



Medical Management of Type B Aortic Dissection (TBAD) & Acute Aortic Syndromes

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No Disclosures

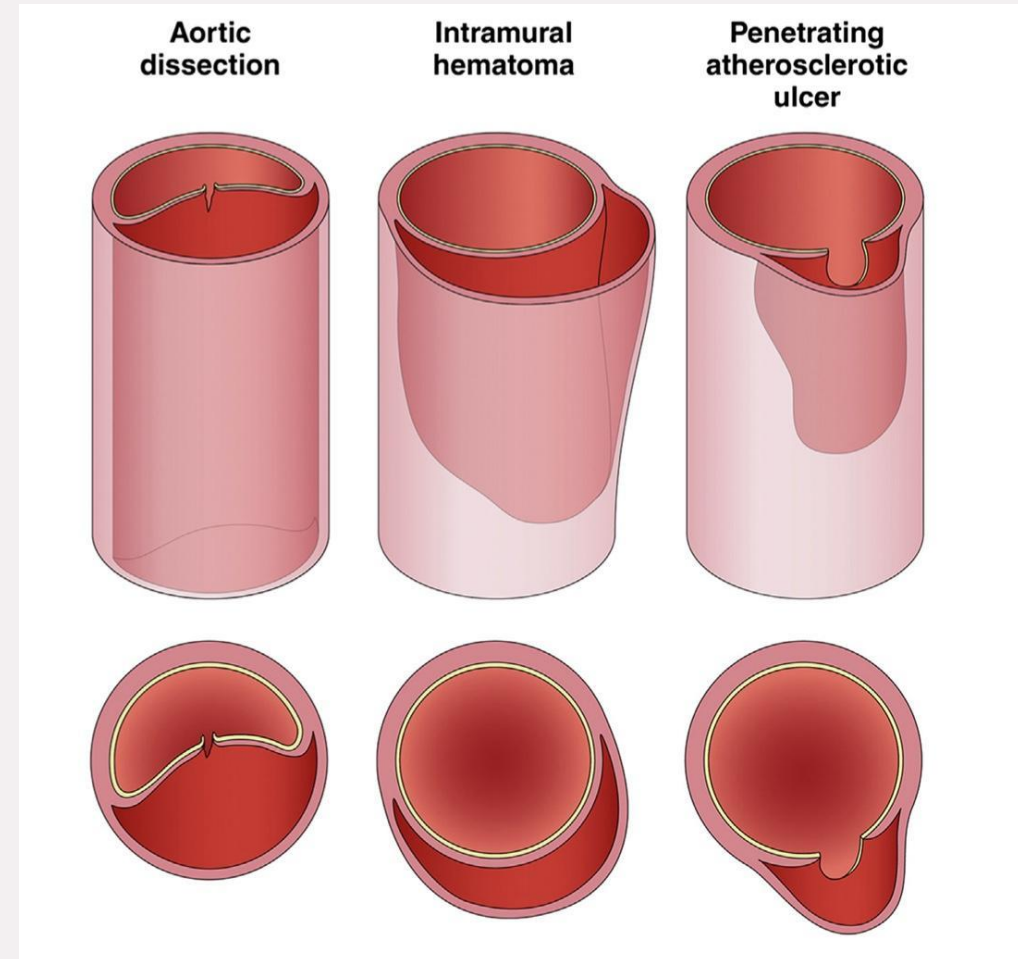
Objectives

- Medical management of descending acute aortic syndromes
- Identifying appropriate drug classifications and proper use
- Transition from intravenous to oral medications
- Identifying resistant / refractory HTN & treatment options
- Challenges to medical management



Acute Aortic Syndromes

- Intramural Hematoma (IMH)
- Penetrating Aortic Ulcer (PAU)
- Aortic Dissection
 - Stanford Type A
 - Stanford Type B
- Traumatic Aortic Injury

