Chapter e31: Acute Hypertensive Crisis

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CHAPTER SUMMARY FROM THE PHARMACOTHERAPY HANDBOOK

For the Chapter in the Schwinghammer Handbook, please go to Chapter 10, Hypertension.

KEY CONCEPTS

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1. Hypertensive crisis is an acute condition of very high blood pressure (BP), with either a systolic BP (SBP) > 180 mm Hg, diastolic (DBP) > 120 mm Hg, or both.
2. The presence of new or worsening target end-organ damage differentiates hypertensive emergency from hypertensive urgency.
3. Autoregulation of perfusion is a key physiological concept that explains the pathophysiology of hypertensive crisis.
4. The affected organs during a hypertensive emergency commonly include the heart, lungs, brain, vasculature, kidneys, and eyes.
5. Hypertensive urgency does not require rapid (ie, immediate) BP reduction because the benefit does not outweigh the risk. A more gradual BP reduction over several hours to days is optimal. Hypertensive urgency is managed by resuming omitted antihypertensive therapy, increasing current doses of antihypertensives, or adding additional agents to achieve control.
6. Hypertensive emergency is a medical emergency that requires acute hospitalization, frequent monitoring, and, in most cases, intravenous (IV) antihypertensive therapy to control BP.
7. The goal for managing hypertensive emergencies is to prevent additional organ damage. Target BP goals are different than those for chronic treatment of high BP, and the timeframe for achieving goals is determined by the organ systems affected and comorbities.
8. Despite no clear mortality benefit with the use of IV antihypertensive agents, their use is still the standard of care intended to reduce further organ damage. There are multiple IV antihypertensive infusions to choose from. The type of organ damage present, clinical characteristics of the patient, and pharmacological properties of the medication should guide therapy selection.
9. Medication nonadherence is a modifiable risk factor that commonly leads to hypertensive crises. Interventions aimed at improving adherence (eg, patient education regarding the importance of medication adherence, simplification of medication regimens, use of fixed-dose combination antihypertensives products, use of low-cost generic agents) and periodic, scheduled follow-up are essential.

BEYOND THE BOOK

BEYOND THE BOOK

To improve your ability to identify the clinical nuances encountered when treating patients with hypertensive crises and also aid in your understanding of the concept of autoregulation, please listen to the podcast and watch the video below.

1. Hypertensive Emergencies Demystified: A Brief Clinical Review on the management of hypertensive crisis—HelixTalk: https://www.rosalindfranklin.edu/academics/college-of-pharmacy/helixtalk/helixtalk-episode-134-hypertensive-emergencies-demystified-a-brief-clinical-review/
    - The discussion of hypertensive emergency uses an illustrative case in which a patient presents with acute ischemic stroke to highlight the complexities in care with which these patients present.
2. Autoregulation—Baroreceptors—Rishi Desai (Khan Academy): https://www.youtube.com/watch?v=R07V4NOwfsk&t=602s

INTRODUCTION

As implied by its nomenclature, an acute hypertensive crisis is both a temporal and numerical characterization of dangerously elevated blood pressure (BP) that requires prompt assessment and clinical intervention. However, this broad terminology does not distinguish between patients who require chronic versus emergent interventions to control BP and prevent or minimize complications. For example, some patients with acute hypertensive crisis require emergent escalation to intensive care and intravenous (IV) antihypertensive therapy while others can be managed less aggressively by resuming or adjusting chronic antihypertensive treatment and monitoring.

The American College of Cardiology (ACC) and the American Heart Association (AHA) characterize an acute hypertensive crisis as a rapid onset of very high BP (systolic [SBP] > 180 mm Hg and/or diastolic [DBP] > 120 mm Hg).[1] While the joint guidelines by the European Society of Cardiology and the European Society of Hypertension define the BP values slightly differently (SBP ≥ 180 mm Hg and DBP ≥ 110 mm Hg), both the European and American guidelines agree that patients must be classified based on clinical presentation rather than a BP reading alone.[1,2] Patients with acute hypertensive crisis and evidence of new or worsening target organ damage are characterized as a *hypertensive emergency* while those without evidence of target organ damage are characterized as a *hypertensive urgency*. Both conditions require acute attention and evaluation, but the treatment algorithms differ based on clinical presentation.

There is debate about the most appropriate terminology to use when characterizing acute hypertensive crisis. In clinical practice, indiscriminate use and interpretation of the nomenclature confound patient evaluation and treatment decisions. Improper management of an acute hypertensive crisis can lead to serious adverse outcomes. Therefore, clinicians need to clearly understand the guideline-based definitions, use consistent and appropriate terminology when communicating to other providers about patients with acute hypertensive crisis, and, most importantly, manage these patients safely and effectively. This chapter will use guideline-based definitions to help clinicians identify, characterize, and manage an acute hypertensive crisis.

EPIDEMIOLOGY

Estimates of the prevalence of hypertensive crisis and, more specifically, hypertensive urgencies and emergencies, are difficult to describe due to variations in definitions of the condition. Approximately 5 out of every 1,000 patients admitted to the emergency department present with a hypertensive crisis.[3] Two out of 1,000 admissions to the emergency department are diagnosed with a hypertensive emergency.[4] For patients with a previous diagnosis of hypertension, 6 out of 1,000 admissions to the emergency department present with a hypertensive emergency.[4] Of all patients with hypertensive crisis, approximately 60% to 75% of these patients present with hypertensive urgency versus 25% to 40% who present with a hypertensive emergency.[5] Demographically, there is an unclear relationship with gender though some believe there are slightly more cases in women.[6] Patient characteristics associated with the most risk include advanced age (eg, 65 years or older), Black ancestry, and low income (eg, lowest quartile of income).[4,6]

Clinical outcomes associated with acute hypertensive crisis are poor. The estimated 1-year mortality rate is over 79% for untreated patients.[7] Patients admitted with hypertensive crisis to emergency departments have a 90-day hospital readmission rate and mortality of 37% and 4.6%, respectively, underscoring the burden and impact of this condition.[8]

ETIOLOGY

The etiology of acute hypertensive crisis is often medication-related, although other causes are possible. Medication nonadherence is the single most common risk factor for acute hypertensive crisis.[9] In addition, the withdrawal effects precipitated by missing doses of certain antihypertensives, such as β-blockers and clonidine, may exacerbate a hypertensive crisis. Drug-drug or drug-disease state interactions (eg, sympathomimetic medications) and the use of illicit substances with vasoactive effects (eg, cocaine, methamphetamine, ecstasy) can also be sources of a medication-related hypertensive crisis. Secondary causes of hypertensive crises include alcohol withdrawal, pheochromocytoma, obstructive sleep apnea, renal artery stenosis, severe thyroid disorders, and hyperaldosteronism.[10] Common medical and pharmacological causes for hypertensive crisis are summarized in Table e31-1.

TABLE e31-1

Common Medical and Pharmacological Causes of Hypertensive Crisis

Medical	
Organ System	**Causative Examples**
Brain	Ischemic or hemorrhagic stroke
Lungs	Obstructive sleep apnea
Heart	Primary hypertension
Kidney	Renal artery stenosis
Endocrine	Hyperaldosteronism, pheochromocytoma, Cushing syndrome, severe thyroid disorders
Pharmacological	
Condition	**Causative Examples**
Nonadherence with prescribed antihypertensive therapy	Patient misconceptions
	Lack of access
Withdrawal of antihypertensive therapy	β-blockers, clonidine
Vasoactive substances	Cocaine, amphetamines, ecstasy
Acute withdrawal of substances and medications	Ethanol, opioids
Drug-drug interactions	Serotonin syndrome
Drug-food interactions	Tyramine containing foods with monoamine oxidase inhibitors
Drug-disease state interactions	NSAIDs, sympathomimetics in patients with hypertension

NSAIDs, nonsteroidal anti-inflammatory drugs.

Data from References 30 and 31.

PATHOPHYSIOLOGY

3 The pathophysiology of acute hypertensive crisis is multifactorial. Although not fully understood, failure of autoregulation of blood flow and inappropriate activation of the renin–angiotensin–aldosterone system (RAAS) likely play key roles in developing hypertensive crisis.[12] Several medical and pharmacological conditions may lead to sympathetic hyperactivity and result in severe elevations in BP. Examples of these conditions include pheochromocytoma, acute intoxication or withdrawal of certain medications, and obstructive sleep apnea. Pheochromocytomas (adrenal tumors) and paragangliomas (non-adrenal tumors) both release catecholamines (epinephrine, norepinephrine, and dopamine). These catecholamines bind to α_1 receptors on vascular smooth muscle, causing vasoconstriction, and β_1 receptors on the heart, causing tachycardia.[13] Similarly, intoxication with

cocaine, amphetamines, or other sympathomimetic medications also increases catecholamines causing similar effects. Withdrawal of substances and medications that blunt the sympathetic nervous system (eg, ethanol, opioids, clonidine, β-blockers) can cause an abrupt rebound of catecholamine release and subsequent hypertensive crisis.[14] Additionally, obstructive sleep apnea enhances sympathetic outflow and catecholamine release, which increases BP. Both renal artery stenosis and hyperaldosteronism upregulate the RAAS, leading to vasoconstriction, sodium and water retention, and subsequent BP elevations.[10] For a more detailed explanation of the pathophysiology of hypertension, please see Chapter 30, "Hypertension."

2 While these mechanisms may lead to acute elevations of BP, the additional pathophysiological changes precipitated by target organ damage may further contribute to the overarching pathophysiology of the disease.[15] Thus, the pathophysiology of acute hypertensive crisis is best understood by categorizing it as hypertensive urgency or hypertensive emergency and, in the case of a hypertensive emergency, subclassifying further by the type(s) of organ damage present.

Autoregulation of Blood Pressure

3 4 The concept of autoregulation is a key component of the pathophysiological mechanism underlying hypertensive emergency. Under normal physiologic circumstances, autoregulation maintains stable blood flow to organs despite alterations in perfusion pressure via alterations in vascular resistance. In response to changes in BP, autoregulation typically maintains perfusion pressure and blood flow to organs when BP is below 180/120 mm Hg for patients with usually well-controlled BP. Autoregulation curves may vary depending on the patient's baseline average BP (Fig. e31-1). Patients with sustained, uncontrolled hypertension tend to have rightward shifts of the autoregulation curve and can typically tolerate higher BP than patients with normal BP at baseline.[16] Once a patient-specific critical point on the autoregulation curve is reached, excessive vasoconstriction will decrease perfusion to vital organs. Additionally, there may be areas where blood vessels can no longer maintain adequate resistance and vasodilation occurs. This abrupt vasoconstriction and isolated areas of vasodilation may lead to precipitous drops in perfusion and contribute to target organ dysfunction.[12] Organs most susceptible to dysfunction due to an acute hypertensive crisis include the heart, arterial vasculature, brain, kidney, and eyes (Fig. e31-2).

FIGURE e31-1

Autoregulation and the effect on cerebral blood flow.

