Hypertensive Crises

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KEYWORDS

• Blood pressure • Hypertension • Urgency • Emergency • Encephalopathy • Stroke

HOSPITAL MEDICINE CLINICS CHECKLIST

1. Blood pressure (BP) exists on a continuum ranging from hypotension to malignant hypertension (HTN).
2. An elevated BP reading should be confirmed by repeating it in different limbs.
3. Patients with elevated BP should be triaged as HTN urgency or emergency based on symptoms/signs/testing, and not merely based on absolute BP numbers.
4. Patients with HTN urgency can be managed outpatients with close follow-up, or as inpatients.
5. HTN emergencies are preferably managed in an intensive care unit setting.
6. In HTN emergency, prompt reduction of BP by about 25% in the first few hours is appropriate, except in patients with ischemic stroke, in whom BP reduction is not recommended unless it is very high. Aggressive reduction of BP is necessary in aortic dissection.
7. Choice of drug depends on clinical presentation/physical findings/laboratory testing.

DEFINITIONS

1. What is the definition of hypertensive crisis?

The Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure[1] classifies 4 stages of blood pressure (BP):

- Normal BP: systolic BP (SBP) lower than 120 mm Hg and diastolic BP (DBP) lower than 80 mm Hg

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- Prehypertension: Prehypertension (pre-HTN) is defined as SBP 120 to 139 mm Hg or DBP 80 to 89 mm Hg
- Stage 1 hypertension (HTN): SBP 140 to 159 mm Hg or DBP 90 to 99 mm Hg
- Stage 2 HTN: SBP ≥160 mm Hg or DBP ≥100 mm Hg

HTN is defined as an SBP of 140 mm Hg or higher or DBP of 90 mm Hg or higher, measured on 2 or more occasions.[1] There is no consensus regarding a cutoff value to define hypertensive crisis, but it is often described as an SBP higher than 180 mm Hg or a DBP higher than 120 mm Hg.[2]

2. What are the different types of hypertensive crises, and how are they differentiated?

Hypertensive crisis can be further classified as a hypertensive urgency or hypertensive emergency, depending on the presence or absence of end-organ involvement:

- Hypertensive urgency is defined as an SBP higher than 180 mm Hg or a DBP higher than 120 mm Hg in the absence of, or minimal, target end-organ damage.[2]
- Hypertensive emergency is most consistently seen with a DBP higher than 120 mm Hg, which irrevocably causes end-organ damage including, but not limited to, the cardiac, renal, and central nervous systems.[3] It accounts for 25% to 30% of all hypertensive crises. The absolute BP elevation is not a necessary criterion for the diagnosis of HTN emergency as long as there is evidence of acute end-organ damage.

EPIDEMIOLOGY

1. What is the incidence and prevalence of hypertensive crisis in the United States and worldwide?

HTN affects an estimated 68 million (1 in 3 adult Americans).[4] About half (47%) of patients with high BP have their condition under control.[4] It is estimated that 1% to 2% of the HTN population will present with hypertensive crisis.[5] Nearly 3.2% of patients presenting to the emergency room have a hypertensive crisis. Zampaglione and colleagues[6] evaluated the prevalence of hypertensive crisis in an emergency department during a 12-month period and the frequency of end-organ damage during the first 24 hours after presentation. The investigators found 76% of the hypertensive crises to be hypertensive urgencies and 24% hypertensive emergencies, representing more than one-fourth of all medical urgencies/emergencies.

As with HTN, hypertensive crises are more prevalent in the elderly and the non-Hispanic black population. Men are affected 2 times more often than women.[7,8] Severe HTN is seen more frequently in noncompliant individuals, black men, persons of lower socioeconomic status, and the elderly.[9]

ETIOLOGY

1. What are the most frequent causes of hypertensive emergency and urgency?

Acute and severe BP elevation can occur as a complication of essential HTN, secondary HTN, or can happen de novo. In general, 8% of patients with hypertensive emergencies and 28% with hypertensive urgencies presenting to the emergency room are unaware of having a diagnosis of HTN.[9]

- The most common precipitant is medication noncompliance.[9] Withdrawal syndrome from centrally acting antihypertensives, peripheral β-blockers, or α-blockers can cause an increase in sympathetic flow.
- In previously normotensive individuals, numerous recreational (eg, cocaine, phencyclidine, amphetamines) or prescription drugs (eg, oral contraceptives, linezolid, nonsteroidal anti-inflammatory drugs, monoamine oxidase [MAO] inhibitors) can increase risk for a hypertensive crisis. Withdrawal from alcohol can also precipitate hypertensive crisis.[10]
- Any secondary causes of HTN can lead to a hypertensive crisis (**Box 1**).[11]

