Risk factors for hypertensive crisis: importance of out-patient blood pressure control

James E Tisdalea,b,d, Mike B Huangb,e and Steven Borzakc,f


Objectives. The purpose of this study was to identify independent risk factors for development of hypertensive crisis.

Methods. This was a retrospective, case-controlled study. Cases were 143 patients who presented during a 3-year period to the Emergency Department with the diagnosis of hypertensive crisis, defined as systolic pressure $\geq$180 mmHg and/or diastolic pressure $\geq$110 mmHg and symptoms of hypertensive emergency during the Emergency Department presentation. Controls were 485 patients with hypertension, matched to cases on the basis of age, sex and race, who were not admitted to the Emergency Department with an episode of hypertensive crisis during the study period. Co-morbid conditions were identified from computerized health system databases and medical records. Out-patient blood pressures were obtained from medical records from randomly selected out-patient clinic visits.

Results. The average blood pressure during Emergency Department presentation in patients with hypertensive crisis was 197 ± 21/108 ± 14 mmHg. Less successful out-patient systolic blood pressure control was an independent risk factor for hypertensive crisis [odds ratio (OR) 1.30 (1.18–1.42), per 10 mmHg, $P = 0.001$]. Higher out-patient diastolic blood pressures [OR 1.21 (0.99–1.43 per 10 mmHg, $P = 0.07$] and history of heart failure [OR 3.48 (0.94–12.94), $P = 0.06$] trended towards independence as risk factors.

Conclusion. Less effective blood pressure control, based on out-patient systolic blood pressure measurements, is an independent risk factor for an Emergency Department presentation due to hypertensive crisis.

Keywords. Blood pressure, hypertension, risk factors.

Introduction

Hypertensive crises are a common cause of medical urgencies or emergencies diagnosed in emergency rooms. Identification of risk factors for development of hypertensive crisis is important, so that specific patients at increased risk can be targeted for more aggressive therapy and/or risk factor intervention for the prevention of morbidity associated with acute severe blood pressure elevations. However, risk factors for the development of hypertensive crisis have not been studied extensively. A hypertensive crisis is known to occur more commonly in males and in African-Americans. In addition, hypertensive crises are known to occur with a peak incidence between the ages of 40 and 50 years. Other risk factors that predispose patients with hypertension to hypertensive crisis have not been determined. Intuitively, it may be expected that patients with less effective out-patient blood pressure control are at higher risk of experiencing an episode of hypertensive crisis, but this has never been reported in a published trial. Existing data have shown that non-adherence with antihypertensive medications independently increases the odds of severe, uncontrolled hypertension, suggesting that poorer blood pressure control may indeed be a risk factor for hypertensive crisis. The influence of co-morbid conditions such as heart failure or renal failure on the risk of hypertensive crisis is also
unknown. Heart failure is associated with elevated plasma concentrations of vasoconstricting substances such as norepinephrine, angiotensin II, endothelin, aldosterone and vasopressin, and heart failure and renal dysfunction are associated with fluid retention, all of which may be expected to predispose patients with chronic hypertension to hypertensive crisis. The purpose of this study was to identify risk factors for development of hypertensive crisis in patients with chronic hypertension. We hypothesized that the risk of hypertensive crisis is increased in patients with: (i) poorly controlled out-patient blood pressure; (ii) heart failure; and/or (iii) chronic renal dysfunction.

Methods

This was a retrospective, case-controlled study. Sources of data were the Henry Ford Health System database, the Health Alliance Plan database and review of medical records. The Henry Ford Health System database maintains information on all in-patients and ambulatory patients treated within the health system. Information maintained in this database includes demographics, in-patient and ambulatory clinic diagnoses according to the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9) codes, procedures, emergency room visits, billing codes, and other clinical and financial information. The Health Alliance Plan is a health maintenance organization owned and operated by Henry Ford Hospital, and its database provides information regarding prescribed drug therapy for enrolled patients.

