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REVIEW

High-Risk Patients with Hypertension: Clinical Management Options

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Abstract: Hypertension, one of the most common human diseases worldwide, affects nearly 1 billion individuals. Complaints related to hypertension are commonly evaluated and treated in the acute care settings such as emergency departments and acute care medical clinics. The evaluation, treatment, and disposition of these patients require thorough knowledge of potential complications and treatment options. This manuscript details a structured approach to evaluating high-risk patients with acute hypertension-related complaints and provides recommendations for treatment and disposition.

Keywords: hypertension, malignant hypertension, emergency treatment

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Introduction

Hypertension, defined in adults as arterial blood pressure greater than 140/90 mmHg, is one of the most common human diseases in the world. Hypertension affects nearly 1 billion people worldwide and between 58 and 65 million people in the United States.[1,2] In the United States, treatment of hypertension is the most common reason for clinic visits to primary care providers and the most common indication for prescription drugs.[3]

Hypertension is also one of the most commonly encountered diseases in acute care settings such as emergency departments, urgent care centers, and acute care medical clinics.[4] In such settings, on occasion, hypertension may be the primary impetus for patient presentation, but more commonly hypertension is incidentally identified during evaluation of a different complaint. Elevated blood pressure identified in the acute care setting without associated symptoms of end-organ injury does not require immediate treatment with medications. However, these encounters do represent an important opportunity for providers and patients to develop a plan for lowering blood pressure over time with a goal of reducing the long-term risk of cardiovascular disease. On the other hand, when severely elevated blood pressure has resulted in acute end-organ damage, such as encephalopathy, acute heart failure, or acute kidney injury, a true hypertensive emergency is present and immediate intervention with antihypertensive therapy is needed.[5] Approximately 1% to 2% of people in the United States with chronic hypertension experience an episode of hypertensive emergency in their lifetime.[6]

Complications of Chronic Hypertension

Over time, uncontrolled hypertension leads to remodeling of the cardiovascular system and increases the risk for end-organ damage, such as myocardial infarction, heart failure, stroke, aortic dissection, and kidney failure.[5] Repeated contraction against increased afterload caused by chronic hypertension results in left ventricular hypertrophy and eventually impaired diastolic filling as the hypertrophied ventricle fails to fully relax. These cardiac changes may progress to left ventricular chamber dilation and systolic dysfunction due to compression of subendocardial vessels and non-coronary artery mediated myocardial ischemia. In the arteries, chronic hypertension leads to cellular remodeling that narrows the lumen of small vessels and atherosclerosis in large vessels, particularly the coronary, carotid, and cerebral arteries; these arterial changes greatly increase the risk of myocardial infarction, stroke, and kidney failure.[7] Chronic antihypertensive treatment to maintain normal blood pressure decreases the relative risk of myocardial infarction and heart failure by 20% to 25% and of stroke by 30% to 40%.[8]

Complications of Acute Hypertension

Severely elevated blood pressure in patients without a history of hypertension or with chronic hypertension can cause acute end-organ dysfunction and can manifest clinically as a hypertensive emergency. The organs most sensitive to acute hypertension are the brain, heart, and kidneys. Within the brain, severe hypertension can overwhelm protective autoregulation mechanisms leading to diffuse vasogenic edema with vasospasm and arterial ischemia; when persistent, the syndrome recognized as hypertensive encephalopathy may develop resulting in altered mental status, headache, and vomiting and may progress to seizures, coma, and death if untreated. Acute hypertension also produces a substantial rise in afterload, which, when greater than the maximal potential systolic force of the heart, can precipitate acute heart failure manifested by pulmonary edema, shortness of breath, and eventually respiratory failure. Chronic hypertension causes endothelial dysfunction in the small arteries of the kidney, leading to impairment of normal arterial autoregulation. Thus, in the setting of severe, acute hypertension, kidney arterioles are unable to properly dilate, and increased systemic blood pressure and intraglomerular pressure cause ischemia and impaired filtration. Patients presenting with acute myocardial infarction and stroke often have concurrent acute hypertension as well. Though not necessarily manifestations of a hypertensive emergency, blood pressure monitoring and control are also important management considerations in these diseases.

