

# Evaluation of hypertensive urgency management in out-of-hospital unit

---

**Raos, Dominik**

**Professional thesis / Završni specijalistički**

**2021**

*Degree Grantor / Ustanova koja je dodijelila akademski / stručni stupanj:* **University of Zagreb, School of Medicine / Sveučilište u Zagrebu, Medicinski fakultet**

*Permanent link / Trajna poveznica:* <https://um.nsk.hr/um:nbn:hr:105:334873>

*Rights / Prava:* [In copyright](#)/[Zaštićeno autorskim pravom.](#)

*Download date / Datum preuzimanja:* **2024-09-14**



*Repository / Repozitorij:*

[Dr Med - University of Zagreb School of Medicine Digital Repository](#)



SVEUČILIŠTE U ZAGREBU  
MEDICINSKI FAKULTET

**DOMINIK RAOS**

**EVALUATION OF HYPERTENSIVE URGENCY  
MANAGEMENT IN OUT-OF-HOSPITAL UNIT**

**Završni specijalistički rad**

Zagreb, 2021.

# ZAVOD ZA HITNU MEDICINU ZAGREBAČKE ŽUPANIJE

Mentor: izv. prof. dr. sc. Ingrid Prkačin, prim. dr. med.

Koautori: Paštrović Frane, Petar Krešimir Okštajner, Vodanović Marko

Redni broj rada: \_\_\_\_\_

## TABLE OF CONTENTS

ABSTRACT .....	1
INTRODUCTION.....	3
PATIENTS AND METHODS .....	5
RESULTS .....	7
DISCUSSION .....	8
CONCLUSION .....	10
REFERENCES.....	11
ACKNOWLEDGEMENTS .....	15
SAŽETAK .....	16
ŽIVOTOPIS .....	18

## LIST OF TABLES

Table 1: General characteristics, clinical findings and outcomes of hypertensive patients with hypertensive urgency and control group of hypertensive patients without hypertensive urgency.....	13
Table 2: Differences in blood pressure recording in the hypertensive urgency group according to the use of benzodiazepine therapy. ....	14

## **ABSTRACT**

**BACKGROUND.** Hypertensive urgencies are common conditions treated in out-of-hospital Emergency Medical Service units, whereas treatment of hypertensive emergencies from current guidelines is hospital based. Current guidelines do not cover in detail the management of hypertensive urgencies, let alone their management in out-of-hospital setting. Our main goal was to evaluate adherence to the existing guidelines.

**PATIENTS AND METHODS.** We analyzed data collected by out-of-hospital Emergency Medical Service unit set up in the Community Health Center in the town of Sveti Ivan Zelina, Croatia. During the one-year period, a total of 2911 patients were treated by Emergency Medical Service unit. Arterial hypertension was the primary diagnosis in 177 (6%) patients, of which 143 patients met the inclusion criteria. We further divided patients into two groups, i.e. hypertensive urgency group (blood pressure >180/120 mm Hg) and control group (systolic blood pressure <180 mm Hg). Different combinations of medications were used, including nitrates, antihypertensives, and anxiolytics.

**RESULTS.** The mean systolic blood pressure reduction was  $19.5 \pm 7.1\%$  in the hypertensive urgency group and  $10.1 \pm 7\%$  in control group. The biggest drop in systolic blood pressure ( $21.9 \pm 5.2\%$ ) was recorded in hypertensive urgency group patients that received the AT + nitrate + benzodiazepine combination (14% of patients). Less patients that received benzodiazepines were referred to the Integrated Hospital Emergency Admission Unit (4% vs. 23%;  $p=0.013$ ).

**CONCLUSION.** Patients presenting with hypertensive urgency tend to be treated more aggressively, and there is a place for anxiolytic therapy in hypertensive urgency management. Further research is needed to make definite conclusions.

**Keywords:** hypertensive urgency, prehospital, out-of-hospital emergency medicine

## **LIST OF ABBREVIATIONS**

HE	Hypertensive emergency
HU	Hypertensive urgency
SBP	Systolic blood pressure
DBP	Diastolic blood pressure
EMS	Emergency medical service
AH	Arterial hypertension
GP	General practitioner
AT	Antihypertensive therapy

## INTRODUCTION

Hypertension is quantitatively the most important risk factor for premature cardiovascular disease (1,2). Most people who have hypertension have no symptoms at all; this is why it is known as the 'silent killer' (3). Current estimates are that about 1% to 2% of patients with hypertension will have a hypertensive crisis at some point in their lifetime (4). Hypertensive crisis is a frequently used term, which includes both hypertensive emergency and hypertensive urgency. Hypertensive emergency (HE) is acute elevation of systolic blood pressure (SBP >180 mm Hg, DBP >120 mm Hg) accompanied by end organ damage primarily in eyes, brain, heart, aorta and kidney (1,5). Hypertensive urgency (HU) is defined as acute elevation of blood pressure above the often used arbitrary limit of systolic blood pressure (SBP) >180 mm Hg and/or diastolic blood pressure (DBP) >120 mm Hg, without end organ damage (5). The prevalence of arterial hypertension in general public adults in Croatia is 37.5% (6). Around 5% of patient visits to the out-of-hospital Emergency Medical Service (EMS) units in Croatia are associated with hypertension. However, most of the patients do not present with HE (7). There are several up-to-date guidelines available for treating chronic hypertension; they address the management of HE and HU mostly in hospital environment, but there are no definite guidelines on pre-hospital management of HE and HU (1,8). The primary goal of intervention in hypertensive crisis is to safely reduce blood pressure in order to prevent end organ damage. The appropriate therapeutic approach to each patient will depend on their clinical presentation. History data, physical examination and instrumental evaluation determine the following management that could be oral (for urgencies) or intravenous (for emergencies) antihypertensive drugs (7).

