HYPERTENSIVE Cardiac-EMERGENCY

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Case

- *96-year-old woman who takes diltiazem and furosemide and presents with pulmonary edema.*
- *Her triage BP reading is 220/130 mm Hg, and her respiratory rate is 28 breaths per minute while sitting in a tripod position.*
- *As you are waiting for portable radiography, the nurse asks how you want to manage the patient's BP.*

Cardiac remodeling

- Cardiac remodeling
    1. Elevated SVR increases left ventricular (LV) myocardial wall tension and oxygen demand.
        - » In hypertensive emergencies, myocardial perfusion may not be able to adequately maintain the increased myocardial oxygen demand, which can lead to myocardial ischemia and even infarction.

- Aggarwal M., Khan I.: Hypertensive crisis: hypertensive emergencies and urgencies. *Cardiol Clin* 24. 135-146.2006

Cardiac remodeling

2. Patients with long-standing hypertension may also have LV hypertrophy, which in itself increases myocardial oxygen demand.
    - » This increased LV mass can also cause some degree of coronary artery compression, leading to decreased luminal blood flow.
- Left ventricular hypertrophy (LVH) by Echocardiographic criteria
    - » 19% of men and 24% of women;
- LVH by electrocardiogram (ECG) criteria
    - » only 1.3% of both men and women.

- Aggarwal M., Khan I.: Hypertensive crisis: hypertensive emergencies and urgencies. *Cardiol Clin* 24. 135-146.2006
- Haider AW, Larson MG, Benjamin EJ, Levy D. Increased left ventricular mass and hypertrophy are associated with increased risk for sudden death. J Am Coll Cardiol.1998;32(5):1454-1459. (Prospective cohort; 3661 patients)

Cardiac remodeling

- Patients who meet ECG criteria for LVH also face an increased risk of:
  - CAD, heart failure, ventricular arrhythmias, CVA disease, and sudden death.
    - The increased risk of sudden death is theorized from a combination of increased myocardial oxygen consumption, compression of endocardial capillaries, and decreased ability to dilate veins, which reduce perfusion.
    - In addition, action potential prolongation, altered repolarization, and excessive myocardial fiber stretching may potentiate ventricular arrhythmias.

- Rials SJ, Wu Y, Xu X, Filart RA, Marinchak RA, Kowey PR. Regression of left ventricular hypertrophy with captopril restores normal ventricular action potential duration, dispersion of refractoriness, and vulnerability to inducible ventricular fibrillation. *Circulation.* 1997;96(4):1330-1336. (**Rabbit model**)
- Kannel WB, Gordon T, Castelli WP, Margolis JR. Electrocardiographic left ventricular hypertrophy and risk of coronary heart disease: the Framingham study. Ann Intern Med. 1970;72(6):813-822. (Prospective, observational; 5127patients)

HTN and Atrial fibrillation

- Hypertension has been associated with a 70% increase in risk for atrial fibrillation,
  - after adjustments for age, sex, and associated conditions.
- A prospective observational study of 4731 patients illustrated a 39% increase in risk for atrial fibrillation for every 5-mm increment in atrial enlargement.
- Atrial fibrillation increased the risk for stroke 3- to 5-fold after adjustments for other risk factors.

- Kannel WB, Wolf PA, Benjamin EJ, Levy D. Prevalence, incidence, prognosis, and predisposing conditions for atrial fibrillation: population-based estimates. Am J Cardiol. 1998;82(8A):2N-9N. (Prospective, observational; 4731patients

HTN and MI

- Hypertension can increase the frequency of MI.
- A prospective population-based study
  - when SBP increased from less than 120mmHg to 141-159 mmHg
    - 4902 adults older than 64 years showed an increased rate of MI from 10 to 22 per 1000-person-years and
    - in-total mortality from 22 to 29 per 1000-person-years.
- Increases in systolic BP above 159mmHg were associated with a further 30% to 40% relative increase in rates of MI and mortality.

- Psaty BM, Furberg CD, Kuller LH, et al. Association between blood pressure level and the risk of myocardial infarction, stroke and total mortality: the cardiovascular health study. *Arch Intern Med.* 2001;161(9):1183-1192. (**Prospective, observational;4902 patients**)

Acute Pulmonary Edema

- Gandhi and colleagues
  - used TTE to evaluate LV ejection fraction during acute episodes of hypertensive pulmonary edema
    - concluded that the cause of acute heart failure in patients with hypertensive crisis may be due to diastolic dysfunction secondary to ischemia.

- Gandhi S.K., Powers J.C., Nomeir A., et al: The pathogenesis of acute pulmonary edema associated with hypertension. *N Engl J Med* 344. 17-22.2001;

Incidence

- **Hypertensive crises may present in 3% of ED visits and 27% of all medical urgencies/emergencies**
  - based on study of patients presenting to ED at single hospital in Italy between 1992 and 1993
  - 449 patients with hypertensive crises evaluated
    - 3.2% of all 14,209 patients who presented to ED
    - 27.4% medical urgencies/emergencies
      - among 108 patients with **hypertensive emergencies**
        - » mean age 67 years
        - » mean blood pressure 210/130 mm Hg
        - » 8% had unknown hypertension at time of presentation
- estimated 0.6% medical service admissions annually attributed to hypertensive emergency

- Hypertensive urgencies and emergencies. Prevalence and clinical presentation Hypertension 1996 Jan;27(1):144
- Hypertensive crisis profile. Prevalence and clinical presentation; Arq Bras Cardiol 2004 Aug;83(2):131-6; 125

Hypertensive Emergencies

- The most common forms of end-organ damage in hypertensive emergencies, in order of decreasing frequency, are:
  (1) cerebral infarction or hemorrhage;
  (2) acute pulmonary edema;
  (3) Hypertensive encephalopathy; and
  (4) Aortic dissection.

- Perez MI, Musini VM. Pharmacological interventions for hypertensive emergencies [edited/substantively amended October 19, 2007]. *Cochrane Database Syst Rev.* 2008;(1):CD003653. (**Review**)

Likely risk factors

- **lack of primary care physician and noncompliance with treatment associated with increased risk of severe, uncontrolled hypertension in an urban population**
  - based on case-control study
  - 93 pts with severe, uncontrolled hypertension were compared with 114 control patients with hypertension
  - risk factors for severe, uncontrolled hypertension after adjusting for multiple factors
    - lack of primary care physician (adjusted odds ratio 3.5, 95% CI 1.6-7.7)
    - noncompliance with treatment for hypertension (adjusted odds ratio 1.9, 95% CI 1.4-2.5)

Likely risk factors

- **less effective outpatient blood pressure control associated with increased risk of hypertensive crisis**
  - based on retrospective case-control study
  - 143 pts with hypertensive crisis were compared with 485 controls without hypertensive crisis
  - risk factors for hypertensive crisis
    - less successful outpatient systolic blood pressure control ($p < 0.001$)
    - higher outpatient diastolic blood pressures ($p = 0.07$)
    - history of heart failure ($p = 0.06$)

- Risk factors for hypertensive crisis: importance of out-patient blood pressure control; Fam Pract 2004 Aug;21(4):420

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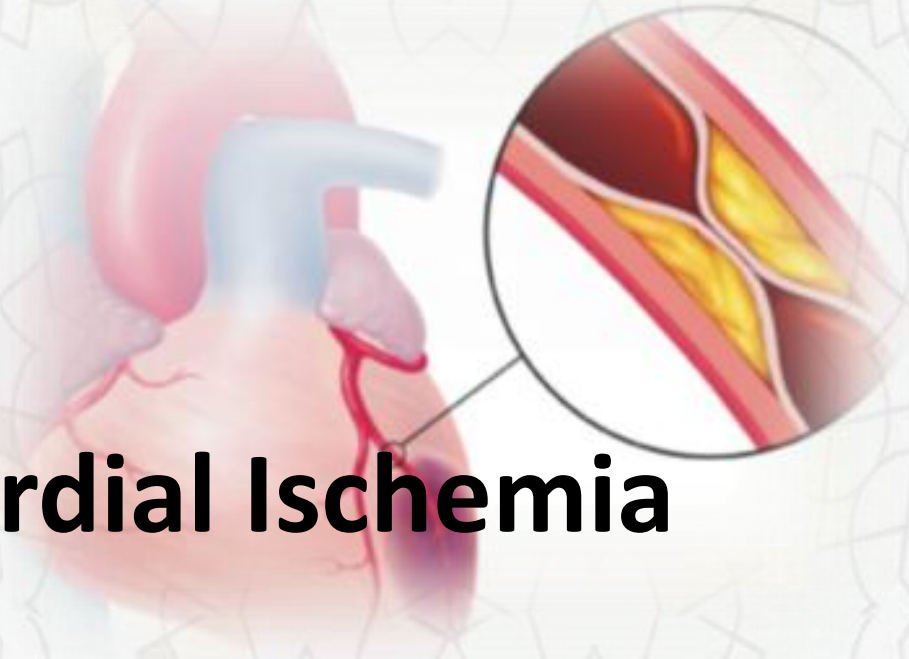
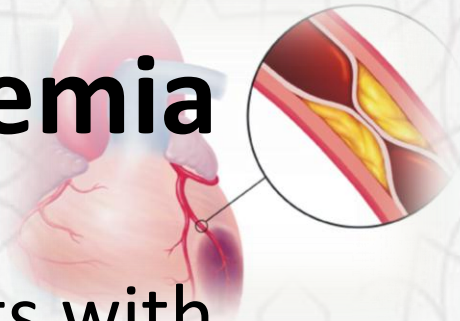


Acute Myocardial Ischemia

Acute Myocardial Ischemia



- Preferred agents in treating patients with hypertensive emergencies with evidence of ischemia include:
  - Nitrates that can lower LV preload and improve coronary blood flow
  - ß-blockers that can reduce heart rate, decrease afterload, and improve diastolic coronary perfusion.

