Adherence With Antihypertensive Drug Therapy and the Risk of Heart Failure in Clinical Practice

Giovanni Corrao, Federico Rea, Arianna Ghirardi, Davide Soranna, Luca Merlino, Giuseppe Mancia

Abstract—Randomized clinical trials have shown that antihypertensive treatment reduces the risk of heart failure (HF). Limited evidence exists, however, on whether and to what extent this benefit is translated into real-life practice. A nested case–control study was carried out by including the cohort of 76 017 patients from Lombardy (Italy), aged 40 to 80 years, who were newly treated with antihypertensive drugs during 2005. Cases were the 622 patients who experienced hospitalization for HF from initial prescription until 2012. Up to 5 controls were randomly selected for each case. Logistic regression was used to model the HF risk associated with adherence to antihypertensive drugs, which was measured by the proportion of days covered by treatment (PDC). Data were adjusted for several covariates. Sensitivity analyses were performed to account for possible sources of systematic uncertainty. Compared with patients with very low adherence (PDC, ≤25%), low, intermediate, and high adherences were associated with progressively lower risk of HF, reduction in the high-adherence group (>75%) being 34% (95% confidence interval, 17%–48%). Similar effects were observed in younger (40–70 years) and older (71–80 years) patients and between patients treated with angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, and diuretics. There was no evidence that adherence with calcium-channel blockers reduced the HF risk. Antihypertensive treatment lowers the HF risk in real-life practice, but adherence to treatment is necessary for a substantial benefit to take place. This is the case with a variety of antihypertensive drugs. **(*Hypertension*. 2015;66:742-749. DOI: 10.1161/HYPERTENSIONAHA.115.05463.)**

Key Words: antihypertensive agents ■ heart failure ■ medical record linkage ■ medication adherence

A large number of epidemiological studies has shown that hypertension is a major risk factor for heart failure (HF).[1] It has further been documented that (1) the hypertension-related risk of HF is not irreversible because in randomized clinical trials (RCTs), antihypertensive drug treatment is accompanied by a substantial reduction of HF incidence[2,3] and (2) although some differences may exist,[3] the HF reduction can be obtained with several antihypertensive drug classes,[3] which implies that the benefit largely depends on blood pressure (BP) lowering per se.[2]

A consensus exists that in real life, adherence with the antihypertensive treatment regimen is low[4,5] and that this affects to a major extent the reduction of BP[6] and the protection against cerebrovascular and coronary events.[7] However, few investigations have so far assessed the effect of adherence with antihypertensive treatment on the risk of HF in the setting of clinical practice[8] making the real-world evidence on this issue still incompletely known. This is an important gap of knowledge because HF is (1) the most common cause of hospitalization in the elderly,[9] with a high hospital readmission, mortality rate,[10,11] and cost[12] and (2) more and more frequently diagnosed[13] because of ageing of the population and better survival of patients from an acute coronary event.

We carried out a population-based case–control investigation, nested into a large cohort of patients on antihypertensive drug treatment with the aim of assessing the relationship between long-term adherence to the prescribed treatment regimen and risk of the first hospitalization for HF. Data were also separately analyzed for the drug class prescribed to find whether the effect of adherence on HF was different for different antihypertensive treatments.

Methods

Setting

The data used for this study were retrieved from the healthcare utilization databases of Lombardy, a region of Italy which accounts for ≈16% (≈10 millions) of its population. In Italy, the whole population is covered by the National Health Service, and in Lombardy, this has been associated since 1997 with an automated system of databases to collect a variety of information. Details of healthcare utilization databases of the Lombardy Region and of their use in the field of cardiovascular diseases have been reported elsewhere.[4,7,10,11]

Cohort Selection and Follow-Up

The target population included Lombardy residents, aged 40 to 80 years, who were beneficiaries of the National Health Service. Of

Received April 22, 2015; first decision May 3, 2015; revision accepted July 2, 2015.

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This paper was sent to Takayoshi Ohkubo, Guest Editor, for review by expert referees, editorial decision, and final disposition.

