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- **More than 35 years of clinical experience both in Internal Medicine & Nephrology**
- **Fellow of American college, Royal college Edin and National Academy of Medical Science**
- Awarded **Searle oration** (2002), **Dr Shurvir Singh Visiting Professorship** (2003),**State Award by Delhi Governmen**t (2007-8), **IMA Distinguished Doctors award** (2009), **IMA National President Appreciation Award** & **IMA Medachievers award** (2014)
- ***NABH Assessor (clinical trial) 2015***
- **Governing body member of API and executive member of ICP**
- **Governing Council Member, ACP India chapter**
- **Past President; Hypertension Society of India**
- **President; North Zone-Indian Society of Nephrology**
- **More than 150 publications in national and international peer reviewed journals**

Hypertension in Special Situations

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Contents of Presentation

- Epidemiology of Hypertension
- Factors Contributed to High Blood Pressure
- Hypertension in special situations –
  - Diabetes Mellitus
  - Cerebrovascular Disease
  - Pregnancy
  - Elderly
  - Chronic Kidney Disease
  - CAD & CCF
  - COPD, Dyslipidaemia & Obesity
  - Resistant Hypertension
- Summary

Introduction

World Health Day 2013

World Health Organization

- Hypertension is a **silent**, **invisible killer** that rarely causes symptoms.
- We live in a rapidly **changing environment.**
- Throughout the world, human health is being shaped by:
  - **Demographic ageing**
  - **Rapid urbanization**
  - **The globalization of unhealthy lifestyles**
- Increasingly, wealthy and resource-constrained countries are facing the same health issues.
- As a result **Non-communicable diseases have overtaken** infectious diseases as the world's leading cause of mortality.
- Increasing public awareness is key, as is access to early detection.

A global brief on HYPERTENSION

Silent killer, global public health crisis

World Health Day 2013

World Health Organization

- Globally cardiovascular disease accounts for approximately 17 million deaths a year, nearly one third of the total.
- Of these complications of hypertension account for 9.4 million deaths worldwide every year.
- Hypertension is responsible for at least 45% of deaths due to heart disease and 51% of deaths due to stroke.