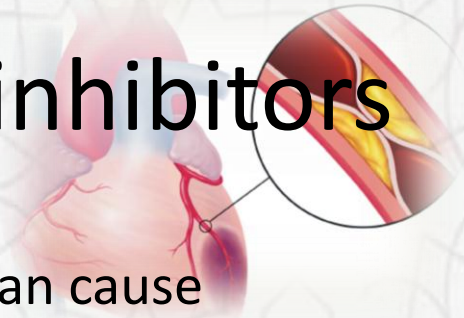
- Frohlich E.D.: Target organ involvement in hypertension: a realistic promise of prevention and reversal. *Med Clin North Am* 88. 1-9.2004

Acute Myocardial Ischemia

- Nitroglycerin reduces preload and decreases myocardial oxygen consumption by decreasing left ventricular end-diastolic volume and myocardial wall tension.
- This makes nitroglycerin the preferred agent in the setting of hypertensive emergencies complicated by myocardial ischemia.

- Chobanian AV, Bakris GL, Black HR et al. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Hypertension. 2003; 42: 1206-52.
- Kitiyakara C, Guzman NJ. Malignant hypertension and hypertensive emergencies. *J Am Soc Nephrol*. 1998; 9:133-42.
- Grossman E, Ironi AN, Messerli FH. Comparative tolerability profile of hypertensive crisis treatments. *Drug Saf*. 1998; 19:99-122.

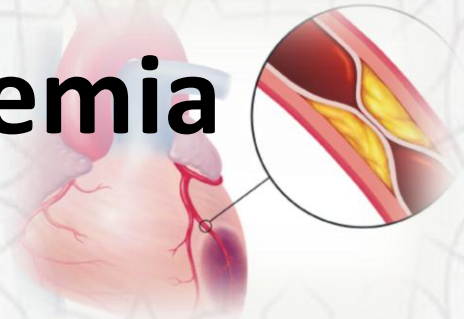
phosphodiesterase-5 (PDE5) inhibitors



- Nitrates given in the presence of a PDE5 inhibitor can cause profound hypotension for up to 48 hours.
- Within 48 hours acute MI & Tadalafil
  - there is no contraindication to using usual therapy such as aspirin, heparin, percutaneous coronary intervention, or thrombolytics,
  - nitrates should not be given.
    - In one study, standing SBP fell below 85 mm Hg in more patients receiving tadalafil compared with placebo ($p < 0.05$), with no difference in the response to sublingual nitroglycerin after 48, 72, and 96 hours.
- Within 48 hours after the last dose of a PDE5 inhibitor, ischemic chest pain can be treated with b-blockers, CCBs, morphine, oxygen, and aspirin; nitrates should be avoided.

- Kloner RA, Hutter AM, Emmick JT et al. Time course of the interaction between tadalafil and nitrates. J Am Coll Cardiol.2003; 42:1855-60.

Acute Myocardial Ischemia



- **ß-blockers**
  - 14% risk reduction in mortality through 7 days and a 23% reduction in long-term mortality.
    - A meta-analysis of prefibrinolytic era trials involving more than 24,000 patients receiving b-blockers
  - In-hospital ß-blockers reduce infarct size and rates of mortality, postinfarction ischemia, and nonfatal acute MI.
  - I.V. b-blockers may also be beneficial for non-ST-segment elevation MI acute coronary syndrome.

- Chae C, Hennekes C. Beta blockers. In: Hennekens C, ed. Clinical trials in cardiovascular disease: a companion to Braunwald's heart disease. Philadelphia: Saunders; 1999:79-94.
- Chen ZM, Pan HC, Chen YP et al. Early intravenous then oral metoprolol in 45,852 patients with acute myocardial infarction: randomised placebocontrolled trial. Lancet. 2005; 366:1622-32.

Acute Myocardial Ischemia

- Enalaprilat has been associated with increased mortality when given during first 24 hours of MI
- Nitroprusside may increase mortality when infused shortly after onset of acute MI
- Hydralazine should be avoided, as it can induce a reflex tachycardia and increase cardiac work.

3. Rhoney D, Peacock WF. Intravenous therapy for hypertensive emergencies, part 1. Am J Health Syst Pharm. 2009 Aug 1;66(15):1343-52.
5. Rhoney D, Peacock WF. Intravenous therapy for hypertensive emergencies, part 2. Am J Health Syst Pharm. 2009 Aug 15;66(16):1448-57

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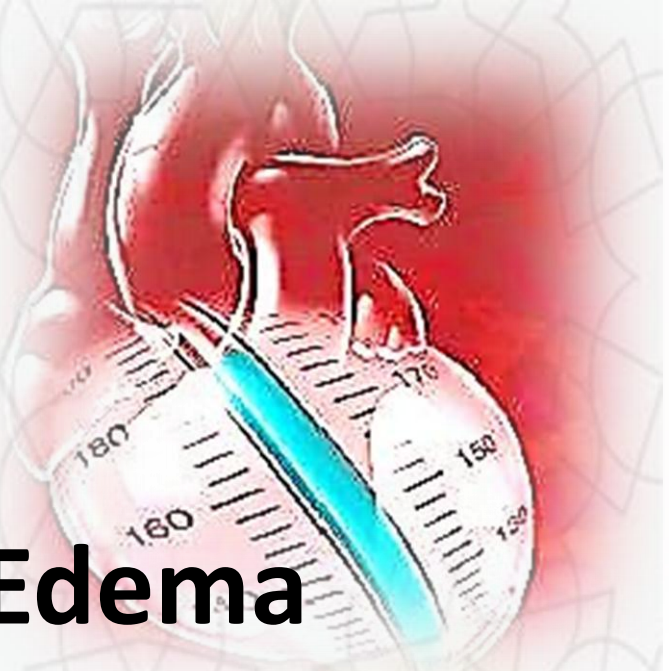


Acute Pulmonary Edema

Acute Pulmonary Edema

- incidence of 36%, making it the second most common sign of end-organ damage.
- nearly 50% of patients with APE are hypertensive (SBP of >140 mm Hg).
- Heart failure can occur in a hypertensive crisis but it can also be a risk factor for the development of hypertensive crisis.

- Aggarwal M., Khan I.: Hypertensive crisis: hypertensive emergencies and urgencies. Cardiol Clin 24. 135-146.2006;
- Tisdale J.E., Huang M.B., Borzak S.: Risk factors for hypertensive crisis: importance of out-patient blood pressure control. *Fam Pract* 21. 420-424.2004;

Acute Pulmonary Edema

- Mortality in acute heart failure is inversely proportional to BP levels.
- Pts. cannot maintain their BP are at high risk for a poor outcome.
- The goal of treatment in acute heart failure is to:
  - improve symptoms, BP control, left atrial pressure, and cardiac output.

83. Nieminen MS, Harjola VP. Definition and epidemiology of acute heart failure syndromes. *Am J Cardiol.* 2005;96(6A):5G- 10G. (**Review**)
84. Gheorghiade M, Abraham WT, Albert NM, et al. Systolic blood pressure at admission, clinical characteristics, and outcomes in patients hospitalized with acute heart failure. *JAMA.* 2006;296(18):2217-2226. (**Retrospective, cohort; 48,612patients**)

Acute Pulmonary Edema

- treatment requires both preload and afterload reduction
  - options include:
    - Nitrates (nitroglycerin or nitroprusside)
    - Diuretics
    - Angiotensin-converting enzyme (ACE) inhibitors
      - » Enalapril
    - A new 3rd generation calcium-channel blocker
      - » Clevidipine

2. Marik PE, Varon J. Hypertensive crises: challenges and management. Chest. 2007 Jun;131(6):1949-62. full-text, correction can be found in Chest 2007 Nov;132(5):1721.
5. Rhoney D, Peacock WF. Intravenous therapy for hypertensive emergencies, part 2. Am J Health Syst Pharm. 2009 Aug 15;66(16):1448-57.

Acute Pulmonary Edema

- Nitrates (nitroglycerin and nitroprusside) are:
  - vasodilators that act on both venous and arterial systems, although nitroglycerin is much more selective for dilation of veins.
- IV nitroglycerin or nitroprusside
  - as adjuvant to diuretic therapy for relief of dyspnea in patients admitted with acutely decompensated heart failure in absence of symptomatic hypotension
  - (ACCF/AHA Class IIb, Level A)

Acute Pulmonary Edema

- Nitrates:
  - Cochrane review
  - systematic review of 4 randomized trials evaluating nitrates Pts. with acute heart failure syndrome
  - no trials comparing nitrates to placebo reported outcomes for efficacy
- symptom relief and haemodynamic variables
  - no significant difference between nitrate vasodilator therapy and alternative interventions.
- Nitrates may be associated with a lower incidence of adverse effects after three hours compared with placebo.

