Hypertension: Perioperative Implications

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What is blood pressure?

- **BP = CO x TRP**
- **MAP = (SP + 2DP)/3**
- **SBP largely determined by CO**
- **DBP largely determined by TRP**

Stages of Hypertension

<table>
<thead>
<tr>
<th>Type of Hypertension</th>
<th>Systolic BP</th>
<th>Diastolic BP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt; 120</td>
<td>&lt; 80</td>
</tr>
<tr>
<td>Pre-hypertension</td>
<td>120 – 139</td>
<td>80 – 89</td>
</tr>
<tr>
<td>Stage 1 hypertension</td>
<td>140 – 159</td>
<td>90 – 99</td>
</tr>
<tr>
<td>Stage 2 hypertension</td>
<td>&gt; 160</td>
<td>&gt; 100</td>
</tr>
<tr>
<td>Malignant hypertension</td>
<td>&gt; 200/140</td>
<td>&gt; 110 – 115</td>
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</table>

Controlling Mean Blood Pressure

CAUSES OF SECONDARY HYPERTENSION

- Disorders of the adrenal gland
- Kidney disease
- Drugs
  - Corticosteroids
  - Nonsteroidal anti-inflammatory drugs
  - Weight loss drugs
  - Cold medications
  - Migraine medications
- Sleep apnea
- Coarctation of the aorta
- Preeclampsia
- Pheochromocytoma
- Thyroid and parathyroid problems
Hormonal Mechanisms
- Renin-angiotensin-aldosterone system
  - Renin is synthesized & stored in juxtaglomerular cells (renal afferent arterioles)
  - ↓ perfusion → ↑ renin release
  - ↑ catecholamine → ↑ renin release
  - Angiotensin II → renin release
  - Angiotensin → (renin) → angiotensin I → ACE → angiotensin II

Normal Blood Pressure Regulation
Blood Pressure = Cardiac Output × PVR
- Physiologically CO and PVR is maintained minute to minute by arterioles and post-capillary venules
- Kidney = volume of intravascular fluid
- Baroreflex, humoral mechanism and renin-angiotensin-aldosterone system regulate all sites
- Nitric oxide
- In hypertensive patients
  - Baroreflex and renal blood-volume control system set at higher level
- Antihypertensives interfere with one of these mechanisms

The Renal response
- Control intravascular volume
- Long-term blood pressure control
- Control intravascular volume
- Reduction in renal pressure
- Increased absorption of salt and water
- Decreased pressure in renal arterioles or sympathetic activity
- Renin production - angiotensin II production
- Angiotensin II:
  - Causes direct constriction of renal arterioles
  - Stimulation of aldosterone synthesis
  - Sodium absorption and increase in intravascular blood volume

Baroreceptor reflex arc
- Postural baroreflex:
  - Aorta
  - Carotids

Benefits of Lowering BP

<table>
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<tr>
<th>Condition</th>
<th>Average Percent Reduction</th>
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<tbody>
<tr>
<td>Stroke incidence</td>
<td>35 – 40%</td>
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<tr>
<td>Myocardial infarction</td>
<td>20 – 25%</td>
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<tr>
<td>Heart failure</td>
<td>50%</td>
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</tbody>
</table>

National Heart, Lung and Blood Institute, www.nhlbi.nih.gov
Minority Populations
- In general, treatment similar for all demographic groups.
- Socioeconomic factors and lifestyle important barriers to BP control.
- Prevalence, severity of HTN increased in African Americans.
- African Americans demonstrate somewhat reduced BP responses to monotherapy with BBs, ACEIs, or ARBs compared to diuretics or CCBs.
- These differences usually eliminated by adding adequate doses of a diuretic.

National Heart, Lung and Blood Institute, www.nih.gov

Hypertension and Diabetes
- Hypertension co-exists with type II in about 40% at age 45 rising to 60% at age 75.
- 70% of type II patients die from cardiovascular disease.
- At least 60% of patients will require 2 or 3 antihypertensive agents to achieve tight control.

