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Changes in Kidney Function in a Population With Essential Hypertension in Real Life Settings

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Original Paper

Introduction. Hypertension has been identified as one of the commonest modifiable determinants for chronic kidney disease progression. A variety of antihypertensive drugs are available and their effect on kidney function has been investigated by a large number of randomized controlled trials. Observational studies, although scarcely been used, outpatient can reflect everyday practice, where drug exposures vary over time, and may provide an alternative for detecting longitudinal changes in kidney function.
Materials and Methods. We applied mixed model repeated measures analysis to investigate the effect of antihypertensive drug categories and their combinations on kidney function change over time in a cohort of 779 patients with essential hypertension, using the data from a Greek hypertension outpatient clinic. Antihypertensive drugs were grouped in 5 categories. Their effect was evaluated and their combinations with and without renin-angiotensin-system inhibitors (RASI) to each other. In addition, the combination of RASI with calcium channel blockers (CCBs) was studied.
Results. Diuretics, RASI, CCBs, and beta-blockers had a significant renoprotective and blood pressure lowering effect. Combinations with RASI had a smaller beneficial effect on kidney function compared to CCBs (0.75 mL/min/1.73 m^2 per year of drug use versus 0.97 mL/min/1.73 m^2). There was no additional effect when combining RASI with CCBs. However, the lowering effect on systolic blood pressure was greater (-0.83 mm Hg per year of drug use, $P < .001$).
Conclusions. RASI were found to have a smaller, although significant, renoprotective effect. There was no additional effect on kidney function when combining RASI with CCBs.

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INTRODUCTION

Hypertension is a major cardiovascular risk factor and has been identified in randomized clinical trials and epidemiological studies as the 2nd commonest modifiable determinant for chronic kidney disease (CKD) progression, after diabetes mellitus.[1-3] A large number of clinical studies have investigated the effect of antihypertensive treatment on kidney function.[4] It is clear that optimal blood pressure control is the main objective of antihypertensive therapy; however, each antihypertensive drug class has unique characteristics and some drugs have been shown to have direct effects on intrarenal mechanisms, resulting in additional renal protection beyond lowering systemic blood pressure.[5,6]

Randomized controlled trials involve careful

selection of participants that may not be representative of the general population. Individual effects of drug classes cannot be evaluated in this context. Observational studies using clinical databases can reflect everyday practice, where drug exposures vary over time and may provide an alternative to clinical trial data for detecting longitudinal changes in blood pressure. The analysis of such data can present a methodological challenge because of missing data, heterogeneity of follow-up intervals, and great variability in drug use within and between patients.[7] This study aimed to investigate the effect of antihypertensive drug categories and their combinations on kidney function change over time in patients with essential hypertension, using the data from a Greek hypertension outpatient clinic.

MATERIALS AND METHODS

Study Design

We conducted a retrospective cohort study using the database of an outpatient hypertension clinic, in order to investigate the effect of antihypertensive treatment on kidney function and blood pressure control in patients with essential hypertension in the complex real world settings, accounting for the variability of the data of everyday clinical practice.

Population

Data was extracted from the computerized medical records of hypertension outpatient clinics of the 1st Department of Internal Medicine of AHEPA University Hospital in Thessaloniki, Greece. Participants were adults with essential hypertension, followed up for at least 3 years between January 1990 and July 2011 that were not on end-stage renal disease. Patients with diabetes mellitus at baseline, as well as patients with secondary forms of hypertension, primary kidney disease, chronic use of nonsteroidal anti-inflammatory drugs or corticosteroids, cancer, active liver disease, pregnancy, and alcohol or drug abuse were excluded from the study. The patients were followed up until last study visit or loss to follow up.

Patients were divided into 3 subgroups according to the frequency of follow-up, in order to investigate whether shorter intervals between visits at the outpatient clinic are associated with better blood pressure control and better kidney function preservation. The first group included those with a mean visit rate less than 1 year, the second group consisted of people who had a mean visit frequency between 1 and 2 years, and the last one included patients coming less often (mean visit rate more than 2 years). Moreover, patients were divided within the interval groups based on the mean systolic blood pressure (SBP) during the follow-up (less than 140 mmHg, between 140 mm Hg and 159 mmHg, and equal or greater than 160 mm Hg).