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these, those who received at least 1 antihypertensive drug prescription during 2005 were identified, and the first dispensation was defined as the index prescription. Antihypertensive drugs included diuretics, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, β-blockers, and calcium-channel blockers (CCBs) initially dispensed as monotherapy. Patients with an initial prescription of ≥2 antihypertensive drugs were excluded to reduce the range of hypertension severity, given that compared with monotherapy, need of multiple drug treatment reflects an increased risk of cardiovascular events, including HF.[14] Exclusion was extended to other patient categories, such as patients who (1) received at least 1 antihypertensive drug prescription within the 5 years before the index prescription, to limit inclusion to newly treated individuals; (2) had been hospitalized for cardiovascular disease or used drugs for coronary heart disease or HF, within the 5 years before the index prescription to limit data collection to the setting of primary cardiovascular prevention; (3) were beneficiaries of the National Health Service from <5 years before the start of prescription; and (4) did not reach at least 1 year of follow-up. Patients who had previously received ≥1 prescriptions of digitalis were also excluded because the use of digitalis might represent a proxy of existing HF. The remaining patients were included into the final cohort whose members accumulated person-years of follow-up from the date of the index prescription until the earliest date among hospital admission for HF, death, emigration, or December 31, 2012.

Selection of Cases and Controls

When the effect of time-dependent exposure on rare events needs to be investigated in the context of large databases, the nested case–control design is a valid alternative to the cohort design.[15] The case–control study was thus nested into our cohort of incident antihypertensive drug users. Cases were members of the cohort who during follow-up were hospitalized for HF (International Classification of Disease-9 code 428.x) or hypertensive HF (402.01, 402.11, and 402.91). The earliest date of hospitalization with one of these codes was considered as the event date.

For each case patient, 5 controls were randomly selected from the cohort to be matched for sex, age at cohort entry, and the date of index prescription. Controls had to be at risk of the outcome when the matched case had it.

Measuring Adherence With Antihypertensive Medication

For each case and control, all antihypertensive drugs dispensed during follow-up were identified. The period covered by an individual prescription was calculated by dividing the total amount of the drug prescribed for the defined daily dose. For overlapping prescriptions, the patient was assumed to have taken the drugs contained in the first prescription before starting the second. Adherence was measured by the cumulative number of days in which the antihypertensive drug was available divided by the days of the overall follow-up, the ratio expressing the PDC.[16] Four categories of adherence were considered, that is, very low (≤ 25%), low (26%–50%), intermediate (51%–75%), and high (>75%) PDC values.

Covariates

In addition to the categories of adherence, information included covariates measured at baseline, that is, (1) the antihypertensive drug class used at index prescription, (2) use of statins and antidiabetic and antidepressant agents within the 5 years before the index prescription, and (3) the Charlson comorbidity index[17] that was calculated via the diagnostic information provided by the inpatient charts within the 5 years before the index prescription. Information also included covariates measured during follow-up, that is, (4) the number of antihypertensive drug classes, (5) the switching between antihypertensive drugs, (6) the addition of other cardiovascular drugs (nitrates, digitalis, and antiarrhythmic drugs) to the antihypertensive treatment regimen, and (7) the number of prescribing physicians.

Data Analysis

The χ^2 test, or its version for the trend, was used when appropriate to test for differences between cases and controls. Conditional logistic regression models were fitted to estimate the odds ratio, and its 95% confidence interval (CI), of HF hospitalization in relation to the PDC categories, using the shortest category (≤25%) as reference. Adjustments were made for the above reported covariates. Odds ratio trends were tested, when feasible, according to the statistical significance of the regression coefficient of the recoded variable obtained by scoring the corresponding categories. The effect of PDC categories on the HF risk was evaluated for the entire cohort, as well as for sex and age strata at index prescription, and classes of antihypertensive drugs prescribed.

Sensitivity Analyses

To verify the robustness of our findings, 3 sensitivity analyses were performed. One, we categorized exposure to antihypertensive drugs according to quartiles of PDC rather than to predefined categories as in the main analysis. Two, to check whether our estimates were affected by the adopted criteria for defining the outcome, the earliest date between the first HF hospitalization or the first prescription of digitalis was considered as the outcome. Three, the potential bias associated with unmeasured confounders was investigated by the rule-out approach described by Schneeweiss[18] whose aim is to detect the extension of the overall confounding required to fully account for the exposure–outcome association, thus moving the observed point estimate to the null. We set the possible generic unmeasured confounder (1) to have a 10% or 50% prevalence in the study population; (2) to increase hospitalization for HF ≤10-fold more in patients exposed than in those unexposed to the confounder, and (3) to be ≤10-fold more or less common in high- than very low-adherent patients.

All analyses were performed using the Statistical Analysis System Software (version 9.2; SAS Institute, Cary, NC). Statistical significance was set at the 0.05 level. All *P* values were 2-sided.

Results

Patients

The distribution of the exclusion criteria is shown in Figure 1. The 76 017 patients included into the study cohort accumulated 502 818 person-years of observation (on average, 6.6 years per patient) and generated 622 first hospital admissions for HF. These 622 case patients were matched to 3110 controls.