- **Nitrates for acute heart failure syndromes**, Cochrane Database Syst Rev 2013 Aug 6;(8):CD005151

Acute Pulmonary Edema:

- Sodium nitroprusside is thought to be the be agent for acute pulmonary edema precipitated by a hypertensive crisis.3
- Sodium nitroprusside decreases both preload and afterload.
- It has a rapid onset of action and a short half-life.
  - Cyanide toxicity is extremely rare.
  - Thiocyanate toxicity is also uncommon and occurs only with high doses of nitroprusside in patients with renal insufficiency.19

- Ram C.V.: Current concepts in the diagnosis and management of hypertensive urgencies and emergencies. Keio J Med 39. 225-236.1990;

Acute Pulmonary Edema:

- **Nitroprusside:**
  - **sodium nitroprusside may be associated with reduced mortality in patients with acute decompensated heart failure**
    - retrospective cohort study
    - 175 patients admitted with acute decompensated heart failure with cardiac index ≤ 2.1 L/minute/m^2
    - 78 were treated with sodium nitroprusside
    - comparing patients treated with sodium nitroprusside vs. controls
    - all-cause mortality 29% vs. 44% (p = 0.005, NNT 7)

- **Sodium nitroprusside for advanced low-output heart failure.** J Am Coll Cardiol 2008 Jul 15;52(3):200
- **Nitroprusside in decompensated heart failure: what should a clinician really know?** Curr Heart Fail Rep 2009 Sep;6(3):182

Acute Pulmonary Edema:

- The ACEP clinical policy for treatment of CHF
  - ***Level B recommendations***
    - Administer intravenous nitrate therapy to patients with acute heart failure syndromes and associated dyspnea.

- Silvers SM, Howell JM, Kosowsky JM, Rokos IC, Jagoda AS. American College of Emergency Physicians. Clinical policy: critical issues in the evaluation and management of adult patients presenting to the emergency department with acute heart failure syndromes. *Ann Emerg Med.* 2007;49(5):627-669. (**Consensus**)

Acute Pulmonary Edema:

- **Diuretics,**
  - specifically loop diuretics, are commonly used to treat acute heart failure.
  - Few studies ?? On efficacy on mortality
  - The Japanese Multicenter Evaluation of Long-Versus Short-Acting Diuretics in Congestive Heart Failure (J-MELODIC) study
    - Azosemide, compared with furosemide, reduced the risk of cardiovascular death or unplanned admission to hospital for congestive HF

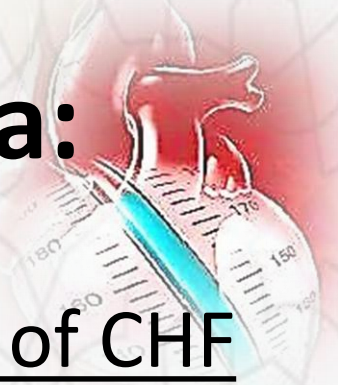
- Cotter G, Metzkor E, Kaluski E, et al. Randomised trial of high-dose isosorbide dinitrate plus low-dose furosemide versus high-dose furosemide plus low-dose isosorbide dinitratein severe pulmonary oedema. Lancet. 1998;351(9100):389-393. (Prospective, randomized; 104 patients)
- **Superiority of long-acting to short-acting loop diuretics in the treatment of congestive heart failure.** Circ J. 2012;76(4):833-42.

Acute Pulmonary Edema

- **Diuretics**
  - **American College of Cardiology Foundation and American Heart Association (ACCF/AHA) recommendations**[6]
    - in hospitalized patients
      - promptly treat patients with significant fluid overload with IV loop diuretics to reduce morbidity (ACCF/AHA Class I, Level B)
    - if diuresis inadequate to relieve congestion, intensification of diuresis may be done with either of
      - higher doses of IV loop diuretics (ACCF/AHA Class IIa, Level B)
      - addition of second diuretic (such as thiazide) (ACCF/AHA Class IIa, Level B)

- J Am Coll Cardiol. 2013;62(16):e147-e239.

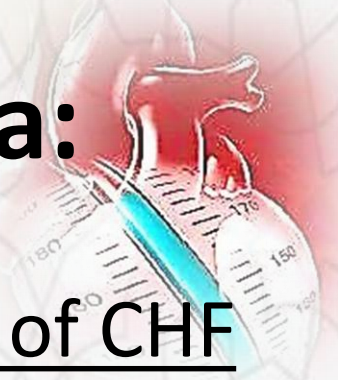
Acute Pulmonary Edema:



- The ACEP clinical policy for treatment of CHF
  - ***Level B recommendations***
    - Treat patients with moderateto- severe pulmonary edema resulting from acute heart failure with furosemide in combination with nitrate therapy.
    - Nevertheless, ACEP cautions against aggressive diuretic use.

- Silvers SM, Howell JM, Kosowsky JM, Rokos IC, Jagoda AS. American College of Emergency Physicians. Clinical policy: critical issues in the evaluation and management of adult patients presenting to the emergency department with acute heart failure syndromes. *Ann Emerg Med.* 2007;49(5):627-669. (**Consensus**)

Acute Pulmonary Edema:



- The ACEP clinical policy for treatment of CHF
  - ***Level C recommendations.***
    - Aggressive diuretic monotherapy is unlikely to prevent the need for endotracheal intubation compared with aggressive nitrate monotherapy.
    - Diuretics should be administered judiciously, given the potential association between diuretics, worsening renal function, and the known association between worsening renal function at index hospitalization and long-term mortality.

- Silvers SM, Howell JM, Kosowsky JM, Rokos IC, Jagoda AS. American College of Emergency Physicians. Clinical policy: critical issues in the evaluation and management of adult patients presenting to the emergency department with acute heart failure syndromes. *Ann Emerg Med.* 2007;49(5):627-669. (**Consensus**)

Natriuretic Peptide

- The natriuretic (B-type) natriuretic peptide (BNP), which is derived from ventricular myocardium—act in multiple ways to decrease BP.
  - promotes diuresis by stimulating salt wasting,
  - acts as a vasodilator by activating the guanylate cyclase pathway and
  - it inhibits the renin-angiotensin system.

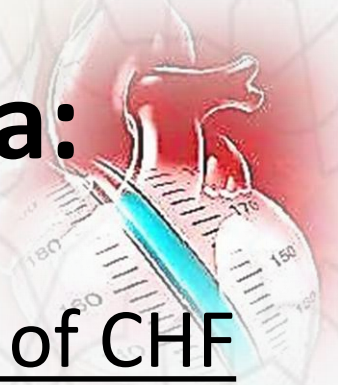
- Nesiritide, (exogenous BNP), was initially proposed as a substitute for nitroglycerin and diuretics in the treatment of decompensated heart failure,
  - superiority in emergent management has not been demonstrated.27
  - Some conflicting evidence implies an increased risk of short-term death in patients treated with nesiritide.

- Publication Committee for the VMAC Investigators (Vasodilatation in the Management of Acute CHF). Intravenous nesiritide vs nitroglycerin for treatment of decompensated congestive heart failure: a randomized controlled trial [published correction appears in *JAMA.* 2002;288(5):577]. JAMA. 2002;287(12):1531-1540. (**Prospective, randomized; 246 patients**)
- Sackner-Bernstein JD, Kowalski M, Fox M, Aaronson K. Short-term risk of death after treatment with nesiritide for decompensated heart failure: a pooled analysis of randomized controlled trials. *JAMA.* 2005;293(15):1900-1905. (**Metaanalysis; 862 patients**)
- Arora RR, Venkatesh PK, Molnar J. Short and long-term mortality with nesiritide. *Am Heart J.* 2006;152(6):1084-1090. (**Meta-analysis; 1717 patients**)

Acute Pulmonary Edema

- **Nesiritide**:
  - IV nesiritide may be considered as adjuvant to diuretic therapy for relief of dyspnea in patients admitted with acutely decompensated heart failure in absence of symptomatic hypotension
  - vasodilator, biosynthetic form of human B-type natriuretic peptide
  - in acute heart failure
    - Nesiritide improves hemodynamic function more effectively than IV nitroglycerin or placebo, but not clearly more effective on symptom improvement
    - inconsistent evidence regarding increased risk of mortality.
  - adverse effects may include hypotension, renal dysfunction, ventricular tachycardia, bradycardia

Acute Pulmonary Edema:



- The ACEP clinical policy for treatment of CHF
  - ***Level C recommendations***
    1. Because of the lack of clear superiority of nesiritide over nitrates in acute heart failure syndrome and the current uncertainty regarding its safety, nesiritide generally should not be considered first line therapy for acute heart failure syndromes.

- Silvers SM, Howell JM, Kosowsky JM, Rokos IC, Jagoda AS. American College of Emergency Physicians. Clinical policy: critical issues in the evaluation and management of adult patients presenting to the emergency department with acute heart failure syndromes. *Ann Emerg Med.* 2007;49(5):627-669. (**Consensus**)

Acute Pulmonary Edema:

- **Hypertonic saline**
  - **addition of hypertonic saline to high-dose furosemide may reduce mortality and hospital readmission for patients with advanced refractory heart failure**
    - **Effects of high-dose furosemide and small-volume hypertonic saline solution infusion in comparison with a high dose of furosemide as bolus in refractory congestive heart failure: long-term effects.** Am Heart J 2003 Mar;145(3):459 (107 patients aged 65-90 years with advanced refractory heart failure)
      - furosemide 500-1,000 mg IV plus hypertonic saline (150 mL of 1.4%-4.6% saline) twice daily over 30 minutes for 6-12 days,
      - furosemide 500-1,000 mg IV twice daily without hypertonic saline
      - » mortality 45% vs. 87% ($p < 0.001$, NNT 3)
    - Short-term effects of hypertonic saline solution in acute heart failure and long-term effects of a moderate sodium restriction in patients with compensated heart failure with New York Heart Association class III (Class C) (SMAC-HF Study). Am J Med Sci 2011 Jul;342(1):27 (1,771 patients)
      - **furosemide 250 mg IV plus hypertonic saline** (150 mL of 1.4%-4.6% saline) twice daily over 30 minutes for 6-12 days, and dietary sodium intake during treatment and after discharge 120 mmol/day
      - **furosemide 250 mg IV twice daily without hypertonic saline** for 6-12 days, and dietary sodium intake during treatment and after discharge 80 mmol/day
      - » readmission for worsening heart failure in 18.5% vs. 34.2% ($p < 0.001$, NNT 7)
      - » mortality 12.9% vs. 23.8% ($p < 0.001$, NNT 10)

Acute Pulmonary Edema:

- Angiotensin-converting enzyme (ACE) inhibitors such as enalapril can be used to reduce afterload and hence improve cardiac output.

