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Factors associated with differences in anti-hypertensive drug treatment: results from the MONICA Augsburg Population Surveys 1989/90 and 1994/95

Summary

Objective: To investigate in a population-based sample of hypertensive men and women the impact of factors that determine frequency and pattern of antihypertensive treatment.

Methods: We used pooled data of two independent surveys conducted 1989/90 and 1994/95 in the Augsburg region among men and women aged 25 to 74 years. Co-morbidity and cardiovascular risk factors were assessed by questionnaire and examination. Multivariate and polytomous logistic regression analyses were used to assess treatment patterns adjusting for cofactors.

Results: Among a total of 9 795 survey participants, 2 279 men and 1 699 women were hypertensive with 30 % of men and 43 % of women using antihypertensive drugs. Hypercholesterolemia was unrelated and smoking even inversely related to treatment (adjusted odds ratio OR = 0.7, 95 % CI 0.56–0.92). Women were more likely to be treated than men (adjusted OR = 1.6, 95 % CI: 1.34–1.82). Furthermore, women on monotherapy used diuretics significantly more often than men (adjusted OR relative to betablocker use 2.8, 95 % CI: 1.6–4.8).

Conclusions: We identified several determinants of drug treatment among hypertensives in the community. During the study period antihypertensive treatment seemed to be determined primarily by clinical disease but not by concomitant cardiovascular risk factor status, such as male gender, smoking, or hypercholesterolemia.

Keywords: Antihypertensive treatment – Population study – Determinants – Gender difference.

Hypertension is a major risk factor for cardiovascular disease. Adequate antihypertensive treatment has been shown to decrease cardiovascular risk and to increase life-expectancy in both men and women and is thus accepted as an effective measure to decrease hypertension related morbidity and mortality (Collins & MacMahon 1994). However, differences in the degree of antihypertensive treatment of men and women with hypertension and in their patterns of drug use have been reported for the MONICA Augsburg as well as for other national and international population-based studies (Gasse et al. 1999; Meyer 1994; Klungel et al. 1997). Despite a lower prevalence of hypertension, Augsburg women used antihypertensive drugs, proportionally, more frequently than men. In addition, women used more often diuretics in monotherapy as well as in combination therapy but less often calcium channel blockers (Gasse et al. 1999). According to the recommendations for the management of arterial hypertension at the time of the surveys, treatment should be initiated based on the level of blood pressure, but also in patients with mild hypertension in the presence of co-morbidity, other cardiovascular risk factors, or end organ damage (Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure 1988; 1990; 1993). The choice of drugs followed the stepped care approach but also should be determined by co-morbidity and by the individual response to a drug (Deutsche Liga zur Bekämpfung des hohen Blutdruckes 1988; 1990; 1994). Thus, the differences described may be accounted for by different distributions of these determinants of treatment in men and women.

The objective of this study was to analyse the frequency of factors related to antihypertensive treatment in men and women with hypertension. We further analysed to what extent those determinants could help to explain differences in treatment rates and in the choice of antihypertensive drugs.

Methods

Study design and population

The collaborative WHO-MONICA Project was initiated in the early 1980s to monitor trends and determinants in cardiovascular disease morbidity and mortality in men and women from 27 countries over a period of 10 years (WHO Monica Project Principal Investigators 1988). The present investigation is based on data from the MONICA Augsburg Project in Southern Germany. Two independent, randomly selected, representative samples of the population of the city of Augsburg and the two surrounding counties were examined in 1989/90 (S2) and 1994/95 (S3). Both surveys comprised the age groups 25 to 74 years. In an earlier paper from the MONICA Augsburg study we reported that prevalence and treatment rates of hypertension remained almost constant between 1989/90 and 1994/95 (Gasse et al. 1999). Changes in antihypertensive treatment patterns were basically restricted to increased use of ACE-inhibitors and calcium channel blockers but the major increments had occurred between 1984/85 and 1989/90. As there were thus no substantial differences with regard to the management of hypertension between S2 and S3, we pooled the data of both studies for the present investigation.

Participation was 76.9% in S2 ($n = 4940$) and 74.9% in S3 ($n = 4856$). In each survey, the participants were interviewed and examined in an identical manner by intensively trained observers with highly standardised methods (WHO Monica Project 1990). Interview questions comprised information on medical history and lifestyle factors such as smoking, alcohol consumption, physical activity, and dietary patterns. All medications taken during the week prior to the interview were assessed identically in S2 and S3. The participants were asked to bring all their drug packages to the interview. Drug names, dosages, and the route of administration were recorded. Antihypertensive drugs were preparations containing diuretics, betablockers, calcium channel blockers, and ACE-inhibitors as well as aldosteronantagonists, peripherally and centrally acting vasodilators and reserpine. These categories were chosen according to the pertinent guidelines for antihypertensive therapy of the German Hypertension League (Deutsche Liga zur Bekämpfung des hohen Blutdruckes 1988; 1994).

Blood pressure was measured with identical methods during the two surveys (Hense et al. 1995). Hypertension was defined as present in a study participant if the systolic blood pressure (SBP) was equal to or greater than 140 mmHg and/or the diastolic blood pressure (DBP) was equal to or greater than 90 mmHg and/or antihypertensive treatment was taken (Joint National Committee on Prevention, Detec-

tion, Evaluation, and Treatment of High Blood Pressure 1988, 1990, 1993). Treated hypertensives were defined as participants currently using at least one antihypertensive drug and reporting a history of hypertension. Among treated hypertensives we identified those who received antihypertensive treatment with a single drug containing only one active agent (monotherapy).

