Original Article

Factors Associated with Successful Blood Pressure Control in Hypertensive Urgency Patients after 12-Week Treatment

Khamphukaew T, MD[1], Mitsungnern T, MD[2], Imoun S, MNS[3], Kotruchin P, MD, PhD[2]

[1] Emergency Medicine Unit, Nongbualamphu Hospital, Nongbualamphu, Thailand
[2] Department of Emergency Medicine, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand
[3] Department of Emergency Nursing, Srinagarind Hospital, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand

Background: Hypertensive urgency is a common presentation in the emergency room (ER). Current practice guidelines suggest that it is not necessary to meet a strict blood pressure (BP) target in ER. But patients should achieve the BP goal within weeks or a few months. However, there is limited data on the follow-up BP outcome and its determinants.

Objective: To evaluate factors associated with successful BP control for hypertensive urgency patients after a 12-week treatment.

Materials and Methods: A retrospective cohort study conducted at a university hospital in the Northeast of Thailand from 1st January 2012 to 31st December 2016. We enrolled hypertensive urgency patients who visited ER and received standard treatment and followed-up in the Hypertensive Crisis Clinic for 12 weeks.

Results: A successful BP control (<140/90 mmHg) was observed in 129 patients (56.1%). The factor that associated with a successful BP control was the achievement of three-lifestyle modification including medication adherence, aerobic exercise, and salt restriction (OR 1.79; 95% CI, 1.01 to 3.19; $p = 0.048$), not the baseline BP, number of medication, and underlying diseases.

Conclusion: Lifestyles modification was an effective strategy to achieve a targeted BP in the hypertensive urgency patient. Therefore, patients should be educated and encouraged to have healthy lifestyles.

Keywords: Hypertensive crisis, Emergency, Lifestyles modification, Thai, Salt restriction

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Hypertensive crisis is a common problem that brings patients to emergency room (ER), whether the patient has any symptoms or not[1]. There are two subcategories of hypertensive crisis; 1) Hypertensive emergency and 2) Hypertensive urgency, depending on the presence or absence of acute target organ damage[2]. The present study targeted the hypertensive urgency group which generally has minimal symptoms and without target organ damage[2,3].

Hypertensive urgency patients, although, have lower acute complications, but without appropriate blood pressure (BP) control, they are at very high risk for developing cardiovascular diseases in the long term[3,4]. It is not uncommon that untreated hypertensive urgency gives rise to a sustained high BP and end organ damage, sooner or later[4]. Therefore, ER physicians often prescribe oral anti-hypertensive medications and attempt to lower BP during patient's admission in the ER[1,5]. According to the present HT guidelines, before discharge, the doctor should prescribe oral anti-hypertensive medications and schedule a proper follow-up date for the patient[6]. However, little is known about the BP outcome and factors that are associated with BP control in a long-term follow-up. The previous studies have largely been retrospective reviews looking at small numbers of patients or focused on the short-term outcome[7-9].

Correspondence to:
Kotruchin P.
Emergency Cardiovascular Unit, Emergency Medicine Department, Faculty of Medicine, Khon Kaen University, Khon Kaen 40002, Thailand.
Phone: +66-65-5269422, **Fax:** +66-43-366870
E-mail: kpraew@kku.ac.th

Objective

To evaluate factors that associated with successful BP control for hypertensive urgency patients after a 12-week treatment.

Materials and Methods

This is a retrospective cohort study in a Hypertensive Crisis Clinic, Department of Emergency Medicine of a university hospital, Khon Kaen, Thailand. The study population was patients who visited the ER according to hypertensive crisis between 1st January 2012 and 31st December 2016. The inclusion criteria were as follow: Age ≥18 years old, had completed a 12-week follow-up, and had taken stable dose of anti-hypertensive medications within the past 4 weeks. The patients with hypertensive emergency, pregnant women, those who were lost to follow-up or were referred to other hospitals or clinics, and those with incomplete data were excluded from the final analysis. The study protocol was approved from the Khon Kaen University

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Ethics Committee in Human Research (HE591608).

Sample size calculation

The sample size was calculated by using the rule of thumb for 16 factors that had potential to affect the BP control rate from prior literatures (sex, hypertension, diabetes mellitus (DM), dyslipidemia, chronic kidney disease (CKD), gout, obesity, body mass index (BMI), smoking, systolic BP (SBP), diastolic BP (DBP), mean arterial pressure (MAP), medication, treatment time, and serum creatinine (Cr)). The estimated lost to follow-up rate was 40%; therefore, the total sample size of 220 was indicated.

