Clinical Policy: Critical Issues in the Evaluation and Management of Adult Patients in the Emergency Department With Asymptomatic Elevated Blood Pressure

From the American College of Emergency Physicians Clinical Policies Subcommittee (Writing Committee) on Asymptomatic Hypertension:
Stephen J. Wolf, MD (Subcommittee Chair)
Bruce Lo, MD, RDMS
Richard D. Shih, MD
Michael D. Smith, MD
Francis M. Fesmire, MD (Committee Chair)

Approved by the ACEP Board of Directors, February 6, 2013

Supported by the Emergency Nurses Association, February 27, 2013

0196-0644/$-see front matter

http://dx.doi.org/10.1016/j.annemergmed.2013.05.012

[Ann Emerg Med. 2013;62:59-68.]

ABSTRACT

This clinical policy from the American College of Emergency Physicians is the revision of a 2006 policy on the evaluation and management of adult patients with asymptomatic elevated blood pressure in the emergency department.[1] A writing subcommittee reviewed the literature to derive evidence-based recommendations to help clinicians answer the following critical questions: (1) In emergency department patients with asymptomatic elevated blood pressure, does screening for target organ injury reduce rates of adverse outcomes? (2) In patients with asymptomatic markedly elevated blood pressure, does emergency department medical intervention reduce rates of

adverse outcomes? A literature search was performed, the evidence was graded, and recommendations were given based on the strength of the available data in the medical literature.

INTRODUCTION

Hypertension is a highly prevalent condition worldwide, carrying significant risk for cardiovascular, renal, and neurologic morbidity and mortality.[2] In 2008, it was estimated that approximately 30% of all adults in the United States were affected, with fewer than 50% undergoing appropriate pharmacologic treatment.[3] The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC 7) reviewed the health risks and outcomes of chronic untreated elevated blood pressure and the benefits of long-term control.[2] That report goes on to make diagnostic and treatment recommendations for primary care physicians.[2] Unfortunately, the long-term primary care outcomes data are often extrapolated broadly to the acute urgent and emergent setting, with limited evidence leading to inconsistent diagnostic and treatment recommendations for patients with elevated blood pressure in the emergency department (ED).[2,4]

Hypertensive emergencies occur when acute target organ injury (ie, cardiovascular, renal, or neurologic) exists in the setting of markedly elevated blood pressures.[2,5] When these complications are clinically apparent or highly suspected because of concomitant signs or symptoms, evaluation and treatment of markedly elevated blood pressure is often initiated expeditiously. However, when signs or symptoms of acute target organ injury are not clinically apparent or suspected, the recommendations for evaluation, treatment, and follow-up are less clear in the ED.

In 2006, Karras et al[6] reported that the majority of ED patients with markedly elevated blood pressure did not receive evaluation, medications, or instructions as traditionally described in the literature. Baumann et al[7] showed that providers overestimate how often they reassessed patients' blood pressures and how often they referred them for follow-up. Collins et al[8] suggested that even when identification of hypertension and targeted patient teaching in the ED occurred, it did not lead to improved outpatient follow-up.

This clinical policy is a revision of the 2006 American College of Emergency Physicians (ACEP) "Clinical Policy: Critical Issues in the Evaluation and Management of Adult Patients With Asymptomatic Hypertension in the Emergency Department."[1] The previous policy provided guidance for physicians practicing in the ED by addressing 2 critical issues: (1) the accuracy and reliability of blood pressure readings in the ED for screening asymptomatic patients for hypertension, and (2) whether there is benefit of rapid lowering of elevated blood pressures in the ED. The 2006 recommendations supported the referral of patients with *persistently* elevated blood pressure in the ED for primary care follow-up. Additionally, the authors noted that the initiation of treatment for asymptomatic hypertension in the ED was not necessary when patients had follow-up, stating that they could find no evidence demonstrating improved patient outcomes or decreased mortality or morbidity with acute management of elevated blood pressure in the ED.[1]

In this revision, 2 critical questions were addressed: (1) In ED patients with asymptomatic elevated blood pressure, does screening for target organ injury reduce rates of adverse outcomes? (2) In patients with asymptomatic markedly elevated blood pressure, does ED medical intervention reduce rates of adverse outcomes?

