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Prescription of antihypertensive agents to haemodialysis patients: time trends and associations with patient characteristics, country and survival in the DOPPS

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Abstract

Background. Haemodialysis patients were studied in 12 countries to identify practice patterns of prescription of antihypertensive agents (AHA) associated with survival.

Methods. The sample included 28 513 patients enrolled in DOPPS I and II. The classes of AHA studied were beta blocker (BB), angiotensin-converting enzyme inhibitor (ACEI), angiotensin receptor blocker (ARB), peripheral blocker, central antagonist, vasodilator, long-acting dihydropyridine calcium channel blocker (CCB), short-acting dihydropyridine CCB and non-dihydropyridine CCB. To reduce bias due to unmeasured confounders, the associations with mortality were assessed by separate Cox models based on patient-level prescription and facility prescription practice.

Results. An increase in prescription of ARBs (9.5%) and BBs (9.1%) was observed from DOPPS I to II. Prescription of AHA classes varied significantly by country, ranging for BBs from 9.7% in Japan to 52.7% in Sweden and for ARBs from 5.5% in Italy to 21.3% in Japan in DOPPS II. Facilities that treated 10% more patients with ARBs had, on average, 7% lower all-cause mortality, independent of patient characteristics and the prescription patterns of other antihypertensive medications ($P = 0.05$). Significant and independent associations with reduction in cardiovascular mortality were observed for ARBs (RR = 0.79; $P = 0.005$) and BBs (RR = 0.87, $P = 0.004$) in analyses of patient-level prescriptions. These associations in the facility-level model followed the same direction.

Conclusions. DOPPS data show large variations across countries in AHA prescription for haemodialysis patients.

The data suggest an association between ARB use and reduction in all-cause mortality, as well as with the use of BBs and reduction in cardiovascular mortality among haemodialysis patients.

Keywords: antihypertensive agents; cardiovascular; haemodialysis; mortality

Introduction

Findings from clinical trials among patients without end-stage renal disease (ESRD) have contributed markedly to improved outcomes for patients at elevated risk of cardiovascular events [1–4]. The use of angiotensin-converting enzyme inhibitors (ACEI) and angiotensin receptor blockers (ARB) has been associated with improved survival in these patients [5,6]. Although the benefit of beta blockers (BB) has been questioned in patients with uncomplicated hypertension [7], there is strong evidence that BBs improve survival in patients with cardiac diseases, particularly coronary artery disease (CAD) [8,9].

Congestive heart failure (CHF) and CAD are important contributors to the reduced survival of patients on maintenance haemodialysis (HD) [10–12]. It has been suggested that the survival of these patients could be improved by increasing the use of cardiovascular medications, such as antihypertensive agents (AHA), with proven beneficial effects in the non-ESRD population [13]. There is evidence, however, that a large fraction of patients on dialysis with cardiac disease do not receive appropriate treatment with medications such as ACEIs, ARBs and BBs, at least in part because of nephrologists' concerns regarding the possibility of adverse reactions [14,15].

Using a representative sample of haemodialysis patients from 12 countries enrolled in the Dialysis Outcomes and Practice Patterns Study (DOPPS), we assessed the frequency of prescription of several classes of AHA and patient characteristics associated with each prescription. We then assessed which classes of AHA were associated with lower risk of all-cause and cardiovascular mortalities.

Methods

Data for these analyses were from the DOPPS, an international, prospective, observational study of practice patterns and associated outcomes involving maintenance haemodialysis facilities and patients. The present study includes data from 16 327 patients from the first phase (DOPPS I) and 12 186 patients from the second phase (DOPPS II). DOPPS I data were collected in five European countries (101 facilities from France, Germany, Italy, Spain and the United Kingdom), Japan (65 facilities) and the United States (145 facilities). Data collection began in 1996 in the United States, 1998 in Europe and 1999 in Japan and continued through 2001. DOPPS II began in 2002 and continued through 2004. It included dialysis facilities from the DOPPS I countries, as well as from Australia, Belgium, Canada, New Zealand and Sweden. There were 308 facilities in DOPPS I and 340 in DOPPS II. Nationally representative samples of dialysis facilities were recruited in each country. Within each participating facility, study patients were randomly selected. Institutional review boards in each country approved the study, and informed patient consent was obtained in accordance with local requirements. The details of the study design have been presented elsewhere [16,17].