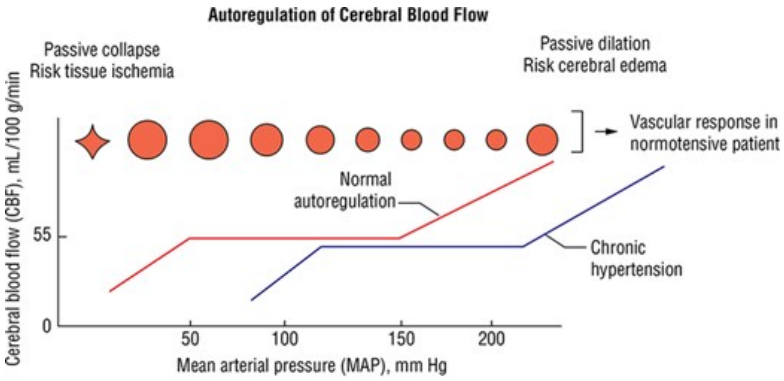
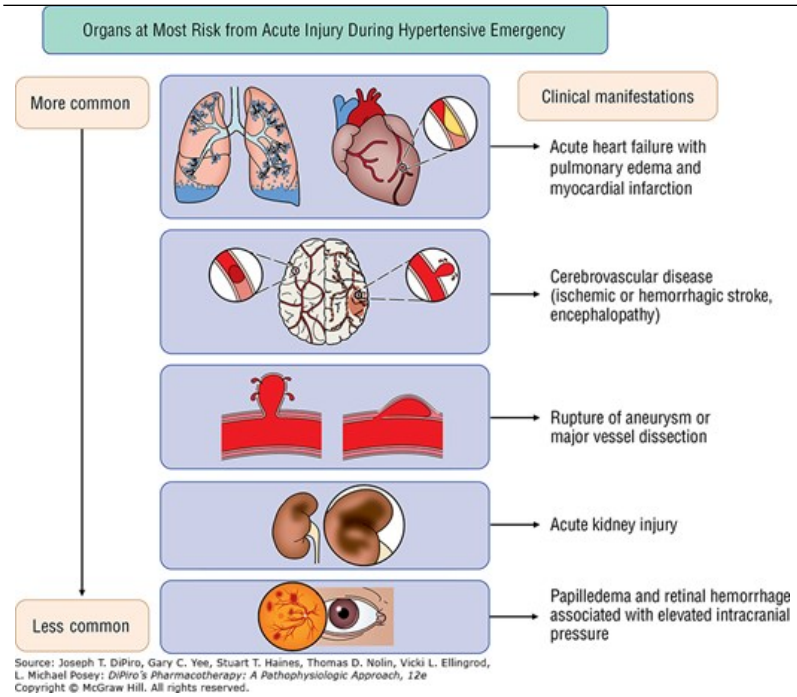


FIGURE e31-2

Organs at most risk from acute injury during hypertensive emergency. *(Data from References 4, 17, and 18.)*



Additionally, target end-organ damage may be caused by the overactivation of the RAAS pathway. Decreases in perfusion may cause upregulation of the RAAS mechanisms, which further increase vasoconstriction. The resulting increase in vasoconstrictive peptides, including angiotensin II, norepinephrine, endothelin, and antidiuretic hormone, worsen local tissue ischemia. Excessive vasoconstriction also leads to endothelial damage, platelet activation and aggregation, and further target organ dysfunction.[16]

Hypertensive Urgency

Patients with hypertensive urgency present with extreme elevations in BP *without* signs or symptoms of new or worsening target organ dysfunction. However, these patients are at risk of impending target organ dysfunction because of severe BP elevations. Commonly, the elevations of BP seen during hypertensive urgency are secondary to antihypertensive therapy being withdrawn.[1]

Hypertensive Emergency and Target Organ Dysfunction

4 In the setting of hypertensive emergency, target organ dysfunction represents an acute change in organ function from baseline. For example, a patient with no prior history of kidney disease may present with acute kidney injury secondary to severe elevations in BP which would qualify as a hypertensive emergency. In contrast, acute elevations in BP in a patient with a history of chronic kidney disease (CKD) secondary to longstanding hypertension should only be classified as a hypertensive emergency if chronic kidney function is worsening or if new target organ dysfunction is identified. In this section, types of target organ dysfunction will be further summarized.

Cardiovascular

Myocardial Infarction

Acute elevations in BP can lead to endothelial damage in coronary arteries. Subsequent activation of the coagulation cascade and platelet aggregation can lead to ischemia and further release of vasoactive peptides, potentiating the endothelial damage. Ischemia may irreversibly lead to infarction of the myocytes if BP is not rapidly controlled.[15]

Acute Decompensated Heart Failure

Patients presenting with acute decompensated heart failure (ADHF) may have underlying reduced or preserved ejection fraction. Patients with a history of baseline heart failure, including systolic or diastolic dysfunction, are at a higher risk for ADHF from severe hypertension due to the inability

of the left ventricle to overcome increased afterload, the pressure that the heart must overcome to achieve adequate cardiac output. Acute increases in afterload place patients at risk for pulmonary edema.[15]

Aortic Dissection

Aortic dissection can result from shear stress on the aortic wall. Over time, elevated BP can lead to tearing of the intima, or the innermost layer, of the aorta, which allows blood to pool in the aortic wall and form a "false lumen." This reduces the critical supply of blood flow to organs relying on downstream perfusion. Arterial branches of the aorta may also become compressed as the dissection extends distally, leading to organ ischemia.[19]

Neurological

Acute Stroke

Cerebral autoregulation typically allows for constant cerebral blood flow in the capillaries from a mean arterial pressure (MAP) of 60 to 150 mm Hg. When the BP exceeds this upper limit, progressive vasoconstriction and areas of vasodilation can occur. Cerebral ischemia may result from this disrupted autoregulation and endothelial injury resulting from sustained elevations in BP. Areas of vasodilation can also lead to disruptions of the blood-brain barrier, cerebral edema, and microhemorrhages. Additionally, a complicating factor in ischemic stroke is that acute BP lowering can increase ischemia, especially in the penumbra surrounding the ischemic core. High BP may also lead to a hemorrhagic transformation of the ischemic area or cause continued bleeding in the setting of intracerebral hemorrhage (ICH) or subarachnoid hemorrhage.[19,20]

Hypertensive Encephalopathy

Disruptions in the blood-brain barrier and cerebral edema secondary to severely elevated BP may lead to a condition known as hypertensive encephalopathy.[19] This is thought to occur as a result of the elevated BP exceeding the brain's ability for autoregulation. Increased vascular permeability causes extravasation of intravascular fluid into the brain, which leads to a broad range of nonspecific neurological symptoms.[16]

Kidney

Acute Kidney Injury

Patients with chronic uncontrolled hypertension are predisposed to endothelial dysfunction in the renal arteries, including the afferent arteriole. The resultant structural changes can lead to progressive narrowing of vessels and fibrosis, which impair the autoregulation mechanisms of the kidney. During acute, severe elevations in BP, intraglomerular pressure is no longer preserved by autoregulation, leading to acute renal ischemia.[19]

Ocular

Acute Retinopathy

Acute retinopathy is an ocular complication of hypertensive crisis. Patients with acute, severe elevations in BP may develop retinal hemorrhages, exudates, and papilledema due to increased intracranial pressure, leading to rapid and progressive vision loss.[19]

Other

Pre-eclampsia

Pre-eclampsia is defined as BP greater than or equal to 140/90 mm Hg on two readings at least 4 hours apart any time after 20 weeks gestation or one reading of 160/110 mm Hg or more plus proteinuria.[21] Other types of maternal target organ dysfunction in this syndrome include acute kidney injury, acute liver injury, neurological complications such as seizures, and hematological complications such as clotting abnormalities. This syndrome is triggered by the release of pro-inflammatory cytokines from the placenta during times of placental stress. These stressors may be multifactorial and include uteroplacental malperfusion and other mismatch states between maternal perfusion and the metabolic demands of the placenta and the fetus. Pre-eclampsia can ultimately lead to maternal and fetal morbidity and mortality if not managed rapidly.[22]

CLINICAL PRESENTATION

CLINICAL PRESENTATION: Hypertensive Crisis

General

May appear asymptomatic (hypertensive urgency) or with evidence of target organ dysfunction (hypertensive urgency)

Symptoms

Headache, nausea, vomiting, confusion, epistaxis, shortness of breath, chest pain, dizziness, paresthesia, vision changes

Signs

SBP > 180 mm Hg and/or DBP > 120 mm Hg, focal neurological deficits, crackles on lung auscultation

Routine laboratory tests guided by symptoms

Blood urea nitrogen/serum creatinine with estimated glomerular filtration rate (using CKD-EPI Creatinine Equation 2021 [https://www.kidney.org/professionals/kdoqi/gfr_calculator/formula]), serum electrolytes (sodium, potassium), blood glucose, complete blood counts, toxicology screens, pregnancy tests, cardiac troponins

Other tests

Electrocardiogram, chest radiographs, fundoscopic examination of the eye, computerized tomography of the head

Target organ damage

- Brain (ischemic or hemorrhagic stroke, encephalopathy, cerebral edema)
- Eyes (papilledema, retinal hemorrhage)
- Heart (acute heart failure, myocardial infarction)
- Vascular (rupture of aneurysm or major vessel dissection)
- Kidney (acute or acute on chronic kidney injury)

The clinical presentation of patients with a hypertensive crisis can vary greatly due to the broad definition of the condition. In addition to the extremely elevated BP, presenting symptoms commonly include headache, epistaxis, shortness of breath, chest pain, neurological deficits such as focal weakness or vision changes, dizziness, or paresthesia.[18,23,24] More specifically, patients with hypertensive *urgency* may present with mild or no symptoms since no target organ damage is present despite the markedly elevated BP. Patients with hypertensive urgency more commonly complain of headaches or non-specific symptoms.[17] In contrast, those with a hypertensive *emergency*, who by definition have acute target organ damage present, are more likely to present with neurological symptoms, dyspnea, and/or chest pain but may also describe other nonspecific symptoms.[17] Clinicians should be aware of the common presenting symptoms and promptly evaluate target organ systems when assessing the patient.

A comprehensive history of medical conditions, surgeries, and medications should be obtained for all patients.[25] This interview should include the onset of any symptoms and concurrent ingestions of any vasoactive substances (eg, prescription medication, non-prescription medications, dietary supplements, herbals, illicit drugs). Nonadherence with prescription BP medications is a common cause of hypertensive crises, requiring clinicians to evaluate and assess adherence.[26] A detailed timeline of the ingestion of any illicit vasoactive substances (eg, cocaine, methamphetamine) is also helpful in determining a cause. Remember to screen carefully for drug-drug and drug-supplement interactions when investigating for acute causation of the hypertensive crisis. A classic drug-food interaction known to cause an acute hypertensive crisis is between tyramine-containing food and

monoamine oxidase inhibitors, sometimes known as the "cheese effect."[27] Tyramine is an amino acid found in various foods, including strong or aged cheeses, fermented foods like sauerkraut and kimchi, aged and fermented meats, tap and unpasteurized beer, and pickled herring.[28] The enzyme monoamine oxidase A can prevent the absorption of tyramine by metabolizing it in the gut wall. In the presence of a nonselective monoamine oxidase inhibitor (eg, selegiline, phenelzine, tranylcypromine, isocarboxazid), tyramine is absorbed systemically and converted to norepinephrine, which causes a significant acute elevation in BP.[28] Lastly, recent changes in dietary behavior may also be useful information to obtain for additional reasons. For example, acute changes in dietary sodium intake (eg, recent large-sodium meal) may be a causative factor in precipitating a hypertensive crisis in sodium-sensitive or at-risk patients.[26]

Blood Pressure Assessment

Obtaining accurate BP reading in patients being evaluated for hypertensive crisis is critical. Factors such as poor assessment technique can lead to misdiagnosis and inappropriate treatment of elevated BP. Unfortunately, initiating inappropriate treatment interventions in response to an inaccurately measured BP reading can cause harm. Thus, clinicians should observe and verify that appropriate techniques were used to measure BP before recommending treatment regimens. Knowledge of the correct techniques can help clinicians troubleshoot in patients where traditional BP assessments may be challenging, not possible, or not recommended to ensure accurate BP measurements are recorded. Some examples include patients who are obese or underweight, patients with upper extremity amputation, and patients with certain post-surgical conditions (eg, mastectomy, presence of an arteriovenous fistula). Chapter 30, "Hypertension," contains a more detailed discussion regarding BP measurement techniques.

