

Acute Hypertension: A Systematic Review and Appraisal of Guidelines

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ABSTRACT

Background: Few clinical practice guidelines provide management recommendations for acute hypertensive episodes except in the context of specific conditions such as pregnancy and stroke.

Methods: We performed a systematic search to identify guidelines addressing acute hypertension and appraised the guidelines using the Appraisal of Guidelines for Research and Evaluation (AGREE II) validated quality assessment tool. Two reviewers independently appraised and one extracted key recommendations. Literature on secondary hypertension, hypertension in pregnancy, preeclampsia/eclampsia, stroke, aortic dissection, and pheochromocytoma was excluded.

Results: Three guidelines were identified, sponsored by the American College of Emergency Physicians (ACEP), the National Heart, Lung, and Blood Institute (NHLBI), and the European Society of Hypertension (ESH) in conjunction with the European Society of Cardiology (ESC). AGREE II yielded mean domain (%) and overall assessment scores (1-7) as follows: NHLBI: 73%, 5.5; ACEP: 67%, 5.5; and ESH/ESC: 56%, 4.5. In hypertensive emergencies, the NHLBI guideline recommends reducing mean arterial pressure by $\leq 25\%$ for the first hour, and then to 160/100-110 mmHg by 2-6 hours

with subsequent gradual normalization in 24-48 hours. The ESH/ESC has similar recommendations. The ACEP does not address guidelines for hypertensive emergency but focuses on whether screening for target organ damage or medical intervention in patients with asymptomatic elevated blood pressure in emergency departments reduces the rate of adverse outcomes, concluding that routine screening does not reduce adverse outcomes, but patients with poor follow-up may benefit from routine screening.

Conclusion: NHLBI and ESH/ESC guidelines are high quality and provide similar recommendations for management of asymptomatic acute hypertensive episodes and hypertensive emergencies. Additional research is needed to inform clinical practice guidelines for this common condition.

INTRODUCTION

In 2000, nearly 1 billion people—more than one-quarter of the world's adult population—were estimated to have hypertension, and by 2025, that number is expected to rise to 1.56 billion.¹ The national and international burden of hypertension has been addressed by many evidence-based guidelines,²⁻¹² but these guidelines primarily provide recommendations for chronic hypertension that is almost exclusively managed in the outpatient setting. Moreover, guidelines for chronic hypertension rely on the accuracy of blood pressure measurements for risk stratification that are obtained under prescribed conditions as opposed to, for example, the acute care setting.¹³

Few studies have addressed the epidemiology of acute hypertensive episodes. Shorr et al examined the prevalence of acute hypertension in a retrospective cohort study using administrative data collected by 114 acute care hospitals from 2005-2007.¹⁴ Among 1,290,804 adults, acute hypertension (defined as systolic blood pressure [SBP] ≥ 180 mmHg in the emergency department [ED]) occurred in 178,131 patients (13.8%). Hypertensive emergency is a condition that affects approximately 1% of all patients with

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chronic hypertension,^{15,16} and hypertensive emergency accounts for 27.5% of all ED visits for medical urgencies and emergencies.¹⁷

Risk factors for hypertensive emergency include female sex, obesity, coronary artery disease, somatoform disorder, a high number of antihypertensive medications, and noncompliance to medication prescription. Perhaps most important, noncompliance contributes significantly to the risk of having an acute hypertensive emergency and increases with the number of antihypertensive medications prescribed.¹⁸ Other risk factors include sedentary lifestyle, increased age, and Caucasian race.¹⁹ Despite the burden of acute hypertensive episodes, few clinical practice guidelines exist outside of specific conditions such as pregnancy and stroke. The objective of this study was to identify clinical practice guidelines for management of acute hypertensive episodes and to appraise the quality of these guidelines. We hypothesized that existing clinical practice guidelines might vary in quality and in key management recommendations.

METHODS

Search Strategy

We performed a literature search to identify guidelines using multiple data sources including MEDLINE, the (US) National Guideline Clearinghouse, international guidelines search engines, and websites of relevant specialty societies. To search MEDLINE, we applied the following search strategy: {("hypertension[Title]" OR "blood pressure[Title]") AND ("treatment[Title/Abstract]" OR "management [Title/Abstract]") AND ("guideline[Title]" or "recommendation[Title]" or "guidelines[Title]")}. This MEDLINE search syntax served as the basis for all other search strategies. All searches were limited to the adult population (age ≥ 18 years).