Extensive patient-level data have been collected for the DOPPS. Baseline data included sociodemographic variables, comorbidities and treatment variables including dialysis dose and medication prescriptions. Longitudinal data were abstracted at approximately 4-month intervals. A complete list of prescribed medications for each patient was collected every 4 months in DOPPS I and yearly in DOPPS II. The medication list underwent an extensive cleaning, validation and coding process. A physician or clinical pharmacist performed all medication coding using a semi-automated process developed for the DOPPS. The following nine classes of AHA were included in the analysis: BB, ACEI, ARB, peripheral blocker, central antagonist, vasodilator, long-acting dihydropyridine calcium channel blocker (CCB), short-acting dihydropyridine CCB and non-dihydropyridine CCB.

In these analyses, we studied the initial cross-sections of patients (n = 8445 and 8905 in DOPPS I and II, respectively) to ensure representativeness of prevalent HD patients. Logistic regression models were used to estimate odds ratios (ORs) for the associations between the prescription of each class of antihypertensive medication and patient characteristics, adjusted for age, sex, race, time on dialysis, dialysis dose by single-pool Kt/V (spKt/V), 14 summary comorbid conditions, country and study phase. The comorbid conditions included history of CAD, CHF, cardiovascular disease other than CAD or CHF, cancer, cerebrovascular disease, peripheral vascular disease, diabetes mellitus, gastrointestinal bleeding, HIV/AIDS, lung disease, hypertension, neurological disease, psychiatric disease and recurrent cellulitis/gangrene.

Cox regression models estimated the relative risk (RR) of the associations between each class of antihypertensive medication and mortality (both all-cause and cardiovascular), adjusted for the same covariates included in the logistic regressions and the concomitant prescription of the other classes of antihypertensive medications. Cardiovascular causes of death were defined as those attributed to acute myocardial infarction, hyperkalaemia, pericarditis (including cardiac tamponade), atherosclerotic heart disease, cardiomyopathy, cardiac arrhythmia, cardiac arrest (causes unknown), valvular heart disease, pulmonary oedema or CHF. These models were stratified by country and study phase, and the sandwich estimator was used to correct for facility clustering [18].

The associations between each class of AHA and mortality using Cox regression models were assessed in two ways. One method examined the association between each individual's prescription of antihypertensive medication and patient-level outcomes. The second method investigated the relationship between a facility's practice of prescribing antihypertensive medication and patient-level outcomes. Facility practice was represented by the fraction of patients in the dialysis facility prescribed a specific class of antihypertensive medication.

To refine our facility practice estimates, the values were adjusted for measured patient case-mix characteristics, similar to an instrumental variable approach [19–21]. The case-mix adjusted percentage of patients prescribed each AHA class was estimated by fitting a linear mixed effects model where AHA class was the dependent variable, all other factors were independent variables and the facility was treated as a random effect. The intercept for the random effect represents the 'expected' level of AHA class prescription at each facility given the patient case mix and was used as the predictor variable in survival models.

Results

Baseline characteristics and prescription of AHA

Overall, 64.0% (5405/8455) of patients in DOPPS I and 65.7% (5847/8905) in DOPPS II were prescribed at least one of the studied classes of AHA. Table 1 shows baseline characteristics by antihypertensive class prescribed, in the baseline cross-sections of patients in DOPPS I and II. After adjusting for comorbid conditions, the odds of prescription of the studied classes of AHA were significantly higher for younger patients. The adjusted odds of prescription of any class of AHA were also significantly higher for patients who were male, black, on dialysis less than 1 year or had CAD, hypertension or diabetes. CHF was associated with higher odds of AHA prescription in the unadjusted model

Table 1. Patient characteristics by prescription of any of the studied antihypertensive agents (AHA) in a cross-section of DOPPS I and DOPPS II