In a longitudinal study, Saguner and colleagues[12] identified several risk factors significantly associated with hypertensive crises: female sex, higher grade of obesity, the presence of hypertensive heart disease, the presence of a somatoform disorder, a higher number of antihypertensive drugs, and nonadherence to medication. Nonadherence to medication was the most important factor associated with hypertensive crises. Other risk factors include suboptimal treatment of HTN as an outpatient,[13] the lack of a primary care physician and medical insurance,[14] being a black male, lack of resources, smoking, diabetes, autumn season, and the morning hours between 6 AM and 12 noon.[15]

PATHOPHYSIOLOGY

1. What is the pathophysiology of hypertensive crisis?

The exact mechanisms underlying both primary (essential) HTN and hypertensive crises are not totally understood. The initial event appears to be an abrupt increase in BP from a known or unknown stimulus followed by compensatory mechanisms arising from the vascular endothelium. Initially the endothelium releases the vasodilator nitric oxide in an attempt to compensate for the change in vasoreactivity. The arterioles sense an increase in BP and, in turn, arterial smooth muscle contracts in an effort to reduce the increase in BP and to limit the effect of the BP at the cellular level. A vicious cycle occurs, with prolonged arterial vasoconstriction leading to more endothelial dysfunction and an inability to release more nitric oxide, resulting only in a further increase in BP. Therefore, patients with chronic HTN have more smooth-muscle hypertrophy because of a sustained elevation in BP, allowing temporary and incomplete end-organ protection at the capillary level. By contrast, normotensive patients who undergo an abrupt increase in BP do not have the same degree of smooth-muscle hypertrophy. Thus, even small abrupt rises in BP can induce a hypertensive crisis in normotensives, partly because of the capillary damage that occurs.[16]

Regardless of the initial stimulus, there appears to be a complex interaction of the renin-angiotensin-aldosterone system, sympathetic nervous system, and endothelial dysfunction. The renin-angiotensin-aldosterone system is thought to be critically responsible for BP changes, owing to water and sodium retention. The sympathetic nervous system also affects BP, especially in times of stress and exercise. The sympathetic nervous system can cause arterial vasoconstriction and can raise cardiac output. The mechanical shear forces on the vascular wall result in endothelial damage and dysfunction. Endothelial dysfunction results in the expression of inflammatory markers that promote coagulation, platelet aggregation, and vasoconstriction.[17] There is also evidence that angiotensin II activates the expression of genes for proinflammatory cytokines, causing a direct toxic effect to the vessel wall.[18]

Box 1
Causes of hypertensive crises

1. Medication noncompliance
2. Suboptimal treatment of essential HTN
3. Renovascular disease
   - Renal artery stenosis: atheroma or fibromuscular dysplasia
   - Polyarteritis nodosa
   - Takayasu arteritis
4. Renal parenchymal disease
   - Glomerulonephritis
   - Tubulointerstitial nephritis
   - Systemic sclerosis
   - Hemolytic uremic syndrome
   - Thrombotic thrombocytopenic purpura
   - Systemic lupus erythematosus
   - Renal cell carcinoma
5. Endocrine
   - Pheochromocytoma
   - Cushing syndrome
   - Primary hyperaldosteronism
   - Renin-secreting tumor
6. Drugs
   - Antihypertensive drug withdrawal (eg, clonidine, β-blockers)
   - Cocaine, phencyclidine, sympathomimetics, erythropoietin, cyclosporine
   - Amphetamines
   - Lead intoxication
   - Interactions with monoamine oxidase inhibitors
   - Alcohol withdrawal
7. Autonomic hyperreactivity
   - Guillain-Barré syndrome
   - Acute intermittent porphyria
8. Central nervous system
   - Head injury
   - Cerebral infarction
   - Cerebral hemorrhage
   - Brain tumor
   - Spinal cord injury
9. Pregnancy-related
   - Preeclampsia
   - Eclampsia

Modified from Johnson W, Nguyen ML, Patel R. Hypertension crisis in the emergency department. Cardiol Clin 2012;30(4):535; with permission.

