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ORIGINAL RESEARCH ARTICLE

Antihypertensive Treatment Patterns and Blood Pressure Control in Older Adults: Results from the Berlin Aging Study II

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Abstract

Background Hypertension is highly prevalent in older adults and represents a major public health issue since recognition, awareness, treatment and control are insufficient. Analyses of prescription patterns in conjunction with clinical parameters can provide novel insights into the current practice of hypertension management and help to identify barriers to sufficient hypertension control.

Methods A cross-sectional analysis was conducted. Prevalence of hypertension, patterns of antihypertensive therapy, and determinants of blood pressure (BP) control were examined in the Berlin Aging Study II cohort, including 1654 community-dwelling older adults (60–85 years of age).

Results Of the participants, 75.9% had hypertension; 40.6% of these were not prescribed BP medications. Lack of hypertension awareness, younger age, absence of comorbidities, not being on a statin, and not having visited a physician in the past 3 months were associated with lack of treatment. Forty-two percent of treated hypertensive individuals received monotherapy and 58.0% received combination therapy. Renin–angiotensin–aldosterone system (RAAS) inhibitors, and β-blockers were most commonly prescribed, while calcium channel blockers were least prescribed. Only 38.5% of treated hypertensive individuals had their BP controlled to < 140/90 mmHg. Number and choice of BP medications were not predictive of BP control; neither were age, glycated hemoglobin (HbA_{1c}), kidney function, or number of healthcare visits. However, female sex, lower low-density lipoprotein cholesterol (LDL-C) levels and current smoking, amongst others, were positively associated with BP control. There was evidence of significant effect modification by statins in the association of LDL-C and BP.

Conclusion The majority of older adults do not reach BP goals. Antihypertensive prescription patterns do not conform to current guidelines. Using more BP medications was not associated with higher odds of BP control. Lowering LDL-C might be favorable in terms of BP control.

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Key Points

Analyses of prescription patterns can provide insights into the current practice of hypertension management in order to overcome insufficient hypertension treatment and control.

In this cohort of community-dwelling older adults, a large proportion of hypertensive older adults were not prescribed blood pressure (BP) medications (40.6%). Antihypertensive prescription patterns did not conform to current guidelines. Only 58.0% of treated hypertensive individuals received combination therapy, and only 38.5% of treated hypertensive individuals had their BP controlled to < 140/90 mmHg.

In this cohort, renin–angiotensin–aldosterone system (RAAS) inhibitors and β-blockers were most commonly prescribed.

Being female, having lower low-density lipoprotein cholesterol, and being a current smoker were positively associated with BP control.

1 Introduction

Hypertension in older adults is a major public health issue. Hypertension is the largest contributor to loss of global disability-adjusted life-years [1]. The prevalence of hypertension increases with age [2]. In Germany, the proportion of people with hypertension was recently estimated to be about 71.0% among individuals aged 65–79 years [3].

Reducing systolic blood pressure (SBP) is effective in preventing stroke and heart failure, among other cardiovascular endpoints, and the benefits are established, regardless of age and frailty status [4, 5]. Moreover, treatment of hypertension can also prevent worsening of cognition in older individuals [6]. Benefits may occur as soon as 1–2 years after the start of treatment [7]. Unfortunately, awareness, recognition, treatment and control of high blood pressure (BP) remain insufficient at all ages, but particularly among older adults [3, 8, 9].

Management of hypertension in Germany is based on treatment recommendations of the European Society of Hypertension (ESH) and the European Society of Cardiology (ESC) [10]. These guidelines recommend initiation of treatment in all older adults with SBP ≥ 160 mmHg, with systolic target levels between 140 and 150 mmHg, and in fit older adults < 80 years, they recommend target levels < 140 mmHg. Indeed, the optimal BP target currently is a matter of intense debate, since at least the recent release of the results of the SPRINT trial, which demonstrated relevant benefits in older subjects treated to an SBP target of < 120 mmHg compared to < 140 mmHg [5].

On the other hand, serious treatment-related events, such as hypotension, syncope and falls, electrolyte imbalances and acute kidney injury (AKI) are relevant concerns, which may affect therapy goals and prescription patterns [11]. Likewise, in the treatment of older adults, consideration of common geriatric syndromes such as frailty, polypharmacy, sarcopenia, and anticholinergic side effects of drugs [12] is important.

