Critical Review Form
Therapy

PGY-4

Patel KK, Young L, Howell EH, Hu B, Rutecki G, Thomas G, Rothberg MB. Characteristics and Outcomes of Patients Presenting With Hypertensive Urgency in the Office Setting. JAMA Intern Med. 2016 Jul 1;176(7):981-8.

Objectives: To test the hypothesis that "ambulatory patients with hypertensive urgency would have low rates of cardiovascular events in the short term and that referral to the hospital would not improve outcomes." (p. 982)

Methods: This retrospective cohort study was conducted at the Cleveland Clinic Healthcare System between January 1, 2008 and December 31, 2013. Patients presenting to any outpatient office with hypertensive urgency (defined as a systolic blood pressure [SBP] ≥180 mmHg or diastolic blood pressure [DBP] ≥ 110 mmHg) were eligible for inclusion. Patients who were pregnant, those referred to the hospital for symptoms, and those referred to the hospital for treatment of a condition other than hypertension were excluded. Patients were analyzed according to whether they were sent home from the office or referred to the hospital, either to the ED or for direct admission.

Patients were followed for 6 months following the index office visit. Patients referred to the ED were then matched to patients sent home in a 2:1 fashion using propensity matching. Outcomes measured included the incidence major adverse cardiac events (MACE) at 7 days, 1 month, and 6 months. Also evaluated was the incidence of uncontrolled hypertension at one month and six months, defined as a most recent blood pressure reading of at least 140/90 mmHg.

Out of 59836 office visits meeting criteria for hypertensive urgency during the study period, 851 were excluded, leaving 58535 patients in the final analysis. The mean age was 63.1 years, 57.7% were women, and 76.0% were white. The mean SBP was 182.5 mmHg and the mean DBP was 96.4 mmHg. Of this cohort, 426 (0.7%) were referred to the hospital.

Guide		Comments
I.	**Are the results valid?**	
A.	**Did experimental and control groups begin the study with a similar prognosis?**	
1.	Were patients randomized?	No. This was a retrospective, observational study. Patients were matched in a 2:1 fashion to case and

		control groups using propensity matching. Despite this effort to balance the two groups, the study is at high risk of selection bias.
2.	Was allocation concealed? In other words, was it possible to subvert the randomization process to ensure that a patient would be "randomized" to a particular group?	N/A. Patients were not randomized.
3.	Were patients analyzed in the groups to which they were randomized?	N/A. Patients were analyzed based on whether or not they were referred to the hospital from the clinic, but this was not a randomized controlled trial.
4.	Were patients in the treatment and control groups similar with respect to known prognostic factors?	No. Prior to propensity matching, patients sent to the hospital had overall higher blood pressure (mean SBP 16 mmHg higher, mean DBP 11 mmHg higher, $p < 0.001$), were more likely to have a SBP > 200 mmHg (51.2% vs. 9.9%), were more likely to have a history of hypertension (96.2% vs. 73.0%), and were more likely to have a history of chronic kidney disease (16.7% vs. 10.4%). Patients sent to the hospital were also much more likely to be African-American (36.9% vs. 19.6%).
B.	**Did experimental and control groups retain a similar prognosis after the study started?**	
1.	Were patients aware of group allocation?	Yes. This was retrospective study, making blinding impossible. It is unlikely, given the outcomes, that performance bias on the part of the patients would have affected the outcomes.
2.	Were clinicians aware of group allocation?	Yes. As above, clinicians were not blinded due to the retrospective nature of this study, as well as the intervention being assessed (decision to refer to the hospital vs. discharge home).
3.	Were outcome assessors aware of group allocation?	Likely yes. "All outcomes were identified electronically via codes from the *International Classification of Diseases, Ninth Revision*, and then manually adjudicated through medical record review by 2 independent reviewers." (p. 982) It is not stated whether these reviewers were blinded to group allocation. Cardiologists and neurologists making the diagnoses in the record would not have been blinded to group allocation (observer bias).
4.	Was follow-up complete?	No. Loss to follow-up occurred in 13.6% of patients referred to the hospital and 21.6% of