Clinicians should resist the temptation to react aggressively to a single elevated BP reading. A single BP value may not be the best indication of the overall clinical picture. For example, a patient presenting in acute pain or with anxiety may exhibit an elevated BP with no other symptoms of target end-organ damage. In these cases, hypertension is manifesting as a symptom of a painful event or anxiety. With appropriate treatment of the pain or anxiety, elevations in BP attributable to those conditions may quickly normalize. However, patients with an extremely elevated BP must receive prompt attention and further clinical follow-up. Since the clinical situations in which patients with reportedly high BP can vary greatly, a clinician must evaluate each elevated value in the context of the patient's clinical situation, symptoms, and medical history. A high BP reading should be repeated minimally two to three times about 1 to 2 minutes apart and averaged to assess the clinical situation more accurately.[26] Clinicians should also check BP readings on both arms.[29] A significant difference between the two readings may indicate an aortic dissection, a medical emergency requiring immediate workup, and a compelling indication for rapid BP lowering.

Target Organ Damage Assessment

The hallmark of managing a hypertensive crisis is differentiating between hypertensive urgency and hypertensive emergency. This differentiation will ultimately guide clinicians to an appropriate treatment regimen. It is important to note the time course of the elevation of the BP. Patients not known to be hypertensive can present with target organ damage if the BP elevation is rapid and acute. Target organ damage may occur in patients that do not meet the traditional BP parameters used to define a hypertensive crisis. Additionally, patients with chronic hypertension may be conditioned to high pressures via shifts in autoregulation and can present with no symptoms. Therefore, reliance on BP readings alone to diagnose and manage hypertensive crises can be misleading and potentially lead to adverse outcomes due to inappropriate treatment decisions. The patient's history of present illness, the time course of the BP elevation, and presenting symptoms are good clues to the potential presence of target organ damage and the need for emergent interventions. However, some symptoms can be nonspecific. Therefore, a systematic approach to evaluation is helpful to minimize the risk of missing an affected organ system.

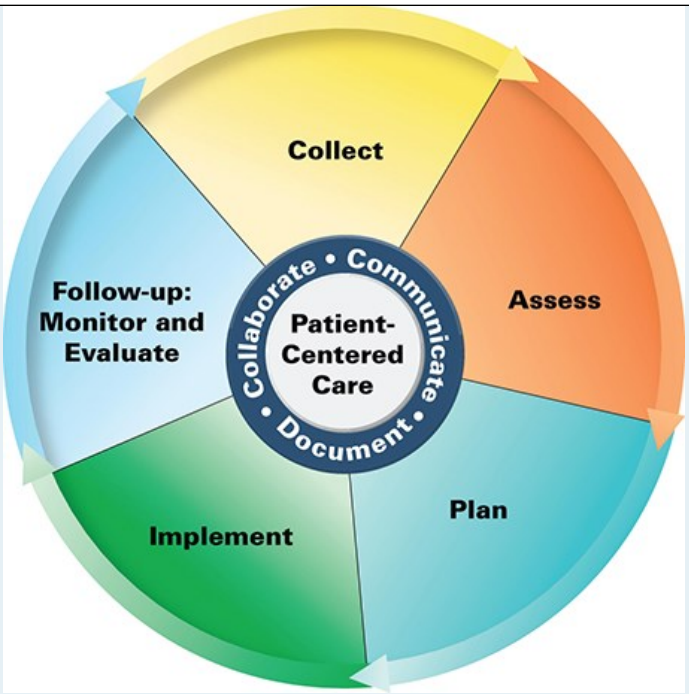
A systematic approach to patient evaluation generally starts from the top-down, commencing with a neurological assessment. Patients should be evaluated for any focal neurological deficits which may be indicative of a stroke. Common signs of stroke include facial asymmetry, unilateral weakness or paresthesia, confusion, visual changes, dizziness or imbalance, or a sudden headache. Another non-stroke neurological condition presenting as a hypertensive emergency is hypertensive encephalopathy. Hypertensive encephalopathy, which is the result of cerebral edema and elevations in intracranial pressure, may manifest as headache, vomiting, confusion, visual changes, seizures, and coma. This diagnosis should be considered after other conditions have been eliminated from the differential diagnosis.[16] Neurological imaging may assist with diagnosing both stroke and hypertensive encephalopathy and is required in patients presenting with neurological symptoms.[29] Fundoscopic examination of the eye is another important means to evaluate target organ damage and should be part of a patient's clinical workup.[29] Important clinical findings from fundoscopic examination include arteriolar narrowing, retinopathy, hemorrhages (flame, blot, or dot), and papillary edema.[12,25,29] If the patient reports chest pain,

acute coronary syndrome (ACS) should be on the differential diagnosis prompting a more detailed evaluation of symptoms, including onset, quality, duration, and precipitating and mitigating factors. Complaints of shortness of breath should be followed up with evaluations of oxygen saturation and auscultation of the lungs. Crackles on auscultation may be a sign of pulmonary edema and potentially heart failure. A chest radiograph assists in confirming the diagnosis of heart failure. Peripheral edema in the extremities and jugular venous distention can also be signs of volume overload and cardiac failure. An electrocardiogram is needed to detect cardiac ischemia and arrhythmias from ischemia or heart failure. An echocardiogram can confirm the clinical findings of cardiac dysfunction. Discordance between BP readings taken on different extremities may suggest an aortic dissection prompting an additional emergent workup.[16] An abdominal examination is also necessary to evaluate for aortic aneurysms.[12]

Laboratory assessment of patients presenting with a hypertensive crisis is critical to detecting target organ damage and selecting appropriate pharmacotherapy. Basic metabolic panels including electrolytes, glucose, serum creatinine, and complete blood cell counts are useful initial laboratory assessments.[16,29] An evaluation of kidney function is essential since the kidneys are at-risk organs. Evidence of acute kidney injury or acute-on-chronic kidney injury is important to detect since kidney disease is common in this population and may inform pharmacotherapy decisions.[29] Therefore, it is important to evaluate current serum creatinine and previously reported values to note trends in kidney function. New or worsening hematuria and proteinuria on urinalysis are indicative of kidney damage. Laboratory evidence consistent with acute kidney damage or acute-on-chronic kidney injury (eg, acute elevations in serum creatinine in patients with CKD) would be sufficient to classify a hypertensive emergency. Chapter 30, "Hypertension," contains a complete discussion of the laboratory assessment necessary in patients that require further diagnosis of secondary causes of hypertension. Patients suspected of illicit drug use should have a toxicologic urinalysis to confirm the presence of causative substances. In women of childbearing age, pregnancy tests are also necessary to assist with the diagnosis of pre-eclampsia or eclampsia and guide pharmacotherapy decisions with the safety of the fetus in mind. Patients who are pregnant with acute onset severe hypertension during their pregnancy require a specific workup for pre-eclampsia due to the high maternal and fetal risk for morbidity and mortality. In the absence of proteinuria, the diagnosis can be made with new onset of thrombocytopenia (platelet count < 100,000/mm^3 [100×10^9/L]), renal insufficiency (serum creatinine > 1.1 mg/dL [97 µmol/L] or doubled from baseline), impaired liver function (transaminases two times the upper limit of normal), pulmonary edema, or new-onset headache unresponsive to medication and not due to an alternative diagnosis. Pre-eclampsia can be further categorized by the presence of severe features which include BP of 160/110 mm Hg or more on two readings at least 4 hours apart, thrombocytopenia, renal insufficiency, impaired liver function (elevated transaminases as above or severe persistent right upper quadrant or epigastric pain unresponsive to medications), or visual disturbances. Eclampsia occurs when there are new-onset tonic-clonic, focal, or multifocal seizures that cannot be explained by other conditions (eg, epilepsy, stroke, drug use).

PATIENT CARE PROCESS

Patient Care Process* for the Management of Hypertensive Crisis



Collect

- Patient characteristics (eg, age, race, sex, pregnancy)
- Patient history (past medical/surgical, family, social, eg, dietary habits, tobacco use, alcohol use, illicit use)
- Blood Pressure (BP) readings (when, how obtained, usual BP range)
- Current or recent use of prescription medications or substances (eg, prior antihypertensive medication use, over-the-counter medications, dietary supplements, illicit substances) (Table e31-1)
- Objective data
  - BP, heart rate (HR), height, weight, and BMI
  - Physical exam results (chest auscultation, fundoscopic exam, neurological exam)
  - Labs (eg, serum electrolytes, SCr, blood urea nitrogen)
  - Other diagnostic tests when indicated (eg, ECG, echocardiogram, brain imaging)

Assess

- Presence of target end-organ damage (eg, myocardial infarction, stroke, new or worsening kidney function) (Fig. e31-2)
- Adherence to antihypertensive medications
- Drug-drug, drug-food, and drug-disease state interactions that cause hypertension
- BP goal and timeframe to achieve the goal based on target end-organ damage
- Appropriate antihypertensive infusion(s), if necessary, to achieve BP goals
- Appropriateness and effectiveness of the current antihypertensive regimen

Plan*

- Medication therapy regimen including specific antihypertensive(s), dose, route, frequency, and duration; specify the continuation and discontinuation of existing therapies (Table e31-3)
- Monitoring parameters including efficacy (eg, BP, cardiovascular events, kidney health), safety (medication-specific adverse effects, new or worsening tissue ischemia), and timeframe
- Patient education (eg, the purpose of treatment, dietary and lifestyle modification, medication therapy, adherence)
- Referrals to other providers when appropriate (eg, physician, dietician)
- Appropriate transition from parenteral to oral antihypertensive therapy

Implement*

- Facilitate medication administration in a timely manner (Table e31-2)
- Communicate dosing, titration, and monitoring parameters of acute antihypertensive therapy with clinical team
- Use motivational interviewing and coaching strategies to maximize medication adherence

Follow-up: Monitor and Evaluate

- Determine BP goal attainment and resolution of target end-organ damage (Fig. e31-3)
- Presence of adverse effects