World Health Day 2013

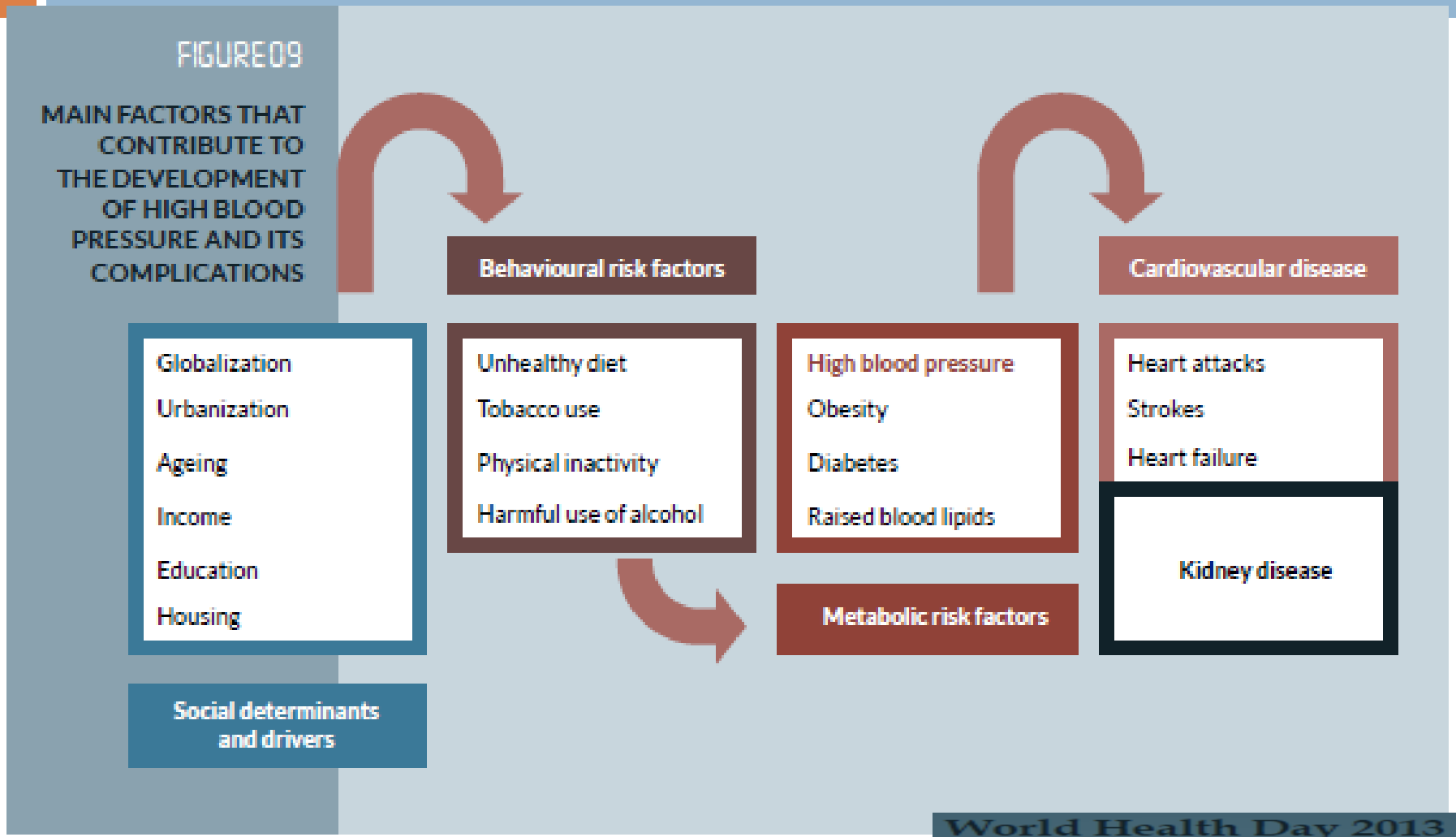
World Health Organization

Prevalence of Hypertension:India

- Prevalence of hypertension: ***25% in Urban India and 10 -15% in Rural India.***
- Overall prevalence of hypertension in India ***by 2020 will be 159.46/1000 population.***
- In the INTERHEART and INTERSTROKE study, hypertension accounted for 17.9% and 34.6% of population attributable risk of various cardiovascular risk factors for coronary artery disease and stroke respectively.