The treatment of HE is usually carried out in hospital intensive care units with intravenous antihypertensive agents (9). Current guidelines recommend reduction of SBP by no more than 25% within the first hour, and then gradual reduction to normal SBP over the next 24 to 48 hours (9). On the other way, HU may in general be treated with oral antihypertensive on outpatient basis, and the target BP should be achieved over hours to days (10,11). Emotional reactivity and anxiety are associated with blood pressure elevations (12,13). When facing a patient with HU, the clinician will not only choose an appropriate antihypertensive agent, but will also assess how rapidly the blood pressure must be lowered. The main problem is that literature does not offer enough data to support one timetable over another (11). In an out-of-hospital environment, such as EMS unit, where a single EMS team is on duty and covers both field interventions and walk-in patients, long observations and follow-up are not always possible.

Our main goal was to evaluate adherence of pre-hospital EMS physicians to the available guidelines, and estimate whether they tended to be overly aggressive in lowering blood pressure due to the lack of observation and follow-up, as well as the patient extreme anxiety if dismissed without a significant SBP decrease.



## **PATIENTS AND METHODS**

We analyzed data from medical records of the EMS unit set up in the Community Health Center in the town of Sveti Ivan Zelina, branch of the Zagreb County Institute of Emergency Medicine, for a period of one year. The study was submitted to and approved by the institutional Committee on Ethics and Research. During the above-mentioned period, a total of 2911 patients were treated in EMS unit set up in the community health center and in 177 (6%) cases the primary diagnosis was arterial hypertension. Records from field interventions or interventions at patient home were not included in the research. Patients with HE and patients without two blood pressure measurements or recorded times of those measurements were excluded from the study.

A total of 143 patients met all the criteria for this study, 44 men and 99 women. The patients were divided into two groups. The first group consisted of 52 patients with AH, but without HU, and the second one consisted of 91 patients with the criteria for HU (SBP >180 mm Hg and/or DBP >120 mm Hg). Data included age, gender, therapy, blood pressure upon pre-hospital EMS unit admission, control blood pressure measurements after therapy administration, time from first to last measurement, referral to Integrated Hospital Emergency Admission Units, home, or general practitioner (GP). Patient therapy included antihypertensive therapy (AT; angiotensin-converting enzyme (ACE) inhibitors, calcium channel blockers, diuretics, fixed combinations); nitrates (isosorbide-dinitrate and glyceryl trinitrate pump spray); anxiolytics (benzodiazepines), urapidil ( $\alpha$ 1-adrenoceptor antagonist and 5-HT<sub>1A</sub> receptor agonist).

Descriptive analysis was performed for qualitative variables and quantitative results were presented as mean and standard deviation. Kolmogorov-Smirnov test was used to determine the normality of distribution of the tested parameters. Mann-Whitney U test was used to determine the significance of results. To compare qualitative variables,  $\chi^2$ -test and Fisher exact test were used depending on the sample size. Data analysis was performed by the IBM SPSS® software version 25.0 (IBM Corp., Armonk, NY, USA).

## RESULTS

General characteristics, clinical findings and outcomes of hypertensive patients with HU and control group of hypertensive patients without HU are shown in Table 1. Women predominated in both groups. There was no difference in the sex distribution of subjects in either group. There was no statistical significance between the groups in the number of patients having received medicines at home prior to arrival to EMS unit, but it was less common in HU group. In the HU group, 28% of patients received AT + nitrate combination, 18% nitrate, 16% nitrate + benzodiazepine, and 14% AT + nitrate + benzodiazepine with the biggest drop in SBP ( $21.9\pm 5.2\%$ ). Five percent of patients in the HU group received oral urapidil as monotherapy. AT as the only medication administered was the least aggressive option with  $14.1\pm 5.0\%$  drop in SBP during the follow-up. Control group patients received AT + nitrate combination (15%); nitrate + benzodiazepine (13%); and benzodiazepine (13%). The most significant drop in SBP ( $17.7\pm 5.0\%$ ) was recorded in patients that received the AT + nitrate + benzodiazepine combination (8% of patients). The mean SBP decrease percentage regardless of therapeutic choice was  $10.1\pm 7\%$ . In the HU group, the mean SBP reduction was  $19.5\pm 7.1\%$ . Patients with HU had longer periods between the first and last blood pressure measurements ( $26\pm 10$  min vs.  $34\pm 15$  min;  $p=0.017$ ). Thirteen of the 91 patients treated in the HU group were referred to the Integrated Hospital Emergency Admission Unit. Less patients having received benzodiazepines were re-referred to the integrated hospital emergency admission units (4% vs. 23%;  $p=0.013$ ) (Table 2.).