METHODOLOGY

This clinical policy was created after careful review and critical analysis of the medical literature. Searches of MEDLINE and MEDLINE InProcess were performed. All searches were limited to English-language sources and human studies. Specific key words/phrases and years used in the searches are identified under each critical question. In addition, relevant articles from the bibliographies of included studies and more recent articles identified by committee members and reviewers were included.

This policy is a product of the ACEP clinical policy development process, including expert review, and is based on the existing literature; when literature was not available, consensus of emergency physicians was used. Expert review comments were received from emergency physicians, family physicians, cardiologists, nephrologists, and individual members of the American Academy of Family Physicians, the American Heart Association Council for High Blood Pressure Research, the American Society of Nephrology, and the Emergency Nurses Association. Their responses were used to further refine and enhance this policy; however, their responses do not imply endorsement of this clinical policy. Clinical policies are scheduled for revision every 3 years; however, interim reviews are conducted when technology or the practice environment changes significantly. The ACEP was the funding source for this clinical policy.

All articles used in the formulation of this clinical policy were graded by at least 2 subcommittee members for strength of evidence. The articles were classified by the subcommittee members into 3 classes of evidence on the basis of the design of the study, with design 1 representing the strongest design and design 3 representing the weakest design for therapeutic, diagnostic, and prognostic clinical reports, respectively (Appendix A). Articles were then graded on dimensions related to the study's methodological features, including but not necessarily limited to randomization processes, blinding, allocation concealment, methods of data collection, outcome measures and their assessment, selection and misclassification biases, external validity, generalizability, and sample size. Articles received a final grade (Class I, II, III) on the basis of a predetermined formula, taking into account the design and study quality (Appendix B). Articles identified with fatal flaws or that were not relevant to the critical question received an "X" grade and were not used in formulating recommendations for this policy. Grading was done with respect to the specific critical

questions; thus, the level of evidence for any one study may vary according to the question. As such, it was possible for a single article to receive different levels of grading as different critical questions were answered from the same study. Question-specific level of evidence grading may be found in the Evidentiary Table included at the end of this policy.

Clinical findings and strength of recommendations about patient management were then made according to the following criteria:

Level A recommendations. Generally accepted principles for patient management that reflect a high degree of clinical certainty (ie, based on strength of evidence Class I or overwhelming evidence from strength of evidence Class II studies that directly address all of the issues).

Level B recommendations. Recommendations for patient management that may identify a particular strategy or range of management strategies that reflect moderate clinical certainty (ie, based on strength of evidence Class II studies that directly address the issue, decision analysis that directly addresses the issue, or strong consensus of strength of evidence Class III studies).

Level C recommendations. Other strategies for patient management that are based on Class III studies or, in the absence of any adequate published literature, based on panel consensus. In instances in which consensus recommendations are made, this is specifically indicated next to the recommendation.

There are certain circumstances in which the recommendations stemming from a body of evidence should not be rated as highly as the individual studies on which they are based. Factors such as heterogeneity of results, uncertainty about effect magnitude and consequences, and publication bias, among others, might lead to such a downgrading of recommendations.

When possible, clinically oriented statistics (eg, likelihood ratios, number needed to treat) were presented to help the reader better understand how the results may be applied to the individual patient. For a definition of these statistical concepts, see Appendix C.

This policy is not intended to be a complete manual on the evaluation and management of patients with asymptomatic elevated blood pressure but rather a focused examination of critical issues that have particular relevance to the current practice of emergency medicine.

It is the goal of the Clinical Policies Committee to provide an evidence-based recommendation when the medical literature provides enough quality information to answer a critical question. When the medical literature does not contain enough quality information to answer a critical question, the members of the Clinical Policies Committee believe that it is equally important to alert emergency physicians to this fact.