Hypertension in Older Persons
- More than two-thirds of people over 65 have HTN.
- This population has the lowest rates of BP control.
- Treatment, including those with isolated systolic HTN, should follow same principles of general care of HTN.
- Lower initial drug doses may be indicated to avoid symptoms, but standard doses and multiple drugs will be needed to reach BP targets.

Adapted from JNC 7 Express: National Heart, Lung and Blood Institute, www.nih.gov

Hypertension in Women
- Oral contraceptives (OCs) may increase BP, and BP should be checked regularly. In contrast, HRT does not raise BP.
- Development of HTN with OC use—consider other forms of contraception.
- Pregnant women with HTN should be followed carefully. Methyldopa, BBs, and vasodilators, preferred for the safety of the fetus. ACEI and ARBs contraindicated in pregnancy.

Adapted from JNC 7 Express: National Heart, Lung and Blood Institute, www.nih.gov

Perioperative Risk
- Anesthesia & surgery
  - Physiologically stressful
  - May exacerbate or uncover underlying disease processes
- Complications include
  - MI
  - Difficulty oxygenating
  - Difficulty ventilating
  - Risk CVA
- Stratify risk
  - Good preoperative assessment
  - No matter what age

CNS
- ↑ risk of stroke
- ↑ risk of neurocognitive dysfunction

RENAI
- ↑ risk of renal dysfunction
- Hypovolemia

WOUND
- Surgical bleeding
- Anastomotic disruptions
Keeping the head in Neutral

- Contoured Head Rest
- Neuro Tongs

If patient emerges from general anesthesia and complains of visual impairment
- Believe the patient
- Period of Hypotension must be considered
- Treated as an emergency!!!

Preoperative Assessment of Hypertension

Hypertension
- Urgent surgery
  - Appropriate anesthetic to control BP
  - Proceed to surgery
- Asymptomatic
  - BP ≤ 180
  - Appropriate anesthetic technique
  - Hematology, WBC
  - SMA 12
  - Urine protein, glucose, sp gr, sodium
  - Chest x-ray
  - Multi-lead EKG (V1, V5, and II)

Visual Impairment

If patient emerges from general anesthesia and complains of visual impairment
- Believe the patient
- Period of Hypotension must be considered
- Treated as an emergency!!!

Pre-anesthetic considerations

- Men are more apt to have hypertension than are women
- May account for overall higher male surgical mortality rate
- Blacks have a higher incidence of hypertension compared to Caucasians
- Blacks also have a higher chance of developing malignant hypertension and are at higher risk of debilitating strokes.

Pre-anesthetic considerations

- Obesity is a common denominator
  - one study found a genuine association between BP and body weight
  - Independent of the upper arm circumference that might affect BP measurement
  - Make sure the cuff is adequate for the patient

- Smoking
  - No statistically significant relationship to development of hypertension in the presence of normal oxygenation and normocarbia

Pre-anesthetic considerations

- Examination of blood vessels in eye grounds
  - Extracranial and peripheral arteries
  - Whether autoregulation of cerebral blood flow is intact

- Measurement of BP in both arms and legs

- Hematocrit, WBC
- SMA 12
- Urine protein, glucose, sp gr, sodium
- Chest x-ray
- Possible flat plate of abdominal

Physical Exam
**When to discontinue drugs prior to surgery**

- **Historically**
  - Drugs were D/C'd prior to anesthesia
  - Aimed at preserving a functionally intact autonomic nervous system during anesthesia
- **Policy established when the primary treatment was reserpine**
  - Developed circulatory collapse with General Anesthesia
  - Swings in BP did not differ from patients not on antihypertensive drugs

**Etiology of Intraoperative Hypertension**

- **Intubation hypertension**
- **Inadequate anesthesia**
- **Hypercapnia**
- **Hypoxemia**
- **Pharmacological adjuvants**
- **Pheochromocytoma**
- **Surgical procedures**
- **Bladder distension**
- **Extubation hypertension**