## DISCUSSION

None of the available guidelines assessing HU management offer a definite timeline ideal for SPB reduction. However, slowly and safely decreasing SBP over hours to days is advised (11). The choice of specific AH drugs depend on the underlying causes of the crisis, patient demographics, comorbidities and cardiovascular risk (11). For emergencies, a maximum blood pressure reduction by 20%-25% within the first hour is considered appropriate, with further gradual decrease over the next 24-48 h to reach normal blood pressure levels. In case of HU, gradual blood pressure lowering over 24-48 h with an oral medication is the best approach (1,11). In an out-of-hospital environment, long-term observation of a patient is not possible, which often results in more aggressive treatment and EMS overuse (14). Medical conditions for which EMS utilization can be considered avoidable are overrepresented (14). When we compared our data with those from other parts of Croatia, the incidence of hypertension in EMS unit was higher (the primary diagnosis was arterial hypertension in 6% of cases) than in Varaždin County (4.8%) (7). The incidence of HU was higher among females, the same as in other reference data (71%) (7). Adherence to chronic AT was higher in the AT group with-out HU (40/52 (77%) in AT group and 43/91 (47%) in HU). According to the available guidelines, adherence to therapy is one of the most important problems and a very common failure in patients with HU (1). Thirteen of the 91 patients treated in the HU group were referred to the Integrated Hospital Emergency Admission Unit, mostly because of the longer follow-up or additional workup was necessary. An interesting fact to point out is that none of the antihypertensive used during the research had the time to action onset shorter than one hour, and our average follow-up time was  $34 \pm 15$  minutes. Blood pressure reduction in HU is best achieved with oral medication with benzodiazepines, as we witnessed in our

EMS. As far as we know, a systematic patient and doctor education program for hypertensive disorders does not exist in any country. Our data analysis showed the use of benzodiazepines in HU to be useful and have a much greater role in HU management than presumed. Differences in the settings, personnel, variety of antihypertensive drugs administered and time spent for observation should be taken into consideration when interpreting every case.

## **CONCLUSION**

Choosing the right antihypertensive therapy and dosage for a patient with HU is a challenge for every EMS physician, especially in an out-of-hospital environment. There is no unified approach and every patient needs to be assessed individually, however, structured approach through some form of guidelines, especially designed for out-of-hospital environment, could provide benefit for patients.

## REFERENCES

1. Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M et al. 2018 ESH / ESC Guidelines for the management of arterial hypertension Eur Heart 2018; 39: 3021-2104.
2. Lawes CMM, Hoorn S Vander, Rodgers A, Society I. Global burden of blood-pressure-related disease, 2001. Lancet. 2008; 371: 1513–8.
3. Prkačin I, Cavrić G, Dabo N, Kasumović D, Šantek L, Balenović D. Hitna stanja vezana uz hipertenziju. Liječ Vjesn 2014; 136 (Supp.2): 100-3.
4. Marik PE, Varon J. Hypertensive Crises, Challenges and Management. Chest. The American College of Chest Physicians; 2007;131(6):1949–62.
5. Baumann BM. Systemic Hypertension. In: Tintinalli JE, Stapczynski JS, Ma OJ, Yealy DM, Meckler GD, Cline DM, editors. Tintinalli's Emergency Medicine, A Comprehensive Study Guide. Eighth Edi. McGraw-Hill; 2016. p. 399–409.
6. Kralj V, Erceg M, Čukelj P. Epidemiologija hipertenzije u Hrvatskoj i svijetu Epidemiology of hypertension in Croatia and worldwide. Cardiol Croat. 2017;16(3):41.
7. Simić A, Lukačević M. Arterijska hipertenzija u izvanbolničkoj hitnoj medicinskoj službi – retrospektivna analiza podataka bolesnika zbrinutih u Zavodu za hitnu medicinu Varaždinske županije Arterial hypertension in outpatient emergency practice – retrospective analysis of hyp. Cardiol Croat. 2017;12(3):64.
8. Whelton PK, Carey RM, Aronow WS, Casey DEJ, Collins KJ, Dennison Himmelfarb C, et al. 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. J Am Coll Cardiol 2018; 71:e127-e248.
9. Vamsi V, Kamath P, Achappa B, Prkacin I. Redefiniendo urgencia hipertensiva y emergencia hipertensiva maligna. Rev Cient Cient Med 2019; 22 (1):77-8.