Five major classes of drugs are commonly recommended for first-line therapy of hypertension, angiotensin-converting enzyme inhibitors (ACE-Is), angiotensin receptor blockers (ARBs), β-blockers (BBs), calcium channel blockers (CCBs) and thiazide diuretics [10], since they have proved to be equally effective regarding cardiovascular outcomes. However, little is known about drug class-dependent benefits and detriments in the elderly [13]. Indeed, according to the ESH/ESC guidelines, CCBs or diuretics are preferentially recommended in elderly patients with isolated systolic hypertension [14], whereas in patients with chronic kidney disease (CKD), diabetes, or metabolic syndrome, ACE-Is or CCBs are favored. There is consensus that in the majority of older adults, two or more antihypertensive drugs are required to attain BP control [10], which ideally would include a diuretic plus CCB and/or ACE-I or ARB in accordance with the current body of evidence and the guidelines [10].

Although intervention studies have proven that BP can be effectively lowered to target levels, it remains a challenge to translate those attempts into routine clinical practice [5, 15]. In part, the reasons are obvious or well known (e.g., poor adherence with pharmacotherapy is well recognized as one of the main barriers to achieving hypertension control [16]), but otherwise, there remains a lack of clarity. Therefore, analyses of real-life prescription patterns in conjunction with clinical parameters can be of great value, as they can provide novel insights into the current practice of hypertension management and help to identify barriers to sufficient hypertension control.

The aims of the present study were (1) to determine the prevalence of hypertension and attainment of BP control in the Berlin Aging Study II (BASE-II) sample, a cohort of community-dwelling older adults (60–85 years of age); (2) to examine patterns of antihypertensive treatment; and (3) to investigate factors that are associated with BP control.

2 Methods

2.1 Study Sample

This was a cross-sectional analysis of baseline data from BASE-II. BASE-II was launched to investigate factors associated with "healthy" and "unhealthy" aging, and has been described previously in detail [17, 18]. Briefly, BASE-II was recruited as a convenience sample from the greater Berlin metropolitan area by means of advertisements in local newspapers and the Berlin public transport system. In 2009–2014, 2172 participants (~ 75% aged 60–85 years and ~ 25% aged 20–35 years) were enrolled in the medical part of the study. All participants gave written informed consent, and the study was approved by the Ethics Committee at Charité-Universitätsmedizin Berlin (EA2/029/09). Datasets of 1654 older participants of BASE-II included complete data on BP measurements and medication.

2.2 Blood Pressure (BP)

BP was measured in the seated position. Two BP measurements were taken, one on the left and one on the right arm, and the mean was used in all further analyses. Hypertension was defined as SBP ≥ 140 mmHg and/or diastolic blood pressure (DBP) ≥ 90 mmHg or use of BP medications [19]. BP control was defined as SBP < 140 mmHg and DBP < 90 mmHg in treated hypertensive individuals. Treated individuals with SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg were classified as "uncontrolled" [20]. Awareness was assessed by the question: "Have you ever been told that you have hypertension or elevated blood pressure?".

2.3 Covariates

All blood and urine parameters were measured in a central certified laboratory using standardized protocols, as previously described [21]. Diagnoses were obtained by integration of information from medical examination, medical history, and further diagnostics such as laboratory tests (for details, see Bertram et al. [17]). Participants were asked to bring their medication plan and packets of all drugs used on a regular basis. Study staff took a comprehensive medication history (including indication, dosage, start, and side effects). BP medications were considered in the analysis without information on dosing and taking scheme. Body mass index (BMI) was calculated as weight in kilograms divided by the square of the height in meters; waist and hip circumferences were measured in light clothes. CKD was defined as estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73 m^2 (Chronic Kidney Disease Epidemiology Collaboration [CKD-EPI] formula) and/or albumin–creatinine ratio > 30 mg/g.

2.4 Statistics

In descriptive statistics, values are expressed as percentages, mean ± standard deviation or median and interquartile range.

