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Hospital and out-of-hospital mortality in 670 hypertensive emergencies and urgencies

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Abstract

Long-term mortality in patients with acute severe hypertension is unclear. The authors aimed to compare short-term (hospital) and long-term (12 months) mortality in these patients. A total of 670 adults presenting for acute severe hypertension between January 1, 2015, and December 31, 2015, were included. A total of 57.5% were hypertensive emergencies and 66.1% were hospitalized: 98% and 23.2% of those with hypertensive emergencies and urgencies, respectively (P = .001). Hospital mortality was 7.9% and was significantly higher for hypertensive emergencies (12.5% vs 1.8%, P = .001). At 12 months, 106 patients died (29.4%), mainly from hypertensive emergencies (38.9% vs 8.9%, P = .001). Median survival was 14 days for neurovascular emergencies and 50 days for cardiovascular emergencies. Patients with hypertensive emergencies or urgencies had bad long-term prognosis. Short-term mortality is mainly caused by neurovascular emergencies, but cardiovascular emergencies are severe, with high mortality at 12 months. These results justify better follow-up and treatment for these patients.

1 | INTRODUCTION

Hypertension is one of the most common chronic diseases, with a prevalence of approximately 40% in European countries.[1] The prevalence of severely high blood pressure (BP) ranges from 1% to 15% of patients treated for hypertension in the literature.[2,3] Although optimal therapeutic strategies have been defined for patients with chronic hypertension, less is known about patients with acute severe elevations in BP who present to the hospital or general practitioners.[4] The management of severely elevated BP depends on the presence or absence of acute end organ damage. Hypertensive emergencies are defined as large elevations in systolic BP (SBP) or diastolic BP (DBP) (≥180 mm Hg or ≥110 mm Hg, respectively) associated with impending or progressive organ damage such as hypertensive encephalopathy, cerebral infarction, intracranial hemorrhage, acute pulmonary edema, aortic dissection, acute renal failure, or eclampsia. Isolated large BP elevations without acute organ damage (hypertensive urgencies) are often associated with treatment discontinuation or reduction as well as with anxiety and should not be considered an emergency but be treated by reinstitution or intensification of drug therapy and treatment of anxiety.[4] Emergencies almost always require an immediate reduction of BP, most often with a titratable short-acting intravenous antihypertensive agent to prevent or limit progressive end organ damage. A narrative review that included analyses of 373 articles tried to redefined these two groups, highlighting the fact that hypertensive emergencies are a group of diseases that are related to acute hypertension caused by catecholamines, the sympathetic nervous system, the vascular endothelium, and acute stress. Hypertension is linked with the disease of one or more organs (myocardium, kidney, brain) in which it has a key role in the appearance of the pathology. In hypertensive urgency, the stress has a low intensity, and the organs can endure this stress without being damaged.[5]

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Epidemiological and clinical characteristics of hypertensive emergencies and urgencies have been described in the literature. A recent report from the Nationwide Emergency Department Sample of the United States showed that the incidence of adult emergency department visits for acute hypertension increased monotonically in 2006 to 2013 from 170 340 to 496 894.[6] Hypertensive emergencies accounted for 63 406 visits (677 per million adult emergency department visits overall) in 2006 and 176 769 visits (1670 per million) in 2013. A large American cohort of 1588 consecutive patients with acute severe hypertension from the STAT registry was analyzed in 2009.[7] The median age of the cohort was 58 years, 49% were women, 56% were black, and 27% had a prior admission for acute hypertension. A second European cohort of 164 prospectively enrolled patients from 25 general practices in Switzerland was recently described.[8] The median age of these patients was 71 years, 63% were women, and 65% had preexisting hypertension. Only approximately two thirds of patients were given immediate BP-lowering medication and only 6% were immediately admitted to the hospital.

Data on short- and long-term mortality are interesting. In the STAT registry, hospital and 90-day outcomes were described.[7] The hospital mortality was 6.9%: 0.3% for hypertensive urgencies and 11% for hypertensive emergencies. At 90 days, mortality was 11%: 4% for urgencies and 16% for emergencies, with 4% lost to follow-up. Merlo and colleagues[8] reported that 27% of patients with a hypertensive emergency vs 6% of those with a hypertensive urgency had experienced a cardiovascular event at 12 months. An American retrospective analysis of 567 patients admitted with hypertensive emergencies found that long-term mortality was 12% per year after 3.1 years of follow-up.[9]

Our objective was therefore to describe and compare short-term (hospital) and long-term (12 months) mortality between patients with hypertensive emergencies and urgencies.