Cardiovascular disease medication was defined as the use of antiarrhythmics other than betablockers or calcium channel blockers, or cardioactive agents, such as digoxin, and nitrates. Participants who reported the use of diuretics, calcium channel blockers, betablockers, or ACE-inhibitors but no history of hypertension were also categorised as users of cardiovascular medication.

Cardiovascular risk factors and co-morbidity

Cardiovascular risk factors and co-morbidity were determined either by physical examinations or by structured interview. Non-fasting blood samples were drawn under standardised conditions (WHO Monica Project 1990; Keil et al. 1988). Total cholesterol was categorised as hypercholesterolemia if equal to or greater than 250 mg/dl according to the European Atherosclerosis Society (1987). Body mass index (BMI) was calculated as weight/height^2 (kg/m^2). Obesity was defined as $\text{BMI} \geq 30 \text{ kg/m}^2$ according to Bray (1978). Participants with missing data on total cholesterol levels or BMI and consequently on the derived variables hypercholesterolaemia or obesity were included in the analyses as such and compared with participants who had no hypercholesterolemia or were not obese respectively. Smoking status was ascertained by self-reporting. Regular smoking of more than 10 cigarettes per day was considered as a cardiovascular risk factor.

Diabetes, angina and heart failure, asthma and bronchitis, and presence of varicosis were also ascertained by self-reporting. The presence of varicosis was included in the analyses because it has been suggested that higher frequency of diuretic use in women may be related to a higher prevalence of varicose veins and phlebitis in women and the subsequent occurrence of oedemas in the legs (Madar & Widmer 1990; Carpentier & Priollet 1994). The participants were asked whether they had suffered from any of the diseases within the year prior to the interview. History of stroke or myocardial infarction (MI) were obtained by asking the participants if they had ever experienced a stroke or MI which was diagnosed by a physician. The answers to these questions could take three levels (yes/no/don't know). The three levels were included as such (dummy variables) in the statistical models. Participants who answered "yes" or "don't know" were separately compared with those participants who answered "no" to the respective question.

Educational attainment was estimated by recording years of schooling completed. The variable was then dichotomised into <10 years (low) and ≥ 10 years (high). Age was categorised in ten year age groups. Family history of cardio- or cerebrovascular disease was present if the reported cause of death of the mother or father was MI or stroke.

Statistical analysis

We present frequency estimates for antihypertensive treatment, cardiovascular risk factors, and concomitant clinical diseases among male and female hypertensives. We report adjusted odds ratios (OR) for risk factors and co-existing diseases to evaluate the association between these factors and antihypertensive treatment. Mean blood pressure values are reported for treated and untreated hypertensives. Percentiles for the systolic and diastolic blood pressure, blood cholesterol, and BMI are presented. Multivariate logistic regression was performed to control for a potential confounding by risk factors and co-morbidity of the association between sex and antihypertensive treatment patterns. We restricted the analysis of individual drug classes and sex to patients receiving antihypertensive monotherapy because the choice of drugs in combination therapy may be determined by several different factors which cannot be adequately controlled for in the analysis. We used polytomous logistic regression analysis controlling for potential co-factors of antihypertensive treatment. The polytomous logistic regression is an extension of the multivariate logistic regression for a polytomous outcome variable. Multiple categories may be created with one designated as a referent, and the other categories compared one at a time to the referent using separate logistic models for each comparison (Rothman & Greenland 1998). In this investigation, the outcome variable has four mutually exclusive categories of drug exposure: diuretics, betablockers, calcium channel blockers, and ACE-inhibitors, exposure to betablockers is used as the reference category as it was fairly equally frequent in men and women. We report relative odds ratios (ROR) for the use of diuretics, calcium channel blockers, and ACE-inhibitors compared with the use of betablockers. Statistical analyses were performed with the PC version of the Statistical Analysis System (SAS 6.11), Intercooled Stata 6.0 for windows, and MEDCALC, version 4.03.

Results

Among the 9795 (4886 men, 4909 women) participants of the two surveys, the prevalence of hypertension was 47% ($n = 2\,279$) for men and 35% ($n = 1\,699$) for women. Hypertensive women were more likely than men to have an education of less than 10 years, to be obese, to use CVD medi-

cation, or to report a family history of cardiovascular disease. Women reported less often regular smoking of more than 10 cigarettes per day and a history of MI (Tab. 1).

Thirty percent ($n = 674$) of hypertensive men and 43% ($n = 725$) of hypertensive women reported the use of antihypertensive drugs. Women were 1.77 (95% confidence interval (CI) 1.56–2.02) times more likely to report treatment than men. After adjustment for co-morbidity, other cardiovascular risk factors and age the OR for the association of being female with treatment status was reduced to 1.6 (95% CI 1.34–1.82) indicating that sex differences were explained to only a small degree by the factors controlled for in this analysis (Tab. 2). Independent, significantly positive relations with treatment status were additionally found for age, diabetes, obesity, history of MI and stroke, angina, heart failure, and use of other cardiovascular disease (CVD) medication. While the association with hypercholesterolemia was almost null, a significantly inverse association was found between smoking and treatment (adjusted OR = 0.72, 95% CI 0.56–0.92) (Tab. 2).