10. Rodriguez MA, Kumar SK, Caro M De. Hypertensive Crisis. *Cardiol Rev.* 2010;18(2):102–7.
11. Maloberti A, Cassano G, Capsoni N et al. Therapeutic approach to hypertension urgencies and emergencies in the emergency room. *High Blood Press Cardiovasc Prev* 2018;25(2): 177-89
12. Ifeagwazi CM, Egberi HE, Chukwuorji JC. Emotional reactivity and blood pressure elevations : anxiety as a mediator Emotional reactivity and blood pressure elevations : anxiety. *Psychol Health Med.* 2017; 22:640-5.
13. Pan Y, Cai W, Qi C, Dong W, An T, Yan J. Association between anxiety and hypertension: a systematic review and meta-analysis of epidemiological studies. *Neuropsychiatr Dis Treat.* 2015; 11:1121–30.
14. Kostanj D, Ben M, Keglevi MV. Ambulatory Care Sensitive Conditions at Out-of-hospital Emergence Services in Croatia : A Longitudinal Study Based on Routinely Collected Data. *Coll Antropol.* 2014; 38(2): 143–8.
15. Rubin S, Cremer A, Boulestreau R, Rigothier C, Kuntz S, Gosse P. Malignant hypertension: diagnosis, treatment and prognosis with experience from the Bordeaux cohort. *J Hypertens.* 2019; 37: 316–24.



**Table 1:** *General characteristics, clinical findings and outcomes of hypertensive patients with hypertensive urgency and control group of hypertensive patients without hypertensive urgency*

	Patients with AH* without HU†	Patients with HU†	p
Patients in the group	52	91	
Women (%)	67	71	0,676
Age (years)	59±14	67±11	0,02
First SBP measured (mmHg)	162±12	197±15	
Last SBP measured (mmHg)	145±9	158±17	<0,01
Therapy applied prior to EMS visit (%)	40	43	0,718
Referred to the Integrated hospital emergency admission unit (%)	4	21	0,052
Time from the first to the last measurement (min)	26±10	34±15	0,017

\* AH - arterial hypertension; †HU - hypertensive urgency; SBP - systolic blood pressure; EMS - emergency medical service

**Table 2:** *Differences in blood pressure recording in the hypertensive urgency group according to the use of benzodiazepine therapy*

	No anxiolysis	Anxiolysis	p
Number of patients	55	36	
Women (%)	69%	73%	0,688
Age (years)	66±12	69±10	0,208
First SBP* measured (mmHg)	197±17	196±14	0,853
Last SBP* measured (mmHg)	162±20	153±14	0,08
Percentage of the SBP* drop (%)	17,9%±7,9%	21,9%±5,2%	0,03
Referred to the Integrated hospital emergency admission unit (%)	23%	4%	0,013

**\*SPB - systolic blood pressure**

## **ACKNOWLEDGEMENTS**

No potential conflicts of interest relevant to this article were reported. All authors contributed to acquiring and interpreting data, reviewed/edited the manuscript. P.F. and O.P.K. contributed to interpreting data and wrote, reviewed/edited the manuscript. V.M. and R.D. reviewed/edited the manuscript. R.D. and I.P. are taking responsibility for the contents of the article.

**Conflict of Interest:** None to declare.

## SAŽETAK

### ZBRINJAVANJE BOLESNIKA S HIPERTENZIVNOM KRIZOM U IZVANBOLNIČKIM UVJETIMA

Hipertenzivna hitna stanja zbrinjavaju se najčešće u izvanbolničkom okruženju u slučaju hitnosti bez oštećenja ciljnih organa, dok hipertenzivnu hitnoću s oštećenjem ciljnih organa treba zbrinuti u bolničkim uvjetima. Trenutne kao i prethodne smjernice nemaju jasne preporuke o zbrinjavanju bolesnika s hipertenzivnom krizom koja obuhvaća oba navedena pojma. Cilj ovoga istraživanja bio je procijeniti primjenu i pridržavanje postojećih smjernica za liječenje hipertenzivne krize u izvanbolničkim uvjetima.

**METODE:** Analizirali smo podatke bolesnika koji su zbrinuti u izvanbolničkoj medicinskoj hitnoj službi Sv. Ivan Zelina u razdoblju od godine dana. Ukupno je bilo 2911 bolesnika, od toga je hipertenzija kao primarna dijagnoza bila u 177 (6 %) bolesnika, od kojih je 143 imalo uključne kriterije o podacima primijenjenog liječenja. Bolesnici su podijeljeni u dvije skupine: skupina s hipertenzivnom hitnošću (krvni tlak  $>180/120$  mm Hg) bez oštećenja ciljnih organa i kontrolna skupina (krvni tlak  $<180/120$  mm Hg). Uspoređivane su razlike u primjeni antihipertenzivnih i anksiolitičkih (benzodiazepin) lijekova.

**REZULTATI:** U skupini hipertenzivne hitnosti sniženje krvnog tlaka iznosilo je  $19,5 \pm 7,1$  %, a u kontrolnoj skupini  $10,1 \pm 7$  %. Najveće sniženje krvnog tlaka zabilježeno je u bolesnika s hipertenzivnom hitnošću koji su primali kombiniranu antihipertenzivnu terapiju uz dodatak nitrata i benzodiazepina ( $21,9 \pm 5,2$  %), 14 % bolesnika.