- Baumann B.M., Cline D.M., Pimenta E.: Treatment of hypertension in the emergency department. J Am Soc Hypertens 5. 366-377.2011;

Acute Pulmonary Edema:

- Cooperative New Scandinavian Enalapril Survival Study II (CONSENSUS II)
  - showed a trend toward increased mortality when enalapril was administered within 24 hours of acute MI, may be due to hypotension after drug administration.

- Swedberg K, Held P, Kjekshus J et al. Effects of the early administration of enalapril on mortality in patients with acute myocardial infarction. Results of the Cooperative New Scandinavian Enalapril Survival Study II (CONSENSUS II). N Engl J Med. 1992; 327:678-84.

Acute Pulmonary Edema:

- **Angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs):**
  - **sublingual ACE inhibitor may produce faster clinical improvement**
    - 48 pts. with acute pulmonary edema randomized to captopril (12.5 mg if systolic blood pressure 90-110 mm Hg, 25 mg if systolic blood pressure > 110 mm Hg) vs. placebo sublingually
    - reduction in distress at 30 minutes was to 57% vs. 75% of initial distress, but no significant difference at 40 or 75 minutes
    - Acad Emerg Med 1996 Mar;3(3):205
  - **captopril may produce greater hemodynamic improvements than nitroglycerin in severe heart failure**
    - 24 patients with severe heart failure randomized to captopril 25 mg vs. nitroglycerin 0.8 mg sublingually in crossover trial
    - comparing captopril vs. nitroglycerin
      - increase in cardiac index +49% vs. + 25% ($p < 0.001$)
      - increase in stroke volume index +53.5% vs. +26% ($p < 0.001$)
      - increase in stroke work index +55% vs. +28% ($p < 0.001$)
      - time to onset of change in hemodynamic parameters 12-19 minutes vs. 16-22 minutes (not significant)
    - Int J Cardiol 1990 Jun;27(3):351

Acute Pulmonary Edema:

- The ACEP clinical policy for treatment of CHF
  - ***Level C recommendations***
    1. Angiotensin-converting enzyme (ACE) inhibitors may be used in the initial management of acute heart failure syndromes, although patients must be monitored for first dose hypotension.

- Silvers SM, Howell JM, Kosowsky JM, Rokos IC, Jagoda AS. American College of Emergency Physicians. Clinical policy: critical issues in the evaluation and management of adult patients presenting to the emergency department with acute heart failure syndromes. *Ann Emerg Med.* 2007;49(5):627-669. (**Consensus**)

Acute Pulmonary Edema:

- calcium-channel blocker (clevidipine)
  - Clevidipine selectively inhibits extracellular calcium influx through L-type channels resulting in smooth muscle relaxation; thus it decreases peripheral vascular resistance.
    - An advantage of clevidipine is that it undergoes metabolism by plasma esterases, thus it is independent of renal or hepatic function.11

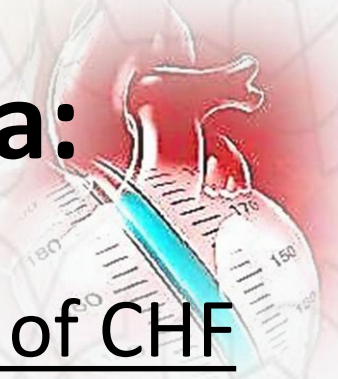
- Marik P., Rivera R.: Hypertensive emergencies: an update. Curr Opin Crit Care 17. 569-580.2011;

Acute Pulmonary Edema:

- **Clevidipine**
  - **reported to be effective for treating hypertensive emergencies in adult**
    - In this study, 89% of patients achieved target BP within 30 minutes of starting clevidipine.
    - based on case series
      - 126 adults ≥ 18 years old who presented to emergency department with severe hypertension (systolic blood pressure > 180 mm Hg and/or diastolic blood pressure > 115 mm Hg) were treated with clevidipine
      - 108 of 117 patients (92.3%) who received ≥ 18 hours of clevidipine did not require additional IV antihypertensive agents

Ann Emerg Med 2009 Mar;53(3):329

Acute Pulmonary Edema:



- The ACEP clinical policy for treatment of CHF
  - ***Level B recommendations***
    - for use of continuous positive airway pressure (CPAP) to help treat pulmonary edema and decreasing respiratory effort, reducing the need for intubation.
      - Use 5 to 10 mm Hg CPAP as therapy for dyspneic patients with acute heart failure syndrome without hypotension or the need for emergent intubation to improve heart rate, respiratory rate, blood pressure, and reduce the need for intubation, and possibly inhospital mortality.
        - » This recommendation is based on results from 6 small studies.

- Silvers SM, Howell JM, Kosowsky JM, Rokos IC, Jagoda AS. American College of Emergency Physicians. Clinical policy: critical issues in the evaluation and management of adult patients presenting to the emergency department with acute heart failure syndromes. *Ann Emerg Med.* 2007;49(5):627-669. (**Consensus**)

In Summery

7th Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure

- The initial goal of therapy in hypertensive emergencies is to reduce mean arterial BP by no more than 25% (within minutes to 1 hour), then if stable, to 160/100–110 mmHg within the next 2–6 hours.
- Excessive falls in pressure that may precipitate renal, cerebral, or coronary ischemia should be avoided.
  - For this reason, short-acting nifedipine is no longer considered acceptable in the initial treatment of hypertensive emergencies or urgencies.

7th Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure

- If this level of BP is well tolerated and the patient is clinically stable, further gradual reductions toward a normal BP can be implemented in the next 24–48 hours.
- There are exceptions to the above recommendation
  - patients with an ischemic stroke in which there is no clear evidence from clinical trials to support the use of immediate antihypertensive treatment,
  - patients with aortic dissection who should have their SBP lowered to <100 mmHg if tolerated, and
  - patients in whom BP is lowered to enable the use of thrombolytic agents

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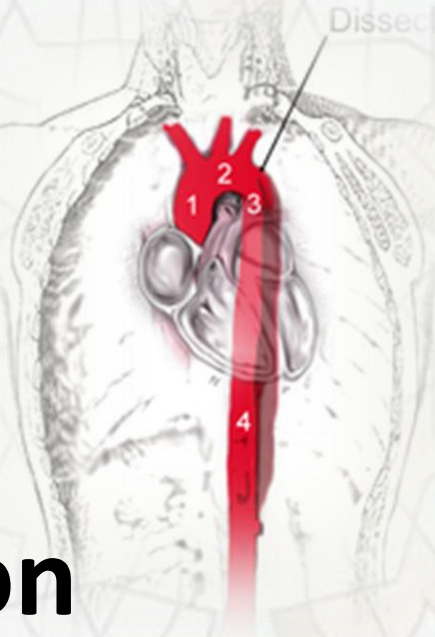
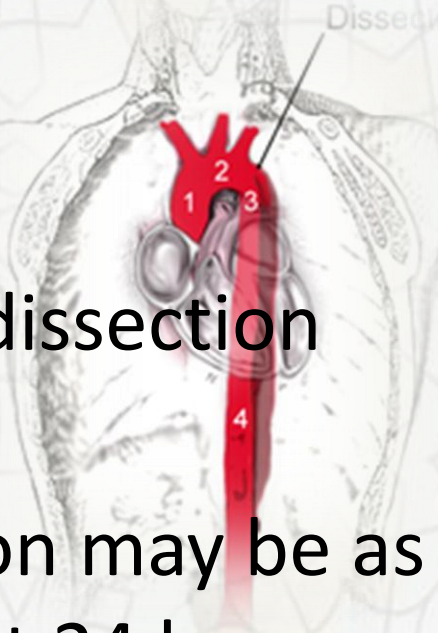