Analysis of the association between sex and treatment stratified for cardiovascular diseases indicated an interaction between cardiovascular diseases and sex, that is, sex differences diminished in the presence of cardiovascular diseases. Thus, we performed separate logistic regression analyses to investigate the association between treatment status and sex and other factors among hypertensive participants with and without cardiovascular disease. For these analyses the variables history of MI or stroke, angina, heart failure, and CVD medication were combined into one dichotomised variable of CVD. Twenty-seven percent ($n = 841$) of hypertensives without CVD and 62% ($n = 558$) of hypertensives with CVD reported antihypertensive therapy. The ORs of the association between treatment status and sex or the other factors among hypertensive participants without CVD did not differ materially from those ORs obtained from the full model (Tab. 3, Tab. 2). By contrast, among hypertensives with CVD sex differences and increasing treatment rates with age were not detected.

The mean systolic and diastolic blood pressure values in treated hypertensives were significantly lower than in untreated hypertensives (SBP: 147.4 vs 149.4 mmHg, $p = 0.006$ (men), and 151.2 vs 148.1 mmHg, $p = 0.0001$ (women); DBP: 89.6 vs 84.7 mmHg $p < 0.0001$ (men), and 88.7 vs 82.7 mmHg, $p < 0.0001$ (women)), but only a third of treated men and women achieved normal blood pressure values lower than 140/90 mmHg (men: 33.1%; women: 31.9%).

Percentiles for systolic and diastolic blood pressure levels, blood cholesterol and BMI are presented in the Appendix (Tab. A1 and A2).

Table 1 Frequency (%) of baseline characteristics, men and women with hypertension. Pooled MONICA Augsburg Surveys 1989/90 and 1994/95

	Total (n = 3978) No (%)	Men (n = 2279) No (%)	Women (n = 1699) No (%)
Survey			
1989/90	1957 (49.2)	1138 (49.9)	819 (48.2)
1994/95	2021 (50.8)	1141 (50.1)	880 (51.8)
Antihypertensive treatment			
yes	1399 (35.1)	674 (29.6)	725 (42.7)
no	2579 (64.9)	1605 (70.4)	974 (57.3)
Age (years)			
25–34	252 (6.3)	202 (8.9)	50 (2.9)
35–44	472 (11.9)	322 (14.1)	150 (8.8)
45–54	816 (20.5)	453 (19.9)	363 (21.4)
55–64	1124 (28.3)	605 (26.5)	519 (30.5)
65–74	1314 (33.0)	697 (30.6)	617 (36.3)
Blood pressure levels			
< 140/90 mmHg	456 (11.5)	225 (9.9)	231 (13.6)
140/90 mmHg – 159/94 mmHg	2052 (51.6)	1190 (52.2)	862 (50.7)
≥ 160/95 mmHg	1470 (36.9)	864 (37.9)	606 (35.7)
Educational level			
low	2740 (68.9)	1382 (60.6)	1358 (79.9)
high	1238 (31.1)	897 (39.4)	341 (20.1)
Diabetes			
yes	325 (8.2)	175 (7.7)	150 (8.8)
don't know	226 (5.7)	132 (5.8)	94 (5.5)
no	3653 (86.1)	1315 (86.5)	1455 (85.7)
Smoking (10 cig/day)			
yes	520 (13.1)	391 (17.2)	129 (7.6)
no	3458 (86.9)	1888 (82.8)	1570 (92.4)
Hypercholesterolaemia			
yes	1680 (42.2)	921 (40.4)	759 (44.7)
missings	116 (2.9)	43 (1.9)	73 (4.3)
no	2182 (94.5)	1265 (57.7)	867 (51.0)
Obesity			
yes	1251 (31.4)	611 (26.8)	640 (37.7)
missings	50 (1.3)	28 (1.2)	22 (1.3)
no	2677 (67.3)	1640 (72.0)	1037 (61.0)
History of MI			
yes	219 (5.5)	158 (6.9)	61 (3.6)
no	3809 (94.5)	2121 (93.1)	1638 (96.4)
History of stroke			
yes	123 (3.1)	80 (3.5)	43 (2.5)
no	3855 (96.9)	2199 (96.5)	1656 (97.5)
Angina pectoris			
yes	293 (7.4)	176 (7.7)	117 (6.9)
don't know	225 (5.7)	110 (4.8)	115 (6.8)
no	3460 (86.9)	2121 (87.5)	1467 (86.3)
Heart failure			
yes	324 (8.1)	167 (7.3)	157 (9.2)
don't know	204 (5.1)	95 (4.2)	109 (6.4)
no	3450 (86.8)	2199 (88.5)	1433 (84.3)
Use of CVD medication			
yes	511 (12.8)	275 (12.1)	296 (17.4)
no	3467 (87.2)	2004 (87.9)	1403 (82.6)
Family history of MI or stroke			
yes	1060 (26.6)	536 (23.5)	524 (30.8)
no	2918 (73.4)	1743 (76.5)	1175 (69.2)

CVD: Cardiovascular disease; MI: Myocardial infarction.

