

Association between hypertensive urgencies and subsequent cardiovascular events in patients with hypertension

Marianne Vlcek^a, Andreas Bur^a, Christian Woisetschläger^a, Harald Herkner^a, Anton N. Laggner^a and Michael M. Hirschl^b

Objective To determine whether patients with hypertensive urgency have a higher risk for subsequent cardiovascular events compared with hypertensive patients without this event.

Methods Overall, 384 patients with hypertensive urgency and 295 control patients were followed up for at least 2 years. Hypertensive urgency was defined as a systolic blood pressure above 220 mmHg and/or a diastolic blood pressure above 120 mmHg without any evidence of acute end-organ damage. The control group consisted of patients admitted to the emergency department with a systolic blood pressure between 135 to 180 mmHg and a diastolic blood pressure between 85–110 mmHg. The number of cardiovascular events defined as acute coronary syndrome, acute stroke, atrial fibrillation, acute left ventricular failure and aortic aneurysm were consecutively analyzed during follow-up. The median follow-up time was 4.2 years (interquartile range 2.9–5.7 years). Twenty-six patients of the urgency group and 23 patients of the control group were lost for follow-up.

Results Overall, 117 (17%) patients had nonfatal clinical cardiovascular events and 13 had (2%) fatal cardiovascular events. The frequency of cardiovascular events was significantly higher in patients with hypertensive urgencies

(88 vs. 42; $P = 0.005$). The Cox regression analysis identified age ($P < 0.001$) and hypertensive urgencies ($P = 0.035$) as independent predictors for subsequent cardiovascular events.

Conclusions Hypertensive urgencies are associated with an increased risk for subsequent cardiovascular events in patients with arterial hypertension. *J Hypertens* 26:657–662 © 2008 Wolters Kluwer Health | Lippincott Williams & Wilkins.

Journal of Hypertension 2008, 26:657–662

Keywords: acute coronary syndrome, hypertension, hypertensive crisis, hypertensive urgency, outcome, prognosis

Abbreviations: BMI, body mass index; BP, blood pressure; CI, confidence interval; ECG, electrocardiogram; ED, emergency department; JNC, Joint National Committee; LV, left ventricle; NSTEMI, non-ST-elevation myocardial infarction; STEMI, ST-elevation myocardial infarction; UAE, urinary albumin excretion; UAP, unstable angina pectoris

^aDepartment of Emergency Medicine, General Hospital, University of Vienna and ^bMedical Department, Landeskrankenhaus St. Pölten, Austria

Correspondence to Michael M. Hirschl, MD, Landeskrankenhaus St. Pölten, 3. Medical Department, Propst-Fuehrer-Strasse 4, A-3100 St. Pölten, Austria, Europe
Tel: +43 2742 3007 2318; fax: +43 2742 3001 4959;
e-mail: Michael.Hirschl@stpoelten.lknoe.at

Received 15 July 2007 Revised 24 November 2007
Accepted 28 November 2007

Introduction

Hypertensive urgencies are a frequently observed reason for admission to the emergency department (ED) [1–4]. This clinical condition is defined as severely elevated blood pressure (BP) – usually above 220 mmHg in systolic and/or above 120 mmHg in diastolic – without any evidence of acute end organ damage [5]. The recommendations for the treatment of hypertensive urgencies include a slow reduction of BP within 24 h by using oral antihypertensive agents. A clinical follow-up should be done within 24–48 h after the hypertensive urgency [6–8]. Whereas the recommendations for diagnosis and treatment of hypertensive urgencies are well established, data about the impact of hypertensive urgencies on the prognosis as well as on the occurrence of subsequent cardiovascular events in hypertensive patients are not available yet. We, therefore, aimed a prospective study to investigate the association between hypertensive urgencies and subsequent cardiovascular events in hypertensive patients.

