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The prevalence of monotherapy and combination therapy in hypertension in China from 2019 to 2021: A nationwide population-based cross-sectional study

Xiaoyang Luo MD[1,2] | Wei Liu MD[1] | Ningling Sun MD[3] | Peili Bo MD[4] | Yuanyuan Chen MD[3] | Qinghua Han MD[5] | Nanfang Li MD[6] | Xinzheng Lu MD[7] | Jianjun Mou MD[8] | Gang Sun MD[9] | Yuqing Zhang MD[10]

[1]Cardiovascular Department, Beijing Hospital, National Center of Gerontology, Institute of Geriatric Medicine, Chinese Academy of Medical Science, Beijing, China

[2]Cardiovascular Department, The Second Hospital of Shanxi Medical University, Taiyuan, China

[3]Cardiovascular Department, Peking University People's Hospital, Beijing, China

[4]Cardiovascular Department, Qilu Hospital of Shandong University, Jinan, China

[5]Cardiovascular Department, The First Hospital of Shanxi Medical University, Taiyuan, China

[6]Cardiovascular Department, Xinjiang Uigur Municipal People's Hospital, Urumqi, China

[7]Cardiovascular Department, Jiangsu Province Hospital, Nanjing, China

[8]Cardiovascular Department, The First Affiliated Hospital of Xi'an Jiaotong University, Xi'an, China

[9]Cardiovascular Department, The Second Affiliated Hospital of Baotou Medical College, Baotou, China

[10]Cardiovascular Department, Fu Wai Hospital, Center for Cardiovascular Diseases, Beijing, China

Correspondence
Wei Liu, Cardiovascular Department, Beijing Hospital, National Center of Gerontology, Institute of Geriatric Medicine, Chinese Academy of Medical Science, Beijing 100010, China.
Email: tgyliuw@163.com; liuweibjyy@163.com

Ningling Sun, Cardiovascular Department, Peking University People's Hospital, Beijing 100032, China.
Email: sunnl@263.net

Abstract

There are no nationwide surveys on antihypertensive drugs in China. In order to assess the current status of antihypertensive drug therapy in patients with hypertension and analyzed factors that may affect combination therapy, using convenience sampling, we recruited 305,624 patients with hypertension from the Chinese Cardiovascular Association Database-Hypertension Center between January 2019 and December 2021. Chi-squared test was performed to analyze the administered antihypertensive drug types and their combinations in different hospital settings. Logistic regression was used to assess the factors influencing combination therapy. We found around 33.1% of the participants had stage 2 and above hypertension, of which 67.9% were treated with combination therapy. In community or general hospitals, the most common monotherapy was calcium channel blockers (CCB), angiotensin-converting enzyme inhibitor/angiotensin II receptor inhibitor (ACEI/ARB) and diuretic were the main single-pill combinations (SPCs), and ACEI/ARB and CCB were the main free combination. From 2019 to 2021, the rates of combination therapy increased (58.8%–64.1%) with SPCs from 25.9% to 31.0% and free combination from 31.9% to 32.6%.

Patients aged < 60 years, with stage 2 and above hypertension, with an education level of high school and above, visiting general hospitals, living in the eastern region of China, with hypertension risk factors and comorbidities, and without anxiety or depression were more likely to receive combination therapy (all $P < .05$). The combination therapy use rate increased yearly and the rate of SPCs rose obviously. Individual, hospital, and regional differences in patients with hypertension influenced combination therapy.

KEYWORDS
free combination, hypertension, monotherapy, single-pill combinations

1 | INTRODUCTION

Hypertension is associated with the occurrence and development of various cardiovascular diseases.[1] Studies have shown that for every 20 mmHg increase in systolic blood pressure (SBP) or 10 mmHg increase in diastolic blood pressure (DBP) the risk of cardiovascular and cerebrovascular diseases doubles.[2,3] Hypertension is a prevalent condition, with an incidence of 27.9% in China between 2012 and 2015. It is associated with high disability and mortality rates. However, a national survey in China revealed low awareness levels of hypertension, a treatment rate of less than 50%, and a control rate of less than 17%.[1]