Recommendations offered in this policy are not intended to represent the only diagnostic and management options that the emergency physician should consider. ACEP clearly recognizes the importance of the individual physician's judgment. Rather, this guideline defines for the physician those strategies for which medical literature exists to provide support for answers to the critical questions addressed in this policy.

Scope of Application. This guideline is intended for physicians working in EDs.

Inclusion Criteria. This clinical policy is intended for patients aged 18 years or older who present to the ED with asymptomatic elevated blood pressure *without* signs and symptoms of acute target organ injury.

Exclusion Criteria. This guideline is not intended to address the care of patients who present to the ED with signs or symptoms of acute hypertensive emergencies (ie, patients with clinical findings that suggest acute target organ injury such as acute stroke, cardiac ischemia, pulmonary edema, encephalopathy, and congestive heart failure), pregnant patients, those with end-stage renal insufficiency, emergent conditions that are likely to cause elevated blood pressure not directly related to acute target organ injury (eg, trauma, other pain syndromes), and acute presentations of serious medical conditions associated with hypertension such as stroke, myocardial infarction, and congestive heart failure.

Definition

Although there is no uniformly accepted definition for markedly elevated blood pressure in the literature, in 2003, JNC 7 classified stage 2 hypertension (ie, the more severe classification) as systolic blood pressure greater than or equal to 160 mm Hg or diastolic blood pressure greater than or equal to 100 mm Hg.[2] However, many clinical studies use a systolic blood pressure greater than or equal to 180 mm Hg or diastolic blood pressure greater than or equal to 110 mm Hg. This policy considers markedly elevated blood pressure to be consistent with the JNC 7 definition of stage 2 hypertension.

Asymptomatic hypertension and hypertensive urgency are frequently used terms to denote markedly elevated blood pressures without clinical evidence of acute target organ injury with or without the established diagnosis of hypertension. Therefore, the term *asymptomatic markedly elevated blood pressure* is used where asymptomatic hypertension had previously been used in the published literature.

CRITICAL QUESTIONS

1. In ED patients with asymptomatic elevated blood pressure, does screening for target organ injury reduce rates of adverse outcomes?

Patient Management Recommendations

Level A recommendations. None specified.

Level B recommendations. None specified.

Level C recommendations. (1) In ED patients with asymptomatic markedly elevated blood pressure, routine screening for acute target organ injury (eg, serum creatinine, urinalysis, ECG) is not required.

(2) In select patient populations (eg, poor follow-up), screening for an elevated serum creatinine level may identify kidney injury that affects disposition (eg, hospital admission).

Key words/phrases for literature searches: hypertension, blood pressure, elevated blood pressure, asymptomatic, mass screening, hospital emergency service, emergency, and variations and combinations of the key words/phrases, years January 1995 through August 2011. From the literature search, 20 articles were selected for further review and grading. In addition, relevant articles from the bibliographies of included studies and more recent articles identified by committee members and reviewers were included.

Current emergency medicine literature, including standard textbooks, does not give definitive advice about which patients who present with asymptomatic markedly elevated blood pressures should receive screening tests.[9,10] In JNC 7, routine laboratory testing, including an ECG for left ventricular hypertrophy or ischemia, chest radiograph (CXR) for cardiomegaly or pulmonary edema, serum creatinine level for renal dysfunction, and urinalysis for proteinuria, is recommended before initiating therapy.[2] However, the JNC report was geared for primary care physicians and does not address patients presenting to the ED. This critical question will focus on the utility of testing in ED patients presenting with asymptomatic elevated blood pressure.