The characteristics of cases and controls are shown in Table 1. At the date of the index prescription, (1) mean age of cases and controls was 67 years and 54% of the patients were men; (2) angiotensin-converting enzyme inhibitors were the most common initial drugs in both cases and controls; (3) more cases than controls started with diuretics, this being the case either for the loop (7% versus 5%) and for the other diuretic (5% versus 3%) types; (4) the proportion of patients on treatment with antidiabetic drugs and having comorbidities (Charlson score) was significantly higher among cases than among controls. During follow-up, most patients had a very low adherence to antihypertensive medicaments, cases being worse than controls. With respect to controls, cases also received a larger variety of antihypertensive agents, showed a greater rate of switching between antihypertensive drug classes, experienced >1 prescribing physician, and were more frequently treated with other cardiovascular drugs.

Adherence With Antihypertensive Therapy and Risk of HF

The risk of HF hospitalization associated with adherence to antihypertensive drugs is shown in Table 2. Compared with very low-adherence group, the risk exhibited a significant and marked progressive reduction as adherence increased to the low, intermediate, and high categories. There was also evidence that the risk was increased among patients who used

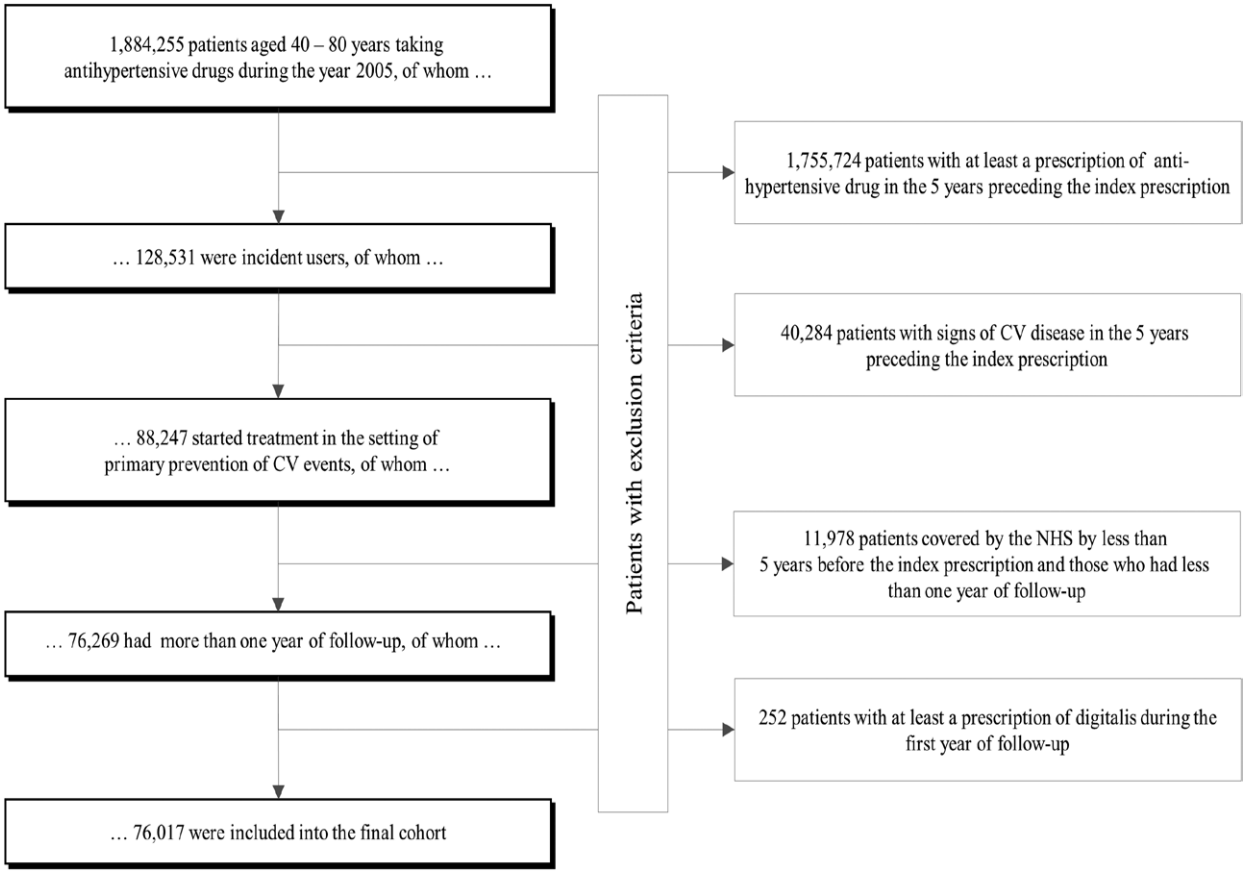

Figure 1. Flow-chart of inclusion and exclusion criteria. CV indicates cardiovascular.

a larger variety of antihypertensive agents, switched between antihypertensive drug classes, experienced >1 prescribing physician, and added other cardiovascular medicaments during follow-up. The risk decreased among users of statins, whereas the opposite happened for those who used antidiabetic agents. There was a significant linear trend toward increasing HF risk as the Charlson score increased.