Methods

General data

The study was performed at the Department of Emergency Medicine of the General Hospital Vienna, Austria, which is a tertiary care hospital with 2000 beds. The design of the study was a prospective data collection to evaluate the frequency of cardiovascular events and the prognosis of patients after hypertensive urgency. The initial data collection was performed from January to December 1999 and the follow-up was closed in December 2005.

Inclusion criteria

All patients admitted to the ED with hypertensive urgency were consecutively included to the study. Hypertensive urgency was defined as a systolic BP above 220 mmHg and/or a diastolic BP above 120 mmHg without any evidence of end-organ damage [5]. The inclusion criteria for the control group were the evidence of an arterial hypertension with a systolic BP above 140 mmHg

Table 1 Classification of the control group according to JNC VI criteria and reasons of admission to the emergency department

	Stage ^a		
	1	2	3
No. of patients	178 (60%)	87 (30%)	30 (10%)
Reasons of admission to the emergency department			
Headache (%)	27	36	34
Faintness (%)	12	5	2
Vertigo (%)	14	12	14
Arrhythmia (%)	28	17	18
Vomitus (%)	10	5	3
Dyspnea (%)	8	22	24
Others (%)	1	3	5

^a According to the Joint National Committee on Prevention, Detection, and Treatment of High Blood Pressure (JNC VI) criteria [5].

and/or diastolic BP above 90 mmHg. The hypertensive patients of the control group were consecutively included and classified according to the Joint National Committee on Prevention, Detection, and Treatment of High Blood Pressure (JNC VI) guidelines. The reasons for admission to the ED are summarized in Table 1.

Exclusion criteria

All patients with evidence of end-organ damage, namely acute coronary syndrome, acute left ventricular failure, acute stroke, aortic dissection, acute renal failure, and hypertensive encephalopathy were excluded from the study. Patients with malignant hypertension, that is evidence of severe hypertensive retinopathy assessed by fundoscopy, were also excluded from further analysis. Additionally, pregnant women, patients with chronic renal insufficiency [serum creatinine >176 $\mu\text{mol/l}$ (2.0 mg/dl)], with known secondary hypertension and with a history of coronary artery disease or stroke were not eligible for follow-up.

Emergency department procedure

Patients with hypertensive urgencies were treated with oral antihypertensive drugs, either with amlodipine (dose: 5 to 10 mg) or captopril (dose: 12.5 to 25 mg). All patients were discharged from hospital after marked reduction in BP.

Initial follow-up procedure

All patients of both groups (hypertensive urgency group and control group) were invited to attend the Hypertension Unit of the General Hospital for a detailed evaluation of their medical history on the day after their admission.

The initial follow-up procedure included a clinical BP measurement, an assessment of medical history (current antihypertensive drug treatment, duration of hypertension), a physical examination, a 12-lead ECG, an echocardiography to assess left ventricular hypertrophy, a sonography of the kidneys and renal arteries, a blood sampling to assess fasting blood glucose, total cholesterol, triglycerides, and serum creatinine, and a 24-h urine

sampling to determine microalbuminuria. In patients with suspected renal artery stenosis a CT-angiography was performed to exclude those who had it. According to the criteria of the International Diabetes Federation, the incidence of the metabolic syndrome, namely elevated waist circumference (abdominal obesity: male >94 cm, female >80 cm); increased serum triglycerides greater than 150 mg/dl; decreased high-density lipoproteins (male <40 mg/dl, female <50 mg/dl); arterial BP above 140/90 mmHg, fasting blood glucose above 100 mg/dl or diagnosed diabetes, was assessed in these patients [9].

Clinical blood pressure measurements

The first clinical BP measurement was done on the day after the admission to the ED. During the physician's visit (8–11), BP was measured in a quiet environment with a mercury sphygmomanometer with the patient in a sitting position after 5 min of rest, following the recommendations of the British Hypertension Society [10]. Systolic and diastolic BP values (Korotkoff phase I and phase V, respectively) were measured at 5-min intervals and a mean of three consecutive measurements was calculated for each visit. For any patient, consecutive sphygmomanometric measurements were obtained by the same medical doctor on the same visit.

