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FULL RESEARCH PAPER
Arterial Hypertension

Profile and management of hypertensive urgencies and emergencies in the emergency cardiology department of a tertiary hospital: a 12-month registry

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Aims Currently there are scarce epidemiological data regarding prevalence, clinical phenotype, and therapy of hypertensive urgencies (HU) and emergencies (HE). The aim of this article was to record the prevalence, clinical characteristics, and management of patients with HU and HE assessed in an emergency department (ED) of a tertiary hospital.

Methods and results The population consisted of patients presenting with HE and HU in the ED (acute increase in systolic blood pressure (BP) ≥ 180 mmHg and/or diastolic BP ≥120 mmHg with and without acute target organ damage, respectively). Of the 38 589 patients assessed in the ED during a 12-month period, 353 (0.91%) had HU and HE. There were 256 (72.5%) cases presented as HU and 97 (27.5%) as HE. Primary causes for both HU and HE were stress/anxiety (44.9%), increased salt intake (33.9%), and non-adherence to medication (16.2%). Patients with HU reported mainly dizziness/headache (46.8%) and chest pain (27.4%), whereas those with HE presented dyspnoea (67%), chest pain (30.2%), dizziness/headache (10.3%), and neurological disorders (8.2%). In HE, the underlying associated conditions were pulmonary oedema (58%), acute coronary syndrome (22.6%), and neurological disorders/stroke (7.2%). All HE cases were hospitalized and received intensive healthcare, including dialysis.

Conclusion This 1-year single-centre registry demonstrates a reasonable prevalence of HU and HE contributing to the high volume of visits to the ED. Stress, increased salt intake and non-adherence were main triggers of HE and HU. Dizziness and headache were the prevalent symptoms of HU patients while heart failure was the most common underlying disease in patients with HE.

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Graphical Abstract

Key question(s)

12month registry recording:

Prevalence

Clinical characteristics

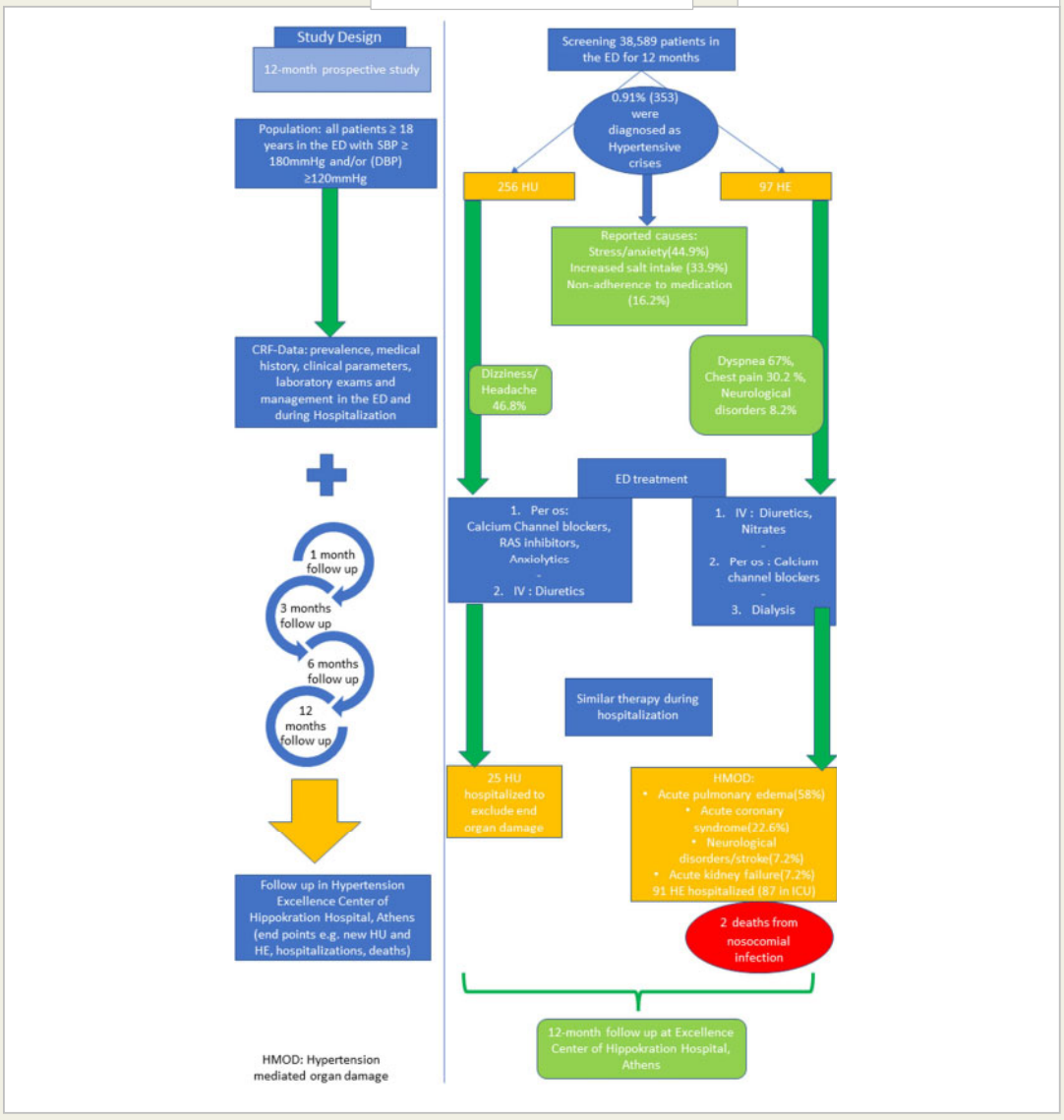
Management of patients with HU and HE in the ED and during hospitalization.