Statistical analysis

Baseline characteristic data are shown as mean $\pm$ standard deviation (SD) or percentage (%). An independent sample t-test and a Chi-square test were used to compare between groups for continuous variables and categorical variables, respectively. A probability value <0.05 was considered statistically significant. Univariate analysis and multivariate analysis were used to identify factors that affect BP control. All statistical analyses were performed with SPSS for Mac version 20.0, registered to Khon Kaen University.

Operating definitions

BP control: The present study defined "controlled BP" in accordance to the 2018 ESC/ESH Guidelines for the management of arterial hypertension, which recommended that the first objective of treatment should be to lower BP to <140/90 mmHg in all patients[6]. Therefore, the "controlled BP group" referred to patients who had BP <140/90 mmHg after the 12-week treatment.

Hypertensive urgency: The present study defined hypertensive urgency by using the definition from the 2018 ESC/ESH Guidelines for the management of arterial hypertension; "Severe hypertension in patients presenting to the emergency department in whom there is no clinical evidence of acute HMOD"[6]. And the threshold for severe hypertension was the SBP of $\geq$180 mmHg and/or DBP of $\geq$120 mmHg.

ER discharge plan and Hypertensive Crisis Clinic: According to our hospital's ER workflow, hypertensive urgency patient who visits ER will be treated by ER physician or ER resident. The choice and number of anti-hypertensive medications (both in ER and as home medication) are chosen by the doctor based on the present standard practice guidelines. Every patient will be scheduled to the Hypertensive Crisis Clinic within the next 2 weeks for the first visit, then every 12 weeks later on. The Hypertensive Crisis Clinic was established in the year 2013 with 3 goals; easy access, efficient use of resource and no delay in treatment. The clinic's treatment strategies including making patients team members, gives adequate time, and uses the stage of change theory for encouraging healthy lifestyles. The clinic consists of doctors who are responsible for pharmacological treatments and a hypertension-specialized nurse who is responsible for providing health education, ensuring follow-up, reinforcing the BP goal and healthy lifestyles, and keeping contact with patients regularly. The follow-up schedule is every 2 to 4 weeks by online messaging after the first visit at the ER and then at least every 3 months at the clinic. Pharmacological treatment in the clinic is judged according to standard hypertension guidelines. The health education about lifestyles modification consists of 1) Medication adherence, 2) Aerobic exercise in hypertensive patients, and 3) Healthy foods and salt restriction.

Results

During the 5-year study period, there were 1,336 hypertensive crisis patients visited the emergency department, among them, 964 patients had hypertensive urgency. After excluded patients who were referred to other hospitals or clinics, patients with incomplete data, and patients who lost to follow-up, 229 eligible patients were included for the final analysis.

Baseline characteristics: Mean age was 59.9$\pm$12.0 years old, and 38.4% were men. More than half of the patients were known to have hypertension (57.2%). Most common co-morbidities were DM and dyslipidemia, 14.4% and 10.5%, respectively. Initial mean SBP and mean DBP were 199.2$\pm$17.7 mmHg and 109.9$\pm$14.2 mmHg. At ER discharge, mean SBP and mean DBP were 162.3$\pm$17.4 mmHg and 92.3$\pm$13.7 mmHg. Mostly 1 or 2 combinations of anti-hypertensive drugs were prescribed in the ER (84.8%). However, there was also 3-drug combinations prescribed (13.1%). The mean emergency department (ED) time was 196.6$\pm$97.2 minutes (3.3$\pm$1.6 hours). Most common anti-