ZAKLJUČAK: Bolesnike koji se očituju hipertenzivnom hitnosti bez oštećenja ciljnih organa (hipertenzivna urgencija) potrebno je liječiti kombiniranom terapijom u kojoj ima mjesta za dodatnu anksiolitičku terapiju benzodiazepinom. Daljnja istraživanja pokazat će značenje toga zaključka.

## **ŽIVOTOPIS**

Rođen sam 25.05.1987. godine u Zagrebu gdje sam završio osnovnu školu i prirodoslovno matematičku gimnaziju. Diplomom doktora medicine stekao sam 2012. godine na Medicinskom fakultetu Sveučilišta u Splitu. Poslijediplomski specijalistički studij Hitna medicina upisao sam 2018. godine na Medicinskom fakultetu Sveučilišta u Zagrebu. Objavio sam nekoliko stručnih radova i sudjelovao na više domaćih i međunarodnih znanstveno stručnih skupova djelatnika hitne medicine. Pripravnički staž za doktora medicine započeo sam krajem 2013. u KB Sveti Duh. Od srpnja 2014. godine zaposlen sam u Zavodu za hitnu medicinu Zagrebačke županije, u ožujku 2017. godine imenovan sam voditeljem ispostave hitne medicinske službe grada Sveti Ivan Zelina.

# EVALUATION OF HYPERTENSIVE URGENCY MANAGEMENT IN OUT-OF-HOSPITAL UNIT

DOMINIK RAOS<sup>1</sup>, FRANE PAŠTROVIĆ<sup>1</sup>, PETAR KREŠIMIR OKŠTAJNER<sup>1</sup>, MARKO VODANOVIĆ<sup>1</sup> and INGRID PRKAČIN<sup>2</sup>

<sup>1</sup>Institute of Emergency Medicine of Zagreb County, Zagreb and <sup>2</sup>Merkur University Hospital, Department of Internal Medicine, Emergency Unit, Zagreb, University of Zagreb, School of Medicine Zagreb, Croatia

**Background:** Hypertensive urgencies are common conditions treated in out-of-hospital Emergency Medical Service units, whereas treatment of hypertensive emergencies from current guidelines is hospital based. Current guidelines do not cover in detail the management of hypertensive urgencies, let alone their management in out-of-hospital setting. Our main goal was to evaluate adherence to the existing guidelines. **Patients and Methods:** We analyzed data collected by out-of-hospital Emergency Medical Service unit set up in the Community Health Center in the town of Sveti Ivan Zelina, Croatia. During the one-year period, a total of 2911 patients were treated by Emergency Medical Service unit. Arterial hypertension was the primary diagnosis in 177 (6%) patients, of which 143 patients met the inclusion criteria. We further divided patients into two groups, i.e. hypertensive urgency group (blood pressure >180/120 mm Hg) and control group (systolic blood pressure <180 mm Hg). Different combinations of medications were used, including nitrates, antihypertensives, and anxiolytics. **Results:** The mean systolic blood pressure reduction was 19.5±7.1% in the hypertensive urgency group and 10.1±7% in control group. The biggest drop in systolic blood pressure (21.9±5.2%) was recorded in hypertensive urgency group patients that received the AT + nitrate + benzodiazepine combination (14% of patients). Less patients that received benzodiazepines were referred to the Integrated Hospital Emergency Admission Unit (4% vs. 23%; p=0.013). **Conclusion:** Patients presenting with hypertensive urgency tend to be treated more aggressively, and there is a place for anxiolytic therapy in hypertensive urgency management. Further research is needed to make definite conclusions.

**KEY WORDS:** hypertensive urgency, pre-hospital, out-of-hospital emergency medicine

**ADDRESS FOR CORRESPONDENCE:** Assoc. Prof. Ingrid Prkačin, MD, PhD  
Merkur University Hospital  
Ivana Zajca 19  
10 000 Zagreb, Croatia  
Tel: 0038512353-470; fax: 0038512431-393  
E-mail: ingrid.prkacin@gmail.com

## INTRODUCTION

Hypertension is quantitatively the most important risk factor for premature cardiovascular disease (1,2). Most people who have hypertension have no symptoms at all; this is why it is known as the 'silent killer' (3). Current estimates are that about 1% to 2% of patients with hypertension will have a hypertensive crisis at some point in their lifetime (4). Hypertensive crisis is a frequently used term, which includes both hypertensive emergency and hypertensive urgency. Hypertensive emergency (HE) is acute elevation of systolic blood pressure (SBP >180 mm Hg, DBP >120 mm Hg) accompanied by end organ damage primarily in

eyes, brain, heart, aorta and kidney (1,5). Hypertensive urgency (HU) is defined as acute elevation of blood pressure above the often used arbitrary limit of systolic blood pressure (SBP) >180 mm Hg and/or diastolic blood pressure (DBP) >120 mm Hg, without end organ damage (5). The prevalence of arterial hypertension in general public adults in Croatia is 37.5% (6). Around 5% of patient visits to the out-of-hospital Emergency Medical Service (EMS) units in Croatia are associated with hypertension. However, most of the patients do not present with HE (7). There are several up-to-date guidelines available for treating chronic hypertension; they address the management of HE and HU mostly in hospital environment, but there are no definite guide-

lines on pre-hospital management of HE and HU (1,8). The primary goal of intervention in hypertensive crisis is to safely reduce blood pressure in order to prevent end organ damage. The appropriate therapeutic approach to each patient will depend on their clinical presentation. History data, physical examination and instrumental evaluation determine the following management that could be oral (for urgencies) or intravenous (for emergencies) antihypertensive drugs (7).