2 | METHODS

2.1 | Population

Adults (≥18 years) who presented to the emergency department of Timone Hospital for acute severe hypertension between January 1, 2015, and December 31, 2015, were eligible for inclusion. Severe hypertension was defined as one BP measurement ≥180 mm Hg systolic and/or ≥110 mm Hg diastolic confirmed after 5 minutes of rest.[4] End organ damage was defined as the presence of one of the following findings: encephalopathy, ischemic stroke, intracerebral hemorrhage, subarachnoid hemorrhage, acute heart failure, acute coronary syndrome, or aortic dissection. End organ damage was screened with brain imaging, chest radiography, brain natriuretic peptide, echocardiography, ECG, troponin-I, coronarography, or aortic imaging. Patients with acute renal failure and patients with preeclampsia/eclampsia could not be included because they were admitted to another hospital with a nephrology and obstetrical department. Patients with organ damage were classified as having hypertensive emergencies, and patients without organ damage were classified as having hypertensive urgencies.

2.2 | Data collection

Data at inclusion were collected retrospectively from the hospital's computer database. Patient demographics, medical history, BP, presenting symptoms at admission, timing and mode of antihypertensive therapy, type of organ damage, and hospital-associated events were analyzed. Long-term outcome information was collected by two medical doctors who called the patients' general practitioners to evaluate mortality at 12 months. Short-term mortality was defined as in-hospital mortality, and long-term mortality was defined as mortality at 12 months. Informed consent was obtained, and procedures were approved by the local human research ethics committee.

2.3 | Statistical analysis

Qualitative variables are presented as numbers and percentages, and quantitative variables are presented as mean ± standard deviation or median with range (minimum, maximum). Associations between qualitative variables were assessed using the chi-square test or Fisher exact test if the expected numbers were less than five. Associations between continuous and qualitative variables were assessed using Student *t* test or the Mann-Whitney nonparametric test if the variables were not normally distributed. The statistical significance threshold was set at $P < .05$. Statistical analyses were performed using IBM SPSS Statistics, version 20.0.

3 | RESULTS

3.1 | Baseline population

From January 1, 2015, to December 31, 2015, 670 patients presented to the emergency department of Timone Hospital for acute severe hypertension and were enrolled. Table 1 presents the characteristics of the entire population. The mean age of the entire cohort was 73.0 ± 16 years, with 55% women. In total, 385 (57.5%) cases were hypertensive emergencies, and 285 (42.5%) were hypertensive urgencies. There were 530 (79.1%) patients with preexisting hypertension, and 470 (70.1%) took antihypertensive drugs: 199 (29.7%) took a single drug, 161 (24.0%) took a two-drug combination (fixed combinations or separate drugs), and 110 (16.4%) took three or more drugs.

Table 2 summarizes the type of hypertensive emergencies observed, of which 53.0% were cardiovascular emergencies (acute pulmonary edema, acute coronary syndrome, aortic dissection) and 45.9% were neurovascular emergencies (ischemic stroke, intracerebral or subarachnoid hemorrhage, malignant hypertension). Although patients with hypertensive emergencies were older than those with hypertensive urgencies (mean age 76.6 ± 18 vs 67.2 ± 15 years, $P = .001$), all other variables were similar in both groups (Table 1).

Antihypertensive treatment included a renin-angiotensin system blocker for 280 patients (59.6%, n = 470), calcium antagonists for 191

TABLE 1 Population characteristics of the entire cohort, hypertensive emergencies and hypertensive urgencies