Measurements and Assessments of Predictors

A validated mercury sphygmomanometer was used, with appropriate cuff size, to obtain at least 2 blood pressure measurements. Kidney function was assessed by estimated glomerular filtration rate (GFR), which was calculated by the simplified the Modification of Diet in Renal Disease study equation.[8] Diabetes mellitus was identified based on a physician diagnosis, use of antidiabetic drugs, or a fasting serum glucose greater than 125 mg/dL at baseline.

Antihypertensive Drug Exposure

A variety of substances were used throughout the cohort. These were classified into the following categories: angiotensin-converting enzyme inhibitors (ACEIs), angiotensin receptor antagonists (ARBs), beta-blockers, calcium channel blockers (CCBs), dihydropyridines (dihydropyridines), and nondihydropyridines, diuretics (thiazides, chlorthalidone, furosemide, and amiloride), and other drugs, which included central acting agents and alpha-blockers. Exposure to treatment was assessed by the number of days each pharmacological entity was used.[9]

Moreover, we identified combinations of antihypertensive categories and compared their blood pressure lowering effect and renoprotective effect. We compared combinations with or without a renin-angiotensin system inhibitor (RASI). We compared also the following combinations: (a) including a RASI but no CCB, (b) including a CCB but not a RASI, (c) combinations of RASI with CCBs, and (d) other combinations.

Statistical Analysis

For the analysis of the continuous effect of antihypertensive treatment on blood pressure and kidney function (GFR), we used repeated measures

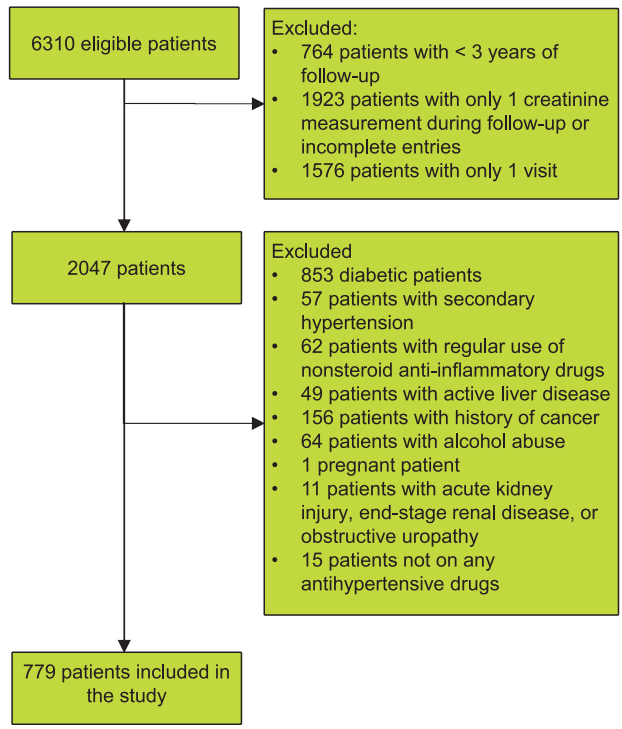
analysis in a mixed effects model. Random intercept and random slope were included in the model to encounter effectively the variability of different baseline and different trajectories between subjects and within subjects. Unstructured covariance structure was used, which allows for the variance and the correlation between any two measurements to be different at all time points, ie, obtaining unique estimates for the variance of subject-specific intercepts, slopes, and covariances.[10,11] The mean differences of GFR, SBP, diastolic blood pressure (DBP), and mean arterial pressure (MAP) between the interval subgroups, as well as between SBP groups for GFR, were evaluated in a similar model.

Descriptive statistics were used to evaluate baseline characteristics of the population, as well as summarize antihypertensive drug use. All analyses were performed using the the SPSS software (Statistical Package for the Social Sciences, version 20.0, SPSS Inc, Chicago, IL, USA). All *P* values were considered significant at .05 level.