Diagnosis and Evaluation in the Acute Setting

In accordance with the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC-7), the diagnosis of hypertension should be "based on

the average of 2 or more properly measured, seated blood pressure readings on each of two or more office visits."[9] Normal systolic and diastolic blood pressures are defined as <120 mmHg and 80 mmHg, respectively.[9] Prehypertension, a new classification included in the JNC-7 report, identifies patients with systolic blood pressure between 120 and 139 mmHg or diastolic blood pressure between 80 and 89 mmHg as an at risk population that needs education on lfestyle modification to prevent hypertension.[9] Stage I hypertension is defined by a systolic blood pressure between 140 and 159 mmHg or diastolic blood pressure between 90 and 99 mmHg.[9] JNC-7 defines stage 2 hypertension as systolic blood pressure > 160 mmHg or diastolic blood pressure > 100 mmHg.[9] This is especially important as more than 10% of individuals with hypertension meet stage 2 criteria, which are associated with a significantly increased risk of pressure-related cardiovascular mortality. This risk increases twofold with each 20/10 mmHg increment increase above the "ideal" 115/75 mmHg standard.[10]

Individuals often present acutely to emergency department or outpatient clinics with elevated blood pressure. The National Hospital Ambulatory Medical Care Survey reported that more than 40% of patients treated in emergency departments in the United States had moderate (ie, blood pressure > 140–159/90–99 mmHg) or severe (ie, blood pressure > 160/100 mmHg) elevations in their blood pressure.[11] Although many of these patients have been diagnosed previously with chronic hypertension that is inadequately treated, Ong et al reported that 33% of adults with hypertension are unaware of it, complicating the accurate diagnosis of hypertension in the acute care setting.[12] The emergency department provides an opportunity to identify patients with untreated hypertension who might not otherwise be evaluated by physicians. This prompted the American College of Emergency Physicians (ACEP) to publish a clinical policy in 2006 recommending that individuals with persistently elevated blood pressure (ie, defined as 2 or more systolic blood pressure readings > 140 mmHg or 2 or more diastolic blood pressure readings > 90 mmHg) be referred for evaluation of possible hypertension.[4]

The challenge for clinicians is to determine whether these individuals have undiagnosed or untreated hypertension or transient elevations due to their acute medical condition (eg, pain, injury, anxiety).[13] A new diagnosis of hypertension in the acute care setting should not be based on a single elevated blood pressure measurement. Serial blood pressure measurements should be performed using proper technique with appropriate sized blood pressure cuff while the patient is not under acute duress. The use of an inappropriately small blood pressure cuff in a large adult often results in a falsely elevated measurement. Prior studies have reported that most emergency department patients experience a spontaneous decrease in blood pressure on subsequent measurements.[4,14–17] Although many physicians believe that patient stress and anxiety significantly increase blood pressure measurements, one emergency department–based study found that pain scores showed only a slight positive correlation with change in systolic blood pressure ($r = 0.18$, $r^2 = 0.03$, $P = 0.03$) and was not correlated with diastolic blood pressure. In the same study, anxiety was not related to changes in blood pressure measurements.[13]

An additional requirement when evaluating patients with elevated blood pressure in the acute care setting is to determine whether the individual is experiencing any acute clinical symptoms related to previously undiagnosed hypertension or chronically undertreated hypertension. Individuals who have multiple elevated blood pressure measurements but are otherwise asymptomatic do not need emergent blood pressure reduction. Hypertensive emergencies, defined by the presence of acute end-organ damage, typically occur only in the setting of moderate or severe hypertension and are most common in patients with undertreated chronic hypertension.[18] According to the JNC-7 report, immediate hospitalization and parenteral drug therapy is required when patients present with a hypertensive emergency defined by marked blood pressure elevations (systolic blood pressure ≥ 180 mmHg or diastolic blood pressure ≥ 110 mmHg) and acute target-organ damage. Acute end-organ damage includes encephalopathy, myocardial infarction, unstable angina, pulmonary edema, eclampsia, stroke, life-threatening arterial bleed, or aortic dissection.[19] Classic symptoms of hypertensive emergencies including altered mental status and acute focal neurologic deficits or visual disturbances suggest ongoing neurologic damage while chest discomfort and dyspnea

suggest cardiac injury. Isolated headache, epistaxis, or dizziness do not indicate acute target-organ injury and are not diagnostic for a hypertensive emergency requiring emergent treatment to achieve blood pressure reduction.[20–23]