	All patients (N = 670)	Hypertensive emergencies (n = 385)	Hypertensive urgencies (n = 285)	*P* value
Age, mean (SD)	73.0 ± 16	76.6 ± 18	67.2 ± 15	**.001**
Women, No. (%)	371 (55.0)	205 (53.2)	166 (58.2)	.198
SBP, mean (SD)	197.8 ± 22.5	197.2 ± 21	199.0 ± 24	.335
DBP, mean (SD)	98.91 ± 19	99.3 ± 20	98.0 ± 18	.364
SBP post treatment, mean (SD)	173.8 ± 25	174.0 ± 24	172.4 ± 26	.111
DBP post treatment, mean (SD)	88.2 ± 20.25	88.8 ± 22.2	87.7 ± 18	.093
Preexisting hypertension, No. (%)	530 (79.1)	295 (76.6)	235 (82.4)	.468
Hypertension drug, No. (%)	470 (70.1)	278 (72.2)	192 (67.3)	.121
Calcium antagonists	191 (40.6, n = 470)	110 (39.5, n = 278)	81 (42.2, n = 192)	
Diuretics	185 (39.3)	131 (47.1)	54 (28.1)	
β-Blockers	173 (36.8)	119 (42.8)	54 (28.1)	
Angiotensin receptor blockers	150 (31.9)	82 (29.5)	68 (35.4)	
ACEIs	130 (27.7)	74 (26.6)	56 (29.2)	
Others	56 (11.9)	32 (11.5)	24 (12.5)	
Monotherapy, No. (%)	199 (29.7)	105 (27.2)	94 (32.9)	.120
Two-drug combination, No. (%)	161 (24.0)	101 (26.2)	60 (21.0)	.112
≥3-drug combination, No. (%)	110 (16.4)	72 (18.7)	38 (13.3)	.062

Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; DBP, diastolic blood pressure; SBP, systolic blood pressure; SD, standard deviation. Boldface indicates significance at $P < .05$.

TABLE 2 Type of hypertensive emergencies

Hypertensive emergencies (n = 385)	No. (%)
Acute pulmonary edema	144 (37.4)
Ischemic stroke	128 (33.7)
Intracerebral or subarachnoid hemorrhage	44 (11.4)
Acute coronary syndrome	53 (13.8)
Aortic dissection	7 (1.8)
Malignant hypertension	5 (1.3)
Others	4 (1)

patients (40.6%), diuretics for 185 patients (39.3%), β-blockers for 173 patients (36.8%), and other drugs (centrally active agents and α-receptor blockers) for 56 patients (11.9%) (Table 1). The distribution of drug types was similar across the two groups, with renin-angiotensin system blockers being most common, followed by calcium antagonists and diuretics.

The most common presenting symptoms at admission were focal neurologic deficit (n = 152, 22.7%), dyspnea (n = 122, 18.2%), dizziness (n = 83, 12.3%), chest pain (n = 77, 11.5%), headache (n = 63, 9.4%), and other various symptoms (n = 143, 21.3%) (Table 3). The three most frequent symptoms among patients with hypertensive emergencies were focal neurologic deficit (n = 140 [36.3%] vs n = 12 [4.2%] for hypertensive urgencies, $P = .001$), dyspnea (n = 113 [29.3%] vs n = 9 [3.6%] for hypertensive urgencies, $P = .001$), and chest pain (n = 52 [13.5%] vs n = 25 [8.8%] for hypertensive urgencies, $P = .001$). The three most frequent symptom categories among patients with hypertensive urgencies were uncategorized (other) symptoms (n = 122 [42.8%] vs n = 31 [0.8%] for hypertensive emergencies, $P = .001$), headache (n = 53 [18.6%] vs n = 10 [2.6%] for hypertensive emergencies, $P = .001$), and dizziness (n = 50 [17.5%] vs n = 33 [8.6%] for hypertensive emergencies, $P = .001$). Other symptoms included vision disorders, edema, tinnitus, vomiting, and abdominal pain.

Comparison of initial treatment between hypertensive emergencies and urgencies showed more oral administration and intravenous boluses for hypertensive urgencies (62.5% [n = 178] vs 9.4% [n = 32], $P = .001$) and more infusions or specific treatments for hypertensive emergencies (76.0% [n = 260] vs 19.7% [n = 56], $P = .001$) (Table 4). There were 43 missing data points for hypertensive emergencies. Others treatments included intravenous β-blockers for hypertensive emergencies and rest and/or analgesic/anxiolytic treatment for hypertensive urgencies.

3.2 | Short-term outcomes and mortality

Overall, 443 patients in the entire cohort were hospitalized (66.1%), with 377 (98%) hospitalizations for hypertensive emergencies and 66 (23.2%) for hypertensive urgencies ($P = .001$) (Table 5).

Hospital mortality was 7.9% (n = 53) and was significantly higher for hypertensive emergencies (n = 48 [12.5%]) than for hypertensive urgencies (n = 5 [1.8%], $P = .001$).