RESULTS

Population Selection and Characteristics

From a total number of 6310 patients, 1923 had no follow-up monitoring of kidney function or incomplete entries of medication, 1576 had attended the clinic only once, and 764 had less than 3 years of follow-up. From the rest, 2047 patients; 853 were diabetic patients; 11 patients developed acute kidney injury, obstructive uropathy, or end-stage renal disease during follow-up; 15 patients were not on any antihypertensive medication; and 389 patients had either secondary forms of hypertension or chronic use of nonsteroidal anti-inflammatory drugs or steroids, history of cancer, active liver disease, pregnancy or alcohol abuse (Figure). Finally, 779 patients were included with a median follow-up of 7.02 years (interquartile range, 4.51 to 10.31). Of these patients, 148 (20.2%) had a GFR equal or greater to 90 mL/min, 481 (65.7%) had a GFR between 60 mL/min and 89 mL/min, 90 (12.3%) had a GFR between 45 mL/min and 59 mL/min, and 3 (1.8%) had a GFR between 30 mL/min and 44 mL/min. Table 1 describes the



Flowchart of study population.

Table 1. Baseline Characteristics and Follow-up*

Characteristics	All Patients	Frequency of Visit		
		< 1 Year	1 to 2 Years	> 2 Years
Number of patients	779	405	228	146
Age, y	57.7 ± 9.8	58.1 ± 10.5	57.6 ± 9.1	60.2 ± 9.0
Sex				
Male	240 (30)	127 (31)	63 (28)	50 (34)
Female	539 (70)	278 (69)	165 (72)	96 (66)
Systolic blood pressure, mm Hg	150 ± 15	149 ± 16	151 ± 14	149 ± 16
Diastolic blood pressure, mm Hg	90 ± 9	90 ± 9	90 ± 8	87 ± 8
Mean arterial pressure, mm Hg	110 ± 9	110 ± 9	111 ± 8	108 ± 9
Body mass index, kg/m^2	30.3 ± 4.4	30.2 ± 4.3	30.5 ± 4.7	30.5 ± 4.8
Glomerular filtration rate, mL/min	75.8 ± 16.6	75.1 ± 16.9	75.5 ± 15.3	75.6 ± 21.7
Smoker	140 (18)	81 (20)	40 (17)	19 (13)
Median follow-up (interquartile range), y	7.02 (4.51, 10.31)	5.53 (3.95, 8.57)	7.63 (5.29, 10.79)	8.84 (6.44, 12.29)

*Values are mean ± standard deviation for continuous variables and frequency (percent) for categorical variables, unless otherwise specified.

baseline characteristics of the study population.

Follow-up Intervals

The median return visit interval was 83 days (interquartile range, 27 to 265). Assessing the patients defined by follow-up interval groups, there were no significant differences at baseline between group means for age ($F(12,762) = 1.180$, $P = .31$), SBP ($F(2,761) = 0.949$, $P = .39$), DBP ($F(2,755) = 0.431$, $P = .65$), MAP ($F(2,755) = 0.938$, $P = .39$), and GFR ($F(2,716) = 1.805$, $P = .17$), as determined by the 1-way analysis of variance. The sex distribution was similar across the three groups ($x^2(2) = 1.29$, $P = .52$). Follow-up time was significantly longer in lower-visit frequency groups, as it was shown in the Kruskal-Wallis test analysis ($P < .001$).

In mixed models adjusted for age and sex, lower frequency of visit was associated with higher mean SBP, DBP, and MAP over time; however, this was not found to be significantly associated with GFR change (Table 2). In a separate analysis including SBP groups along with interval groups, frequency of follow-up was not found to have a significant effect on kidney function change as above; however, the worse SBP control had a significant negative impact on GFR (β estimate = -7.5 and $P = .003$ for SBP greater than 160 mm Hg and β estimate = -3.0 and $P = .045$ for SBP of 140 mm Hg to 159 mm Hg, compared to patients with mean SBP during follow-up less than 140 mm Hg). It is notable that the less frequent the attendance to the hypertension clinic was, the higher the percentage of uncontrolled SBP was, as it is depicted in Table 3.