Aortic Dissection

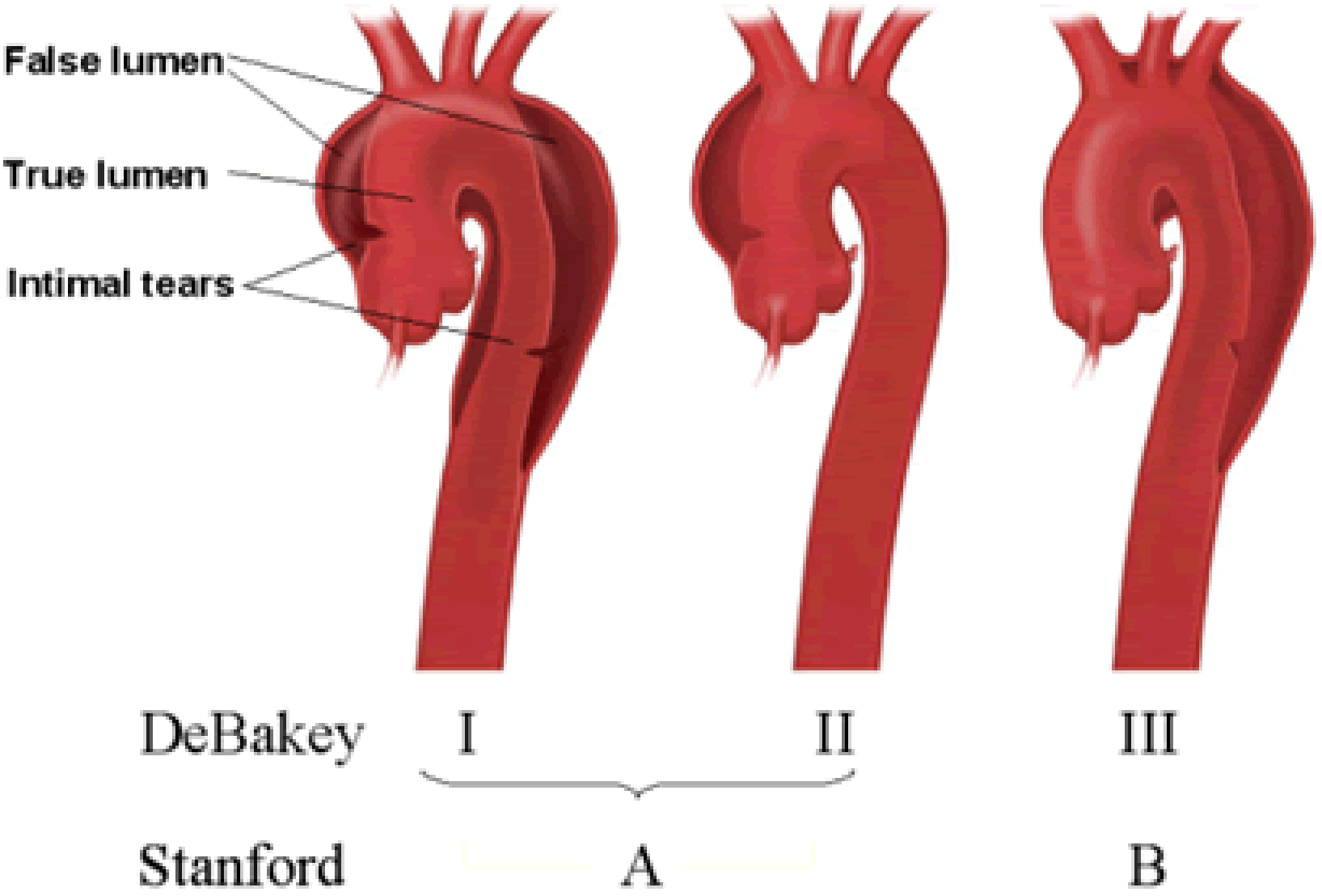
Aortic Dissection



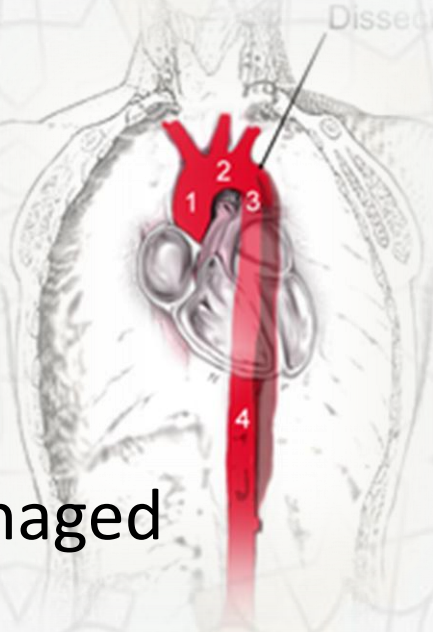
- 75% of patients with acute aortic dissection have underlying hypertension.
- Death rate in acute aortic dissection may be as high as 1% per hour during the first 24 hours.

- Braverman AC. Aortic dissection: prompt diagnosis and emergency treatment are critical. Cleve Clin J Med 2011;78(10):685–96.
- Hagan PG, Nienaber CA, Isselbacher EM, et al. International Registry of Acute Aortic Dissection (IRAD): new insights from an old disease. JAMA 2000;283:897–903.

Anatomy and Classification of Aortic Dissection

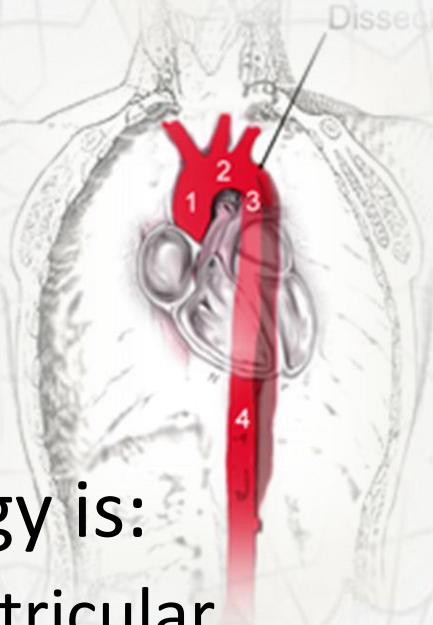


Aortic Dissection



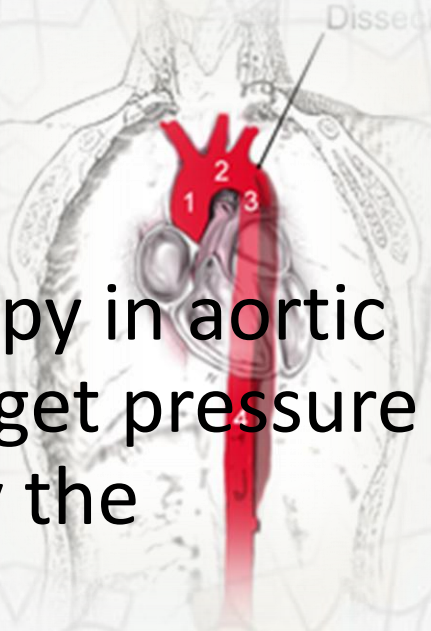
- A type-A dissection is
  - a surgical emergency
  - a type-B dissection can often be managed medically.
- If the vascular surgery consultant determines that emergency surgery is not needed, prompt BP reduction to a target systolic BP of less than 120 mm Hg and reduction in heart rate to below 65 beats/min should be instituted.

Aortic Dissection



- The aim:
  - avoid progressive intimal dissection
- The theory in management strategy is:
  - that reducing the force of left ventricular contractions, thus dilating the vessels, will enhance laminar flow and lessen stress on the aortic wall.
  - Turbulent flow is increased by using a vasodilator alone.

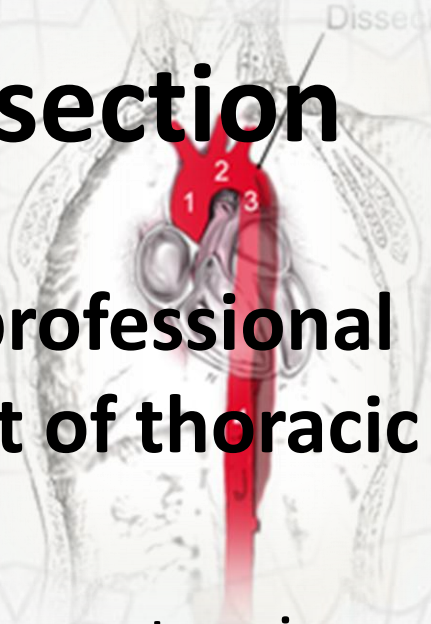
Aortic Dissection



- The goal of antihypertensive therapy in aortic dissection is unique in that the target pressure is the lowest pressure tolerated by the patient.
- Systolic levels of 100 to 120 mm Hg are ideal.
- In addition to lowering the BP, the emergency clinician should attempt to slow the heart rate to reach a target of 60 to 70 beats per minute; these numbers are not evidence-based.

- Khan IA, Nair CK. Clinical, diagnostic, and management perspectives of aortic dissection. Chest. 2002;122(1):311- 328. (Review)
- Nienaber CA, Eagle KA. Aortic dissection: new frontiers in diagnosis and management, part II: therapeutic management and follow-up. Circulation. 2003;108(6):772-778. (Review)

aortic aneurysm and dissection

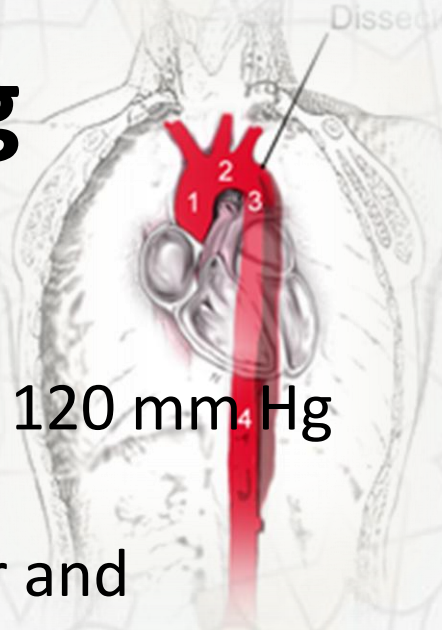


- **Joint recommendations from 10 professional societies for medical management of thoracic aortic disease:**
  - give antihypertensive therapy to hypertensive patients to achieve goal of < 140/90 mm Hg (in patients without diabetes) or
  - < 130/80 mm Hg (in patients with diabetes or chronic renal disease)

aortic aneurysm and dissection

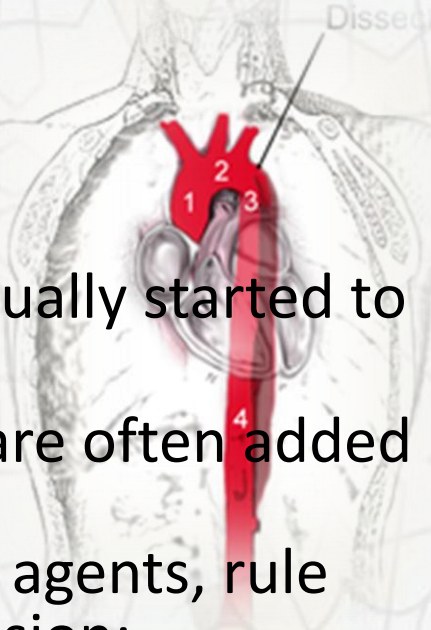
- **Treatment overview:**
  - initial management of acute aortic dissection (type A and B) includes
    - hemodynamic stabilization
    - monitoring urine output and cardiac rhythm
    - pain relief with morphine
    - limiting propagation of false lumen by controlling aortic shear stress (via blood pressure and rate control)
    - reducing systolic blood pressure to 100-120 mm Hg and heart rate to < 60 beats/minute