Inclusion and Exclusion Criteria

We included guidelines and systematic reviews that focus on the treatment and management of acute hypertension in adults. Literature relevant to secondary hypertension, hypertension during pregnancy, preeclampsia/eclampsia, acute stroke, aortic dissection, pheochromocytoma, unpublished draft guidelines, and clinical protocols was excluded. We included guidelines in English published between January 1, 2003, and June 15, 2014. We excluded guidelines derived entirely from other guidelines and those without detailed information on development.

Quality Assessment and Extraction of Recommendations

We reviewed selected guidelines using the validated Appraisal of Guidelines for Research and

Evaluation (AGREE II) instrument to objectively assess the quality of each guideline.²⁰⁻²³ AGREE II consists of 23 items organized into 6 domains: (1) scope and purpose, (2) stakeholder involvement, (3) rigor of development, (4) clarity of presentation, (5) applicability, and (6) editorial independence.

Each item was scored from 1 (strongly disagree) to 7 (strongly agree) depending on how much the appraiser believed the guideline adhered to the provided criteria. The overall quality of each guideline was scored using the same scale. Appraisers then decided whether they would recommend the use of the guideline with or without modifications. Guidelines were independently rated by 2 authors (KJP and LAB). Domain scores were calculated by the following formula:²³

$$\frac{(\text{obtained score} - \text{minimum possible score})}{(\text{maximum possible score} - \text{minimum possible score})}$$

The maximum possible score = $7 \times$ number of items in domain \times number of appraisers. The minimum possible score = $1 \times$ number of items in domain \times number of appraisers. Domain scores $< 50\%$ are generally considered low quality.²⁴⁻²⁷ One reviewer (KJP) extracted recommendations from the guidelines.

RESULTS

Selected Guidelines

After reviewing titles and/or abstracts from articles that qualified under our inclusion/exclusion criteria (Figure), we identified 3 reference guidelines (Table 1):

1. "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 (ACEP)²⁸
2. "Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure" from the National Heart, Lung, and Blood Institute (NHLBI)¹¹
3. "2013 ESH/ESC Guidelines for the Management of Arterial Hypertension" from the European Society of Hypertension (ESH) and the European Society of Cardiology (ESC)⁴

Guidelines for Hypertensive Urgency or Emergency

Guidelines for treating hypertension from the NHLBI's Seventh Joint National Committee (JNC 7)¹¹ recommend treating hypertensive emergencies by reducing mean arterial pressure by $\leq 25\%$ in the first hour, then to 160/100-110 mmHg by 2-6 hours,