**Classification of Anti-hypertensive drugs**

- **ACE inhibitors** — captopril, Ramipril
- **β-blockers** — propranolol, atenolol
- **Calcium channel blockers** — verapamil, felodipine
- **Diuretics** — thiazides
- **α1-Blockers** — prazosin, terazosin
- **Angiotensin II antagonist** — losartan
- **α-over β-blockers** — Labetalol
- **Central sympatholytics** — methyldopa, clonidine
- **Neuron blockers** — reserpine
- **Ganglion blockers** — pentolinium

**Antihypertensive Drugs**

- **Diuretics:**
  - Increase excretion of Na+ and H2O
  - Where goes sodium so goes water
  - Decrease in blood volume
  - Decreased BP

**Diuretics**

- Thiazide
  - Hydrochlorothiazide (HydroDIURIL, Esidrix)
  - Indapamide (Dynacirc)
- Loop diuretics
  - Furosemide (Lasix)
  - Bumetadine (Burmex)
  - Ethacrynic acid (Edecrin)
- K+ sparing
  - Amiloride (Midamor)
  - Spironolactone (Aldactone)
  - Triamterene (Dyrenium)
- Osmotic
  - Mannitol (Osmitrol)
  - Urea (Ureaphil)
- Other
  - Combination — HCTH +
  - Trandolapril (Ozardil)
  - Atenolol (Tenormin)
Diuretics

- **Site of Action**: Renal Nephron
- **Mechanism of Action**:
  - Urinary Na+ excretion
  - Urinary water excretion
  - Extracellular Fluid and/or Plasma Volume
- **Effect on Cardiovascular System**:
  - Acute decrease in CO
  - Chronic decrease in TPR, normal CO
  - Mechanism(s) unknown

- **Site of Action**: Renal Nephron

- **Adverse Reactions**:
  - Dizziness
  - Electrolyte imbalance/depletion
  - Hypokalemia
  - Hyperlipidemia
  - Hyperglycemia (Thiazides)
  - Gout

- **Contraindications**:
  - Hypersensitivity
  - Compromised kidney function
  - Cardiac glycosides (K+ effects)
  - Hypovolemia
  - Hyponatremia

- **Therapeutic Considerations**:
  - Thiazides (most common diuretics for HTN)
  - Start with lower potency diuretics
  - Used to treat mild to moderate HTN
  - Combined with lower dietary Na+ intake, K+ supplement or high K+ food
  - K+ Sparing (combination with other agent)
  - Loop diuretics (severe HTN, or with CHF)
  - Osmotic (HTN emergencies)
  - Maximum antihypertensive effect reached before maximum diuresis - 2nd agent indicated

Peripheral α-1 Adrenergic Antagonists

- **Drugs**: prazosin (Minipres), terazosin (Hytrin)
- **Site of Action**: Peripheral arterioles, smooth muscle

- **Mechanism of Action**: Competitive antagonist at α-1 receptors on vascular smooth muscle.

- **Effects on Cardiovascular System**:
  - Vasodilation, reduces peripheral resistance
  - CRITICAL POINT! Blocking α-receptors on vascular smooth muscle allows muscle relaxation, dilation of vessel, and reduced resistance.

- **Contraindications**:
  - Hypersensitivity

- **Adverse Effects**:
  - Nausea; drowsiness; postural hypotension

- **Therapeutic Considerations**:
  - No reflex tachycardia
  - Use with diabetes, asthma, and/or hypercholesterolemia
  - Mild to moderate hypertension
  - Combined with diuretic, β-antagonist
Central Sympatholytics (α-2 Agonists)

Drugs: clonidine (Catapres), methyldopa (Aldomet); dexmetetomidine (Precedex)

- Site of Action
  - CNS medullary cardiovascular centers
  - clonidine: direct α-2 agonist
  - methyldopa: "false neurotrans."
- Mechanism of Action
  - CNS α-2 adrenergic stimulation
  - Peripheral sympathoinhibition
  - Decreased norepinephrine release
- Effects on Cardiovascular System
  - Decreased NE → vasodilation → Decreased TPR

**CRITICAL POINT!**
Stimulation of α-2 receptors in the medulla decreases peripheral sympathetic activity, reduces tone, vasodilation and decreases TPR.