The relationship between adherence with antihypertensive medicaments and HF risk according to age and sex is shown in Figure 2. Low- and intermediate-adherence categories were pooled to increase the power in the middle adherence groups. A significant linear progressive decrease of HF risk as adherence increased was observed in both younger and older patients. This was the case also in men, whereas the trend did not reach the statistical significance in women. A progressive decrease of HF risk for increasing levels of adherence was seen for diuretic, angiotensin-converting enzyme inhibitor, and angiotensin receptor blocker treatment, whereas the trend was not significant for β-blockers and CCBs (Figure 3).

Sensitivity Analyses

The relationships described above did not substantially change by (1) varying the criteria for categorization of adherence with antihypertensive drug therapy or (2) adopting a more demanding criterion for defining the outcome. Taking the lowest quartile as reference, the odds ratio of HF decreased to 0.88 (95% CI, 0.67–1.16), 0.77 (95% CI, 0.58–1.02), and 0.70 (95% CI, 0.56–0.88) as the PDC quartiles increased. Similarly, the odds ratio of HF decreased from 0.99 (95% CI, 0.79–1.24) to 0.72 (95% CI, 0.57–0.91) and 0.67 (95% CI, 0.55–0.81) by using an alternative criterion for defining the outcome, that is, that based not only on hospitalization but also on incident digitalis prescription.

The results of the residual confounding analysis obtained by the rule-out approach are shown in Figure 4. Assuming that patients with high adherence to antihypertensive drugs (1) had a 3-fold higher odds of exposure to the confounder than those with very low adherence and (2) the confounder prevalence in the study population was 10% or 50%, the analysis shows that confounding should increase the HF risk by 7.5-fold or 4.5-fold (10% and 50% prevalence, respectively) to nullify the observed protective effect of high adherence on hospitalization for HF weaker confounder; outcome associations are required for confounders more intensely unbalanced between patients with very low and high adherence, but increases of HF risk of 4-fold and 2-fold are still required for a confounder prevalence of 10% and 50%, respectively, to move to the null the effect on HF of adherence to treatment.

Discussion

The most important finding of our study is that in patients newly treated with antihypertensive drugs in a real-world setting, the risk of hospitalization for HF decreases markedly and progressively as adherence to the prescribed antihypertensive drug regimen increases. This provides evidence that the protective effect of antihypertensive treatment on HF documented in RCT[3] is

Table 1. Characteristics of the 622 Case Patients Hospitalized for Heart Failure and the Corresponding 3110 Controls

Characteristics	Case Patients	Controls	*P* Value*
Baseline			
Men	334 (54%)	1670 (54%)	MV
Age, mean (SD)	67 (10.0)	67 (10.0)	MV
Antihypertensive drug class			
Diuretics	76 (12%)	237 (8%)	0.005
ACEIs	230 (37%)	1248 (40%)	
ARBs	109 (18%)	568 (18%)	
β-Blockers	88 (14%)	469 (15%)	
CCBs	119 (19%)	588 (19%)	
Other treatments			
Statins	102 (16%)	608 (20%)	0.068
Antidiabetic agents	109 (18%)	337 (11%)	<0.001
Antidepressant agents	81 (13%)	456 (15%)	0.287
Charlson comorbidity index score			
0	526 (85%)	2810 (90%)	<0.001
1	40 (6%)	130 (4%)	
≥2	56 (9%)	170 (6%)	
During follow-up			
Adherence with antihypertensive therapy†			
Very low	285 (46%)	1283 (41%)	0.042
Low	93 (15%)	405 (13%)	
Intermediate	82 (13%)	432 (14%)	
High	162 (26%)	990 (32%)	
No. of antihypertensive classes			
1	263 (42%)	1600 (51%)	<0.001
2	165 (27%)	834 (27%)	
≥3	194 (31%)	676 (22%)	
Switching between antihypertensive drugs	429 (69%)	1883 (61%)	<0.001
>1 prescribing physician	51 (8%)	189 (6%)	0.049
Concomitant CV treatments			
Digitalis	11 (2%)	15 (0%)	<0.001
Nitrates	34 (5%)	58 (2%)	<0.001
Antiarrhythmic drugs	21 (9%)	50 (2%)	0.003

ACEIs indicate angiotensin-converting enzyme inhibitors; ARBs, angiotensin receptor blockers; CCBs, calcium-channel blockers; CV, cardiovascular; and MV, matching variable.