Routine diagnostic testing in healthy appearing individuals with elevated blood pressure is rarely helpful.[17,24] In individuals with concerning presentations for an acute hypertensive urgency or emergency, the JNC-7 recommendations for diagnostic testing prior to initiating antihypertensive therapy include an electrocardiogram, urinalysis, blood glucose, hematocrit, basic metabolic panel, and a fasting lipid panel.[19] A chest radiograph is often performed in the acute care setting especially in patients with cardiopulmonary complaints.[24] These studies are intended to determine whether the individual exhibits any findings of acute target-organ injury (ie, left ventricular hypertrophy, myocardial injury, underlying cardiac dysfunction, and chronic kidney disease) that may not be overtly visible on clinical assessment. A complete physical examination and alternative advanced testing might be required to exclude other target organ damage such as stroke, peripheral arterial disease, and retinopathy.[19] Clinicians should order additional laboratory or imaging studies based on the patient's condition and symptoms.

Treatment of the Severely Elevated Blood Pressure

Hypertensive emergency

Hypertensive emergency is defined as elevated blood pressured associated with acute or progressive end-organ damage and requires immediate reduction in blood pressure.[25] Often, diastolic blood pressure is greater than 140 mmHg. Hypertensive urgency is characterized by markedly elevated blood pressure without associated severe symptoms or target organ damage. The target organs of interest include the cardiovascular system (acute aortic dissection, heart failure, myocardial infarction), the cerebrovascular system (hypertensive encephalopathy, atherothrombotic brain infarction with severe hypertension, intracerebral hemorrhage, subarachnoid hemorrhage), and the renal system (acute glomerulonephritis, renovascular hypertension, renal crisis from collagen-vascular disease, and severe hypertension after kidney transplantation). In the setting of pregnancy, eclampsia and pre-eclampsia are also considered hypertensive emergencies and urgencies, respectively.

Expert opinion recommends immediate reduction in blood pressure for patients with hypertensive emergency, generally using parenteral medications. It should be noted that there are no data supporting superiority of one drug over another, and there is no definitive data that immediate reduction in blood pressure reduces morbidity or mortality.[26] Therefore, the choice regarding which medication to use should be based on patient characteristics (especially the type and location of end-organ injury that is present) and clinician familiarity with the drug. In addition, the risks of too rapidly reducing blood pressure and causing a watershed infarct of the brain or kidney should be taken into consideration. The choice of parenteral antihypertensive medication should be guided by the ability to provide adequate supervision of administration, achieve gradual and controlled reduction in blood pressure while avoiding target-organ damage, and avoid inherent drug toxicity.[25] Given these restrictions, the use of nitroprusside is no longer recommended in the treatment of hypertensive emergency due to the risk of relative hypotension with significant reduction in cerebral blood flow and increase in intracranial pressure,[27] vomiting, muscle twitching, and thiocyanate and cyanide toxicity.[18]

Commonly used parenteral drugs in the treatment of hypertensive emergency include nicardipine, esmolol, and labetalol (Table 1). Nicardipine is a dihydropyridine calcium channel blocker that results in steady, progressive blood pressure reduction with little change in heart rate when administered as a continuous infusion.[28] Esmolol is a relatively cardioselective beta blocker that is rapidly metabolized by blood esterases and has a short half-life of approximately 9 minutes. Labetalol is a beta blocker with some alpha antagonist activity that is safe and effective when given by bolus or continuous infusion.[29,30] Labetalol should be avoided in cases where left ventricular dysfunction may be worsened by beta blockade.