Key finding(s)

38,589 patients. 256 with HU and 97 with HE.
Stress, increased salt intake and non-adherence to medication as causes for BR rise.
Most HU patients presented dizziness/headache, while most HE reported dyspnea with pulmonary edema receiving intensive health care.

Take-home message

Comparable prevalence, clinical phenotype and therapy of HU and HE with other studies.
Worst clinical profile of HE requires careful, intensive treatment both in the ED and during hospitalization.
Need to further harmonize the everyday clinical practice with current guidelines.



Design of the study and major results of registering characteristics and management of hypertensive urgencies and emergencies.

Keywords Hypertensive urgencies • Hypertensive emergencies • Pharmacological treatments • Hospitalizations

Introduction

Hypertension emergencies (HE) are heterogenous disorders in which blood pressure (BP) levels above 180/110 mmHg are associated with acute organ damage[1–9] which is potentially life threatening and requires careful lowering of BP.[10–15] The term hypertensive urgencies (HU) describes severe hypertension with lack of organ damage[1,2] and the appropriate therapy comprises of oral drugs with usually no need for hospitalization. However, these hypertensive patients are at high risk mandating a close clinical follow-up.[16,17] It is of importance that the cumulative incidence of HU and HE is estimated at 0.5–1% of all hypertensive patients and ∼1 of 200 patients in the emergency departments (ED) present with HE.[18–21] This incidence seems unaltered over the last decades despite the current improvements in hypertension therapy and overall cardiovascular risk factors management.[22,23] The mainstay pathophysiological mechanisms for HU and HE involve activation of the renin–angiotensin system (RAS), diffuse vascular damage,[6,24] and dysfunction of organ haemodynamic autoregulation.[3] Although the clinical presentation is by and large variable, the prognosis of patients with HE has been significantly improved.[18,25]

Nowadays, although hypertension treatment strategies are well defined by international guidelines, few evidence-based recommendations are available on acute severe hypertension.[6] Epidemiological data on prevalence and clinical features of patients referred to the ED are limited along with diagnostic and management algorithms in spite of their relevance from a public health perspective.[18–21,26]

Based on the above there is a current need for more data on the epidemiology, clinical aspects, and therapeutic trends of HU and HE. There is a need to understand the phenotype of these cases and the 'gaps' in their management. Therefore, the aim of this study was to evaluate the incidence of HU and HE, describe their clinical and laboratory characteristics, as well as to present the therapeutic management in a tertiary general hospital during a period of 12 months.

Methods

The study was conducted in 'Hippokration General Hospital of Athens', gathering all the necessary data of HU and HE at their attendance in the ED during every day clinical routine and their therapeutic and diagnostic management in departments of admission. The population consisted of all patients, aged 18 years and over, visiting the ED of Hippokration hospital either due to increased BP levels or other reasons and who presented elevated BP that required further assessment. The study started in December 2017 and the BP cut-off values for the diagnosis of HU and HE were those adopted by the 2013 ESC/ESH guidelines [systolic blood pressure (SBP) ≥ 180 mmHg and/or diastolic blood pressure (DBP) ≥120 mmHg].[27] In addition, written or oral informed consent was obtained by patient or authorized relatives. Women affected by eclampsia, pre-eclampsia, and HELLP syndrome were not included, as they were generally referred to the Obstetrics Clinics without visiting the ED of the study hospital.

A structured case report form was used by doctors to collect the necessary data for each patient. Full medical history, previous medication, possible causes of acute rise of BP, the clinical characteristics, signs, symptoms, somatometric features, demographics as well as the physical examination, laboratory tests, management of patients, and the time remaining in the ED before discharge or admission were registered. We also recorded the management of these patients during hospitalization and hard endpoints of morbidity and mortality (Supplementary material online, *Table*).

All patients underwent physical examination and BP measurement by doctors according to the protocol.[27] The average of the last two out of three consecutive BP measurements taken 1 min apart with a validated sphygmomanometer (OMRON M6) in both arms, in supine/sitting and standing position was recorded.[27]

Patients were classified as HE or HU on the basis of presence or absence of acute and progressive end-organ damage (diagnosed using clinical data and diagnostic tests when appropriate) and were managed accordingly. Hypertension-mediated organ damage was excluded based on 12-lead electrocardiogram, transthoracic echocardiography, chest radiography, biochemical analysis, funduscopic examination, brain computed tomography, magnetic resonance imaging, and chest contrast enhanced computed tomography.

Direct doctor attendance in the ED for the scope of the registry, medical records of both the ED and clinics were all used to register the necessary data. Enrolment continued until completion of the 12 months collecting time frame, since 1 December 2017 to 30 November 2018. Furthermore, all patients were scheduled for predetermined follow-up visits in the European Society of Hypertension Excellence Center at Hippokration Hospital to record endpoints, such as new HU and HE, new hospitalizations and deaths from both cardiovascular and non-cardiovascular causes for a period of 12 months after the initial visit at the ED. All procedures followed the internal hospital protocols and the study protocol was approved by the institutional ethics committee.

Statistical analysis

Analysis of all data was performed by SPSS 25 (SPSS Inc., Chicago, IL, USA) software. Results are presented as a mean ± standard deviation for continuous variables and absolute numbers (percentages) for categorical variables. The differences between variables were analysed by either the Student's *t*-test or the χ^2 for continuous and categorical variables, respectively. Statistical significance was considered $P < 0.05$.