*According to χ^2 test (antihypertensive agent used at entry, switching between antihypertensive drugs, concomitant use of other drugs, and no. of prescribing physician) or its version for the trend (categories of the Charlson comorbidity index score, adherence with antihypertensive therapy, and no. of antihypertensive classes).

†Adherence was measured according to the proportion of days with antihypertensive drugs available with respect to the days of overall follow-up. Categories are the following: very low, ≤25%; low, 26%–50%; intermediate, 51%–75%; and high, >75%.

transferable to real-life conditions. It also emphasizes, however, the paramount importance for the magnitude of this protective effect of abiding by the prescribed antihypertensive medicaments.

In line with previous investigations,[4,5] our study shows that adherence with antihypertensive drug therapy is extremely poor in real-life medicine, the number of patients in whom the prescribed drugs were available for less than half of the overall follow-up exceeding 50%. This makes improvement of adherence with antihypertensive medicaments, a fundamental goal to pursue for protecting patients against HF. Our study also agrees with a post hoc analysis of an intervention trial performed in Australia[19] that better adherence to treatment is accompanied by HF protection in old hypertensive patients, a finding of obvious importance because in old individuals, HF plays a crucial role as a cause of death, hospitalization, and healthcare-related costs.[9,12] However, in the Australian study, better adherence to treatment was found to guarantee a lesser degree of protection in younger patients, whereas in our

Table 2. Effect of Adherence With Antihypertensive Drug Therapy and of Other Factors on the Risk of Hospitalization for Heart Failure

Effect	OR*	95% CI
Adherence with antihypertensive therapy		
Very low	1.00	Reference
Low	0.83	0.63–1.10
Intermediate	0.73	0.55–0.98
High	0.66	0.52–0.83
P trend	<0.001	
No. of antihypertensive classes		
1	1.00	Reference
2	1.28	1.02–1.60
≥3	1.99	1.57–2.53
Switching between antihypertensive drugs	1.61	1.32–1.95
>1 prescribing physician	1.22	1.02–1.46
Concomitant CV treatments		
Digitalis	2.65	1.13–6.18
Nitrates	2.63	1.66–4.17
Antiarrhythmics	1.65	0.96–2.86
Other treatments		
Statins	0.71	0.56–0.91
Antidiabetic agents	1.69	1.31–2.17
Antidepressant agents	0.82	0.63–1.07
Charlson comorbidity index score		
0	1.00	Reference
1	1.48	1.01–2.16
≥2	1.55	1.12–2.14

CI indicates confidence interval; CV, cardiovascular; and OR, odds ratio.
*Adjusted OR and 95% CI, estimated with conditional logistic regression.

study, adherence to antihypertensive treatment had a similarly marked protective effect in patients younger and older than 70 years, in line with the conclusion of meta-analyses of RCT.[20] In this context, it should be mentioned that in the Australian study, adherence to treatment was self-reported and expressed in dichotomized form (yes or not), 2 fallible means to measure this variable that cannot match our measurement of adherence by objective (prescription renewal) and continuous form data.[16]

Our study provides the following additional results. One, better adherence with antihypertensive drug treatment prevents HF in men, but it does not offer evidence for a similar beneficial effect in women. This cannot be accounted for by a sex-related effect of antihypertensive drugs on BP or hypertension-related complications because meta-analyses of RCT have not shown sex-related differences in antihypertensive treatment effects.[21] Furthermore, real-life BP control has frequently been reported to be better in women than in men.[22] However, because no RCT has so far compared treatment effects between sexes, the sex difference seen in this study, as well as more in general the protective effects of antihypertensive drugs in men and women, deserves further investigation. Two, our results show that the relationship between improved adherence to treatment and reduction of HF holds for several different treatments, such as diuretics, angiotensin-converting enzyme inhibitors, and angiotensin receptor blockers, the trend being qualitatively similar, although not statistically significant, also for β-blockers. This suggests that the greater protection against HF seen with better adherence to drug treatment is because of a better BP control, a conclusion supported by the evidence that adherence to treatment and achieved BP values exhibit a close relationship.[23] Three, no clear relationship between adherence to antihypertensive drug treatment and protection against HF was detected for CCBs. This has an apparent bearing with the results of some meta-analyses of RCT that, while effectively reducing the risk of stroke and coronary disease, CCBs do not match other antihypertensive drugs as far as protection against HF is concerned, possibly because they adversely affect neurohumoral factors involved in HF prognosis.[3] However, this is unlikely to be the only explanation of our observations because RCTs have also shown that CCBs can reduce the HF risk when BP reduction occurs.[3,24] Thus, the lack of relationship between adherence to CCB treatment and HF risk remains at least in part unexplained. Finally, our findings suggest that in real life, other factors are relevant to protection against HF. The risk of HF was significantly greater in patients in whom during follow-up antihypertensive treatment switched from the original prescription to other drugs, used a wider range of antihypertensive agents, and more frequently changed the prescribing physician possibly because all these factors reflect treatment failure or greater difficulties to achieve BP control. Also, there was a greater HF risk in patients under antidiabetic drugs, which is attributable to the importance of diabetes mellitus as a risk factor for HF,[25] as well as to the limited effect of antidiabetic treatment on diabetic-related macrovascular complications.[26] Finally, the risk of HF was less in individuals with when compared with those without administration of statins. This implies a protective effect of lipid-lowering treatment on HF, a benefit, however, not yet unequivocally demonstrated in RCT.[27]