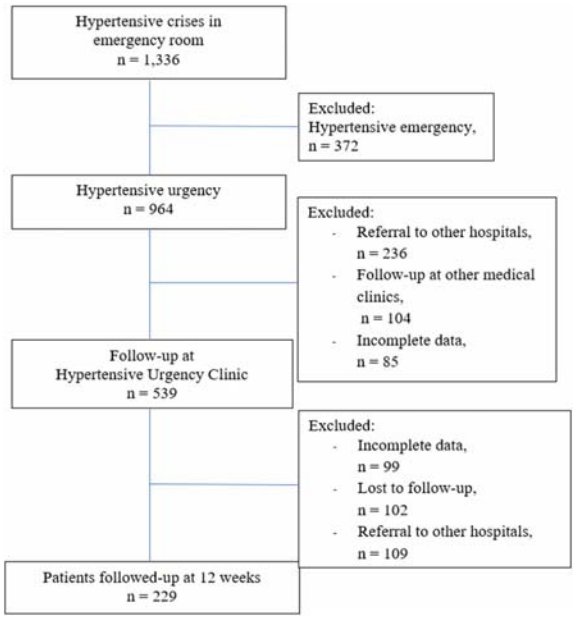

Figure 1. Flow of study patients.

hypertensive drug regimen for home medication was monotherapy (56.8%), and 26.2% of the patients had home blood pressure monitoring (HBPM) (Table 1).

Comparison between groups: Mean age was similar between two groups. The uncontrolled BP group had lower numbers of men than the controlled BP group, 45.5% vs. 54.5%, $p = 0.67$. The striking difference was the significantly higher numbers of DM patients in the uncontrolled group, 75.8% vs. 24.2% in the controlled BP group ($p<0.001$). Initial mean SBP in the uncontrolled BP group was significantly higher, 203.8±16.5 mmHg vs. 195.7±17.9 mmHg, $p<0.001$, while, DBP was not significantly different between uncontrolled BP and controlled BP group (111.0±14.0 mmHg vs. 109.0±14.4 mmHg, $p<0.001$). The SBP and DBP at ER discharge between two groups were not significantly different, 164.2±18.0 mmHg vs. 161.5±16.9 mmHg, $p = 0.243$ and 91.5±12.1 mmHg vs. 92.9±14.9 mmHg, $p = 0.429$, in the uncontrolled BP and controlled BP group, respectively. The controlled BP group was prescribed a single anti-hypertensive drug (monotherapy) as home medication more often, 64.6% vs. 35.4% of the uncontrolled BP group ($p = 0.004$). Many patients in both groups had HBPM, 41.7% and 58.3% in the uncontrolled BP and controlled BP group, respectively. Regarding lifestyles modification, the controlled BP group had significantly higher rate of medical adherence (56.3%) and aerobic exercise (60.5%) than the uncontrolled

Table 1. Baseline characteristics

	Total population (n = 229)	Controlled BP (n = 129)	Uncontrolled BP (n = 100)	*p*-value
Age, year (mean ± SD)	59.9±12.0	59.7±12.2	60.2±11.8	0.742
Men, n (%)	88 (38.4)	48 (54.5)	40 (45.5)	0.666
Known HT, n (%)	131 (57.2)	66 (50.4)	65 (49.6)	0.035
Underlying, n (%)				
DM	33 (14.4)	8 (24.2)	25 (75.8)	<0.001
DLP	24 (10.5)	9 (37.5)	15 (62.5)	0.049
CKD	4 (1.8)	3 (75.0)	1 (25.0)	0.447
Gout	5 (2.2)	2 (40.0)	3 (60.0)	0.456
BMI, kg/m^2	25.9±4.4	25.5±4.3	26.5±4.6	0.094
Office blood pressure, mmHg (mean ± SD)				
SBP				
ER initial	199.2±17.7	195.7±17.9	203.8±16.5	<0.001
ER discharge	162.3±17.4	161.5±16.9	164.2±18.0	0.243
1st visit (week 2)	152.2±21.7	146.2±19.9	160.0±21.6	<0.001
2nd visit (week 12)	140.0±20.6	128.3±11.5	155.1±19.8	<0.001
DBP				
ER initial	109.9±14.2	109.0±14.4	111.0±14.0	0.291
ER discharge	92.3±13.7	92.9±14.9	91.5±12.1	0.429
1st visit (week 2)	86.7±13.8	85.4±13.9	88.4±13.6	0.110
2nd visit (week 12)	80.4±13.2	76.2±11.0	85.9±13.8	<0.001
MAP				
ER initial	139.7±12.1	137.9±12.4	142.0±11.6	0.012
ER discharge	115.8±12.6	115.8±13.2	115.7±11.8	0.969
ER treatment (number of medications), n (%)				
1	97 (42.4)	59 (60.8)	38 (39.2)	0.239
2	97 (42.4)	51 (52.6)	46 (47.4)	0.326
3 or more	30 (13.1)	15 (50)	15 (50)	0.450
ER time, minute (mean ± SD)	196.6±97.3	197.8±97.7	195.2±97.2	0.840
Home medication (number of medications), n (%)				
1	130 (56.8)	84 (64.6)	46 (35.4)	0.004
2	71 (31.0)	36 (50.7)	35 (49.3)	0.259
3 or more	26 (11.4)	9 (34.6)	17 (65.4)	0.010
Home blood pressure monitoring, (%)	60 (26.2)	35 (58.3)	25 (41.7)	0.710
Lifestyles modification*				
Medicine adherence, n (%)	205 (89.5)	129 (56.3)	100 (43.7)	0.016
Salt restriction, n (%)	186 (81.2)	110 (59.1)	76 (40.9)	0.074
Aerobic exercise, n (%)	162 (70.7)	98 (60.5)	64 (39.5)	0.048
Creatinine at ER, mg/dl	210 (91.7)	0.87±0.30	0.86±0.33	0.950