Results

Of the 38 589 patients assessed in the ED during a period of 12 months, 353 (0.91%) had HU and HE, out of which 256 (72.5%) presented as HU and 97 (27.5%) as HE. The mean age of the patients was 67.4 ± 12.9 years and 49% were males. Moreover, patients with HE compared with HU were older by 8 years, had lower haematocrit by 4%, more increased creatinine by 0.7 mg/dL and troponin values by 228.4 pg/mL. Patients with HE compared with those with HU had higher SBP levels in ED by 5 mmHg, as well as heart rate (HR) by 13 b.p.m. All the above differences proved statistically significant, while there were no differences in DBP (*Table 1*).

Previous history of diagnosis of hypertension was present in 80% of HE and HU cases. The previous antihypertensive treatment in the two groups involved RAS inhibitors, diuretics, β-blockers, calcium channel blockers, central acting agents, and aldosterone antagonists, while more HE patients had already been prescribed ≥3 drug categories for hypertension. Nitrates were reported as baseline therapy on admission in 6.8% of all patients (15.6% of HE vs. 2.8% of HU, $P < 0.0001$). Patients with HE compared with HU had higher prevalence of coronary heart disease, heart failure, chronic kidney disease, diabetes mellitus, dyslipidaemia, and chronic obstructive sleep

Table 1 Clinical, demographic, and laboratory data in the emergency department

	Total ($n = 353$)	Hypertensive emergencies ($n = 97$)	Hypertensive urgencies ($n = 256$)	P
Age (years)	67 ± 13	73 ± 12	65 ± 13	<0.0001
Gender (males), *n* (%)	173 (49)	50 (51.5)	123 (48)	0.558
Body mass index (kg/m^2)	28.9 ± 5.8	29.1 ± 6.1	28.8 ± 5.7	0.725
Obesity (BMI > 30 kg/m^2) (%)	38.4	37.8	38.8	0.876
History of hypertension (%)	80	86.4	77.2	0.60
History of dyslipidaemia (%)	57.6	78.1	48.3	<0.0001
History of diabetes mellitus (%)	26.9	42.7	19.8	<0.0001
History of active smoking (%)	27.6	26	28.3	0.682
SBP (mmHg)	196 ± 20	200 ± 21	195 ± 19	0.020
DBP (mmHg)	102 ± 15	103 ± 15	101 ± 15	0.212
HR (b.p.m.)	85 ± 19	94 ± 21	81 ± 16	<0.0001
Haematocrit (%)	41 ± 5	39 ± 6	43 ± 5	<0.0001
Creatinine (mg/dL)	1.1 ± 0.8	1.6 ± 1.3	0.9 ± 0.3	<0.0001
Glucose (mg/dL)	139 ± 60	171 ± 74	124 ± 47	<0.001
High sensitivity TnI (pg/mL)	83.7 ± 541	241.4 ± 954	13 ± 52	0.001

All clinical parameters and laboratory exams are taken at first medical contact in the emergency department.
BMI, body mass index; DBP, diastolic blood pressure; HR, heart rate; *n*, number of patients; *P*, statistical significance ($P < 0.05$); SBP, systolic blood pressure; TnI, serum troponin.

apnoea. Comorbidities, previous medication, and their relative differences between the two groups are listed in *Tables 1* and *2*.

The putative causes for both HU and HE were excessive stress (44.9%), increased salt intake (33.9%), non-adherence to medication (16.2%), and drug-induced rise of BP (13.1%) (*Figure 1*). Stress refers to reported feeling of anxiety, restlessness, and insomnia. Salt/dietary represents daily consumption of over a teaspoon of salt (over 5.7 g of salt and over 2.4 g of sodium) or consumption of savoury foods the previous hours. Nonadherence refers to antihypertensive medication and drug-induced rise of BP mostly to nonsteroidal anti-inflammatory drugs and corticosteroids. Analysis showed statistically significant differences between the two groups for causes of BP rise such as excessive stress/anxiety mostly for HU (30.2% of HE vs. 46.1% of HU, $P < 0.0001$) and change of antihypertensive medication the previous 7 days (11.5% of HE vs. 4.6% of HU, $P = 0.032$) and infection (24% of HE vs. 7.7% of HU, $P < 0.0001$) mainly for HE.

Patients with HU reported mainly dizziness/headache, chest pain, and dyspnoea, while patients with HE mostly presented with dyspnoea, chest pain, dizziness/headache, and neurological disorders (*Table 3*). Predominant organ damage in the HE group was pulmonary oedema (58%), acute coronary syndrome (22.6%), neurological disorders/stroke (7.2%), and acute kidney failure (7.2%) (*Figure 2*).

Cases with HU were treated by orally administered calcium channel blockers, RAS inhibitors, anxiolytics, and intravenous (i.v.) diuretics, while HE received i.v. nitrates and diuretics as well as p.o. calcium channel blockers (*Figure 3*). Moreover, HE compared with those with HU remained in the ED less time (181 ± 134 vs. 297 ± 177 min, respectively, $P < 0.0001$).

Regarding hospitalizations, 116 patients were admitted in the clinics of our hospital, 91 out of 97 HE and 25 out of 256 HU. The majority of HE (87) was admitted in the intensive care unit. Naturally, patients with HE had longer in-hospital stay than patients with HU (6.9 ± 6.1 vs. 4.3 ± 2.6 days, $P = 0.039$). Moreover, we recorded a mean impairment of renal function among the hospitalized population expressed as a mean serum creatinine increase by 0.11 mg/dL ($P = 0.011$). Also, an SBP/DBP reduction of 63/27 mmHg was observed from admission until hospital discharge. A more gradual fall of BP was observed in HU. Patients with HU were mostly treated with oral therapy comprised of RAS inhibitors (79.1%), calcium channel blockers (62.5%), β-blockers (62.5%), and diuretics (58.3%). Patients with HE initially received i.v. nitrates (67.4%) and diuretics (67.5%) and treatment regimen shifted to orally administered preparations during the following hospital stay. Six patients with HE underwent haemodialysis due to acute kidney injury and one male was introduced into peritoneal dialysis improving congestion and renal function, while two male patients of HE died from nosocomial infection during the first long hospitalization.

