Original Science

Referral verses Early Treatment for Emergency Department Identified Hypertension: a Randomized Controlled Pilot Study Assessing Patient Compliance and Outcomes

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Abstract

Introduction: No randomized controlled trials (RCT) have assessed the safety or efficacy of initiating antihypertensive therapy at ED discharge for ED identified hypertension.

Methods and Materials: Patients with BP of > 160/90 mmHg on second measurement were randomized to follow-up referral or an antihypertensive medication prescription. Patients were interviewed via telephone at 3 weeks for compliance, symptoms, and outcome. Charts were reviewed for 3 years for serious complications.

Results: Eighty patients were enrolled, 77 interviewed. Follow-up compliance was 59.5% in the treatment group, 48.6% controls (a sample size of 350 patients would achieve statistical significance). Non-serious symptom rate was 33.3% in treatment group; 25.7%, controls. Mean systolic BP dropped between first, second (down 7 mm Hg), third measure (down 9 mmHg), and at clinic follow up (down 14 mmHg); 30 mm Hg total. Diastolic BP fell 14 mm Hg. There was no statistically significant difference in BP reduction between treatment groups at 3 week follow-up. Hypertension was confirmed in 75% of patients. Complications at 3 years post enrollment: 1 non-fatal stroke, 1 deterioration in renal function, and 1 patient died of cancer.

Conclusion: A funded RCT of 350 patients could demonstrate the safety and efficacy of initiating treatment for ED identified hypertension.

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Introduction

In the United States, over 40% of patients presenting to the Emergency Department (ED) have moderately to severely elevated blood pressure (BP).[1] In patients who do not carry a diagnosis of chronic hypertension, it is a challenge for emergency physicians to differentiate reactive hypertension from undiagnosed, untreated hypertension.[2] While a single abnormal measurement may not correlate with actual, underlying HTN, studies have shown that 26% to 70% of ED patients with an initial BP elevation will have persistently increased BP upon ambulatory clinic follow-up.[3-6]

In many instances, the finding of an elevated BP in the ED is incidental and from the perspective of related consequences, patients are asymptomatic.[7] There is widespread

confusion among ED physicians however, regarding the ideal approach to management of these individuals leading to divergent practice patterns.[8-11] Accordingly, inappropriate treatment (both under and over) is common,[5,11-16] which increases the likelihood of adverse outcomes.

The American College of Emergency Physicians recommends that patients with elevated blood pressure be referred for reassessment and treatment of elevated blood pressure.[17] However, emergency physicians overestimate the likelihood of timely follow-up for elevated blood pressure.18 Furthermore, patient compliance severely limits ACEP's follow up recommendation. Follow-up rates vary widely after an emergency department visit,[19-24] with a high of over 90% for insured patients with orthopedic injuries,[22] to 19% for uninsured patients with medical complaints.[24] Retrospectively, using our ED hypertension registry, we observed that hypertensive ED patients given a prescription for an antihypertensive medication at discharge followed up with a physician more frequently than those not receiving a prescription (76.1% vs 64.6%).[25]

The safety and efficacy of initiating antihypertensive therapy at ED discharge for ED identified hypertension has never been determined with a randomized controlled trial (RCT). The current study randomized patients to a prescription for an antihypertensive medication at discharge, or referral for follow up alone to examine patient outcomes, ongoing symptoms and/or medication side effects, and patient compliance.

Specific Aims

1. Determine if hypertensive ED patients (Systolic BP > 160-200 mm Hg or diastolic BP > 100-120 mm Hg) who are given a prescription for an antihypertensive medication at ED discharge follow-up with a primary care doctor more often at 3 weeks after the initial ED visit compared to patients in the referral only group.
2. Determine the rate of adverse events/side effects among patients receiving anti-hypertensive medication compared to the control group during the 3-week follow-up period.
3. Determine whether initiation of antihypertensive agents in the ED will lower systolic and diastolic blood pressure within 3 weeks of the initial ED visit.

Methods and Materials

Design: Randomized, non-blinded comparison of referral to primary care follow-up (control) verses an antihypertensive medication prescription prescribed at ED discharge plus referral for ED patients with persistently elevated BP > 160/100 mmHg on second measure. The study used a convenience sample based the availability of study investigators' non-clinical time to enroll patients while the physician on duty could serve as the treating physician, better serving as the patient's advocate.

Setting: Single, university-based emergency department with an annual volume of approximately 90,000 patients.