Echocardiography

A standard methodology was employed in the study to assess left ventricular hypertrophy [11]. Echocardiography was recorded on videotapes and analyzed following the recommendations of the American Society of Echocardiography [12]. Two-dimensionally guided M-mode tracings were used, if correctly oriented, to measure left ventricle (LV) structures, whereas linear measurements of LV structure were obtained in two-dimensional parasternal long-axis view in the presence of low parasternal windows. LV measurements were averaged from two to five cardiac cycles. End-diastolic LV dimensions were used to calculate LV mass according to the formula described by Devereux [13].

Determination of microalbuminuria

Urinary albumin excretion (UAE) was measured using an immunonephelometric assay (Behring Institute, Marburg, Germany). Aliquots of urine were taken from the 24-h, stored in glass tubes at 4°C, and were analyzed 1–7 days after collection. The intra-assay and interassay variabilities of the method in our laboratory were 3 and 7%, respectively. Microalbuminuria was defined as UAE of 30–300 mg/day.

Fundoscopy

Hypertensive retinopathy was assessed directly from fundoscopy by a single ophthalmologist who was blinded to BP levels and echocardiographic data. The fundoscopic grades were classified according to the gradings published by Keith *et al.* [14] and Grosso *et al.* [15].

Long-term follow-up

The long-term treatment of the patients was done by the general practitioners according to the recommended guidelines of the JNC VI. All patients, who were alive 1 year after the acute event, were invited to be admitted to the Hypertension Unit for a physical examination, for an assessment of BP and an interview about cardiovascular events requiring hospitalization during the past 12 months.

Assessment of cardiovascular events

The incidence of cardiovascular events during the time of follow-up was recorded. A minimal of 6 months of follow-up was required for being included in the analysis. Cardiovascular events included acute coronary syndrome, atrial fibrillation requiring hospitalization, sudden cardiac death, acute ischemic or hemorrhagic stroke, acute left ventricular failure, and acute aortic dissection.

The acute coronary syndrome included the ST-elevation myocardial infarction (STEMI: ST-segment elevations of more than 0.1 mV in two corresponding leads and a typical rise and fall of cardiac enzymes), the NON-ST-elevation myocardial infarction (NSTEMI: combination of typical chest pain and an increase of biochemical markers as troponin I or T) and unstable angina pectoris (UAP) with the need of coronary angiography and/or intervention. Atrial fibrillation was included in the data, if the patient was admitted to the hospital and received a therapeutic intervention, that is, an application of antiarrhythmic drugs or electrical cardioversion. Acute stroke was defined if the patient was admitted to the hospital because of neurological symptoms like aphasia, hemianopsia, paresthesia or paresis, and the computer tomography of the brain revealed an ischemic or hemorrhagic area. Acute left ventricular failure was included if hospitalization was required due to a pulmonary edema confirmed by chest radiograph.

Fatal events were retrieved from the Statistical Department of the Austrian government, which collected the causes of death of all patients who died in a hospital in Austria. Patients who died of a noncardiovascular cause were considered event free until death. Nonfatal events of the first 12 months were assessed by the interview of the patients at the Hypertension Unit 1 year after the initial evaluation. After the first year, the patients were called each year to acquire information about optional hospitalization during the last 12 months. In case of a prior hospitalization, the patients were invited to visit the Hypertension Unit to review the discharge letter of the hospital and all medical reports related to prior hospitalization.

Statistical analysis

Data are presented as mean and standard deviation or 95% confidence interval (CI). Categorical variables are given as counts and percentage. Patients with hypertensive

urgency were compared to controls. For univariate comparison of continuous variables, a *t*-test was used, as data were at least near normally distributed. For univariate comparison of categorical data, χ^2 tests or Fisher's exact test were adequate. Odds ratios and 95% CIs were calculated. In the univariate analysis the following variables were included: gender, smoking, creatinine, diabetes, cholesterol, age, microalbuminuria, left ventricular hypertrophy, systolic and diastolic BP, unknown hypertension and evidence of a hypertensive urgency. Variables were only included to the Cox regression analysis if they reached a statistical significance in the univariate analysis. To adjust for potential confounders, a multivariate Cox regression model was developed. Cardiovascular event was the dependent variable, and the independent variable was hypertensive urgency with the covariates age, left ventricular hypertrophy, systolic BP, cholesterol and microalbuminuria.