Although there was no significant difference between HU and HE regarding the male to female ratio, gender analysis resulted in some parametric differences. Males compared with females were heavier (86.6 ± 16.2 vs. 75.5 ± 17.5 kg, $P < 0.0001$) and taller (172.8 ± 6.1 vs. 161.5 ± 7 cm, $P < 0.0001$), whereas females had larger hips circumference (109.3 ± 19.6 vs. 104.1 ± 9.8 cm, $P = 0.048$). In addition, men had higher SBP (199 ± 19.5 vs. 194 ± 19 mmHg, $P = 0.014$), DBP (104 ± 15 vs. 100 ± 15 mmHg, $P = 0.005$) and higher prevalence of atrial fibrillation (20.1% vs. 9.4%, $P = 0.017$). More men compared with women were asymptomatic (15.5% vs. 3.7%, $P < 0.0001$), while females more frequently described non-specific symptoms such as dizziness or headache (43.8% vs. 27.1%, $P = 0.002$). Furthermore, male patients reported more often comorbidities such as coronary artery disease (36.1% vs. 11.5%, $P < 0.0001$), heart failure (23.2% vs. 10.9%, $P = 0.004$), chronic kidney disease (15.9% vs. 8.3%, $P = 0.042$), and smoking (34.9% vs. 20.5%, $P = 0.005$), as well as excessive physical activity as a probable cause for BP elevation (5.7% vs. 1.3%,

Table 2 Associated comorbidities and hypertension drug treatment in patients with hypertensive emergencies and urgencies

	Total ($n = 353$)	Hypertensive emergencies ($n = 97$)	Hypertensive urgencies ($n = 256$)	P
Coronary artery disease (%)	23	40.6	15	<0.0001
Heart failure (%)	16.3	32.3	9	<0.0001
Chronic kidney disease (%)	11.4	25	5.2	<0.0001
Stroke (%)	8.1	9.4	7.6	0.596
Atrial fibrillation (%)	18.2	27.1	14.2	0.007
Peripheral artery disease (%)	6.8	7.3	6.6	0.833
Chronic obstructive pulmonary disease (%)	11	18.8	7.6	0.004
RAS-inhibitors (%)	58.3	60.4	58.3	0.727
Calcium channel blockers (%)	28.7	34.3	26.5	0.162
Diuretics (%)	38.1	55.2	30.3	<0.0001
β-Blockers (%)	38	51	33	0.003
Central-acting agents (%)	6.5	13.5	3.3	0.001
Aldosterone antagonists (%)	5.2	14.6	1.4	<0.0001
One antiHTN drug (%)	18.9	9.4	23.2	0.004
Two antiHTN drugs (%)	30	27.1	31.3	0.458
Three antiHTN drugs (%)	17.9	24	15.2	0.063
≥4 antiHTN drug (%)	10.4	21.9	5.2	<0.0001

All comorbidities represent medically diagnosed previous disease, while medication refers to prescribed antihypertensive drugs prior to the event. Heart failure refers to heart failure with preserved, mid-range, and reduced ejection fraction.
antiHTN, antihypertensive categories; P, statistical significance ($P < 0.05$); RAS-inhibitors, renin–angiotensin system inhibitors.

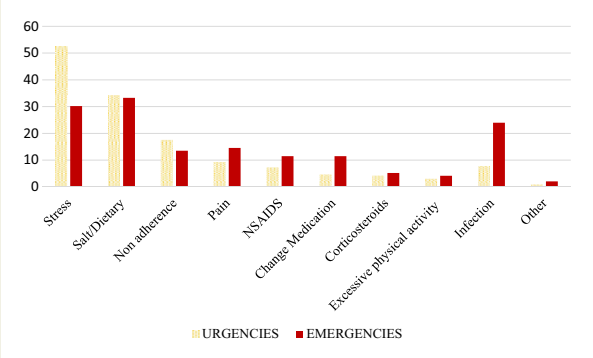


Figure 1 Reported causes of hypertensive urgencies and emergencies. Solid fill represents hypertensive emergencies while pattern fill represents urgencies. Stress refers to reported feeling of anxiety, restlessness, and insomnia. Salt/dietary represents daily consumption of over a teaspoon of salt (over 5.7 g of salt and over 2.4 g of sodium) or consumption of savoury foods the previous hours. Nonadherence refers to antihypertensive medication. Pain represents reported acute subjective feeling of pain, often confirmed by clinical signs. Change of medication refers to antihypertensive medication the last 7 days prior to the event. Excessive physical activity represents an exertion for each patient's everyday activities. Other refers to other causes such as consumption above the suggested daily amount of alcohol per sex, urinary retention, and other reported causes. NSAIDS, nonsteroidal anti-inflammatory drugs.

$P = 0.042$). Finally, female patients suffered more frequently from thyroid disease (32.7% vs. 7.3%, $P < 0.0001$) and had greater rate of acute pain (14.7% vs. 7.1%, $P = 0.039$), excessive stress and anxiety (51.7% vs. 37.9%, $P = 0.018$) as probable causes of BP rise.