		patients sent home.
II.	**What are the results ?**	
1.	How large was the treatment effect?	<u>In unadjusted analysis:</u> • Patients sent to the hospital were more likely to have MACE at 7 days (RR 4.5, 95% CI 1.1 to 18), but not at 8-30 days (RR 2.3, 95% CI 0.57 to 9.2) or 1-6 months (RR 1.1, 95% CI 0.42 to 3.0). • Hospital admission rates were higher among patients referred to the hospital, both at 7 days (RR 2.1, 95% CI 1.5 to 2.8) and 8-30 days (RR 1.7, 95% CI 1.3 to 2.2). <u>Following propensity matching:</u> • There was no difference in the incidence of MACE between those referred to the hospital and those sent home at 7 days and 8-30 days (0.5% vs. 0%, RR ∞, 95% CI 0 to ∞), or at 1-6 months (RR 1.0, 95% CI 0.30 to 3.3). • Patients referred to the hospital were more likely to be admitted by 7 days (RR 1.8, 95% CI 1.1 to 2.7), and at 8-30 days (RR 1.6, 95% CI 1.1 to 2.3). • Patients sent home were more likely to have uncontrolled hypertension at one month (86.3% vs. 81.9%, p = 0.04), but there was no difference at 6 months.
2.	How precise was the estimate of the treatment effect?	See above.
III.	**How can I apply the results to patient care?**	
1.	Were the study patients similar to my patient?	Likely yes. This study enrolled patients seen in one of the clinics of the Cleveland Health Center and found to have elevated blood pressure without symptoms of end-organ damage. In this study, presumably all patients had access to follow-up as they were being seen in clinic, which would not apply to a large segment of our population. In addition, despite the authors' intentions, it seems likely that patients sent to the hospital were more likely to have some concerning signs or symptoms (leading to the plan to refer to the hospital).
2.	Were all clinically important outcomes considered?	Mostly yes. While MACE is a clinically appropriate, patient-centered outcome, hospital admission is substantially less important and more likely to be a result of the decision to send the patient to the hospital rather than the result of a

		concerning finding. The authors also did not consider acute or chronic renal failure, patient satisfaction, mortality, or quality of life.
3.	Are the likely treatment benefits worth the potential harm and costs?	No. This study indicates that the incidence of MACE in the 7 days to one month following discharge from a clinic visit with asymptomatic yet significantly elevated blood pressure is extremely low (0.1 and 0.2%, respectively), and that referral to the hospital does not seem to reduce this incidence. Overall, it would appear to be safe to discharge such patients home unless there is another, compelling reason to send them to the hospital.

Limitations:

1. **This was a retrospective, observational study at high risk of selection bias despite the use of propensity matching to attempt to balance the two groups being assessed.**

2. **No information was provided regarding who abstracted data from the medical record, or what sort of form was used to record abstracted data (Gilbert 1996 and Worster 2004).**

3. **No power analysis/sample size calculation was performed.**

4. **There was a high loss to follow-up in this study, approaching 20% overall (attrition bias).**

5. **It is notable that over 80% of patients in both groups had uncontrolled hypertension one month following the index office visit, suggesting either inadequate treatment or some degree of medication compliance.**

6. **The authors provided no measures of effect size or 95% confidence intervals.**

Bottom Line:

This retrospective, observational study of patients seen in clinic with asymptomatic yet significantly elevated blood pressure (SBP ≥ 180 or DBP ≥ 110) found a very low rate of adverse events among patients discharged home (0.1% at 7 days and 0.2% at 30 days). There was no difference in the rates of adverse events between those referred to the hospital and those sent home after propensity matching, despite higher rates of hospital admission at 7 days following the clinic visit.