Table 2 Frequency (%) of cardiovascular risk factors and diseases and adjusted^a odds ratios (OR) (and 95% confidence intervals) for the association with treatment status. Men and women with hypertension. Pooled MONICA Augsburg Surveys 1989/90 and 1994/95

	Total (n = 3 978) No (%)	Treated No	Untreated No	Adjusted OR
Survey				
1989/90 ^b	1957 (49.2)	673	1284	1.0
1994/95	2021 (50.8)	726	1295	1.07 (0.93–1.24)
Sex				
male ^b	2 279 (57.3)	674	1 605	1.0
female	1 699 (42.7)	725	974	1.56 (1.34–1.82)
Age (years)				
25–34 ^b	252 (6.3)	12	240	1.0
35–44	472 (11.9)	71	401	3.21 (1.76–6.36)
45–54	816 (20.5)	220	596	5.30 (3.00–10.26)
55–64	1 124 (28.3)	476	648	8.52 (4.86–16.41)
65–74	1 314 (33.0)	620	694	9.25 (5.27–17.83)
Educational level				
low	2 740 (68.9)	1 046	1 694	1.08 (0.91–1.28)
high ^b	1 238 (31.1)	353	885	1.0
Diabetes				
yes	325 (8.2)	198	127	1.94 (1.50–2.51)
don't know	226 (5.7)	52	174	0.48 (0.34–0.68)
no ^b	3 427 (86.1)	1 149	2 278	1.0
Smoking (10 cig/day)				
yes	520 (13.1)	103	41	0.72 (0.56–0.92)
no ^b	3 458 (86.9)	1 286	2 162	1.0
Hypercholesterolaemia				
yes	1 680 (42.2)	610	1 070	0.90 (0.78–1.05)
missings	116 (2.9)	48	68	0.87 (0.56–1.36)
no ^b	2 182 (54.9)	741	1 441	1.0
Obesity				
yes	1 251 (31.4)	554	697	1.68 (1.44–1.95)
missings	50 (1.3)	25	25	1.46 (0.76–2.81)
no ^b	2 677 (67.3)	820	1 857	1.0
History of MI				
yes	219 (5.5)	155	64	1.97 (1.40–2.79)
no ^b	3 809 (94.5)	1 244	2 515	1.0
History of stroke				
yes	123 (3.1)	89	34	2.68 (1.85–4.50)
no ^b	3 855 (96.9)	1 310	2 545	1.0
Angina pectoris				
yes	293 (7.4)	221	72	3.19 (2.32–4.42)
don't know	225 (5.7)	122	103	1.74 (1.25–2.41)
no ^b	3 460 (86.9)	1 056	2 404	1.0
Heart failure				
yes	324 (8.1)	229	95	2.59 (1.94–3.48)
don't know	204 (5.1)	109	95	1.41 (0.99–1.99)
no ^b	3 450 (86.8)	1 061	2 389	1.0
Use of CVD medication				
yes	511 (12.8)	328	243	0.91 (0.72–1.15)
no ^b	3 467 (87.2)	1 071	2 336	1.0
Family history of CVD				
yes	1 060 (26.6)	434	626	1.17 (1.0–1.37)
no ^b	2 918 (73.4)	965	1 953	1.0

^a Adjusted for all other variables simultaneously.^b Reference group.

MI: Myocardial infarction; CVD: Cardiovascular disease; OR: Odds ratio.

Table 3 Adjusted^a odds ratios (OR) (and 95% confidence intervals) for the association with treatment status. Hypertensives with and without cardiovascular diseases. Pooled MONICA Augsburg Surveys 1989/90 and 1994/95

	Hypertensives without cardiovascular disease (n = 3084) OR (95% CI)	Hypertensives with cardiovascular disease (n = 894) OR (95% CI)
Survey		
1989/90 ^b	1.0	1.0
1994/95	1.07 (0.90–1.26)	1.08 (0.82–1.43)
Sex		
male ^b	1.0	1.0
female	1.68 (1.41–2.00)	0.96 (0.72–1.28)
Age (years)		
25–34 ^b	1.0	1.0
35–44	3.96 (2.02–8.69)	0.41 (0.04–3.26)
45–54	6.39 (3.37–13.74)	0.81 (0.10–5.27)
55–64	10.82 (5.74–23.20)	0.95 (0.12–6.05)
65–74	11.99 (6.35–25.74)	0.82 (0.10–5.17)
Educational level		
low	1.14 (0.94–1.38)	0.88 (0.63–1.21)
high ^b	1.0	1.0
Diabetes		
yes	2.12 (1.54–2.93)	1.71 (1.16–2.57)
don't know	0.46 (0.30–0.67)	0.95 (0.46–2.05)
no ^b	1.0	1.0
Smoking (10 cig/day)		
yes	0.72 (0.54–0.95)	0.67 (0.38–1.18)
no ^b	1.0	1.0
Hypercholesterolemia		
yes	0.85 (0.72–1.01)	1.08 (0.81–1.44)
missings	1.00 (0.56–1.74)	0.69 (0.36–1.32)
no ^b	1.0	1.0
Obesity		
yes	1.73 (1.45–2.06)	1.42 (1.05–1.93)
missings	0.87 (0.31–2.15)	3.33 (1.20–11.88)
no ^b	1.0	1.0
Family history of MI or stroke		
yes	1.19 (0.99–1.43)	1.08 (0.80–1.47)
no ^b	1.0	1.0

^a Adjusted for all other variables simultaneously.^b Reference group.

MI: Myocardial infarction.