Discussion

The main findings of the present registry in the Emergency Cardiology department of a tertiary general hospital during a 12-month period were the following: First, the combined prevalence for HU and HE was 0.91% out of which 27.5% had HE. Secondly, apart from non-adherence to therapy the contribution of stress and increased salt intake were presumptive causes of severe BP increase. Thirdly, pulmonary oedema and coronary syndromes are the more frequent clinical conditions associated with HE, followed by stroke and acute kidney damage differentiating our registry from previous ones.[18–21,25,28,29] Lastly, long-acting calcium channel blockers, RAS inhibitors, and anxiolytics were used for oral treatment of high BP, while nitrates and diuretics were the most common i.v. therapy of HE.

The combined prevalence for HU and HE was 0.91% in the totality of cases, out of which 27.5% had HE. The HU cases contribute majorly in the high volume of unnecessary visits in the ED that could be avoided since they could be optimally managed in the outpatient setting. The previously reported prevalence is ranging from two times lower to three times higher values in European studies (from 0.46%

Table 3 Symptoms reported in the emergency and urgency groups

Symptoms	Emergencies ($n = 97$)	Urgencies ($n = 256$)	P
Asymptomatic (%)	0.0	13.6	<0.0001
Headache/dizziness (%)	10.3	46.8	<0.0001
Epistaxis (%)	1	3.6	0.199
Chest pain (%)	30.2	27.4	0.611
Dyspnoea (%)	67	10	<0.001
Faintness (%)	1	3.2	0.262
Vomitus (%)	1	6.3	0.039
Palpitations (%)	0.0	2.7	0.101
Neurological deficit (%)	8.2	0	<0.0001
Other (%)	1.4	2.8	0.105

n, number of patients; *P*, statistical significance ($P < 0.05$).

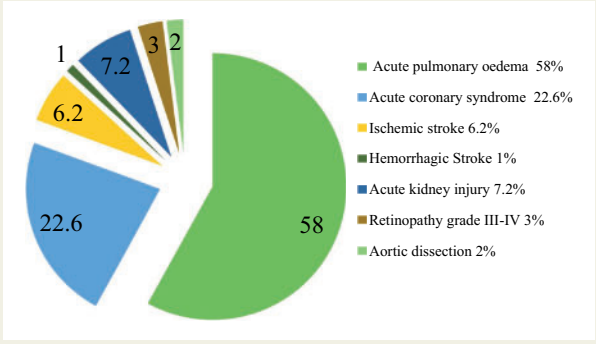


Figure 2 Target organ damage in the hypertensive emergency group (%).

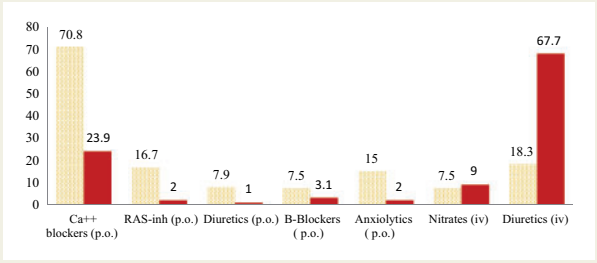


Figure 3 Management of hypertensive urgencies and emergencies in the emergency cardiology department. Solid fill represents hypertensive emergencies while pattern fill represents urgencies. Ca^{++} blockers, calcium channel blockers; i.v., intravenous; p.o., orally; RAS-inh, renin–angiotensin system inhibitors.

to 3.16%)[18–21] and others from the USA (reporting a prevalence of 2–4%)[28,29] and Brazil (0.5%).[25] Climatical and geographical differences among countries in the northern hemisphere (the USA and European countries) and countries in South America (Brazil) and Africa, as well as different BP cut-off values for determining HU and HE could partially explain these differences. Regarding our work, we have adopted BP thresholds consistent with the 2013 ESC/ESH guidelines (SBP ≥ 180 mmHg and/or DBP ≥120 mmHg), since the beginning of our study was in December 2017,[27] and not the current ones.[1]

The study presented a slightly higher prevalence of HE in men and in older individuals. The first difference could mainly be due to the exclusion of pregnant women with HE, mainly eclampsia. The ageing effect on large artery stiffness and related comorbidities like hypertension, coronary artery disease, heart failure, chronic kidney disease, dyslipidaemia, and diabetes mellitus could explain why older individuals had more HE.[5,6,9–11,23] In terms of comparison, the results of Andrade *et al.*[30] were also similar regarding the high percentage of the previous hypertension, dyslipidaemia, smoking, and diabetes in HE. Other trials could not confirm the statistical significance of the causal effect of these comorbidities to HE.[31]

Regarding the worst clinical phenotype of men compared with women one could suggest that male gender predisposes to HE events which is in agreement with the study conducted by Pinna *et al.*[20] and Martin *et al.*[25] On the other hand, Zampaglione *et al.*[18] did not report any differences between the two sexes regarding HE events.

Both higher SBP and DBP in HE was shown in this study pointing out that the magnitude of BP elevation constitutes an important factor for end-organ damage in contrast with the data of Zampaglione *et al.* (for SBP) and Pinna *et al.* (for SBP and DBP) and in agreement with others.[31] Moreover, elevated HR at first measurement in the ED, anaemia, and impaired renal function complete the worst profile of this group in the current registry. Andrade *et al.*[30] reported no difference between the two groups of HE and HU for creatinine, but there were significantly higher creatinine levels in the combined HE and HU group in comparison with normotensives and well controlled hypertensives. Augmented BP and HR could be attributed to the leading pathophysiological pathways for HU and HE which involve activation of the RAS, sympathetic nervous system overdrive,[32] diffuse vascular damage,[6,24] and dysfunction of haemodynamic autoregulation.[3,5–19]

The main reported causes for HU and HE were excessive stress and increased salt intake, leaving non-adherence to medication in the third place, a finding not in agreement with all previous evidence.[18–21,28,29] It is notable that non-adherence to medication is a frequent but often overrated cause of HU and HE.[33] The use of smartphone applications together with telemonitoring of BP could contribute to better hypertension management by enforcing physician–patient relation and adherence to medication.[1] Excess sodium intake clearly plays a major role in euvolaemia of patients especially the older ones with stiffer vasculature,[34,35] partially explaining the older age of HE group in our registry that reported salt as the most frequent cause.