Table 3. Percentage of Patients in Each Mean Systolic Blood Pressure Category Over the Follow-up Period by Interval Visits Groups

Systolic Blood Pressure Category, %	Visit Interval		
	< 1 Year	1 to 2 Years	> 2 Years
< 140 mm Hg	40.0	24.1	25.0
140 mm Hg to 159 mm Hg	49.6	62.3	53.8
≥ 160 mm Hg	10.4	13.6	21.2

Table 4. Persistence in Medication Use

Medication Category	Mean Use, y*	Persistence Rate, %
Renin-angiotensin-system inhibitors	5.19 ± 4.12	84.3
Angiotensin-converting enzyme inhibitors	4.63 ± 4.19	44.7
Angiotensin receptor blockers	3.01 ± 2.81	86.8
Calcium channel blockers	5.18 ± 4.04	83.5
Dihydropyridines	4.52 ± 3.81	74.7
Nondihydropyridines	3.45 ± 3.63	52.1
Diuretics	5.13 ± 4.14	77.4
Beta-blockers	5.28 ± 4.52	63.8

*Values are mean ± standard deviation.

Medication Use

Table 4 shows the persistence of drug use, depicted as the average total years of drug use. Persistence rates were assessed as the number of patients still using the drug category at the last visit divided by the total number of patients that had been prescribed the medication. The results reveal that RASI had the greater persistence rate (84.3%), although similar to CCBs (83.5%), followed by diuretics (77.4%). Angiotensin-converting enzyme inhibitors had a lower persistence rate than ARBs (44.7% versus 86.8%), and nondihydropyridine had a lower persistence rate than dihydropyridine (52.1% versus 74.7%). The characteristics of patients using the studied drug combinations during the course of treatment are shown in Table 5 and they were similar among the different groups.

Effect of Antihypertensives on Kidney Function and Blood Pressure Control

In univariable analyses, adjusting for SBP, all drug categories, apart from "other drugs," were found to have significant renoprotective effects (positive estimates), where β estimates represent the change of GFR in mL/min/1.73m^2 by each year

Table 2. Changes Over the Follow-up Period by Interval Visits Groups*

Parameter	Visits Every 1 to 2 Years		Visits Longer Than Every 2 years	
	Beta Estimate ± Standard Error	*P*	Beta Estimate ± Standard Error	*P*
Systolic blood pressure	4.20 ± 0.86	< .001	4.73 ± 1.09	< .001
Diastolic blood pressure	1.42 ± 0.39	< .001	1.69 ± 0.49	.001
Mean arterial pressure	2.37 ± 0.47	< .001	2.71 ± 0.60	< .001
Glomerular filtration rate	-0.24 ± 1.18	.08	0.28 ± 1.46	.85

*Reference group is patients with visit rate less than a year. Analysis is adjusted for age and sex.

Table 5. Characteristics of Patients With Different Treatment Combinations*

Drug Combinations	Including RASI	Without RASI	CCB Plus RASI	RASI Without CCB	CCB Without RASI	Other Combinations
Number of patients	577	322	423	340	267	117
Sex						
Male	169 (29)	77 (24)	127 (30)	93 (27)	63 (24)	21 (18)
Female	408 (71)	77 (76)	127 (70)	93 (73)	63 (76)	21 (82)
Age, y	65.0 ± 8.9	61.9 ± 10.2	66.6 ± 8.3	62.1 ± 9.3	62.4 ± 10.7	60.5 ± 8.4
Systolic blood pressure, mm Hg	145 ± 16	145 ± 16	147 ± 16	143 ± 16	144 ± 16	147 ± 15
Diastolic blood pressure, mm Hg	85 ± 8	85 ± 8	85 ± 8	86 ± 7	85 ± 8	87 ± 8
Body mass index, kg/m2	30.6 ± 4.6	31.1 ± 4.8	30.5 ± 4.7	30.7 ± 4.4	30.9 ± 4.9	31.6 ± 4.6
Glomerular filtration rate, mL/min	75.8 ± 21.0	75.8 ± 21.0	75.8 ± 21.0	78.6 ± 19.9	75.9 ± 20.7	78.7 ± 20.8
Smokers	115 (80)	45 (86)	87 (79)	64 (81)	40 (85)	11 (91)
Duration of use	4.53 ± 3.90	4.14 ± 3.67	3.46 ± 3.34	3.39 ± 3.31	3.38 ± 3.30	3.67 ± 3.46