Multiple logistic regression models were computed to estimate multivariable-adjusted associations of BP treatment (no treatment but evidence of hypertension as reference group) and age, GFR (mL/min/1.73 m^2), BMI, awareness of hypertension, statin use, type 2 diabetes, sex, having visited a general practitioner (GP)/physician in the past 3 months (binary) and coronary artery disease (CAD). Furthermore, multiple logistic and linear regression models were used to estimate adjusted association of BP control (no BP control as reference group) and SBP (continuous variable). Covariates in the final models were age (years), waist circumference, sex, low-density lipoprotein cholesterol (LDL-C) (mg/dL), glycated hemoglobin (HbA_{1c}) (%), statin use, number of BP medications, GFR by CKD-EPI formula (GFR_{EPI}) < 60 mL/min/1.73 m^2, current smoking, heart rate (bpm) and sodium (mmol/L), CAD and number of visits to a physician in the past 3 months. The variables to be included in the multiple regression models were identified both based on associations seen in univariate analyses and based on knowledge that they might act as a confounder. Effect modification by sex and statin use was assessed by running stratified analyses. Pairwise correlation coefficients were assessed to identify potential multicollinearity. Statistical significance was set at $p < 0.05$. We used IBM SPSS Statistics version 24.

3 Results

3.1 Prevalence of Hypertension and Antihypertensive Treatment Patterns

The mean age was 68.7 ± 3.7 years, and 51.4% of the participants were female. The mean BMI was 26.8 ± 4.2 kg/m^2. Further basic characteristics of the sample are provided in Table 1.

Mean SBP was 143.7 ± 18.8 mmHg, and mean DBP was 83.1 ± 10.9 mmHg. A total of 686 participants (41.5%) had normotensive BP levels (SBP < 140 and DBP < 90 mmHg), 651 participants (39.4%) had a measured SBP of 140–159 and/or DBP of 90–99 mmHg, 239 participants (14.4%) had a measured SBP of 160–179 and/or DBP of 100–109 mmHg, and 78 participants (4.7%) had severely elevated BP levels of ≥ SBP 180 and/or DBP 110 mmHg.

Of all participants, 75.9% were classified as having hypertension (measured BP ≥ 140/90 mmHg or use of BP medication).

Of these, 40.6% did not receive any BP medications, while the remaining 59.4% of hypertensive individuals were prescribed one or more BP medications. According to multivariable logistic regression analyses, lack of awareness, being younger, and not having visited a physician/GP in the

Table 1 Cohort characteristics ($n = 1654$)

Characteristic	Percentage
60–69 years	64.1
70–79 years	35.2
≥ 80 years	0.7
Sex, female	51.5
Hypertension	75.9
Awareness	59.9
With antihypertensive treatment	59.4
thereof controlled	38.5
Diabetes mellitus, type 2	12.6
Obesity	19.0
CKD	16.3
CAD*	4.0
Lipid disorder*	36.4

Missing: BMI ($n = 12$), CKD ($n = 30$), CAD ($n = 11$), lipid disorder ($n = 12$), awareness ($n = 2$), obesity ($n = 12$)

CAD coronary artery disease, *BMI* body mass index, *CKD* chronic kidney disease

*Self-reported

preceding 3 months, as well as better kidney function, having no history of CAD, and not being on a statin were associated with the lack of treatment (see supplementary Table S2 in the electronic supplementary material).

Among treated hypertensive individuals, 42.0% received monotherapy, 32.3% received dual therapy, 20.3% received triple therapy, and 5.4% were prescribed four or more BP medications ("polytherapy").

BBs (43.6%) were the most commonly prescribed drug class, followed by ARBs (40.3%), thiazide/thiazide-like diuretics (37.3%), ACE-Is (35.2%), CCBs (28.1%), other antihypertensives (4.4%) and α1-blockers (0.8%). Taken together, 75.5% of treated participants were prescribed either an ACE-I or ARB (Table 2). There were no significant differences in this distribution between individuals aged 60–70 years and individuals aged 70–80 years (Table 2).

Altogether, there were 49 different, unique combinations of BP medication classes. Again, the largest proportion received monotherapy with BBs (14.6%), followed by monotherapy with ACE-Is (12.3%) or ARBs (9.5%). ARB plus thiazide (9.1%) and ACE-I plus BB (5.4%) were the most common combinations.

Thiazides were almost completely neglected in monotherapy, amounting to a proportion of only 2.6%, whereas thiazides were commonly used in combination therapy, being included in 78.1% of all triple-therapy regimens. Likewise, only one in ten individuals with monotherapy used a CCB (9.9%), whereas CCBs were commonly prescribed (56.3%) in triple therapy (Table 2).

Notably, 7.5% of all treated hypertensive individuals were prescribed drugs rated as potentially inadequate medications (PIMs) for older adults, according to the PRISCUS and Fit fOR The Aged (FORTA) lists [22, 23], including α1-blockers, moxonidin, verapamil, spironolacton, and aliskiren.