In 2008, Karras et al[11] published a Class II observational study on testing asymptomatic patients with markedly elevated blood pressure in 3 different urban EDs. They enrolled 109 patients (83% black) with a systolic blood pressure of greater than or equal to 180 mm Hg or diastolic blood pressure of greater than or equal to 110 mm Hg and without symptoms of acute hypertensive target organ damage. Their primary endpoint of the frequency of clinically meaningful unanticipated test results, as determined by the treating physician, was found in 7 patients (6%; 95% confidence interval [CI] 2% to 11%). No abnormal test result was believed to be related to acute markedly elevated blood pressure. However, several abnormalities were considered to be a result of chronically elevated blood pressure, including 4 patients with elevated creatinine levels, 3 patients with proteinuria, and 2 patients with abnormal ECG results. Other clinically meaningful results were not believed to be due to elevated blood pressures; these incidental findings included 3 nonhemolytic anemias and 1 abnormal CXR result.

Similarly, in a Class III observational study, Nishijima et al[12] screened 167 asymptomatic patients with elevated blood pressure (98% black) in 2 urban EDs. They included patients aged 18 years or older with a diastolic blood pressure of greater than or equal to 100 mm Hg, excluding those receiving hemodialysis, pregnant patients, or patients with a chief complaint suggestive of high risk for target organ damage. They found 12 patients (7.2%; 95% CI 3% to 11%) who had unanticipated basic metabolic profile results that led to hospitalization, as determined by the primary investigators on chart review. Of these, 10 patients were admitted for new-onset or worsening renal dysfunction and 2 patients were admitted for hyperglycemia.

In both of these studies, despite a lack of standardized endpoints and the potential for a lack of generalizability, there is a suggested benefit in identifying patients with elevated creatinine levels, which may alter disposition.[11,12]

In an older Class III study, Bartha and Nugent[13] evaluated the usefulness of an ECG and CXR in 109 patients as part of a routine evaluation within 2 months of enrollment into a hypertensive clinic. Sixty-nine patients had ongoing treatment of hypertension, with a mean blood pressure of 146/95 mm Hg, and 47 patients had previously untreated hypertension, with a mean blood pressure of 158/113 mm Hg. Fifty-three of 109 patients (49%; 95% CI 39% to 58%) had an abnormal ECG finding and 24 of 102 (24%; 95% CI 16% to 33%) had an abnormal CXR result. In all, 4 patients had a change in management, 2 patients with abnormal CXR results leading to unrelated pulmonary diagnosis and 2 with abnormal ECG results associated with coronary artery disease. No abnormality was thought to be related to elevated blood pressure. Although it was not an ED study, the utility of screening ECG and CXR was found to be of no added value to short-term management.

Currently, there is very little evidence to guide the practitioner about which patients to test who present to the ED with asymptomatic elevated blood pressure. No current study measured adverse outcomes on the basis of the decision to test patients with asymptomatic elevated blood pressure. Of the available evidence, ED screening for creatinine level may identify a small group of patients with renal dysfunction in the setting of asymptomatic markedly elevated blood pressure. However, it is unclear how this frequency compares with that of patients who present with normal or near-normal blood pressures. No other diagnostic screening tests appear to be useful.

2. In patients with asymptomatic markedly elevated blood pressure, does ED medical intervention reduce rates of adverse outcomes?

Patient Management Recommendations

Level A recommendations. None specified.

Level B recommendations. None specified.

Level C recommendations. (1) In patients with asymptomatic markedly elevated blood pressure, routine ED medical intervention is not required.

(2) In select patient populations (eg, poor follow-up), emergency physicians may treat markedly elevated blood pressure in the ED and/or initiate therapy for long-term control. [Consensus recommendation]

(3) Patients with asymptomatic markedly elevated blood pressure should be referred for outpatient follow-up. [Consensus recommendation]

Key words/phrases for literature searches: hypertension, blood pressure, asymptomatic, elevated blood pressure, treatment, hospital emergency service, emergency, emergency department, antihypertensive agents, and variations and combinations of the key words/phrases, years January 2005 through August 2011.

From the literature search, 23 articles were selected for further review and grading. In addition, relevant articles from the bibliographies of included studies and more recent articles identified by committee members and reviewers were included.