*Values are mean ± standard deviation or frequency (percentage). RASI indicates renin-angiotensin-system inhibitor and CCB, calcium channel blocker.

of drug use. The CCBs, diuretics, and beta-blockers had similar β estimates; however, RASI had a smaller renoprotective effects. The beneficial effect of antihypertensive drugs was beyond the effect of blood pressure, since SBP was included in the model as a covariate. Moreover, all drug categories, apart from "other drugs," had significant and similar negative β estimates for SBP (representing the change in mm Hg by each year of drug use), with a slightly greater lowering effect for RASI (Table 6).

Drug combinations including RASI were compared to drug combinations without RASI in mixed models analysis. Both groups were found to have significant renoprotective and blood pressure lowering effects by each year of drug use. Including a RASI in the treatment regime was found to have a greater lowering effect on SBP; however, the β estimate for GFR was smaller. When comparing combinations including either a RASI or a CCB, both groups had significant positive estimates for GFR, with a higher β estimate for combinations of CCB, and similar significant negative estimates for SBP. The combination of RASI with CCB had a greater lowering effect on SBP than using either of these categories separately. However, no additional renoprotective effect was found (P = .26). When neither a RASI nor a CCB were used, the effect on kidney function was not found to be significant (Table 7).

All analyses were adjusted for age, sex, body mass index, and smoking status. Age had a significant negative effect on GFR, which is biologically plausible and is consistent with the aging kidney. Body mass index and smoking status were not found to have any significant effects on GFR; however, body mass index was significantly associated with higher SBP.

DISCUSSION

The present study showed that through the variety of follow-up and drug use, outpatient clinic data can effectively be used for evaluating the impact of antihypertensive medication on blood pressure control and kidney function. Closer follow-up was associated with better blood pressure control, probably providing more opportunities for intensification of medication as well as enhancing treatment adherence.[12,13] All categories of antihypertensive drugs were found to

Table 6. Univariable Analysis of the Effect of Antihypertensive Drug Categories*

Covariate	Estimated Glomerular Filtration Rate		Systolic Blood Pressure	
	Beta Estimate ± Standard Error	*P*	Beta Estimate ± Standard Error	*P*
Renin-angiotensin-system inhibitors	0.50 ± 0.13	< .001	-0.55 ± 0.09	< .001
Calcium channel blockers	0.67 ± 0.14	< .001	-0.52 ± 0.09	< .001
Diuretics	0.60 ± 0.14	< .001	-0.47 ± 0.09	< .001
Beta-blockers	0.66 ± 0.16	< .001	-0.40 ± 0.10	< .001
Other medications	0.84 ± 0.58	.15	1.42 ± 0.37	< .001

*Beta estimates represent changes in kidney function in mL/min/1.73m^2 and changes in systolic blood pressure in mm Hg. For medications, the change is per year of medication use.

Table 7. Multivariable Analysis of Combinations of Antihypertensive Drug Categories*