Table 2 Distribution of BP medication classes prescribed to individuals receiving treatment for hypertension ($n = 745$)

	ACE-I	BB	Thiazides	ARB	CCB	Alpha1	Other
Total	35.2	43.6	37.3	40.3	28.1	0.8	4.4
Age categories							
60–69 years	35.9	44.5	37.3	39.4	26.3	1.2	4.4
70–79 years	33.8	42.9	37.3	41.9	30.8	0.3	3.9
≥ 80 years*	50.0	25.0	37.5	25.0	12.5	0.0	25.0
Sex							
Male	37.0	41.2	34.7	41.7	30.3	1.0	3.6
Female	33.1	46.2	40.1	38.7	25.6	0.6	5.3
Therapy mode							
Mono	29.4	34.8	2.6	22.7	9.9	0	0.6
Dual	39.0	39.0	46.9	48.5	24.9	0	1.7
Triple	40.4	57.0	78.1	54.3	56.3	0.7	13.2
Poly (≥ 4)	37.5	90.0	97.5	75.0	82.5	12.5	17.5

All values are %

ACE-I angiotensin-converting enzyme inhibitor, *Alpha1* α1 receptor blocker, *ARB* angiotensin receptor blocker, *BB* β-blocker, *BP* blood pressure, *CCB* calcium channel blocker

*Only $n = 12$

3.2 Controlled and Uncontrolled Hypertension

Only 38.5% of all individuals receiving BP medications had their hypertension controlled to target levels of < 140/90 mmHg. Women were more likely than men to have controlled hypertension (42.6% vs. 34.7%, $p = 0.027$). There were no significant differences regarding proportions of controlled BP between separate age strata, e.g., individuals aged 60–69 years and 70–79 years. The characteristics of treated hypertensive individuals according to the number of BP medications used are provided in supplementary Table S1 (see the electronic supplementary material).

In our sample, 45% of participants treated with three BP medications were controlled compared to only 36.9% or 37.6% with monotherapy or dual therapy, respectively. However, our data only provided weak evidence (p value of 0.118) against the null hypothesis that there is no association between BP control and number of antihypertensive drugs.

Yet, it should be mentioned that controlled BP at an above-average frequency was found with the combination of CCB plus ARB plus thiazide (50% of participants on this therapy were controlled to < 140/90 mmHg) and with ACE-I plus thiazide (46.9%). Notably, among subjects on BB monotherapy, the frequency of BP control was above average (45%), whereas subjects on monotherapy with ARBs, ACE-Is, thiazides, or CCBs were less likely to attain BP control (30–37%).

As shown in Table 3, among treated controlled and uncontrolled hypertensive individuals, the average number of BP medications was almost equal [2 (1–3) vs. 2 (1–2), $p = 0.170$]. Furthermore, there was no evidence of differential choices of drug classes between controlled and uncontrolled individuals. Proportions of monotherapy and dual therapy were similar among uncontrolled and controlled individuals, but there was some weak evidence that triple therapy was more frequent among controlled compared to uncontrolled participants ($p = 0.066$). Interestingly, age, BMI and waist circumference, HbA_{1c}, and eGFR were comparable in both groups. Also, there were no differences in the proportions of controlled and uncontrolled individuals who had visited a physician or GP in the preceding 3 months, but individuals with controlled hypertension reported slightly more visits to any clinician as compared to individuals with uncontrolled hypertension.

Noticeably, those with controlled hypertension had lower mean LDL-C levels, lower heart rate and significantly lower serum sodium levels. They were more likely to receive a lipid-lowering treatment with a statin than those with uncontrolled hypertension and were almost twice as likely to report current smoking.

Results of the multiple logistic regression analyses are provided in Table 4. Female sex, lower LDL-C levels, lower heart rate, lower serum sodium levels and current smoking were independently associated with hypertension control.

Also, linear regression, adjusted for sex, age, WC, HbA_{1c}, heart rate, number of BP medications, statin use, serum sodium levels and current smoking status, provided reasonable evidence to suggest that lower LDL-C levels in addition to current smoking, being female, lower heart rate and serum sodium levels and lower age were significantly associated with a lower SBP, treated as a continuous variable.