The treatment of HE is usually carried out in hospital intensive care units with intravenous antihypertensive agents (9). Current guidelines recommend reduction of SBP by no more than 25% within the first hour, and then gradual reduction to normal SBP over the next 24 to 48 hours (9). On the other way, HU may in general be treated with oral antihypertensives on outpatient basis, and the target BP should be achieved over hours to days (10,11). Emotional reactivity and anxiety are associated with blood pressure elevations (12,13). When facing a patient with HU, the clinician will not only choose an appropriate antihypertensive agent, but will also assess how rapidly the blood pressure must be lowered. The main problem is that literature does not offer enough data to support one timetable over another (11). In an out-of-hospital environment, such as EMS unit, where a single EMS team is on duty and covers both field interventions and walk-in patients, long observations and follow-up are not always possible.

Our main goal was to evaluate adherence of pre-hospital EMS physicians to the available guidelines, and estimate whether they tended to be overly aggressive in lowering blood pressure due to the lack of observation and follow-up, as well as the patient extreme anxiety if dismissed without a significant SBP decrease.

## PATIENTS AND METHODS

We analyzed data from medical records of the EMS unit set up in the Community Health Center in the town of Sveti Ivan Zelina, branch of the Zagreb County Institute of Emergency Medicine, for a period of one year. The study was submitted to and approved by the institutional Committee on Ethics and Research. During the above-mentioned period, a total of 2911 patients were treated in EMS unit set up in the community health center and in 177 (6%) cases the primary diagnosis was arterial hypertension. Records from field interventions or interventions at patient home were not included in the research. Patients with HE and patients without two blood pressure measurements or recorded times of those measurements were excluded from the study. A total of 143 patients met all the criteria for this study, 44 men and 99 women. The patients were divided into two groups. The first group

consisted of 52 patients with AH, but without HU, and the second one consisted of 91 patients with the criteria for HU (SBP >180 mm Hg and/or DBP >120 mm Hg). Data included age, gender, therapy, blood pressure upon pre-hospital EMS unit admission, control blood pressure measurements after therapy administration, time from first to last measurement, referral to Integrated Hospital Emergency Admission Units, home, or general practitioner (GP). Patient therapy included antihypertensive therapy (AT; angiotensin-converting enzyme (ACE) inhibitors, calcium channel blockers, diuretics, fixed combinations); nitrates (isosorbide-dinitrate and glyceryl trinitrate pump spray); anxiolytics (benzodiazepines), urapidil ( $\alpha$ 1-adrenoceptor antagonist and 5-HT<sub>1A</sub> receptor agonist).

Descriptive analysis was performed for qualitative variables and quantitative results were presented as mean and standard deviation. Kolmogorov-Smirnov test was used to determine the normality of distribution of the tested parameters. Mann-Whitney U test was used to determine the significance of results. To compare qualitative variables,  $\chi^2$ -test and Fisher exact test were used depending on the sample size. Data analysis was performed by the IBM SPSS® software version 25.0 (IBM Corp., Armonk, NY, USA).

## RESULTS

General characteristics, clinical findings and outcomes of hypertensive patients with HU and control group of hypertensive patients without HU are shown in Table 1. Women predominated in both groups. There was no difference in the sex distribution of subjects in either group. There was no statistical significance between the groups in the number of patients having received medicines at home prior to arrival to EMS unit, but it was less common in HU group. In the HU group, 28% of patients received AT + nitrate combination, 18% nitrate, 16% nitrate + benzodiazepine, and 14% AT + nitrate + benzodiazepine with the biggest drop in SBP (21.9±5.2%). Five percent of patients in the HU group received oral urapidil as monotherapy. AT as the only medication administered was the least aggressive option with 14.1±5.0% drop in SBP during the follow-up. Control group patients received AT + nitrate combination (15%); nitrate + benzodiazepine (13%); and benzodiazepine (13%). The most significant drop in SBP (17.7±5.0%) was recorded in patients that received the AT + nitrate + benzodiazepine combination (8% of patients). The mean SPB decrease percentage regardless of therapeutic choice was 10.1±7%. In the HU group, the mean SBP reduction was 19.5±7.1%. Patients with HU had longer periods between the first and last blood pressure measurements (26±10 min vs. 34±15 min; p=0.017).