Hospital mortality was mainly attributable to neurovascular emergencies (n = 34 [70.8%] vs n = 14 [29.1%], for cardiovascular emergencies).

TABLE 3 Symptoms of hypertensive emergencies and urgencies at presentation in the emergency department for the entire cohort

Presenting symptoms	All patients (N = 670) No. (%)	Hypertensive emergencies (n = 385) No. (%)	Hypertensive urgencies (n = 285) No. (%)	*P* value
Headache	63 (9.4)	10 (2.6)	53 (18.6)	.001
Focal neurologic deficit	152 (22.7)	140 (36.3)	12 (4.2)	.001
Chest pain	77 (11.5)	52 (13.5)	25 (8.8)	.001
Dizziness	83 (12.3)	33 (8.6)	50 (17.5)	.001
Epistaxis	30 (4.5)	1 (0.3)	29 (10.2)	.001
Dyspnea	122 (18.2)	113 (29.3)	9 (3.6)	.001
Others	143 (21.3)	31 (0.8)	122 (42.8)	.001

TABLE 4 Type of antihypertensive treatment administered in the emergency department

Hypertension drug	Hypertensive emergencies (n = 342) No. (%)	Hypertensive urgencies (n = 285) No. (%)	*P* value
Oral amlodipine	13 (3.8)	79 (27.7)	.001
Oral nicardipine	6 (1.8)	50 (17.5)	.001
Intravenous nicardipine bolus	13 (3.8)	49 (17.2)	.005
Intravenous nicardipine infusion	57 (17.7)	22 (7.7)	.005
Intravenous furosemide	130 (38.0)	9 (3.2)	.001
Intravenous uradipil	15 (4.4)	20 (7.0)	.074
Intravenous nitroglycerine	58 (17.0)	5 (1.8)	.001
Others	50 (14.6)	51 (17.9)	.432

Other hypertension drugs included intravenous β-blockers for hypertensive emergencies and rest and/or analgesic/anxiolytic treatment for hypertensive urgencies.

3.3 | Long-term mortality

Mortality data at 12 months were available for 360 patients: 247 who presented with hypertensive emergencies and 113 who presented with hypertensive urgencies (Table 5).

Of these, 106 patients had died at 12 months (29.4% [n = 360]), mainly from hypertensive emergencies (n = 96/247 [38.9%] vs n = 10/113 [8.9%] for hypertensive urgencies, *P* = .001).

Of the patients who did not die in the hospital, 53 patients had died at 12 months (17.3% [n = 307]). Patients with hypertensive emergencies had significantly higher 12-month mortality (48 patients, 24.1% [n = 199]) than those with hypertensive urgencies (5 patients, 4.6% [n = 108]; *P* = .001).

Of the 96 deaths associated with hypertensive emergencies, 58 (60.4%) were among patients with neurovascular emergencies and 38 (39.6%) were among patients with cardiovascular emergencies. Median survival was 14 days for neurovascular emergencies and 50 days for cardiovascular emergencies.

4 | DISCUSSION

We demonstrated that both hypertensive emergencies and urgencies are severe forms of hypertension with very poor short- and long-term prognoses. Long-term mortality at 12 months was 29.4% for the entire cohort, 17.3% excluding patients who died during the initial hospitalization and 38.9% for hypertensive emergencies. Few data were available in the literature regarding the long-term mortality of patients with acute severe hypertension. Malignant hypertension was identified retrospectively in 315 European patients (33% women; mean age 49.4 years, 17.5% black) referred to the City Hospital, Birmingham, from 1965 to 1995.[10] After a median follow-up period of 33 months, 48.0% had died (126/262, with 53 lost to follow-up). The estimated annual mortality was 17.5%. A second cohort of 567 American patients with hypertensive emergencies was analyzed by Alfonso and colleagues.[11] The authors conducted a retrospective analysis of admissions to two major medical centers that service a predominantly inner-city population. The mean age was 58.0 years, 91% of patients were black, and 46.7% were men. Troponin elevation was observed in 32.3% of patients, and mortality over a mean follow-up of 3.1 years was 37%. The two independent predictors of mortality were age and history of coronary artery disease. The estimated annual mortality was 12%. This mortality rate was high but lower than that in our population, primarily because of the exclusion criteria in the analysis by Alfonso and colleagues: the study excluded patients with acute coronary syndrome, obstructive coronary artery disease requiring intervention during the index admission, or ECG-documented ventricular or supraventricular

