Underdiagnosis of Isolated Systolic and Isolated Diastolic Hypertension

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Systolic and diastolic hypertension independently predict the risk of adverse cardiovascular events. It remains unclear how systolic pressure, diastolic pressure, and other patient characteristics influence the initial diagnosis of hypertension. Here, we use a cohort of 146,816 adults in a large healthcare system to examine how elevated systolic and/or diastolic blood pressure measurements influence initial diagnosis of hypertension and how other patient characteristics influence the diagnosis. Thirty-four percent of the cohort were diagnosed with hypertension within 1 year. In multivariable logistic regression of the diagnosis of hypertension, controlling for covariates, isolated systolic hypertensive measures (odds ratio [OR] 0.42 [95% confidence interval {CI} 0.41 to 0.43]) and isolated diastolic hypertensive measures (OR 0.32 [95% CI 0.31 to 0.33]) were less likely to lead to hypertension diagnosis when compared with combined hypertensive measures. Higher levels of systolic blood pressure had a greater impact on hypertension diagnosis (OR 1.77 [95% CI 1.75 to 1.79] per Z-score) than did higher levels of diastolic blood pressure (OR 1.34 [95% CI 1.32 to 1.36] per Z-score). Older age, non-white race/ethnicity, and medical comorbidities all predicted the establishment of a diagnosis of hypertension. Isolated systolic and isolated diastolic hypertension are underdiagnosed in clinical practice, and several patient-centered factors also strongly influence whether a diagnosis is made. In conclusion, our findings uncover a care gap that can be closed with increased attention to the independent influence of systolic and diastolic hypertension and the various patient-centered factors that may impact hypertension diagnosis. **© 2020 Elsevier Inc. All rights reserved.** **(Am J Cardiol 2021;141:56−61)**

Patients with hypertension have elevated risk of adverse cardiovascular events, and reducing blood pressure is known to reduce these risks.[1,2] Diagnosing hypertension is a critical first step in order to treat with interventions such as diet, exercise, and antihypertensive medications.[1] Many patients with potentially treatable hypertension remain undiagnosed,[3,4] with missed diagnoses particularly likely among women[3] and young adults.[4,5] In particular, lower recognition of isolated diastolic hypertension might lead to underdiagnosis of young adults.[5] Hypertension diagnosis may also vary according to race/ethnicity.[6] Both systolic and diastolic blood pressure are routinely recorded during outpatient visits, offering an opportunity to identify hypertension, but only a minority of those with multiple high values recorded receive diagnosis and treatment.[1,4,7−9] Both systolic and diastolic hypertension strongly and independently predict the risk of adverse cardiovascular outcomes,[10] but the relative contribution of these two components of blood pressure to the initial diagnosis of hypertension remains unknown. Therefore, we sought to examine the impact of systolic and diastolic blood pressure elevations on the initial diagnosis of hypertension in a large population of adults in an integrated healthcare delivery system.

Methods

This is a retrospective, data-only, cohort study, focused on the diagnosis of incident essential hypertension among members of a large, membership-based integrated healthcare delivery system. The study was conducted in Kaiser Permanente Northern California, a system with >4 million members that are demographically representative of the broader population of Northern California.[11] KPNC has an outpatient and inpatient electronic medical record with electronic medication prescription and electronic documentation of diagnoses via an EMR Problem List. Medication prescriptions are filled at plan pharmacies and require the prescribing clinician to identify a diagnosis linkage for every prescription.[12] In particular, prescribing an antihypertensive medication requires the provider to electronically link this prescription to an existing or new diagnosis of hypertension. KPNC members choose, or are assigned, a personal primary care physician (PCP). The source of blood pressure measurements was recorded for all measures as

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obtained from a PCP visit or another visit type. Blood pressure control has been an important priority within KPNC, resulting in higher rates of blood pressure control compared with other systems of care delivery.[13]