Cases

Cases were patients who presented to the Emergency Department at Henry Ford Hospital with the diagnosis of hypertensive crisis during a 3-year period. Hypertensive crisis was defined as systolic blood pressure ≥180 mmHg and/or diastolic blood pressure ≥110 mmHg, in the presence of symptoms known to be associated with hypertensive emergency, based on ICD-9 codes assigned in the Emergency Department. Patients were initially included in the case group if the primary or secondary Emergency Department diagnosis was hypertension or a clinical manifestation of hypertensive crisis (Table 1). The following ICD codes were used to establish initially the Emergency Department diagnosis of hypertensive crisis: hypertension (401); hypertension, benign or malignant (401.0); hypertension, benign or malignant with congestive heart failure (402.01); hypertension, unspecified (401.9); hypertension, unspecified with congestive heart failure (402.91); hypertensive encephalopathy (437.2); aortic dissection (441.0); acute renal failure (584); unstable angina (411.1); and acute coronary insufficiency (411.89). Patients were excluded if the primary reason for admission was head injury or cerebrovascular accident. A total of 305 Emergency Department patients were assigned one of these ICD-9 codes. Medical records of these patients were reviewed to determine blood pressures during the Emergency Department presentation. Patients were included in the final case group only if the Emergency Department blood pressure was ≥180 mmHg systolic and/or ≥110 mmHg diastolic. Of the 305 patients who were assigned to one of the above ICD-9 codes, 143 patients met the inclusion criteria, and were included as cases of hypertensive crisis.

Controls

A total of 21,371 patients were identified in the Henry Ford Health System database with the ICD-9 code for hypertension (401). Controls were defined as patients with hypertension who were not admitted to the Emergency Department with an episode of hypertensive crisis.

<table>
<thead>
<tr>
<th>Signs/symptoms</th>
<th>Clinical manifestations/symptoms and physician-assigned diagnoses used to classify patients presenting to the Emergency Department with severely elevated blood pressure into the hypertensive crisis case group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute heart failure</td>
<td>Shortness of breath; crackles/rales suggestive of pulmonary oedema on chest auscultation; jugular venous distension; chest X-ray suggestive of pulmonary oedema; physician-assigned diagnosis of heart failure</td>
</tr>
<tr>
<td>Unstable angina or acute coronary insufficiency</td>
<td>Crushing, squeezing chest pain, chest tightness, chest pressure, with or without radiation to arms or jaw; physician-assigned diagnosis of unstable angina or acute coronary syndrome</td>
</tr>
<tr>
<td>Aortic dissection</td>
<td>Back or chest pain radiating to the arms; widening of the mediastinum on chest X-ray; echocardiogram, CT scan or MRI indicating aortic dissection; physician-assigned diagnosis of aortic dissection</td>
</tr>
<tr>
<td>Hypertensive encephalopathy</td>
<td>Mental status changes; physician-assigned diagnosis of hypertensive encephalopathy</td>
</tr>
<tr>
<td>Acute renal failure</td>
<td>Elevated serum creatinine; diminished urine output; physician-assigned diagnosis of acute renal failure</td>
</tr>
</tbody>
</table>

CT = computed tomography; MRI = magnetic resonance imaging.
crisis during the 3-year study period. Control patients were matched to the case population on the basis of age (±5 years), sex and race. Matching for age, sex and race was performed because these factors had been identified previously as risk factors for hypertensive crisis, and matching for these variables therefore allowed us to evaluate other risk factors in a matched population. Of the 21,371 patients identified as having received the diagnosis of hypertension, 485 were matched to the case group for age (±5 years), sex and race, and on this basis were selected as the control group. This sample size in the control group was selected because it allowed calculation of a statistically significant odds ratio (OR) of ≥2.0.

Randomization was performed using a random number generator feature available in Microsoft Excel version 7.0.

**Data collection**

Co-morbid conditions were identified from the computerized databases and medical records. To assess the degree of blood pressure control during treatment, blood pressures were obtained from medical records documented during randomly selected out-patient clinic visits.

**Statistical analysis**

Univariate analysis of risk factors for an Emergency Department visit due to hypertensive crisis was performed. Student’s unpaired t-test was used for parametric data, whereas chi-square or Fisher’s exact test was used for non-parametric data as appropriate. To identify independent risk factors for an Emergency Department visit due to hypertensive crisis, factors with a univariate P-value ≤0.30 were incorporated into a multivariate logistic regression analysis. Multivariate ORs for Emergency Department visits due to hypertensive crisis were calculated.