The timely administration of appropriate treatment can prevent or delay the occurrence of hypertension-related complications. Some studies have suggested that monotherapy effectively lowers blood pressure (BP) in only a subset of patients with hypertension, with the remainder requiring combination therapy.[4–6] However, combination therapy is not routinely administered in China, resulting in a low control rate of hypertension.[7] To standardize the diagnosis, treatment, and management of hypertension and improve the BP control rate in patients, the Chinese Cardiovascular Association (CCA) Database-Hypertension Center collected data from multiple centers regarding the administration of antihypertensives and personal characteristics of patients with hypertension. This study aimed to analyze the choice of antihypertensive drug therapy, particularly combination therapy to provide suggestions for the selection of antihypertensive drugs for patients with hypertension in China.

2 | METHODS

2.1 | Data source and study population

The aim of establishing the CCA Databases–Hypertension Center was to bridge the gap between general hospitals and community hospitals. General hospitals are usually the lead hospitals and need to establish cooperation systems with at least three community hospitals (also known as satellite hospitals), including joint consultation and referral systems for patients with hypertension. To be identified as a lead hospital, a hospital needs to meet the following conditions: (1) cardio-

vascular internal medicine is a dominant discipline in the region, and it can provide other medical institutions in the region with diagnosis and treatment of complex cases and continuing education; (2) the hospital establish an information sharing platform with three or more surrounding satellite hospitals; (3) the hospital is equipped with at least one intelligent sphygmomanometer that can transmit BP data in real-time; (4) the hospital has basic laboratory and imaging examination conditions; (5) the hospital has an available hypertension clinic and ward; (6) the hospital has available educational facilities. To be identified as a satellite hospital, a hospital needs to meet the following conditions: (1) the team of internal medicine physicians has the ability to diagnose and treat mild hypertension; (2) the hospital is equipped with at least one intelligent sphygmomanometer that can transmit BP data in real-time; (3) the hospital has available educational facilities. According to the CCA requirements, a lead hospital and all satellite hospitals that associated with the lead hospital have a combined population of not less than 500, and the number of patients in a satellite hospital must not be less than 100.

Data were collected from the CCA Database-Hypertension Center by staff having a medical background. Using convenience sampling, patients with hypertension included in the database between January 1, 2019 and December 31, 2021, were selected as the study population. Data on patient demographics (age, sex, height, weight, body mass index [BMI], ethnic group, education level, and place of residence) and clinical characteristics (hospital attended, BP at clinical visit, clinical visit date, risk factors, hypertension course, comorbidities, psychological status, and antihypertensive medication) were collected.

2.2 | BP measurements, diagnostic criteria, and definitions

The automatic sphygmomanometer validated according to standardized conditions and protocols was preferred. BP was measured sequentially in both upper arms, using an appropriate cuff size for the arm circumference by a trained physician or nurse, after the patient had sat still for five min in the hospital outpatient room. The upper arm with the highest BP was defined as the measurement arm and BP was measured three times in that arm. The average of the last two measurements was calculated every day. However, if the difference between

the two SBP or DBP measurements was over 10 mmHg, another measurement was made, and the average of the last two was calculated.[6,8] On three consecutive days, the same doctor or nurse repeat above steps of BP measurement, and only the last 2 days of BP values were recorded.

The types and names of antihypertensive drugs were consistent with those of the Joint National Committee and Chinese definitions.[7,9] Hypertension was diagnosed in patients with an SBP of at least 140 mmHg or a DBP of at least 90 mmHg in the absence of antihypertensive medications, and in patients with a history of hypertension and receiving antihypertensive medications, regardless of their BP measurements.[8] Clinical visit date was defined as the first visit day to the current lead or satellite hospital. Patients with hypertension were classified according to their office BP at the clinical visit: below stage 2 hypertension (SBP < 160 mmHg and/or DBP < 100 mmHg) and; stage 2 and above hypertension (SBP ≥160 mmHg and/or DBP ≥100 mmHg). Controlled hypertension was defined as an average SBP of < 140 mmHg and an average DBP of < 90 mmHg in people with hypertension; patients not meeting these criteria were considered as uncontrolled hypertension.

