DIAGNOSIS AND MANAGEMENT OF RESISTANT HYPERTENSION

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LEARNING OBJECTIVES

• DEFINITION OF RESISTANT HYPERTENSION

• IDENTIFICATION AND MANAGEMENT OF RESISTANT HYPERTENSION

• TREATMENT MODALITIES: PHARMACOLOGIC, NONPHARMACOLOGIC AND EXPERIMENTAL THERAPIES
INTRODUCTION

• HYPERTENSION IS THE LEADING RISK FACTOR FOR CARDIOVASCULAR DISEASE, STROKE, DISABILITY AND DEATH

• 2017 AHA GUIDELINES REDUCED THE BP THRESHOLD FOR INITIATION OF ANTIHYPERTENSIVE THERAPY TO > 130/80 IN PATIENTS WITH KNOWN CVD OR ASCVD RISK SCORE OF > 10%.

• PREVALENCE OF TREATMENT RESISTANT HYPERTENSION IS 12-15% AMONG ADULTS TREATED FOR HYPERTENSION

• THESE PATIENTS ARE AT HIGHER RISK OF POOR OUTCOMES BASED ON PRIOR OBSERVATIONAL STUDIES.

• PATIENTS WITH RESISTANT HYPERTENSION ARE 47% MORE LIKELY TO SUFFER MI, HEART FAILURE, STROKE, CKD OR DEATH OVER 3.8 YEARS OF FOLLOW UP. (DAUGHTERY ET AL. INCIDENCE AND PROGNOSIS OF RESISTANT HYPERTENSION IN HYPERTENSIVE PATIENTS. CIRCULATION. 2012;125:1635-42)
DEFINITION OF RESISTANT HYPERTENSION

• BP THAT REMAINS ELEVATED DESPITE USE OF 3 ANTIHYPERTENSIVE AGENTS (INCLUDING A DIURETIC) AT THE MAXIMALLY TOLERATED DOSES

• ALSO INCLUDES PATIENTS WHO BP IS CONTROLLED ON ≥ 4 ANTIHYPERTENSIVE MEDICATIONS ("CONTROLLED RH")

• EXCLUDES PATIENTS WITH “WHITE COAT EFFECT” AND MEDICATION NONCOMPLIANCE

• THESE PATIENTS ARE AT HIGHER RISK OF CVD EVENTS AND DEATH

• ALSO MORE LIKELY TO HAVE A SECONDARY CAUSE OF HYPERTENSION COMPARED WITH THOSE WHO ARE CONTROLLED ON MEDICATIONS
PSEUDORESISTANT HYPERTENSION
APPROACH TO RESISTANT HYPERTENSION

• CONFIRM TREATMENT RESISTANCE
• ASSESSMENT OF OVER THE COUNTER SUPPLEMENTS
• DETERMINATION OF MEDICATION ADHERENCE
  • 25% OF PATIENTS NEWLY INITIATED ON ANTIHYPERTENSIVES FAIL TO FILL THEIR PRESCRIPTION
  • REVIEW OF STUDIES ON MEDICATION ADHERENCE IN PATIENTS WITH HYPERTENSION IDENTIFIED RATES OF NONADHERENCE RANGING FROM 7% USING PHARMACY REFILL RECORDS TO > 60% USING SERUM DRUG LEVELS IN A REFERRAL CLINIC
  • THERE IS NO GOLD STANDARD FOR MEASURING ADHERENCE - PILL COUNT, SELF-REPORTING AND PRESCRIPTION REFILL DATA ARE SIMPLE AND WIDELY USED.
AMBULATORY BP MONITORING

• VALUABLE TOOL FOR BP ASSESSMENT AND INDICATIONS FOR THIS INCLUDE:
  • SUSPECTED WHITE COAT HYPERTENSION
  • SUSPECTED EPISODIC HYPERTENSION (EX. PHEOCHROMOCYTOMA)
  • HYPERTENSION RESISTANT TO INCREASING MEDICATIONS
  • AUTONOMIC DYSFUNCTION

• WORN FOR 24-48 HOURS AND MEASURES BP EVERY 20 MINUTES DURING DAYTIME AND 30 MINS DURING THE NIGHT

• DATA PROVIDED BY THE ABPM INCLUDES THE 24 HOUR AVERAGE BP, AWAKE BP, NIGHTTIME BP, NOCTURNAL DIPPING
NOCTURNAL DIPPING

- The average nocturnal blood pressure is 15 percent lower than daytime values in both normotensive and hypertensive patient.