Hydralazine and intravenous nitroglycerin are also available, though their use is generally restricted to more narrow indications. Hydralazine is a direct vasodilator that can be given intravenously or intramuscularly. When used alone in older patients, its use can result in compensatory increases in cardiac output. Nitroglycerin is also a potent vasodilator that

Table 1. Parenteral drugs for the treatment of hypertensive emergency.[10,25]

Drug	Dose	Onset	Duration	Common side effects*
Nicardipine	5–15 mg/hour	5–10 min	1–4 hour	Headache, flushing, nausea, tachycardia
Esmolol	250–500 μg/kg/min for 4 min, then 50–300 μg/kg/min	1–2 min	10–20 min	Nausea
Labetalol	20–80 mg q10 min	5–10 min	3–6 h	Nausea, scalp tingling, burning throat, dizziness, heart block
Hydralazine	5–20 mg	10–20 min	1–4 h	Headache, vomiting, worsening angina
Nitroglycerin	20–500 μg/min	2–5 min	5–10 min	Headache, vomiting, methemoglobinemia, tolerance with prolonged use

Note: *All carry the risk of hypotension and dizziness.

decreases preload and in higher doses, afterload.[18] It is very effective for patients with acute hypertensive heart failure and is often used as an adjunct for patients with suspected acute coronary ischemia.

Additional options for the treatment of hypertensive emergencies include fenoldopam, clevidipine, and phentolamine. Fenoldopam is a peripheral dopamine-I agonist that maintains or increases renal perfusion while lowering blood pressure.[31] Clevidipine is an ultra–short-acting dihydropyridine calcium channel blocker that reduces blood pressure by selective arterial dilation, reducing afterload without affecting cardiac filling pressure or causing reflex tachycardia.[32] Phentolamine is an alpha blocker specifically used in the treatment of pheochromocytoma and tyramine-, cocaine-, or methamphetamine-induced catecholamine crises.

Hypertensive Urgency

The treatment of hypertensive urgency is generally by oral medications, preferably using the same medications patients are already taking. In fact, the focus in treatment of hypertensive urgency should be less on the blood pressure and more on identifying the proximate cause for the abrupt increase in blood pressure. Therefore, treatment should also address hypoxia, pain, volume overload, bladder distension, disturbed sleep, or other sources of autonomic instability. The goal should be to avoid rapid or precipitous reduction in blood pressure, which may precipitate adverse events such as watershed cerebrovascular infarct.

As in the treatment of hypertensive emergency, there are no data to support the use of one medication over another in the treatment of hypertensive urgency. The patient and the medical provider's familiarity with the drug should guide choice of therapy.

Oral medications that may be considered include captopril, labetalol, and clonidine. Captopril is a fast-acting oral angiotensin-converting enzyme inhibitor (ACEI) that can be administered sublingually as well as orally.[33] Care should be used in patients with volume depletion and renal insufficiency, and patients with an activated renin-angiotensin system may experience abrupt, marked blood pressure reduction.[34]

Labetalol, the alpha and beta blocker, can be given in 100 mg and 200 mg doses every hour. Clonidine is a central alpha agonist that has the side effect of sedation. Though effective for acute blood pressure reduction, it is also well known to cause rebound hypertension with missed doses in chronic use and should not be prescribed to patients with anticipated low medication adherence.

Diuretics such as furosemide or bumetanide may be used to lower blood pressure in patients with fluid overload and to prevent the loss of potency of other antihypertensive medications that cause fluid retention while they lower blood pressure. Care should be taken to avoid causing volume depletion, which increases renin and cause vasoconstriction and raise blood pressure.

The use of oral nifedipine is no longer recommended because it may induce rapid and significant fall in blood pressure in an uncontrolled manner, increasing the risk of cerebral hypoperfusion and watershed infarcts.[35]

Patient Disposition

Patients who seek care in the emergency department for hypertensive emergency should be admitted to the hospital, generally under intensive care. Intensive monitoring using an arterial line may be needed to most effectively use titratable medications.

Close monitoring is required to avoid precipitous and potentially harmful hypotension.

Patients with hypertensive urgency should be thoroughly and carefully evaluated in the emergency department and may require admission to the hospital to clearly define whether or not end-organ damage is present. Importantly, there is no evidence-based threshold to determine a safe blood pressure for discharge.[25] The cutoff of 180/115 mmHg is generally recommended based on expert opinion, but it is an arbitrary cutoff without supporting data. Care should be taken when evaluating patients with elevated blood pressure to first determine whether they have symptoms that may represent end-organ damage. Following an evaluation that does not reveal end-organ damage, blood pressure should be carefully and judiciously lowered over time. The key for effective management of such individuals is outpatient follow-up.