Inclusion criteria: age > 18 years; BP > 160/100 mmHg on second measure, 15 minutes after the first measurement while sitting comfortably; absence of an indication for admission to the hospital; non-pregnant; safe for discharge home, with or without a prescription for an antihypertensive medication in the judgement of the treating physician in the ED (non-investigator); patient willing and able to give written informed consent prior to study enrollment.

Exclusion criteria: Acute illness or injury requiring immediate intervention to prevent or limit a life-threatening event; blood pressure on the second measure that is above 200 mm Hg systolic, or 120 mmHg diastolic; patients with an indication to receive intravenous antihypertensive medication to reduce blood pressure prior to the 15 period minute of rest between the 1st and second measurement; patients with known hypertension who have been on antihypertensive medication within the past six months; pregnancy.

Sample Size Calculations: Observational data from the Hypertension Registry at Wake Forest University found that patients given an anti-hypertension medication prescription had follow-up rates of 76%, while hypertensive ED patients referred without being given a prescription had follow-up rates of 65%. Based on the retrospective data, for the primary outcome, a sample size of 224 patients yielded 80% power to detect a significant difference in follow up rates; a sample size of 300 patients would be required to yield 90% power to detect a significant difference in follow-up rate between groups.

Analysis Plan/Statistical methods: Chi-Square/Fishers Exact Test was used to assess the differences in frequency of categorical variables. Student's t-test and analysis of variance for repeated measures were be used to compare blood pressures between groups. Logistic regression analyses were used to assess the association of outpatient follow-up (yes/no) with treatment conditions and change in systolic and diastolic blood pressures.

Study Procedures: Block randomization was used (block sizes of 10) with a computer generated randomization schedule. If randomized to treatment, the patient's treatment physician selected an antihypertensive agent based on the patient's comorbidities based on JNC7 guidelines.[26] All consented patients received follow-up help from study personnel. Patients in the treatment group that expressed difficulty in purchasing an antihypertensive medication received an ED consultation with social services for medication access. Patients were called and assisted in making an appointment if they initially experienced resistance from physician office or clinic administrative staff.

Interviews: Patients were interviewed concerning follow-up compliance with a primary care physician and compliance with taking medicine if in the treatment group. Specifically, patients were asked if they were experiencing any symptoms that they believed were related to their elevated blood pressure or their medication if they were on medicine. Requests for records (form signed by patient at enrollment) were faxed to PCP offices so follow-up blood pressure values could be obtained.

Chart Review: Charts were reviewed up to 3 years post study enrollment to check for an ongoing diagnosis of hypertension and any significant complications of hypertension.

Human Subjects Protection: Informed consent was obtained from all patients; the protocol and consent were approved by the authors' institutional review board.

Results

Over 30 months, from January 2010, through June 2012, eighty-three patients were consented, 42 were randomized to the treatment arm, 41 control arm. Three control patients were withdrawn: 2 at the patient's request because the patient asked for a prescription off the study protocol, and 1 patient because the consultant requested hospital admission to manage a skin abscess larger than originally suspected. Eighty patients completed the full enrollment and ED discharge process. Seventy-seven patients were reached for interviews (96.25%). Our study group had a mean age of 54.5 years, 57.5% male 42.5% female, 57.5% African-American, 1.25% Hispanic, and 41.25% white.

Presenting Complaints: Thirteen patients (16%) presented with symptoms commonly associated with hypertension, with uncontrolled hypertension as their sole diagnosis: headache (6) asymptomatic hypertension found during routine measurement (5), and dizziness (2). The remaining 67 patients (84%) presented with a wide range of complaints and primary diagnoses, but also were diagnosed with uncontrolled hypertension. Of the 80 patients enrolled, 60 patients (75%) complained of pain while in the ED. In the group confirmed to have hypertension at short term follow-up (detailed below), 77% of those patients had complained of pain in the ED.

Follow-up Compliance: Forty-two patients (54.52%) followed up with a primary care physician as referred, representing 59.52 % of the treatment group, and 48.57% of the control group. This difference is not statistically significant. A sample size of 350 patients would be required to show statistical significance. Factors potentially contributing to follow-up compliance were entered in to a multivariate model including treatment group, prior history of hypertension, second blood pressure readings, and presence of ongoing symptoms. No factor had a statistically significant association with follow up compliance given the sample size of 77 patients with complete follow-up data. Of the 42 patients in the treatment group, 25 (59.5%) filled their prescription and followed up with a PCP, 10 filled the prescription but stopped taking the medicine by the time of the follow-up interview, 7 never filled the prescription.