****Collaborate with patients, caregivers, and other healthcare professionals.***

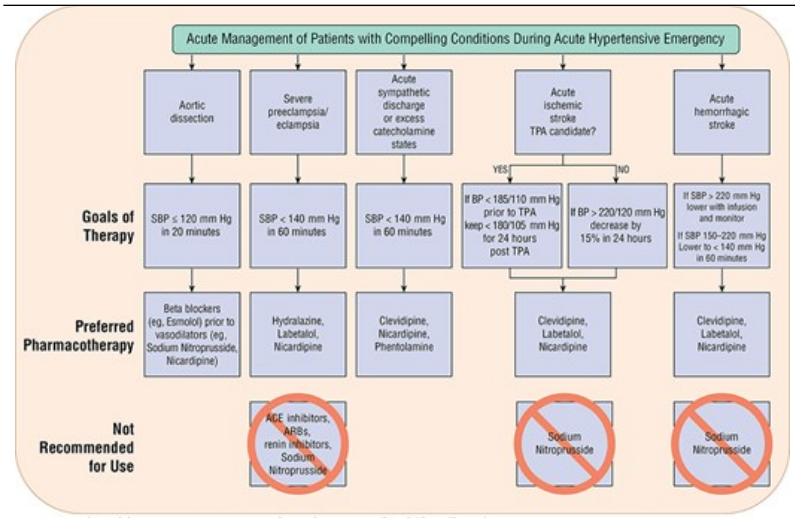
TREATMENT

Treatment Goals

[7,8] The goals of treatment for patients presenting with hypertensive crises are to carefully assess and characterize the degree of hypertension, evaluate for any precipitating risk factors, characterize the condition as hypertensive urgency or emergency based on the presence of acute target organ damage, and safely reduce the BP to specific goals in an appropriate timeframe, based on compelling indications.[1] Ultimately, clinical goals, including the selection of appropriate BP targets, are determined by the classification (hypertensive urgency or emergency) and the presence of compelling indications. In patients with evidence of acute target organ damage (hypertensive emergency), the primary goal is to avoid further worsening the organ damage by lowering BP quickly and safely. Since the long-term consequences of a further worsening of organ damage can have profound clinical impacts, selecting the right treatment course is paramount. Selecting appropriate pharmacotherapy based on the presence of compelling indications, clinical presentation, and pharmacological properties of the antihypertensives may minimize long-term health consequences (Fig. e31-3).[1,29]

FIGURE e31-3

Summary of treatment recommendations for hypertensive emergencies based on specific target organ damage. (ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; BP, blood pressure; SBP, systolic blood pressure; TPA, tissue plasminogen activator.)



Blood Pressure Goals

Hypertensive Urgency

Hypertensive urgency is characterized as patients presenting with BP elevations greater than 180/120 mm Hg without the presence of target organ damage. Despite using the term "urgency" in the description of the condition, there is little data to support that patients with hypertensive urgency are at acute, urgent risk for negative sequelae.[30] For example, a review of patients with hypertensive urgency presenting to outpatient care centers found the rate of major adverse cardiovascular events within seven days to be low (<0.5%) in patients admitted to the hospital and an even lower (<0.1%) in patients sent home.[31] While patients with hypertensive urgency are at risk of the long-term adverse effects of uncontrolled hypertension, in the short term, these risks are minimal in the absence of acute target organ damage. In fact, the consequences of acutely and aggressively lowering BP in patients with hypertensive urgency, such as ischemic stroke, myocardial infarction, and renal ischemia, may outweigh any derived benefit. The ACC/AHA Guideline offers no specific BP goal in the acute management of hypertensive urgency.[1] Acute BP lowering, referral to the emergency department, or hospital admission is not recommended for patients with hypertensive urgency.[1]

Hypertensive Emergency

Specific BP goals for patients with a hypertensive emergency are determined by the target organ damage present. Table e31-2 summarizes BP goals for hypertensive emergencies.

TABLE e31-2

Target Organ Damage, Blood Pressure Targets, and Medication Choices for Hypertensive Emergencies

Target Organ Damage	Blood Pressure Target	IV Antihypertensive Selection
Acute kidney injury	Reduce BP by a max of 25% in the first hour, then to 160/100-110 mm Hg over the next 2-6 hours, then to normal over the next 24-48 hours	Most IV antihypertensives are acceptable Use caution with prolonged use of sodium nitroprusside due to renal clearance of the toxic metabolite thiocyanate Avoid enalaprilat due to the risk of worsening AKI
Acute decompensated heart failure with pulmonary edema	Reduce BP by a max of 25% in the first hour, then to 160/100-110 mm Hg over the next 2-6 hours, then to normal over the next 24-48 hours	Nitroglycerin or sodium nitroprusside (nicardipine and clevidipine are acceptable alternatives) Avoid β-blockers or non-dihydropyridine calcium channel blockers
Aortic dissection	HR < 60 beats per minute AND SBP ≤ 120 mm Hg within the first hour, ideally within the first 20 minutes	Initiate β-blocker before a vasodilator (eg, nicardipine, clevidipine, or nitroprusside) to prevent reflex tachycardia
Intracranial hemorrhage	If SBP > 220 mm Hg lower and monitor; if SBP 150-220 mm Hg, SBP < 140 mm Hg in 60 minutes	Nicardipine, clevidipine, or labetalol
Ischemic stroke	BP < 185/110 mm Hg before starting tPA and < 180/105 mm Hg during tPA infusion SBP < 220 mm Hg if not receiving tPA	Nicardipine, clevidipine, or labetalol
Hypertensive encephalopathy	Reduce BP by a max of 25% in the first hour, then to 160/100-110 mm Hg over the next 2-6 hours, then to normal over the next 24-48 hours	Most IV antihypertensives are acceptable
Acute coronary syndromes	Reduce BP by a max of 25% in the first hour, then to 160/100-110 mm Hg over the next 2-6 hours, then to normal over the next 24-48 hours	Esmolol, labetalol, nitroglycerin, nicardipine, or sodium nitroprusside Use caution with non-dihydropyridine calcium channel blockers Avoid β-blockers in the setting of reduced ejection fraction, bradycardia (HR < 60 bpm), hypotension (SBP < 100 mm Hg), poor peripheral perfusion, second or third-degree heart block, or reactive airway disease
Severe pre-eclampsia or eclampsia	SBP < 140 mm Hg in the first hour	Hydralazine, labetalol, or nicardipine Enalaprilat (any ACEi, ARB, renin inhibitors) and nitroprusside contraindicated
Pheochromocytoma crisis	SBP < 140 mm Hg in the first hour	β-blockers ± nicardipine or clevidipine
Retinopathy	Reduce BP by a max of 25% in the first hour, then to 160/100-110 mm Hg over the next 2-6 hours, then to normal over the next 24-48 hours	Most IV antihypertensives are acceptable Avoid fenoldopam

ACEi, angiotensin-converting enzyme inhibitor; AKI, acute kidney injury; ARB, angiotensin receptor blocker; bpm, beats per minute; HR, heart rate; tPA, tissue plasminogen activator.

Data from References 1 and 32-35.

General Approach to Treatment

Prevention

9 Counseling patients on the importance of medication adherence is a crucial measure in preventing hypertensive crises. Many patients with underlying chronic hypertension are asymptomatic and may not feel compelled to take medications consistently. Importantly, patients must have access to prescribed antihypertensives. Generic medications should be used whenever possible to avoid cost-related barriers to care. Additionally, appropriate nonpharmacological therapy must be recommended for all patients (see Chapter 30, "Hypertension"). Patients should also be instructed to consult with their pharmacist before initiating any new over-the-counter medications, which can potentially lead to poor BP control (eg, nonsteroidal anti-inflammatory drugs [NSAIDs]).

Hypertensive Urgency Treatment

5 Patients presenting with hypertensive urgency should be managed conservatively by initiating, reinitiating, or intensifying oral antihypertensive medications and implementing nonpharmacological interventions (eg, sodium restriction, removing medications or other substances that can increase BP). Guideline recommended antihypertensive medications should be chosen whenever possible. These treatments are discussed in more detail in Chapter 30, "Hypertension." Patients should not be required to seek evaluation in the emergency department unless target organ damage is suspected.[1] Aggressive lowering of BP with IV antihypertensives is not indicated in the absence of target organ damage; the risks associated with precipitous BP drops outweigh any benefit of intensive BP control. Patients with chronically uncontrolled hypertension will have shifts in autoregulation that make intensive BP lowering suboptimal for organ perfusion. Therefore, overly aggressive BP lowering places patients at risk for ischemic complications. For this reason, a gradual lowering of BP with oral antihypertensives to goal is the safest treatment approach in patients with hypertensive urgency.[36]

Hypertensive Emergency Treatment

6 7 8 Suspected target organ dysfunction in the setting of extreme BP elevations constitutes a medical emergency and patients should be promptly referred to the emergency department for further management.[1] Because acute target organ disease is present, the benefit of rapid BP lowering with IV antihypertensives generally outweighs the risk of potential ischemic complications described previously. Patients with hypertensive emergency require admission to the intensive care unit to accommodate the frequency of monitoring and administration of antihypertensive therapy via continuous IV infusion. The goal of treatment with IV antihypertensives is to prevent worsening organ dysfunction by targeting specific BP goals. However, treatment with IV antihypertensives has not been proven to reduce mortality in randomized controlled trials.

Pharmacotherapy

General Considerations

8 The ideal antihypertensive used to treat hypertensive emergencies should have a fast onset and offset of action, predictable pharmacokinetics, and minimal adverse effects. The route of administration that generally has the most rapid onset is IV, with continuous IV infusions providing the most optimal pharmacokinetics (Table e31-3). Continuous IV infusions of antihypertensive medications allow for the ability to titrate the dose to the desired effect. Thus, doses can be rapidly up-titrated to achieve intensive BP control but if BP decreases too rapidly, the dose of the infusion can also be readily decreased in order to minimize adverse effects related to hypotension such as ischemia. Intermittent dosing of antihypertensives on an as-needed basis is usually not ideal, given that precipitous and unpredictable drops in BP could occur. Rather than maintenance of the BP in a tight range, intermittent dosing causes more variation, and patients may experience more episodes above and below the desired BP range. Some scenarios may warrant intermittent IV boluses of an antihypertensive, however, generally continuous infusions are preferred.