Indian Guidelines on Hypertension JAPI 2013

Factors Contributed to High Blood Pressure



World Health Day 2013

World Health Organization

Hypertension Management

Starts with lifestyle modification,,,,,,

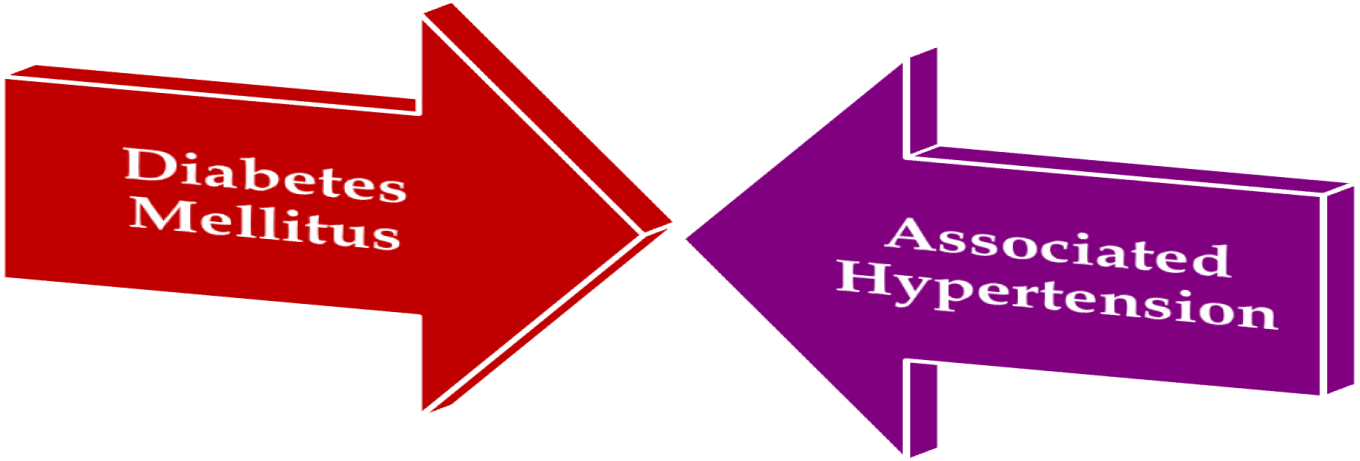
Life Style Modification

American Heart Association®

Modification	Recommendation	Approximate SBP Reduction (Range)**
Reduce weight	Maintain normal body weight (body mass index 18.5–24.9 kg/m^2)	5–20 mm Hg/10 kg
Adopt DASH*[5] eating plan	Consume a diet rich in fruits, vegetables, and low-fat dairy products with a reduced content of saturated and total fat	8–14 mm Hg
Lower sodium intake[6]	a. Consume no more than 2,400 mg of sodium/day; b. Further reduction of sodium intake to 1,500 mg/day is desirable since it is associated with even greater reduction in BP; and c. Reduce intake by at least 1,000 mg/day since that will lower BP, even if the desired daily sodium intake is not achieved	2–8 mm Hg
Physical activity	Engage in regular aerobic physical activity such as brisk walking (at least 30 min per day, most days of the week)	4–9 mm Hg
Moderation of alcohol consumption	Limit consumption to no more than 2 drinks (e.g., 24 oz beer, 10 oz wine, or 3 oz 80-proof whiskey) per day in most men, and to no more than 1 drink per day in women and lighter weight persons	2–4 mm Hg