Treatment setting



- acute aortic dissection
  - target systolic blood pressure (SBP) is < 120 mm Hg within 5-10 minutes
  - treatment usually requires beta blocker and vasodilator
  - if vasodilator used without beta blocker, reflex tachycardia may develop and aggravate dissection
  - options include
    - for beta blocker – esmolol Or metoprolol
    - for vasodilator - nicardipine, nitroprusside or fenoldopam

Aortic Dissection



- I.V. ß-blockers with esmolol or labetalol is usually started to reduce shear stress on the aorta.
- Other agents such as sodium nitroprusside are often added

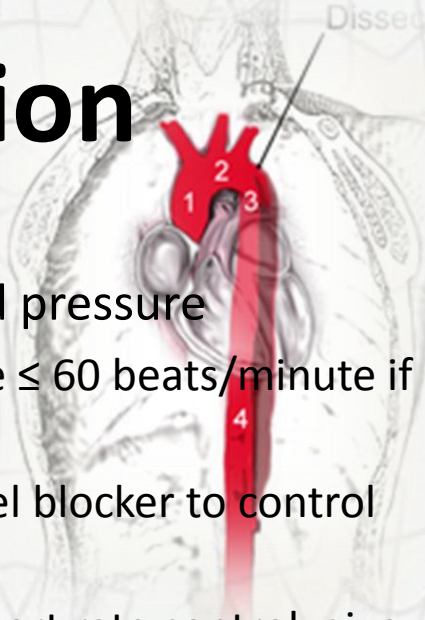
- if BP refractory to multiple antihypertensive agents, rule out reversible secondary causes of hypertension:
  - Renal artery hypertension or acute pain from the.
- Calcium channel blockers: 2nd line interventions.
- If the aortic dissection is complicated by organ ischemia, limb ischemia, or refractory pain, surgical or endovascular therapy may be necessary.

- Braverman A.C.: Aortic dissection: prompt diagnosis and emergency treatment are critical. Cleve Clin J Med 78. (10): 685-696.2011;
- 24 Braverman A.C., Thompson R., Sanchez L.: Diseases of the aorta. In: Bonow R.O., Mann D.L., Zipes D.P., et al ed. Braunwald's heart disease, 9th edition ElsevierPhiladelphia2011:

Acute aortic dissection

- It is important that ß-blockers precedes the administration of any drug that may cause reflex tachycardia or a reflex positive inotropic effect, as this may exacerbate the dissection.
- This BP level should be maintained for as long as it is tolerated or until intraoperative control of the aorta is accomplished.

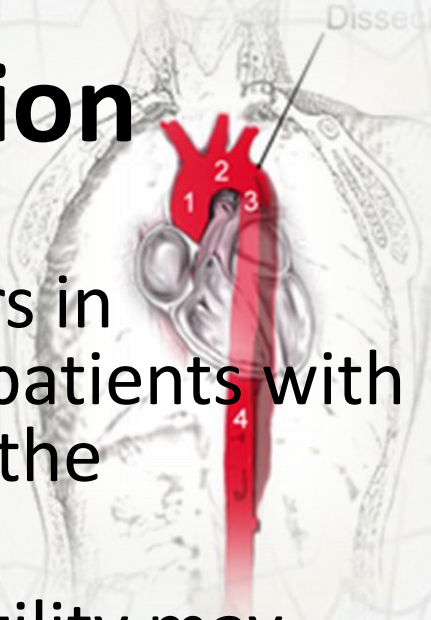
Acute aortic dissection



- for initial management controlling heart rate and blood pressure
  - start IV ß-blockers and titrate to achieve target heart rate ≤ 60 beats/minute if no contraindications
  - if contraindications to beta blockade, use calcium channel blocker to control heart rate
  - if systolic blood pressure > 120 mm Hg after adequate heart rate control, give IV ACE inhibitors and/or other vasodilators to reduce blood pressure to level that maintains adequate end-organ perfusion
    - use ß-blockers cautiously in setting of acute aortic regurgitation (will block compensatory tachycardia)
    - do NOT start vasodilator therapy before rate control (to avoid associated reflex tachycardia that may increase aortic wall stress) (ACC/AHA Class III, Level C)
    - acute thoracic dissection of descending aorta should be managed medically unless life-threatening complications develop (ACC/AHA Class I, Level B)

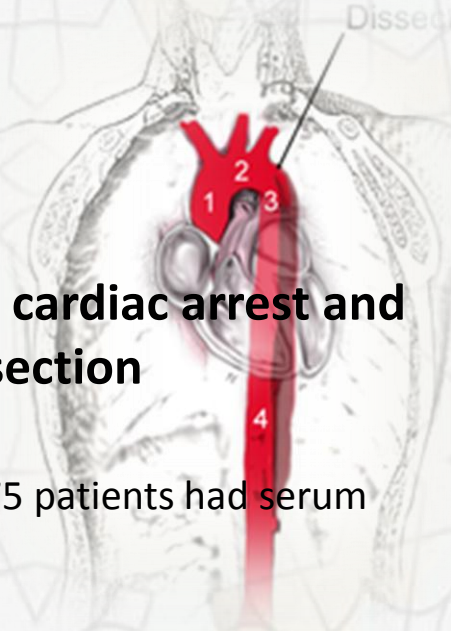
- ACC/AHA Aortic Dissection Guideline

Acute aortic dissection



- The one exception to using ß-blockers in combination with a vasodilator is in patients with acute aortic regurgitation caused by the dissection.
- In these patients, the loss of contractility may reduce forward flow and perfusion, thus causing more harm than good.96
- esmolol
  - has also been used in patients with relative contraindications to b-blocker therapy,67,71-75 and it lowers BP to a degree comparable to that achieved with sodium nitroprusside.73

Prognosis



- **elevated cardiac troponin I levels associated with cardiac arrest and mortality in patients with acute type A aortic dissection**
  - based on retrospective cohort study
  - 148 patients admitted for acute type A aortic dissection, 75 patients had serum cardiac troponin I measured
  - in-hospital mortality 25.9%
  - 15.6% had preoperative cardiac circulatory arrest
  - predictors of preoperative cardiac circulatory arrest included
    - hypotension
    - shock
    - pericardial effusion
    - tamponade
    - elevated cardiac troponin I
  - elevated cardiac troponin I also associated with higher in-hospital mortality

- J Cardiovasc Surg (Torino) 2001 Oct;42(5):647

In Summery

7th Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure

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  - patients with an ischemic stroke in which there is no clear evidence from clinical trials to support the use of immediate antihypertensive treatment,
  - patients with aortic dissection who should have their SBP lowered to <100 mmHg if tolerated, and
  - patients in whom BP is lowered to enable the use of thrombolytic agents

Drug	Mechanism of Action	Dose	Onset	Duration	Clinical Situations	Precautions
Sodium Nitroprusside	Direct arterial and venous vasodilator	0.25 – 10 mcg/ kg/ min	1-2 min	3-4 minutes after stopping infusion	Used in all clinical situations of hypertensive emergency. Caution in neurological emergencies as it can decrease cerebral blood flow and in ACS can cause coronary steel.	Elevated Intracranial pressure Cerebrovascular and cardiovascular insufficiency Renal impairment Hepatic impairment
Nitroglycerin	Venous vasodilator	5 – 200 mcg/ kg. min	2-5 min	5-10 min	Commonly used for ACS and ADHF	Concomitant use of phosphodiesterase 5 inhibitors. Raised intracranial pressure Inferior ST-elevation myocardial infarction.
Labetalol	Combined Alpha and beta adrenergic blocker	IV bolus: 20mg over 2 min Infusion: 1-2 mg/ min	2-5 min after bolus	2-4 hours after stopping infusion	Aortic dissection, and neurological emergencies	Severe bradycardia Bronchial asthma Recent cocaine use Pheochromocytoma Acute decompensated heart failure
Fenoldopam	Peripheral dopamine 1 receptor agonist	0.1- 1.6 mcg / kg/ min	10 min	1 hour after stopping	Useful in hypertensive emergencies complicated by renal failure	Sulfite allergy Hypokalemia
Nicardipine	Dihydropyridine Calcium channel blocker, vasodilator	5 – 15mg / hr	10 min	2 -6 hours	Post op hypertension and neurological emergencies	Advanced aortic stenosis Renal impairment Acute decompensated heart failure
Clevidipine	Ultra short acting dihydropyridine Ca channel blocker	2-16 mcg/ kg/ min	1-5 min	5 minutes after stopping	Potentially useful in most hypertensive emergencies ; studied extensively in post operative cardiac surgery patients	Allergy to soy products and egg products Advanced aortic stenosis Acute decompensated heart failure
Hydralazine	Direct arterial vasodilator	IV bolus: 10-20 mg IV	10 – 20 min	1-4 hours	Pre eclampsia and eclampsia	Dissecting aortic aneurysm.