Between January 1, 2008 and December 31, 2015, we enrolled all adult members not previously identified as hypertensive who had either 2 successive elevated outpatient blood pressure measurements (within 2 years of each other) or any 2 elevated measurements within 30 days, subject to the following inclusion criteria: (1) the second of these measurements (the index measurement) was made in internal medicine or family practice clinic, and (2) the patient was a member of the plan for 2 full years before and 1 full year after their index hypertension diagnosis. Requiring 2 years prior membership minimized the chance that patients were being actively treated for hypertension but had not yet filled a prescription at a KPNC pharmacy; requiring one year of enrollment after the index date ensured consistent information about hypertension diagnosis and treatment. None of the included subjects were on antihypertensive medications.

For all subjects, we obtained patient characteristics including age (transformed to ln(age) for use in models), sex, race/ethnicity, body mass index and medical comorbidities including congestive heart failure, coronary artery disease, diabetes mellitus, a history of stroke, hypercholesterolemia, and tobacco use (current or former). PCP visits were also recorded.

Outpatient blood pressure measures in KPNC were obtained with validated automated oscillometric blood pressure cuff systems (Mindray Accutorr [Mahwah, NJ] & Welch Allen [Skaneateles Falls, NY]) by a medical assistant or nurse trained in guidelines-based recommendations for blood pressure measurement,[1] as previously described.[10,13] All clinic blood pressures were directly entered into the electronic medical record as previously described.[10,13]As all outpatient blood pressure measurements in routine clinical practice were obtained, measurements were taken across the regular clinical hours of operation, not at a particular time of day. We included all outpatient blood pressure measurements for all subjects identified by our inclusion/exclusion criteria as described above, including patients in long-term care, but inpatient blood pressure measurements were not included.

The primary outcome measure was identification of hypertension as an ongoing problem within a year of the index measurement. Patients were identified as positive for hypertension identification as of the day when they either had hypertension recorded in the problem list component of their EMR chart or had a medication ordered with a diagnosis of hypertension linked to the medication prescription. Medications ordered to treat hypertension were captured by electronic prescription for an antihypertensive medication together with a diagnosis of hypertension electronically linked to the prescription (all medications in KPNC are electronically prescribed and each prescription requires electronic linkage to a specific diagnosis). Having a diagnosis of hypertension recorded at a visit was not sufficient unless the condition was identified as an ongoing problem by addition of hypertension to the EMR problem list or by linkage to an antihypertensive medication prescription. We used this strict definition because false positives are likely when one relies on a single diagnosis entered during a visit, particularly as EMR charting rules require that every visit must have at least one entered diagnosis.

We sought to identify how initial hypertension diagnosis was influenced by the type of high blood pressure (systolic and diastolic elevation, isolated systolic elevation, or isolated diastolic elevation), the magnitude of recorded pressures, patient demographics, and medical comorbidities. We used multivariable logistic regression to explore the impact of the level and type of hypertension on the probability of initial hypertension diagnosis. For models including presence of hypertension according to measured blood pressure, consensus definitions based on guidelines present at the time of the study period were used (systolic $\geq$140 mm Hg, diastolic $\geq$90 mm Hg).[1] For models including continuous systolic and diastolic pressures, blood pressures measured in mmHg were converted to Z-scores ($\pm$standard deviations from the study population mean) as previously described,[10] to avoid creating bias from the differing range of values for systolic compared with diastolic blood pressure. Where indicated, multivariable models included control for subject characteristics, medical comorbidities, and visits to their personal PCP as described above. Specific covariates included in each model are presented along with results. Bivariate analyses were performed with the Chi-square test for categorical variables and Student's *t* test for continuous data. Statistical analyses were performed with SAS version 9.4 (Cary, NC).

Approvals: The KPNC Institutional Review Board approved this retrospective data-only study with waiver of informed consent.

Results

We identified 146,816 patients with incident, recurring high blood pressure measurements, based on a threshold of $\geq$140 mm Hg for systolic blood pressure or $\geq$90 mm Hg for diastolic blood pressure. We calculated descriptive statistics and bivariate relationships between predictors and the primary outcome measure (hypertension diagnosis within 1 year). Table 1 shows baseline patient characteristics at the time of the index visit.