BP = blood pressure, HT = hypertension, DM = diabetes mellitus, DLP = dyslipidemia, CKD = chronic kidney disease, BMI = body mass index, SBP = systolic blood pressure, DBP = diastolic blood pressure, MAP = mean arterial pressure, ER = emergency room
* Life style modification was evaluated at 8 to 12 weeks

BP group. Serum creatinine of the two groups was not significantly difference (0.87±0.30 mg/dl in the controlled BP group and 0.86±0.33 mg/dl in the uncontrolled BP group, $p = 0.950$) (Table 2).

Factors associated with successful blood pressure control: The patients with known hypertension, DM, and the patients who were prescribed more than one anti-hypertensive drugs as home medication had 44% (OR 0.56, 95% CI 0.33 to 0.96, $p = 0.037$), 80% (OR 0.20, 95% CI 0.09 to 0.46, $p<0.001$), and 51% (OR 0.49, 95% CI 0.29 to 0.84, $p = 0.010$) less likely to achieved goal BP (<140/90 mmHg) in a 12-week follow-up. On the other hand, the patients who had their lifestyles modified successfully were almost 2 times likely to achieve the BP goal than those who did not modified their lifestyles (OR 1.98, 95% CI 1.15 to 3.40, $p = 0.013$) (Table 2).

However, in a multivariate analysis, the only factor that had significant negative effect on achieving the BP goal was DM (OR 0.26, 95% CI 0.11 to 0.63, $p = 0.003$), and the only positive factor that associated with achieving the BP goal was successful lifestyles modification (OR 1.79, 95% CI 1.01 to 3.19, $p = 0.048$) (Table 3).

Discussion

Results from the 5-year retrospective cohort study showed that hypertensive urgency patients with DM were less likely to have their BP under controlled after 12-week treatment compared with those without DM. Interestingly, the only significant factor that associated with a successful BP control was a complete lifestyles modification including medication adherence, aerobic exercise, and salt restriction. Neither BP level nor number of anti-hypertensive medications

Table 2. Factors associated with successful blood pressure at 12 weeks by univariate analysis

Factors	Odds ratio	95% CI	*p*-value
Age, per one year	0.99	0.97, 1.02	0.741
Men	0.89	0.52, 1.52	0.667
Known HT	0.56	0.33, 0.96	0.037
DM	0.20	0.09, 0.46	<0.001
DLP	0.43	0.18, 1.02	0.054
CKD	2.36	0.24, 22.99	0.461
Gout	0.51	0.08, 3.11	0.465
BMI, per 1 kg/m^2	0.95	0.89, 1.01	0.095
Discharge SBP, per 1 mmHg	0.99	0.98, 1.01	0.243
Discharge DBP, per 1 mmHg	1.08	0.99, 1.03	0.427
Discharge MAP, per 1 mmHg	1.00	0.98, 1.02	0.969
ER medication >1 drug	0.67	0.39, 1.14	0.138
ER time >4 hours	0.89	0.50, 1.56	0.679
Home medication >1 drugs	0.49	0.29, 0.84	0.010
Successful lifestyles modification*	1.98	1.15, 3.40	0.013
Creatinine at ER, per 1 mg/dl	1.03	0.43, 2.45	0.950

HT = hypertension, DM = diabetes mellitus, DLP = dyslipidemia, CKD = chronic kidney disease, BMI = body mass index, SBP = systolic blood pressure, DBP = diastolic blood pressure, MAP = mean arterial pressure, ER = emergency room
* Successful lifestyles modification defined as medicine compliance 100%, salt restriction <3 grams per day and aerobic exercise at least 3 days per week.