Characteristic	DOPPS I		DOPPS II		OR for AHA versus no AHA (*P*-value)*	
	AHA ($n = 5405$)	No AHA ($n = 3040$)	AHA ($n = 5847$)	No AHA ($n = 3058$)	Unadjusted	Adjusted**
Demographics						
Age (mean)	59.3	60.9	62.1	62.9		
<45 years (%)	19.4	17.6	15.9	15.6	1.00 (ref)	1.00 (ref)
45–64 years (%)	48.3	47.7	46.7	47.5	0.96 (0.33)	0.79 (<0.001)
65–74 years (%)	29.8	31.9	34.0	33.4	0.95 (0.24)	0.73 (<0.001)
75+ years (%)	2.5	2.7	3.4	3.5	0.88 (0.16)	0.69 (0.003)
Male (%)	58.5	53.4	58.3	55.2	1.26 (<0.001)	1.09 (0.03)
Black (%)	20.8	11.9	11.1	6.3	1.34 (<0.001)	1.23 (<0.001)
Haemodialysis <1 year (%)	24.0	17.8	22.8	18.6	1.51 (<0.001)	1.32 (<0.001)
Comorbidities (%)						
Coronary artery disease	39.4	30.2	49.3	38.9	1.34 (<0.001)	1.26 (<0.001)
Congestive heart failure	32.0	25.0	31.6	24.6	1.21 (<0.001)	1.02 (0.63)
Other cardiac diagnosis	33.6	32.5	36.5	36.3	1.04 (0.22)	0.96 (0.27)
Hypertension	84.7	53.6	86.5	61.6	4.41 (<0.001)	4.15 (<0.001)
Diabetes	37.3	25.6	38.4	26.5	1.50 (<0.001)	1.32 (<0.001)
Cerebrovascular disease	16.6	13.5	18.2	15.3	1.19 (<0.001)	1.06 (0.21)
Peripheral vascular disease	22.2	19.7	28.0	23.0	1.19 (<0.001)	1.08 (0.13)
Cancer	7.5	10.0	11.6	11.6	0.78 (<0.001)	0.93 (0.21)
Gastrointestinal bleed	7.3	6.3	6.0	5.6	0.98 (0.66)	0.89 (0.10)
Lung disease	9.5	8.9	10.4	11.4	0.87 (0.006)	0.90 (0.09)
HIV/AIDS	0.6	0.5	0.6	0.4	0.61 (0.0003)	0.72 (0.15)
Neurological disorder	8.5	8.3	11.5	11.4	0.81 (<0.001)	0.75 (<0.001)
Psychiatric disease	18.7	18.6	19.1	18.7	0.85 (<0.001)	0.95 (0.23)
Recurrent cellulitis/gangrene	7.3	7.9	8.0	8.0	0.77 (<0.001)	0.63 (<0.001)
spKt/V (per 0.1)	1.36	1.39	1.44	1.43	0.96 (<0.001)	0.87 (0.02)

*Based on DOPPS I and II combined.
**Adjusted model includes all variables listed in table, plus phase of DOPPS & country of residence; also accounts for facility clustering.

but not in the multivariable model. This finding was partly explained by the adjustment for hypertension.

Prescriptions of specific classes of AHA were also significantly associated with certain cardiovascular diagnoses ($P < 0.05$, data not shown). For patients with CAD, higher adjusted odds of prescription were observed for BBs [adjusted odds ratio (AOR) = 1.54] and non-dihydropyridine CCBs (AOR = 1.28) compared to no AHA. ACEIs and ARBs were not significantly associated with the odds of prescription for CAD. For patients with diabetes, lower significant odds of prescription were observed for BBs (AOR = 0.84) and higher odds were observed for ACEIs (AOR = 1.41), ARBs (AOR = 1.15), non-dihydropyridine CCBs (AOR = 1.25), central antagonists (AOR = 1.20) and long-acting dihydropyridine CCBs (AOR = 1.16). The adjusted odds of prescription of each class of AHA were significantly higher for patients with hypertension. Each of these AORs was adjusted for simultaneous prescription of any of the other studied classes of AHA.

In an analysis restricted to countries participating in both phases of DOPPS, a trend was observed for prescription of certain classes of AHA from DOPPS I to DOPPS II (Figure 1). From DOPPS I to II, prescription of BBs increased from 17.3% to 26.4% and prescription of ARBs more than tripled, from 3.9% to 13.4%. By contrast, prescription of CCBs decreased from 45.5% to 39.8% from DOPPS I to II. ACEI prescription was similar in DOPPS I (21.7%) and II (20.5%).