CLINICAL PRESENTATION

1. What are the presenting symptoms of a hypertensive crisis?

There may be signs and symptoms associated with a hypertensive crisis, or its manifestations may be silent. Silent hypertensive crisis has been found to be especially common in young black men.[10] For symptomatic patients, the symptoms will ultimately depend on the organ(s) affected. These symptoms may include chest pain (myocardial ischemia or infarction), back pain (aortic dissection), dyspnea (pulmonary edema or congestive heart failure), seizures, nausea/vomiting, or altered consciousness (hypertensive encephalopathy).[18] The most widespread signs and symptoms at presentation for hypertensive urgency are headache (22%), epistaxis (17%), faintness (10%), psychomotor agitation (10%), chest pain (9%), and dyspnea (9%).[6]

A detailed history is essential; it is vital to inquire about the onset, duration, and severity of HTN, prior organ damage with associated symptoms, recreational drug and alcohol use, a list of medications (antihypertensive regimen with dosing and over-the-counter preparations), compliance with the antihypertensive regimen, and time and dose of the most recent ingested treatment.

2. What are the important physical findings in hypertensive crises?

The physical examination should initially focus on proper BP measurement in both upper limbs with an appropriately sized BP cuff, and to evaluate for any evidence of end-organ damage. Pulses should be palpated and compared in the upper and lower extremities. BP readings in the supine, sitting, and standing positions are required to measure volume status. Carotid arteries and abdominal arteries should be auscultated for bruits.[19]

A comprehensive cardiovascular examination is of value. An elevated jugular venous pressure, third heart sound, and/or pulmonary rales are evidence of heart failure. A prominent/displaced apical impulse or a harsh interscapular murmur is suggestive of coarctation of the aorta. Other significant elements include a fundoscopic examination for the presence of hemorrhages, papilledema, or exudates (confirming a hypertensive retinopathy), and a thorough neurologic examination to assess for stroke, somnolence, stupor, visual loss, focal deficits, seizures, or coma.[20]

3. What are the most common hypertensive emergency syndromes?

In a study of the prevalence of end-organ complications in hypertensive crisis, central nervous system and cardiovascular abnormalities were the most frequent.[6] The reported complications are outlined in **Table 1**.

Cerebral Infarction

Cerebral infarction is generally caused by 1 of 3 pathogenic mechanisms: atherosclerotic disease in extracranial and large intracranial arteries; embolism from the heart; or intracranial small-vessel disease (lacunar infarcts).[21] Lacunar infarcts are strongly associated with long-standing HTN; they are defined as small (<15 mm diameter) subcortical infarcts (usually located in the basal ganglia, thalamus, internal capsule, corona radiata, and the brainstem) that result from occlusion of a single perforating artery. The most important clinical feature is the presence of a focal neurologic deficit in the absence of cognitive symptoms or signs (except in the case of thalamic infarcts) and visual field defects.[22]

Table 1
Percentage of hypertensive emergencies

Type of Hypertensive Emergency	%
Cerebral infarction	24.5
Acute pulmonary edema	22.5
Hypertensive encephalopathy	16.3
Acute congestive heart failure	14.3
Acute myocardial infarction or unstable angina	12.0
Intracerebral or subarachnoid hemorrhage	4.5
Eclampsia	4.5
Aortic dissection	2.0

Hypertensive Encephalopathy

Hypertensive encephalopathy is defined as an acute neurologic syndrome in the setting of severe HTN. Symptoms include severe headache, nausea, vomiting, visual disturbances, confusion, and focal or generalized weakness. Signs include disorientation, focal neurologic defects, focal or generalized seizures, and nystagmus. If not adequately treated, hypertensive encephalopathy can lead to cerebral hemorrhage, coma, and death, but with proper treatment it is completely reversible.[23] It is mainly a clinical diagnosis. Stroke, subarachnoid hemorrhage, mass lesions, seizure disorder, and vasculitides need to be ruled out.

Myocardial Ischemia/Infarction

Activation of the renin-angiotensin-aldosterone system in HTN constricts systemic vasculature and thereby increases myocardial oxygen demand by increasing left ventricular wall tension. Increasing wall tension leads to hypertrophy of the left ventricle, which further increases oxygen demand on the heart. A second effect of the hypertrophy is that the newly thickened ventricle can cause coronary compression and decreased luminal blood flow. Concomitant atherosclerosis worsens the wall-to-lumen ratio, further decreases coronary flow reserve, and leads to coronary ischemia.[24]

Left Ventricular Failure and Acute Pulmonary Edema

In certain cases, despite increasing wall tension, the left ventricle cannot hypertrophy enough to overcome the acute increase in systemic vascular resistance. This inability to compensate leads to left ventricular failure and a back-up of flow causing pulmonary edema. Second, neurohormonal activation of the renin-angiotensin-aldosterone system leads to increased sodium content and increased total body water. In addition, left ventricular hypertrophy leads to focal ischemia and subsequent inadequate diastolic filling, which can result in imbalance between left ventricular contraction and relaxation, leading to pulmonary edema[25]; this will clinically manifest as acute heart failure. Patients will present with dyspnea, chest pain, and rales and S3 gallop on examination.