TABLE e31-3

Intravenous Antihypertensive Medications

Medication	Dose	Onset (minutes)	Duration (minutes)	Adverse Effects	Indications and Precautions
Clevidipine	1-2 mg/hr IV infusion (Maximum dose: 32 mg/hr) Dose may be doubled at 90-second intervals toward BP goal; as BP approaches goal, titrate by smaller increments every 5-10 minutes (every 1-2 mg/hr increase in dose will reduce BP by approx. 2-4 mm Hg systolic BP)	2-4	5-15	Hypotension, headache, nausea, tachycardia, hyper-triglyceridemia	Most hypertensive emergencies; caution with coronary ischemia; contraindicated in soy or egg allergy, defective lipid metabolism, and severe aortic stenosis
Enalaprilat	1.25-5 mg IV every 6 hours	15-30	360-720	Hypotension	Acute left ventricular heart failure; avoid in acute myocardial infarction, eclampsia, acute kidney injury; precipitous fall in pressure in high-renin states; variable response
Esmolol	250-500 mcg/kg/min IV bolus (optional), and then 50-100 mcg/kg/min IV infusion; may repeat bolus after 5 minutes or increase infusion to 300 mcg/min Titrate infusion by 50 mcg/kg/min no more than every 4 minutes until at goal	1-2	10-20	Hypotension, bradycardia, nausea, asthma, first-degree heart block, HF	Aortic dissection; perioperative; avoid in patients treated with a β-blocker, bradycardic, or decompensated HF
Fenoldopam	0.1-0.3 mcg/kg/min IV infusion Increase infusion by 0.05-0.1 mcg/kg/min every 15 minutes until at goal	<5	30	Hypotension, tachycardia, headache, nausea, flushing	Most hypertensive emergencies; caution with glaucoma
Hydralazine	10-20 mg IV every 4-6 hours (maximum dose: 40 mg)	10-20	60-240	Hypotension, tachycardia, flushing, headache, vomiting, aggravation of angina	Eclampsia
Labetalol	10-20 IV bolus followed by 20-80 mg every 10 minutes until BP controlled followed by 0.5-2 mg/min IV infusion Increase infusion by 0.5 mg/min every 15 minutes until at goal	5-10	180-360	Hypotension, vomiting, scalp tingling, bronchoconstriction, dizziness, nausea, bradycardia, heart block, orthostatic hypotension	Most hypertensive emergencies except acute HF or heart block
Nicardipine	2.5-5 mg/hr IV infusion Increase infusion by 2.5 mg/hr every 5-15 minutes until at goal	5-10	15-30 (may exceed 240)	Hypotension, tachycardia, headache, flushing, local phlebitis	Most hypertensive emergencies except acute HF; caution with coronary ischemia

Nitroglycerin	5-200 mcg/min IV infusion Increase infusion by 5 mcg/min every 3-5 minutes; if no response at a dose of 20 mcg/min, increase infusion by 10-20 mcg/min every 3-5 minutes until at goal	2-5	5-10	Hypotension, headache, vomiting, methemoglobinemia, tolerance with prolonged use	Coronary ischemia
Sodium nitroprusside	0.25-10 mcg/kg/min IV infusion Increase infusion by 0.5 mg/kg/min every 3 minutes until at goal	Seconds	1-2	Hypotension, nausea, vomiting, muscle twitching, sweating, thiocyanate and cyanide intoxication	Most hypertensive emergencies; caution with high intracranial pressure, azotemia, or chronic kidney disease

HF, heart failure.

[5] [6] Oral antihypertensives with relatively quick onsets of action have been utilized in the setting of severely elevated BP. The rationale for use in this setting is that these medications correct BP readings more rapidly than oral antihypertensives with longer onset times. However, treatment of asymptomatic severe hypertension (hypertensive urgency) with rapid-acting, "as-needed" oral antihypertensives is not warranted. Instead, guideline-recommended therapies should inform treatment decisions. Additionally, oral antihypertensives should not be used in the setting of target organ damage (hypertensive emergency), as their effects are not as rapid or predictable as IV antihypertensives. Oral antihypertensives should only be utilized if vascular access is unavailable.

Calcium Channel Blockers (CCBs)

Calcium channel blockers (CCBs) act by inhibiting the entry of calcium ions into cells through voltage-gated calcium channels thus preventing cellular depolarization. CCBs can be broadly characterized by their chemical structure as dihydropyridine (DHP) or non-dihydropyridine (non-DHP). DHP CCBs act preferentially on the vascular smooth muscle cells to promote smooth muscle relaxation. They have minimal effect on the calcium channels in the myocytes and, therefore, do not typically have direct effects on heart rate or contractility. Conversely, non-DHP CCBs are more selective for the cardiac myocytes and have more effects on the cardiac conduction system.[37] DHP CCBs are the primary agents from this class used in hypertensive emergencies. Please refer to Chapter 30, "Hypertension," for more information on the types of CCBs.

Nicardipine

Nicardipine, a short-acting IV DHP CCB, has become a mainstay of therapy for hypertensive emergencies due to its pharmacokinetics and predictable pharmacodynamics (eg, effect on BP). Nicardipine crosses the blood-brain barrier and causes cerebral vascular smooth muscle relaxation. Because of these properties, nicardipine is useful in patients with neurological hypertensive emergencies. Nicardipine may have variable effects on cardiac function because it causes coronary artery vasodilation and increases perfusion. However, it may also cause reflex tachycardia, which increases myocardial oxygen demand. The net effect, therefore, tends to be relatively neutral. Nicardipine is contraindicated in patients with severe aortic stenosis. Nicardipine clearance may be affected by severe kidney or hepatic impairment, so titrations should be made more slowly in these patients. During prolonged infusions of nicardipine, patients should be monitored for volume overload because the dilution required for IV administration (0.1 mg/mL) can result in patients receiving nearly 2 liters of fluid during a 24-hour period at high doses. Other common adverse drug reactions associated with nicardipine use include headache, hypotension, and tachycardia.[37,38]

Clevidipine

Clevidipine is an IV DHP CCB that acts as a vasodilator on arterioles. Compared with nicardipine, clevidipine has the added benefit of more rapid onset and offset of action and lack of accumulation in organ impairment. In clinical trials, clevidipine was associated with faster BP control and less precipitous BP drops than other agents.[39,40] However, it was not associated with better clinical outcomes overall. Clevidipine undergoes rapid hydrolysis by plasma esterases to inactive metabolites. Clevidipine is formulated as a lipid emulsion, so caution is warranted when using it for prolonged durations, as hypertriglyceridemia can occur. Additionally, because lipid formulations have a higher risk of bacterial or fungal

contamination, lines must be changed every 12 hours to minimize the risk of infection. It is also contraindicated in patients with soy or egg allergy, lipid metabolism defects, or acute pancreatitis in the setting of hyperlipidemia. Clevidipine is also contraindicated in severe aortic stenosis.[37,39,40]

Vasodilators

Nitroglycerin

Nitroglycerin induces smooth muscle relaxation via its conversion to nitric oxide (NO), activating guanylate cyclase and cyclic guanosine 3′,5′-cyclic monophosphate (GMP) in smooth muscle cells, causing vasodilation. Nitroglycerin has a rapid onset and offset, making it useful for emergent use and providing ease of titration. Nitroglycerin is primarily a venodilator. However, it also causes arteriole vasodilation at high doses (>60 mcg/min). Because nitroglycerin is a potent venodilator, cardiac preload reductions can be achieved even at low doses (≤60 mcg/min), making it useful in treating patients with acute HF. It is more challenging to utilize nitroglycerin for other indications (eg, stroke, aortic dissection) due to dose-limiting side effects such as headache and reflex tachycardia. Additionally, tachyphylaxis, or loss of efficacy, can occur relatively quickly during nitroglycerin administration, requiring continuous reassessments for the need to increase the dose. For this reason, IV nitroglycerin should not be used for more than 24 to 48 hours.[37,41] Nitroglycerin and other nitrates are contraindicated in patients who have received phosphodiesterase-3 inhibitors (ie, avanafil, sildenafil, tadalafil, vardenafil) due to the risk of profound hypotension.[42] To avoid this interaction, nitrates should be avoided until at least 12 hours after the last dose of avanafil, 24 hours after the last dose of sildenafil or vardenafil, and 48 hours after the last dose of tadalafil. Nitroglycerin is also contraindicated in patients with known or suspected elevations in intracranial pressure.

Sodium Nitroprusside

Sodium nitroprusside is a prodrug that is converted to its active form via dissociation of NO and cyanide upon interaction with sulfhydryl groups on erythrocytes and other plasma proteins. Similar to nitroglycerin, once NO is released, guanylate cyclase and cyclic GMP are activated in smooth muscle cells, causing vasodilation.[43] Sodium nitroprusside was traditionally used as one of the first-line agents for hypertensive emergency given its potent arteriole and venous dilation effects and short onset and half-life (minutes). However, it is now used less frequently due to several theoretical drawbacks. Accumulation of toxic metabolites, including cyanide, may occur in patients with kidney or hepatic impairment. Normally, the liver converts cyanide to thiocyanate, which is subsequently excreted by the kidneys. In patients with severe liver impairment, cyanide can accumulate, which is 100 times more toxic than thiocyanate, and should be avoided in these patients. With kidney impairment, thiocyanate toxicity can occur. However, because thiocyanate is less toxic than cyanide, the risk of thiocyanate toxicity in patients, including those with kidney impairment, is low when low doses (max dose 2 mcg/kg/min) are administered for short periods (<24 hours). Concerns regarding the possibility of sodium nitroprusside raising intracranial pressure also limit its use in patients with intracranial pathologies at risk for elevations of intracranial pressure. Additionally, in patients with coronary artery disease, redistribution of oxygenated blood from ischemic areas with less vasodilation toward nonischemic regions, a phenomenon known as “coronary steal,” has been reported as a potential concern. Finally, patients with hypovolemia or diastolic dysfunction may experience excessive hypotensive effects with sodium nitroprusside. Although it is used less frequently, the potency of sodium nitroprusside makes it a good option for patients who fail to respond adequately to other IV antihypertensive medications.[37,41]

Hydralazine

Hydralazine is a peripheral arterial vasodilator that is available in both IV and oral formulations. Hydralazine can be administered on an intermittent, as-needed basis, although its use is limited given its unpredictable effects on BP. While onset typically occurs within 30 minutes and the duration of activity is normally 12 hours or less, the effects on BP can persist for up to 100 hours, especially in patients that are slow acetylators. Hydralazine should be avoided in patients susceptible to worsening target organ damage due to the risk of precipitous BP drops. Therefore, hydralazine is not considered first-line therapy. Furthermore, hydralazine has been reported to induce myocardial ischemia in patients who experience rebound tachycardia. For this reason, in patients with a history of cardiac disease, hydralazine should only be used after a β-blocker is administered to avoid rebound tachycardia unless concomitant bradycardia is present.[37,41]

Some clinicians inappropriately use oral hydralazine to treat hypertensive urgency in the hospital setting. Although theoretically useful for acute BP elevations because it produces peak plasma concentrations in 1 to 2 hours, oral hydralazine should generally be avoided due to unpredictable pharmacokinetics and the possibility of prolonged duration of action. Additionally, in the absence of target organ damage, there is currently no indication to treat acutely elevated BP.[44]

Fenoldopam

Fenoldopam is a selective peripheral dopamine type 1 (D_1) receptor agonist. The pharmacologic effect of D_1 receptor stimulation is arterial vasodilation, including those in the renal and mesenteric vasculature. Consequently, fenoldopam reduces BP and preserves renal blood flow. Fenoldopam contains sodium metabisulfite, so it should not be used in patients with sulfite allergies or intolerance. Fenoldopam should also be avoided in patients with increased intraocular pressure, such as glaucoma, as it causes dose-dependent increases in intraocular pressure. It is unclear if fenoldopam affects intracranial pressure, so it should generally be avoided in neurological hypertensive emergencies.[37,45]