- Inability of the BP to fall by 10 percent during sleep is called nondipping.

- The underlying mechanisms of nondipping are unknown, but intrinsic renal defects may contribute as well as melatonin levels.

- Independent of the degree of hypertension, nondipper status has been found to be a risk factor for progression to LVH, heart failure, and other cardiovascular complications.

- The presence of sleep apnea should be evaluated in nondippers.

- Reversal of nondipping with nocturnal dosing of antihypertensives is of uncertain benefit. There have not been trials powered for this intervention.
LIFESTYLE FACTORS CONTRIBUTING TO RH

• OBESITY: ADIPOSITY RESULTS IN ENHANCED SALT SENSITIVITY, VASCULAR DYSFUNCTION AND ACTIVATION OF THE RAS
• INCREASED SODIUM INTAKE THAT LEADS TO VOLUME EXPANSION, VASCULAR DYSFUNCTION, ARTERIAL STIFFNESS, IMPAIRED RAS
• ETOH CONSUMPTION
• PHYSICAL INACTIVITY
ASSESS FOR SECONDARY HYPERTENSION

- PRIMARY ALDOSTERONISM
- RENAL PARENCHYMAL DISEASE
- RENAL ARTERY STENOSIS
- PHEOCHROMOCYTOMA
- SLEEP DISORDERS
- COARCTATION OF THE AORTA

- LESS COMMON ENDOCRINE ETIOLOGIES
  - HYPO/HYPERTHYROIDISM
  - HYPERCALCEMIA
  - CONGENITAL ADRENAL HYPERPLASIA
  - ACROMEGALY
  - CUSHING SYNDROME
PRIMARY ALDOSTERONISM

• ALDOSTERONE PRODUCTION IS HIGH AND IS INDEPENDENT OF THE RENIN-ANGIOTENSIN (RAS) SYSTEM AND WHERE ALDOSTERONE IS NOT SUPPRESSED BY SODIUM LOADING

• ASSOCIATED WITH MAJOR INCREASE IN CV EVENTS COMPARED TO THOSE WITH PRIMARY HYPERTENSION INCLUDING STROKE, MI AND ATRIAL FIBRILLATION

• ASSOCIATED WITH LEFT VENTRICULAR HYPERTROPHY, DIASTOLIC DYSFUNCTION AND HEART FAILURE

• OBSERVATIONAL STUDIES SUGGEST THAT 20% OF PATIENTS WITH RESISTANT HYPERTENSION HAVE PRIMARY ALDOSTERONISM
SCREENING FOR PRIMARY ALDOSTERONISM

- RATIO OF PLASMA ALDOSTERONE: RENIN RATIO (ARR)
- SAMPLE SHOULD BE TAKEN IN THE MORNING AND THE PATIENT SHOULD BE SEATED FOR 30 MINS BEFORE SAMPLE IS OBTAINED
- POSITIVE SCREENING OCCURS WHEN ARR > 30 OR > 20 IF THE PLASMA ALDOSTERONE IS > 16NG/DL
- NOTE: HYPOKALEMIA CAN REDUCE ALDOSTERONE SECRETION, SO THIS SHOULD BE REPLETED WITH ORAL POTASSIUM PRIOR TO THE STUDY
- AGENTS SUCH AS ALDACTONE, EPLERENONE, ACE, ARBS SHOULD BE DISCONTINUED FOR AT LEAST 1 MONTH PRIOR TO TESTING
PRIMARY ALDOSTERONISM

• IF SCREENING IS POSITIVE, THEN CONFIRMATORY TESTING CAN BE PERFORMED (SALINE SUPPRESSION TEST, ORAL SALT LOAD OR CAPTOPRIL TEST)

• IF THIS IS CONFIRMED, THEN THE SUBTYPE CLASSIFICATION CAN BE DETERMINED BY ADRENAL VENOUS SAMPLING

• UNILATERAL DISEASE CAN BE TREATED WITH A LAPARASCOPIC ADRENALECTOMY

• BILATERAL DISEASE (IDIOPATHIC HYPERALDOSTERONISM) WILL SHOW IMPROVED BP CONTROL WITH WITH ALDACTONE OR EPLERENONE
RENAL PARENCHYMAL DISEASE