Aortic Dissection

Dilation of the aorta caused by atherosclerosis and high BP tears the intima of the vessel, allowing a surge of blood into the aortic wall. The blood driven by pulsatile pressure separates the arterial wall into 2 layers. Clinically, patients complain of

retrosternal or interscapular chest pain that migrates to the back. If dissection extends proximally, it can lead to aortic insufficiency, pericardial effusion, or myocardial ischemia. Dissection can lead to compression or occlusion of a branch of the aorta and subsequently lead to organ ischemia. Clinical signs that are notable with dissection include discrepancies between pulses, murmur of aortic insufficiency, and neurologic deficits.[26]

Acute Kidney Injury

Renal insufficiency can be the cause or result of hypertensive crisis. In patients with chronic HTN renal autoregulation is impaired, resulting in an increase of intraglomerular pressure with increasing systemic arterial pressure. This increase in pressure can cause ischemic injury and fibrosis.[16] Hypertensive crisis can occur in acute glomerulonephritis, hemolytic uremic syndrome, renal artery stenosis, patients on hemodialysis receiving erythropoietin with an accelerated rate of increase in hematocrit, and renal transplant patients, especially those on cyclosporine and corticosteroids.[18]

Clinical presentations that suggest renal involvement include proteinuria, elevated serum creatinine, hypokalemic metabolic alkalosis, and microangiopathic hemolytic anemia.[27] The level of renal recovery relates to the degree of renal impairment at presentation and the underlying renal disorder.

Hypertensive Retinopathy

In 1914, the term "malignant HTN" was coined after findings of severe HTN, renal failure, retinopathy with papilledema, uremia, and accelerated death. Since then, multiple studies have looked at retinopathy in the setting of HTN. Some retinal changes such as arteriole narrowing are considered a result of chronic HTN. Nowadays, malignant HTN refers to a hypertensive crisis in the setting of papilledema and retinal hemorrhages and exudates. Ophthalmoscopy may be useful in recognizing acute hypertensive target-organ damage such as hypertensive encephalopathy, but the absence of retinal exudates, hemorrhages, or papilledema does not exclude the diagnosis.[28]

Preeclampsia

Preeclampsia is characterized as a syndrome of pregnancy-induced HTN, edema, and proteinuria in a pregnant woman after the 20th week of gestation. Eclampsia is the end result of this spectrum and is associated with acute HTN, edema, proteinuria, and concomitant seizures.[29] The pathophysiologic mechanisms of this spectrum are not well understood, but an increased responsiveness to vasoconstrictors, especially angiotensin II, and a decreased sensitivity to endothelium-derived vasodilators have been described. Pregnancy-induced HTN usually resolves spontaneously after delivery.[11]

DIAGNOSIS

1. What should the initial workup include?

Following thorough history and physical examination, initial workup should include laboratory studies such as serum electrolytes, blood urea nitrogen, serum creatinine level, blood cell count, and peripheral smear. An electrocardiogram should be done to exclude myocardial ischemia and left ventricular hypertrophy, and a chest radiograph (CXR) should be obtained to look for pulmonary congestion, cardiac enlargement, and widened mediastinum. Urine analysis (UA) is indicated for assessment of

proteinuria and tubular casts. A computed tomography (CT) scan of the head should be obtained in a patient presenting with neurologic symptoms (**Table 2**).[30]

2. What further testing should be done to differentiate the etiology of hypertensive crisis?

Further imaging studies should be performed based on the clinical presentation and the initial workup. If the physical examination or clinical picture is consistent with aortic dissection (severe chest pain, unequal pulses and widened mediastinum on CXR), a contrast CT scan or magnetic resonance image of the chest should be obtained promptly to rule out aortic dissection. Transesophageal echocardiography also has excellent sensitivity and specificity for aortic dissection, but this study should not be performed until adequate BP control has been achieved.[20]

In patients presenting with shortness of breath, a transthoracic echocardiogram may help to distinguish between diastolic, systolic, and valvular dysfunction. Many patients, particularly the elderly, obese, and/or diabetic patients, have a normal ejection fraction; in such patients, heart failure is due to isolated diastolic dysfunction.[31]

A sudden increase in BP in a patient with undiagnosed HTN or the presentation in a young patient (<25 years) suggests a secondary source. Workup for secondary causes should include a noninvasive imaging study of the kidneys and renal arteries, along with hormonal screening for excess aldosterone, cortisol, and catecholamine states. It is important to distinguish renal parenchymal disease from renovascular HTN to direct further testing appropriately. Secondary HTN is traditionally classified by organ system into renal causes, endocrine causes, and other causes, including obstructive sleep apnea (**Table 3**).[30]