Drug use patterns among hypertensives receiving antihypertensive monotherapy

Among treated hypertensives receiving antihypertensive monotherapy (646/1399) women reported the use of diuretics more than twice as often as men (32.9% vs 14.6%), the absolute percentage difference was 18.3%, 95% CI 11.9–24.7. Conversely, women used calcium channel blockers less often than men (21.4% vs 34.1%; percentage difference –12.7%, 95% CI –5.9 to –19.5). The use of betablockers and ACE-inhibitors did not significantly differ

between women and men (betablockers: 37.3% vs 43.0; ACE-inhibitors: 8.4% vs 8.4%). We selected betablocker use as the reference category. Including an interaction term for female sex and presence of varicosis and adjusting for co-variables in the polytomous logistic regression analyses, women were still more likely to use diuretics in antihypertensive monotherapy than men. The ROR was 2.77, (95% CI 1.61–4.75). By contrast, the sex difference in calcium channel blocker use diminished to an ROR = 0.96, 95% CI 0.59–1.56 (Tab. 4). The ROR of the interaction term was 3.87 (95% CI 1.15–13.04) for the association of diuretics with betablockers, and 3.28 (95% CI 1.05–10.27) for the association of calcium channel blockers with betablockers. Other determinants that independently influenced the choice of antihypertensive drug classes were identified. Age increased strongly the likelihood of reporting the use of diuretics while the presence of angina decreased the use of diuretics and increased that of calcium channel blockers. Quite expectedly, diuretics and calcium channel blockers were more frequently used compared with betablockers among participants reporting asthma or bronchitis, as were, among diabetics, ACE-inhibitors.

Discussion

We report here that treatment differences between men and women with hypertension were only partly explained by the presence of co-existing clinical conditions or other cardiovascular risk factors. Hypertensive women remained more likely to be treated than men even when confounding factors potentially related to treatment decisions were accounted for. Of note, once that cardiovascular diseases were clinically manifest women and men received antihypertensive treatment with the same probability. Only a third of treated hypertensives had their blood pressure values controlled (<140/90 mmHg). With regard to the types of antihypertensive drugs used in monotherapy, substantially higher utilisation of diuretics by women was unrelated to co-factors. By contrast, lower use of calcium channel blockers by women observed in crude analyses was completely explained by concomitant conditions.

Higher treatment rates of hypertensive women of about 50% must be evaluated in the context of general health care utilisation patterns. There is good evidence for the contention that women generally use medications more often than men (Meyer 1994; Bjerrum et al. 1998). Thus, it can be assumed that differences in treatment rates are not particularly disease related but rather due to varying health behaviours and other factors not controlled for in this investigation (Meyer 1994; Bjerrum et al. 1998; Verbrugge 1982).

Table 4 Relative Odds Ratios (ROR) for the use of diuretics, calcium channel blockers, ACE-inhibitors versus β -blockers, using polytomous logistic regression, adjusted for all other variables simultaneously. Hypertensives receiving monotherapy. Pooled MONICA Augsburg Surveys 1989/90 and 1994/95

	Diuretics/ β -blockers ROR (95% CI)		Calcium channel blockers/ β -blockers ROR (95% CI)		ACE inhibitors/ β -blockers ROR (95% CI)	
Sex (men reference)	2.77	(1.61–4.75)	0.96	(0.59, 1.56)	1.23	(0.59, 2.59)
Age (years)						
25–34 (reference)						
45–54	2.11	(0.68–6.60)	1.38	(0.51–3.73)	1.50	(0.44–5.12)
55–64	4.04	(1.36–12.02)	2.83	(1.13–7.13)	0.67	(0.19–2.42)
65–74	8.83	(3.03–25.75)	5.71	(2.25–14.50)	2.50	(0.75–8.36)
History of MI	0.35	(0.12–0.97)	0.74	(0.40–1.35)	0.91	(0.29–2.86)
Angina	0.33	(0.14–0.80)	2.63	(1.40–4.95)	0.69	(0.22–2.19)
Asthma or bronchitis	3.21	(1.69–6.09)	1.93	(1.03–3.60)	1.94	(0.78–4.79)
Diabetes	2.73	(1.22–6.14)	2.88	(1.34–6.23)	6.73	(2.67–16.96)
Heart failure	0.91	(0.44–1.88)	1.55	(0.86–2.83)	0.65	(0.22–1.91)
History of stroke	1.07	(0.28–4.20)	3.31	(1.25–8.74)	3.86	(1.09–13.67)
Hypercholesterolemia	0.88	(0.52–1.32)	0.78	(0.51–1.21)	1.11	(0.59–2.09)
Obesity	2.13	(1.37–3.31)	1.80	(1.19–2.73)	0.84	(0.43–1.63)
Smoking	0.86	(0.35–2.11)	0.90	(0.41–1.98)	0.62	(0.19–1.99)
Survey 89/90 (reference)	0.39	(0.25–0.63)	0.90	(0.58–1.39)	1.45	(0.76–2.76)
Survey 94/95						
Educational level	1.45	(0.82–2.56)	1.19	(0.77–1.93)	0.64	(0.32–1.24)
Use of CVD medication	1.72	(0.90–3.28)	0.73	(0.40–1.35)	0.95	(0.36–2.50)
Varicosis	0.80	(0.42–1.58)	0.54	(0.26–1.1)	1.47	(0.59–3.63)
Female gender and varicosis (interaction)	3.87	(1.15–13.04)	3.28	(1.05–10.27)	1.47	(0.30–7.11)

MI: Myocardial infarction; CVD: Cardiovascular disease; CI: confidence interval.

Among such factors may count a higher frequency of doctor contacts by women, or differences in health concepts and also in therapy compliance.

