypertensive patients had other comorbidities, such as diabetes, hyperlipidemia, stroke, and cardiovascular disease, their MPRs were significantly increased. We also found that the MPR increased as the number of prescriptions for hypertension increased. This finding was also consistent with a previous report that found that the use of CCBs, β-blockers, and ARBs was associated with higher MPRs.[36]

There were several major findings on the relationships among the MRCI, medical specialties, and MPRs in newly diagnosed hypertensive patients. First, by using the NHIRD in Taiwan, we found that the MRCI was a negative factor associated with the MPR among newly diagnosed hypertensive patients. This finding was consistent with those of previous reports.[11,13,16,17,19,28,38,39] One possible explanation of this finding is that the MPR of antihypertensive therapy might be improved by decreasing the numbers of drugs, pill counts, or the dosing frequency.[13,16,17,38,39] However, few studies have considered dosage forms and additional directions to measure the medication regimen complexity. In the MRCI results, we found that the score for additional directions tended to be higher in the low-MPR group, which suggests that simplifying additional directions could improve the MPR.

Second, the finding that medical specialties were associated with the MPR is consistent with those of previous reports.[11,34,35] The MPRs of patients who visited the same medical specialty were greater than those of patients who visited different medical specialties. We also found that the specialty of either family medicine or cardiology was one of the most visited

for the first diagnosis of hypertensive patients, and over half of all patients visited the same medical specialty. The endocrinology and metabolism specialty had the highest MPR, and family medicine and other medical specialties had lower MPRs. This finding was similar to that of a previous study.[11] They found that the MPR for the internal medicine specialty (33.6%) was higher than those for family medicine (26.3%) and cardiology (17.6%). Interestingly, the MRCI was highest for cardiology and lowest for family medicine. One reason for the lower MPR and MRCI for family medicine might be that comprehensive physical checkups were typically performed. After the checkup, newly diagnosed hypertensive patients would receive their first antihypertensive medications by a family medicine specialist; subsequently, patients may be treated for hypertension in other medical specialties depending on the patients' comorbidities. We also found that patients who were treated by endocrinology and metabolism specialists had higher prevalences of diabetes and hyperlipidemia than did the patients treated by other medical specialists. Patients who have more comorbidities might seek health care more regularly, which could lead to a higher MPR for the endocrinology and metabolism specialty. Another possible explanation is that the MPR will be higher because patients are referred to the endocrinology and metabolism specialty for the management of the comorbid disease.

5.1. Strengths and limitations

This study had several strengths: this was a nationwide descriptive study and the results should be applicable to other populations, the study included a large number of newly diagnosed hypertensive patients, the study used the NHIRD and pharmacy claims data to define the MPR and MRCI, and the study analyzed all patients who visited the same medical specialties to reduce the influence of confounding factors. Further studies are needed to examine the long-term trends in the associations among MRCIs, medical specialties, and MPRs in hypertensive patients.

Despite these strengths, this study had some limitations that should be considered. First, medication adherence was not examined in this study. The study used the NHIRD in Taiwan, so the situations under which the patients took their medications were not actually observed. Second, other potential factors related to the MPR (e.g., ethnicity, educational level, marital status, attitude, self-efficacy, social support, and side effects of antihypertensive drugs) were not available in the NHIRD. Third, BP was not measured in this study. Because the data in the database were presented to ensure patient confidentiality, the data could not be linked to the clinical records of an individual, so the database lacked data from physical examinations and laboratory testing. Finally, we adopted a mean MPR for multiple medications during the 1-year follow-up; however, this did not consider the temporal trend of antihypertensive drugs. Thus, the overall MPR might be underestimated for multipharmacy patients with an addition of another antihypertensive drug.

6. Conclusion

We found that MRCI and medical specialties were significantly associated with MPR in newly diagnosed hypertensive patients. Regarding regimen complexity, both dosing frequency and additional directions were inversely associated with the MPR. We suggest that simple dosage forms and medication directions, low dosing frequency, and fixed-dose combination therapy should be considered. For patients who visited the same specialty during the 1-year follow-up, those who were treated by endocrinology and metabolism specialists had higher MPRs than did those who were treated by family medicine specialists.

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