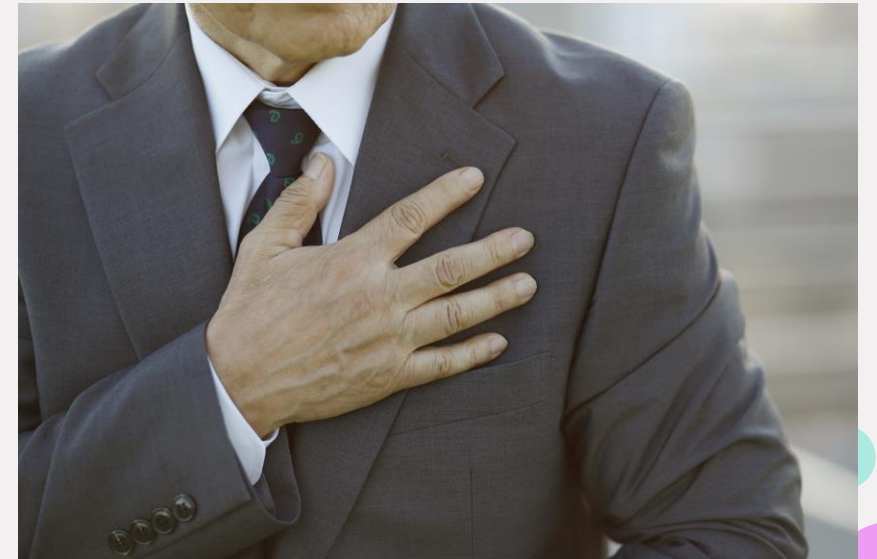


Causes / Risk Factors

- Uncontrolled hypertension
- Coronary artery disease
- Congenital disorders
 - Marfan Syndrome
 - Ehlers-Danlos Syndrome
 - Loeys-Dietz Syndrome (Vascular type)
- Congenital valve disorders
- Iatrogenic (Aortic surgery)
- Inflammatory disorders (Aortitis)
- Smoking (Tobacco)
- Hyperlipidemia
- Illicit drug use (Cocaine)
- Trauma (Blunt Aortic Injuries)
- Age (> 60)
- Sex (Male)
- Ethnicity (African descent)
- Pregnancy
- Extreme exertion

Presenting Symptoms

- Hypertension or hypotension
- Acute onset of pain
 - Back
 - Chest
 - Abdomen and flank
- End organ dysfunction due to malperfusion
 - Renal failure
 - Bowel ischemia
 - Acute limb ischemia
 - Spinal cord ischemia
 - Altered mental status
 - Loss of consciousness / stroke
- Acute shortness of breath
- Paresthesias
 - Loss of sensation in upper extremities
 - Loss of sensation in lower extremities
- Anxiety
- Impending doom
- Cardiac tamponade
- Rupture



Comprehensive Medical Exam

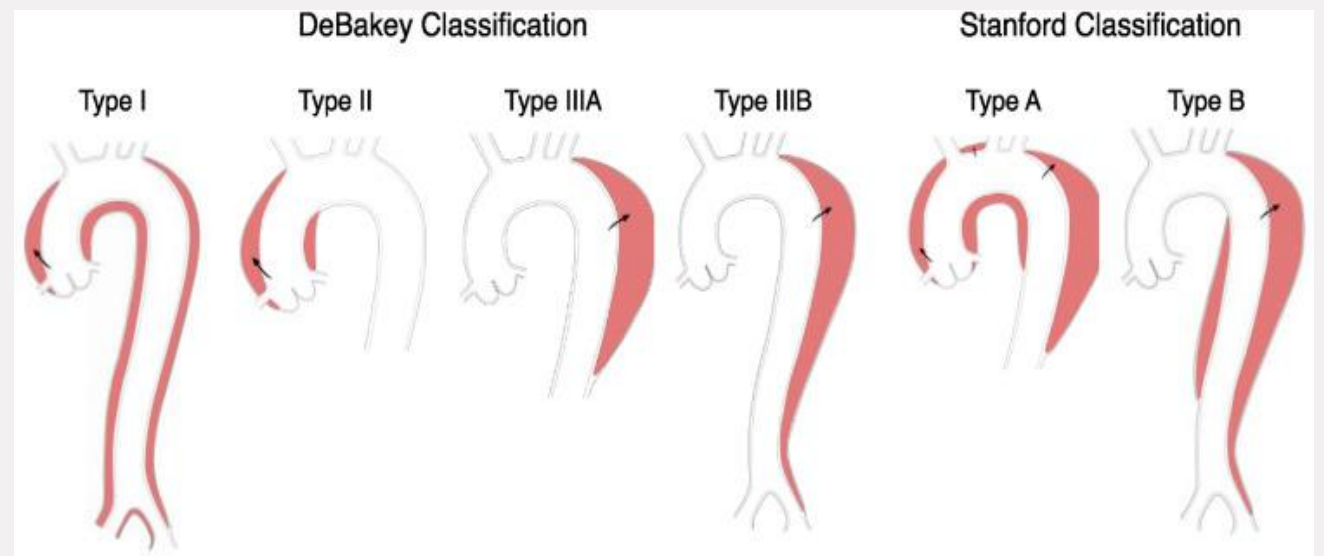
- History and physical
- Labs
- Blood pressure (bilateral upper extremities)
- Chest X-ray (widened mediastinum)
- Electrocardiogram (EKG)
- **CT Angiogram- including Chest Abdomen and Pelvis**
 - *CTA head and neck may be applicable*
- Transthoracic echocardiogram (TTE)
- Transesophageal echocardiogram (TEE)