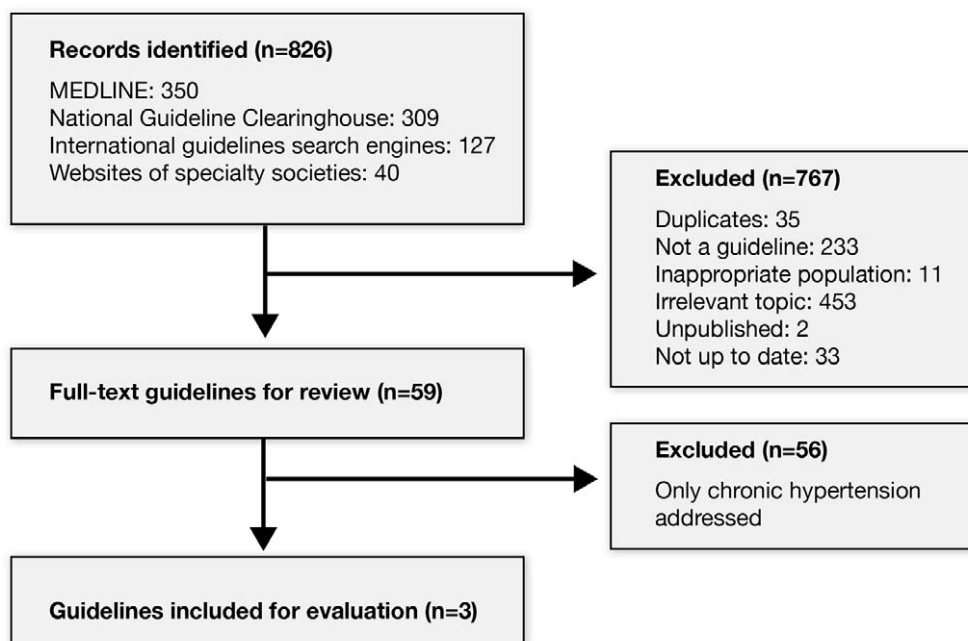


Figure. Extraction of selected guidelines.

with further gradual normalization of blood pressure within the next 24-48 hours. Table 2 lists parenteral drugs for treatment of hypertensive emergency per JNC 7. The 2014 report from the panel members appointed to the Eighth Joint National Committee,² however, is more limited regarding scope of topics compared to JNC 7 and does not address acute hypertension. The 2013 guidelines for the management of arterial hypertension from the ESH and the

ESC⁴ define hypertensive emergency as elevations in SBP >180 mmHg or diastolic blood pressure (DBP) >120 mmHg associated with progressive or impending organ dysfunction. In cases other than acute stroke, pulmonary edema, or aortic dissection, ESH/ESC guidelines recommend reducing blood pressure by <25% during the “first hours” followed by subsequent cautious reduction (without specification of how many hours). The medications recom-

Table 1. Characteristics and Scope of Selected Guidelines

Selected Guidelines			
Title	Clinical policy: critical issues in the evaluation and management of adult patients in the emergency department with asymptomatic elevated blood pressure ²⁸	Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure ¹¹	2013 ESH/ESC guidelines for the management of arterial hypertension ⁴
Sponsoring Organization	American College of Emergency Physicians	National Heart, Lung, and Blood Institute	European Society of Hypertension (ESH) and European Society of Cardiology (ESC)
Region, Publication Year	United States, 2013	United States, 2003	Europe, 2013
Stated Scope, Purpose, Aims	Does screening for target organ injury in emergency department (ED) patients with asymptomatic elevated blood pressure reduce rates of adverse outcomes, and does ED medical intervention reduce rates of adverse outcomes?	Evidence-based prevention and management of hypertension	Evidence-based prevention and management of hypertension

Table 2. Key Recommendations from Selected Guidelines

Selected Guidelines	Asymptomatic Elevated Blood Pressure (Hypertensive Urgency)	Blood Pressure Lowering Target/Timing in Hypertensive Emergency
American College of Emergency Physicians, 2013 ²⁸	<ul style="list-style-type: none"> • Routine screening for acute target organ injury (eg, serum creatinine, urinalysis, and electrocardiogram) is not required. • 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). • Routine emergency department (ED) medical intervention is not required. • 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. • Patients with asymptomatic markedly elevated blood pressure should be referred for outpatient follow-up. 	Not addressed
National Heart, Lung, and Blood Institute, 2003 ¹¹	<ul style="list-style-type: none"> • Some patients may benefit from treatment with an oral, short-acting agent, such as captopril, labetalol, or clonidine, followed by several hours of observation. • There is no evidence to suggest that failure to aggressively lower blood pressure in the ED is associated with any increased short-term risk to the patient who presents with severe hypertension. 	<ul style="list-style-type: none"> • Reduce mean arterial pressure $\leq 25\%$ for first hour, then to 160/100-110 mmHg by 2-6 hours, followed by gradual normalization in 24-48 hours. • Listed parenteral drugs: Vasodilators: sodium nitroprusside, nicardipine, fenoldopam, nitroglycerin, enalaprilat, and hydralazine. Adrenergic inhibitors: labetalol, esmolol, and phentolamine.
European Society of Hypertension/European Society of Cardiology, 2013 ⁴	<ul style="list-style-type: none"> • Isolated large blood pressure elevations without acute organ dysfunction should not be considered an emergency but treated by reinstitution or intensification of drug therapy and treatment for anxiety. • No specific agents mentioned for hypertensive urgency. 	<ul style="list-style-type: none"> • Reduce blood pressure by $<25\%$ during “first hours” and then subsequent cautious reduction. • Intravenous agents most usually employed: labetalol, sodium nitroprusside, nicardipine, nitrates, and furosemide.