Table 3. Factors associated with successful blood pressure control at 12 weeks by multivariate analysis

Factors	Adjusted odds ratio	95% CI	*p*-value
Known HT	0.83	0.46, 1.52	0.553
DM	0.26	0.11, 0.63	0.003
DLP	0.63	0.25, 1.63	0.341
BMI, per 1 kg/m^2	0.95	0.89, 1.02	0.152
ER medication >1 drug	0.72	0.41, 1.28	0.268
Home medication >1 drug	0.73	0.40, 1.35	0.315
Successful lifestyles modification*	1.79	1.01, 3.19	0.048

HT = hypertension, DM = diabetes mellitus, DLP = dyslipidemia, BMI = body mass index, ER = emergency room
* Successful lifestyles modification defined as medicine adherence 100%, salt restriction <3 grams per day and aerobic exercise at least 30 minutes per day and 3 days per week

had significant impact on BP control.

A study in Japan found that hypertensive patients who had DM as comorbidity were less likely to achieve BP control which was similar to our study[10]. However, a study in Turkey found opposite results. They reported that patients who had both DM and HT were more likely to achieve goal BP[11]. This difference might be explained by ethnicities. Japanese and Thai are similar and are different from the Turkish. Furthermore, in the study from Turkey, there were more patients with CKD (70%) and cardiovascular diseases (14%) than our study, which might affect the medication chosen and the BP goal[11].

In the present study, initial BP level and BP level before ER discharge were not associated with BP outcome at the 12th week follow-up. The results were in line with a study by Nakprasert, et al, they reported that BP before ER discharge (≥180 mmHg vs. <180 mmHg) was not associated with achieving goal BP at 2nd week follow-up[8]. However, another study of hypertensive urgency patients showed that BP before ER discharge had an impact on achieving goal BP (<140/90 mmHg) at a 2nd week follow-up[7]. When looked into details, these two studies had a different BP level before ER discharge (180 mmHg in the prior study vs. 160 mmHg in the latter, respectively), which might effect the inconsistent results.

In Thailand, hypertensive urgency patients, who visit ER usually, are treated by ER physicians or residents. The choice and number of anti-hypertensive medications may be varied according to preferences and experiences of doctors. In the present study, the authors found that numbers of medication both for immediate treatment in the ER and for home medication did not have any impact on achieving the BP goal after 12-weeks treatment. These results were consistent with prior studies[8,9,11]. Two studies were performed in Thai population. They compared one with two or more anti-hypertensive medication and found that there was no different in the BP control rate[7,8]. These results imply that the number of medication might not replace the importance of dosage and type of medication prescribed. However, little is known about dosage and type of anti-hypertensive medication. Further study may be required. Another important point to consider is adherence. It is prerequisite to achieve the BP goal. In any diseases, without adherence to medications, the treatment goal cannot be reached.

The main result of the present study was to find that the significant determinant of achieving a goal BP at 12th week was a complete lifestyles modification. Medication adherence was mentioned before and was known for its relevance to a long-term BP achievement in systematic review and meta-analysis[12]. Aerobic exercise was proved to decrease BP because it enhances physical regulations by decreasing the sympathetic tone and catecholamine level, followed by blood vessel dilatation and decreasing total vascular resistance: as a result, BP decreases[13,14]. There was a meta-analysis that recommended 30-minute aerobic exercise for 5 days in a week to lower SBP and DBP for 4.7 mmHg and 3.2 mmHg, respectively[15]. This recommendation has been adopted into current hypertension guidelines[6]. Salt restriction has been a back bone of lifestyles modification in hypertensive patients. Salt or sodium leads to vascular stiffness and increased total vascular resistance as well as vasoconstriction, resulting in hypertension[16]. There was a meta-analysis in African-Americans, Caucasians, and Asians, both hypertensive and normotensive subjects that reported the impact of salt restriction on BP level. One gram of salt restriction per day resulted in decreasing 0.94 mmHg and 0.62 mmHg of SBP and DBP, respectively[17].