Table 1. General characteristics, clinical findings and outcomes of hypertensive patients with hypertensive urgency and control group of hypertensive patients without hypertensive urgency

	Patients with AH without HU	Patients with HU	p
Number of patients	52	91	
Women (%)	67	71	0.676
Age (years)	59±14	67±11	0.02
First SBP measured (mm Hg)	162±12	197±15	
Last SBP measured (mm Hg)	145±9	158±17	<0.01
Therapy applied prior to EMS visit (%)	40	43	0.718
Referred to Integrated Hospital Emergency Admission Unit (%)	4	21	0.052
Time from first to last measurement (min)	26±10	34±15	0.017

AH = arterial hypertension; HU = hypertensive urgency; SBP = systolic blood pressure; EMS = Emergency Medical Service

Thirteen of the 91 patients treated in the HU group were referred to the Integrated Hospital Emergency Admission Unit.

Less patients having received benzodiazepines were referred to the integrated hospital emergency admission units (4% vs. 23%;  $p=0.013$ ) (Table 2).

Table 2. Differences in blood pressure recording in the hypertensive urgency group according to the use of benzodiazepine therapy

	No benzodiazepine	Benzodiazepine	p
Number of patients	55	36	
Women (%)	69%	73%	0.688
Age (years)	66±12	69±10	0.208
First SBP measurement (mm Hg)	197±17	196±14	0.853
Last SBP measurement (mm Hg)	162±20	153±14	0.08
Percentage of SBP drop (%)	17.9±7.9%	21.9±5.2%	0.03
Referred to Integrated Hospital Emergency Admission Unit (%)	23%	4%	0.013

SPB = systolic blood pressure

## DISCUSSION

None of the available guidelines assessing HU management offer a definite timeline ideal for SPB reduction. However, slowly and safely decreasing SBP over hours to days is advised (11). The choice of specific AH drugs depend on the underlying causes of the crisis, patient demographics, comorbidities and cardiovascular risk (11). For emergencies, a maximum blood pressure reduction by 20%-25% within the first hour is considered appropriate, with further gradual decrease over the

next 24-48 h to reach normal blood pressure levels. In case of HU, gradual blood pressure lowering over 24-48 h with an oral medication is the best approach (1,11). In an out-of-hospital environment, long-term observation of a patient is not possible, which often results in more aggressive treatment and EMS overuse (14). Medical conditions for which EMS utilization can be considered avoidable are overrepresented (14). When we compared our data with those from other parts of Croatia, the incidence of hypertension in EMS unit was higher (the primary diagnosis was arterial hypertension in 6% of cases) than in Varaždin County (4.8%) (7). The incidence of HU was higher among females, the same as in other reference data (71%) (7). Adherence to chronic AT was higher in the AT group without HU (40/52 (77%) in AT group and 43/91 (47%) in HU). According to the available guidelines, adherence to therapy is one of the most important problems and a very common failure in patients with HU (1). Thirteen of the 91 patients treated in the HU group were referred to the Integrated Hospital Emergency Admission Unit, mostly because of the longer follow-up or additional workup was necessary. An interesting fact to point out is that none of the antihypertensives used during the research had the time to action onset shorter than one hour, and our average follow-up time was 34±15 minutes. Blood pressure reduction in HU is best achieved with oral medication with benzodiazepines, as we witnessed in our EMS. As far as we know, a systematic patient and doctor education program for hypertensive disorders does not exist in any country. Our data analysis showed the use of benzodiazepines in HU to be useful and have a much greater role in HU management than presumed. Differences in the settings, personnel, variety of antihypertensive drugs administered and time spent for observation should be taken into consideration when interpreting every case.

## CONCLUSION

Choosing the right antihypertensive therapy and dosage for a patient with HU is a challenge for every EMS physician, especially in an out-of-hospital environment. There is no unified approach and every patient needs to be assessed individually, however, structured approach through some form of guidelines, especially designed for out-of-hospital environment, could provide benefit for patients.