• CHRONIC KIDNEY DISEASE IS BOTH A CAUSE AND A COMPLICATION OF UNCONTROLLED HYPERTENSION

• CREATININE > 1.5 MG/DL WAS A STRONG PREDICTOR OF FAILURE TO ACHIEVE BP GOALS IN THE ALLHAT TRIAL

• TREATMENT RESISTANCE IS RELATED TO INCREASED SODIUM AND FLUID RETENTION, LEADING TO VOLUME EXPANSION

• MAY ALSO NEED TO EVALUATE FOR OTHER SECONDARY CAUSES OF HYPERTENSION INCLUDING RENAL ARTERY STENOSIS, PRIMARY ALDOSTERONISM, OR OTHER ENDOCRINE ETIOLOGIES.
SPECIAL CONSIDERATIONS TO PATIENTS WITH CKD

- Higher doses of diuretic are required
- Chlorthalidone is more effective in lowering BP
- Torsemide may be preferred in advanced CKD due to greater bioavailability and can be dosed daily
- Consider combination of thiazide and loop diuretic for to augment diuresis
- Be very cautious with ARB in CKD patients as they are more prone to develop hyperkalemia
RENAL ARTERY STENOSIS

• RECENT STUDIES SUGGEST THAT UP TO 24% OF OLDER PATIENTS (MEAN AGE 71 YEARS) WITH RESISTANT HYPERTENSION HAVE SIGNIFICANT RENAL ARTERIAL DISEASE

• MOST COMMON CAUSE IS ATHEROSCLEROTIC DISEASE, BUT OTHER ETIOLOGIES ARE FIBROMUSCULAR DYSPLASIA, RENAL DISSECTION, TAKAYASU ARTERITIS, RADIATION FIBROSIS, RENAL ARTERY OBSTRUCTION FOLLOWING AORTIC STENT GRAFTS

• CLINICAL MANIFESTATIONS RANGE FROM ASYMPTOMATIC, ACCELERATING HYPERTENSION, TO RENAL INSUFFICIENCY
PATHOPHYSIOLOGY OF RENOVASCULAR HYPERTENSION

• IMPAIRMENT OF RENAL ARTERIAL BLOOD FLOW RESULTS IN ACTIVATION OF THE RENIN-ANGIOTENSIN-ALDOSTERONE AXIS WITH SEQUELAE THAT INCLUDE: VASOCONSTRICTION, SODIUM AND WATER RETENTION, ALDOSTERONESECRETION, SYMPATHETIC NERVOUS SYSTEM ACTIVATION, VASCULAR REMODELING, AND RESULTANT HYPERTENSION

• Renal duplex ultrasound is a valuable first line study that provides hemodynamic information.

• Measures the velocity in the renal arteries and in the aorta.

• If the renal-aortic ratio (RAR > 3.5), then there is hemodynamically significant lesion.

• If there is evidence of disease, would be reasonable to consider a CT or MRI to assess anatomy prior to any intervention.

• CT is limited in atherosclerotic disease with a great deal of calcification.
TREATMENT OPTIONS

• MEDICAL THERAPY WITH ACE OR ARB Confirms a long term mortality benefit

• INDICATIONS FOR INTERVENTION WITH RENAL STENTING INCLUDE:
  • CARDIAC DISTURBANCE – FLASH PULMONARY EDEMA OR ACS WITH SEVERE HYPERTENSION
  • RESISTANT HYPERTENSION
  • ISCHEMIC NEPHROPATHY WITH CKD AND GLOBAL RENAL ISCHEMIA (UNILATERAL SIGNIFICANT RAS WITH SOLITARY KIDNEY OR BILATERAL SIGNIFICANT RAS) WITHOUT OTHER EXPLANATION
STENTING AND MEDICAL THERAPY FOR ATHEROLOGINOTIC RENAL-ARTERY STENOSIS