Emergency physicians frequently face the decision of whether to treat markedly elevated blood pressure with no overt signs of target organ injury. Longitudinal data continue to suggest that controlling blood pressure *over time* reduces the incidence of target organ damage, morbidity, and mortality.[2] Acute treatment of patients with markedly elevated blood pressure in the presence of acute target organ injury has long been recommended.[4,14,15] However, a 2008 Cochrane review of 15 randomized controlled trials between 1983 and 2004 found insufficient evidence to support or refute this practice.[16]

Since 2005, a limited number of studies have been published directly addressing appropriate indications for medical treatment of asymptomatic markedly elevated blood pressure in the ED. Two studies suggest that observation with ED medical intervention is reasonable[17,18]; however, data to suggest an appropriate timeframe for outpatient follow-up for these patients are lacking. The Class II study by Grassi et al[17] explored the safety of a "wait, then treat" approach in 549 asymptomatic ED patients with markedly elevated blood pressure (≥180 mm Hg systolic and/or ≥110 mm Hg diastolic). Enrolled patients were without overt evidence of acute target organ injury or previous cardiac, renal, or brain disease. The authors showed that 175 of 549 patients (32%; 95% CI 28% to 36%) had a spontaneous decrease in their blood pressure with 30 minutes of quiet rest, as defined by a blood pressure of less than 180/110 mm Hg and at least a 20 mm Hg decrease in systolic or 10 mm Hg decrease in diastolic blood pressure. Nonresponders were treated with one of 3 immediate-acting antihypertensive agents that were similarly effective in all but 78 of 549 patients (14%; 95% CI 11% to 17%), with the remaining 14% being referred for "personalized treatment and follow-up." No serious hypertension-related or postintervention adverse events occurred in any enrolled patient on telephone follow-up 48 to 72 hours after discharge from the ED.

A Class III study, the VA Cooperative Trial of 1967, was a randomized placebo-controlled trial of 143 male patients with diastolic blood pressure of 115 mm Hg to 130 mm Hg.[18] No adverse outcomes in either group were demonstrated during the initial 3 months of enrollment. Four of 70 patients in the placebo group (6%; 95% CI 2% to 14%) versus 0 of 73 patients in the treatment group (0%; 95% CI 0% to 5%) developed significant complications within 4 months of enrollment, including sudden death, ruptured aortic aneurysm and death, severely elevated blood urea nitrogen level, and congestive heart failure. However, within 20 months, 27 of 70 patients (39%; 95% CI 27% to 51%) treated with placebo and 2 of 73 patients (3%; 95% CI 0.3% to 9.5%) treated with antihypertensive drugs experienced adverse events (absolute risk reduction 36%; number needed to treat=3).

Finally, it is generally accepted that the rapid lowering of markedly elevated blood pressure in the asymptomatic patient has the potential to do harm.[1,14,19-22] However, in selected social or clinical situations (eg, poor follow-up, limited access to care, older patients, black patients), emergency physicians may choose to initiate treatment for markedly elevated blood pressure in the asymptomatic patient before discharge to gradually lower the blood pressure and/or initiate long-term control.[11,12,23] In this situation, a significant portion of these patients' blood pressures spontaneously decrease without intervention during the 60 and 90 minutes after the initial blood pressure measurement in the ED.[17,24]

FUTURE RESEARCH

Given the limited literature on the optimal evaluation, management, and follow-up of ED patients with asymptomatic markedly elevated blood pressure, suggested future research topics include the following:

- What is the optimal screening for ED patients with asymptomatic markedly elevated blood pressures as it relates to patient outcomes (eg, short- and long-term adverse events, long-term target organ disease)?
- What is the optimal management for ED patients with asymptomatic markedly elevated blood pressures as it relates to patient outcomes?
- Does writing a prescription from the ED or administering an oral dose of medication in the ED change outcomes?
- What is the ideal interval for patient follow-up to minimize adverse patient outcomes?

Relevant industry relationships: There were no relevant industry relationships disclosed by the subcommittee members.