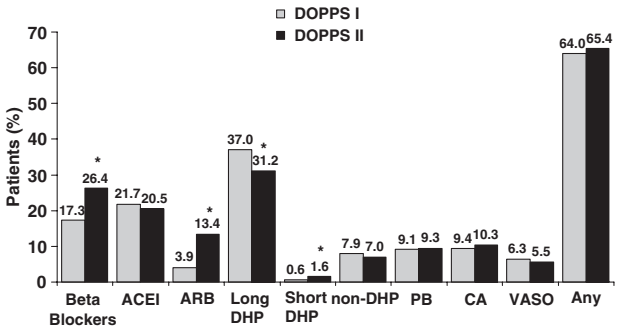

Fig. 1. Percentage of patients with prescription antihypertensive agents in prevalent samples from countries that participated in both phases of DOPPS. *$P < 0.05$ compared with DOPPS I. ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; DHP, dihydropyridine calcium channel blocker; PB, peripheral blocker; CA, central antagonist; VASO, vasodilator.

Prescription of AHA by country

The data shown in Table 2 are from a DOPPS II cross-section. The percentage of patients with prescription of any class of AHA was higher in the United States (76.8%) and Canada (77.5%) than in other countries (from 46.5% in Italy to 68.8% in Germany). Prescription of specific classes of AHA also varied significantly by country, even when adjusted for differences in demographic characteristics, comorbidities and years on dialysis.

Table 2. Percentage of patients with prescription of different classes of antihypertensive agents (AHA) by country, in a cross-section of DOPPS II

	Patients (%)										
	ANZ	Belgium	Canada	France	Germany	Italy	Japan	Spain	Sweden	UK	USA
N (facilities)	–	–	–	–	–	–	–	–	–	–	–
N (patients)	512	535	600	516	588	566	1720	600	546	552	2190
Cardiac medication											
Any AHA	65.2**	55.3*	77.5*	61.4**	68.8	46.5**	63.8	50.8**	66.8	60.1*	76.8
Beta blockers	26.2**	30.5	46.0*	25.6**	41.0	11.0**	9.7**	13.2**	52.7**	29.0**	42.7
ACEI	27.5*	21.9*	37.3**	21.5	33.8**	14.1	11.9	13.2**	17.4	22.5*	26.8
ARB	9.4	8.0	14.5	10.7	17.3**	5.5	21.3**	11.0	17.4*	9.6	10.5
Peripheral blockers	4.3	3.0	8.2	1.9	5.8	8.8	11.5	14.2	5.9	13.2	7.9
Central antagonists	1.8	0.9	9.2	1.0	14.8	9.7	12.3	0.2	0.7	0.9	14.9
Vasodilators	2.7	4.5	5.8	13.0	3.9	2.3	1.2	4.2	0.9	2.5	9.6
CCB: non-dihydropyridines	9.4	3.0**	7.3	5.8	10.6*	5.5	7.4	6.7*	1.6**	3.6**	7.3
CCB: long-acting dihydropyridines	21.7*	16.3**	37.5**	21.1*	20.4	21.2	39.5**	26.7	28.9	25.0	35.4
CCB: short-acting dihydropyridines	0.0	0.2	0.2	1.7	1.1	0.2	4.5	0.3*	0.4	0.0	0.6

ANZ, Australia–New Zealand; ACEI, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; CCB, calcium channel blocker.
$^{**}P < 0.005$, $^{*}P < 0.05$ compared with US percentages, adjusted for variables in Table 1, phase of DOPPS, and accounting for facility clustering.
Note: the percentages are not adjusted and represent the actual patients on medications.

Countries most commonly prescribing each class of AHA, by patient, were: Sweden for BBs prescription (52.7%), Canada for ACEIs (37.3%), Japan for ARBs (21.3%), Spain for peripheral blockers (14.2%), France for vasodilators (13.0%) and Germany for non-dihydropyridine CCBs (10.6%). The United States (14.9%) and Germany (14.8%) had similar percentages of patients with prescription of central antagonists. Italy had the lowest percentage of patients prescribed ARBs (5.5%). Prescription of long-acting and short-acting dihydropyridine CCBs was most common in Japan (39.5% and 4.5%, respectively). Japan was also the country with the lowest percentage of patients prescribed BBs (9.7%). Countries with significantly higher adjusted percentages of prescription of ARBs than the United States were Japan (21.3%), Sweden (17.4%) and Germany (17.3%). Japan (9.7%), Italy (11.0%) and Spain (13.2%) had the lowest percentages of patients who were prescribed BBs. Similar to Sweden, the prescription of BBs was >40% in Canada (46%), the United States (42.7%) and Germany (41%).