Data processing was performed with MS Excel 97 for Windows and SPSS 7.5 for Windows. A two-sided *P* value less 0.05 was considered statistically significant.

Results

General data

The general characteristics of the patients are demonstrated in Table 2. Overall, 384 patients with hypertensive urgency and 295 patients of the control group were followed up for a median time of 4.2 years (interquartile range 2.9–5.7 years). Malignant hypertension was noted in 11 (2.8%) patients of the urgency group and four (1.4%) patients of the control group. Additionally, 26 patients of the urgency group and 23 patients of the control group were lost for follow-up. The reasons for the loss of follow-up were address unknown (*n* = 25; urgency: *n* = 15, control group: *n* = 10), refusal to visit the Hypertension Unit (*n* = 14; urgency: *n* = 8, control group: *n* = 6) and no access to hospital data (*n* = 10; urgency: *n* = 7, control group: *n* = 3). The general data of patients lost for follow-up did not differ from the patients included to the study protocol (see Table 3).

Patients with hypertensive urgencies were older (56 vs. 50 years; *P* = 0.0001), had a higher rate of left ventricular hypertrophy (16 vs. 10%; *P* = 0.02), a higher rate of microalbuminuria (27 vs. 19%; *P* = 0.01) and a higher rate of dyslipidemia (72 vs. 64%; *P* = 0.04) The frequency of patients unaware of hypertension was significantly higher in the urgency group compared to the control group (21 vs. 15%; *P* = 0.03). The percentage of patients with acknowledged but untreated hypertension was also significantly higher in patients with hypertensive urgency (22 vs. 14%, *P* = 0.03).

Course of BP

BP values measured at the initial examination and 1 year later are summarized in Table 4. Systolic and diastolic BP

Table 2 General data at study entry

	Hypertensive urgency (n = 384)	Control group (n = 295)	P value
Gender (female/male)	185 (48)/199 (52)	147 (50)/148 (50)	NS
Age (years ± SD)	56 ± 12	50 ± 15	0.0001
Unknown hypertension ^a	81 (21)	43 (15)	0.02
Current antihypertensive treatment	299 (78)	254 (86)	0.006
Obesity (BMI > 30 kg/m ²)	90 (23)	63 (21)	NS
Smoking	64 (17)	67(23)	NS
Diabetes	59 (15)	37 (13)	NS
Dyslipidemia ^b	276 (72)	190 (64)	0.04
Metabolic syndrome ^c	93 (24)	75 (25)	NS
Duration of hypertension [years (IQR)]	7.9 (6.9–8.9)	7.4 (6.3–8.6)	NS
Left ventricular hypertrophy	62 (16)	30 (10)	0.02
Microalbuminuria ^d	103 (27)	55 (19)	0.01
Hypertensive retinopathy (stage I and II) ^e	91 (23)	67 (23)	NS
Serum creatinine (μmol/l)/(mg/dl)	91.1 (14.1)/1.0 (0.16)	92.8 (11.5)/1.02 (0.13)	NS

Percentage values are shown in parentheses. IQR, interquartile range. ^aThe following criteria were used to define unknown hypertension: no assessment of arterial blood pressure by a medical doctor until admission to the emergency department, no knowledge about arterial hypertension, no prescription of antihypertensive drugs. ^bTotal cholesterol greater than 6.5 mmol/l or greater than 250 mg/dl. ^cMetabolic syndrome: elevated waist circumference (abdominal obesity: male >94 cm, female >80 cm); serum triglycerides >150 mg/dl; high-density lipoproteins (male <40 mg/dl, female <50 mg/dl); arterial blood pressure >140/90 mmHg, fasting blood glucose >100 mg/dl or diagnosed diabetes. ^dMicroalbuminuria defined as urinary excretion of microalbumin between 30 and 300 mg/day. ^eHypertensive retinopathy was classified according to the criteria of Keith–Wagener: generalized or focal narrowing of retinal arterioles, arteriolar thickening, hemorrhage exudates or papilledema – patients with a hypertensive retinopathy stages III and IV were excluded according to the inclusion and exclusion criterias.