β-Blockers

Labetalol

Labetalol is a mixed α_1 and nonselective β_1 and β_2 adrenergic antagonist, with β activity predominating in a 7:1 ratio over the alpha activity for the IV formulation (compared to oral labetalol which has a 3:1 ratio). The selectivity and physiologic effects of labetalol vary depending on the formulation used. Antagonism of α_1 occurs in vascular smooth muscle, decreasing systemic vascular resistance. β_1 antagonism occurs in the myocardium and decreases heart rate and contractility while β_2 antagonism occurs mainly in the pulmonary artery smooth muscle, causing bronchoconstriction (although this is not the predominant effect). Labetalol can be administered as intermittent IV boluses or as a continuous IV infusion. Labetalol bolus dosing is useful as a loading dose preceding a continuous infusion or an intermittent dosing strategy utilized on an as-needed basis. In a true hypertensive emergency, sustained BP control with a continuous infusion is usually more appropriate than intermittent dosing strategies. However, labetalol boluses could also be helpful as add-on therapy when an IV infusion is being used at maximum dosage. Labetalol is useful in situations where heart rate and BP control are both warranted. Labetalol has a longer duration of action (2-4 hours) than other commonly used IV antihypertensives, making titrations more complicated and necessitating more caution when doing so. Generally, other agents such as nicardipine provide more rapid BP control than labetalol. Labetalol is contraindicated in the setting of severe bradycardia, second- or third-degree heart block, ADHF, and reactive airway diseases due to its nonselective β activity.[37,46]

Esmolol

Esmolol is a rapid-acting selective β_1 adrenergic antagonist, with its main effects being heart rate reduction and no effect on systemic vascular resistance. Because of its cardioselectivity, esmolol is typically administered concomitantly with a vasodilating medication to treat hypertensive emergencies. In other words, esmolol is useful as an adjunct when heart rate control is needed in addition to rapid BP reduction but generally cannot achieve adequate reductions on its own. Esmolol should be avoided in patients with bradycardia, second- or third-degree heart block, or ADHF due to its negative chronotropic and inotropic properties. Esmolol is generally well-tolerated in patients with reactive airway disease, given its cardioselectivity.[37,41]

Metoprolol

Metoprolol is a cardioselective β-blocker. IV metoprolol is typically only administered as an intermittent dose and, therefore, is not an ideal medication for BP control in the setting of hypertensive emergencies. Metoprolol may be used to prevent or treat rebound tachycardia associated with vasodilatory antihypertensive medications (eg, hydralazine).[37]

Alternative Medication Classes

Enalaprilat

Enalaprilat is an IV angiotensin-converting enzyme (ACE) inhibitor that exerts its effect via inhibition of the conversion of ACE I into ACE II, which is a potent vasoconstrictor. IV enalaprilat can be administered as an intermittent, as-needed bolus. Peak effects may not be observed until 4 hours after administration and prolonged effects can be observed for up to 12 hours. Thus, it is not an ideal agent for managing a hypertensive emergency. Enalaprilat is contraindicated in the setting of acute kidney injury and hyperkalemia.[37,41]

Clonidine

Like oral hydralazine, oral clonidine is also utilized inappropriately by some clinicians to treat acutely elevated BP in the setting of hypertensive crisis. Clonidine acts via central α_2 agonism to reduce sympathetic outflow, which, in turn, decreases BP. Clonidine is available as an oral tablet and a transdermal patch. In patients with a hypertensive emergency, oral clonidine should only be used if IV access cannot be obtained; the transdermal formulation has no role in the treatment of hypertensive crisis. Oral clonidine has an onset of action of 0.5 to 1 hour with maximum effects at 2 to 4 hours. Clonidine should generally be avoided for long-term use due to the potential for tolerance, hypertensive crisis upon withdrawal of the medication, adverse effects (eg, bradycardia, sedation, dizziness), and lack of outcome data.[47,48] (See Chapter 30, "Hypertension.")

Medications to Avoid

Immediate-release (IR) oral formulations of nifedipine, a DHP CCB, have been used historically to acutely treat elevated BP. Oral and sublingual IR formulations of nifedipine produce rapid and profound BP decreases after administration that has also been reported to cause myocardial ischemia, even at low doses. For this reason, IR nifedipine formulations should not be used in the management of a hypertensive crisis.[48,49]

Compelling Indications

Figure e31-3 summarizes treatment recommendations when specific target organ damage is present.

Intracerebral Hemorrhage (ICH)

Patients with ICH have an increased risk of mortality and functional morbidity. When presenting with this form of stroke, patients also commonly have high elevated BP in the acute setting. Rapid control of BP is thought to reduce mortality and functional morbidity. Because the risk of re-hemorrhage and hematoma expansion may be high in the acute phase of presentation, early control of BP might mitigate this risk and improve functional outcomes. Two landmark trials have examined the effect of early aggressive BP lowering versus a more conservative approach to BP management in this patient population.[50,51] The first of these trials randomized patients to SBP goals of <140 mm Hg or <180 mm Hg via any pharmacological means within 6 hours of stroke onset and reported no difference in the primary outcome of death or severe disability between groups.[50] However, secondary results showed potentially improved functional outcomes in patients in the more aggressively controlled group.

Similarly, the Antihypertensive Treatment of Acute Cerebral Hemorrhage II trial, or ATACH-2, randomized patients to the same BP goals but within 4.5 hours of stroke onset using continuous infusions of nicardipine to meet the BP goals.[51] There was no difference in death or severe disability as the primary outcomes between the two treatment groups. Additionally, there was an increased risk of adverse kidney events within 7 days in patients in the intensive BP lowering group. Due to the inconclusive outcomes of these trials, the ideal BP goal in patients with an ICH is not known.

While the optimal BP target, timing of intervention, and pharmacologic agent of choice for managing elevated BP in patients with ICH remain unclear, major medical organizations offer guidance on acute BP management in this patient population. The 2015 AHA/American Stroke Association (ASA) guideline on the management of spontaneous ICH, published before the results of the ATACH-2 trial were available, recommends an SBP goal of less than 140 mm Hg in patients presenting with SBPs between 150 and 220 mm Hg without any contraindications.[33] In patients presenting with SBPs greater than 220 mm Hg, they state it is reasonable to lower the BP using continuous infusion of antihypertensive medications in closely monitored patients. The 2017 ACC/AHA hypertension guideline warns that for patients presenting with SBP of 150 to 220 mm Hg, acute BP lowering to a goal SBP of less than 140 mm Hg within 6 hours is not beneficial and may potentially cause harm.[1] For those presenting with an SBP greater than 220 mm Hg, the hypertension guideline states it is reasonable to lower BP with a continuous infusion of antihypertensive medications. The National Institute for Health Care and Excellence in the United Kingdom recommends a goal SBP goal of 130 to 140 mm Hg for patients with an ICH presenting within six hours, including patients presenting with SBP greater than 220 mm Hg, provided no contraindications are present.[32]

While the debate continues concerning the optimal BP goal in patients with acute ICH, the important take-home point is that patients should be closely monitored for any signs of ischemia during acute BP lowering. To minimize BP fluctuations, infusions of nicardipine or clevidipine could be considered first-line agents for acute BP control. Enteral antihypertensives can be started as soon as there is access and should be titrated as tolerated for long-term BP control. Sodium nitroprusside is generally avoided in patients with ICH, secondary to the risk for elevations in intracranial pressure due to extravasated intracranial blood and the concern over the medication itself causing elevations in intracranial pressure.

Acute Ischemic Stroke

Acute BP management during an acute ischemic stroke is a balance between preserving cerebral perfusion and minimizing the risk of intracerebral hemorrhage via hemorrhagic conversion of stroke infarcts, especially for those patients who are candidates for fibrinolytic therapy (eg, alteplase). In the stroke penumbra, the area surrounding the infarcted brain tissue, autoregulation is dysfunctional, and cerebral perfusion pressure is more directly related to BP values.[1] Aggressive BP lowering can, therefore, decrease perfusion, causing further ischemia. However, uncontrolled BP may pose a risk of hemorrhagic conversion of the ischemic stroke.

The decision to administer reperfusion therapy is the critical junction in the pathway for determining BP goals during acute ischemic stroke. If patients are not candidates for reperfusion therapy, decreasing BP by 15% is considered reasonable if the BP is greater than or equal to 220/120 mm Hg.[35] However, for patients who are candidates for IV alteplase, the AHA/ASA guideline recommends that the BP be controlled to less than 185/110 mm Hg before administering IV alteplase.[35] During alteplase infusions, the guideline recommends maintaining BP at less than or equal to 180/105 mm Hg.[35] It is essential to monitor BP carefully during alteplase infusions and for 24 hours after completing the infusion. BP elevations above the guideline-specific ranges are thought to increase the risk of cerebral bleeding associated with alteplase administration. Readers are encouraged to visit Chapter 39, "Stroke," for more details regarding monitoring patients receiving IV alteplase for acute ischemic stroke.

Careful selection and dosing of the appropriate antihypertensive medication is important to maintain the balance of perfusion and BP control. In patients without contraindications, as-needed IV bolus doses of labetalol or continuous infusions of nicardipine or clevidipine are the medications of choice for acute BP control.[35] Intermittent IV boluses of hydralazine or enalaprilat are alternatives that may also be considered.[35]

Hypertensive Encephalopathy

When evaluating patients for hypertensive encephalopathy, clinicians must assure that the symptoms are not attributable to an intracerebral hemorrhage, ischemic stroke, or some other intracranial or vascular pathology (eg, aortic dissection). These conditions may alter the more conservative BP goals recommended for patients with hypertensive encephalopathy. Therefore, the decision to treat a patient for hypertensive encephalopathy is usually based on their symptoms after other neurological conditions have been excluded. Carefully monitored reduction in BP can reverse symptoms while minimizing the risk of ischemic complications. While randomized controlled trials evaluating BP management in hypertensive encephalopathy are lacking, a decrease in BP of not more than 25% in the first hour is reasonable.[52] IV infusions of nicardipine and clevidipine are commonly used as initial therapy.

Acute Coronary Syndromes (ACS)

When a patient with hypertensive crisis presents with an ACS, rapid BP lowering is indicated to lessen cardiac ischemia. When managing hypertensive emergencies in the setting of an ACS, nitroglycerin is a first-line medication due to its ability to cause smooth muscle relaxation and coronary artery dilation. Additionally, nitroglycerin provides symptomatic relief of accompanying chest pain or discomfort. β-Blockers are also indicated in all patients with ACS in the absence of contraindications. IV β-blockers are recommended in patients with ACS and tachyarrhythmias or uncontrolled hypertension. In patients with evidence of or who are at risk for developing cardiogenic shock, β-blocker use should be deferred. CCBs such as nicardipine or clevidipine may be used cautiously, taking care to avoid rebound tachycardia, which could increase myocardial oxygen demand and worsen ischemia.[42,53] Sodium nitroprusside is associated with increased mortality in patients with acute myocardial infarction complicated by left ventricular heart failure, presumably due to coronary steal, and should be avoided in this setting.[54] Refer to Chapter 34, "Acute Coronary Syndromes," for information on the management of patients with ACS.