Monotherapy was defined as the use of only one type of antihypertensive drug, whereas combination therapy was defined as the use of two or more antihypertensive pills (free combination) or any type of single-pill combination (SPC), which includes only a SPC and SPC with other antihypertensive drugs. BMI was calculated as weight (kg) divided by the squared value of height (m^2); a BMI ≥28.0 was considered to indicate obesity.[10] Participants who smoked > 400 cigarettes previously and smoked at the time of the examination were classified as current smoking.[11] People who drank three or more drinks per day and drank at the time of the examination were defined as current drinking.[12] Diabetes was diagnosed as glycosylated hemoglobin A1c≥6.5%, previous diagnosis of diabetes and/or chronic hypoglycemic drug usage.[13] Coronary lumen diameter stenosis ≥50% in the main artery or its major branches confirmed by angiography, computed tomography angiography or magnetic resonance imaging was diagnosed as coronary heart disease (CHD).[14] Patients filled out questionnaires of Patient Health Questionnaire-9 (PHQ-9) and 7-item generalized anxiety disorder score (GAD-7). Depression was diagnosed when PHQ-9≥5 scores and anxiety was diagnosed when GAD-7≥5 scores.[15,16] Grading details are provided in Supplemental Digital Content 1.

2.3 | Statistical analyses

SPSS software (version 26.0; IBM Corporation, Armonk, NY) was used for database management and statistical analyses. Categorical variables are expressed as constituent ratios or rates, and continuous variables are expressed as mean ± standard deviation. We compared the characteristics of the patients in the controlled hypertension group and uncontrolled hypertension group using the Chi-squared test for categorical variables and Student's t-test for continuous variables.

Chi-squared test to was used analyze monotherapy and combination therapy in community and general hospitals. Multiple comparative analyses of the monotherapy, free combination, and SPC group were made using Bonferroni's correction. Multivariate logistic regression analysis was used to analyze the factors influencing combination therapy. The significance level α was equal to 0.05, and two-sided P-value < .05 was considered as statistically significant.

3 | RESULTS

3.1 | Patient characteristics

In this study, a total of 1409 hospitals participated in the accreditation between January 2019 and December 2021 from 34 provinces in China, including 310 lead hospitals and 1099 satellite hospitals. An average of 217 patients were enrolled in each hospital (least number in Deqing County Wukang town community hospital, n = 100, and highest number in Lanzhou First People's Hospital, n = 3,967).

A total of 356,783 patients with hypertension were included in the database between January 2019 and December 2021 along with the required information. The exclusion criteria were patients: (1) aged < 18 years, > 100 years, or no age provided (n = 733); (2) height < 140 cm, > 200 cm, or no height provided (n = 494); (3) weight < 40 kg, > 120 kg, or no weight provided (n = 795); (4) education information missing (n = 609); (5) geographical region information missing (n = 803); (6) SBP ≤60 mmHg, ≥250 mmHg, or information missing (n = 330); (7) DBP ≤40 mmHg, ≥180 mmHg, or information missing (n = 250); and (8) no antihypertensive drug treatment (about 47,145 cases in total, including 40,116 patients who refused to administer antihypertensive drugs, and 7,029 patients who were reluctant to answer). A total of 305,624 patients were included in the study, which involved 1,409 hospitals in 34 provinces in China. The Ethics Committee of the National Center for Institute of Geriatric Medicine, Chinese Academy of Medical Sciences/Beijing Hospital approved our study protocol.

The characteristics of the 305,624 study participants are summarized in Table 1. The participants had an average age of 64.7 ± 12.5 years and an average office BP of 147/86 mmHg. Among the participants, 52.7% (n = 161,177) were males, 28.4% (n = 86,658) attended community hospitals, 50.2% (n = 153,434) lived in the east of China, 61.9% (n = 189,137) had uncontrolled hypertension and 33.1% (n = 101,219) had stage 2 and above hypertension.

Compared to the participants with controlled hypertension, participants with uncontrolled hypertension were more likely to visit general hospitals, live in the central and western regions of China, have lower educational status, current smoking, current drinking, receive combination therapy, have not used antihypertensive drugs before and have a history of obesity, stroke, anxiety, and depression. Participants with controlled hypertension were more likely to be older, have a longer duration of hypertension, and have a history of diabetes and CHD, compared with participants with uncontrolled hypertension.