values were significantly higher in patients with hypertensive urgencies ($P=0.0001$ and $P=0.008$, respectively) at the initial evaluation. During the period of follow-up, goal of BP control – defined as BP values below 135 and 85 mmHg – was achieved in 197 (51%) patients after hypertensive urgency and in 169 (57%) patients of the control group ($P=0.12$).

Cardiovascular events in different patient groups

Overall, 130 patients had a cardiovascular event and 13 patients died during the follow-up period (Table 5). The frequency of cardiovascular events was significantly higher in patients with hypertensive urgencies (88 vs. 42; $P=0.005$). Whereas no significant differences were observed between both groups concerning fatal cardiovascular events (hypertensive urgency, $n=6$; control group, $n=7$), a significantly higher frequency of nonfatal cardiovascular events was noted in patients with hypertensive urgencies ($P=0.005$). A significant difference was noted with regard to the occurrence of acute coronary syndrome ($P=0.03$) and acute left ventricular failure ($P=0.02$) between both groups.

Association between hypertensive urgencies and subsequent cardiovascular events

The Kaplan–Meier plot demonstrating the probability of cardiovascular events of the different patient groups is presented in Fig. 1. We found a statistically significant higher frequency of cardiovascular events in patients with hypertensive urgency as compared with patients having hypertension stage 1 or 2 over a mean observational period of 4.2 years ($P=0.04$). In the Cox regression analysis including hypertensive urgency, age, left ventricular hypertrophy, clinical BP values, and microalbuminuria only age ($P<0.001$) and the occurrence of hypertensive urgency ($P=0.04$) were revealed to be independent predictors of cardiovascular events (Table 6).

Discussion

In this study we describe the prognosis during 5 years of follow-up among consecutive patients admitted to the ED with hypertensive urgencies. These patients had a higher rate of cardiovascular events during follow-up compared with those without a history of urgency. To our knowledge, this finding has never been reported

Table 3 Comparison of general data between patients included to the study and those, who were lost during follow-up

	Hypertensive urgency (n = 384)	Control group (n = 295)	Loss of follow-up (n = 49)
Gender (female/male)	185 (48)/199 (52)	147 (50)/148 (50)	24 (49)/25 (51)
Age (years ± SD)	56 ± 12	50 ± 15	52 ± 12
Unknown hypertension	81 (21)	43 (15)	10 (20)
Current antihypertensive treatment	299 (78)	254 (86)	34 (69)
Obesity (BMI > 30 kg/m ²)	90 (23)	63 (21)	11 (22)
Smoking	64 (17)	67(23)	12 (25)
Diabetes	59 (15)	37 (13)	8 (16)
Dyslipidemia	276 (72)	190 (64)	32 (65)
Duration of hypertension [years (IQR)]	7.9 (6.9–8.9)	7.4 (6.3–8.6)	7.6 (6.4–8.5)

Percentage values are shown in parentheses. IQR, interquartile range.

Table 4 Summarized BP values measured at the initial examination

	Hypertensive urgency (n = 384)	Control group (n = 295)	P value
Clinical BP values at baseline			
Clinical SBP (mmHg)	152 ± 15	146 ± 14	0.0001
Clinical DBP (mmHg)	88 ± 9	86 ± 8	0.008
Clinical BP values 1 year after inclusion in the study			
Clinical SBP (mmHg)	136 ± 13	134 ± 11	0.06
Clinical DBP (mmHg)	80 ± 9	80 ± 8	0.86

BP, blood pressure; DBP, diastolic blood pressure; SBP, systolic blood pressure.

before and indicates the impact of hypertensive urgency on the cardiovascular risk of hypertensive patients.