Acute Decompensated Heart Failure (ADHF) with Pulmonary Edema

Patients with acute pulmonary edema and severe elevations in BP (often referred to as "flash pulmonary edema") can present with respiratory distress and hypoxemia due to fluid overload. Because acute cardiogenic pulmonary edema is often associated with excessive increases in afterload, afterload reduction is a mainstay of therapy. To achieve afterload reduction, IV antihypertensives should be titrated to a BP reduction of about 25% in the first hour.[1]

Nitroglycerin is a treatment of choice for BP reduction in the setting of ADHF with pulmonary edema.[55] Nitroglycerin causes venous dilation at low

doses (≤60 mcg/min) and arterial vasodilation at higher doses (>60 mcg/min).[56] Since nitroprusside is both a potent arterial and venous vasodilator, it is a good option for patients who display an inadequate response to nitroglycerin.[57] An IV loop diuretic such as furosemide should also be administered as soon as possible to help manage fluid overload. Early use (within 60 minutes of presentation to the emergency department) of IV diuretics has been associated with improvements in oxygenation and in-hospital mortality for patients with ADHF.[58] Refer to Chapter 37, "Acute Decompensated Heart Failure," for more details on the management of ADHF.

Aortic Dissection

Aortic dissections are worsened by aortic wall stress. BP, heart rate, and the velocity of ventricular contraction all contribute to aortic wall stress. β-Blockers are first-line to minimize wall stress by controlling all three contributing factors. It is crucial to control heart rate first, as vasodilatory IV antihypertensives may lead to reflex tachycardia, worsening aortic wall stress. Because aortic dissection can rapidly lead to decompensation and death, heart rate should be reduced to and maintained at less than 60 beats per minute (bpm), and SBP lowered to less than 120 mm Hg. Ideally, achievement of both heart rate and BP goals should occur within 20 minutes, which is notably more aggressive than with other types of target organ damage.

The choice of β-blocker depends on patient-specific factors. In a patient who might be expected to have an intolerance to a β-blocker, such as those with heart failure or asthma, esmolol should be considered due to its short half-life. Labetalol possesses both α- and β-blocking properties and may be more effective in achieving heart rate and BP goals in patients with aortic dissection. However, the longer half-life of labetalol is a disadvantage because it cannot be titrated as easily as esmolol. Other parenteral pharmacotherapy options include metoprolol and propranolol.[34] These medications also have long half-lives and, therefore, should not be administered via continuous infusion.

Once the heart rate goal is achieved, an additional IV antihypertensive from an alternative class may be utilized in combination with the β-blocker if BP remains above goal. An IV vasodilator such as sodium nitroprusside or nicardipine would be appropriate add-on therapy.[34]

Supportive therapies depend on the severity of the aortic dissection. Dissections in the ascending aorta (type A dissections) are considered surgical emergencies. Type B dissections, or descending aortic dissections, may be managed medically or surgically depending on the severity. Because pain may contribute to tachycardia and hypertension, adequate analgesia is crucial for patients with aortic dissection.[34]

Acute Kidney Injury

Patients with acute kidney injury due to hypertensive crisis require BP lowering of about 25% in the first hour. Because of this, medications that may cause precipitous BP drops or worsen kidney perfusion should be avoided.[1] In a hypertensive emergency with acute kidney injury, DHP CCBs should be considered first. Although labetalol is not nephrotoxic, it was associated with greater BP variation than nicardipine in multiple studies.[59] An alternative option for the management of hypertension-associated acute kidney injury is fenoldopam. Fenoldopam has renoprotective effects that may reduce the risk of requiring renal replacement therapy.[37] ACE inhibitors such as enalaprilat should be avoided in the setting of hypertensive acute kidney injury due to the potential to worsen kidney function.

Severe Hypertension in Pregnancy

Due to the high risk associated with pre-eclampsia and eclampsia, treatment with IV antihypertensive therapy should be initiated within 30 to 60 minutes or as soon as possible to target an SBP less than 140 mm Hg. First-line agents include IV hydralazine or IV labetalol. The American College of Obstetricians and Gynecologists guideline suggests that oral IR nifedipine may also be used for this indication. However, IR nifedipine has largely fallen out of favor due to increased rates of severe adverse drug reactions and the risk of myocardial ischemia.[21] If used to treat hypertensive crisis during pregnancy, IR nifedipine should be reserved as a third-line agent.

In patients with pre-eclampsia with severe features, seizure prophylaxis with magnesium sulfate is indicated. Magnesium is the medication of choice for preventing eclampsia, which is the convulsive presentation of gestational hypertension. Magnesium is administered as a bolus dose of 4 to 6 grams over 15 to 30 minutes at the onset of labor, followed by a 1- to 2-gram per hour continuous infusion for at least 24 hours after delivery. Close laboratory, cardiac, and respiratory monitoring is required to ensure that the patient is not experiencing magnesium toxicity.[21]

Pheochromocytoma Crisis

The treatment of choice for pheochromocytoma crisis is α-adrenergic blockade with phenoxybenzamine or doxazosin. These medications are utilized temporarily until surgical resection of the tumor can occur. It is not recommended to use β-blockers until adequate β-blockade can be achieved. Without α-blocking medications, β-blockade can cause unopposed α-receptor stimulation, increasing vasoconstriction and worsening the hypertensive crisis. However, once treatment is initiated with an α-receptor antagonist, tachycardia can be further managed with a β-blocker. If an additional agent is needed to control BP, CCBs or metyrosine (catecholamine synthesis inhibitor) may be used.[60]

Transitioning from IV to Oral

After patients with a hypertensive emergency are stabilized on an IV antihypertensive regimen, transition to oral antihypertensives should be considered. Ideally, patients should be started on an agent with which they can be maintained long term. Before this transition is made, it should be confirmed that target organ damage is no longer worsening and that it is appropriate and safe to utilize the patient's gastrointestinal tract. Additionally, BP should be at or near the recommended goal depending on the underlying organ dysfunction for at least two consecutive readings before the transition is made.[61]

Choice of oral antihypertensive should follow evidence-based guidelines and patient-specific factors (Chapter 30, "Hypertension"). IV therapy should be continued while oral therapy is started in a stepwise fashion. If a patient has a home antihypertensive regimen, this should be resumed or intensified. Individual oral antihypertensive pharmacokinetic properties should be considered when determining how rapid titrations can be made. Quick but safe transitions from IV to oral antihypertensive therapy can reduce ICU and hospital length of stay and reduce healthcare costs.[62]

EVALUATION OF THERAPEUTIC OUTCOMES

Patients being managed with IV antihypertensives should have BP checked at least every 15 minutes while medication doses are titrated. Some patients may require more frequent monitoring depending on the clinical status and medication being used. Once a stable dose has been reached, BP readings may be performed every 1 hour. While not required, many patients with a hypertensive emergency will have continuous BP monitoring performed via an arterial line placement.

Laboratory monitoring during treatment of hypertensive emergency is dependent upon the type of target organ dysfunction present and the antihypertensive regimen used. If the emergency involves bleeding into a critical organ site (eg, aortic dissection), complete blood counts should be monitored to follow hemoglobin and hematocrit concentrations trends. In addition, a comprehensive metabolic panel should be obtained to assess for kidney or hepatic injury and electrolyte disturbances. Triglyceride levels may be warranted in patients on prolonged infusions of clevidipine.

Repeated symptomatic and diagnostic assessments are also important. Physical exams should be repeated regularly during hospitalization to monitor for new, worsening, or the resolution of symptoms specific to the affected target organ systems. Repeat diagnostic imaging may also be required depending on the type of target organ dysfunction identified (eg, ICH).

CONCLUSION

Treating patients with hypertensive crises is complex and requires a detailed evaluation of symptoms, history (medical, medication, and dietary), and careful measurement of BP. In patients without evidence of target organ damage (hypertensive urgency), conservative management (eg, resumption of or adjustments to chronic antihypertensive therapy) is often sufficient. Patients with evidence of target organ damage (hypertensive emergency) must be treated as a medical emergency. Prompt identification of target organ damage and treatment to patient-specific goals can prevent adverse effects of tissue ischemia and progressive target organ damage. Careful consideration to the diagnosis of target organ damage is necessary when treating patients with hypertensive crisis. Once target organ damage is identified, clinicians should utilize patient-specific factors and guideline-recommended BP goals to outline acute treatment plans and select the appropriate antihypertensive treatment. Clinicians should familiarize themselves with the contraindications and adverse effect profiles of available antihypertensive medications to ease management decisions. IV infusions of antihypertensives are generally preferred, but other routes may be considered in specific circumstances. Initial dosing and dose titrations are also key to patient management. Lastly, treatment plans do not end with the selection and initiation of appropriate pharmacotherapy. Frequent monitoring of BP and the clinical and laboratory markers of target organ damage is important to minimize adverse events and document clinical success.

Achievement of treatment goals is best when patients are cared for by interprofessional care teams, in which all members contribute their expertise.

ABBREVIATIONS

ACC	American College of Cardiology
ACS	acute coronary syndromes
ACE	angiotensin-converting enzyme
ADHF	acute decompensated heart failure
AHA	American Heart Association
ASA	American Stroke Association
ATACH	Antihypertensive Treatment of Acute Cerebral Hemorrhage
BP	blood pressure
BPM	beats per minute
CCB	calcium channel blocker
CKD	chronic kidney disease
D_1	dopamine type 1
DBP	diastolic blood pressure
DHP	dihydropyridine
GMP	guanosine 3′,5′-cyclic monophosphate
HF	heart failure
ICH	intracerebral hemorrhage
IR	immediate release
IV	intravenous
MI	myocardial infarction
NSAID	nonsteroidal anti-inflammatory drug
NO	nitric oxide
RAAS	renin–angiotensin–aldosterone system
SBP	systolic blood pressure

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SELF-ASSESSMENT QUESTIONS

Use the following scenario to answer questions 1 to 3:

A 72-year-old female presents to the emergency department with complaints of shortness of breath. Blood pressure is 234/116 mm Hg. A chest x-ray reveals bilateral diffuse hazy infiltrates. Past medical history includes coronary artery disease, heart failure, hypertension, and osteoporosis. Home medications include alendronate 70 mg once weekly, aspirin 81 mg daily, furosemide 20 mg twice daily, losartan 100 mg daily, metoprolol XL 100 mg daily, and rosuvastatin 40 mg daily. The patient reports consuming a significant amount of fried and salty foods while attending a barbeque.

1. How should this patient's hypertension be classified?

   A. Prehypertension

   B. Stage 1 hypertension

   C. Hypertensive urgency

   D. Hypertensive emergency

2. Which of the following blood pressure targets is the *most appropriate* for this patient?

   A. 25% reduction over the first hour then 160/100 to 110 mm Hg over the next 2 to 6 hours.

   B. 50% reduction over the first hour then 140/100 to 110 mm Hg over the next 2 to 6 hours.

   C. Immediately decrease the blood pressure to a goal of <140/90 mm Hg within 1 hour.

   D. Immediately decrease the blood pressure to a goal of <120/80 mm Hg within 1 hour <140/90 mm Hg as soon as possible.

3. In addition to IV furosemide, which of the following represents the *best* medication regimen to manage this patient's acute hypertension?