This study has several elements of strength. One, the investigation was based on a large unselected population, which was made possible because in Italy, a cost-free healthcare system involves virtually all citizens. Two, the drug prescription database provided highly accurate data because pharmacists are required to report prescriptions in detail to obtain reimbursement, and incorrect reports about the dispensed drugs have legal consequences.[28] Three, participants were identified at the time of their initial antihypertensive drug therapy, a new-user approach that reduced the potential for selection bias.[29] Four, patients were included only if there was no previous evidence (drug treatment or hospitalization) of HF for several years. Finally, the data provided by the main analysis were confirmed by many sensitivity analyses.

Limitations

Our study has limitations. One, because of privacy regulations, hospital records were not available for scrutiny, which means that diagnosis of HF could not be checked. Although the diagnostic accuracy for identification of HF has been shown to be high,[30] because of the lack of evidence from up-to-date studies performed in the healthcare system of the region we study, misclassification cannot be completely excluded in our setting. Two, adherence with treatment was derived from drug prescriptions, that is, a widely used method to estimate adherence

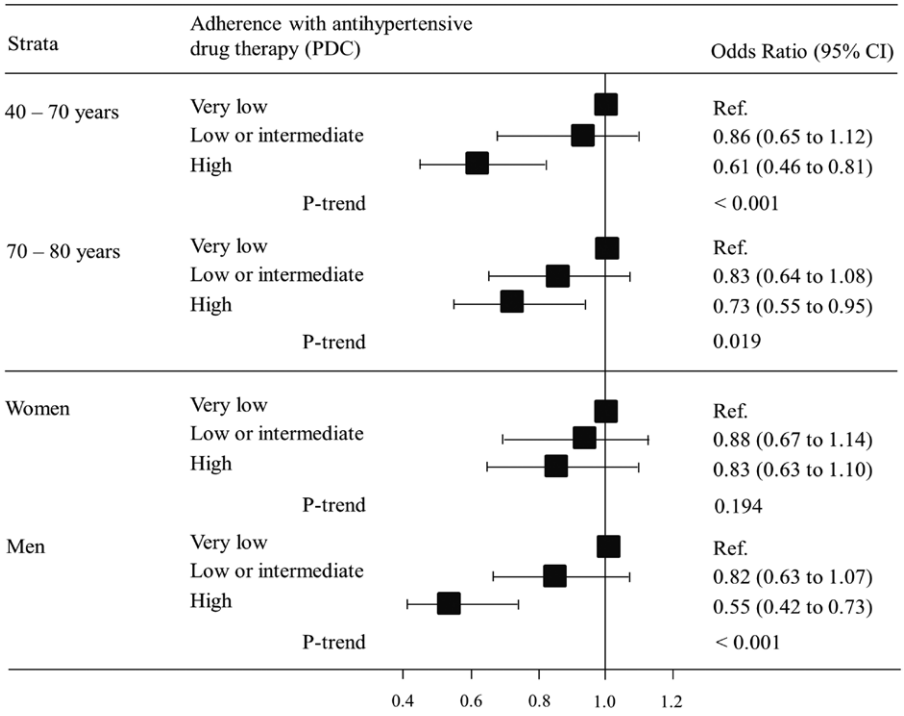

Figure 2. Effect of adherence with antihypertensive drug therapy on the odds ratio of hospitalization for heart failure according to age and sex. Adherence was measured according to the proportion of days with antihypertensive drugs available with respect to the days of overall follow-up (PDC). Categories are the following: very low, ≤25%; low, 26%–50%; intermediate, 51%–75%; and high, >75%. Odds ratio and 95% confidence interval (CI), estimated with conditional logistic regression. Estimates are adjusted for the covariates listed in Table 1.