We show here on the population level that antihypertensive treatment is closely associated with co-existing disease and end organ involvement. This appears to indicate that physicians in the Augsburg area managed their hypertensive patients in compliance with guidelines recommending consideration of concurrent disease in the decision for treatment (Deutsche Liga zur Bekämpfung des hohen Blutdruckes 1994). By contrast, this did not fully apply to the presence of other cardiovascular risk factors, such as smoking and hypercholesterolemia which did not seem to play a role in the decision to start antihypertensive treatment in the early 1990s in this Southern German community. In fact, there was a significantly lower use of treatment by about 30% in hypertensives who smoked. Amazingly, this underutilisation of antihypertensive therapy persisted in magnitude even in those having clinically manifest cardiovascular disease. We determined cholesterol levels during our surveys. There is thus the possibility that the treating physicians were un-

aware of hypercholesterolemia in their patients because blood tests had not been done recently. These findings may be of particular interest in light of the discussion about the undertreatment of hypertension (Furberg et al. 1994; Klungel et al. 1998b; Klungel et al. 1999).

In this investigation, the most frequently used drug classes in antihypertensive monotherapy were betablockers and diuretics in women and betablockers and calcium channel blockers in men.

Overall the choice of antihypertensive drug classes in monotherapy was in consent with pertinent antihypertensive treatment recommendations and information available at that time (Deutsche Liga zur Bekämpfung des hohen Blutdruckes 1988; Deutsche Liga zur Bekämpfung des hohen Blutdruckes 1994; Estacio & Schrier 1998; Lewis et al. 1993) and confirmed the results of another study on this topic (Klungel et al. 1998a). Despite these consistent relations, the investigated factors did not fully account for the sex differences in the use of diuretics. It could be perceived that the higher frequency of diuretic use in women might be related to a higher prevalence of varicose veins and phlebitis

in women and the subsequent occurrence of edemas in the legs (Madar & Widmer 1990; Carpentier & Priollet 1994). In fact, the presence of varicosis was a strong and significant predictor for diuretic use only in women but this did not explain their higher use of diuretics. There may be another explanation for sex differences in diuretic use. Our analyses of hypertensives with and without cardiovascular risk factors indicate that women are treated more often than men only if cardiovascular disease is not present. Diuretics have been shown to be safe and effective for step one therapy of uncomplicated hypertension and women seem to respond to diuretics particularly well (Freis 1996). As different frequency and pattern of treatment in men and women with hypertension can only partly be explained by co-factors, antihypertensive drug use seems influenced by factors beyond purely medical reasoning. These may include attitudes and preferences of patients and physicians, and of drug marketing strategies (Klungel et al. 1998a; Whelton & Brancati 1993).

A potential drawback of our study is that hypertension prevalence estimates are based on the average of the last two of three measurements taken on one occasion. They were not confirmed by measurements at subsequent occasions which might have led to an overestimation of hypertension in this population (Kouame et al. 1996; Klungel et al. 1998c). Nevertheless, the extent of this overestimation is probably not differential for men and women and, therefore, could not have affected the treatment rates or medication patterns. Furthermore, we could not validate the self-reported antihypertensive medication or co-morbidity against clinical or pharmacy records for this investigation. However, as antihypertensive medication is usually taken over a long time and the co-factors considered in this investigation are chronic conditions we are confident that this information is valid.

As we only investigated factors in monotherapy our results cannot be interpreted in relation to the choice of drugs in combination therapy, which is usually prescribed to patients with more severe hypertension. In these patients the choice of drugs may be determined by several different factors, which we could not adequately control for in this analysis.

It should also be noted that ACE-inhibitors have partially replaced other drug classes in monotherapy in recent years as it could already be seen between 1984 and 1995 (Gasse et al. 1999). Thus, the results of the study may not fully apply to the current pattern of antihypertensive drug use.

In conclusion, antihypertensive treatment rates are influenced by clinical disease but not by risk factor status. Different

frequency and pattern of treatment in men and women with hypertension can only partly be explained by co-factors. Thus, antihypertensive drug use seems modified by factors beyond purely medical reasoning. They deserve more attention as they appear to exert a major impact on the management of hypertension in the population. The consequences of sex differences in hypertension management with regard to differential outcomes remain to be investigated.

Zusammenfassung

Unterschiede in der Behandlung der Hypertonie und damit assoziierte Faktoren: Ergebnisse der MONICA Augsburg Bevölkerungsstudien 1989/90 und 1994/95

Fragestellung: Untersuchung des Einflusses von Faktoren auf die Häufigkeit und das Muster der Bluthochdruckbehandlung in einer bevölkerungsbezogenen Stichprobe von Männern und Frauen mit Hypertonie.

Methoden: Wir verwendeten die kombinierten Daten von zwei unabhängigen Querschnittsuntersuchungen aus den Jahren 1989/90 und 1994/95 in der Augsburger Region. Begleiterkrankungen und kardiovaskuläre Risikofaktoren wurden mithilfe eines Fragebogens und körperlicher Untersuchungen ermittelt. Multivariate und polytome logistische Regressionsanalyse wurden angewandt, um für potentiell beeinflussende Ko-Faktoren für die Behandlung kontrollieren zu können.