Relevant industry relationships are those relationships with companies associated with products or services that significantly impact the specific aspect of disease addressed in the critical question.

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Evidentiary Table.

Study	Year	Design	Intervention(s)/Test(s)/ Modality	Outcome Measure/Criterion Standard	Results	Limitations/ Comments	Class
Karras et al[11]	2008	Prospective cross-sectional at 3 academic sites	Laboratory testing for patients with either systolic blood pressure ≥180 mm Hg or diastolic blood pressure ≥110 mm Hg	Primary endpoint: frequency of clinically meaningful unanticipated abnormalities that led to hospital admission, further testing, consultation, or modification of the patient's medication	57/109 (52%; 95% CI 43% to 62%) patients and unanticipated abnormal laboratory results, with 7 (6%; 95% CI 2% to 11%) patients having "clinically meaningful" abnormalities; of the 7, only 5 were possibly related to acute hypertensive end-organ damage, whereas 0 had abnormalities directly related to severe hypertension	No standard criteria for clinically meaningful abnormalities; predominantly black population	II
Nashijima et al[12]	2010	Prospective cross-sectional at 2 academic sites	Basic metabolic profile for patients with diastolic blood pressure of ≥100 mm Hg	Primary endpoint: admission secondary to abnormal basic metabolic profile; secondary endpoint: prevalence of GFR <60 mL min^{-1} 1.73 m^{-2}	12/167 (7.2%; 95% CI 3% to 11%) patients admitted for abnormalities on basic metabolic profile (10 for renal dysfunction, 2 for elevated glucose); 27/167 (16.2%; 95% CI 11% to 21%) patients had GFR <60 mL min^{-1} 1.73 m^{-2}, with 12 <30 mL min^{-1} 1.73 m^{-2}	Admission criterion was not standardized; predominantly black population	III

Evidentiary Table (continued).

Study	Year	Design	Intervention(s)/Test(s)/ Modality	Outcome Measure/Criterion Standard	Results	Limitations/ Comments	Class
Bartha and Nugent[13]	1978	Retrospective cohort	CXR/ECG screening for patients with diastolic blood pressure >105 mm Hg	Management decision related to CXR or ECG findings	53/109 (49%; 95% CI 39% to 58%) patients had an abnormal ECG result and 24/102 (24%; 95% CI 16% to 33%) had an abnormal CXR result; 2 patients had change in management from abnormal CXR result, but none because of hypertension	Population studied was from hypertensive clinic	III
Grassi et al[17]	2008	Randomized, open-label, cohort study	Efficacy and safety of stepped therapeutic strategy with a nested, randomized, open-label, parallel comparison of 3 intermediate-acting antihypertensive medications	Severely elevated blood pressure ≥180/110 mm Hg repeated after 30 min of rest; nonrest responders were treated and reassessed at 60 and 120 min; excluded: acute target organ dysfunction, previous heart, renal, or brain disease, recent surgery, acute trauma, infectious disease, acute psychiatric disease; treatment: single oral dose (amlodipine 5 mg, perindopril 4 mg, or labetolol 200 mg); all followed at 48 to 72 h	N=549 after 155 excluded; 175/549 (32%; 95% CI 28% to 36%) patients responded to rest; 296/374 (79%; 95% CI 75% to 83%) nonrest responders responded to oral medication (53% in first h, 26% in second h); 78/374 (21%; 95% CI 17% to 25%) nonrest responders, or 78/549 (14%; 95% CI 11% to 17%) of total cohort, did not respond to rest or medication; there was no statistical difference in response rates based on the oral medicine used; no severely elevated blood pressure–related or postintervention major or minor events were reported	Allocation groups randomized but not blinded; rest period limited by ED crowding; no responders referred to "personalized treatment and follow-up"	II

Evidentiary Table (continued).