Renal parenchymal disease is the most common cause of secondary HTN. Normal renal parenchymal imaging on ultrasonography, the absence of hydronephrosis, and a bland urinary sediment argue against this etiology. Coupled with drug-resistant HTN, this should prompt further renal vascular imaging, either with renal artery Doppler, CT angiography (CTA), or magnetic resonance angiography (MRA). As the use of gadolinium with MRA has been associated with nephrogenic systemic fibrosis (NSF),

Table 2
Initial workup

Laboratory Tests and Imaging Studies	Elements to Look For
Blood cell count and peripheral smear	Schistocytes (HUS)
Serum electrolytes	Hypernatremia, hypokalemia (both seen in Hyperaldosteronism)
BUN, serum creatinine	AKI
ECG	Acute coronary syndrome, LVH
CXR	Widened mediastinum (aortic dissection) Bilateral pulmonary infiltrates (pulmonary edema)
UA	Proteinuria (nephrotic syndrome) Granular casts (AKI) RBC casts (nephritic syndrome)
Head CT	Intracranial hemorrhage (either intraparenchymal or subarachnoid)

Abbreviations: AKI, acute kidney injury; BUN, blood urea nitrogen; CT, computed tomography; CXR, chest radiography; ECG, electrocardiography; HUS, hemolytic uremic syndrome; LVH, left ventricular hypertrophy; RBC, red blood cells; UA, urine analysis.

Table 3
Workup for secondary causes

Tests	Elements to Look For
Renal ultrasonography	Hydronephrosis, renal parenchymal disease
Abdominal CT	Hydronephrosis, adrenal masses
Abdominal CT angiography	Renal artery stenosis
Magnetic resonance angiography	Renal artery stenosis
Renal biopsy	Glomerular diseases, tubulointerstitial diseases
8 AM serum aldosterone and renin levels	Screening test for hyperaldosteronism
Fractionated plasma metanephrines	Pheochromocytoma
24-h urinary metanephrines	Pheochromocytoma
Thyroid-stimulating hormone and free thyroxine	Hyperthyroidism, hypothyroidism
Low-dose overnight dexamethasone suppression test	Cushing syndrome

a life-threatening sclerosis of the skin and connective tissues, certain institutions prefer CTA in patients with renal insufficiency. Contrast-induced nephropathy is generally reversible and can be prevented in part by preprocedural hydration and *N*-acetylcysteine.[32] NSF, on the other hand, is irreversible.[33]

Clinical features should guide the investigation of hormonal secondary causes. Primary hyperaldosteronism is increasingly recognized as a correctable cause for resistant HTN; thus, screening with serum aldosterone and plasma renin activity should be considered early in the evaluation, especially if hypokalemia is present. Pheochromocytoma is rare but should be considered in patients who have markedly labile BP, particularly those with orthostatic hypotension, tachycardia, or dizzy spells. All patients who have HTN should be evaluated for thyroid disease (hyperthyroid and hypothyroid states), particularly if their BP is not controlled. Directed testing of the adrenal cortisol axis is usually reserved for patients with clinical evidence of cortisol excess (eg, central obesity, pigmented striae, hyperglycemia) or for those with an incidentally discovered adrenal mass.[30]

MANAGEMENT

1. Where should patients with a hypertensive crisis be managed?

There are no guidelines on where to manage a patient with hypertensive crisis. There is general consensus that patients with HTN emergencies should be managed in the intensive care unit, as this allows for simultaneous control of various factors that predispose to high BP and the use of intravenous antihypertensive therapy. Patients with HTN urgency can be managed as outpatients or on medical floors, as these patients can be treated with oral antihypertensive medications and the need for early and controlled reduction in BP is not urgent.

2. What is the goal in lowering BP in a patient with hypertensive urgency?

The goal in most cases of HTN urgency is to lower the BP gradually over 24 to 48 hours, usually with oral medications. The risk of rapid correction of BP outweighs the benefits in patients with HTN urgency.[20] These patients can be managed in the outpatient

setting as long as the patient is compliant with use of medication, diet, and regular monitoring of BP. For patients at high risk for cardiovascular or cerebrovascular disease, and those unlikely to comply with changes in the prescribed medication regimen, admission to the hospital for initial management of BP should be considered.

3. What is appropriate initial therapy for hypertensive urgency?

There is no single drug of choice in this setting. The choice of medication should be based on individual patient characteristics and medical history.[1] For instance, calcium-channel blockers and thiazide-like diuretics are preferred over angiotensin-converting enzyme (ACE) inhibitors and β-blockers as monotherapy in African Americans. In patients with proteinuria, ACE inhibitors are the preferred agents. Some experts initiate therapy with 2 agents, 1 of which is a thiazide diuretic if the BP is 20/10 mm Hg or more above goal.[1] This approach can be considered in patients who have close follow-up and are not at high risk for cerebrovascular disease.