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Table 2
Special indications and warnings for parenteral medications

	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, theoretical "coronary steal" (shunting of blood from diseased vessels to well-perfused vessels may produce coronary ischemia)
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[a]	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 Aggarwal M, Khan I. Hypertensive crisis: hypertensive emergencies and urgencies. Cardiol Clin 2006;24:135–46; and Acelajado MC, Calhoun DA. Resistant hypertension, secondary hypertension, and hypertensive crises: diagnostic evaluation and treatment. Cardiol Clin 2010;28:639–54

Table 1
Parenteral medications used for treatment of hypertensive crisis

	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 secs 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	↓	↑

Table 3
Target blood pressure goals

Hypertensive Emergency	Target Blood Pressure
Hypertensive encephalopathy	MAP lowered by maximum 20% or to DBP 100–110 mm Hg within first hour then gradual reduction in BP to normal range over 48–72 h
Ischemic stroke	MAP lowered no more than 15%–20%, DBP not less than 100–110 mm Hg in 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	MAP lowered by 20%–25%
Hypertensive retinopathy	MAP lowered by 20%–25%
Left ventricular failure	MAP to 60–100 mm Hg
Aortic dissection	SBP 100–120 mm Hg
Acute renal insufficiency	MAP lowered by 20%–25%
Pregnancy-induced hypertension	SBP 130–150 mm Hg and DBP 80–100 mm Hg
Postoperative hypertension	MAP lowered by 20%–25% (not based on published guidelines)
Myocardial ischemia/infarct	MAP to 60–100 mm Hg
Hyperadrenergic states	MAP lowered by 20%–25% (not based on published guidelines)

Parenteral drugs for treatment of hypertensive emergencies in adults*

Drug	Dose range	Onset of action (minutes)	Duration of action (minutes)	Adverse effects*	Role*
Vasodilators					
Clevidipine	1 to 2 mg/hour as IV infusion with rapid titration. Most patients respond to 4 to 6 mg/hour and are treated with maximum doses of 16 mg/hour or less. NOTE: Delivered in lipid emulsion. 1000 mL maximum per 24 hours (equivalent to 21 mg/hour) due to lipid load restriction.	2 to 4	5 to 15	Atrial fibrillation, nausea, lipid formulation contains potential allergens (eg, soy, egg)	Hypertensive emergencies including postoperative hypertension.
Enalaprilat	1.25 to 5 mg every 6 hours IV.	15 to 30	~6 to >12 hours	Precipitous fall in pressure in high-renin states; variable response, headache, dizziness	Acute left ventricular failure. Due to slow onset and long duration of effect, rarely used. Avoid use in AMI, renal impairment, or pregnancy.
Fenoldopam	0.1 microgram/kg per minute as IV infusion titrated to a maximum of 1.6 microgram/kg per minute.	5 to 10	30 to 60	Tachycardia, headache, nausea, flushing	Most hypertensive emergencies, including aortic dissection. Use caution or avoid with glaucoma or intracranial hypertension.
Hydralazine	10 to 20 mg IV	10 to 20 IV	1 to ≥4 hours IV	Sudden precipitous drop in blood pressure, tachycardia, flushing, headache, vomiting, aggravation of angina	In general, hydralazine should be avoided due to its prolonged and unpredictable hypotensive effect. Labetalol and nicardipine are generally preferred choices for treatment of eclampsia.
	10 to 40 mg IM	20 to 30 IM	4 to 6 hours IM		
Nicardipine	5 to 15 mg/hour as IV infusion. Some patients may require up to 30 mg per hour.	5 to 15	~1.5 to ≥4 hours	Tachycardia, headache, dizziness, nausea, flushing, local phlebitis, edema	Most hypertensive emergencies, including aortic dissection and pregnancy-induced. Avoid use in acute heart failure. Caution with coronary ischemia.
Nitroglycerin (glyceryl trinitrate)	5 to 100 micrograms/minute as IV infusion.	2 to 5	5 to 10	Hypoxemia, tachycardia (reflex sympathetic activation), headache, vomiting, flushing, methemoglobinemia, tolerance with prolonged use	Potential adjunct to other IV antihypertensive therapy in patients with coronary ischemia (ACS) or acute pulmonary edema.
Nitroprusside	0.25 to 10 micrograms/kg per minute as IV infusion. To minimize risk of cyanide toxicity infusion duration should be as short as possible and not exceed 2 micrograms/kg per minute. Patients who receive higher doses (ie, >500 microgram/kg at a rate exceeding 2 microgram/kg per minute) should receive sodium thiosulfate infusion to avoid cyanide toxicity.	0.5 to 1	1 to 10	Elevated intracranial pressure, decreased cerebral blood flow, reduced coronary blood flow in CAD, cyanide and thiocyanate toxicity, nausea, vomiting, muscle spasm, flushing, sweating	In general, nitroprusside should be avoided due to its toxicity. If other appropriate agents (eg, nicardipine, fenoldopam) are unavailable, can be used for treating aortic dissection after control of heart rate with beta-blockade. Nitroprusside should be avoided in patients with AMI, CAD, CVA or elevated intracranial pressure, renal or hepatic impairment.
Adrenergic inhibitors					
Esmolol	250 to 500 microgram/kg loading dose over 1 minute; then initiate IV infusion at 25 to 50 microgram/kg per minute; titrate incrementally up to maximum of 300 microgram/kg per minute.	1 to 2	10 to 30	Nausea, flushing, bronchospasm, first-degree heart block, infusion site pain; half-life prolonged in setting of anemia	Aortic dissection, perioperative hypertension. Avoid use in acute decompensated heart failure.
Labetalol	Initial bolus of 20 mg IV followed by 20 to 80 mg IV bolus every 10 minutes (maximum 300 mg). **OR** 0.5 to 2 mg/minute as IV infusion following an initial 20 mg IV bolus (maximum 300 mg per 24 hours).	5 to 10	2 to 4 hours	Nausea/vomiting, paresthesias (eg, scalp tingling), bronchospasm, dizziness, nausea, heart block	Most hypertensive emergencies including myocardial ischemia, aortic dissection, hypertensive encephalopathy, pregnancy, and postoperative hypertension. Avoid use in acute decompensated heart failure. Use cautiously in obstructive or reactive airway.
Metoprolol	Initially 1.25 to 5 mg IV followed by 2.5 to 15 mg IV every 3 to 6 hours.	20	5 to 8 hours	Refer to labetalol	Aortic dissection, myocardial ischemia, perioperative hypertension. Avoid use in acute decompensated heart failure.
Phentolamine	5 to 15 mg IV bolus every 5 to 15 minutes.	1 to 2	10 to 30	Tachycardia, flushing, headache, nausea/vomiting	Alternative option for catecholamine excess (eg, adrenergic crisis secondary to pheochromocytoma or cocaine overdose).

AMI: acute myocardial infarction; CAD: coronary artery disease; CVA: cerebrovascular accident.

* Intravenous short-acting agents for treatment of hypertensive emergency should be administered immediately by clinicians who are trained and experienced in their titration using continuous non-invasive electronic monitoring of blood pressure, heart rate, and ECG. Patients should be admitted to an intensive care unit as rapidly as possible. A combination of IV agents is often selected depending upon the acute indication. Refer to topic(s) for suggested combinations.

• Hypotension may occur with all agents.

References:

1. *Marik PE, Varon J. Hypertensive crises: challenges and management. Chest 2007; 131:1949.*
2. *Chobanian AV, Bakris GL, Black HR, et al. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Hypertension 2003; 42:1206.*
3. *Varon J. Treatment of acute severe hypertension: Current and newer agents. Drugs 2008; 68:283.*

Note: Recommendations for parenteral treatment of hypertensive emergencies were not addressed in the JNC 8 guideline (James PA, Oparil S, Carter BL, et al. 2014 Evidence-based guideline for the management of high blood pressure in adults: Report from the panel members appointed to the Eighth Joint National Committee (JNC 8). JAMA 2014; 311:507).

SUMMARY

- Management of hypertensive crisis in the ED will continue to challenge clinicians because of the lack of randomized clinical trials. Expert opinion and sound clinical judgment will continue to guide the management of hypertension crisis until such trials are completed.
- Hypertensive crisis persists largely because of medication nonadherence, poorly controlled chronic hypertension, substance abuse, and poor access to primary care.
- A few key principles should be noted:
    1. verify BP readings before initiating treatment;
    2. patients presenting with a hypertensive emergency should have their MAP reduced by 20% to 25% within the first hour, with the exception being ischemic stroke and aortic dissection as noted in Table 3;
    3. hypertensive urgencies should be treated with oral, not parental, agents;
    4. appropriate testing to differentiate hypertensive urgencies versus emergencies should be done; and
    5. once BP is stabilized with parenteral therapy, the transitionnto oral therapy can begin within 6 to 12 hours.