Within one year of the index measurement, 34.0% were diagnosed with hypertension (either prescribed an antihypertensive medication for a linked diagnosis of hypertension or had a diagnosis of hypertension recorded as a chronic problem in the EMR problem list).

The type of blood pressure elevation (systolic or diastolic) strongly influenced whether incident hypertension was diagnosed within a year. Isolated systolic hypertensive measures (systolic $\geq$140 mm Hg with diastolic <90 mm Hg) were the most common type of hypertensive measures found among subjects diagnosed with hypertension, with combined hypertension (systolic $\geq$ 140 mm Hg and diastolic $\geq$90 mm Hg) being the second-most common (Table 2). Isolated diastolic hypertensive measures were present in only 9% of subjects diagnosed with hypertension, while 17% of subjects not diagnosed with hypertension had isolated diastolic measures (Table 2).

Table 1
Baseline patient characteristics according to diagnosis of hypertension

Variable	Diagnosis of hypertension: Yes (n = 46929)	No (n = 99887)	P value
Age (years)	54.5 (54.4-54.6)	51.8 (51.7-51.8)	<0.001
Women	23465 (50.0%, 49.6-50.4%)	50344 (50.4%, 50.1-50.6%)	0.1
White	25154 (53.6%, 53.2-53.9%)	58335 (58.4%, 58.1-58.6%)	<0.001
Black	4271 (9.1%, 8.8-9.3%)	7392 (7.4%, 7.3-7.5%)	
Hispanic	7228 (15.4%, 15.1-15.6%)	15583 (15.6%, 15.4-15.8%)	
Asian	6805 (14.5%, 14.2-14.7%)	11088 (11.1%, 10.9-11.3%)	
Other Ethnicity/Unknown	3567 (7.6%, 7.4-7.8%)	7492 (7.5%, 7.4-7.7%)	
Diabetes mellitus	3145 (6.7%, 6.5-6.9%)	3796 (3.8%, 3.7-3.9%)	<0.001
Atrial fibrillation	845 (1.8%, 1.7%-1.9%)	1699 (1.7%, 1.6%-1.8%)	0.24
CAD or History of MI	470 (1.0%, 0.9-1.1%)	700 (0.7%, 0.6-0.7%)	<0.001
Prior stroke	141 (0.3%, 0.3-0.3%)	200 (0.2%, 0.2-0.2%)	<0.001
Hyperlipidemia	1408 (3.0%, 2.8-3.1%)	2298 (2.3%, 2.2-2.3%)	<0.001
Congestive heart failure	329 (0.7%, 0.6-0.7%)	400 (0.4%, 0.4-0.5%)	<0.001
Body Mass Index (kg/m^2)	30.4 (30.3-30.4)	29.9 (29.8-29.9)	<0.001
Tobacco use (current)	1596 (3.4%, 3.2-3.5%)	2298 (2.3%, 2.3-2.4%)	<0.001
Tobacco use (former)	1784 (3.8%, 3.6-3.9%)	4396 (4.4%, 4.2-4.5%)	<0.001
Primary Care Provider visit	28956 (61.7%, 61.3-62.0%)	51942 (52.0%, 51.7-52.2%)	<0.001

In multivariable logistic regression of the diagnosis of hypertension within 1 year, combined hypertensive measures had the greatest influence on hypertension diagnosis, while isolated systolic hypertensive values had an intermediate influence, and isolated diastolic hypertensive values had the least impact on the diagnosis of hypertension (Table 3). This relationship persisted after control for the full list of measured covariates (Table 3). Several individual covariates, such as age, non-white race/ethnicity, and medical comorbidities were each independently associated with a hypertension diagnosis being made, while prior smoking had a negative association with hypertension diagnosis (Table 3).