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Surgical vs. Medical Management

- **Surgical Management – Emergency**
 - Stanford Type A / DeBakey type I and II
 - Complicated Stanford Type B / DeBakey type III
- **Medical Management – Uncomplicated TBAD**
 - Impulse control
 - Blood pressure and heart rate control
- **Surgical – Acute**
 - Failed medical management / High Risk



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Uncomplicated vs Complicated TBAD

Features of complicated, uncomplicated, and high-risk acute type B aortic dissection (TBAD)

UNCOMPLICATED

No high-risk features
No malperfusion
No rupture

COMPLICATED

Malperfusion
Rupture

HIGH RISK

True lumen diameter > 22 mm
Total aortic diameter > 40 mm
Radiographic malperfusion
Refractory pain
Hemothorax
Refractory hypertension
Readmission

Medical Management for Descending Acute Aortic Syndromes

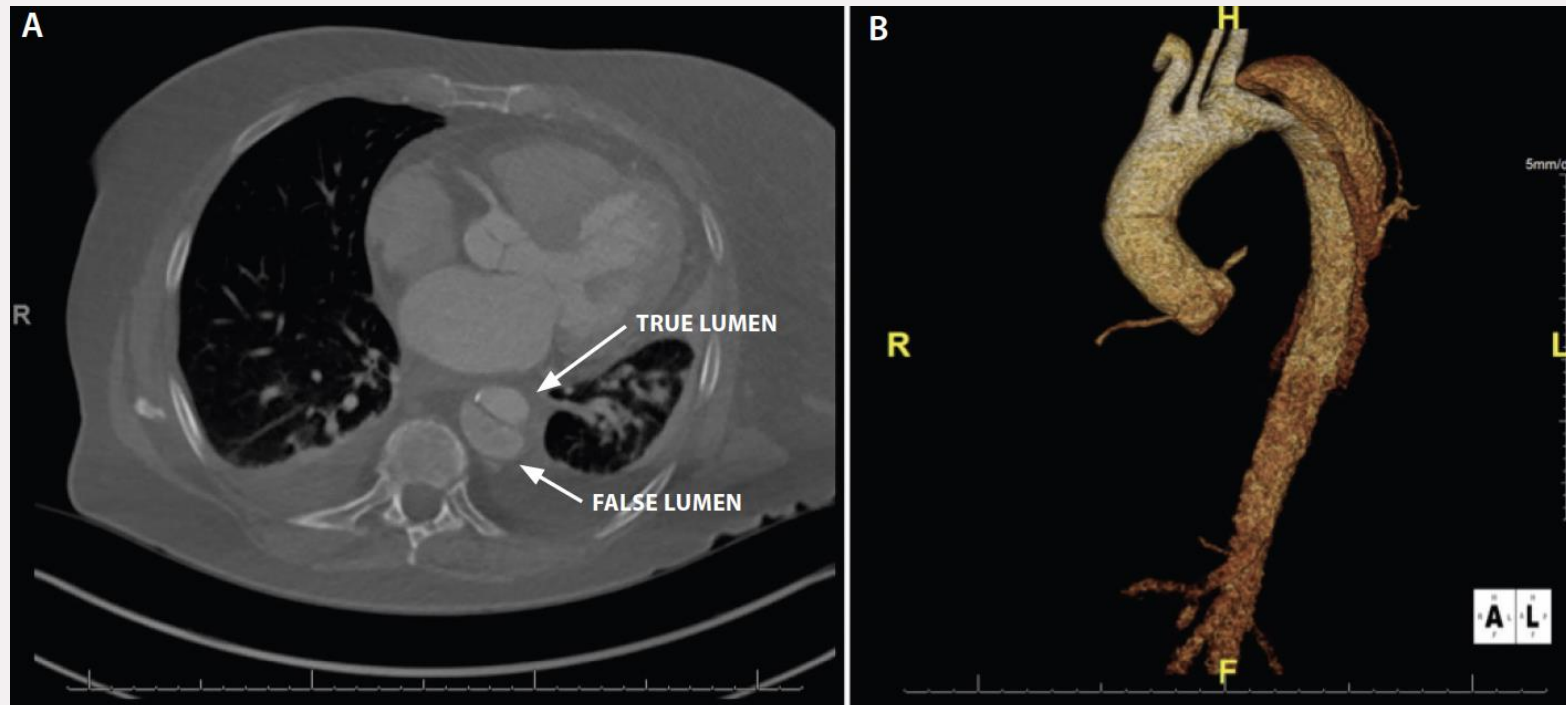
- **Treatment of choice** for any descending aortic syndrome
- Mainstay of treatment **throughout the continuum** of care
 - Pre-op, intra-op, post-op, non-op & outpatient
- **Goal of medical management**
 - Reduce shearing forces
 - Reduce contractility
 - Reduce pressure / rate pressure product
 - Relieve pain
- **Outcome**
 - Stop propagation of defect
 - Allow for remodeling
 - Reduce malperfusion
 - **Prevent aneurysmal formation / rupture**