## REFERENCES

1. Williams B, Mancia G, Spiering W *et al.* 2018 ESH / ESC Guidelines for the management of arterial hypertension. *J Hypertens* 2018; 36(10): 1953-2041.
2. Lawes CMM, Hoorn S Vander, Rodgers A, Society I. Global burden of blood pressure-related disease, 2001. *Lancet* 2008; 371: 1513-8.
3. Prkačin I, Cavrić G, Dabo N, Kasumović D, Šantek L, Balenović D. Hitna stanja vezana uz hipertenziju. *Lijec Vjesn* 2014; 136 (Supl. 2): 100-3. (in Croatian)
4. Marik PE, Varon J. Hypertensive crises, challenges and management. *Chest* 2007; 131(6): 1949-62.
5. Baumann BM. Systemic hypertension. In: Tintinalli JE, Stapczynski JS, Ma OJ, Yealy DM, Meckler GD, Cline DM, editors. *Tintinalli's Emergency Medicine, A Comprehensive Study Guide*. Eighth edition. McGraw-Hill; 2016. p. 399-409.
6. Kralj V, Erceg M, Čukelj P. Epidemiologija hipertenzije u Hrvatskoj i svijetu / Epidemiology of hypertension in Croatia and worldwide. *Cardiol Croat* 2017; 16(3): 41.
7. Simić A, Neseck Adam V, Lukačević M. Arterijska hipertenzija u izvanbolničkoj hitnoj medicinskoj službi – retrospektivna analiza podataka bolesnika zbrinutih u Zavodu za hitnu medicinu Varaždinske županije / Arterial hypertension in outpatient emergency practice – retrospective analysis of hypertensive patients at the Emergency Medicine Department of Varaždin County. *Cardiol Croat* 2017; 12(3): 64.
8. Whelton PK, Carey RM, Aronow WS *et al.* 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. *J Am Coll Cardiol* 2018; 71: e127-e248.
9. Vamsi V, Kamath P, Achappa B, Prkacin I. Redefiniendo urgencia hipertensiva y emergencia hipertensiva maligna. *Rev Cient Med* 2019; 22 (1): 77-8.
10. Rodriguez MA, Kumar SK, Caro MD. Hypertensive crisis. *Cardiol Rev* 2010; 18(2): 102-7.
11. Maloberti A, Cassano G, Capsoni N *et al.* Therapeutic approach to hypertension urgencies and emergencies in the emergency room. *High Blood Press Cardiovasc Prev* 2018; 25(2): 177-89.
12. Ifeagwazi CM, Egberi HE, Chukwuorji JC. Emotional reactivity and blood pressure elevations: anxiety as a mediator. *Psychol Health Med* 2017; 22: 640-5.
13. Pan Y, Cai W, Qi C *et al.* Association between anxiety and hypertension: a systematic review and meta-analysis of epidemiological studies. *Neuropsychiatr Dis Treat* 2015; 11: 1121-30.
14. Kostanj D, Ben M, Keglevi MV. Ambulatory care sensitive conditions at out-of-hospital emergency services in Croatia: a longitudinal study based on routinely collected data. *Coll Antropol* 2014; 38(2): 143-8.
15. Rubin S, Cremer A, Boulestreau R *et al.* Malignant hypertension: diagnosis, treatment and prognosis with experience from the Bordeaux cohort. *J Hypertens* 2019; 37: 316-24.

## SAŽETAK

### ZBRINJAVANJE BOLESNIKA S HIPERTENZIVNOM KRIZOM U IZVANBOLNIČKIM UVJETIMA

D. RAOS<sup>1</sup>, F. PAŠTROVIĆ<sup>1</sup>, P.K. OKŠTAJNER<sup>1</sup>, M. VODANOVIĆ<sup>1</sup> I I. PRKAČIN<sup>2</sup>

<sup>1</sup>Zavod za hitnu medicinu Zagrebačke županije, Velika Gorica i <sup>2</sup>Klinička bolnica Merkur, Klinika za unutarnje bolesti, Sveučilište u Zagrebu, Medicinski fakultet, Zagreb, Hrvatska

Hipertenzivna hitna stanja zbrinjavaju se najčešće u izvanbolničkom okruženju u slučaju hitnosti bez oštećenja ciljnih organa, dok hipertenzivnu hitnoću s oštećenjem ciljnih organa treba zbrinuti u bolničkim uvjetima. Trenutne kao i prethodne smjernice nemaju jasne preporuke o zbrinjavanju bolesnika s hipertenzivnom krizom koja obuhvaća oba navedena pojma. Cilj ovoga istraživanja bio je procijeniti primjenu i pridržavanje postojećih smjernica za liječenje hipertenzivne krize u izvanbolničkim uvjetima. *Metode:* Analizirali smo podatke bolesnika koji su zbrinuti u izvanbolničkoj medicinskoj hitnoj službi Sv. Ivan Zelina u razdoblju od godine dana. Ukupno je bilo 2911 bolesnika, od toga je hipertenzija kao primarna dijagnoza bila u 177 (6 %) bolesnika, od kojih je 143 imalo uključne kriterije o podacima primijenjenog liječenja. Bolesnici su podijeljeni u dvije skupine: skupina s hipertenzivnom hitnošću (krvni tlak >180/120 mm Hg) bez oštećenja ciljnih organa i kontrolna skupina (krvni tlak <180/120 mm Hg). Uspoređivane su razlike u primjeni antihipertenzivnih i anksiolitičkih (benzodiazepin) lijekova. Rezultati: U skupini hipertenzivne hitnosti sniženje krvnog tlaka iznosilo je 19,5±7,1 %, a u kontrolnoj skupini 10,1±7 %. Najveće sniženje krvnog tlaka zabilježeno je u bolesnika s hipertenzivnom hitnošću koji su primali kombiniranu antihipertenzivnu terapiju uz dodatak nitrata i benzodiazepina (21,9±5,2 %), 14 % bolesnika. *Zaključak:* Bolesnike koji se očituju hipertenzivnom hitnošću bez oštećenja ciljnih organa (hipertenzivna urgencija) potrebno je liječiti kombiniranom terapijom u kojoj ima mjesta za dodatnu anksiolitičku terapiju benzodiazepinom. Daljnja istraživanja pokazat će značenje tog zaključka.

**KLJUČNE RIJEČI:** hipertenzivna hitnost, izvanbolničko okruženje, izvanbolnička hitna medicina