TABLE 5 Short- and long-term outcomes

Outcome	All patients (N = 670), No. (%)	Hypertensive emergencies (n = 385), No. (%)	Hypertensive urgencies (n = 285), No. (%)	*P* value
Hospitalization	443 (66.1)	377 (98)	66 (23.2)	.001
Hospital mortality	53 (7.9)	48 (12.5)	5 (1.8)	.001
Neurovascular emergencies		34 (70.8, n = 48)		
Cardiovascular emergencies		14 (29.1, n = 48)		
12-mo mortality excluding hospital mortality	53 (17.3, n = 307)	48 (24.1, n = 199)	5 (4.6, n = 108)	
Total 12-mo mortality	106 (29.4, n = 360)	96 (38.9, n = 247)	10 (8.9, n = 113)	.001
Neurovascular emergencies		58 (60.4, n = 96)		
Cardiovascular emergencies		38 (39,6, n = 96)		

tachycardia. A third study focused on 164 patients presenting to their general practitioner with severely elevated BP. At 12 months, 16.4% experienced a cardiovascular event and 5% had died. These results differ from ours because 60% of the patients in this study had initially asymptomatic BP elevation and only 9% had hypertensive emergencies.[8] Finally, Vlcek and colleagues[12] studied the association between hypertensive urgencies and subsequent cardiovascular events in patients with hypertension. They showed that only 13 patients (2%) with hypertensive urgencies had fatal cardiovascular events at 2 years but they classified patients who died of a noncardiovascular cause as event free until death.

Short-term mortality was 7.9% in our study and significantly higher for hypertensive emergencies (12.5%) than for hypertensive urgencies (1.8%). This was consistent with the literature. In the STAT registry, the hospital mortality rate was 6.9% (11% for hypertensive emergencies and 0.3% for hypertensive urgencies).[7] Hospital deaths were more common in patients with intracranial hemorrhage (20%). A subanalysis of the STAT registry focusing on 432 patients with a primary neurological admission diagnosis showed 24% mortality at 90 days.[13] The authors identified three factors associated with poor prognosis for patients with neurovascular hypertensive emergencies: lower minimum BP values, less rebound hypertension, and a higher frequency of neurologic deterioration. Our work showed that neurovascular emergencies have a poorer prognosis than cardiovascular emergencies early on. We also demonstrated that median survival was 14 days after hospital admission for patients with neurovascular emergencies and 50 days for patients with cardiovascular emergencies. Short-term mortality was primarily caused by neurovascular emergencies but cardiovascular emergencies were also severe and had a significant impact on long-term mortality.

The prevalence and types of hypertensive urgencies in our cohort are interesting. In the literature, hypertensive urgencies are more frequent (75%) than hypertensive emergencies (25%).[14–16] In contrast, in our population, there was a majority of hypertensive emergencies (57.5%). However, 23.2% of patients with hypertensive urgencies required hospitalization. In-hospital and long-term mortality were significantly lower for patients with hypertensive urgencies than for patients with hypertensive emergencies but were nevertheless high: 1.8% in the hospital and 8.9% at 12 months. Merlo and colleagues[8] reported a 6% cumulative incidence of cardiovascular events at 12 months among patients with hypertensive urgencies. Various factors seemed to confer risk for hypertensive emergencies: black race,[10] male sex, and specific symptoms.[15]

5 | STUDY STRENGTHS AND LIMITATIONS

The strength of our work is the large number of patients, but there are some limitations. The first is that enrollment occurred only in the emergency department; therefore, we probably missed patients with hypertensive emergencies who were directly admitted to specialized departments and we could not include patients with nephrology emergencies and obstetrical emergencies, who were admitted to another hospital. Retrospectively, we observed an excessive use of intravenous treatment for urgencies and we will introduce a more moderate management protocol using rest and oral therapy for these patients. Retrospective collection of data may also have missed otherwise eligible patients. Unfortunately, we failed to collect data on race, body mass index, smoking, and cardiovascular history. Finally, it was difficult to contact all of the general practitioners during the telephone follow-up and to collect the causes of the death.

6 | CONCLUSIONS

Both hypertensive emergencies and urgencies are severe forms of hypertension with high short- and long-term mortality. Short-term mortality is mainly caused by neurovascular emergencies, but cardiovascular emergencies are also severe, with high mortality at 12 months. These results justify better follow-up and treatment of these patients.

CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

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