mended for lowering blood pressure in the ESH/ESC guidelines are the same as those suggested for treating malignant hypertension (defined by the ESH/ESC guidelines as a hypertensive emergency associated with ischemic organ dysfunction): nicardipine, labetalol, sodium nitroprusside, nitrates, and furosemide, as these can be administered as an intravenous infusion and titrated to avoid hypotension and exacerbation of ischemic damage. The ESH/ESC guidelines state that recommendations are limited because of the lack of randomized controlled trials comparing conservative vs aggressive regimens in reducing blood pressure. Other guidelines, such as those from the National Institute of Health

and Care Excellence (formerly the National Institute of Health and Clinical Excellence),²⁹ explicitly exclude accelerated hypertension or acute hypertension in emergency settings. A summary of recommendations from the selected guidelines is presented in Table 2.

Guidelines for Acute Hypertensive Episodes in the Emergency Department

With the support of the ACEP, Wolf et al reviewed the literature to synthesize evidence-based guidelines on hypertension management in adult patients with asymptomatic elevated blood pressure without evidence of acute target organ

Table 3. Quality Assessment: AGREE II Domain Scores

AGREE II Domain	ACEP, 2013 ²⁸	NHLBI, 2003 ¹¹	ESH/ESC, 2013 ⁴	Mean, Selected Guidelines
Scope and purpose, %	97	61	64	74
Stakeholder involvement, %	58	61	36	52
Rigor of development, %	84	66	52	67
Clarity of presentation, %	94	92	92	93
Applicability, %	8	100	48	52
Editorial independence, %	58	58	42	53
Mean across domains, %	67	73	56	65
Overall assessment, 1-7	5.5	5.5	4.5	5.2

ACEP, American College of Emergency Physicians; AGREE II, Appraisal of Guidelines for Research and Evaluation; ESH/ESC, European Society of Hypertension/European Society of Cardiology; NHLBI, National Heart, Lung, and Blood Institute.

damage or hypertensive urgency (ie, SBP ≥ 180 mmHg or DBP ≥ 110 mmHg) in the ED setting.²⁸ Pregnant patients and patients with hypertensive emergencies, end-stage renal disease, and emergent states (eg, stroke, myocardial infarction, congestive heart failure, trauma, and pain) causing hypertension were excluded. The review was designed to address 2 critical questions:

1. In patients admitted to the ED with asymptomatic elevated blood pressure, does screening for target organ injury reduce rates of adverse outcomes?
2. In patients with asymptomatic markedly elevated blood pressures, does ED medical intervention reduce rates of adverse outcomes?

No level A (high quality) or B (moderate quality) recommendations resulted. Several level C (low quality) recommendations resulted and are provided in Table 2.

Quality Assessment

All 3 guidelines were reviewed using AGREE II and generally showed a high degree of agreement between the independently rated scores. The mean score for all domains combined for each guideline was $>50\%$. However, only the NHLBI guideline achieved $>50\%$ on all individual domain scores. The ACEP guidelines received a low score for the domain of applicability (8%) because no mention was made of facilitators or barriers to guideline implementation. Objective or quantifiable criteria to audit or monitor recommendations were also lacking. Despite this flaw, the ACEP guidelines obtained a high overall score from high ratings in other areas, especially in the domains of scope and purpose, rigor of development, and clarity of presentation. The ESH/ESC guidelines were wide in scope and scored well in clarity of presentation but fell below 50% in the domains of stakeholder involvement, applicability, and editorial independence.

AGREE II yielded mean domain (%) and overall assessment scores (1-7) as follows: NHLBI: 73%, 5.5; ACEP: 67%, 5.5; and ESH/ESC: 56%, 4.5. Table 3 presents a summary of domain and overall quality assessment scores.

DISCUSSION

Current Guidelines Addressing Acute Hypertension

The identification of only 3 guidelines demonstrates the scarcity of clinical practice recommendations on the subject of acute hypertension.^{30,31} Overall, the NHLBI and ESH/ESC guidelines were of high quality and provided similar recommendations for management of asymptomatic acute hypertensive episodes and hypertensive emergencies. However, the guidelines that we identified lacked specific treatment recommendations for acutely elevated asymptomatic blood pressure in patients hospitalized for other causes.