- RANDOMIZED PATIENTS TO MEDICAL THERAPY OR MEDICAL THERAPY + RENAL ARTERY STENTING IN A 1:1 FASHION
- MEDICAL THERAPY INCLUDED ARB, HCTZ AND CCB
- PRIMARY END POINT WAS THE OCCURRENCE OF A MAJOR CARDIOVASCULAR OR RENAL EVENT — A COMPOSITE OF DEATH FROM CARDIOVASCULAR OR RENAL CAUSES, STROKE, MYOCARDIAL INFARCTION, HOSPITALIZATION FOR CONGESTIVE HEART FAILURE, PROGRESSIVE RENAL INSUFFICIENCY, OR THE NEED FOR PERMANENT RENAL-REPLACEMENT THERAPY
Stenting and Medical Therapy for Atherosclerotic Renal-Artery Stenosis. Cooper et al., January 2, 2014

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<th>End Point</th>
<th>Stenting plus Medical Therapy (N = 415)</th>
<th>Medical Therapy Only (N = 472)</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value</th>
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<td>Primary end point: death from cardiovascular or renal causes, stroke, myocardial infarction, hospitalization for congestive heart failure, progressive renal insufficiency, or permanent renal replacement therapy</td>
<td>63 (15.1)</td>
<td>69 (15.8)</td>
<td>0.94 (0.76–1.17)</td>
<td>0.58</td>
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Components of primary end point:
- Death from cardiovascular or renal causes: 20 (4.4) vs. 20 (4.2)
- Stroke: 12 (2.6) vs. 16 (3.4)
- Myocardial infarction: 30 (6.5) vs. 27 (5.7)
- Hospitalization for congestive heart failure: 27 (5.9) vs. 26 (5.5)
- Progressive renal insufficiency: 68 (14.8) vs. 77 (16.3)
- Permanent renal replacement therapy: 4 (0.9) vs. 3 (0.6)

Secondary clinical end point:
- Death from any cause: 63 (15.7) vs. 76 (16.1) | 0.80 (0.58–1.12) | 0.20 |
- Death from cardiovascular causes: 43 (8.9) vs. 45 (9.5) | 0.89 (0.58–1.36) | 0.60 |
- Death from renal causes: 2 (0.4) vs. 1 (0.2) | 3.89 (0.17–20.83) | 0.60 |
- Stroke: 16 (3.5) vs. 23 (4.9) | 0.68 (0.36–1.30) | 0.25 |
- Myocardial infarction: 40 (8.7) vs. 37 (7.8) | 1.09 (0.70–1.71) | 0.70 |
- Hospitalization for congestive heart failure: 39 (8.5) vs. 39 (8.5) | 1.00 (0.44–1.56) | 0.99 |
- Progressive renal insufficiency: 77 (18.8) vs. 89 (18.9) | 0.86 (0.44–1.77) | 0.54 |
- Permanent renal replacement therapy: 16 (3.5) vs. 8 (1.7) | 1.98 (0.85–4.52) | 0.11 |

* The hazard ratios were calculated with the use of multivariable proportional-hazards regression. P-values were calculated with the use of the log-rank statistic.

† Only the first event per participant is included in the composite.
‡ Components of the composite are included only if it was the first event contributing to the primary end point.
§ The first event for each component of the primary composite end point is included as a secondary end point.

![Hazard ratio with stenting, 0.94 (95% CI, 0.76–1.17) P=0.58 by log-rank test](image)

### Event-Free Survival (%)
- Stent plus medical therapy
- Medical therapy alone

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DISCUSSION

• NO STATISTICALLY SIGNIFICANT DIFFERENCE BETWEEN THE MEDICAL THERAPY ARM AND THE STENTING ARM

• THE STENTING ARM SAW A REDUCTION IN BP BY 2MMHG, BUT THIS DID NOT CORRELATE TO A REDUCTION OF CLINICAL EVENTS

• LIMITATIONS
  • DEBATE ON THE SEVERITY OF STENOSIS REQUIRED TO JUSTIFY INTERVENTION
  • FMD WAS NOT INCLUDED IN THIS TRIAL
  • SOME PATIENTS WHO WERE SCREENED AND DEEMED TO BE ELIGIBLE WERE NOT ENROLLED IN THE TRIAL, INCLUDING PATIENTS WHO WERE NOT ENROLLED BECAUSE OF THE PREFERENCE OF THEIR PHYSICIAN
FIBROMUSCULAR DYSPLASIA