---

**Results**

**Patient characteristics**

Characteristics of patients included are presented in Table 2. By design, there were no significant differences between the groups in age, sex or race. The average blood pressure during Emergency Department presentation in the case group of patients with hypertensive crisis was 197 ± 21/108 ± 14 mmHg.

**Univariate analysis**

The prevalence of specific co-morbid conditions in the hypertensive crisis versus the control groups is presented in Table 2. A significantly higher proportion of hypertensive crisis patients had a history of heart failure than in the control group. There was a non-significant trend towards a higher frequency of chronic renal insufficiency in the hypertensive crisis group. Of interest, the number of antihypertensive drugs taken was significantly higher in the control group than in the hypertensive crisis group. A significantly higher proportion of patients in the case group were receiving no antihypertensive drug therapy compared with that in the control group (29.5 versus 6.0%, P < 0.001).

The degree of successful out-patient blood pressure control in the two groups is presented in Figure 1. Out-patient control of blood pressure was significantly better in the control group compared with that in the patients who subsequently presented to the Emergency Department with an episode of hypertensive crisis.

**Multivariate analysis**

Independent co-morbid risk factors for an Emergency Department visit due to hypertensive crisis are presented in Table 3. Less successful out-patient blood pressure control, measured in terms of systolic blood...
pressure, was a significant independent risk factor. The odds of an Emergency Department presentation due to hypertensive crisis were increased by 30% for every 10 mm increase in out-patient systolic blood pressure. There were non-significant trends towards history of heart failure and less well-controlled out-patient diastolic blood pressure as independent risk factors. The number of antihypertensive drugs taken was not a significant independent risk factor for hypertensive crisis.

ORs for an Emergency Department presentation due to hypertensive crisis based on varying increments of systolic and diastolic blood pressure are presented in Table 4.

Discussion

The results of this study demonstrate that less effective control of systolic blood pressure on an out-patient basis is an independent risk factor for hypertensive crisis leading to an Emergency Department presentation.

In the present study, average out-patient systolic blood pressures were ~14 mmHg lower in the group of patients who did not present with hypertensive crisis compared with the case group. Average out-patient diastolic blood pressures were 7 mmHg lower in the control group. The odds of an Emergency Department presentation due to hypertensive crisis were increased by 30% for every 10 mmHg increase in out-patient systolic blood pressure, and by 21% for every 10 mmHg increase in out-patient diastolic blood pressure. These data underscore the importance of adequate blood pressure control for reduction in morbidity associated with hypertension. The number of antihypertensive drugs taken was not an independent risk factor for hypertensive crisis, and therefore cannot necessarily be used as an indicator of more refractory (or better controlled) hypertension.

Relatively few studies have been performed to determine risk factors for hypertensive crisis in patients with chronic hypertension. Hypertensive crises occur most commonly in individuals between the ages of 40 and 50 years. African-American race and male sex are also known to be risk factors. In addition, socio-economic and patient factors including lack of a primary care physician, lack of medical insurance and non-adherence to antihypertensive regimens were found independently to increase the odds of severe, uncontrolled hypertension (mean blood pressure 222 ± 28/141 ± 15 mmHg) in an urban population of African-American and Hispanic patients. Illicit drug use or one or more alcohol-related problems were not found to be independent risk factors for severe, uncontrolled hypertension.

In the present study of hypertensive individuals, in which patients were matched for the previously known hypertensive crisis risk factors of age, sex and race, less effective control of out-patient systolic blood pressure was found to be an independent risk factor for hypertensive crisis. Although intuitively expected to be a risk factor, less well-controlled out-patient blood pressure has not been reported previously as a risk factor for hypertensive crisis. However, in a study of 189 patients who underwent digestive tract surgery, mean pre-operative systolic blood pressure was an independent risk factor for development of post-operative hypertensive urgency. In that study, for every 1 mmHg increase in pre-operative systolic blood pressure, the odds ratio for development of post-operative hypertensive urgency was 1.16, representing a 16% increase in risk for every 1 mmHg increase in systolic pressure. Therefore, in the post-surgical setting, higher pre-operative blood pressure is associated with an increased risk of post-operative hypertensive crisis.