Immediate Medical Management

- **Impulse Control**

- Goal systolic blood pressure (SBP) < **120 mmHg**
- Goal heart rate (HR) < **80 bpm**



Initial Medications

Initiate immediately once diagnosis confirmed

Start with IV medications

Drug Class:

First line: Beta Blockers (BB)

AND THEN

Second line: Vasodilators



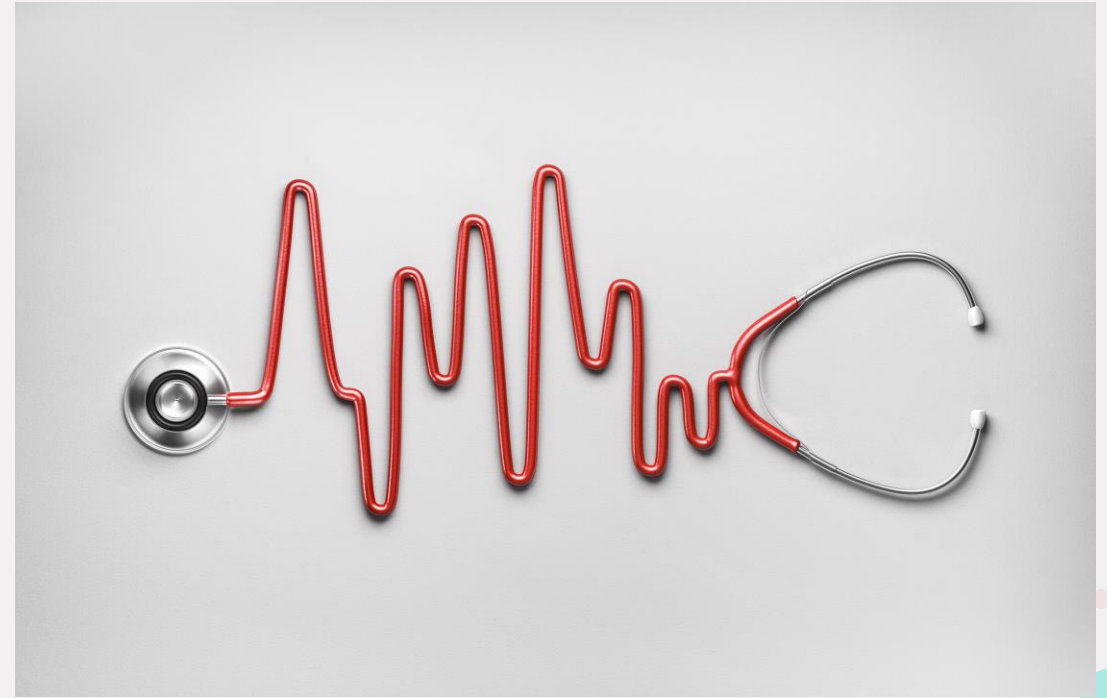
Why are Beta Blockers First?