Conclusion

Elevated blood pressure is a common condition that can be associated with life threatening target organ damage. The evaluation, treatment, and disposition of these patients require thorough knowledge of potential complications and treatment options.

Author Contributions

Conceived and designed the experiments: CDM, WHS, PDL, TWB. Analysed the data: CDM, WHS, PDL, TWB. Wrote the first draft of the manuscript: CDM, WHS, PDL, TWB. Contributed to the writing of the manuscript: CDM, WHS, PDL, TWB. Agree with manuscript results and conclusions: CDM, WHS, PDL, TWB. Jointly developed the structure and arguments for the paper: CDM, WHS, PDL, TWB. Made critical revisions and approved final version: CDM, WHS, PDL, TWB. All authors reviewed and approved of the final manuscript.

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Competing Interests

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Disclosures and Ethics

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References

1. Wright JD, Hughes JP, Ostchega Y, Yoon SS, Nwankwo T. Mean systolic and diastolic blood pressure in adults aged 18 and over in the United States, 2001–2008. *Natl Health Stat Report*. 2011;(35):1–22, 24.
2. Vasan RS, Beiser A, Seshadri S, et al. Residual lifetime risk for developing hypertension in middle-aged women and men: The Framingham Heart Study. *JAMA*. 2002;287(8):1003–10.
3. Egan BM, Zhao Y, Axon RN. US trends in prevalence, awareness, treatment, and control of hypertension, 1988–2008. *JAMA*. 2010;303(20): 2043–50.
4. Decker WW, Godwin SA, Hess EP, Lenamond CC, Jagoda AS. Clinical policy: critical issues in the evaluation and management of adult patients with asymptomatic hypertension in the emergency department. *Ann Emerg Med*. 2006;47(3):237–49.
5. Kaplan NM, Flynn JT. *Kaplan's Clinical Hypertension*. 9th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006.
6. Deshmukh A, Kumar G, Kumar N, et al. Effect of Joint National Committee VII report on hospitalizations for hypertensive emergencies in the United States. *Am J Cardiol*. 2011;108(9):1277–82.
7. Libby P, Ridker PM, Hansson GK. Progress and challenges in translating the biology of atherosclerosis. *Nature*. 2011;473(7347):317–25.
8. Turnbull F, Neal B, Ninomiya T, et al. Effects of different regimens to lower blood pressure on major cardiovascular events in older and younger adults: meta-analysis of randomised trials. *BMJ*. 2008;336(7653):1121–3.