We found a similar bias toward systolic blood pressure in predicting the diagnosis of hypertension when we examined the degree of systolic and diastolic blood pressure elevation as Z-score standardized continuous predictors in multivariable logistic regression of hypertension diagnosis by 1 year (Table 4). This relationship was also robust to control for covariates, and the relationships between age, race/ethnicity, and comorbidities with the diagnosis of hypertension were all maintained (Table 4).

Discussion

We found that combined elevation of systolic and diastolic blood pressure had a greater impact than isolated elevation in either systolic or diastolic blood pressure on the initial diagnosis of hypertension. This underdiagnosis of hypertension was even more apparent for isolated elevation in diastolic blood pressure.

In the current revision of the American College of Cardiology (ACC)/American Heart Association guidelines for the diagnosis and treatment of hypertension issued in 2017, the diagnosis of hypertension in the general population is made when 2 or more blood pressures are obtained with systolic ≥140 and/or diastolic ≥90.[1] Based on the results of the SPRINT trial,[14] the 2017 ACC/American Heart Association revision also recommended diagnosis of hypertension

Table 2
Blood pressure measures according to diagnosis of hypertension

Variable	Diagnosis of hypertension: Yes (n = 46929)	No (n = 99887)	P value
Hypertensive Measure Type			<0.001
Combined (>140/90 mmHg)	19429 (41.4%, 41.0-41.8%)	24273 (24.3%, 24.1-24.6%)	
Isolated systolic (>140 mmHg)	23324 (49.7%, 49.3-50.0%)	58634 (58.7%, 58.4-58.9%)	
Isolated diastolic (>90 mmHg)	4224 (9.0%, 8.8-9.2%)	16981 (17.0%, 16.8-17.2%)	
Mean Blood Pressures			
Systolic (mmHg)	150.8 (150.7-150.9)	145.2 (145.2-145.3)	<0.001
Diastolic (mmHg)	88 (87.9-88.1)	85.4 (85.4-85.5)	<0.001

Categorical measures (Hypertensive Measure Type [type of hypertension found in the index measure]) are presented as *n* (%, 95% CI), and continuous measures (Mean Blood Pressures) are presented as mean (95% CI).

Table 3
Multivariable logistic regression of diagnosis of hypertension by presence of systolic or diastolic hypertension

Variable	Model 1: BP Only Odds ratio (95% CI)	P value	Model 2: Control for covariates Odds ratio (95% CI)	P value
Type of BP Measure				
Systolic ≥ 140 mmHg (vs. combined ≥ 140/90 mmHg)	0.47 (0.46-0.48)	< 0.001	0.42 (0.41-0.43)	< 0.001
Diastolic ≥ 90 mmHg (vs. combined ≥140/90 mmHg)	0.31 (0.29-0.32)	< 0.001	0.32 (0.31-0.33)	< 0.001
ln(Age)			2.49 (2.39-2.60)	<0.001
Female			0.96 (0.94-0.98)	<0.001
Black (vs. White)			1.41 (1.35-1.47)	<0.001
Hispanic (vs. White)			1.19 (1.16-1.23)	<0.001
Asian (vs. White)			1.70 (1.65-1.76)	<0.001
Other / Unknown (vs. White)			1.20 (1.14-1.25)	<0.001
Diabetes mellitus			2.09 (1.96-2.22)	<0.001
Atrial fibrillation			0.93 (0.85-1.01)	0.098
CAD or History of MI			1.55 (1.33-1.80)	< 0.001
Prior stroke			1.24 (0.92-1.66)	0.15
Hyperlipidemia			1.12 (1.04-1.20)	0.004
Congestive heart failure			1.30 (1.08-1.64)	0.007
Body Mass Index (kg/m^2)			1.02 (1.02-1.02)	<0.001
Tobacco use (current)			1.85 (1.66-2.07)	<0.001
Tobacco use (former)			0.95 (0.90-0.99)	0.047
Primary Care Provider visit			1.41 (1.38-1.44)	<0.001

in individuals with high cardiovascular risk above a threshold of ≥130/80,[1] but this change from prior guidelines did not take effect until after the period of our study (2008 to 2015).