- Noninflammatory, nonatherosclerotic disorder that can affect any layer of the arterial wall (intima, media and adventitia).
- Can lead to arterial stenosis, occlusion, aneurysm, dissection, and arterial tortuosity.
- Most commonly affects the renal and carotid arteries, but also found in the external iliac arteries.
- Leads to hypertension due to activation of the renin-angiotensin system due to arterial stenosis.
TREATMENT

• MEDICAL THERAPY
  • INITIAL CLASS OF DRUG IS AN ACE INHIBITOR OR ARB
  • IF BP TARGET IS NOT REACHED, THEN CONSIDER THIAZIDE DIURETIC OR LONG ACTING CALCIUM CHANNEL BLOCKER

• REVASCULARIZATION VIA ANGIOPLASTY
  • THERE ARE NO RANDOMIZED STUDIES TO COMPARE MEDICAL THERAPY AND REVASCULARIZATION. THE DATA FROM RENAL ARTERY STENTING FOR ATHEROSCLEROTIC DISEASE CANNOT BE
  • INDICATIONS FOR PATIENTS WITH FMD AND HYPERTENSION TO UNDERGO REVASCULARIZATION
    • RECENT ONSET OF HYPERTENSION
    • RH ON APPROPRIATE THREE DRUG REGIMEN.
    • INABILITY TO TOLERATE THEIR MEDICATION REGIMEN
SHORT AND LONG TERM OUTCOMES


- Technical success was achieved in all patients.

- Primary patency at 5 years is 66%.

- Restenosis rate is 28% at 5 years.

- Immediate improvement in hypertension was seen in 72% of patients.

- Predictors of long-term clinical benefit:
  - Duration of hypertension < 8 years.
  - Creatinine < 1.5 mg/dL.
  - Ipsilateral kidney size > 9 cm.
PHEOCHROMOCYTOMA

• CATECHOLAMINE-SECRETING TUMORS THAT ARISE FROM CHROMAFFIN CELLS OF THE ADRENAL MEDULLA AND THE SYMPATHETIC GANGLIA

• RARE CAUSE OF RESISTANT HYPERTENSION, ACCOUNTING FOR < 0.2% OF THE PATIENTS WITH HYPERTENSION

• CLASSIC TRIAD OF SYMPTOMS ARE EPISODIC HEADACHES, SWEATING AND TACHYCARDIA
  • LESS COMMON SYMPTOMS INCLUDE EPISODIC HYPERTENSION AND CARDIOMYOPATHY (DUE TO THE CATECHOLAMINE SURGES, SIMILAR TO TAKOTSUBO CARDIOMYOPATHY)
  • SYMPTOMS ARE DUE TO THE HYPERSECRETION OF NOREPINEPHrine, EPINEPHrine OR DOPAMINE
EVALUATION

• DIAGNOSIS IS MADE BASED ON INITIAL BIOCHEMICAL TESTING AND FOLLOW UP IDENTIFICATION VIA IMAGING STUDIES

• DISCONTINUE INTERFERING MEDICATIONS SUCH AS: TRICYCLIC ANTIDEPRESSANTS, LEVODOPA, DRUGS CONTAINING ADRENERGIC RECEPTOR AGONISTS (EX. DECONGESTANTS) FOR AT LEAST 2 WEEKS

• ADDITIONALLY, TESTS SHOULD BE AVOIDED IN SITUATIONS OF APPROPRIATELY INCREASED CATECHOLAMINE LEVELS – IE. PHYSICAL STRESS, HOSPITALIZATION

• SCREENING TEST IS MEASUREMENT OF CIRCULATING CATECHOLAMINE METABOLITES. CATECHOL O-METHYL TRANSFERASE RELEASES NORMETANEPHRINE AND METANEPHRINE FROM THE TUMORS, WHICH ARE MEASURED AS PLASMA FREE OR URINARY FRACTIONATED METANEPHRINES
EVALUATION

• IMAGING SHOULD ONLY BE PURSUED IF BIOCHEMICAL SCREENING IS POSITIVE.