- Contraindications
- Adverse Effects

Beta Blockers

- BBs have been shown to be equivalent to HCTZ in Caucasian patients but more effective in AA and older patients*
- BBs may provide primary protection from CHD and reduce risk of reinfarction.
- BBs can produce LVH regression.
- Some are also used as anti-arythmics.

- Effects on Cardiovascular System
  - Cardiac: Decrease HR, increase CO
  - Renin: Decrease → Decrease Angiotensin II → Decrease TPR

- Adverse Effects
  - Impotence
  - Bradycardia
  - Fatigue
  - Exercise intolerance

- Contraindications
  - Asthma
  - Diabetes
  - Bradycardia

**β-Adrenergic Antagonists**

- Therapeutic Considerations
  - Selectivity
  - Nadolol (Corgard) non selective, but 20 hr 1/2 life
  - Metoprolol (Lopresor) β-1 selective, 3-4 hr 1/2 life
  - Risky in pulmonary disease even selective β₁
  - Available as mixed a/b blocker available-labelatal (Trandate, Normodyne)
  - Use post myocardial infarction - protective
  - Use with diuretic - prevent reflex tachycardia
  - MUST BE CONTINUED DAY OF SURGERY!!

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**Beta Adrenergic Blockers (BBs)**

- Various types include nonspecific beta antagonists, selective beta antagonists, and those with and without intrinsic sympathomimetic activity (ISA).
- In post-MI patients, cardioselective agents are preferred [without ISA].
- Useful for hypertensives with angina, MI, migraine, a. fib. and essential tremor.

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*VA Cooperative Study Group.*

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**Noble: Textbook of Primary Care Medicine, 4th edition, 2010 Mosby.**
Angiotensin converting enzyme inhibitors (ACE)

- Angiotensin Converting Enzyme- Inhibitors
  - enalapril (Vasotec);
  - quinapril (Accupril);
  - fosinopril (Monopril);
  - moexipril (Univasc);
  - lisinopril (Zestril, Prinivil);
  - benazepril (Lotensin);
  - captopril (Capoten)

Angiotensin II Formation

- Ang II Receptor Antagonists
  - losartan (Cozaar);
  - candesartan (Atacand);
  - valsartan (Diovan)

Ang I \rightarrow Ang II

\[ \text{ACE} \]

\[ \text{Ang II} \]

\[ \text{AT1} \]

\[ \text{AT2} \]

Lung

Brain

Kidney

Adr Gland

Effect on Cardiovascular System

ACE Inhibitors

- Volume
- Aldosterone
- Vasopressin
- CO
- Angiotensin II
- Ang II Receptor Antagonists
- Norepinephrine
- Sympathetic response
- HR
- CO
- TPR

Adverse Effects

- Hyperkalemia
- Angiogenic edema (ACE inhibitor)
- Cough (ACE inhibitor)
- Rash
- Itching

Contraindications

- Pregnancy
- Renal insufficiency

Therapeutic Considerations

- Heart failure
- Adjunctive therapy in heart failure
- Often used with diuretics
- IV for hypertensive emergency
- Renal insufficiency

Anti-Angiotensin II Drugs

- Adverse Effects

- Hyperkalemia
- Angiogenic edema (ACE inhibitor)
- Cough (ACE inhibitor)
- Rash
- Itching

- Contraindications

- Pregnancy
- Hypersensitivity

- Therapeutic Considerations

- Diabetes or renal insufficiency
- Adjunctive therapy in heart failure
- Often used with diuretics
- IV for hypertensive emergency - enalapril

Ca++ Channel Blockers

- Site of Action:
  - Vascular smooth muscle

- Mechanism of Action:
  - Blocks Ca++ channel
  - Decreases/prevents contraction

- Effect on Cardiovascular System:
  - Vascular relaxation
  - Decreased TPR

Vasodilators

- Drugs:
  - Hydralazine (Apresoline)
  - Minoxidil (Loniten)
  - Nitroprusside (Nipride)
  - Diazoxide (Hyperstat I.V.)
  - Fenoldopam (Corlopam)