Ongoing Symptoms/Medication Side Effects:
No patient sustained a serious side effect or complication prior to the follow-up phone interview, and/or follow up visit at three weeks post enrollment. In the control group,

25.71% of patients had ongoing symptoms while 33.33% of the treatment group had ongoing symptoms or side effects from the medications. The only symptoms in the treatment group not found in the control group were diuresis (4.76%) and peripheral edema (2.38%). Symptoms common in both groups were headache, dizziness, gastrointestinal irregularity, and fatigue.

Blood Pressure Changes with Time and Treatment: Systolic and diastolic blood pressures were compared between treatment and control groups to assess uniformity of the randomization process and the effect of treatment at three weeks follow up. Table 1 lists the systolic and diastolic changes in blood pressures during the ED stay.

Table 1. Mean Blood Pressures During The Emergency Department Stay

Measure	N	Mean	95%CI in mm Hg
First Systolic BP	80	179.4 mm Hg	175.3-183.4
First Diastolic BP	80	101.4 mm Hg	98.0-104.7
Second Systolic BP at 15 Minutes	80	172.2 mm Hg	168.5-175.8
Second Diastolic BP at 15 minutes	80	100.2 mm Hg	97.1-103.2
Systolic BP at Discharge	45	162.9 mm Hg	156.9-168.9
Diastolic BP at Discharge	45	94.7 mm Hg	89.6-99.8
Systolic BP at Clinic Follow-up	38	149.1 mm Hg	143.4-154.7
Diastolic BP at Clinic Follow-up	38	87.0 mm Hg	83.1-90.7

Abbreviations: BP = blood pressure, PCP = Primary care physician.

Without treatment, mean blood pressure values dropped during the patients' time in the ED. Mean systolic BP dropped 7 mm Hg between the first and the second measurement and 9 mm Hg between second and final ED measurement. At clinic follow up, mean systolic blood pressures were down 14 mmHg. The total drop in systolic blood pressure was 30 mm Hg. Total diastolic BP fell 14 mm Hg from first measure in the ED to clinic follow-up. There was no statistically significant difference in BP reduction between treatment groups during the ED stay, or at the 3 week follow-up, despite the treatment group having been prescribed an antihypertensive medication (see Table 2).

Table 2. Mean Blood Pressures of Control and Treatment Groups

	Control		Treatment	
Measurement	N	Mean (Std Dev)	N	Mean (Std Dev)
First ED Measurement	38	181.8/101.5 mm Hg (19.6/16.4)	42	177.1/101.2 mm Hg (19.0/13.8)
Second ED Measurement	38	171.9/100.2 mm Hg (16.6/12.9)	42	172.4/100.0 mm Hg (16.2/14.5)
Follow-up Clinic Measurement	17	143.3/81.1 mm Hg (10.6/9.13)	25	153.7/91.7 mm Hg (20.1/11.3)
Long Term Follow Up Measurement	36	148.2/88.5 mm Hg (20.7/13.3)	38	144.8/85.7 mm Hg (22.8/13.4)

Table 3. Mean Blood Pressures of Patients with and Without a Prior History of Hypertension

	Prior History of Hypertension		No Prior History of Hypertension	
Measurement	N	Mean (Std Dev)	N	Mean (Std Dev)
First ED Measurement	17	183.5/ 105.4 mm Hg (19.7/15.5)	63	177.7/100.2 mm Hg (16.1/12.7)
Second ED Measurement	17	175.4/106.7 mm Hg (17.4/15.6)	63	171.3/98.4 mm Hg (16.1/12.7)
Follow-up Clinic Measurement	9	144.8/90.0 mm Hg (16.1/11.0)	33	150.4/86.0 mm Hg (17.5/11.7)
Long Term Follow Up Measurement	15	140.2/88.8 mm Hg (15.2/9.1)	59	148.1/86.6 mm Hg (23.0/13.7)

We compared blood pressure characteristics for patients with a prior history of hypertension (17 of 80 patients) with those without a prior history of hypertension. These differences are shown in Table 3. Blood pressures were slightly higher in the ED, and slightly lower at clinic follow-up, but these differences were not statistically different by Students T Test.

Confirmation of ED Identified Hypertension and Management Changes: Forty-two patients (25 treatment, 17 control) followed up with a primary care physician. Of this group, the PCP confirmed the diagnosis of hypertension made by study criteria (> 160/100 on second measure after 15 minutes of rest) made in the ED in 73.8% of patients. If we exclude those patients who self reported a prior diagnosis of hypertension, confirmation drops slightly to 68.75%. In 52.38% of cases, the follow up physician continued the medication started in the ED, or started an antihypertensive for patient in the control group. In 9.52% of cases, a second antihypertensive was added to the medication started in the ED, and in 11.9% of cases, the patient was switched from the antihypertensive medication started in the ED to a new antihypertensive medication. Hydrochlorothiazide was the most common medication chosen by the treating physician in the ED for those patients in the treatment group.