TABLE 1 Characteristics of patients with hypertension.

Analyzed parameter	Controlled hypertension (n = 116,487)	Uncontrolled hypertension (n = 189,137)	Total (n = 305,624)	P-value
Age, years (mean ± SD)	65.6 ± 11.6	64.1 ± 13.0	64.7 ± 12.5	<.001
Sex				<.001
Male	61,072 (52.4)	100,105 (52.9)	161,177 (52.7)	
Female	55,415 (47.6)	89,032 (47.1)	144,447 (47.3)	
Duration of hypertension (years)				<0.001
1–10	44,124 (37.9)	69,673 (36.8)	113,797 (37.2)	
11–20	43,025 (36.9)	58,145 (30.8)	101,170 (33.1)	
>20	12,873 (11.1)	20,089 (10.6)	32,962 (10.8)	
Unknown[a]	16,465 (14.1)	41,230 (21.8)	57,695 (18.9)	
Level of hospital at clinical diagnosis				<.001
Community	43,495 (37.3)	43,163 (22.8)	86,658 (28.4)	
General	72,992 (62.7)	145,974 (77.2)	218,966 (71.6)	
Geographical region of China				<0.001
Eastern	64,211 (55.2)	89,223 (47.2)	153,434 (50.2)	
Central	27,896 (23.9)	57,773 (30.5)	85,669 (28.0)	
Western	24,380 (20.9)	42,141 (22.3)	66,521 (21.8)	
Ethnicity				<.001
Han	112,276 (96.4)	180,101 (95.2)	292,377 (95.7)	
Non-Han	4,211 (3.6)	9,036 (4.8)	13,247 (4.3)	
Education				<.001
Primary school and below	55,033 (47.2)	98,638 (52.1)	153,671 (50.3)	
Middle school	29,953 (25.7)	45,246 (23.9)	75,199 (24.6)	
High school	19,663 (16.9)	27,355 (14.5)	47,018 (15.4)	
College and above	11,838 (10.2)	17,898 (9.5)	29,736 (9.7)	
Risk factors				
Current smoking	16,935 (14.5)	28,730 (15.2)	45,665 (14.9)	<.001
Current drinking	17,172 (14.7)	31,059 (16.4)	48,231 (15.8)	<.001
Obesity	17,237 (14.8)	32,141 (17.0)	49,378 (16.2)	<.001
Comorbidities				
Diabetes	22,436 (19.3)	32,485 (17.2)	54,921 (18.0)	<.001
CHD	29,590 (25.4)	43,095 (22.8)	72,685 (23.8)	<.001
Stroke	11,141 (9.6)	20,952 (11.1)	32,093 (10.5)	<.001
Drug therapy				<.001
Monotherapy	49,039 (42.1)	70,348 (37.2)	119,387 (39.1)	
Free combination	36,312 (31.2)	63,635 (33.6)	99,947 (32.7)	
Single-pill combinations	31,136 (26.7)	55,154 (29.2)	86,290 (28.2)	
Antihypertensive medication history				<.001
Previously used	85,512 (73.4)	118,913 (62.9)	204,425 (66.9)	
Have not used before[a]	16,081 (13.8)	31,419 (16.6)	47,500 (15.5)	
Unknown[b]	14,894 (12.8)	38,805 (20.5)	53,699 (17.6)	
Psychological factors[c]				<.001
Health	100,839 (86.6)	158,156 (83.6)	258,995 (84.7)	
Anxiety	13,939 (12.0)	27,897 (14.7)	41,836 (13.7)	
Depression	995 (0.9)	2,025 (1.1)	3,020 (1.0)	
Anxiety and depression	714 (0.5)	1,059 (0.6)	1,773 (0.6)	

Unless stated otherwise, data are presented as number (percentage).

Abbreviations: SD, standard deviation; CHD, coronary heart disease.

[a]"haven't used before" refers to patients with hypertension who never used antihypertensive drugs before but started to take such drugs at this clinical visit.

[b]Patients did not know or did not wish to answer.