4. What is the goal in lowering BP in a patient with hypertensive emergency?

The goal of lowering BP in patients with HTN emergency is to control BP to terminate ongoing organ damage and prevent further complications, but not to return BP to normal levels.[25] The rate at which lowering takes place, and how much to lower BP, depends on the clinical presentation of the patients. For example, in patients with HTN encephalopathy or malignant HTN, the goal should be to reduce the mean arterial BP (MAP) by about 20% to 25% in the first 24 hours, but in patients with ischemic stroke who do not receive thrombolytic therapy (tissue plasminogen activator), BP should not be reduced except in cases of extreme BP elevation (SBP >220 or DBP >120 mm Hg).[34] **Table 4** lists target BP goals by clinical presentation.

5. What is the appropriate initial therapy for hypertensive emergency?

All patients with HTN emergency should be admitted to an intensive care unit. The room should be quiet and well lit. Patients should be advised to avoid activity that increases heart rate or BP. Patients should be given low-sodium diets, and use of intravenous fluids should be minimized. If intravenous fluids are necessary, use of 5% dextrose or 0.45% saline should be considered as long as serum sodium is normal. Patients should be initiated on intravenous antihypertensive medications as soon as intravenous access is established. The choice of intravenous agent depends on patients' clinical presentation.[25] Starting of simultaneous intravenous and oral medication can result in rapid decline in BP. Hence, it is advisable to first stabilize BP with intravenous agents over the first 24 hours before considering transition to oral agents. **Table 5** lists commonly used intravenous antihypertensive medications. **Table 6** summarizes the special indications of parenteral medications and their associated side effects.

6. Management of HTN emergency in special circumstances

Neurologic Syndromes

The lower limit of cerebral blood flow autoregulation is reached when BP is reduced by 25%. Cerebral ischemia can be precipitated with rapid reductions in BP of greater than 50%.[25] Sodium nitroprusside is the preferred agent, given its rapid onset of action. Labetalol is a good alternative unless there is evidence of severe bradycardia

Table 4
Target blood pressure goals

Hypertensive Emergency	Target Blood Pressure
Hypertensive encephalopathy	Reduce MAP by maximum of 20% or to DBP 100–110 mm Hg within first hour, then gradually lower blood pressure to normal range over 48–72 h
Ischemic stroke	Reduce MAP no more than 15%–20%, and to DBP not less than 100–110 mm Hg in the first 24 h (thrombolytic protocols in stroke may allow slightly more aggressive management)
Ischemic stroke post-tPA	SBP <185 mm Hg or DBP <110 mm Hg
Intracerebral hemorrhage	Reduce MAP by 20%–25%
Hypertensive retinopathy	Reduce MAP by 20%–25%
Left ventricular failure	MAP 60–100 mm Hg
Aortic dissection	SBP 100–120 mm Hg
Acute renal insufficiency	Reduce MAP by 20%–25%
Pregnancy-induced hypertension	SBP 130–150 mm Hg and DBP 80–100 mm Hg
Postoperative hypertension	Reduce MAP by 20%–25% (not based on published guidelines)
Myocardial ischemia/infarct	MAP 60–100 mm Hg
Hyperadrenergic states	Reduce MAP by 20%–25% (not based on published guidelines)

Abbreviations: DBP, diastolic blood pressure; MAP, mean arterial pressure; SBP, systolic blood pressure; tPA, tissue plasminogen activator.

From Johnson W, Nguyen ML, Patel R. Hypertension crisis in the emergency department. Cardiol Clin 2012;30(4):541; with permission.

caused by cerebral edema. Clonidine should not be used, because it can cause central nervous system depression and a prolonged and sustained decrease in BP.[25]

Hypertensive Encephalopathy

One should aim to reduce the MAP by 20% or to a DBP of 100 to 110 mm Hg, whichever is higher, during the first few hours, with subsequent gradual reduction.