AHA and all-cause mortality

All-cause mortality was 16.42/100 patient-years. Figure 2 shows the adjusted relative all-cause mortality risks associated with specific classes of AHA, from analyses based on either patient-level prescription data or on facility prescription practices. Multivariable models were adjusted for the variables in Table 1, as well as pre-dialysis systolic blood pressure (SBP) and for prescription of each of the other studied classes of AHA.

In the analysis of patient-level prescription data, the all-cause mortality was significantly ($P < 0.05$) lower for patients prescribed BBs, peripheral blockers and long-acting dihydropyridine CCBs and marginally significantly lower ($P = 0.06$) for patients prescribed ARBs. In contrast, the mortality risk was significantly higher for patients prescribed short-acting dihydropyridine CCBs.

In the analysis of facility prescription practices, we observed a 7% reduction (RR = 0.93, $P = 0.05$) in all-cause mortality for every 10% increase in patients with prescriptions of ARBs within a facility. The other AHA were not significantly associated with lower all-cause mortality in the facility practice model.

AHA and cardiovascular mortality

The death rate due to cardiovascular causes was 8.12/100 patient-years. The covariates in the analyses of cardiovascular mortality shown in Figure 3 are the same as those shown in Figure 2 for all-cause mortality. In the analysis of patient-level prescription data, BBs (RR = 0.87, $P = 0.004$), ARBs (RR = 0.79, $P = 0.005$) and peripheral blockers (RR = 0.84, $P = 0.01$) were found to be significantly associated with lower risk of cardiovascular death. The risk of cardiovascular death was significantly higher for patients prescribed a short-acting dihydropyridine, a finding consistent with that for all-cause mortality.

In the analysis of facility prescription practices, adjusted for the prescription of other AHA, the strongest association with lower cardiovascular mortality was observed for ARBs. Every 10% increase in patients with ARB prescriptions within a facility was marginally significantly associated with 11% lower cardiovascular mortality (RR = 0.89, $P = 0.06$). The associations of greater facility prescriptions of BBs and ACEIs with cardiovascular mortality were also in the direction of risk reduction (BB: RR = 0.95 per 10%, $P = 0.15$; ACEI: RR = 0.96 per 10%, $P = 0.31$).

As there was significant variation across countries in the means of dialysate sodium concentration and interdialytic weight gain, separate Cox models with adjustments for these two covariates were used to assess the associations between prescription of AHA and mortality. In general, the patterns of the associations remained similar to the adjusted models that did not include these covariates. This was observed both in the patient-level and in the facility-level models.