Covariate	Estimated Glomerular Filtration Rate		Systolic Blood Pressure	
	Beta Estimate ± Standard Error	*P*	Beta Estimate ± Standard Error	*P*
Combinations Including RASI or Not				
RASI combinations	0.47 ± 0.15	.002	-0.62 ± 0.10	< .001
No RASI combinations	0.79 ± 0.21	< .001	-0.45 ± 0.13	.001
Age	-0.53 ± 0.05	< .001	0.37 ± 0.04	< .001
Female sex	-8.33 ± 1.14	< .001	4.78 ± 0.87	< .001
Smoking	2.25 ± 1.34	.09	-0.91 ± 1.02	.37
Body mass index	0.09 ± 0.11	.38	0.57 ± 0.08	< .001
Systolic blood pressure	-0.05 ± 0.02	.03	…	…
Combinations of RASI and CCBs				
RASI without CCB	0.75 ± 0.22	.001	-0.34 ± 0.15	.02
CCB without RASI	0.97 ± 0.26	< .001	-0.48 ± 0.16	.003
RASI and CCB	0.23 ± 0.20	.26	-0.83 ± 0.13	< .001
Other Combinations	0.49 ± 0.34	.15	-0.38 ± 0.22	.08
Age	-0.53 ± 0.05	< .001	0.38 ± 0.04	<.001
Female sex	-8.29 ± 1.14	< .001	4.79 ± 0.87	< .001
Smoking	2.23 ± 1.34	.10	-1.02 ± 1.02	.32
Body mass index	0.09 ± 0.11	.38	0.57 ± 0.08	< .001
Systolic blood pressure	-0.05 ± 0.02	.03	…	...

*Beta estimates represent changes in kidney function in mL/min/1.73m^2 and changes in systolic blood pressure in mm Hg. For medications, the change is per year of medication use. RASI indicates renin-angiotensin-system inhibitor and CCBs, calcium channel blockers.

have a similar significant renoprotective and blood pressure lowering effect in univariable analyses, adjusting for SBP (in the GFR model), age, sex, body mass index and smoking status. When combinations of drug categories were evaluated, it was found that combinations including RASI had a better effect on blood pressure control than combinations without a RASI, while the effect on kidney function for both groups was protective, although slightly smaller for the RASI group. Moreover, the results showed that there was no additional effect on kidney function when combining RASI with CCBs, although the lowering effect on SBP was greater.

Unlike clinical trials, where the drug effects are evaluated in an ideal study setting, the effectiveness and clinical impact of drug use can be confirmed in the target population in real life settings, when outpatient clinic databases are used. These usually include patients with variable intervals of visits, different follow-up periods, and variable number of observations.[14] Moreover, a variety of drugs are used within and between patients for a variable time period. We used mixed model repeated measures analysis, which is the most effective analysis for such databases. Mixed models can overcome limitations of other methods and help understand better the true nature of change, by giving information about individual or group growth trajectories.[8,11]

Real life data are not usually available on large sets of patients. The most widely used clinical database in Europe for pharmacoepidemiological studies is the General Practice Research Database in the United Kingdom (known as the Clinical Practice Research Datalink since March 2012), with millions of patients. Examples of the General Practice Research Database cohort studies related to blood pressure control and drug treatment are one by Delaney and associates, who validated the effect of non-antihypertensive drug treatment on blood pressure,[7] including nonsteroidal anti-inflammatory drugs, statins, warfarin, and proton pump inhibitors, as well as another study by Burke and coworkers, who evaluated the effect of antihypertensive drugs on new-onset diabetes mellitus.[15]

Searching the PubMed (through March 2016), we found only 2 recent retrospective cohort studies that investigated the impact of RASI on CKD progression, using the data from the Veterans Affairs System in the United States. Arora and colleagues, in their recent study (December 2015), showed that the use of RASI was not associated with less hazard of CKD progression or mortality in elderly patients without diabetes mellitus or proteinuria compared to other antihypertensive

medications.[16] This is relevant to our finding of slightly lower magnitude of renoprotective benefit in the group of RASI. On the other hand, Molnar and coworkers found that patients treated with RASI had lower odds of mortality than patients not treated with RASI. However, in this study, patients receiving an ACEI or ARB were more likely to be diabetic with proteinuria, and stratified analysis showed that the effect of RASI on mortality was not significant in nondiabetic patients.[17]

Our study included nondiabetic patients with an average younger age, while the majority of them had normal or only mildly impaired kidney function. The study period was longer in total and evaluated the impact of all antihypertensive drug categories and their combinations on the rate of kidney function change over time, rather than specific cutpoint outcomes. To the best of our knowledge, there is no other study analyzing the change of kidney function over time in real life settings, in terms of antihypertensive medication treatment.