Patients with hypertensive urgencies differed at baseline as compared with the control group in terms of age, initial BP values, frequency of left ventricular hypertrophy and microalbuminuria.

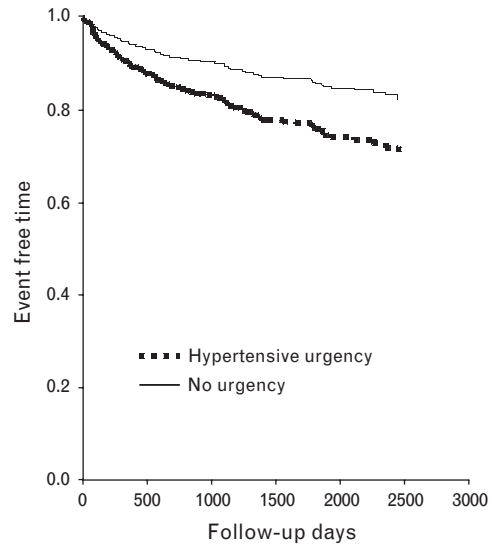
We observed higher initial BP values in the urgency group. The reasons for this BP difference may be a matter of discussion. One possible explanation may be the higher rate of unawareness of hypertension, which resulted in a higher number of patients with uncontrolled BP. This finding is supported by the previous data demonstrating an even higher rate of unawareness in hypertensive patients [16]. An analysis of the characteristics of patients with uncontrolled hypertension in the United States demonstrated that 31% patients are unaware of hypertension [17]. Additionally, Tisdale *et al.* [18] reported that less successful outpatient systolic BP control was an independent risk factor for hypertensive crisis. The urgency group was characterized by a higher rate of unknown hypertension and by a higher proportion of patients with poorly controlled hypertension. These characteristics contributed to the higher initial BP values in the urgency group.

The higher age may also contribute to the BP difference, as an association between older age and increased BP is well documented in a recent analysis of surveys on hypertension in North America and Europe [19]. After 1 year of follow-up, however, the rate of patients with

Table 5 Frequency of first cardiovascular event (fatal and nonfatal) during follow-up

	Hypertensive urgency (n = 384)	Control group (n = 295)	P value
Fatal and nonfatal events			
Fatal cardiovascular events	88	42	0.005
Acute coronary syndrome	5	3	NS
Ischemic stroke	1	3	NS
Hemorrhagic stroke	–	1	NS
Nonfatal cardiovascular events			
Acute coronary syndrome	35	14	0.03
Atrial fibrillation	5	2	NS
Acute left ventricular failure	17	4	0.02
Aortic dissection	–	2	NS
Stroke (ischemic or hemorrhagic)	25	13	NS

Fig. 1



Event-free time interval based on the first occurring cardiovascular event (hypertensive urgency vs. no urgency; P = 0.04).

sufficient BP control was similar in both groups. This may explain the lack of impact of initial BP values on the rate of cardiovascular events during follow-up.

We also observed a higher rate of hypertension-associated end-organ damage in the group of patients with hypertensive urgencies. The frequency of end-organ damage is correlated to the level of BP [20]. It can be assumed that the initially assessed BP values reflect the long-term average of BP in the study population. Therefore, the higher frequency of end-organ damage as left ventricular hypertrophy and/or microalbuminuria may be a result of long-term insufficient BP control in these patients. Both clinical conditions have an independent impact on morbidity and mortality in hypertensive patients [21,22]. Sufficient BP control, however, results in a regression of left ventricular hypertrophy as well as microalbuminuria leading to an improvement of the prognosis of