   A. Enalaprilat 5 mg IV push

   B. Hydralazine 20 mg IV push

   C. Labetalol 1 mg/min IV infusion

   D. Nitroglycerin 10 mcg/min IV infusion

Use the following scenario to answer questions 4 to 6:

A 68-year-old male presents to the emergency department with slurred speech, facial droop, and an unsteady gait. The patient's wife reports the patient was in a normal state of health 2.5 hours ago. Blood pressure readings upon arrival were 196/92 mm Hg and 204/96 mm Hg. Heart rate is 89 bpm. Upon evaluation by the interdisciplinary healthcare team, the patient is diagnosed with ischemic stroke and a decision is made to administer IV alteplase.

4. Which of the following is the *most appropriate* blood pressure target for this patient?

   A. <140/80 mm Hg

   B. <180/105 mm Hg

   C. A 25% reduction in 1 hour

   D. A 50% reduction in 1 hour

5. Which of the following is the *most appropriate* antihypertensive regimen for this patient?

   A. Metoprolol 5 mg IV push

   B. Hydralazine 10 mg IV push

   C. Nicardipine 5 mg/hr IV infusion

   D. Nitroglycerin 5 mcg/min IV infusion

6. Which of the following the *best* represents the risk of rapidly reducing blood pressure in this patient?

   A. Cerebral ischemia

   B. Cerebral hemorrhage

   C. Acute kidney injury

   D. Coronary ischemia

Use the following scenario to answer questions 7 to 9:

A 45-year-old male presents from the primary care physician's office for management of elevated blood pressure. The patient reports having no symptoms and was at the physician's office for a routine physical. Blood pressure in the office was 204/120 mm Hg. As a result, the patient was instructed to immediately report to the emergency department. Blood pressure in the ED is 198/116 mm Hg. Past medical history includes gout and hypertension. Home medications include allopurinol 100 mg daily, amlodipine 10 mg daily, carvedilol 25 mg twice daily, and lisinopril/hydrochlorothiazide 40/25 mg daily but the patient reports running out of medications 4 days ago. The patient also takes acetaminophen occasionally for headaches (about twice monthly).

7. How should this patient's hypertension be classified?

   A. Prehypertensive

   B. Stage 1 hypertension

   C. Hypertensive urgency

   D. Hypertensive emergency

8. Which of the following is the *best* strategy for managing this patient's blood pressure?

   A. Start nicardipine 5 mg/hr IV infusion

   B. Administer clonidine 0.1 mg PO as needed

   C. Administer labetalol 10 mg IV push

   D. Reinitiate home antihypertensives as reported

9. Which if the following is the *most likely cause* for this patient's visit to the emergency department?

   A. Hypertensive emergency at the doctor's office

   B. Interruption of home BP medication regimen

   C. Elevated BP from painful gout attack

   D. Suboptimal doses of antihypertensive medications

Use the following scenario to answer questions 10 to 11:

An 82-year-old male presents with "tearing pain" located in the chest and back. Blood pressure is 182/90 mm Hg and heart rate is 96 beats per minute. A CT scan of the chest reveals a Type B descending aortic dissection. The patient does not report taking any medications at home and does not regularly seek medical care.

10. Which of the following medications can safely be initiated first in this patient?

A. Clevidipine

B. Esmolol

C. Nicardipine

D. Nitroprusside

11. Which of the following best represents clinical goals to prevent additional organ damage in this patient?

A. SBP < 120 mm Hg

B. SBP < 140 mm Hg

C. SBP < 120 mm Hg and HR < 60 bpm

D. SBP < 140 mm Hg and HR < 60 bpm

12. Which of the following physical exam findings are characteristic of aortic dissection?

A. Discordant blood pressure readings on opposite arms

B. Peripheral pitting edema palpated in the lower extremities

C. Papillary edema visualized fundoscopically in both eyes

D. Jugular venous distension was observed unilaterally

Use the following scenario to answer questions 13 to 15:

A 53-year-old female presents to the primary care physician for a checkup and to request medication refills. Home medications include nifedipine XR 30 mg daily, hydrochlorothiazide 12.5 mg daily, valsartan 40 mg daily, ibuprofen 600 mg twice daily as needed for back pain, and metformin 500 mg twice daily. The patient reports adherence with home medications and enjoys drinking multiple sports drinks while playing racquetball. Blood pressure is 188/114 mm Hg. When checked 10 minutes later, blood pressure is 194/112 mm Hg and heart rate is 62 bpm. The patient reports that blood pressure at home is typically about 170/90 mm Hg.

13. Which of the following best represents how this patient's autoregulation curve could be altered due to long-standing uncontrolled hypertension?

A. Shifted to the right which increased the risk of tissue ischemia with acute BP lowering

B. Shifted to the right which increased the risk of cerebral edema with acute BP lowering

C. Shifted to the left which increased the risk of tissue ischemia with acute BP lowering

D. Shifted to the left which increased the risk of cerebral edema with acute BP lowering

14. Which of the following is the *most appropriate* pharmacologic recommendation now?

A. Change nifedipine to equipotent dose of amlodipine

B. Administer IV labetalol now as a one-time injection

C. Change hydrochlorothiazide to furosemide

D. Increase the dose of nifedipine

15. Which of the following counseling points would be *most appropriate* for this patient during this office visit?

A. Avoid excessive physical exertion to prevent further blood pressure elevations

B. Avoid the use of nonprescription medications such as NSAIDs and certain herbal supplements

C. Report to the emergency department for evaluation of extremely elevated blood pressure

D. Limit water and sports drinks intake during periods of intense exercise

SELF-ASSESSMENT QUESTION-ANSWERS

1. **D.** This patient's hypertension can currently be classified as a hypertensive emergency (see "Hypertensive Emergency" section). The patient has acutely elevated blood pressure >180/120 mm Hg with evidence of target end-organ damage. She is experiencing shortness of breath and her chest radiograph shows evidence of fluid overload. This is indicative of acute heart failure which is a type of target end-organ damage.

2. **A.** A 25% blood pressure reduction over the first hour then to 160/100 to 110 mm Hg over the next 2 to 6 hours is recommended to alleviate target end-organ dysfunction while minimizing precipitous blood pressure decreases that could precipitate ischemic complications (see Table e31-2). Alleviation of acute heart failure will prevent the worsening of acute respiratory insufficiency.

3. **D.** Nitroglycerin 10 mcg/min IV infusion would be the most appropriate choice for this patient because the vasodilatory properties of nitroglycerin in combination with the diuretic effect of furosemide will help to decrease pulmonary edema and reduce blood pressure (see Table e31-3). In the setting of acute heart failure, β-blockers such as labetalol should be avoided due to negative inotropic effects that could worsen cardiac output. Hydralazine and enalaprilat should not be used first-line given the unpredictable pharmacodynamic effects and relatively slow onsets of action.

4. **B.** The blood pressure target for patients who are candidates for fibrinolytic therapy (eg, alteplase) is <180/105 mm Hg to minimize the risk of hemorrhagic conversion of ischemic stroke (see Table e31-2). It is not recommended to target goals lower than 180/105 due to the risk of worsening cerebral ischemia.

5. **C.** Nicardipine 5 mg/hr IV infusion is the most appropriate choice for this patient given its ease of titration and predictable pharmacokinetics (see Table e31-3). Nitroglycerin is preferred in patients with cardiac-related target end-organ dysfunction, which is not relevant in this patient. Hydralazine's unpredictable onset and pharmacodynamic effects render it suboptimal for a patient who requires rapid blood pressure control and avoidance of precipitous blood pressure decreases. Metoprolol, while it may have some effect on blood pressure, primarily acts as an agent to reduce heart rate which is not the primary goal in this patient.

6. **A.** Risk of blood pressure decreases that are too rapid include worsening tissue ischemia (see Fig. e31-1). This is especially problematic in the setting of ischemic stroke, where brain perfusion is crucial. Hemorrhagic conversion would be a concern in the setting of uncontrolled hypertension rather than decreased blood pressure. Acute kidney injury and coronary ischemia are both general risks of rapidly lowering blood pressure. However, in the setting of acute ischemic stroke, the risk of cerebral ischemia would be most concerning.

7. **C.** This patient's blood pressure should be classified as hypertensive urgency (see "Hypertensive Urgency" section). He presents with acute elevations >180/120 mm Hg confirmed on multiple readings. However, this patient is asymptomatic with no evidence of target end-organ damage. Therefore, this cannot be classified as an hypertensive emergency.

8. **D.** Because this patient has hypertensive urgency, he should be managed conservatively by reinitiating his home antihypertensives (see "Treatment Hypertensive Urgency" section). He reports running out of medications 4 days prior which could have led to his hypertensive urgency. The patient's medications should be renewed, and he should be counseled on the importance of adherence to the prescribed regimen.

9. **B.** This patient reports running out of medications 4 days prior which could have led to his hypertensive urgency (see Table e31-1). The patient's medications should be renewed, and he should be counseled on the importance of adherence to the prescribed regimen. If blood pressures remain uncontrolled upon the next office visit, then his regimen should be modified accordingly.

10. **B.** Esmolol should be used first-line in this patient due to the presence of aortic dissection (see "Recommendations for Specific Target Organ Damage" section). Patients with aortic dissection must be treated with a rate-controlling medication prior to the use of a medication that causes vasodilation to prevent the risk of rebound tachycardia. Tachycardia must be avoided to minimize shear stress on the damaged aortic wall.

11. **C.** When managing aortic dissection, it is recommended to both treat blood pressure (SBP < 120 mm Hg) and control the heart rate (HR goal < 60 beats/min) within 20 minutes to prevent further organ damage (see Table e31-2).

12. **A.** Discordant blood pressure readings on opposite arms is a characteristic physical exam finding in patients with aortic dissection. Peripheral pitting edema and jugular venous distension would be expected to occur more frequently in the setting of cardiac failure and fluid overload. Papillary edema would be expected to occur in the setting of hypertensive acute retinopathy. (See "Clinical Presentation Blood Pressure Assessment" section.)

13. **A.** As a result of long-standing uncontrolled hypertension, the patient's autoregulation curve is most likely shifted to the right (see Fig. e31-1). This alteration in autoregulation increased the risk of tissue ischemia with acute decrease in BP despite BP readings being in the otherwise "normal" range. The curve is not generally shifted to the left in patients with long-standing hypertension.

14. **D.** Increasing the dose of one of her antihypertensive medications would be the best course of action in this patient (see "Hypertensive Urgency" in "Treatment" section). None of her antihypertensives (nifedipine XR, hydrochlorothiazide, or valsartan) are currently prescribed at optimized doses and could potentially provide better control of her hypertension if increased. It would not be appropriate to switch the patient to a different medication in the same class if the patient is tolerating the medication well. There is no need to add on an additional agent since she is already on three guideline-recommended medications. IV therapy is not an appropriate management strategy for hypertensive urgency.

15. **B.** Avoidance of the use of certain nonprescription medications such as NSAIDs or certain herbal supplements would be an appropriate counseling point in any patient with hypertension but is especially important in the setting of uncontrolled hypertension (see Table e31-1). Avoiding physical exertion or drinking water are not appropriate interventions for this patient. This patient should not report to the emergency department given that there is no suspicion for target end-organ damage.