Our results showed a slightly lower magnitude of renoprotective benefit in the group of RASI. Having been widely studied, ACEIs and ARBs have been shown to protect the glomeruli by reducing intraglomerulus blood pressure and proteinuria.[5,6] However, in our study, patients with diabetes mellitus or glomerulonephritis were not included, and although proteinuria was not regularly monitored, it is unlikely to have been a major factor. Moreover, in our cohort, patients with impaired kidney function were presumably more likely to have a degree of renovascular disease, as patients with other primary and secondary causes of kidney disease were excluded from the study. In such a group of patients, the beneficial effect of RASI may not be the same as in individuals with proteinuria, diabetes mellitus, and CKD. Certainly, it would have been interesting to see the effects of RASI in comparison between diabetics and nondiabetics, if diabetic patients were included in the study.

In addition, calcium antagonists have been shown to be effective for reducing blood pressure, through their vasodilating effect on afferent arteriole of the glomerulus, although this can result in increased transmission of pressure into the glomerulus, when systematic blood pressure is not well controlled. In our study, CCBs were found to have a beneficial effect both in univariable and multivariable analyses.

As far as the combination of RASI with CCBs is concerned, Bakris and colleagues showed that combining an ACEI with a nondihydropyridine CCB can reduce proteinuria to a greater extent than either agent alone in patients with type 2 diabetes mellitus.[18] Moreover, the Irbesartan Diabetic Nephropathy Trial and the African American Study of Kidney Disease and Hypertension showed that dihydropyridines failed to reduce proteinuria and to slow the progression of nephropathy in the absence of agents that block the RASI.[6,19] However, these studies included patients with advanced nephropathy and proteinuria. A post-hoc analysis of another similar study for renal outcomes did not show any significant differences between amlodipine, Lisinopril, and chlorthalidone in hypertensive patients with reduced GFR.[20] A recent meta-analysis of Huang and coworkers examined the effect of the combination of RASI and CCB on kidney function, including 628 hypertensive patients with CKD from 7 randomized controlled trials.[21] The results showed that the combination of RASI with a CCB had a greater lowering effect on SBP compared to RASI monotherapy. However, it did not show any additional renoprotective effect for the combination treatment. These conclusions were consistent with the findings of our study.

Our findings are limited by the fact that we do not know the causes of patients' loss to follow-up and we can only assume deliberately not attending to the clinic, death, or end of the study. In patients for whom the interval between visits was quite extended, we tried to cover as best as possible potential factors affecting kidney function from the history of the patient as it was recorded in the database. However, the results of the study may be biased by morbidity and mortality, since we did not censor that. Moreover, information regarding compliance to medication were not available, and the reasons of changing drug categories during the course of treatment (crossovers) were not systematically documented and could include ineffective blood pressure control or a drug adverse effect.

Finally, proteinuria, a surrogate marker of kidney disease, was not routinely monitored, although, as previously mentioned, we could assume that this was not a significant factor. More accurate and

valuable results can be obtained with increased numbers of patients and years of follow-up, so larger outpatient database studies can evaluate further the antihypertensive drugs' effect on kidney function in the complicated settings of everyday clinical practice.

CONCLUSIONS

The results of the present study implied that outpatient records can be a useful tool in estimating blood pressure control and kidney function change over time, secondary to drug therapy, when appropriate statistical techniques are used. The importance of regular follow-up visits has been depicted in previous studies and is confirmed in the present study, which included patients with variable and longer follow-up intervals. All 5 antihypertensive drug categories had a significant renoprotective effect that was beyond blood pressure control in univariable analysis, although RASI were found to have a slightly smaller beneficial effect on kidney function in a nondiabetic population with essential hypertension. Moreover, there was no additional effect when combining RASI with CCBs, although this combination, as well as combinations including RASI, were found to have a better blood pressure lowering effect.

CONFLICT OF INTEREST

None declared.

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