Site of Action:

- Vascular smooth muscle

Mechanism of Action:

- Hydralazine
  - NO
  - Ca++K+/Na+

Minoxidil

Nitroprusside

Diazoxide

Fenoldopam
Vasodilators

- Effect on cardiovascular system
  - Vasodilation
  - ↓ TPR
- Adverse Effects
  - Reflux esophagitis
  - Increase of gastric NG
  - Lupus - nephritis
  - Cyanide toxicity - nitrates
- Therapeutic Considerations
  - Nitrates – therapy
  - Hydralazine – safe for pregnancy
  - DIazoxide – emergency use severe hypertension

Adverse Effects

- Reflex tachycardia
- Increase Sympathetic NS
- Lupus – nephritis
- Cyanide toxicity - nitrates

Therapeutic Considerations

- Nitrates – therapy
- Hydralazine – safe for pregnancy
- DIazoxide – emergency use severe hypertension

Summary Sites and Mechanisms of Action

- α-2 agonists
- β-blockers
- Receptor antagonists
- Antagonists
- Vasodilators
- Diuretics

CRITICAL POINTS!

1. Can alter CO/TPR of number of sites and/or mechanisms.
2. Antihypertensives mechanistically specific, and alter blood pressure through physiologically diverse effects on CO/TPR.
3. All organ systems and/or effector mechanisms are potential targets.

Summary Important Points Hypertensive Agents

Each class of antihypertensive agent:

- Specific mechanism of action
- Acts at one or more major organ systems
- Acts on a major physiological regulator of blood pressure
- Reduces CO and/or TPR to lower blood pressure
- Specific indications, contraindications, and therapeutic advantages and disadvantages

Logical Combinations

<table>
<thead>
<tr>
<th></th>
<th>Diuretic</th>
<th>β-blocker</th>
<th>CCB</th>
<th>ACE inhibitor</th>
<th>α-blocker</th>
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<tbody>
<tr>
<td>Diuretic</td>
<td>-</td>
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<td>β-blocker</td>
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</table>

* Vasoparal + beta-blocker = absolute contra-indication

Hypertension treatment with some common co-existing conditions

- Heart Failure
  - ACE inhibitors
  - Diuretics
- Myocardial Infarction
  - β-blockers
  - ACE inhibitors
- Diabetes
  - ACE inhibitors
  - AVOID β-blockers
- Isolated systolic hypertension (Older persons)
  - Diuretics preferred
  - Calcium channel antagonist
Agent | Dosage | Onset | Duration
---|---|---|---
Nitroprusside | 0.5 – 10 µg/kg/min | 30-60 sec | 1-5 mins
Nitroglycerine | 0.5 – 10 µg/kg/min | 1 min | 1-5 mins
Esmolol | 0.5-50 µg/kg/min bolus | 1 min | 12-60 mins
Fenoldopam | 0.1 – 1.6 µg/kg/min | 5 mins | 5 mins
Labetolol | 50 – 300 µg/kg/min infusion | 1 min | 12-60 mins
Propranolol | 1-3 mg | 1-2 mins | 4-6 hrs
Labetolol | 5-20 mg | 1-2 mins | 4-8 hrs
Hydralazine | 5-20 mg | 5-20 mins | 4-8 hrs
Nifedipine s/l | 10 mg | 5-10 mins | 4-8 hrs
Nicardipine | 0.25 – 0.5 mg | 1-5 mins | 3-4 hrs
Enalapril | 0.625 – 1 mg | 55 mins | 6-15 mins
Fenoldopam | 0.1 – 1.6 µg/kg/min | 5 mins | 5 mins

Initial treatment of hypertension

- Lifestyle modification first
- No smoking
- Weight control
- Reduce alcohol intake
- Decrease stress
- Sodium control

**Postoperative Concerns**

*Factors associated with Postoperative Hypertension*

- Pain
- Emergence excitement
- Full urinary bladder
- Hypercarbia
- Operative procedure
- Vascular
- Cardiac
- Neck
- Indwelling

**Questions?**