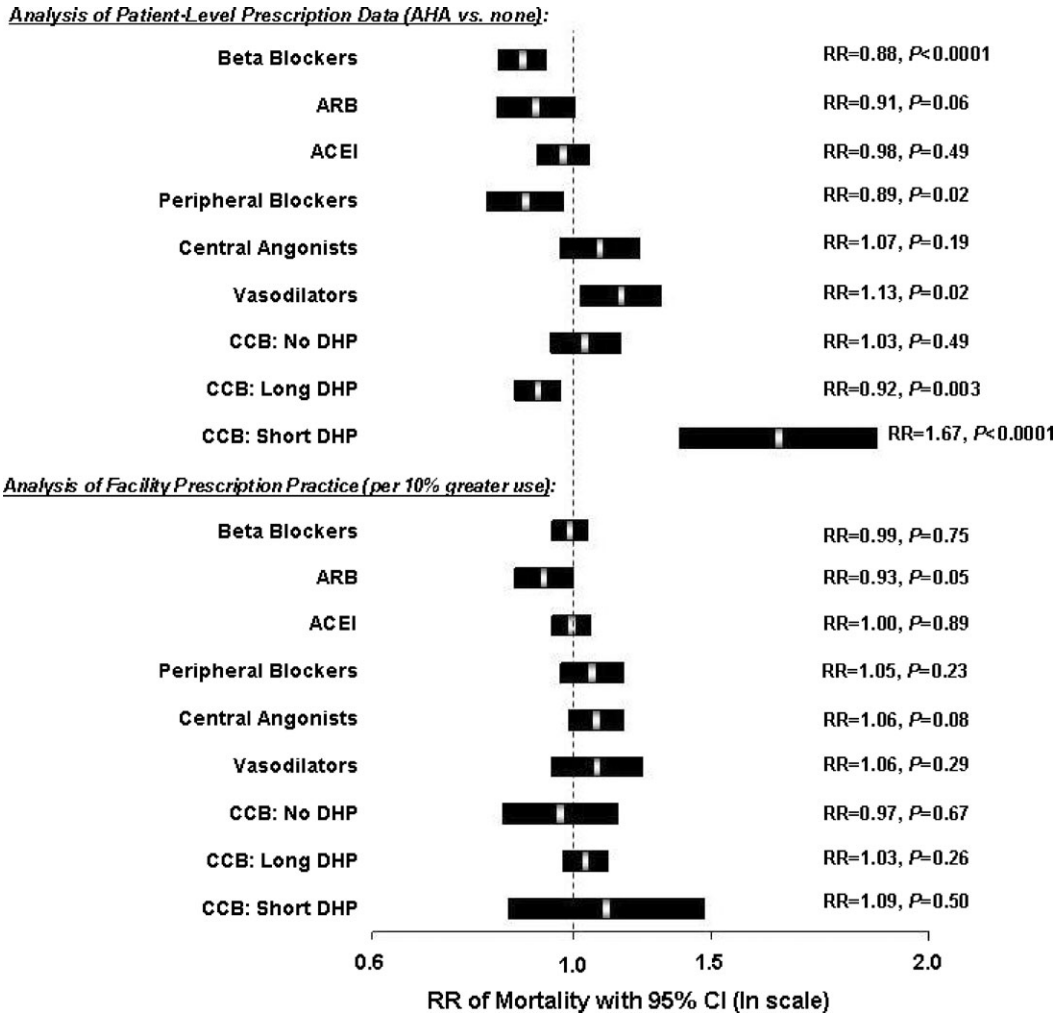

Fig. 2. Adjusted RR (95% CI)* of all-cause mortality associated with each class of antihypertensive agent (AHA). ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB, calcium channel blocker; DHP, dihydropyridine. *By Cox PH analysis, adjusted for the following patient-level data, age, sex, race, time on ESRD, 14 summary comorbid conditions listed in Table 1, pre-dialysis systolic blood pressure and other AHA classes.

Outcomes according to class-specific indications

Certain classes of AHA are recommended preferentially over others for patients with specific comorbidities, such as diabetes, CAD and CHF. However, we found no significant variations in the associations of specific classes of AHA with all-cause or cardiovascular mortality according to the presence or absence of these conditions.

Discussion

The results of this international study of patients on maintenance haemodialysis show important variations in the prescription of AHA by demographic characteristic, diagnosis and region. The data suggest that the odds of prescription of these medications, after adjusting for differences in case mix, were higher for male, black, diabetic and younger patients. In general, the odds of prescription of the studied classes of AHA were also higher for haemodialysis patients in the United States and Canada compared to patients in other DOPPS countries. When countries were compared regarding specific classes of AHA, we observed that ARBs were most commonly prescribed in Japan, Sweden and Germany and BBs were most commonly prescribed in Sweden, Canada, the United States and Germany. These regional differences were not explained by age, sex, race, years of ESRD or prevalence of comorbidities. Regarding temporal trends, an increase in the percentage of patients with prescription of BBs and ARBs was observed from DOPPS I to DOPPS II. No notable change was observed in the percentage of patients prescribed ACEIs. These temporal and regional trends are important because they reflect modifiable practice patterns that might be related to changes in the risks of adverse outcomes over time or by region among haemodialysis patients.

The present study shows statistically significant associations between the prescription of certain AHA and a reduced risk of death in haemodialysis patients. To reduce the effects of bias by indication, we examined the associations