Table 6 Results from the multivariate Cox regression analysis

	Hazard ratio	95% confidence interval	P value
Hypertensive urgency (yes vs. no)	1.50	1.03–2.19	0.035
Age ('per years increase')	1.04	1.03–1.06	<0.001
Microalbuminuria ^a (yes vs. no)	1.45	0.98–2.14	0.06
LV hypertrophy (yes vs. no)	1.16	0.74–1.81	0.30
Systolic blood pressure (per mmHg increase)	1.00	0.99–1.01	0.53
Dyslipidemia ^b	0.83	0.57–1.22	0.52

Cardiovascular event was the dependent variable and the independent variable was hypertensive urgency with the covariates age, left ventricular hypertrophy, systolic blood pressure, cholesterol and microalbuminuria. LV, left ventricle. ^aMicroalbuminuria defined as urinary excretion of microalbumin between 30 and 300 mg/day. ^bTotal cholesterol greater than 6.5 mmol/l or greater than 250 mg/dl.

hypertensive patients [23–25]. The greater extent of BP reduction in the urgency group during the first year of treatment may lead to a comparable rate of hypertension-associated organ damage in both groups after 1 year of follow-up. We, therefore, assume that the differences observed at baseline cannot explain the differences in the event rate between both the groups.

The analysis of cardiovascular events after hypertensive urgency revealed no significant differences with regard to mortality, but showed a significantly higher morbidity in the urgency group compared with the control group. The acute coronary syndrome was the leading cardiovascular event in our study population and occurred more frequently in the urgency group. The strong association between hypertensive crisis and cardiovascular events observed in our study is in line with previously published results demonstrating acute myocardial infarction as the leading cause of death and hospital admission in patients with severely elevated BP [26]. Webster *et al.* [27] demonstrated that nearly 50% of all patients admitted to the ED with a hypertensive emergency died as a result of an acute myocardial infarction during follow-up. The lack of a significant difference of mortality between both groups is mainly due to the similar percentage of patients with sufficient BP control after 1 year. In contrast, morbidity remains higher in patients after hypertensive urgency despite sufficient BP control demonstrating the impact of this event on the health status of hypertensive patients.

In summary, hypertensive urgency occurs preferentially in hypertensive patients with an unknown or poorly controlled hypertension. This fact contributes to the higher frequency of hypertension associated end-organ damage observed at study entry. Despite a sufficient BP control following hypertensive urgency an increased risk for cardiovascular events persists in this group of patients during the follow-up. Therefore, preventive methods, that is, reduction of the number of patients with unknown or poorly controlled hypertension, have to be established to avoid the occurrence of hypertensive urgency.

Acknowledgements

There are no conflicts of interest.