We examined confounding and effect modification (interaction) by sex and statin therapy in the association between BP and LDL-C levels in individuals on antihypertensive treatment (Table 5). There was in fact evidence of relevant effect modification by statin therapy, given that the association of lower LDL-C with lower BP was much stronger and only statistically significant in the presence of statin comedication. Furthermore, there was evidence of effect modification by sex, in terms of the effect being stronger in women than in men.

To note, we obtained congruent results when we examined the relation of SBP and LDL-C levels in the total sample ($n = 1654$), including all older BASE-II participants, regardless of their hypertension and treatment status.

4 Discussion

While an intense debate over lower BP goals of treatment has come up [5, 24], today, the majority of individuals do not reach long-term established target levels [8]. Here, we conducted a cross-sectional, in-depth analysis of BP and antihypertensive medication data, in conjunction with other clinical data from the BASE-II study, a cohort of community-dwelling older adults (mean age 68.7 ± 3.7 years).

First, we found that the prevalence of hypertension (75.9%) was comparable to estimates from previous studies [3, 19], and was also in line with known regional differences in hypertension prevalence and control in Germany [25].

Second, we found that 40.6% of hypertensive individuals did not receive BP medications, which is presumably mainly attributable to insufficient recognition and awareness. Indeed, there was a particularly strong association between hypertension awareness and receiving antihypertensive treatment, with an adjusted odds ratio (OR) of 28.0 [95% confidence interval (CI) 19.5–40.2]. Also, having seen a physician or GP within the last 3 months significantly increased the odds of receiving antihypertensive treatment, as well as greater age, history of CAD, receiving a statin, and lower eGFR.

Third, even among those individuals who received BP medications, still only 38.5% had their BP controlled to < 140/90 mmHg.

Table 3 Characteristics of uncontrolled and controlled hypertensive individuals

	Uncontrolled	Controlled	*P*
Age (years)	69.4 ± 4.1	69.1 ± 3.6	0.291
Female sex	45.0	53.3	0.027
Body mass index (km/m²)	27.9 ± 4.1	28.4 ± 4.7	0.157
Waist circumference (cm)	99.5 ± 11.4	100.1 ± 11.9	0.493
DBP (mmHg)	86.9 ± 9.9	75.2 ± 7.8	<0.001
SBP (mmHg)	155.3 ± 15.0	128.1 ± 8.6	<0.001
Heart rate (bpm)	69.5 ± 12.1	67.8 ± 10.7	0.046
Glucose (mg/dL)	95 (87–105)	94 (87–104)	0.698
HbA_{1c} (%)	5.7 ± 0.67	5.7 ± 0.60	0.293
eGFR (mL/min/1.73 m^2)	75.2 (65.9–85.3)	74.3 (64.3–85.3)	0.596
Potassium (mmol/L)	4.5 ± 0.49	4.5 ± 0.43	0.850
Sodium (mmol/L)	139.7 ± 2.8	139.2 ± 2.8	0.021
LDL-C (mg/dL)	129.9 ± 34.6	119.5 ± 38.4	< 0.001
Antihypertensive drug classes, %			
ACE-I	34.9	35.5	0.866
BB	41.9	46.3	0.236
Thiazides	36.0	39.4	0.358
ARB	41.5	38.3	0.393
CCB	27.5	28.9	0.677
Alpha1	0.9	0.7	1.000[#]
Other	3.9	5.2	0.403
Therapy mode, %			
Mono	43.2	40.1	0.395
Dual	33.0	31.4	0.647
Triple	18.1	23.7	0.066
Poly (≥ 4)	5.6	3.5	0.638
Number of BP medications	2 (1–2)	2 (1–3)	0.170
Number of total prescription drugs	4 (2–5)	4 (3–6)	0.008
Statin use, %	23.8	31.4	0.023
Smoking, current, %	4.6	9.8	0.006
Visited GP/physician ≥ 1 times in the past 3 months, %	81.8	85.5	0.250
No. of visits to a clinician in past 3 months	2 (1–3)	2 (1–3)	0.029
Coronary artery disease, %	6	9.9	0.055

Values are mean ± standard deviation, median (interquartile range) or percentages

Missing: body mass index ($n=4$), waist circumference ($n=6$), heart rate ($n=2$), glucose ($n=23$), HbA_{1c} ($n=32$), eGFR ($n=16$), potassium ($n=18$), sodium ($n=16$), LDL-C ($n=26$), smoking ($n=5$), visited GP/physician ≥ 1 times in the past 3 months ($n=3$), no. of healthcare visits in the past 3 months ($n=4$)