Ergebnisse: Unter den 9795 Teilnehmern der Untersuchung wurden 2279 Männer und 1699 Frauen mit Bluthochdruck identifiziert, von denen 30 % der Männer und 43 % der Frauen die Einnahme von blutdrucksenkenden Mitteln angaben. Hypercholesterolämie war nicht und Rauchen nur invers mit der Behandlung assoziiert. Frauen wurden häufiger behandelt als Männer (adjustiertes OR = 1.6, 95 % KI: 1.34–1.82), jedoch nur bei unkomplizierter Hypertonie. In der Monotherapie erhielten Frauen häufiger Diuretika als Männer (adjustiertes OR relativ zur Einnahme von Betablockern: 2.8, 95 % KI: 1.6–4.8).

Schlussfolgerungen: Die Behandlung des Bluthochdrucks war über den Untersuchungszeitraum hauptsächlich durch das Vorliegen von kardiovaskulären Begleiterkrankungen bestimmt und weniger durch kardiovaskuläre Risikofaktoren wie Hypercholesterolämie, Rauchen oder männliches Geschlecht. Unterschiede in der Häufigkeit und in dem Behandlungsmuster bei Frauen gegenüber Männern mit Bluthochdruck konnten nur zum Teil durch Ko-Faktoren erklärt werden.

Résumé

Facteurs associés aux différences de traitements

antihypertenseurs: résultats des enquêtes populationnelles de MONICA Augsburg, 1989/90 et 1994/95

Objectifs: Examiner dans un échantillon représentatif d'hommes et de femmes hypertendus l'impact de facteurs qui déterminent la fréquence et le type de traitement antihypertenseur.

Méthode: Nous avons utilisé les données groupées de deux enquêtes indépendantes menées en 1989/90 et 1994/95 dans la région de Augsburg parmi de 25 à 74 ans. L'hypertension a été définie comme une pression artérielle égale ou supérieure à 140/90 mmHg ou par la prise de médicaments antihypertenseurs. Les comorbidités et les facteurs de risque cardiovasculaires étaient évalués par questionnaire et examen physique. Les analyses multivariées et par régression logistique polytomique ont été utilisées pour évaluer les types de traitement.

Résultats: Sur un total de 9 795 participants, 2 279 hommes et 1 699 femmes étaient hypertendus avec 30 % d'hommes et 43 % de femmes utilisant des médicaments antihypertenseurs. Le traitement n'était pas associé à l'hypercholestérolémie et était inversement associé au tabac (odds ratio ajusté OR = 0.7, intervalle de confiance (IC) à 95 % : 0.56–0.92). Les femmes étaient plus souvent traitées que les hommes (OR ajusté = 1.6, IC à 95 % : 1.34–1.82). L'analyse détaillée montre que ce résultat ne concerne que les femmes avec une hypertension non compliquée. Les femmes sous monothérapie reçoivent des diurétiques significativement plus souvent que les hommes (OR ajusté par rapport à l'utilisation de beta bloquants : 2.8, IC à 95 % : 1.6–4.8).

Conclusions: Nous avons identifié plusieurs déterminants du traitement médicamenteux parmi les hypertendus de la communauté. Pendant la période de l'étude, le traitement antihypertenseur semblait être déterminé avant tout par la maladie clinique, mais pas par les facteurs de risque cardio-vasculaires concomitants, tels que le sexe masculin, le tabac ou l'hypercholestérolémie.

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Appendix 1

Table A1 Blood pressure (systolic and diastolic), blood cholesterol and BMI in women (n = 1699), MONICA Augsburg Surveys 1989/90 and 1994/95

Age (years)	N*	Percentiles					Mean (SD)
		P10	P25	P50	P75	P90	
Blood pressure (Systolic) (mmHg)							
25 – 29	82	134	139	142	147	152	142.93 (8.22)
30 – 34	120	127.5	135.0	142.0	148.5	153.0	142.28 (11.73)
35 – 39	154	128	134	140	148	156	141.82 (12.48)
40 – 44	168	130	135	142	150	158	144.05 (13.58)
45 – 49	201	129	138	143	154	168	147.46 (17.00)
50 – 54	252	131	140	146	157	167	148.90 (16.03)
55 – 59	303	131	140	148	158	171	149.31 (16.43)
60 – 64	302	132	142	153	165	173	152.96 (17.15)
65 – 69	399	131	141	150	162	171	151.04 (16.99)
70 – 74	298	133	143	151	162	172	152.75 (15.92)
Blood pressure (Diastolic) (mmHg)							
25 – 29	82	71	79	87	92	98	85.50 (10.16)
30 – 34	120	75.5	84.5	91.0	94.5	99.5	89.78 (10.28)
35 – 39	154	81	89	92	97	103	92.14 (9.58)
40 – 44	168	82.0	89.5	93.0	96.0	104.0	93.40 (9.27)
45 – 49	201	81	88	92	98	108	93.54 (10.88)
50 – 54	252	80	88	93	99	104	93.07 (9.81)
55 – 59	303	77	84	91	96	102	90.22 (10.17)
60 – 64	302	72	78	87.5	94.0	100	86.79 (11.72)
65 – 69	399	69	77	84	92	97	83.67 (11.01)
70 – 74	298	67	74	81	88	95	80.69 (11.33)
Blood cholesterol (mg/dl)							
25 – 29	80	166.61	185.80	209.92	248.26	275.73	217.03 (43.43)
30 – 34	118	181.89	202.01	228.45	254.90	277.48	232.76 (42.99)
35 – 39	153	186.53	204.72	229.49	259.29	301.09	236.86 (45.99)
40 – 44	163	188.6	212.08	238.50	265.87	299.54	241.16 (45.03)
45 – 49	201	194.27	211.69	241.88	273.61	315.02	245.18 (46.88)
50 – 54	250	197.48	219.04	245.16	273.60	299.84	249.05 (45.55)
55 – 59	298	196.5	217.90	245.55	275.93	309.99	249.79 (44.34)
60 – 64	295	196.98	218.27	243.81	269.60	306.80	246.40 (42.77)
65 – 69	388	191.3	217.11	246.33	273.22	299.93	246.50 (44.11)
70 – 74	290	187.25	212.46	239.63	266.26	285.75	239.01 (39.09)
BMI (kg/m²)							
25 – 29	81	21.54	23.98	25.70	28.36	31.17	26.20 (3.50)
30 – 34	120	22.80	24.89	26.88	29.76	32.39	27.34 (3.78)
35 – 39	151	23.02	25.20	26.85	29.56	32.70	27.65 (4.32)
40 – 44	168	23.90	25.62	27.64	30.38	33.67	28.26 (3.91)
45 – 49	201	23.94	25.37	27.75	30.30	33.00	28.13 (3.90)
50 – 54	251	24.85	26.27	28.24	30.61	33.42	28.70 (3.75)
55 – 59	302	24.73	26.36	28.02	30.30	33.66	28.73 (3.55)
60 – 64	299	24.40	26.17	28.53	30.91	32.95	28.71 (3.37)
65 – 69	391	23.78	25.97	28.10	30.95	32.91	28.39 (3.77)
70 – 74	287	23.52	25.23	27.76	29.67	31.99	27.79 (3.74)