• RECOMMENDATIONS ARE TO START WITH A CT ABDOMEN FIRST, WITH MRI BEING AN ALTERNATIVE MODALITY

• IF IDENTIFIED, THE PATIENT SHOULD BE REFERRED TO THE SURGICAL TEAM FOR CONSIDERATION OF REMOVAL
SLEEP DISORDERS AND RESISTANT HYPERTENSION

• OSA IS VERY COMMON IN PATIENTS WITH RH, WITH PREVALENCE RATES OF 70-90%.
• WHEN PRESENT, OSA IS OFTEN SEVERE
• THOUGHT TO BE RELATED TO INCREASED FLUID RETENTION AND UPPER AIRWAY EDEMA
• TREATMENT OF PATIENTS WITH OSA AND RH WITH CPAP WILL RESULT IN MODEST REDUCTIONS IN BP
• HOWEVER, RECENT RANDOMIZED STUDY DEMONSTRATED THAT CPAP USAGE DOES NOT REDUCE CVD EVENTS IN PATIENTS WITH OSA AND ESTABLISHED CVD
INITIAL EVALUATION

- BASIC METABOLIC PANEL
- URINALYSIS
- RENIN/ALDOSTERONE LEVELS
- CONSIDER PLASMA FREE METANEPHRINES (OR 24 HOURS URINARY METANEPHRINE) IF SUSPICION OF PHEOCHROMOCYTOMA
- CONSIDER POLYSOMNOGRAPHY
- RENAL ARTERY DOPPLER
  - CONSIDER IN YOUNG PATIENTS WITH NEWLY DIAGNOSED HYPERTENSION
  - CONSIDER IN PATIENTS WITH KNOWN CAD AND WITH ABDOMINAL BRUITS
NON PHARMACOLOGIC LIFESTYLE CHANGES

• WEIGHT LOSS
  • WEIGHT REDUCING DIETS HAVE BEEN SHOWN TO REDUCE BP BY 4.5/3.2MMHG IN A RECENT META-ANALYSIS (347).
  • THE EFFECT OF PHARMACOLOGIC WEIGHT LOSS IS NOT AS CLEAR (IE. ORLISTAT)
  • GUIDELINES SUGGEST THAT OBESE PATIENTS WITH HYPERTENSION VIA CALORIC RESTRICTION AND LIFESTYLE CHANGES AIM FOR 5-10% WEIGHT LOSS.
  • INTERESTINGLY, LONG TERM PERSISTENT OF WEIGHT LOSS AND SUSTAINED BP EFFECTS ARE NOT WELL KNOWN.

• DIETARY SALT RESTRICTIONS
  • ESTIMATED 1G REDUCTION IN DAILY SODIUM INTAKE LEADS TO 2.1MMHG REDUCTION IN BP IN HYPERTENSIVE PATIENTS.
  • THE OPTIMAL INTAKE OF DIETARY SODIUM IS NOT CLEAR – BUT THE GREATEST REDUCTIONS ARE ACHIEVED BY FOLLOWING A MODEST RESTRICTION OF 2G/DAY.
NON PHARMACOLOGIC LIFESTYLE CHANGES

- DASH DIET
- EXERCISE
  - AHA RECOMMENDATIONS ARE 150 MINS/WEEK OF MODERATE TO INTENSE AEROBIC ACTIVITY, SUPPLEMENTED WITH 2-3 SESSIONS OF LIGHT RESISTANCE TRAINING
  - IN THE RH POPULATION, THIS MAY BE DIFFICULT AND LOW INTENSITY PHYSICAL ACTIVITY, 6 MINUTES HOURLY OVER AN 8 HOUR PERIOD IN SEDENTARY INDIVIDUALS LOWERED BP 14MMHG/8MMHG
PHARMACOLOGICAL INTERVENTIONS

• Once identifiable causes of hypertension have been eliminated, therapeutic approaches need to be considered.

• Verify the presence of and address any barriers to adherence.
• Optimize 3-4 medication regimen
  • Should include thiazide diuretic, ACE/ARB, CCB
• Transition to chlorthalidone
• Consider addition of aldactone or eplerenone
• Add a beta blocker if HR permits
• Consider hydralazine (with heart failure patients, this should be added with Imdur)
• Consider minoxidil
DEVICE BASED INTERVENTION FOR RH

- RENAL NERVE DENERVATION
- CENTRAL ARTERIOVENOUS ANASTOMOSIS
RENAL NERVE DENERVATION

• The sympathetic nervous system plays an integral role in the development and also progression of hypertension.