ACE-I angiotensin-converting enzyme inhibitor, *Alpha1* α1 receptor blocker, *ARB* angiotensin receptor blocker, *BB* β-blocker, *BP* blood pressure, *CCB* calcium channel blocker, *DBP* diastolic blood pressure, *eGFR* estimated glomerular filtration rate, *GP* general practitioner, HbA_{1c} glycated hemoglobin, *LDL-C* low-density lipoprotein cholesterol, *SBP* systolic blood pressure

[#] *P* according to Fisher's exact test

Although recent data [3, 8, 26] have suggested relevant increases in the proportions of hypertensive individuals with BP treatment and control in Germany in the past decade, this is not observed in our sample of community-dwelling older adults. Our results are, however, in line with recent European data that indicated only 40% of patients achieve BP control [10], and rather reflect the state of affairs about

Table 4 Predictors of BP control to < 140/90 mmHg among treated hypertensive individuals (multiple logistic regression)

	Odds ratio	95% confidence interval		*P*
Age (years)	0.987	0.959	1.043	0.987
Waist circumference (cm)	1.016	1.000	1.032	0.057
Sex, female	1.872	1.318	2.660	< 0.001
LDL-C (mg/dL)	0.992	0.987	0.997	0.001
HbA_{1c} (%)	0.956	0.721	1.269	0.756
Statin use	0.932	0.619	1.403	0.735
Number of BP medications	1.037	0.866	1.241	0.692
Coronary artery disease	1.528	0.825	2.827	0.177
GFR_{EPI} < 60 mL/min/1.73 m^2	0.701	0.428	1.147	0.157
Current smoking	2.493	1.313	4.732	0.005
Heart rate (bpm)	0.981	0.967	0.996	0.012
Sodium (mmol/L)	0.929	0.875	0.987	0.016
No. of visits to a clinician in past 3 months	1.040	0.973	1.111	0.250

BP blood pressure, *CKD-EPI* Chronic Kidney Disease Epidemiology Collaboration, GFR_{EPI} glomerular filtration rate by CKD-EPI formula, $R^2 = 0.96$, HbA_{1c} glycated hemoglobin, *LDL-C* low-density lipoprotein cholesterol

Table 5 Linear regression of systolic BP on LDL-C, stratified by statin use and sex

		B	SE	*β*	*P*
Without statins	Male	0.008	0.035	0.014	0.827
	Female	0.058	0.034	0.103	0.096
With statins	Male	0.160	0.074	0.219	0.033
	Female	0.201	0.061	0.385	0.002

Adjusted for age, waist circumference, number of BP medications, serum sodium, heart rate, current smoking, and HbA_{1c}

β standardized coefficient, *β* regression coefficient, *BP* blood pressure, *LDL-C* low-density lipoprotein cholesterol, HbA_{1c} glycated hemoglobin, *SE* standard error

2 decades ago in Germany, as described by Sarganas et al. (age group 65–79 years: 65% treated, 32.7% controlled) [26].

4.1 High Use of Monotherapy and β-Blockers, and Low Use of Thiazides

Thus, the question is why so few older adults in the BASE-II cohort achieved adequate BP control (< 140/90 mmHg). To address this, first, we considered patterns of antihypertensive therapy. We found that a surprisingly large proportion of individuals received monotherapy (42.0%), and only 58.0% were prescribed a combination therapy. Presumably, monotherapy is insufficient to achieve BP control in most of these older adults, as there is substantial evidence and even the guidelines state that combination treatment is necessary "to control blood pressure in the majority of patients" [10].

Furthermore, to our surprise, in monotherapy, thiazides, and likewise CCBs, were heavily neglected; whereas in dual, triple and polytherapy, for example, thiazides were included in 46.9, 78.1, and 97.5% of all combinations, respectively. Also, the genuine combination of CCB plus thiazide made up only 0.7% of all prescriptions. This is in strikingly sharp contrast to the current ESC/ESH guidelines [10] explicitly recommending the use of thiazides (and CCBs) as first-line agents in patients with isolated systolic hypertension, which is by far the most prevalent form of hypertension in older adults [27, 28]. In a similar vein, a recent analysis of SPRINT baseline data (the mean age in SPRINT was comparable to the mean age in BASE-II) also found a low use of thiazides (16%) among subjects treated with a single agent [29], whereas in triple and polytherapy thiazides were commonly used. Likewise previous studies from Germany and Europe have shown that diuretics are currently rarely prescribed in monotherapy [30]. According to studies on guideline implementation in primary care, the reasons given by physicians for not prescribing diuretics as first-line therapy were fear of side effects, presumed insufficient BP-lowering effect, and having a preference for other medication classes, among others [30]. Yet, it has been shown, e.g., in the HYVET study, that diuretics are not associated with an increased risk of adverse events [4].