Acute pulmonary oedema and acute coronary syndrome outweighed the prevalence of other end-organ damage due to the fact that our hospital is a reference national centre for percutaneous coronary interventions as well as for the management of patients with heart failure. These findings are discordant with the results by Martin *et al.*,[25] Zampaglione *et al.*,[18] and Pinna *et al.*[20] where the frequency of end-organ damage is almost equally divided between the heart and

brain. The same trend is registered in reported symptoms highlighting the differences with the above studies. Almost 70% of symptoms in the HE group were related with the heart (dyspnoea and chest pain), only 10% involved brain-related symptoms (neurological deficit), and only 1% kidney-related symptoms (urinary retention). Interestingly, elevated concentrations of high sensitivity troponin in HE suggest that acute heart damage is more evident in this entity, magnifying the overall risk. The observed lower rate of strokes since the hospital is not a primary stroke centre and the lack of emergencies in pregnant women because of the absence of Obstetric clinics diversify our results in comparison with other studies.[29,31]

Bringing the centre of attention on therapy, patients with HU in the ED were mostly treated orally with calcium channel blockers, RAS inhibitors, and anxiolytics. It was diazepam and alprazolam that were used in 15% of patients with HU who were treated with anxiolytics. There are reports in the field of neurocardiology that anxiolytics have shown acceptable efficacy for BP reduction in conjunction with decreased need of antihypertensive drugs to achieve desirable BP targets.[15] In the same lines, resting in a quiet room could serve as an alternative to antihypertensive drugs but this was not tested in the registry.[36,37] Nicardipine and urapidil suggested by ESC/ESH guidelines 2018[1] were not available, thus amlodipine was used instead, while there was no therapy with sublingual nifedipine and captopril in contrast to past therapeutic trends.[38,39] Focusing on HE in the ED, patients were mostly treated with i.v. diuretics and nitrates but lacked the use of labetalol and nicardipine due to non-availability at country level. Acknowledgement should be noted that p.o. administration of drugs, which was registered in the last group is not compatible with the current guidelines. Last but not least, we found unjustified high usage of i.v. diuretics in HU like in the Project GEAR.[19]

The trends for therapy are the same during hospitalization for the 91 HE and 25 HU patients. More specifically, during hospitalization calcium channel blockers, RAS inhibitors, diuretics, and β-blockers were mostly administered orally to HU while HE were treated with i.v. nitrates, β-blockers (esmolol and not labetalol) and diuretics during the first days of hospitalization. Moreover, the study reported more intensive treatments used like haemodialysis and peritoneal dialysis as suggested by the current guidelines for HE.[1] Additionally, there was a decline in renal function during hospitalization in our study and this can be interpreted as a causal effect of the combination of end-organ damage and intensified treatment with diuretics especially for the management of HE. Finally, the reported two deaths from nosocomial infections and not from their initial admission diagnosis (acute pulmonary oedema) were due to long duration of hospitalization and high-risk phenotype based on previous medical history of rehospitalizations.[40]

This registry due to design and methodology presents several limitations. First, as an observational study can be limited by unmeasured or unknown confounding as well as by investigator bias. Secondly, the presented results could not be generalized to other settings like the primary care of other countries, due to different geographic regions and health systems. The management of these patients especially for HE in the ED and in clinics showed similarities with others[19] but were not consistent with the current guidelines.[1] Another limitation is the fact that women affected by eclampsia and/or pre-eclampsia were not included[20,29] and fewer patients with stroke were registered due to the organization of the referred hospital. Nevertheless, the 12 months duration of the study and the number of participants along with the detailed data collection strengthen the findings.

The novelties of this study include the extensive recording of each reported cause of HE and HU, identifying other causes as first than the usual ones registered in other studies. Moreover, in the current work, there is a full record of the therapeutic management of the hospitalized patients, regardless of group and the continuous monitoring of the daily BP until hospital discharge. This abundance and adequacy of data are perhaps one of the innovations of this registry.

Future studies should focus in establishing practical methods for more intensive follow-up especially for hypertensive patients with uncontrolled hypertension and worst clinical profile, preventing clinical manifestation of HU and HE. A prospective multinational and multicentre registry such as the ESH registry of hypertensive URGencies and EMergencies (ESH-URGEM) could imprint the current prevalence, phenotype, and management of these patients, as well as their differences between centres and countries.

Conclusion

The current registry provides an updated description of the clinical status and management of HU and HE in a tertiary centre. Stress and high salt consumption are primary causes of increased BP, while pulmonary oedema and coronary syndromes are the more frequent clinical entities for HE. Our findings support that there is an urgent need to construct consensus and homogenize therapy in the acute and chronic setting of HU and HE towards better cardiovascular and overall outcome.

Supplementary material

Supplementary material is available at *European Journal of Preventive Cardiology* online.

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Conflict of interest: There is no conflict of interest declared.

Data availability

The study data can be made available to interested researchers upon request. We cannot place these data in a public storagedue to legal and ethical restrictions.