to treatment in large populations,[31] which requires, however, the assumption that the proportion of days covered by a prescription corresponds to the proportion of days of drug use.[32] Finally, because allocation of antihypertensive drug therapy was not randomized, the results may be affected by confounding. That is, the reduction in HF risk associated with a better adherence to antihypertensive medicaments might have been generated by factors, accompanying but different from a better adherence to antihypertensive drug treatment. However, factors, such as ethnicity or socioeconomic status, can be confidently ruled out because the Lombardy population is largely white, and we have previously found that in Lombardy, income and educational differences play no role in the persistence on antihypertensive drug treatment.[33] Furthermore, it is unlikely that the increased risk of HF in patients with low adherence to antihypertensive drug treatment is accounted for a more compromised clinical status because (1) patients prescribed multiple antihypertensive drugs at the start were excluded to minimize participation in the study of individuals with a more severe hypertension and greater cardiovascular risk[14], (2) data were adjusted for several demographic, therapeutic, and clinical characteristics, (3) although our database did not make BP values available,[32] adjustment included several proxies of the severity of hypertension and the difficulties of achieving therapeutic results, such as the number of antihypertensive drugs, the switching between antihypertensive drug classes, the number of prescribing physicians, and the addition to antihypertensive drug treatment of nonhypertensive cardiovascular agents,[34] and (4) patients with a more severe hypertension and a higher cardiovascular risk are known to have a better rather than a worse adherence to drug treatment.[35] Of course, this does not entirely eliminate the problem of confounding, one aspect of which is that because adherence may be a surrogate for overall health-seeking behavior, patients more adherent to antihypertensive drugs might also have more regularly followed healthy lifestyle advices, more effectively treated other cardiovascular risk factors, or dealt with HF more frequently as out- rather than in-hospital. However, as far as the last 2 possibilities are concerned, (1) data were adjusted for drug treatment of other cardiovascular risk factors and (2) therapy with most cardiovascular drugs was less, equal or only slightly more common in cases than in control patients, at variance with what might be expected from the more thorough medical attention associated with a better health-seeking behavior. Finally, as shown in Figure 4, we calculated that to account for the difference of HF risk between groups with different adherence to treatment, an unmeasured confounder should increase HF risk to such an extent (several folds) to make this explanation of the results, although in principle possible, highly unlikely.

Conclusions

In a real-life setting, antihypertensive therapy with a variety of drugs reduces the risk of HF in both middle age and elderly individuals, but good adherence to the prescribed treatment regimens is a critical factor in making the reduction substantial. This emphasizes the need for physicians and healthcare providers to recognize the importance of adherence to the prescribed treatment regimen to translate into real-life medicine the benefit shown by trials.

Perspectives

Our study confirms the results of previous investigations showing that adherence with antihypertensive medications