Complications and Ongoing Hypertension at 3 Years Post Enrollment: Seventy-four of the original 80 patients enrolled (92.5%), 38 treatment, 36 control, were captured on chart review out to 3 years post enrollment. Serious complications of the entire group included one patient with non-fatal stroke, one patient with deterioration in renal function not requiring dialysis, and 1 patient who died of cancer related complications, presumed to be unrelated to the identification of hypertension in the study. Of those 74 patients captured on chart review, 57 (77.0%) carried the diagnosis of hypertension. If we exclude those patients who self-reported a diagnosis of hypertension prior to enrollment (16 patients), 43 of the 58 remaining patients (74.1%) carried the diagnosis of hypertension.

Discussion

This pilot study of early treatment for ED identified hypertension was underpowered to determine if writing a prescription for an antihypertensive medication at the time of ED discharge significantly enhanced the follow-up compliance in hypertensive patients. Our study design required balancing the fact that some patients presenting to the emergency department with elevated blood pressures will have normal blood pressures at follow up, and we found that 26% of patients in this study were normotensive at follow-up. When investigators raise the numerical threshold used to identify patients as "hypertensive," a greater percentage of patients will have the diagnosis of hypertension confirmed at follow up.[3] However, at the same time, the risk of complications due to untreated hypertension is incrementally higher as blood pressure rises.[27,28] Due to a lack of funding for study staff to enroll patients on a continuous basis, 30 months were required to enroll 80 patients in the study during periods when study authors were available to consent patients and ensure study procedures were followed.

Of patients compliant with short term follow-up, 73.8% of those identified by two blood pressure measurements > 160/100 Hg, 15 minutes apart, were confirmed as hypertensive in an office setting. If we exclude those patients who self-reported a prior diagnosis of hypertension, confirmation drops to 68.75%. Ultimately at 3 year follow up, with, 77% of patients meeting our inclusion criteria of two measurements 15 minutes apart, > 160/100 mm Hg, carried the diagnosis of hypertension. This simple method can be used to identify patients that are highly likely to benefit from follow-up with blood pressure recheck.

The association of pain and elevated has been long understood,[29] however, it appears over estimated as a cause of elevated blood pressures in the emergency department.[6,7] Tanabe and colleagues in their study of 156 emergency department patients sent home with ambulatory blood pressure monitors found no association with pain reported in the ED return of elevated blood pressures in the ED to normal pressures at home. In our study, the majority of patients reported pain in the ED (75%). Of the 42 patients who followed up as instructed, 31 patients were found to be hypertensive, and of those, 77% complained of pain in ED. We caution clinicians that while pain certainly may cause an elevation of blood pressure, attributing significantly elevated blood pressure on repeated measure in emergency department patients are likely to miss patients that should be treated, or followed in the primary care physician's office.

Unlike a recent retrospective study,[30] we did not find that a prescription of an antihypertensive medication significantly reduced blood pressures at 3 week is followup compared to the control group. In the study by Brody et al, the patients prescribed blood pressure medication had significantly higher blood pressures in the ED as compared to those not prescribed antihypertensives, while our treatment and control groups did not have blood pressure differences during their ED stay. Other ED studies have seen a phenomenon of ED blood pressure regressing back to the mean,[31] which could explain some of the drop in blood pressures in both studies. As noted in the retrospective study by Brody et al, we did not see any serious side effects in either group, those given a prescription, and those who received referral only. We saw diuresis and peripheral edema exclusively in the treatment group at a rate less than 5%, but ongoing symptoms are were found in both groups and symptoms of elevated blood pressure can easily be mistaken for side effects of the medication, such as dizziness, fatigue, headache, and gastrointestinal irregularity as seen in our control group.

Limitations

The major limitation of the study is the sample size, being a pilot study. Another limitation of the study is the unblinded design; however, the unblinded design allowed for a physician not connected with the study (the patient's treatment physician) to choose the antihypertensive best suited for the patient when randomized to the treatment arm, which added safety for the patient.

Conclusion

A funded randomized controlled trial of 350 patients would be required to confirm the differences between groups observed in this study are not due to chance, so that the safety and efficacy of initiating treatment for ED identified hypertension could be demonstrated.

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