In our study, there was no direct evidence that diuretics were associated with increased odds of BP control. However, we found that lower serum sodium levels were significantly associated with hypertension control, which may be indicative (surrogate marker) of diuretic responsiveness and adherence. Lower serum sodium levels in the controlled group might be ascribed to more people being adherent in this group. Indeed, a recent analysis could show again that only about half of all patients are taking all their BP medications as prescribed. Therefore, non-adherence is unquestionably one of the main barriers to achieving satisfactory BP control. Adherence rates for diuretics are typically poorest [16].

Of note, in BASE-II, 43.6% of treated hypertensive individuals used BBs. BBs are generally not considered the first choice in the management of hypertension among older adults, since they can lead to a further elevation in SBP [13, 31]. To note, the frequent use of BBs was not due to a high prevalence of CAD or cardiac arrhythmias in the examined participants, which was only 4.7 and 11.7%, respectively. Noteworthy, the common use of BBs is not a singular finding among the BASE-II cohort. Sarganas et al. also showed that a majority of treatment regimens in the German Health Examination Survey 2008–2011 included a BB (54%), and BBs were even positively associated with BP control [8, 26]. Also among National Health and Nutrition Examination

Survey (NHANES) participants, a particularly high use of BBs was found [32].

To sum up, one major finding of this study was that real-life patterns of antihypertensive therapy deviated highly from the current recommendations of the hypertension societies [10] explicitly recommending the use of thiazides and CCBs as first-line agents in the population of older adults, deeming combination therapy inevitable and considering BBs only a second choice [10].

4.2 Antihypertensive Prescription Patterns and BP Control

As a consequence, the fact that hypertension control in our cohort was insufficient and unsatisfactory may be attributed, at least in part, to the described prescription patterns, i.e., a high proportion of individuals being on monotherapy, too little use of diuretics and CCBs, and too frequent use of β-blockers instead of other drug classes. To note, adherence was not assessed in this study, but previous data suggest that the importance of non-adherence is particularly high [16]. Furthermore, physician inertia has been consistently shown to be a major reason for the lack of therapy intensification [33].

We were surprised to find that even in our adjusted analyses an increase in the number of BP medications was not clearly associated with more BP control. Our data only provided some weak evidence that the proportion controlled was higher with triple therapy than with monotherapy or dual therapy ($p = 0.118$), and the frequency of triple therapy was higher among controlled versus uncontrolled participants (23.7, 95% CI 18.7–28.6 vs. 18.1, 95% CI 14.6–21.7), respectively. Anyway, the proportions controlled with mono-, dual, triple or even polytherapy, respectively, were all well below 50%.

In the BASE-II cohort, the mean number of BP medications prescribed was 1.9, both in subjects with controlled and uncontrolled BP. Also, in the standard treatment-group of the SPRINT trial [5], the mean number of drugs was 1.8. Only by careful titration and readjusting of therapeutic regimens a final mean BP of 134 mmHg (baseline 139 mmHg) was achieved without increasing the mean number of drugs, emphasizing the importance of proper drug choice and dosing. Yet, the SPRINT intervention was in fact more complex, including encouragement of lifestyle modifications and measures to monitor and improve adherence.

4.3 Comorbid and Other Factors and BP Treatment and Control

When comparing individuals with mono- versus dual versus triple therapy, we noticed that monotherapy was associated with a rather well clinical-metabolic profile (see supplementary Table S1) in our cohort, whereas with increasing BP medication number, the average clinical-metabolic profile gradually deteriorated. This could be explained by observations that clinicians are more likely to prescribe optimal therapy if the perceived cardiovascular risk is greater. In fact, CKD, cardiovascular disease, diabetes, and higher BMI have been linked with higher chances of optimal treatment and control [20, 26]. On the other hand, there is substantial evidence that CKD, increasing age and obesity impede BP control, necessitating more drugs [34]. In the present study, HbA_{1c}, waist circumference and impaired renal function were not independently associated with BP control, though there was evidence for an association of a higher BMI (adjusted OR 1.08, 95% CI 1.03–1.12) with triple therapy.