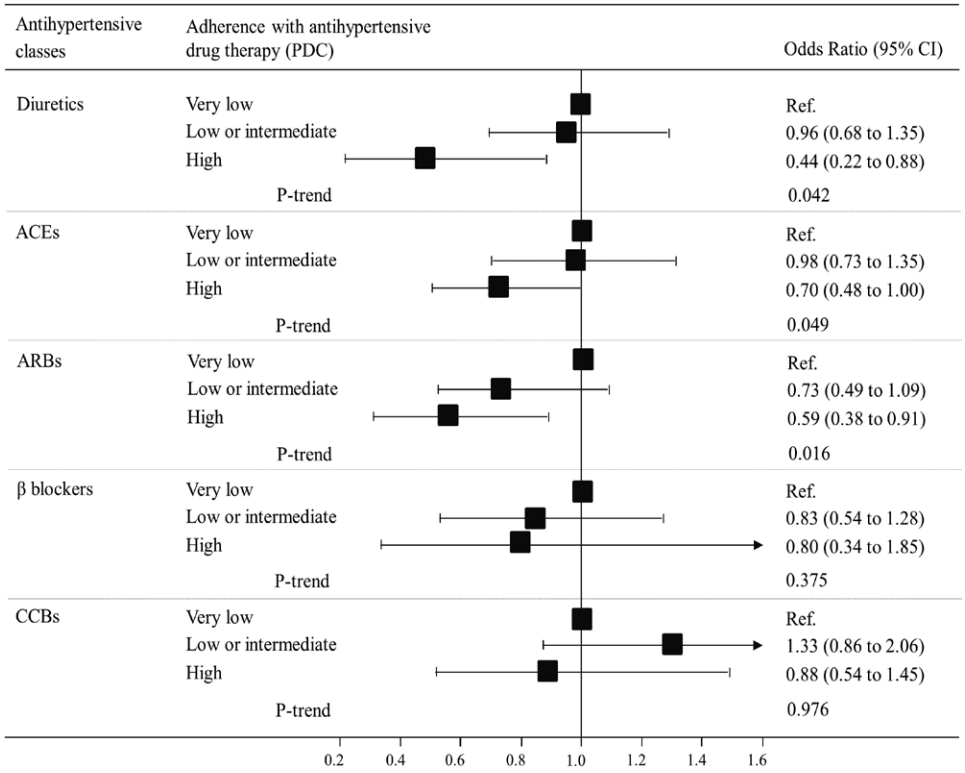

Figure 3. Effect of adherence with specific antihypertensive classes on the reduction in odds ratio of hospitalization for heart failure. Adherence was measured as mentioned in Figure 2. ACEs indicate angiotensin-converting enzymes; ARBs, angiotensin receptor blockers; CI, confidence interval; and PDC, proportion of days covered by treatment.

is extremely poor in real-life practice. Moreover, this study offers evidence that adherence with antihypertensive therapy is associated with a reduction of HF risk. Future studies should concern strategies to achieve better adherence, in particular for patients at high cardiovascular risk, and their clinical and economic implications.

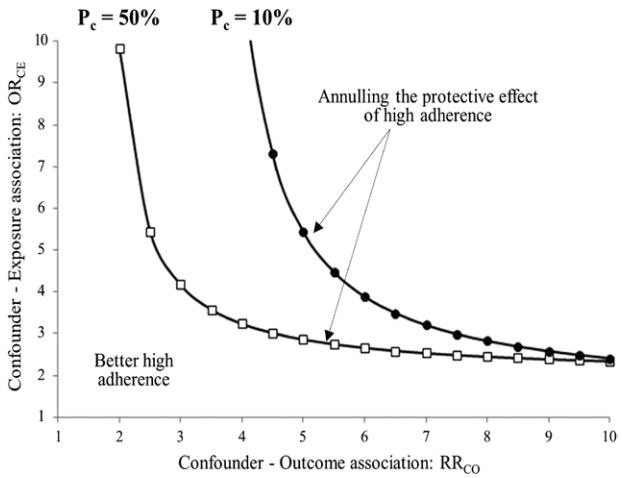

Figure 4. Influence of a confounder on the relationship between heart failure risk (outcome) and adherence with antihypertensive drug treatment (exposure). The graph indicates the RR_{CO}–OR_{CE} combinations (ie, the confounder–outcome and the confounder–exposure associations, respectively) that would be required to move the observed protective effect of adherence to treatment toward the null for 2 possible values of the confounder's prevalence in the study population (P_c=10% and 50%).

Sources of Funding

This study was funded by grants from the Italian Minister for University and Research ('Fondo d'Ateneo per la Ricerca' portion, year 2014).

Disclosures

G. Corrao received research support from the European Community, the Italian Agency of Drug, and the Italian Minister for University and Research. He took part to a variety of projects that were funded by pharmaceutical companies (ie, Novartis and GSK). He also received honoraria as a member of advisory board from Roche. G. Mancia received honoraria for participation as speaker/chairman in national/international meetings from Bayer, Boehringer Ingelheim, CVRx, Daiichi Sankyo, Ferrer, Medtronic, Menarini Int, Merck, Novartis, Recordati, and Servier. The other authors report no conflicts.

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Novelty and Significance

What Is New?

- Randomized clinical trials offer conclusive evidence that antihypertensive drugs are effective in reducing the risk of heart failure.
- Limited evidence exists, however, on whether this benefit is translated into real-life practice.

What Is Relevant?

- Compared with patients with very low adherence with antihypertensive agents, those with higher adherence had progressively lower risk of heart failure, the risk reduction in the high-adherence group being 34%.
- Similar effects were observed in younger (40–70 years), older (71–80 years) patients, and patients treated with angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, or diuretics.

Summary

In the real-life setting, achieving a suitable adherence with antihypertensive medicaments is effective for the primary prevention of hospitalization for heart failure.

Hypertension
Journal of the American Heart Association

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Hypertension. 2015;66:742-749; originally published online July 27, 2015;
doi: 10.1161/HYPERTENSIONAHA.115.05463
Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Print ISSN: 0194-911X. Online ISSN: 1524-4563