[c]The psychological rating scale is described in supplemental digital content 1.
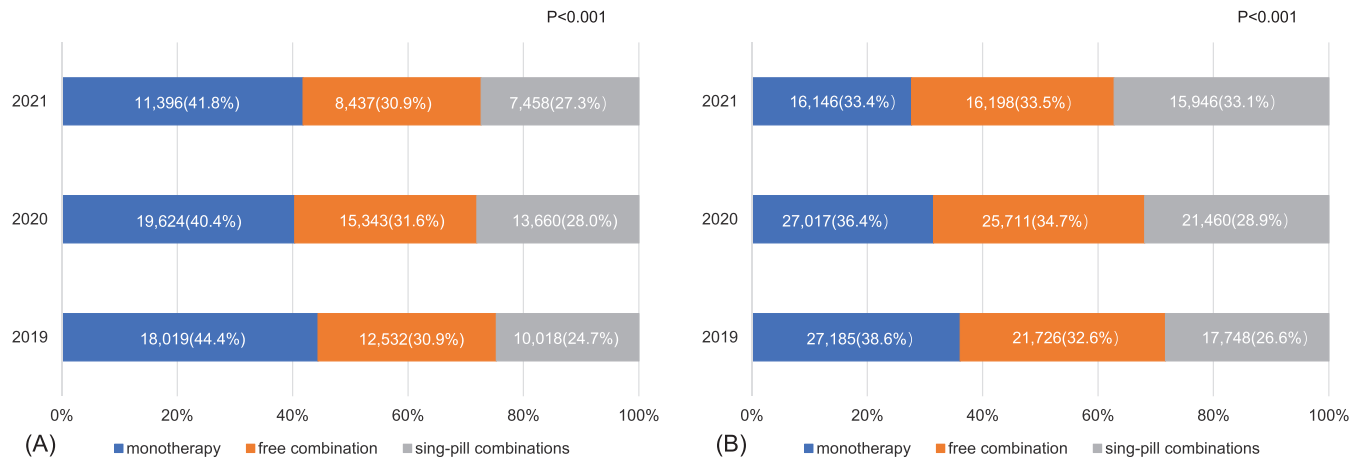
P<0.001

P<0.001

FIGURE 1 Percentage of monotherapy, free combination and single-pill combinations in patients with controlled hypertension (A) and uncontrolled hypertension (B) in 2019–2021. Multiple comparative analyses of the monotherapy, free combination, and single-pill combination groups were performed in (A) and (B), and the *P*-value of Bonferroni's correction was .0167. For patients with controlled hypertension, the pairwise comparison of 3 years in the monotherapy group was statistically significant (*P* < .0167); the comparisons between 2020 and 2019, and 2021 and 2019 in single-pill combinations group were statistically significant (all *P* < .0167), but the comparison between 2020 and 2019 was not significant (*P* > .0167). The pairwise comparison of 3 years in the free combination group was not statistically significant (*P* > .0167). The *P*-values were all less than .0167 after pairwise comparisons among the three groups in (B).

3.2 | Antihypertensive drugs

Of the 305,624 patients with hypertension, 119,387 (39.1%) received monotherapy with a percentage decrease from 41.2% in 2019–35.9% in 2021, and 186,237 (60.9%) received combination therapy with a percentage increase from 58.8% in 2019–64.1% in 2021 (*P* < .001). About 40.4%~44.4% of the patients with controlled hypertension received monotherapy and 30.9%~31.6% of patients were treated with free combination during 2019–2021 as shown in Figure 1A. The percentage of SPCs jumped from 24.7% in 2019–27.3% in 2021 (*P* < .001). Monotherapy and combination therapy in uncontrolled hypertension patients over the 3 years of this study are shown in Figure 1B. The percentage of SPCs had gone up the most, which increased from 26.6% in 2019–33.1% in 2021. However, the decline in the percentage of monotherapy from 38.6% to 33.4% over 3 years for patients with uncontrolled hypertension more obviously than that for the patients with controlled hypertension (from 44.4% to 41.8%) over the same period (*P* < .001).

The specific antihypertensive drugs used are shown in Table 2. Calcium channel blocker (CCB), administered to 53.8% (*n* = 64,226) of the patients receiving monotherapy, was the most commonly used monotherapy, followed by angiotensin II receptor blocker (ARB) and angiotensin-converting enzyme inhibitor (ACEI), which was given to 24.8% (*n* = 29,559) and 10.1% (*n* = 12,082) of the patients, respectively.