Areas of Variation Among Current Recommendations

How rapidly acutely elevated blood pressure should be lowered is controversial,³²⁻³⁵ and recommendations are limited by the lack of high-quality clinical evidence, as no benefit has been shown from rapid blood pressure reduction.^{4,11,32,35,36} The ESH/ESC guidelines do not include specific time frames for lowering blood pressure compared to the NHLBI guidelines of 2003. In the asymptomatic patient, however, the general suggestion is to gradually lower pressure during a period of hours to days^{11,35} (1) to minimize risks associated with rapid blood pressure reduction (eg, myocardial infarction and stroke) or impairment of autoregulatory mechanisms that maintain tissue perfusion,^{11,32-34,37} and (2) to prevent deleterious cardiovascular sequelae that

may result from insufficient or too slow blood pressure reduction.

No current evidence exists showing the benefit of antihypertensive management in patients hospitalized for reasons other than hypertension. Yet many physicians feel strongly compelled to treat blood pressure numbers (often at arbitrary thresholds and when only moderately elevated). In a 2010 survey, approximately 91% of internal medicine residents indicated that discharging patients on an inpatient medication regimen was preferable to the regimen established prior to admission.³⁸ Inpatient decision-making may be extrapolated from blood pressure thresholds from hypertension guidelines, but these thresholds are based on outpatient criteria that are poorly justified.³⁰ The term hypertensive urgency may also have led to overaggressive and rapid treatment of patients with severe but uncomplicated hypertension¹¹ with intravenous therapies such as labetalol and hydralazine.³⁹ These therapies are not without risks, as labetalol (although inhibiting reflex tachycardia) could enhance orthostatic reduction in blood pressure from bed rest⁴⁰ with adverse effects on cerebral perfusion. Rapid reduction of blood pressure from hydralazine can lead to reflex sympathetic output.³⁰ In at least 1 study, when as-needed intravenous medications were not used, hospital length of stay decreased to approximately half (among patients who were treated, only 2.9% had International Classification of Diseases-9 [ICD] codes documenting diagnoses requiring prompt antihypertensive treatment).³⁹

Definitions of Acute Hypertensive Episodes

Normal blood pressure is defined as <120 mmHg SBP and <80 mmHg DBP. The prehypertensive condition extends from 120-139 mmHg SBP and 80-89 mmHg DBP.¹¹ Stage 1 hypertension is defined as 140-159 mmHg SBP and 90-99 mmHg DBP, while stage 2 hypertension is any SBP \geq 160 mmHg and a DBP \geq 100 mmHg.

Acute hypertension, or an acute hypertensive episode, is at times difficult to define and is not easily translatable for reimbursement and coding. Terminologies such as malignant hypertension, accelerated hypertension, hypertensive urgency, and hypertensive emergency have been used to describe acute hypertensive episodes. The definitions of these terms have changed with time as well. The terms hypertensive urgency and hypertensive emergency, despite being the most commonly used in medical education and guidelines, are not tied to reimbursement and coding in the ICD system. Rather, historical terms coined at the turn of the last century are used for reimbursement and coding purposes.

First introduced in 1914 by Franz Volhard and Karl Theodor Fahr,^{41,42} the term malignant hypertension originally described severe hypertension with renal failure, retinopathy with papilledema, fibrinoid necrosis, uremia, and accelerated death. The term has also been used to define marked hypertension with ocular hemorrhages and exudates with papilledema.⁴³ However, the term malignant hypertension relating to encephalopathy or nephropathy has since been removed from use in national and international blood pressure control guidelines.⁴⁴

Accelerated hypertension was first used in 1921 by Keith and Wagener^{41,45} to describe severe hypertension with papilledema and severe retinopathy without findings of renal failure. Accelerated hypertension denotes severely elevated blood pressure (SBP >179 mmHg or DBP >109 mmHg) that is associated with ocular hemorrhages, exudates, and no papilledema (stage 3 Kimmelsiel-Wilson retinopathy).⁴⁶