- Aortic wall stress is affected by blood pressure, rate of ventricular contraction & the velocity of the ventricular contraction.
- **BBs decrease velocity of contraction** – reducing heart rate & blood pressure
- **Antihypertensive agents cause:**
 - Hyperdynamic response
 - Decrease in systemic vascular resistance (vasodilation)
 - Left ventricle to contract with a higher velocity (**compensatory tachycardia**)
- **ONCE** HR < 80 on BB, **THEN** an adjunctive antihypertensive agent can be added **IF** SBP goals are not met.
- **BB prevent reflex tachycardia from vasodilation**

Beta Blockers

Esmolol

- **Dose**
 - Range 25-300 mcg/kg/min continuous infusion
- **Pros**
 - **Anti-tachycardia**
 - *Beta-1 receptor selective*
 - Fast acting (onset dose dependent)
 - Short half-life (~ 9 minutes)
 - Can bolus (immediate effect)
- **Cons**
 - High cost
 - High fluid volume



Beta Blockers

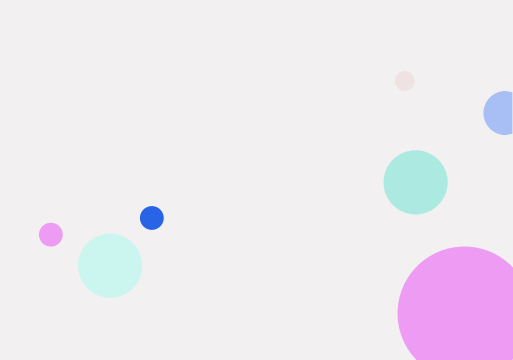
Labetalol

- **Dose**
 - IV push: 20 mg Q 10 minutes PRN (up to 300 mg total dose)
 - Infusion: 0.5-2 mg/minute (max dose of 80 ml/hour), start infusion at 10 ml/hr and titrate
- **Pros**
 - **Anti-HTN and anti-tachycardia**
 - Alpha-1 receptor antagonist
 - *Vasodilator*
 - Non-selective beta (1 & 2) receptor antagonist
 - *Blocks reflex tachycardia from vasodilation*
- **Cons**
 - Infusion not recommended due to long half-life (~5.5 hours)
 - Less effect on beta blockade compared to pure beta 1 blocker (like esmolol)



Beta Blockers

Metoprolol IV

- Beta-1 receptor- selective antagonist
 - Dose
 - Initial dose 5 mg IV push Q 5 minutes as needed (up to 15-20 mg in an hour)
 - Max dose 160 mg IV / 24 hours
 - Onset 10-12 minutes
 - Half Life 5-8 hours
- 

Vasodilators

Now that the betablocker is in effect...

Nicardipine

- **Dose**
 - Initial dose 2.5-5 mg/hr, titrating Q 5-15 minutes by 5 mg, max dose 15 mg/hr
- **Pros**
 - Potent arterial vasodilator
- **Cons**
 - May cause reflex tachycardia due to selective calcium channel blockade / vasodilation
 - Accumulation can occur due to long half life
 - *When goal blood pressure is reached you titrate gtt down to prevent overshooting SBP goal*

Vasodilators

Nitroprusside

- **Dose**
 - 0.1-8 mcg/kg/min
- **Pros**
 - Short acting - onset less than 2 minutes
 - Short half-life - 2 minutes
 - Low cost (newly)
- **Cons**
 - Cyanide metabolite toxicity – EXTREMELY RARE

Pain Control

Multimodal approach

- Acetaminophen
- Muscle relaxers
- Narcotics

Route

- Start with IV route

Finding balance is key...

- Goal is to reduce pain to reduce blood pressure and tachycardia
- Judicious use of analgesic to prevent masking of symptomatic aortic syndromes / signs of malperfusion



Summary of First Steps

1. Obtain diagnosis

2. Start **IV betablocker** immediately

- Esmolol gtt
 - *Labetalol not first choice due to long half life*

3. Once heart rate < 80 bpm and if systolic blood pressure > 120 mmHg, start **IV vasodilator**

- Nicardipine gtt

5. Pain control

6. If systolic blood pressure goals not maintained, add nitroprusside gtt (nicardipine resistance)

- *May be in addition to or alternative to nicardipine*

7. Titrate to resolution of symptoms while avoiding signs of malperfusion

When is Safe to Start Oral Medications?