Intracerebral or Subarachnoid Hemorrhage

Intracranial bleeding can be reduced by lowering the BP by 20% to 25%. Any further decrease can increase the bleed. The current American Heart Association/American Stroke Association (AHA/ASA) guidelines suggest that acute lowering of SBP to a target of 160/90 mm Hg is probably safe.[35]

Ischemic Stroke

BP reduction is not recommended after a stroke, except in cases of extreme BP elevation or if patients receive thrombolytic therapy. For patients with acute ischemic stroke who are treated with thrombolytic therapy, the goal is to bring down the systolic BP to 185 mm Hg or lower and diastolic BP to 110 mm Hg or lower. For patients with acute ischemic stroke who are not treated with thrombolytic therapy, it is recommended not to treat high BP unless HTN is extreme (SBP >220 or DBP >120 mm Hg), or if the patient has another clear indication such as myocardial infarction or aortic dissection. In

Table 5
Parenteral medications used for treatment of hypertensive emergency

Medication	Dosing	Onset of Action	Preload	Afterload	Cardiac Output
Sodium nitroprusside	0.25–10 μg/kg/min IV infusion	Within seconds to minutes	↓	↓↓	No effect
Nitroglycerin	5–100 μg/min IV infusion	1–5 min	↓↓	↓	No effect
Labetalol	20–80 mg bolus every 10 min, or 0.5–2 mg/min IV infusion	5–10 min	No effect	↓	↓
Esmolol	80 mg bolus over 30 s then 150 μg/kg/min IV infusion	1–2 min	No effect	No effect	↓
Hydralazine	10–20 mg IV bolus	10–20 min	No effect	↓	↑
Phentolamine	5–15 mg IV bolus	1–2 min	No effect	↓	↑
Nicardipine	2–15 mg/h IV infusion	5–10 min	No effect	↓	↑
Clevidipine	1–2 mg/h then titrate to maximum 16 mg/h IV infusion	1–4 min	No effect	↓	↑
Fenoldopam	0.1–0.6 μg/kg/min IV infusion	5–10 min	No effect	↓	↑
Enalaprilat	1.25–5 mg every 6 h IV bolus	15–30 min	No effect	↓	↑

Abbreviation: IV, intravenous.
From Johnson W, Nguyen ML, Patel R. Hypertension crisis in the emergency department. Cardiol Clin 2012;30(4):536; with permission.

these settings, there should be cautious lowering of BP by approximately 15% during the first 24 hours after stroke onset.[25]

Myocardial Ischemia

Intravenous parenteral vasodilators, principally nitroprusside and nitroglycerin, are effective, and may reduce mortality in patients with acute myocardial infarction with HTN. β-Blockers can reduce heart rate, decrease afterload, and improve diastolic coronary perfusion. Hydralazine should be avoided, as it can induce a reflex tachycardia and increase myocardial oxygen demand.[36]

Aortic Dissection

The aim of the therapy is to reduce the heart rate, BP, and shear stress on the aortic wall. Once the diagnosis of aortic dissection is made, prompt treatment is essential because the death rate in acute aortic dissection may be as high as 1% per hour during the first 24 hours. Intravenous labetalol is the drug of choice in this setting, to achieve a heart rate lower than 60 beats/min and maintain the systolic BP between 100 and 120 mm Hg or the lowest level that is tolerated. Nitroprusside reduces both preload and afterload, but this should not be used before starting labetalol, as this can cause reflex tachycardia through vasodilatation. Hydralazine and diazoxide should be avoided, as they both increase shear stress on the aortic wall. Type A dissection (ascending aorta) requires immediate surgical intervention in addition to BP control. Type B dissection (descending aorta) can be managed medically unless complications develop.[37]

Table 6
Special indications and warnings for parenteral medications

Medication	Special Indications	Warnings
Sodium nitroprusside	Most hypertensive emergencies	Caution with renal insufficiency; can develop cyanide toxicity, acidosis, methemoglobinemia, increased intracranial pressure, nausea, vomiting, muscle twitching[29]
Nitroglycerin	Most hypertensive emergencies, coronary ischemia	Headache; can develop tolerance, tachycardia, vomiting, methemoglobinemia, flushing
Labetalol	Most hypertensive emergencies, aortic dissection	Avoid in acute heart failure, bradycardia, and bronchoconstrictive disease
Esmolol	Aortic dissection	Avoid in acute heart failure, bronchoconstrictive disease, and heart block
Hydralazine	Eclampsia	Can cause reflex tachycardia, headache
Phentolamine	Catecholamine excess	Flushing, headache, tachycardia
Nicardipine	Most hypertensive emergencies	Avoid in acute heart failure and coronary ischemia; causes reflex tachycardia, nausea, vomiting, headache, increased intracranial pressure
Clevidipine	Most hypertensive emergencies	Atrial fibrillation; avoid in soy allergy
Fenoldopam	Most hypertensive emergencies, acute renal impairment, and/or hematuria	Caution with glaucoma; can cause headache, flushing, tachycardia, local phlebitis
Enalaprilat	Acute left ventricular failure	Avoid in acute myocardial ischemia

Data from Johnson W, Nguyen ML, Patel R. Hypertension crisis in the emergency department. Cardiol Clin 2012;30(4):533–43.