### Table 3

<table>
<thead>
<tr>
<th>Co-morbid condition</th>
<th>Odds ratio (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic renal failure</td>
<td>1.48 (0.43–5.14)</td>
<td>0.54</td>
</tr>
<tr>
<td>History of heart failure</td>
<td>3.48 (0.94–12.94)</td>
<td>0.06</td>
</tr>
<tr>
<td>Out-patient systolic blood pressure</td>
<td>1.30 (1.18–1.42)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Out-patient diastolic blood pressure</td>
<td>1.21 (0.99–1.43)</td>
<td>0.07</td>
</tr>
<tr>
<td>No. of antihypertensive drugs taken</td>
<td>0.89 (0.57–1.41)</td>
<td>0.63</td>
</tr>
</tbody>
</table>

*a Odds ratio based on each 10 mmHg increase in blood pressure.

### Figure 1

Blood pressures during randomly selected out-patient clinic visits. Difference in systolic blood pressure: 13.8 mmHg (95% CI 10.1–17.6 mmHg); difference in diastolic blood pressure: 6.7 mmHg (95% CI 4.4–8.9 mmHg).

- = cases; = controls

### Table 3

Results of the multivariate analysis to determine independent co-morbid risk factors for an Emergency Department visit due to hypertensive crisis

Co-morbid condition                  | Odds ratio (95% CI) | P    |
-------------------------------------|---------------------|------|
| Chronic renal failure               | 1.48 (0.43–5.14)    | 0.54 |
| History of heart failure            | 3.48 (0.94–12.94)   | 0.06 |
| Out-patient systolic blood pressure | 1.30 (1.18–1.42)    | <0.001 |
| Out-patient diastolic blood pressure| 1.21 (0.99–1.43)    | 0.07 |
| No. of antihypertensive drugs taken | 0.89 (0.57–1.41)    | 0.63 |
In addition, as mentioned above, non-adherence with antihypertensive medication has been shown to be a risk factor for hypertensive crisis, presumably as a result of less effective blood pressure control. The design of the present study precluded an analysis of patient compliance with antihypertensive medication, and therefore it is unknown whether the poorer control of out-patient blood pressure in the hypertensive crisis group was a result of medication non-adherence, inadequate response to specific antihypertensive medications or both. In any event, the results of the present study further underscore the importance of adequate blood pressure control for avoidance of episodes of hypertensive crisis.

We hypothesized that a history of heart failure or renal dysfunction is also an independent risk factor for hypertensive crisis. Neither of these conditions independently increased the odds of a hospital presentation with hypertensive crisis. However, a trend towards statistical significance was present for history of heart failure, with an OR of 3.48. Heart failure is associated with well-known elevations in plasma norepinephrine, angiotensin II, endothelin, aldosterone and vasopressin concentrations, all of which are vasoconstricting and/or sodium-retaining substances that may contribute to elevation of blood pressure. Further study is necessary to determine whether heart failure is indeed an independent risk factor for hypertensive crisis, and also to establish whether control of heart failure symptoms or slowing of the progression of heart failure may reduce the risk of hypertensive crisis.

Limitations of this investigation should be acknowledged. This was a retrospective cohort trial, subject to the potential biases of such studies. As mentioned previously, information regarding patient adherence with antihypertensive medications was not available. Therefore, the impact of medication non-adherence as a risk factor for hypertensive crisis could not be evaluated in this study. Additional study is required to define the relative impact of medication non-adherence on the risk of hypertensive crisis.

The blood pressure definition of hypertensive crisis used in this study (>180/110 mmHg) was lower than that used in some previous studies. However, our definition of hypertensive crisis was based both on clinical signs/symptoms of hypertensive crisis that resulted in patient presentation to the Emergency Department and on a presenting blood pressure in the stage 3 range as defined by the sixth report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC-VI) guidelines. The definition of hypertensive crisis used in this study is therefore clinically relevant, and is consistent with the definition of hypertensive crisis as defined in JNC-VI as well as other published definitions.

Clinical implications
Less effective out-patient blood pressure control, as represented by out-patient systolic blood pressure measurements, is an independent risk factor for hypertensive crisis leading to an Emergency Department presentation. More aggressive and successful control of hypertension may therefore reduce the odds of hypertensive crisis in patients with chronic hypertension.

References