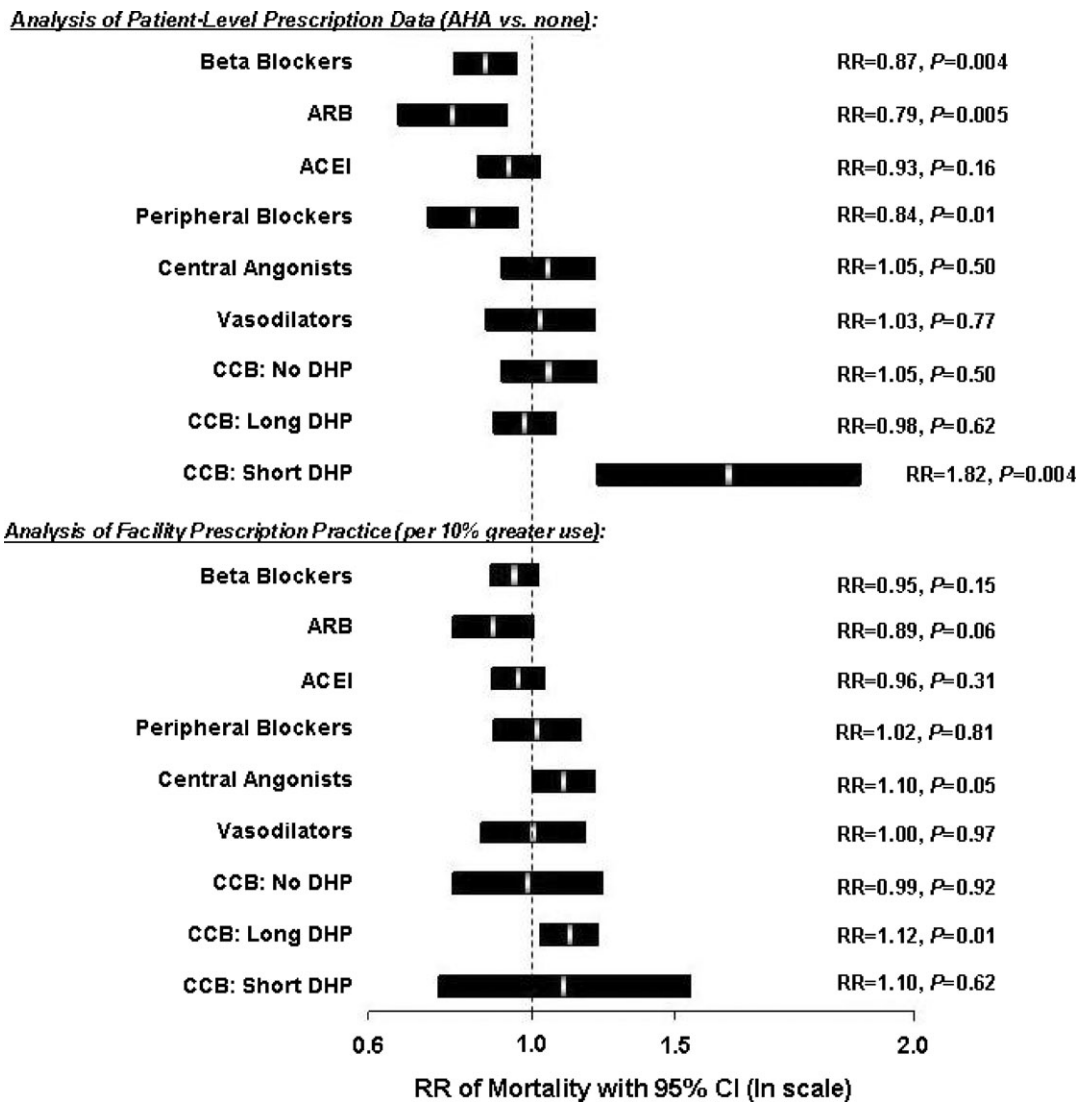

Fig. 3. Adjusted RR (95% CI)* of cardiovascular mortality associated with each antihypertensive agent (AHA). ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB, calcium channel blocker; DHP, dihydropyridine. *By Cox PH analysis, adjusted for the following patient-level data; age, sex, race, time on ESRD, 14 summary comorbid conditions listed in Table 1, pre-dialysis systolic blood pressure and other AHA classes.

with mortality of AHA classes prescribed at the patient level and as a practice pattern at the facility level. However, because this is an observational study, the results need to be confirmed in randomized clinical trials. Our findings suggest that ARB use is associated with lower mortality risk, both all-cause and cardiovascular, among patients on maintenance haemodialysis. The association between the prescription of ARBs and reduced all-cause mortality was marginally significant when assessed at the patient level, but the association became significant when the prescription was analysed at the facility level. Confounding by indication should be viewed as a potential explanation for the lack of statistically significant associations in the patient-level model.

The association of ARB prescription and reduction in mortality, particularly cardiovascular mortality, is consistent with results from clinical trials in non-ESRD populations [22–25].