Beta-blocker (BB) were used in 8.6% (*n* = 10,208) of the patients with hypertension receiving monotherapy, 41.7% (*n* = 4,259) of them had CHD. BB was administered to 3.6% (*n* = 1,614) and 11.6% (*n* = 8,594) of the patients with hypertension in community and general hospitals, respectively. Of the patients receiving BB in community and general hospitals, 19.3% (*n* = 312) and 45.9% (*n* = 3,947), respectively, had CHD.

A total of 186,237 patients were treated with combinations of antihypertensive drugs, of whom 54.1% (100,711) used free combinations and 45.9% (85,526) used SPCs. Of 85,526 patients using SPCs, 52.3% (44,740) were on SPC and also on other types of antihypertensive drugs. The most common free combination was ACEI/ARB (A)+CCB (C), which was taken by 35.7% (*n* = 36,410) of the patients receiving this drug therapy, followed by A+BB (B) (15.6%, *n* = 15,577) and B+C (13.7%, *n* = 13,688). The most frequently used SPC was A+diuretic (D), which was taken by 63.3% (*n* = 54,621) of patients receiving this therapy, followed by A+C (30.5%, *n* = 26,323). In most compositions of free combination and SPCs, ARB accounted for a larger proportion than ACEI. The usage rates of SPCs in community and general hospitals were 25.7% (*n* = 22,259) and 29.2% (*n* = 64,031), respectively.

CCB was the most commonly used monotherapy in patients with diabetes (*n* = 54,921), CHD (*n* = 72,685) and stroke (*n* = 32,093), followed by ARB. In patients with CHD, A+B and A+D were the most commonly used free combination and SPCs, respectively. In patients with diabetes and stroke, A+C was the most commonly used free combination and A+D was the most commonly used SPCs.

3.3 | Factors associated with combination therapy

Forward binary logistic regression analysis was used to analyze 15 variables: age, sex, region, education level, hospital types, hypertension stage, risk factors for hypertension, comorbidities, and psychological factors.

The male patients aged < 60 years with stage 2 and above hypertension, an education level of high school and above, and visiting general hospitals were more likely to receive combination therapy (Figure 2). Patients with hypertension in the eastern region of China were more

TABLE 2 Types of antihypertensive drugs used in patients with hypertension in different hospitals.

Drug therapy	Community hospitals	General hospitals	Total	P-value
Monotherapy				<.001
CCB	26,500 (58.6)	37,726 (50.9)	64,226 (53.8)	
ARB	11,769 (26.0)	17,790 (24.0)	29,559 (24.8)	
ACEI	3,783 (8.4)	8,299 (11.2)	12,082 (10.1)	
BB	1,614 (3.6)	8,594 (11.6)	10,208 (8.6)	
Diuretic	1,588 (3.4)	1,724 (2.3)	3,312 (2.7)	
Total	45,254 (37.9)	74,133 (62.1)	119,387 (100.0)	
Combination therapy				<.001
Free combination				
A+C	10,718 (25.9)	25,692 (17.7)	36,410 (19.6)	
A+B	1,690 (4.1)	13,887 (9.6)	15,577 (8.4)	
B+C	2,656 (6.4)	11,032 (7.6)	13,688 (7.3)	
C+D	725 (1.8)	1,685 (1.2)	2,410 (1.3)	
A+D	642 (1.6)	1,690 (1.2)	2,332 (1.3)	
B+D	143 (0.4)	1,432 (1.0)	1,575 (0.8)	
Other two	540 (1.3)	2,358 (1.6)	2,898 (1.6)	
A+B+C	1,336 (3.2)	10,890 (7.5)	12,226 (6.6)	
A+C+D	508 (1.2)	2,477 (1.7)	2,985 (1.6)	
A+B+D	121 (0.3)	1,852 (1.3)	1,973 (1.1)	
B+C+D	102 (0.2)	1,000 (0.7)	1,102 (0.6)	
Other three	153 (0.4)	2,580 (1.8)	2,733 (1.5)	
A+B+C+D	83 (0.2)	1,706 (1.2)	1,789 (1.0)	
Other four	97 (0.2)	2,250 (1.6)	2,347 (1.3)	
Five and above	12 (0.1)	654 (0.5)	666 (0.4)	
SPCs				
A+D[a]	15,130 (36.6)	39,491 (27.3)	54,621 (29.3)	
A+C[b]	3,319 (8.0)	23,004 (15.9)	26,323 (14.1)	
Other SPCs	3,429 (8.1)	1,153 (0.6)	4,582 (2.2)	
Total	41,404 (22.2)	144,833 (77.8)	186,237 (100.0)	