References

1. Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M, Clement DL, Coca A, de Simone G, Dominiczak A, Kahan T, Mahfoud F, Redon J, Ruilope L, Zanchetti A, Kerins M, Kjeldsen SE, Kreutz R, Laurent S, Lip GYH, McManus R, Narkiewicz K, Ruschitzka F, Schmieder RE, Shlyakhto E, Tsioufis C, Aboyans V, Desormais I; ESC Scientific Document Group. 2018 ESC/ESH Guidelines for the management of arterial hypertension. *Eur Heart J* 2018;**39**:3021–3104.
2. Whelton PK, Carey RM, Aronow WS, Casey DE, Collins KJ, Himmelfarb CD, DePalma SM, Gidding S, Jamerson KA, Jones DW, MacLaughlin EJ, Muntner P, Ovbiagele B, Smith SC Jr, Spencer CC, Stafford RS, Taler SJ, Thomas RJ, Williams KA Sr, Williamson JD, Wright JT Jr. 2017. ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection,

evaluation, and management of high blood pressure in adults: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Soc Hypertens* 2018; **12**:579.e1–579.e73.
3. Peixoto AJ. Acute severe hypertension. *N Engl J Med* 2019;**381**:1843–1852.
4. Naranjo M, Paul M. *Malignant Hypertension*. Treasure Island, FL: StatPearls Publishing, 2020. http://www.ncbi.nlm.nih.gov/books/NBK507701/ (9 February 2021).
5. van den Born BJH, Honnebier UPF, Koopmans RP, van Montfrans GA. Microangiopathic hemolysis and renal failure in malignant hypertension. *Hypertension* 2005;**45**:246–251.
6. van den Born B-JH, Lip GYH, Brguljan-Hitij J, Cremer A, Segura J, Morales E, Mahfoud F, Amraoui F, Persu A, Kahan T, Agabiti Rosei E, de Simone G, Gosse P, Williams B. ESC Council on hypertension position document on the management of hypertensive emergencies. *Eur Heart J Cardiovasc Pharmacother* 2019;**5**: 37–46.
7. Wolffsohn JS, Hurcomb PG. Hypertension and the eye. *Curr Hypertens Rep* 2002; **4**:471–476.
8. August P. Hypertensive encephalopathy: what's in a name? *J Am Soc Hypertens* 2016;**10**:404–405.
9. Papadopoulos DP, Sanidas EA, Viniou NA, Gennimata V, Chantziara V, Barbetseas I, Makris TK. Cardiovascular hypertensive emergencies. *Curr Hypertens Rep* 2015;**17**:5.
10. Weintraub NL, Collins SP, Pang PS, Levy PD, Anderson AS, Arslanian-Engoren C, Gibler WB, McCord JK, Parshall MB, Francis GS, Gheorghiade M; American Heart Association Council on Clinical Cardiology and Council on Cardiopulmonary, Critical Care, Perioperative and Resuscitation. Acute heart failure syndromes: emergency department presentation, treatment, and disposition: current approaches and future aims: a scientific statement from the American Heart Association. *Circulation* 2010;**122**:1975–1996.
11. Wajngarten M, Silva GS. Hypertension and stroke: update on treatment. *Eur Cardiol* 2019;**14**:111–115.
12. Powers WJ, Rabinstein AA, Ackerson T, Adeoye OM, Bambakidis NC, Becker K, Biller J, Brown M, Demaerschalk BM, Hoh B, Jauch EC, Kidwell CS, Leslie-Mazwi TM, Ovbiagele B, Scott PA, Sheth KN, Southerland AM, Summers DV, Tirschwell DL; American Heart Association Stroke Council. 2018. Guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 2018;**49**:e46–e110.
13. ElFarra J, Bean C, Martin JN. Management of hypertensive crisis for the obstetrician/gynecologist. *Obstet Gynecol Clin North Am* 2016;**43**:623–637.
14. Salvetti M, Paini A, Bertacchini F, Stassaldi D, Aggiusti C, Agabiti Rosei C, Muiesan ML. Acute blood pressure elevation: therapeutic approach. *Pharmacol Res* 2018 Apr;**130**:180–190.
15. Grossman E, Nadler M, Sharabi Y, Thaler M, Shachar A, Shamiss A. Antianxiety treatment in patients with excessive hypertension. *Am J Hypertens* 2005;**18**: 1174–1177.
16. Patel KK, Young L, Howell EH, Hu B, Rutecki G, Thomas G, Rothberg MB. Characteristics and outcomes of patients presenting with hypertensive urgency in the office setting. *JAMA Intern Med* 2016;**176**:981–988.
17. Campos CL, Herring CT, Ali AN, Jones DN, Wofford JL, Caine AL, Bloomfield RL, Tillett J, Oles KS. Pharmacologic treatment of hypertensive urgency in the outpatient setting: a systematic review. *J Gen Intern Med* 2018;**33**:539–550.
18. Zampaglione B, Pascale C, Marchisio M, Cavallo-Perin P. Hypertensive urgencies and emergencies. Prevalence and clinical presentation. *Hypertension* 1996;**27**: 144–147.
19. Salvetti M, Paini A, Colonetti E, Tarozzi L, Bertacchini F, Aggiusti C, Stassaldi D, Rosei CA, Rosei EA, Muiesan ML. Hypertensive emergencies and urgencies: a single-centre experience in Northern Italy 2008-2015. *J Hypertens* 2020;**38**:52–58.
20. Pinna G, Pascale C, Fornengo P, Arras S, Piras C, Panzarasa P, Carmosino G, Franza O, Semeraro V, Lenti S, Pietrelli S, Panzone S, Bracco C, Fiorini R, Rastelli G, Bergandi D, Zampaglione B, Musso R, Marengo C, Santoro G, Zamboni S, Traversa B, Barattini M, Bruno G. Hospital admissions for hypertensive crisis in the emergency departments: a large multicenter Italian study. *PLoS One* 2014;**9**:e93542.