Renal Insufficiency

These patients need reduction in systemic vascular resistance without compromising renal blood flow. Fenoldopam improves renal perfusion and diuresis, and has no toxic metabolites. β-Blockers and calcium-channel blockers can be used as well, but have no effect on renal glomerular filtration. In patients with acute renal injury, ACE inhibitors or angiotensin receptor blockers (ARBs) are preferably avoided until the acute renal crisis improves, except in case of scleroderma renal crises whereby ACE inhibitors such as captopril and enalapril are the drugs of choice.[38]

Preeclampsia and Eclampsia

For acute severe BP reduction, it is recommended to use intravenous labetolol or hydralazine, and for chronic severe HTN methyldopa is the drug of choice. Methyldopa acts centrally, and reduces BP and heart rate. ACE inhibitors and ARBs are contraindicated in pregnancy because of their teratogenic effects.[25]

Pheochromocytoma

Phentolamine is an intravenous α1-adrenergic blocker for acute severe hypertensive crisis of pheochromocytoma. Phenoxybenzamine is the oral agent of choice for

chronic and perioperative management. After a week or 10 days of phenoxybenzamine, β-adrenergic blockade should be started. The β-adrenergic blocker should never be started first, because unopposed α-adrenergic receptor stimulation can lead to a further elevation in BP.[11]

Acute Heart Failure/Pulmonary Edema

In this group of patients, nitroprusside or nitroglycerin with a loop diuretic is the regimen of choice. The concomitant venous and arterial dilation improve forward flow and cardiac output. Drugs that increase cardiac workload (hydralazine) or decrease cardiac contractility (labetalol or other β-blockers) should be avoided in the setting of acute pulmonary edema or acute heart failure.[39]

Hyperadrenergic States

Increased adrenergic activity can lead to severe HTN in a variety of clinical settings: autonomic dysfunction, post–spinal cord injury, use of sympathomimetic drugs (cocaine, amphetamines, phencyclidine), or the combination of an MAO inhibitor and the ingestion of tyramine-containing foods. Control of HTN in these disorders can be achieved with phentolamine and nitroprusside. Administration of a β-blocker alone is contraindicated to prevent unopposed α activity and increased BP.

PROGNOSIS

1. What is the prognosis of hypertensive crises?

Data regarding prognosis in hypertensive crises is scarce. It has been reported that 1-year mortality is 79% for patients with untreated hypertensive emergencies,[25] and the 5-year survival among all patients who present with hypertensive crisis is 74%. The most common causes of death described in the literature are renal failure, stroke, myocardial infarction, and heart failure.[40]

Table 7
Performance measure description

Name	Description	Numerator	Denominator	Source	Reference
Hypertension control	Percentage of patients 18–85 y old with a diagnosis of hypertension and whose BP was adequately controlled (<140/90) during the measurement year	Patients from the denominator with last BP measurement with SBP < 140 mm Hg and DBP <90 mm Hg	All patients 18–85 y old with a diagnosis of hypertension during the measurement year	NQF/ NCQA/ CMS-PQRI 2008	National Committee for Quality Assurance

Abbreviations: CMS, Centers for Medicare and Medicaid Services; NCQA, National Committee for Quality Assurance; NQF, National Qualifications Framework; PQRI, Physician Quality Reporting System.

Data from US Department of Health and Human Services, Health Resources and Services Administration. Available at: http://www.hrsa.gov/quality/toolbox/measures/hypertension/index.html. Accessed October 24, 2013.

Frequently, cardiac enzymes are elevated. A retrospective study found that in patients with hypertensive crisis, elevated troponin-I confers a significantly greater risk of major cardiovascular events within the next 2 years.[41]

PERFORMANCE IMPROVEMENT

- The Hypertension Control Clinical Quality Measure is designed to measure the effectiveness of the care and management of patients diagnosed with HTN.
- Modest improvements in BP have been shown to reduce morbidity and mortality. It is estimated that a reduction of SBP of 5 mm Hg in the population would result in[42]:
  - 14% overall reduction in mortality from stroke
  - 9% reduction in mortality from coronary heart disease
  - 7% decrease in all-cause mortality

The National Heart, Lung, and Blood Institute, through the National Blood Pressure Education Program Coordinating Committee, has been increasing awareness, prevention, treatment, and control of HTN, and considerable progress has been made toward achieving the goal of HTN control (**Table 7**).

CLINICAL GUIDELINES

Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Hypertension 2003;42:1206–52.

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