Hypertension is generally an asymptomatic medical condition, and therefore the initial diagnosis of hypertension requires several factors to be present, including recognition of the need for screening (awareness), performance of screening and recording of blood pressure measurements in an accessible fashion, and application of guidelines-based systolic and diastolic hypertension definitions to make the diagnosis.[1] It is estimated that less than half of people with hypertension are aware that they have it.[8,9] Among those treated for hypertension, estimates of blood pressure control are typically low, ranging across studies from 7%[7] to 33%.[8] The process of diagnosing and successfully treating hypertension is therefore a pipeline that suffers from potential inefficiencies at each stage.

Table 4
Multivariable logistic regression of diagnosis of hypertension by systolic or diastolic blood pressure

Variable	Model 1: BP Only Odds ratio (95% CI)	P value	Model 2: Control for covariates Odds ratio (95% CI)	P value
Systolic blood pressure (per Z-score)	1.77 (1.75-1.79)	<0.001	1.69 (1.67-1.72)	<0.001
Diastolic blood pressure (per Z-score)	1.34 (1.32-1.36)	<0.001	1.43 (1.41-1.45)	<0.001
ln(Age)			2.26 (2.17-2.36)	<0.001
Female			0.96 (0.94-0.99)	0.003
Black (vs. White)			1.40 (1.34-1.47)	<0.001
Hispanic (vs. White)			1.22 (1.18-1.26)	<0.001
Asian (vs. White)			1.69 (1.63-1.75)	<0.001
Other/Unknown (vs. White)			1.20 (1.14-1.25)	<0.001
Diabetes mellitus			2.15 (2.01-2.29)	<0.001
Atrial fibrillation			0.99 (0.91-1.09)	0.88
CAD or history of MI			1.74 (1.49-2.03)	<0.001
Prior stroke			1.29 (0.95-1.74)	0.10
Hyperlipidemia			1.15 (1.06-1.24)	<0.001
Congestive heart failure			1.37 (1.11-1.70)	0.004
Body Mass Index (kg/m^2)			1.02 (1.02-1.02)	<0.001
Tobacco use (current)			1.80 (1.61-2.01)	<0.001
Tobacco use (former)			0.95 (0.90-0.99)	0.037
Primary Care Provider visit			1.43 (1.40-1.47)	<0.001

Odds ratios for systolic and diastolic blood pressures are per Z-score (standard deviations from the mean), relative to the mean (Z score of 0).

Significant progress has been made in using organized systems of care to improve blood pressure control among patients already diagnosed with hypertension requiring treatment. For example, deployment of a large-scale hypertension treatment program in the integrated healthcare system from which the present study is derived led to an improvement in hypertension control from 44% to 80%.[13] Home blood pressure telemonitoring with pharmacist management has also been successful in improving blood pressure control.[15]

Far less is known about how integrated systems of care might improve recognition and initial diagnosis of hypertension. It is possible that approaches such as best practice alerts or other methods of provider feedback might help to capture the initial diagnosis of hypertension—similar techniques have shown success in improving hypertension control among patients already diagnosed with hypertension.[13,16] Systems could be designed to identify systolic and/or diastolic hypertensive measures to maximize the chances of capturing the initial diagnosis of hypertension according to published guidelines.[1] Such tools may also be helpful in improving provider awareness of combined hypertension, isolated systolic hypertension, and isolated diastolic hypertension as potentially distinct entities, with different pathophysiological implications.[17]

Provider-assigned diagnosis of hypertension in the presence of hypertensive measures was also strongly influenced by age, race/ethnicity, and medical comorbidities. Each measured comorbidity and each category of race/ethnicity (compared with the group with White race/ethnicity) was associated with an increased probability of hypertension being diagnosed. Our data do not let us determine the underlying cause for the relationship between these predictors and the diagnosis, and we are unable to definitively say if this is a psychological effect, or an effect mediated by the patient, the provider, or both. The decision to record a diagnosis of hypertension is ultimately a provider decision, so it is reasonable to suggest that provider psychology may play a role in patient factors influencing the diagnosis of hypertension. If a patient lacks comorbidities, the provider may be more likely to discount hypertensive measures (and not diagnose hypertension) than if they see such measures in the context of a patient viewed as "at-risk" due to comorbidities. This may explain our finding that smokers are more likely to be diagnosed with hypertension, but prior smokers (those who have quit) are less likely to be diagnosed with hypertension.