Overall, our results added the importance of lifestyles modification because patients who had all three healthy lifestyles were more likely to have their BP controlled in 12th week than those who had not. Until now, lifestyles modification has proved its benefit for BP control in general hypertensive patients. Our study addressed its association with achieving BP controlled in hypertensive urgency patients who presented at ER with extremely high BP. We are aware that this was a retrospective study, therefore, the limitation is missing or incomplete data since the data were obtained from patient's charts collected at the Hypertensive Crisis Clinic.

Conclusion

Lifestyles modification including medication adherence, aerobic exercise, and salt restriction were impactful for BP control in hypertensive urgency patients, independent of underlying diseases, number of anti-hypertensive medications, and BMI. In conjunction to pharmacological treatment, hypertensive urgency patients should be educated and encouraged to have healthy lifestyles.

What is already known for this topic?

Lifestyles modification has been proved its benefit for BP control in general hypertensive patients.

What this study adds?

The present study emphasized the impact of lifestyle modification on achieving a long-term BP targets in hypertensive urgency patients.

Potential conflicts of interest

The authors declare no conflicts of interest.

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ปัจจัยที่เกี่ยวข้องกับความสำเร็จในการควบคุมความดันโลหิตได้ตามเป้าหมายในผู้ป่วยความดันโลหิตสูงวิกฤตหลังการรักษา 12 สัปดาห์

ธนวัฒน์ คำภูแก้ว, ฐปนวงศ์ มิตรสูงเนิน, สุภาพ อิ่มอ้วน, แพรว โคตรุฉิน

ภูมิหลัง: ความดันโลหิตสูงวิกฤตเป็นภาวะที่พบได้บ่อยในห้องฉุกเฉิน คำแนะนำในเวชปฏิบัติที่มีในปัจจุบันคือไม่จำเป็นต้องลดความดันโลหิตลงถึงระดับปกติเมื่อรักษาในห้องฉุกเฉิน แต่ผู้ป่วยควรมีระดับความดันโลหิตอยู่ในเป้าหมายภายในระยะเวลาเป็นสัปดาห์หรือเดือน อย่างไรก็ตามข้อมูลเกี่ยวกับผลลัพธ์ในการรักษาและปัจจัยที่ส่งผลต่อผลลัพธ์ในปัจจุบันยังมีน้อย

วัตถุประสงค์: เพื่อหาปัจจัยที่มีผลต่อความสำเร็จในการควบคุมความดันโลหิตให้ได้ตามเป้าหมายในผู้ป่วยความดันโลหิตสูงวิกฤตภายหลังจากการรักษา 12 สัปดาห์

วัสดุและวิธีการ: เป็นการศึกษาเชิงพรรณนาแบบย้อนหลังในผู้ป่วยความดันโลหิตสูงวิกฤตที่มารักษาที่ห้องฉุกเฉิน โรงพยาบาลมหาวิทยาลัยในภาคตะวันออกเฉียงเหนือของไทย ตั้งแต่ วันที่ 1 มกราคม พ.ศ. 2555 ถึง วันที่ 31 ธันวาคม พ.ศ. 2559 และมีนัดติดตามการรักษาอย่างน้อย 12 สัปดาห์

ผลการศึกษา: กลุ่มที่ควบคุมความดันโลหิตได้ <140/90 มม. ปรอท มีจำนวน 129 ราย (ร้อยละ 56.1) ปัจจัยที่มีผลต่อการควบคุมความดันโลหิตได้ตามเป้าหมายคือการปรับเปลี่ยนพฤติกรรมครบทั้ง 3 อย่าง ได้แก่ การรับประทานยาอย่างสม่ำเสมอ การออกกำลังกายแบบแอโรบิค และการจำกัดเกลือ (OR, 1.79; 95% CI, 1.01 ถึง 3.19; $p = 0.048$) ในขณะที่ค่าความดันตั้งต้น จำนวนของยาลดความดันโลหิต หรือโรคประจำตัวไม่มีผลต่อการควบคุมความดันโลหิต

สรุป: การปรับเปลี่ยนพฤติกรรมในผู้ป่วยความดันโลหิตสูงวิกฤตเป็นปัจจัยที่มีผลทำให้ควบคุมความดันโลหิตได้ตามเป้าหมาย ดังนั้นควรมีการให้ความรู้และสนับสนุนให้ผู้ป่วยมีพฤติกรรมสุขภาพ