Abbreviations: A, ACEI/ARB; B, BB; C, CCB; D, diuretic. A+D; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor inhibitor; BB, beta-blocker; CCB, calcium channel blockers; SPC, single-pill combination.
[a]Represents the SPC composed of ACEIs/ARBs and diuretics, and A+C.
[b]Indicates the SPC composed of ACEIs/ARBs and CCB.

likely to receive combination therapy than those in the central and western regions. Patients with risk factors for hypertension, CHD, diabetes, and no anxiety or depression were more likely to receive combination therapy.

4 | DISCUSSION

A total of 305,624 patients with hypertension from more than 1,400 hospitals in China were included in this study. About 60.9% of these patients were treated with a combination of antihypertensive drugs. CCB was the most common monotherapy, A+C was the most common free combination, and A+D was the most common SPC. Among these, the use of SPCs has significantly increased over the 3 years.

The pathogenesis of hypertension is complex. Patients with significantly elevated BP, target organ damage, and clinical comorbidities require combination therapy. Previous studies have shown that more than 70% of patients with hypertension require combination therapy to effectively control BP.[17,18] In this study, similar proportions of patients received free combination and SPCs. A+C was the main type of free combination administered in community and general hospitals, which is consistent with the 2020 International Society of Hypertension guidelines.[19] A+D was the predominant SPCs used in community and general hospitals, which may be related to the

variation		OR(95% CI)	P value
gender			
male		1	
female		0.980(0.964-0.996)	0.018
age			
≤60yr		1	
>60yr		0.842(0.828-0.856)	<0.001
classification of hypertension			
below stage 2		1	
stage 2 and above		1.450(1.427-1.474)	<0.001
hospital level			
community hospitals		1	
general hospitals		1.860(1.828-1.892)	<0.001
region			
east region		1	
central region		0.892(0.876-0.908)	<0.001
western region		0.971(0.953-0.990)	0.004
degree of education			
did not graduate high school graduate		1	
high school graduate and above		1.154(1.134-1.175)	<0.001
risk factors			
smoking		1.098(1.071-1.125)	<0.001
drinking		1.163(1.136-1.191)	<0.001
obesity		1.325(1.298-1.354)	<0.001
comorbidities			
coronary heart diseases		1.466(1.438-1.494)	<0.001
diabetes		1.168(1.145-1.192)	<0.001
stroke		0.913(0.891-0.936)	<0.001
psychological states			
depression and/or anxious		1	
no depression and/or anxious		0.895(0.876-0.913)	<0.001

FIGURE 2 Factors that may influence the combination therapy. CI, confidence interval; OR, odds ratio.

drug availability in China. SPCs are recommended for combination therapy in the hypertension guidelines worldwide because of their efficacy and notable high compliance rates.[4–7] Thiazide diuretics, which are components of most SPCs, are recommended as first-line antihypertensive drugs by the international guidelines.[20,21] The selection of A+C or A+D should be determined on a case-by-case basis after considering the clinical characteristics of each patient.

CCB, the most commonly used monotherapy in two hospital classes, is suitable for use in Asian populations because of its wide indications, good antihypertensive effects, and lack of absolute contraindications.[22] In this study, ARB was the second most popular monotherapy. ARB is related to target organ protection in patients with hypertension, thus, it is typically the first choice for patients with diabetes and CHD.[23] BB can inhibit sympathetic nerve activity and slow the heart rate, and is therefore suitable for patients with sympathetic nerve excitation. Due to a lack of evidence and the influence of international guidelines, only 6.4% of patients without comorbidities received BB monotherapy. The proportion of BB use in general hospitals was significantly higher than that in community hospitals, which may be related to the higher proportion of patients with CHD in general hospitals. Previous randomized controlled trials revealed that the low heart rate was associated with the occurrence of adverse cardiovascular events in older patients with hypertension,[24] which limits the use of BB in this population.