References

- Zampaglione B, Pascale C, Marchisio M, Cavallo-Perin P. Hypertensive urgencies and emergencies. Prevalence and clinical presentation. *Hypertension* 1996; **27**:144–147.
- Chiang WK, Jamshahi B. Asymptomatic hypertension in the ED. *Am J Emerg Med* 1998; **16**:701–704.
- Cherney D, Straus S. Management of patients with hypertensive urgencies and emergencies: a systematic review of the literature. *J Gen Intern Med* 2002; **17**:937–945.
- Vidt DG. Hypertensive crises: emergencies and urgencies. *J Clin Hypertens (Greenwich)* 2004; **6**:520–525.
- Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure. The Sixth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *Arch Intern Med* 1997; **157**:2413–2446.
- Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *Hypertension* 2003; **42**:1206–1252.
- Guidelines Subcommittee. 1999 World Health Organisation – International Society of Hypertension Guidelines for the Management of Hypertension. *J Hypertens* 1999; **17**:151–183.
- Hirschl MM. Guidelines for the drug treatment of hypertensive crises. *Drugs* 1995; **50**:991–1000.
- Alberti KG, Zimmet P, Shaw J. Metabolic syndrome – a new world wide definition. A consensus statement from the International Diabetes Federation. *Diabet Med* 2006; **23**:469–480.
- Petrie JC, O'Brien ET, Littler WA, de Swiet M. British Hypertension Society. Recommendations on blood pressure measurement. *BMJ* 1986; **293**:611–615.
- Devereux RB, Bella J, Boman K, Gerds E, Nieminen MS, Rokkedal J, *et al.* Echocardiographic left ventricular geometry in hypertensive patients with electrocardiographic left ventricular hypertrophy: the LIFE Study. *Blood Press* 2001; **10**:74–82.
- Schiller NB, Shah PM, Crawford M, Demaria A, Devereux RB, Feigenbaum H, *et al.* Recommendations for quantitation of the left ventricle by two-dimensional echocardiography. American Society of Echocardiography Committee on Standards, Subcommittee on Quantitation of Two-Dimensional Echocardiograms. *J Am Soc Echocardiogr* 1989; **2**:358–367.
- Devereux RB, Alonso DR, Lutas EM, Gottlieb GJ, Campo E, Sachs I, Reichel N. Echocardiographic assessment of left ventricular hypertrophy: comparison to necropsy findings. *Am J Cardiol* 1986; **57**:450–458.
- Keith NM, Wagener HP, Barker NW. Some different types of essential hypertension: their course and their prognosis. *Am J Med Sci* 1939; **197**:837–843.
- Grosso A, Veglio F, Porta M, Grignolo FM, Wong TY. Hypertensive retinopathy revisited: some answers, more questions. *Br J Ophthalmol* 2005; **89**:1646–1654.
- Karras DJ, Ufberg JW, Heipern KL, Cienki JJ, Chiang WK, Wald MM, *et al.* Elevated blood pressure in urban emergency department patients. *Acad Emerg Med* 2005; **12**:835–843.
- Hyman DJ, Pavlik VN. Characteristics of patients with uncontrolled hypertension in the United States. *N Engl J Med* 2001; **345**:479–486.
- Tisdale JE, Huang MB, Borzak S. Risk factors for hypertensive crisis: importance of out-patient blood pressure control. *Fam Pract* 2004; **21**:420–424.
- Wolf-Meier K, Cooper RS, Banegas JR, Giampaoli S, Hense HW, Joffred M, *et al.* Hypertension prevalence and blood pressure levels in 6 European countries, Canada, and the United States. *JAMA* 2003; **289**:2363–2369.
- Verdecchia P, Reboldi GP. Hypertension and microalbuminuria: the new detrimental duo. *Blood Press* 2004; **13**:198–211.
- Schrader J, Luders S, Kulschewski A, Hammersen F, Zuchner C, Venneklaas U, *et al.*, for the MARPLE Study Group. Microalbuminuria and tubular proteinuria as risk predictors of cardiovascular morbidity and mortality in essential hypertension: final results of a prospective long-term study (MARPLE Study). *J Hypertens* 2006; **24**:541–548.
- Koren MJ, Ulin RJ, Koren AT, Laragh JH, Devereux RB. Left ventricular mass change during treatment and outcome in patients with essential hypertension. *Am J Hypertens* 2002; **15**:1021–1028.
- Schmieder RE, Martus P, Klingbeil A. Reversal of left ventricular hypertrophy in essential hypertension. A meta-analysis of randomized double-blind studies. *JAMA* 1996; **275**:1507–1513.
- Schussheim AE, Diamond JA, Phillips RA. Left ventricular midwall function improves with antihypertensive therapy and regression of left ventricular hypertrophy in patients with asymptomatic hypertension. *Am J Cardiol* 2001; **87**:61–65.
- Wenzel RR. Renal protection in hypertensive patients: selection of antihypertensive treatment. *Drugs* 2005; **65** (suppl 2):29–39.
- Herlitz J, Karlson BW, Lindquist J, Sjölin M. Prognosis during five years of follow-up among patients admitted to the emergency department with acute chest pain in relation to a history of hypertension. *Blood Press* 1998; **7**:81–88.
- Webster J, Petrie JC, Jeffers TA, Lovell HG. Accelerated hypertension – pattern of mortality and clinical factors affecting outcome in treated patients. *Q J Med* 1993; **86**:485–493.