Finally, the present study identified a number of factors that were associated with increased odds of BP control in older adults. Women were more likely to have their hypertension controlled. This sex difference has been previously reported [26]. Moreover, epidemiological studies generally have reported lower BP levels among current smokers compared with nonsmokers, which is counterintuitive, but was also evident from our data [35].

4.4 Low-Density Lipoprotein Cholesterol, Lipid-Lowering Therapy and BP Control

Noteworthy, we found that LDL-C levels were significantly lower, and the prevalence of statin use was significantly higher (31.4% vs. 23.8%, $p = 0.023$) among individuals with controlled hypertension. In fact, statin therapy appeared to modify the relationship between LDL-C levels and SBP, in that the positive association of LDL-C and SBP was stronger and only statistically significant in individuals taking a statin (Table 5). The finding of an independent positive association between LDL-C levels and SBP and BP control is very interesting and conceivably of high clinical relevance. Egan et al. have likewise observed more statin use and lower LDL-C among controlled hypertensive individuals [20], and also other groups [36, 37] have previously suggested an association and interaction of LDL-C and BP. Our data suggest that the observed association may reflect a statin-drug effect or an effect caused by statins' cholesterol-lowering action, i.e., a true pathophysiological link between BP and blood lipids [38]. Epidemiological studies have consistently shown that dyslipidemia is a risk factor for incident hypertension [39], and lipid-lowering therapy (with statins) may exert a small but clinically relevant, antihypertensive effect [36, 40, 41]. As to putative mechanisms involved, hypertension and dyslipidemia share common risk factors, such as obesity. Furthermore, dyslipidemia may impair functional (endothelial function) and structural properties of arteries. Moreover, interactions between hypercholesterolemia and angiotensin

(AT1) receptor expression in vascular tissue have been proposed [36, 41]. Future studies, e.g., using Mendelian-randomization approaches, are necessary to further investigate the link between LDL-C levels and BP.

4.5 Limitations and Strengths

The setup of the BASE-II study, providing broad, detailed, and high-quality data, is a strength of this study. However, the sample size is relatively small. Thus, not all differences and associations, which may be clinically and epidemiologically important, may have been detectable (β error). A major confounder in the office measurement of BP is elevated BP related to the "white-coat effect," accounting for up to one-third of all apparent resistant hypertension [10, 42]. This may explain, at least in part, why BP control across all categories in our cohort was poor. On the other hand, "masked hypertension" is common [42], and might have also affected results. Since this is a cross-sectional analysis, we cannot draw conclusions as to causality. Also, BP has only been measured on a single occasion, whereas the diagnosis of hypertension requires at least two measurements per visit and on a least two visits [10]. Thus, there may have been inaccuracy in the classification of hypertension and BP control. There are other factors potentially influencing BP control, e.g., physical activity, nonsteroidal anti-inflammatory drug (NSAID) use, among others, which were not considered in this study. Also, adherence to medical therapy could not be determined and drug dosing was not considered in the analyses. As our cohort was drawn from the general population, their medication is likely to reflect prescription patterns in the population of older adults in the catchment area (Berlin, Germany). However, as BASE-II was a convenience sample, we cannot exclude selection bias.

5 Conclusion

In summary, we found that BP control in a contemporary cohort of community-dwelling older adults in Germany was poor and prescription patterns did not conform to current guidelines. A large proportion of hypertensive older adults were not prescribed any BP medications, and only 58% of treated hypertensive individuals received combination therapy. Importantly, there was no evidence from our data showing that using more BP medications was associated with higher proportions of controlled individuals. Our study suggests, that a large proportion of older adults is treated insufficiently, receiving either no, too little or not the optimum (combination) of drugs, which is likely to be a major contributor to poor BP control. There is a need for focused interventions so that prescription patterns may more closely reflect practice guidelines, which may improve BP control and global outcomes. Finally, the apparent link between LDL-C levels, lipid-lowering treatment and BP deserves more attention.

Compliance with Ethical Standards

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Conflict of interest Maximilian König, Maik Gollasch, Adrian Rosada, Ilja Demuth, Dominik Spira, and Elisabeth Steinhagen-Thiessen declare that they have no conflicts of interest that might be relevant to the contents of this article.

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