• In the 1940s, surgical sympathectomy (lumbar sympathectomy) was shown to dramatically reduce hypertension, cardiac size, and led to improved renal function.

• This was also shown to decrease cardiovascular events in an era before antihypertensive agents were easily accessible.

• Unfortunately, these patients also suffered from orthostatic hypotension, and bowel/bladder incontinence.
SYMPLECTICITY HTN-3

- FIRST SHAM CONTROLLED, PROSPECTIVE RANDOMIZED STUDY IN THE FIELD OF RADIOFREQUENCY BASED RENAL ARTERY DENERVATION.

- NONBLINDED STUDIES HAD PREVIOUSLY SUGGESTED SOME BENEFIT IN EUROPE AND ASIA.

- FAILED TO MEET PRIMARY AND SECONDARY OUTCOMES
  - PRIMARY EFFICACY END POINT WAS THE MEAN CHANGE IN OFFICE SYSTOLIC BLOOD PRESSURE FROM BASELINE TO 6 MONTHS IN THE DENERVATION GROUP, AS COMPARED WITH THE MEAN CHANGE IN THE SHAM CONTROL GROUP.
  - THE STUDY WAS ALSO POWERED FOR ASSESSMENT OF A SECONDARY EFFICACY END POINT: THE CHANGE IN MEAN 24-HOUR AMBULATORY SYSTOLIC BLOOD PRESSURE AT 6 MONTHS
IS RENAL DENERVATION DEAD?

- NO WAY TO REALLY IDENTIFY IF THE NERVES HAVE BEEN ABLATED WITH THE THERAPY.
- HOW MUCH DENERVATION WILL PROVIDE A RESPONSE?
- WOULD CHANGES IN THE CATHETER TECHNOLOGY LEAD TO IMPROVED RESPONSES?
RADIANCE-HTN

- A study utilizing a different catheter technology
- Evaluated the use of renal denervation using endovascular ultrasound technology.
- This was also a multicenter, international, single-blind, randomized, sham-controlled trial.
- 146 were randomized to undergo renal denervation (N=74) or a sham procedure (N=72).
- The reduction in daytime ambulatory systolic blood pressure was greater with renal denervation (−8.5 mm Hg, SD 9.3) than with the sham procedure (−2.2 mm Hg, SD 10.0)
- No major adverse events were reported in either group.
CENTRAL ARTERIOVENOUS FISTULA

- AN OVERLOOKED CAUSE OF RESISTANCE TO CONVENTIONAL ANTIHYPERTENSIVE TREATMENT IS ARTERIAL STIFFNESS

- CREATION OF A AV FISTULA IN THE ILIAC ARTERY AND VEIN ADDS A LOW PRESSURE, HIGHLY COMPLIANT VENOUS SEGMENT TO THE ARTERIAL TREE

- ONE YEAR DATA SUGGESTS THAT CREATION OF THE AV FISTULAS LED TO A LARGE REDUCTION IN OFFICE SYSTOLIC AND DIASTOLIC BPS (26.9 AND 20.1 MM HG, RESPECTIVELY)

Central arteriovenous anastomosis for the treatment of patients with uncontrolled hypertension (the ROX CONTROL HTN study): a randomised controlled trial. The Lancet. VOLUME 385, ISSUE 9978, P1634-1641, APRIL 25, 2015
SUMMARY

• IDENTIFICATION OF RESISTANT HYPERTENSION
  • EXCLUDE PSEUDORESISTANCE – POOR ADHERENCE, WHITE COAT HYPERTENSION, UNTREATED HYPERTENSION, POOR OFFICE BP READINGS

• EXCLUDE SECONDARY CAUSES OF RH
  • PRIMARY ALDOSTERONISM, CHRONIC KIDNEY DISEASE, RAS, PHEOCHROMOCYTOMA, SLEEP DISORDERED BREATHING, THYROID DISEASE

• LIFESTYLE MODIFICATION

• PHARMACOLOGICAL THERAPY

• NEW HORIZONS FOR THERAPY : RENAL DENERVATION AND CENTRAL AV FISTULA CREATION