The association between prescription of BBs and reduction in the mortality risk due to cardiovascular causes is consistent with results from previous clinical trials in dialysis patients with dilated cardiomyopathy [26].

The finding of lower mortality with long-acting dihydropyridine CCB in the adjusted analysis of patient-level prescription data is consistent with data from the USRDS Dialysis Morbidity and Mortality Study Wave II cohort [27], but is not supported by our facility practice analysis. The discrepancy between the results of analyses of patient-level prescription data and facility prescription practice suggests that patients prescribed long-acting dihydropyridine CCBs are, as a whole, healthier than those who are not. Therefore, our results do not offer support for an independent beneficial effect of long-acting dihydropyridine CCBs on survival among haemodialysis patients. The weaker association between short-acting dihydropyridine CCBs in the model using patient-level prescription data compared

to the association observed in the model of facility prescription practice suggests that this class of AHA may have been administered to patients with worse health. The data from the non-ESRD hypertensive population indicate that the use of short-acting dihydropyridine CCBs is associated with more harmful than beneficial effects when compared with other AHA [28]. The very low percentage of patients with short-acting dihydropyridine CCB prescriptions in the DOPPS limits inference about the actual effect of this class of antihypertensive medication in the population on maintenance haemodialysis.

Interestingly, our results suggest that the use of ARBs for haemodialysis patients is strongly associated with lower cardiac and all-cause mortality than the use of ACEIs. In the context of prior studies in non-ESRD populations [24,29], our finding of a more robust association with longer survival for ARBs than ACEIs may be considered unexpected. It is known that ARBs block angiotensin II activity more completely than ACEIs, for which inhibition of the renin–angiotensin system may be limited by angiotensin II generation via non-ACE pathways. However, there is a lack of studies to support the possibility that a more complete blockade by ARBs may explain a more beneficial effect of this class of medication on increasing survival among haemodialysis patients. Consistent with our results regarding ACEIs, a previous clinical trial of 400 ESRD patients treated by haemodialysis found no significant differences in all-cause and cardiovascular mortality between patients randomized to fosinopril or placebo in the intention to treat analysis after adjusting for independent predictors of cardiovascular events [30].

It has been suggested that ARBs are particularly beneficial for improving outcomes in patients with diabetes [31]. For that reason, we assessed the data for a possible interaction between class of medication and diabetes status on the mortality risk in the practice-pattern model. For both ARBs and ACEIs, the associations with mortality risk did not differ significantly according to diabetic status.

Dialysate sodium concentration has been associated with interdialytic weight gain and, therefore, may potentially influence blood pressure, cardiovascular outcomes and prescription of AHA [32,33]. According to our results, however, the associations between prescription of AHA and mortality are independent of the effects of dialysate sodium concentration and IDWG.

In conclusion, this observational study suggests associations between ARBs and the reduction of the risk of all-cause death and between BBs and the reduction of the risk of cardiovascular death among haemodialysis patients. The reason for the stronger association of ARBs than ACEIs with lower mortality risk could not be directly addressed in our study and should be viewed as an intriguing question for future investigation. Our results highlight the need for caution when efficacy and outcome data for AHA in non-ESRD populations are used to guide treatment decisions in haemodialysis patients. The combined results from analyses of both patient-level prescription data and facility prescription practice in this large observational study provide further rationale for a clinical outcomes trial comparing AHA, or combinations of AHA, in haemodialysis patients.

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Optimization of mid-dilution haemodiafiltration: technique and performance

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Abstract

Background. Mid-dilution haemodiafiltration (MD-HDF), reported as a highly efficient convective-mixed technique, has demonstrated serious drawbacks in relation to the high pressure originating inside the blood compartment of the filter during clinical application. This randomized crossover design study was planned to optimize the efficiency of the MD-HDF technique while reducing its inherent risks.

Methods. Fifteen patients on RRT were submitted in random sequence to standard and reverse MD-HDF under similar operating conditions. Efficiency in solute removal was evaluated by measuring urea (U), phosphate (P) and beta2-microglobulin (β2-m), mean dialysate clearances (K_{DQ}) and eKt/V. Blood and dialysate compartment pressures were monitored on-line during the sessions, and instantaneous hydraulic and membrane permeability indexes were calculated.

Results. During standard MD-HDF sessions, unlike with reverse MD-HDF, excessive blood inlet and transmembrane pressure prevented the planned infusion from being maintained. Resistance index and membrane permeability to