21. Saladini F, Mancusi C, Bertacchini F, Spannella F, Maloberti A, Giavarini A, Rosticci M, Bruno RM, Pucci G, Grassi D, Pengo M, Muiesan ML. Diagnosis and treatment of hypertensive emergencies and urgencies among Italian emergency and intensive care departments. Results from an Italian survey: Progetto GEAR (Gestione dell'Emergenza e urgenza in ARea critica). *Eur J Intern Med* 2020;**71**:50–56.
22. Wu P-H, Yang C-Y, Yao Z-L, Lin W-Z, Wu L-W, Chang C-C. Relationship of blood pressure control and hospitalization risk to medication adherence among patients with hypertension in Taiwan. *Am J Hypertens* 2010;**23**:155–160.
23. Saguner AM, Dur S, Perrig M, Schiemann U, Stuck AE, Burgi U, Erne P, Schoenenberger AW. Risk factors promoting hypertensive crises: evidence from a longitudinal study. *Am J Hypertens* 2010;**23**:775–780.
24. Lip GYH, Edmunds E, Nuttall SL, Landray MJ, Blann AD, Beevers DG. Oxidative stress in malignant and non-malignant phase hypertension. *J Hum Hypertens* 2002; **16**:333–336.
25. Martin JFV, Higashiama E, Garcia E, Luizon MR, Cipullo JP. Hypertensive crisis profile. Prevalence and clinical presentation. *Arq Bras Cardiol* 2004;**83**:125–136. 125–130.
26. Salvetti M, Bertacchini F, Saccà G, Muiesan ML. Hypertension urgencies and emergencies: the GEAR Project. *High Blood Press Cardiovasc Prev* 2020;**27**: 129–132.
27. Mancia G, Fagard R, Narkiewicz K, Redon J, Zanchetti A, Böhm M, Christiaens T, Cifkova R, De Backer G, Dominiczak A, Galderisi M, Grobbee DE, Jaarsma T, Kirchhof P, Kjeldsen SE, Laurent S, Manolis AJ, Nilsson PM, Ruilope LM, Schmieder RE, Sirnes PA, Sleight P, Viigimaa M, Waeber B, Zannad F; Task Force Members. 2013 ESH/ESC guidelines for the management of arterial hypertension: the Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *Eur Heart J* 2013;**34**:2159–2219.
28. Deshmukh A, Kumar G, Kumar N, Nanchal R, Gobal F, Sakhuja A, Mehta JL. Effect of Joint National Committee VII report on hospitalizations for hypertensive emergencies in the United States. *Am J Cardiol* 2011;**108**:1277–1282.
29. Janke AT, McNaughton CD, Brody AM, Welch RD, Levy PD. Trends in the incidence of hypertensive emergencies in US Emergency Departments From 2006 to 2013. *J Am Heart Assoc* 2016;**5**:e004511.
30. Andrade DO, Santos SPO, Pinhel MAS, Valente FM, Giannini MC, Gregório ML, De Godoy MF, Souza DRS, Vilela-Martin JF. Effects of acute blood pressure elevation on biochemical-metabolic parameters in individuals with hypertensive crisis. *Clin Exp Hypertens* 2017;**39**:553–561.
31. Astarita A, Covella M, Vallelonga F, Cesareo M, Totaro S, Ventre L, Aprà F, Veglio F, Milan A. Hypertensive emergencies and urgencies in emergency departments: a systematic review and meta-analysis. *J Hypertens* 2020;**38**:1203–1210.
32. Carnagarin R, Matthews V, Zaldivia MTK, Peter K, Schlaich MP. The bidirectional interaction between the sympathetic nervous system and immune mechanisms in the pathogenesis of hypertension. *Br J Pharmacol* 2019;**176**:1839–1852.
33. Overgaauw N, Alsma J, Brink A, Hameli E, Bahmany S, Peeters LEJ, Van Den Meiracker AH, Schuit SCE, Koch BCP, Versmissen J. Drug nonadherence is a common but often overlooked cause of hypertensive urgency and emergency at the emergency department. *J Hypertens* 2019;**37**:1048–1057.
34. Grillo A, Salvi L, Coruzzi P, Salvi P, Parati G. Sodium intake and hypertension. *Nutrients* 2019;**11**: 1970.
35. Rodrigo R, González J, Paoletto F. The role of oxidative stress in the pathophysiology of hypertension. *Hypertens Res* 2011;**34**:431–440.
36. Park SK, Lee D-Y, Kim WJ, Lee SY, Park HS, Kim HW, Kim B, Moon KH. Comparing the clinical efficacy of resting and antihypertensive medication in patients of hypertensive urgency: a randomized, control trial. *J Hypertens* 2017; **35**:1474–1480.
37. Grassi D, O'Flaherty M, Pellizzari M, Bendersky M, Rodriguez P, Turri D, Forcada P, Ferdinand KC, Kotliar C; on behalf of the Group of Investigators of the REHASE Program 6. Hypertensive urgencies in the emergency department: evaluating blood pressure response to rest and to antihypertensive drugs with different profiles. *J Clin Hypertens (Greenwich)* 2008;**10**:662–667.
38. Sarafidis PA, Georgianos PI, Malindretos P, Liakopoulos V. Pharmacological management of hypertensive emergencies and urgencies: focus on newer agents. *Expert Opin Investig Drugs* 2012;**21**:1089–1106.
39. Grossman E, Messerli FH, Grodzicki T, Kowey P. Should a moratorium be placed on sublingual nifedipine capsules given for hypertensive emergencies and pseudoemergencies? *JAMA* 1996;**276**:1328–1331.
40. Sydnor ERM, Perl TM. Hospital epidemiology and infection control in acute-care settings. *Clin Microbiol Rev* 2011;**24**:141–173.