* Numbers of participants of the 5-year age groups of the reported variables may not add up to the total number of participants due to missing information.

Appendix 2

Table A2 Blood pressure (systolic and diastolic), blood cholesterol and BMI in men (n = 2279), MONICA Augsburg Surveys 1989/90 and 1994/95

Age (years)	N*	Percentiles					Mean (SD)
		P10	P25	P50	P75	P90	
Blood pressure (Systolic) (mmHg)							
25 – 29	21	131	139	142	145	148	140.71 (7.03)
30 – 34	29	121	132	139	146	155	139 (12.80)
35 – 39	55	124	130	139	146	151	137.62 (10.78)
40 – 44	95	131	138	142	148	158	143.26 (12.45)
45 – 49	158	129	139	146	154	168	147.26 (15.43)
50 – 54	205	128	139	148	157	178	149.10 (17.74)
55 – 59	234	130	140	148	156	168	148.42 (15.56)
60 – 64	285	132	141	149	161	172	151.13 (16.36)
65 – 69	334	134	142	150	164	174	153.26 (18.01)
70 – 74	283	132	143	153	165	176	154.15 (18.55)
Blood pressure (Diastolic) (mmHg)							
25 – 29	21	87	87	90	94	100	91.19 (6.07)
30 – 34	29	82	90	92	96	100	92.24 (9.39)
35 – 39	55	76	84	92	95	100	90.24 (9.09)
40 – 44	95	81	86	93	98	103	91.97 (9.38)
45 – 49	158	79	85	91	96	102	90.82 (10.03)
50 – 54	205	–	84	91	96	102	90.03 (9.87)
55 – 59	234	74	81	88	94	102	87.84 (10.65)
60 – 64	285	72	79	86	92	98	85.38 (10.52)
65 – 69	334	69	76	83	90	96	82.88 (10.53)
70 – 74	283	64	72	80	87	94	79.46 (12.12)
Blood cholesterol (mg/dl)							
25 – 29	20	173.18	184.55	203.22	234.24	244.45	207.67 (28.34)
30 – 34	27	184.99	197.20	217.11	235.30	256.00	217.31 (31.83)
35 – 39	51	181.89	195.40	217.10	253.87	274.38	224.98 (45.29)
40 – 44	90	176.24	201.24	223.30	244.97	276.29	223.45 (35.05)
45 – 49	154	185.37	208.21	232.26	265.40	288.32	238.07 (42.71)
50 – 54	201	199.31	219.00	245.20	275.70	300.70	246.98 (38.62)
55 – 59	226	202.40	226.80	249.51	278.50	306.60	253.32 (41.17)
60 – 64	274	204.10	228.70	259.10	290.25	316.57	260.94 (48.97)
65 – 69	322	198.30	227.30	253.87	284.06	316.10	256.37 (45.20)
70 – 74	261	203.70	222.80	250.70	282.10	317.80	255.19 (46.17)
BMI (kg/m²)							
25 – 29	20	19.36	21.00	25.34	34.71	42.28	28.12 (8.97)
30 – 34	29	20.05	22.15	28.30	30.75	41.71	28.44 (7.53)
35 – 39	54	20.71	22.23	25.52	29.67	34.23	26.52 (5.38)
40 – 44	95	21.36	23.06	26.57	31.77	36.13	27.77 (6.26)
45 – 49	157	22.36	24.57	27.58	31.76	35.51	28.55 (5.78)
50 – 54	203	23.40	25.44	28.38	32.40	36.92	29.54 (6.06)
55 – 59	231	23.83	26.09	28.65	32.21	35.54	29.20 (4.70)
60 – 64	282	24.03	26.19	29.03	32.92	36.57	29.77 (4.98)
65 – 69	330	23.41	25.78	28.65	31.79	35.47	28.97 (4.53)
70 – 74	276	23.13	25.61	28.25	31.46	34.57	28.72 (4.67)

* Numbers of participants of the 5-year age groups of the reported variables may not add up to the total number of participants due to missing information.