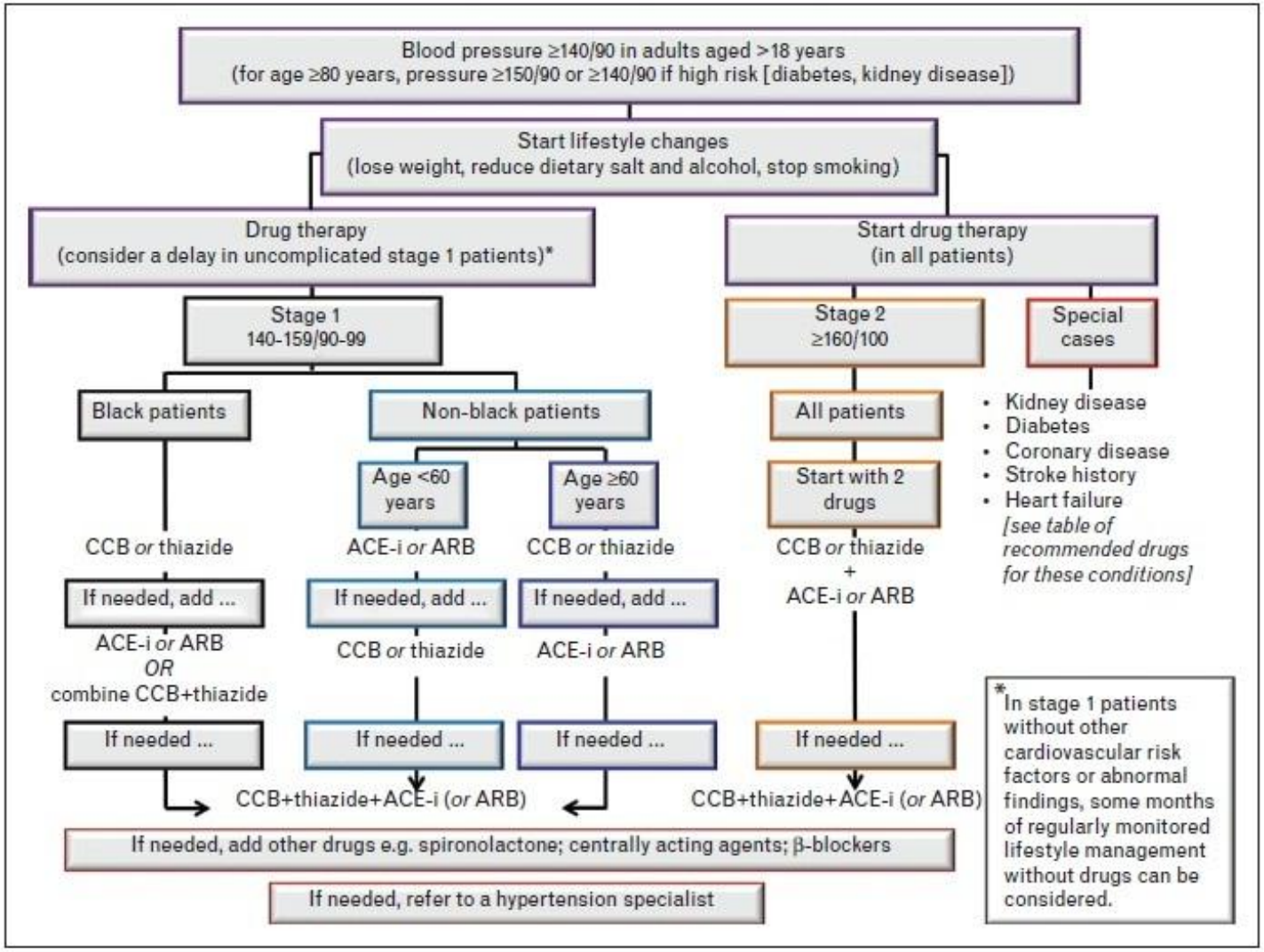

FIGURE 1 Algorithm summarizing the main recommendations of the guidelines. At any stage, it is entirely appropriate to seek help from a hypertension expert if treatment is proving difficult. In patients with stage 1 hypertension in whom there is no history of cardiovascular, stroke or renal events or evidence of abnormal findings, and who do not have diabetes or other major risk factors, drug therapy can be delayed for some months. In all other patients (including those with stage 2 hypertension), it is recommended that drug therapy be started when the diagnosis of hypertension is made. ACE-I, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB, calcium channel blocker; thiazide, thiazide or thiazide-like diuretics. Blood pressure values are mmHg.

TABLE 1. Drug selection in hypertensive patients with or without other major conditions

Patient type	First drug	Add second drug if needed to achieve a BP of <140/90 mmHg	If third drug needed to achieve a BP of <140/90 mmHg
(Part 1) Treatment regimens when hypertension is the only or main condition			
Black patients (African Ancestry): all ages	CCB[a] or thiazide diuretic	ARB[b] or ACE inhibitor (If unavailable can add alternative first drug choice)	Combination of CCB + ACE inhibitor or ARB + thiazide diuretic
White and other non-black patients: aged <60 years	ARB[b] or ACE inhibitor	CCB[a] or thiazide diuretic	Combination of CCB + ACE inhibitor or ARB + thiazide diuretic
White and other non-black patients: aged >60 years	CCB[a] or thiazide diuretic (though ACE inhibitors or ARBs are also usually effective)	ARB[b] or ACE inhibitor (or CCB or thiazide, if ACE inhibitor or ARB used first)	Combination of CCB + ACE inhibitor or ARB + thiazide diuretic
	First drug	**Add second drug if needed to reach a BP of <140/90 mmHg**	**ADD third drug if needed to reach a BP of <140/90 mmHg**
(Part 2) When hypertension is associated with other conditions			
Hypertension and diabetes	ARB or ACE inhibitor Note: in black patients, it is acceptable to start with CCB or thiazide	CCB or thiazide diuretic; Note: in black patients, if starting with CCB or thiazide, would now add ARB or ACE inhibitor	The alternative second drug (thiazide or CCB)
Hypertension and chronic kidney disease	ARB or ACE inhibitor Note: in black patients, good evidence for renal protective effects of ACE inhibitors	CCB or thiazide diuretic[c]	The alternative second drug (thiazide or CCB)
Hypertension and clinical coronary artery disease[d]	β-blocker with ARB or ACE inhibitor	CCB or thiazide diuretic	The alternative second step drug (thiazide or CCB)
Hypertension and stroke history[e]	ACE inhibitor or ARB	Thiazide diuretic or CCB	The alternative second drug (CCB or thiazide)
Hypertension and heart failure	Patients with symptomatic heart failure should usually receive an ARB or ACE inhibitor + β-blocker + diuretic + spironolactone regardless of blood pressure. Dihydropyridine CCB can be added if needed for BP control.		

ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; BP, blood pressure; CCB, calcium channel blocker; eGFR, estimated glomerular filtration rate.
[a]CCBs generally preferred, but thiazides may cost less.
[b]ARBs can be considered because ACE inhibitors can cause cough and angioedema, though ACE inhibitors may cost less.
[c]If eGFR less than 40 ml/min, a loop diuretic, for example, furosemide or torsemide, may be needed.
[d]If previous myocardial infarction, a β-blocker and ARB/or ACE inhibitor are indicated regardless of blood pressure.
[e]If using a diuretic, there is good evidence for indapamide (if available).

Prognosis

- **acute kidney injury associated with increased risk of adverse cardiac events and death in patients with acute severe hypertension (level 2 [mid-level] evidence)**
  - based on retrospective cohort study
  - 1,566 patients with acute severe hypertension (≥ 1 blood pressure measurement > 180 mm Hg systolic or > 110 mm Hg diastolic) and treated with IV antihypertensive therapy were followed for up to 6 months
  - 79% had chronic kidney disease (CKD) at baseline
    - mild CKD in 32.6% (estimated glomerular filtration rate [eGFR] 60-89 mL/min)
    - moderate CKD in 23.7% (eGFR 30-59 mL/min)
    - severe CKD in 11.6% (eGFR < 30 mL/min)
    - end stage renal disease in 11.2%
  - 36% developed acute kidney injury during hospitalization (decrease in eGFR ≥ 25% from baseline)
  - compared to no CKD, any CKD associated with increased risk of
    - heart failure ($p < 0.0001$)
    - non-ST-elevation myocardial infarction ($p = 0.003$)
    - acute kidney injury ($p < 0.007$)
  - compared to no change in eGFR, acute kidney injury associated with increased risk of
    - heart failure ($p \leq 0.0001$)
    - cardiac arrest ($p \leq 0.0001$)
    - 90-day mortality ($p = 0.003$)
  - any acute loss of estimated glomerular filtration rate during hospitalization associated with increased risk of death (odds ratio 1.05, 95% CI 1.01-1.09 per 10 mL/min decline)
  - Reference - Circulation 2010 May 25;121(20):2183 full-text, editorial can be found at Circulation 2010 May 25;121(20):2160 full-text

Prognosis

- **duration of known hypertension and serum urea levels at presentation may predict survival**
  - based on observational study of 315 patients (mean age 49.4 years) with malignant hypertension
  - mortality 40% (most common causes of death were renal failure, stroke, myocardial infarction and heart failure)
  - duration of known hypertension and serum urea level at presentation were main predictors of survival
  - Reference - J Hypertens 1995 Aug;13(8):915

Measuring Blood Pressure

- ED visit is a good opportunity to identify patients with asymptomatic hypertension: 25% to 75% of patients with elevated systolic or diastolic BP in the ED remain hypertensive at follow-up.

- Fleming J, Meredith C, Henry J. Detection of hypertension in the emergency department. Emerg Med J. 2005;22(9):636-640.(Prospective, observational; 213 patients)
- Tanabe P, Persell SD, Adams JG, McCormick JC, Martinovich Z, Baker DW. Increased blood pressure in the emergency department: pain, anxiety, or undiagnosed hypertension? Ann Emerg Med. 2008;51(3):221-229. (Prospective, observational;156 patients)

Measuring Blood Pressure

- A convenience sample of 53 postsurgical patients with arterial lines compared 2 arm cuffs and found greater random error with the large cuff but consistently elevated systolic and diastolic readings with the smaller cuff.

- Karvonen MJ, Telivuo LJ, Jarvinen EJ. Sphygmomanometer cuff size and the accuracy of indirect measurement of blood pressure. Am J Cardiol. May 1964;13:688-693. (Prospective; 53patients)

Treatment setting

- **General principles:**
  - blood pressure goals[()2]
    - in most cases, lower diastolic pressure by 10%-15% or to approximately 110 mm Hg over 30-60 minutes
    - for aortic dissection, lower systolic pressure to < 120 mm Hg rapidly (5-10 minutes)
  - consider starting lower doses or infusion rates in patients > 65 years old[(3)]
  - transition to oral therapy as soon as possible after blood pressure stabilization[(3)]

ATUDER

10. ULUSAL
ACİL TIP KONGRESİ

15 - 18 Mayıs 2014
Gloria Golf Resort Hotel,
Belek-Antalya