- Blood pressure and heart rate at goal (impulse control)
- Resolution of signs of malperfusion (pain)
- No need for emergent surgery
- When GI function is considered reliable



Transitioning to Oral Medications

Calcium Channel Blocker (CCB)

Amlodipine

- Amlodipine 10 mg Q 12 hours x 3 doses (load), then 10 mg PO daily
 - Max dose 10 mg PO daily

Nifedipine

- Nifedipine IR 10 mg PO Q 6 hours
 - To wean off nicardipine gtt
 - Max dose 30 mg PO Q 6 hours
- Nifedipine to XL tablet PO daily when IR tolerated
 - Starting dose 30-90 mg PO Q day
 - Max dose 120 mg/day
- Do NOT give nifedipine via SL route d/t higher risk of excessive acute BP drop

Transitioning to Oral Medications

Betablockers (BB)

Metoprolol Tartrate

- Starting dose as low as 25 mg PO BID
- Maximum daily dose = 450 mg PO daily total
- Maximum frequency Q 6 hours
- Betablocker preferred over alphablocker (AB)

Metoprolol Succinate (XL)

- Starting dose as low as 25 mg PO daily
- Maximum daily dose = 400 mg/daily
- Maximum frequency BID
- Transition to succinate with prolonged inpatient stay vs. outpatient

Conversion: Use same total daily dose if switching from tartrate to succinate

Transitioning to Oral Medications: Additional Beta & Alpha Blockers

May consider these agents when need additional blood pressure control:

Labetalol (Betablocker)

- Starting dose 100 mg PO BID
- Often dosed Q 8 hours
- Maximum daily dose 2400 mg/day
- Con: TID dosing

Carvedilol (Alphablocker)

- Starting dose as low as 3.125 mg PO BID
- Maximum daily dose 50 mg PO BID (HFrEF dosing)
- Con: Alpha Blocker



Transitioning to Oral Medications

ACE (Angiotensin- Converting Enzyme) inhibitor

- **Lisinopril**
 - Starting dose as low as 2.5 mg PO daily
 - Max daily dose 40 (80) mg/day

ARB (Angiotensin II Receptor Blocker)

- **Losartan**
 - Starting dose as low as 25 mg PO daily
 - Max daily dose 150 mg/day [HFrEF dosing])

Add ACE / ARB when able - No AKI, no renal artery dissection / stenosis / malperfusion

What Else is in Our Toolbox?

Diuretics

Potassium Sparing Diuretic / Mineralocorticoid receptor antagonist

Spironolactone

- Starting dose as low as 25 mg PO daily
- Maximum daily dose 100 mg PO daily

Thiazide- like Diuretic

Chlorthalidone

- Starting dose as low as 12.5 mg PO daily
- Maximum daily dose 50 mg PO daily (200 mg daily - edema)

Loop Diuretic

Furosemide

- Starting dose as low as 10 mg PO daily (20 mg PO daily)
- Maximum daily dose 600 mg PO daily (edema)
- Dosing dependent on fluid status
- Do not use for additional BP control other agents are more effective



Spironolactone Gets the GOLD Medal

Spironolactone:

- Decreases both systolic and diastolic blood pressure
- Spironolactone is the most effective for resistant hypertension

Studies demonstrated:

- BP reduction about ~11 - 14 points in spironolactone dosing of 50 mg daily *

Side effects:

- Hyperkalemia
- Renal dysfunction
- Gynecomastia



* Medicine Volume 93, Number 27, December 2014

* Lancet 2015; 386: 2059–68

Desperate Yet?

- Hydralazine 25 mg PO Q 8 hours. Max daily dose = 300 mg / day (blood pressure)
- Clonidine 0.1 mg PO BID-TID. Max daily dose = 2.4 mg / day (blood pressure)
- Diltiazem 120 mg PO daily. Max daily dose = 540 mg / day (heart rate)



Last Resort?

- Doxazosin 4 mg PO daily. Max daily dose = 16 mg / day
- Isosorbide mononitrate ER 30 mg PO daily. Max daily dose = 240 mg / day
- Minoxidil 5 mg PO daily. Max daily dose = 100 mg / day (40 mg/day)
- Enalapril 5 mg PO daily. Max daily dose = 40 mg / day



Remember! Aspirin & Statin

Aspirin

- Reduces intramural thrombi
- Anti-inflammatory effects
- May slow progression of aneurysmal growth

Statin

- Anti-inflammatory
- Lipid lowering effects
- May slow progression of aneurysmal growth
- Improve mortality



Treat Comorbid Risk Factors

- Glucose control
 - Glucose goal < 130
- Smoking cessation
 - Wellbutrin preferred
 - Nicotine Replacement Therapy (NRT) *
 - Nicotinic Agonist *

* *Debated risk / benefit*



Do NOT Forget!