In our study, approximately 80% of the patients with hypertension, diabetes, and CHD were being treated with antihypertensive drugs at the time of the clinical consultation, and therefore had normal BP at that time. The hospital grade was related to the choice of antihypertensive drugs. The higher the hospital, the higher the proportion of combination treatment, which was related to hypertension severity and drug resource allocation. It is more challenging to control BP in patients who smoke, drink alcohol, and are obese.[25–27] Therefore, the proportion of combination therapy was higher in these patients. In addition, patients with comorbidities were more likely to choose combination therapy than others, which might be related to the difficulty in controlling BP in these patients and the lower BP target blood set.[28,29] Although a high proportion of patients with stroke had uncontrolled hypertension, the target BP was higher in these patients than that of the general population, which may explain the small proportion of these patients receiving combination therapy.[30] Patients with higher education levels were more likely to accept combination drug therapy, indicating that educational background could affect the choice of antihypertensive drugs.[31,32]

Overall, the selection of antihypertensive drugs in this study was consistent with the recommendations of national and international guidelines.[4–7] However, certain matters require further investigation. First, the use of ACEIs was much lower than that of ARBs. Many studies have suggested that ACEI and ARB have similar antihypertensive effects,[33–35] but evidence suggests that ACEI can significantly reduce

the risk of adverse cardiovascular events.[36] Accordingly, ACEI should be the first choice of treatment for patients with hypertension who can tolerate these drugs. Second, most patients with hypertension and diabetes received CCB monotherapy, which differed slightly from the recommendations of the guidelines. This may be related to the good tolerance of CCB and their widespread use in primary medical institutions. Third, the application of SPCs in community hospitals remains insufficient, which may be related to drug availability, regional differences, and economic conditions. Therefore, the use of SPCs requires further promotion in these settings. Fourth, SPCs were mainly limited to A+D and A+C, which are indicated for patients with comorbidities, suggesting that the variety of SPCs available in China is insufficient. Thus, there is scope for improvement in terms of selection of the appropriate antihypertensive drug in China.

This study has few limitations. First, factors that may affect the choice of antihypertensive drugs, such as income, occupation, and patient medication compliance, were not analyzed. Second, lifestyle interventions are important aspects of antihypertensive treatment; the effects of this factor on BP were not considered in this study. Although none of the enrolled patients were infected with the novel coronavirus, but quarantine, low physical activity, poor diet, and psychological stress may raise the incidence of hypertension. Some patients with well-controlled BP may need intensive antihypertensive therapy.[37] Third, less commonly used antihypertensive medications, such as alpha-blockers and angiotensin receptor neprilysin inhibitors, were not included in this study, which may have resulted in selection bias. Fourth, although convenience samples are easy and economical to acquire, the extent to which one can generalize the results from the patients in a convenience sample to others in the population is limited.[38]

The novelty of this study is that it is the first to analyze the use of antihypertensive drugs in community and general hospitals in China. The proportions of patients treated with monotherapy, free combination, and SPCs were compared in detail and the rationality of antihypertensive drug use was analyzed. This study findings suggest that improvements are needed to conform to the current guidelines and optimize patient care.

5 | CONCLUSIONS

In conclusion, the rate of combination therapy increased every year, and the rate of SPCs rose obviously in China from 2019 to 2021, especially for uncontrolled hypertension patients. For patients with or without comorbidities, the selection of antihypertensive drugs was roughly consistent with the recommendations of international guidelines. However, SPCs in community hospitals were still relatively insufficient, and for some patients with hypertension combined with diabetes, the first choice of antihypertensive drug was inconsistent with the guidelines. Finally, the individual, hospital and regional differences in patients with hypertension might influence combination therapy.

ORCID

Wei Liu MD https://orcid.org/0009-0005-9131-1211
Ningling Sun MD https://orcid.org/0000-0003-0378-2813
Jianjun Mou MD https://orcid.org/0000-0002-0335-3528
Yuqing Zhang MD https://orcid.org/0000-0001-8142-8305

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.