Hypertensive urgency describes a severe elevation in blood pressure (>180 mmHg SBP and >120 mmHg DBP) without progressive target organ dysfunction. Examples include high levels of stage 2 hypertension associated with severe headache, shortness of breath, epistaxis, pedal edema, or severe anxiety. Most of these patients present as noncompliant or inadequately treated hypertensive individuals with little or no evidence of target organ damage.¹¹

Rodriguez et al describe hypertensive emergency as severe elevation in blood pressure >220/140 mmHg and a DBP >120 to 130 mmHg (complicated by evidence of impending or progressive target organ dysfunction).⁴¹ Examples of end organ dysfunction include hypertensive encephalopathy, intracerebral hemorrhage, acute myocardial infarction, acute left ventricular failure with pulmonary edema, unstable angina pectoris, dissecting aortic aneurysm, acute renal failure, pulmonary edema, and eclampsia. The signs and symptoms of patients with hypertensive emergency vary according to which organ system is affected most severely, but the most common presentation includes dyspnea, chest pain, headache, and neurological deficit.¹⁹

Clinician Attitudes and Current Management of Acute Hypertension

Benson et al⁴⁷ conducted a 2008 survey on the treatment for acute hypertension among 5,574 critical care physician and pharmacist members of the Society of Critical Care Medicine and the American College of Clinical Pharmacy. They found that the mean SBP used to initiate intravenous antihyperten-

sives was 180.9 (range 105-220) mmHg among nonstroke patients. A wide distribution of agents was used, with intermittent intravenous labetalol as the drug of choice among physicians (21.3%) and pharmacists (26.5%). The second-line agent of choice for the nonstroke patient was sodium nitroprusside among physicians (19.8%) and continuous infusion labetalol for pharmacists (19.8%). About 74% of respondents reported not having practice guidelines for treating hypertensive emergencies at their respective institutions. We also do not have treatment guidelines established at our institution.

In addition to the survey conducted by Benson et al⁴⁷, 25 centers in the United States participated in the STAT (Studying the Treatment of Acute hyperTension) registry to “improve understanding of clinical conditions of acute severe hypertension managed in a critical care setting and treated with intravenous antihypertensive drugs.”⁴⁸ Severe hypertension was defined as SBP \geq 180 mmHg and/or DBP \geq 110 mmHg and subarachnoid hemorrhage patients with SBP $>$ 140 mmHg and/or DBP $>$ 90 mmHg. The registry study found that the median time to SBP of $<$ 160 mmHg was 4 hours and SBT increased to $>$ 180 mmHg after initial control in 60% of patients. About 4% of patients had iatrogenic hypotension, and 29% had recurrent, severe hypertension necessitating reinstitution of parenteral therapy. Additionally, an alarming 65% of patients had no documentation of a follow-up appointment being scheduled or attended. Regarding outcomes, the study reported 6.9% in-hospital deaths, 11% admits to 90-day death, 37% 90-day readmissions, and a 9.3% rate of 90-day readmission because of hypertension.

CONCLUSION

Despite numerous national and international guidelines for chronic hypertension, the common problem of acute hypertension is neglected in the literature. Results from the STAT registry and other studies demonstrate that acute severe hypertension in the hospital setting has high rates of mortality and morbidity, especially with new or worsening end organ damage. The problem is associated with poor medical adherence, but alarmingly low rates of follow-up likely contribute to a high recurrence rate. The management of acute severe hypertension is also heterogeneous regarding admission hospital unit (medical ward or intensive care unit), medication use, and blood pressure targets or thresholds. The lack of evidence-based guidance leads to the use of arbitrary targets for blood pressure control or a crude extrapolation of blood pressure targets from guidelines mostly intended for outpatient management. These differences in practice may increase the risk of harm to patients, burden hospital resources (eg,

lower bed availability with longer lengths of stay), and have an impact on the healthcare system overall. Further research and examination of current evidence are needed to provide more detailed information and expand the currently limited resources for clinical practice recommendations for this common condition.

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This article meets the Accreditation Council for Graduate Medical Education and the American Board of Medical Specialties Maintenance of Certification competencies for Patient Care and Medical Knowledge.