- Always betablocker unless contraindicated
- Max dose of one drug before adding a new agent
- Should always include (if able):
 - **Beta blocker**
 - **ARB**
 - **Diuretic**
 - **Spironolactone**
- Consider Nephrology **consultation**



Contraindications to Consider

- Connective Tissue Disorders – Avoid CCB. ARB and ACE preferred.
 - Marfan Syndrome - First line choice betablockers and ARB.
- Heart block – Avoid BB. Avoid CCB in 2nd and 3rd AV block.
- Bradycardia – Avoid BB
- Severe Asthma – Avoid BB
- COPD – Avoid BB
- Hypotension – Avoid CCB



Resistant & Refractory HTN

Resistant

- **3 or more** antihypertensive meds of different classes at max doses & still not meeting BP goal
 - Including a **diuretic**

Refractory

- **5 or more** antihypertensive meds of different classes at max doses & still not meeting BP goal
 - Including long-acting thiazide or thiazide-like diuretic (**chlorthalidone**)
 - One is a mineralocorticoid (aldosterone) receptor antagonist (**spironolactone**)

Resistant HTN Risk Factors

Older age
High baseline blood pressure
Obesity
Excessive dietary salt ingestion
Chronic kidney disease
Diabetes
Left ventricular hypertrophy
Black race
Female sex
Residence in southeastern United States

Medications that can Contribute to Resistant HTN

NSAIDs
Oral contraceptives
Sympathomimetic
Cyclosporine, tacrolimus
Erythropoietin
VEGF inhibitors
Alcohol
Cocaine
Amphetamines
Antidepressants
Glucocorticoids, mineralocorticoids

BP indicates blood pressure; NSAIDs, nonsteroidal anti-inflammatory drugs; and VEGF, vascular endothelial growth factor.

Specialist Work Up

Nephrology

- Renal artery duplex
- Aldosterone
- Renin
- Urine electrolytes

Endocrinology

- CT adrenals with and without contrast
- Cortisol
- Adrenocorticotrophic hormone (ACTH)
- Metanephrines (plasma, urine)
- Thyroid studies

Genetics

- Genetic Testing



Is This Realistic?

Compliance & Safe Discharges

Minimize dosing

- Maximize one agent prior to starting another agent
- TID dosing is challenging

Observe for adverse reactions

- Acute kidney injury
- Electrolyte derangements
- Hypotension

Monitoring

- PCP communication & follow up within 1 week of discharge
- Blood pressure monitoring at home
- Outpatient lab work (basic metabolic panel)

Lifestyle Modifications

- Consider sodium restrictive diet
- Weight loss
- Low impact exercise (walking, swimming) - Avoid Valsalva



Failure of Medical Management

At OUR institution:

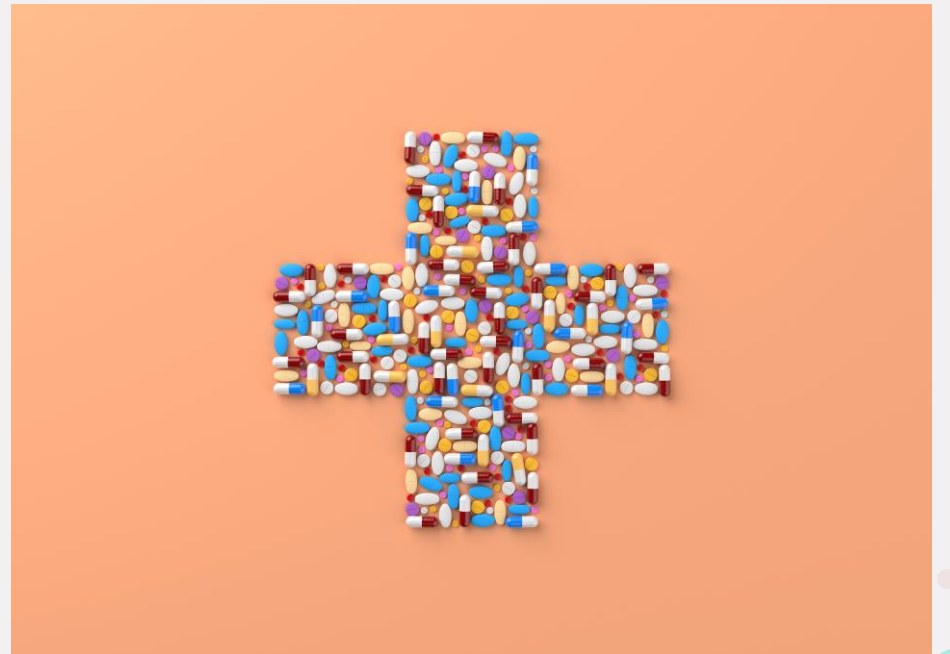
- 5 or more medications without sufficient impulse control and/or symptom control
- Continued pain
- Signs of malperfusion
- Progression serial CT scan (*48-72 hours from onset, if acute signs of malperfusion & 1 month*)