9. Chobanian AV, Bakris GL, Black HR, et al. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. *JAMA*. 2003;289(19): 2560–72.
10. Marx JA, Hockberger RS, Walls RM, Adams J, Rosen P. *Rosen's emergency medicine: concepts and clinical practice*. 7th ed. Philadelphia, PA: Mosby Elsevier; 2010.
11. Pitts SR, Niska RW, Xu J, Burt CW. National Hospital Ambulatory Medical Care Survey: 2006 emergency department summary. *Natl Health Stat Report*. 2008;7:1–38.
12. Ong KL, Cheung BM, Man YB, Lau CP, Lam KS. Prevalence, awareness, treatment, and control of hypertension among United States adults 1999–2004. *Hypertension*. 2007;49(1):69–75.
13. Tanabe P, Persell SD, Adams JG, McCormick JC, Martinovich Z, Baker DW. Increased blood pressure in the emergency department: pain, anxiety, or undiagnosed hypertension? *Ann Emerg Med*. 2008;51(3):221–9.
14. Fleming J, Meredith C, Henry J. Detection of hypertension in the emergency department. *Emerg Med J*. 2005;22(9):636–40.
15. Lebby T, Paloucek F, Dela Cruz F, Leikin JB. Blood pressure decrease prior to initiating pharmacological therapy in nonemergent hypertension. *Am J Emerg Med*. 1990;8(1):27–9.
16. Pitts SR, Adams RP. Emergency department hypertension and regression to the mean. *Ann Emerg Med*. 1998;31(2):214–8.
17. Slovis CM, Reddi AS. Increased blood pressure without evidence of acute end organ damage. *Ann Emerg Med*. 2008;51(Suppl 3):S7–9.
18. Varon J. Treatment of acute severe hypertension: current and newer agents. *Drugs*. 2008;68(3):283–97.
19. Chobanian AV, Bakris GL, Black HR, et al. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *Hypertension*. 2003;42(6):1206–52.
20. Herkner H, Laggner AN, Mullner M, et al. Hypertension in patients presenting with epistaxis. *Ann Emerg Med*. 2000;35(2):126–30.
21. Karras DJ, Kruus LK, Cienki JJ, et al. Evaluation and treatment of patients with severely elevated blood pressure in academic emergency departments: a multicenter study. *Ann Emerg Med*. 2006;47(3):230–6.
22. Karras DJ, Ufberg JW, Harrigan RA, Wald DA, Botros MS, McNamara RM. Lack of relationship between hypertension-associated symptoms and blood pressure in hypertensive ED patients. *Am J Emerg Med*. 2005;23(2): 106–10.
23. Theodosis P, Mouktaroudi M, Papadogiannis D, Ladas S, Papaspyrou S. Epistaxis of patients admitted in the emergency department is not indicative of underlying arterial hypertension. *Rhinology*. 2009;47(3):260–3.
24. Karras DJ, Kruus LK, Cienki JJ, et al. Utility of routine testing for patients with asymptomatic severe blood pressure elevation in the emergency department. *Ann Emerg Med*. 2008;51(3):231–9.
25. Kaplan NM, Victor RG. *Kaplan's Clinical Hypertension*. 10th ed. Philadelphia, PA: Wollters Kluwer Health: Lippincott Williams & Wilkins; 2010.
26. Perez MI, Musini VM. Pharmacological interventions for hypertensive emergencies: a Cochrane systematic review. *J Hum Hypertens*. 2008;22(9):596–607.
27. Immink RV, van den Born BJ, van Montfrans GA, Kim YS, Hollmann MW, van Lieshout JJ. Cerebral hemodynamics during treatment with sodium nitroprusside versus labetalol in malignant hypertension. *Hypertension*. 2008;52(2):236–40.
28. Mansoor GA, Frishman WH. Comprehensive management of hypertensive emergencies and urgencies. *Heart Dis*. 2002;4(6):358–71.
29. Huey J, Thomas JP, Hendricks DR, Wehmeyer AE, Johns LJ, MacCosbe PE. Clinical evaluation of intravenous labetalol for the treatment of hypertensive urgency. *Am J Hypertens*. 1988;1(3, pt 3):284S–9.
30. Leslie JB, Kalayjian RW, Sirgo MA, Plachetka JR, Watkins WD. Intravenous labetalol for treatment of postoperative hypertension. *Anesthesiology*. 1987;67(3):413–6.
31. Murphy MB, Murray C, Shorten GD. Fenoldopam: a selective peripheral dopamine-receptor agonist for the treatment of severe hypertension. *N Engl J Med*. 2001;345(21):1548–57.
32. Pollack CV, Varon J, Garrison NA, Ebrahimi R, Dunbar L, Peacock WFt. Clevidipine, an intravenous dihydropyridine calcium channel blocker, is safe and effective for the treatment of patients with acute severe hypertension. *Ann Emerg Med*. 2009;53(3):329–38.
33. Angeli P, Chiesa M, Caregaro L, et al. Comparison of sublingual captopril and nifedipine in immediate treatment of hypertensive emergencies. A randomized, single-blind clinical trial. *Arch Intern Med*. 1991;151(4):678–82.
34. Postma CT, Dennesen PJ, de Boo T, Thien T. First dose hypotension after captopril; can it be predicted? A study of 240 patients. *J Hum Hypertens*. 1992;6(3):205–9.
35. Shayne PH, Pitts SR. Severely increased blood pressure in the emergency department. *Ann Emerg Med*. 2003;41(4):513–29.