Study	Year	Design	Intervention(s)/Test(s)/ Modality	Outcome Measure/Criterion Standard	Results	Limitations/ Comments	Class
Freis et al (VA Coop Study)[18]	1967	Randomized, placebo-controlled trial	Adverse event rates in patients discharged with markedly elevated blood pressure	Hospitalized patients discharged with diastolic blood pressure 115 mm Hg to 129 mm Hg were randomized 2 mo after discharge to placebo versus treatment; primary outcomes were adverse events during the next 20 mo	N=143; 27/70 (39%; 95% CI 27% to 51%) patients treated with placebo and 2/73 (3%; 95% CI 0.3% to 9.5%) patients treated with hypertensive drugs experienced adverse events within 20 mo; there was no difference in adverse events between the 2 groups during the first 3 mo	All male study population; not ED study	III
Dieterle et al[24]	2005	Prospective observational	ED blood pressure for the diagnosis of hypertension	JNC 7 >160/100 mm Hg without previous diagnosis or untreated and no acute target organ damage; exclusions: life-threatening conditions, hypertensive encephalopathy, suspected intracerebral hemorrhage or ischemic stroke, acute myocardial infarction, acute pulmonary edema, aortic dissection, blood pressure measurement every 5 min for 2 h; primary outcome: diagnosis of hypertension on follow-up using JNC 6 or JNC 7	N=45 (4 lost to follow-up); patients with and without primary outcome were similar; mean blood pressure=176/99 (SD 14/11 mm Hg); 26/41 (61%) patients received a diagnosis of hypertension on follow-up; no difference in mean initial blood pressure by primary outcome; blood pressure ≥165/105 between 60 and 80 min of ED entry was >90% specific for identifying hypertension (AUC=0.8 for systolic blood pressure and 0.76 for diastolic blood pressure); blood pressure <130/80 mm Hg at 60 to 80 min was >90% sensitive for excluding hypertension	Limited sample size	III

AUC, area under the curve; *CI*, confidence interval; *CXR*, chest radiograph; *ECG*, electrocardiogram; *ED*, emergency department; *GFR*, glomerular filtration rate; *h*, hour; *JNC*, Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure; *m,* meter; *mg*, milligram; *min*, minute; *mL*, milliliter; *mm Hg*, millimeters of mercury; *mo*, month; *SD,* standard deviation; *VA Coop,* Veterans Administration Cooperative.

Appendix A. Literature classification schema.*

Design/Class	Therapy†	Diagnosis‡	Prognosis§
1	Randomized, controlled trial or meta-analysis of randomized trials	Prospective cohort using a criterion standard or meta-analysis of prospective studies	Population prospective cohort or meta-analysis of prospective studies
2	Nonrandomized trial	Retrospective observational	Retrospective cohort Case control
3	Case series Case report Other (eg, consensus, review)	Case series Case report Other (eg, consensus, review)	Case series Case report Other (eg, consensus, review)

*Some designs (eg, surveys) will not fit this schema and should be assessed individually.
†Objective is to measure therapeutic efficacy comparing interventions.
‡Objective is to determine the sensitivity and specificity of diagnostic tests.
§Objective is to predict outcome including mortality and morbidity.

Appendix B. Approach to downgrading strength of evidence.

	Design/Class		
Downgrading	**1**	**2**	**3**
None	I	II	III
1 level	II	III	X
2 levels	III	X	X
Fatally flawed	X	X	X

Appendix C. Likelihood ratios and number needed to treat.*

LR (+)	LR (−)	
1.0	1.0	Useless
1-5	0.5-1	Rarely of value, only minimally changes pretest probability
10	0.1	Worthwhile test, may be diagnostic if the result is concordant with pretest probability
20	0.05	Strong test, usually diagnostic
100	0.01	Very accurate test, almost always diagnostic even in the setting of low or high pretest probability

LR, Likelihood ratio.
*Number needed to treat (NNT): number of patients who need to be treated to achieve 1 additional good outcome; NNT=1/absolute risk reduction×100, where absolute risk reduction is the risk difference between 2 event rates (ie, experimental and control groups).