Disease Progression & Survival Rate

Patients who are well controlled on antihypertensive agents:

- **4 years:** 25-30% progress to aortic aneurysm formation
- **5 years:** 50-80% survival rate
- **10 years:** 30-60% survival rate



Summary

- **Goal:** Reduce aortic wall stress via reduced heart rate and blood pressure
 - Initial Heart Rate Target < 80 bpm – **Beta blockers FIRST!**
 - Initial Blood Pressure Target < 120 mmHg
- **Max dose of one drug** before adding additional drug(s)
- **Resistant > 3 max dose medications** (*including diuretic*)
- **Refractory > 5 max dose medications** (*including thiazide and mineralocorticoid receptor antagonist*)
- This can be **extraordinarily difficult** to achieve in patients with
 - Acute aortic dissection-related pain
 - History of severe hypertension (untreated, undertreated, resistant or refractory HTN)

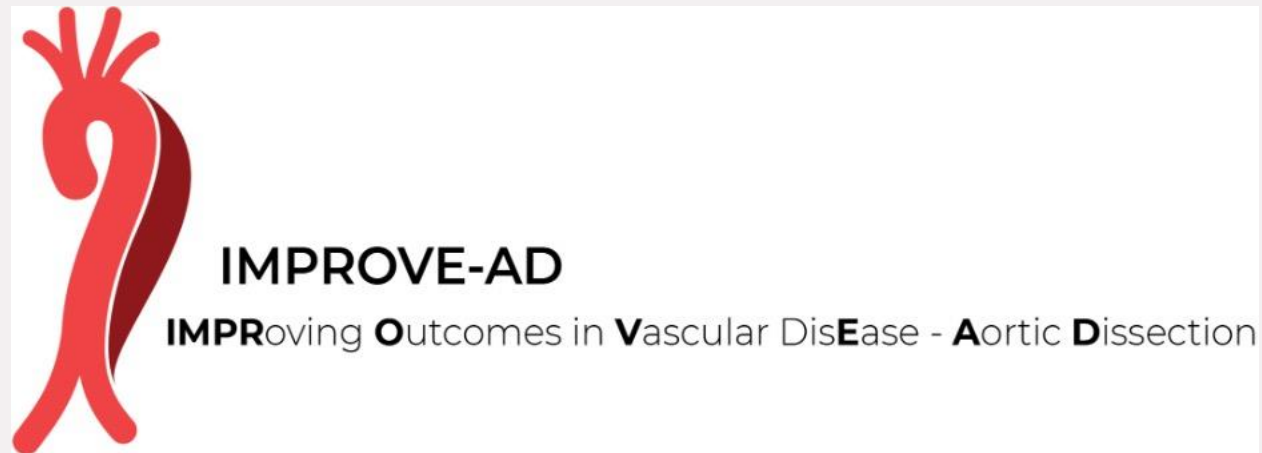


The Future: Research

IMPROVE – AD STUDY

Improving Outcomes in Vascular Disease Aortic Dissection

- Prospective randomized clinical trial assessing clinical outcomes of uncomplicated TBAD
- One group will receive upfront TEVAR along with medical management.
- Other group will receive medical management and routine check ups / surveillance.



The IMPROVE-AD Trial is funded by the National Heart, Lung, and Blood Institute

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Questions?



Thank you!



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