Our study has certain strengths. We analyzed data from an integrated healthcare system in which specific physician actions related to the initial diagnosis of hypertension are recorded as structured data. In the system under study, it is not possible to prescribe medications by an alternative means such as paper prescriptions that would elude electronic capture. It is also not possible in this system to prescribe a medication without providing a diagnosis linkage. The present cohort was derived from a large data set established to study systolic and diastolic hypertension, and these data include broad information on demographics and comorbidities.[10]

This study also has limitations. This is an observational retrospective cohort and therefore subject to the familiar limitations of this design type. We cannot exclude the possibility that some providers may make a diagnosis of hypertension that they feel does not require medication and did not record hypertension in the EMR problem list. It is possible that clinicians may recognize hypertension in some circumstances but not codify until they are ready to treat with medications. It is, however, unlikely that our inability to capture such informal hypertension diagnosis would create a systematic bias regarding the relative influence of systolic versus diastolic blood pressures on initial hypertension diagnosis. Although we have data on many comorbidities as shown in the Tables, we do not have data regarding diet or lifestyle factors. As is common practice, only the diagnosis of hypertension was recorded in the EMR, without subdivision into diagnostic subtypes of combined hypertension, isolated systolic hypertension, or isolated diastolic hypertension.

In conclusion, while both systolic and diastolic hypertension independently convey cardiovascular risk,[10] isolated systolic and isolated diastolic hypertension are underdiagnosed when compared with combined systolic and diastolic hypertension. Of the two, isolated diastolic hypertension appears to suffer most from underdiagnosis. Advanced age, non-white race/ethnicity, and medical comorbidities all independently predict a diagnosis of hypertension. Organized approaches are needed to better recognize the importance of isolated systolic and isolated diastolic hypertension and to clarify how patient-centered factors influence the diagnosis of hypertension.

Authors contribution

Carol Conell: Conceptualization, Methodology, Software, Writing – Original Draft; Alexander Flint: Conceptualization, Methodology, Writing – Original Draft, Writing – Review & Editing, Xiushui Ren: Writing - Review & Editing; Nader M Banki: Writing - Review & Editing; Sheila L Chan: Writing - Review & Editing; Vivek A Rao: Writing - Review & Editing, Nancy J Edwards:; Ronald B Melles: Writing - Review & Editing; Deepak L Bhatt: Writing – Original Draft, Writing – Review & Editing, Supervision.

Disclosure

Dr. Deepak L. Bhatt discloses the following relationships - Advisory Board: Cardax, Cereno Scientific, Elsevier Practice Update Cardiology, Medscape Cardiology, PhaseBio, Regado Biosciences; Board of Directors: Boston VA Research Institute, Society of Cardiovascular Patient Care, TobeSoft; Chair: American Heart Association Quality Oversight Committee; Data Monitoring Committees: Baim Institute for Clinical Research (formerly Harvard Clinical Research Institute, for the PORTICO trial, funded by St. Jude Medical, now Abbott), Cleveland Clinic (including for the ExCEED trial, funded by Edwards), Duke Clinical Research Institute, Mayo Clinic, Mount Sinai School of Medicine (for the ENVISAGE trial, funded by Daiichi Sankyo), Population Health Research Institute; Honoraria: American College of Cardiology (Senior Associate Editor, Clinical Trials and News, ACC.org; Vice-Chair, ACC Accreditation Committee), Baim Institute for Clinical Research (formerly Harvard Clinical Research Institute;

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