Hypertension Management in special situations

Diabetic Hypertension



Diabetic Hypertension

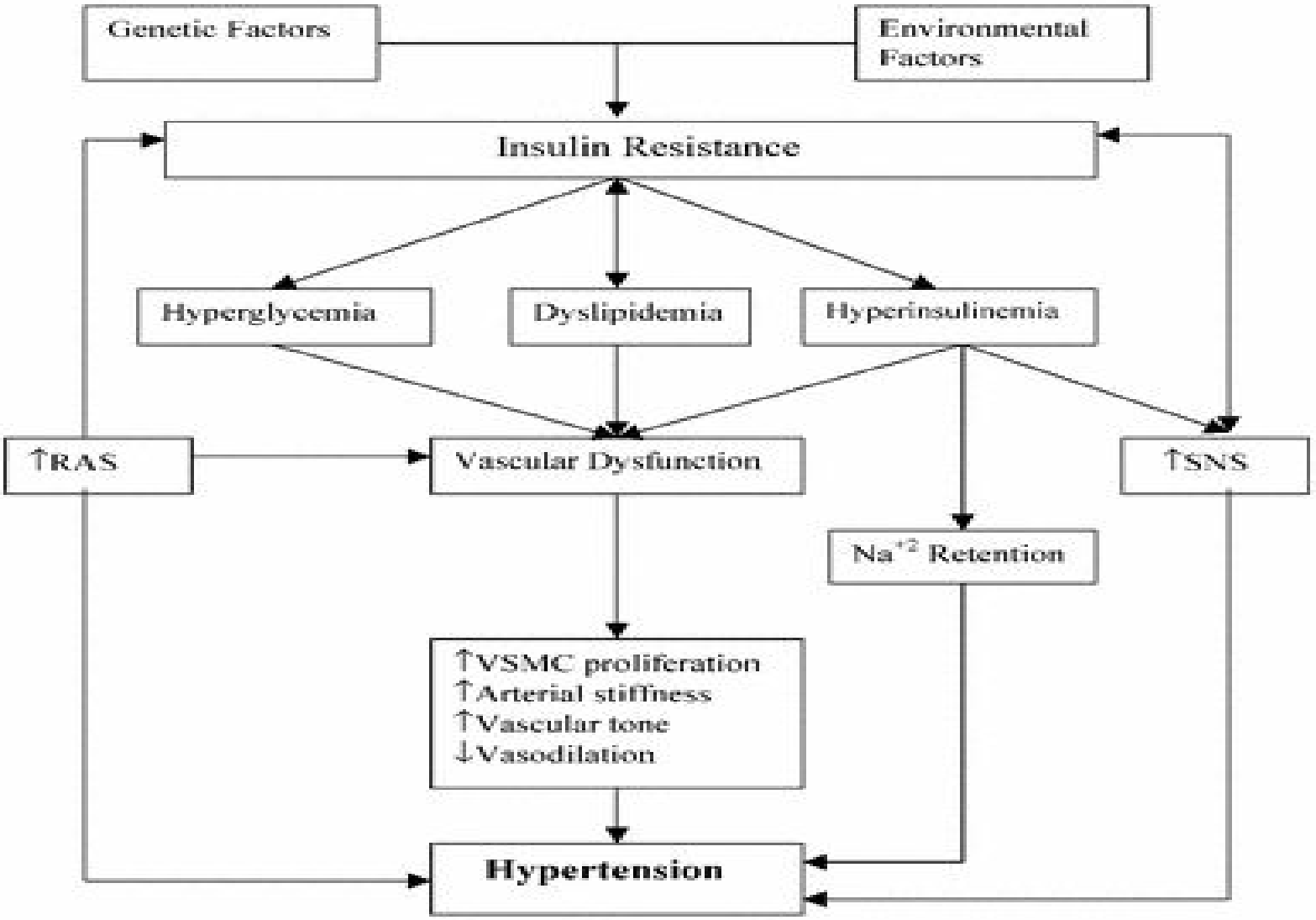
- New onset **DM is 2.5** times in HTN
- **Systolic HTN** more common in DM (65 %)
- Patients with type 1 diabetes, the incidence of hypertension rises from *5 % at 10 yrs duration, to 33 % at 20 yrs, and 70 % at 40 yrs*.
- **30% to 35% of hypertensive patients** are detected to have co-existing diabetes mellitus
- The incidence of *hypertension eventually reaches 75 to 85 % in patients with progressive diabetic nephropathy.*
- Only 1/4 of HTN in DM is controlled

Indian Guidelines on Hypertension JAPI 2013

What Causes HTN in DM

- Metabolic Syndrome
- Excessive RAAS activity is the main mechanism
- HTN due to nephropathy in T2DM – GS - KWL
- Renal scarring - Recurrent pyelonephritis
- Endocrine causes for both HTN & DM
  - Cushing's, Conn's, Pheochromo, Acromegaly
- Coincidental – DM on existing HTN
- Diabetogenic antihypertensive drugs (D and B)
- Drugs causing both HTN & DM – OCP, CS

PATHOGENESIS: High BP in DM



Target Blood Pressure in Diabetes

What Should Be The BP Goal

Guideline	Population	Goal BP, mm Hg	Initial Drug Treatment Options
JNC 8 2014 Hypertension guideline	General ≥60 y	<150/90	**Nonblack:** thiazide-type diuretic, ACEI, ARB, or CCB
	General <60 y	<140/90	**Black:** thiazide-type diuretic or CCB
	Diabetes	<140/90	Thiazide-type diuretic, ACEI, ARB, or CCB
	CKD	<140/90	ACEI or ARB
NICE 2011	General <80 y	<140/90	**<55 y**: ACEI or ARB
	General ≥80 y	<150/90	≥55 y or black: CCB
KDIGO 2012	CKD no proteinuria	≤140/90	ACEI or ARB
	CKD + proteinuria	≤130/80	

JAMA. 2013;():. doi:10.1001/jama.2013.284427

HOT study, UKPDS study & ADVANCE Study support a goal blood pressure for diabetic patients of **less than 140/90 mmHg.**

Choice of Anti-hypertensive agents in Diabetes

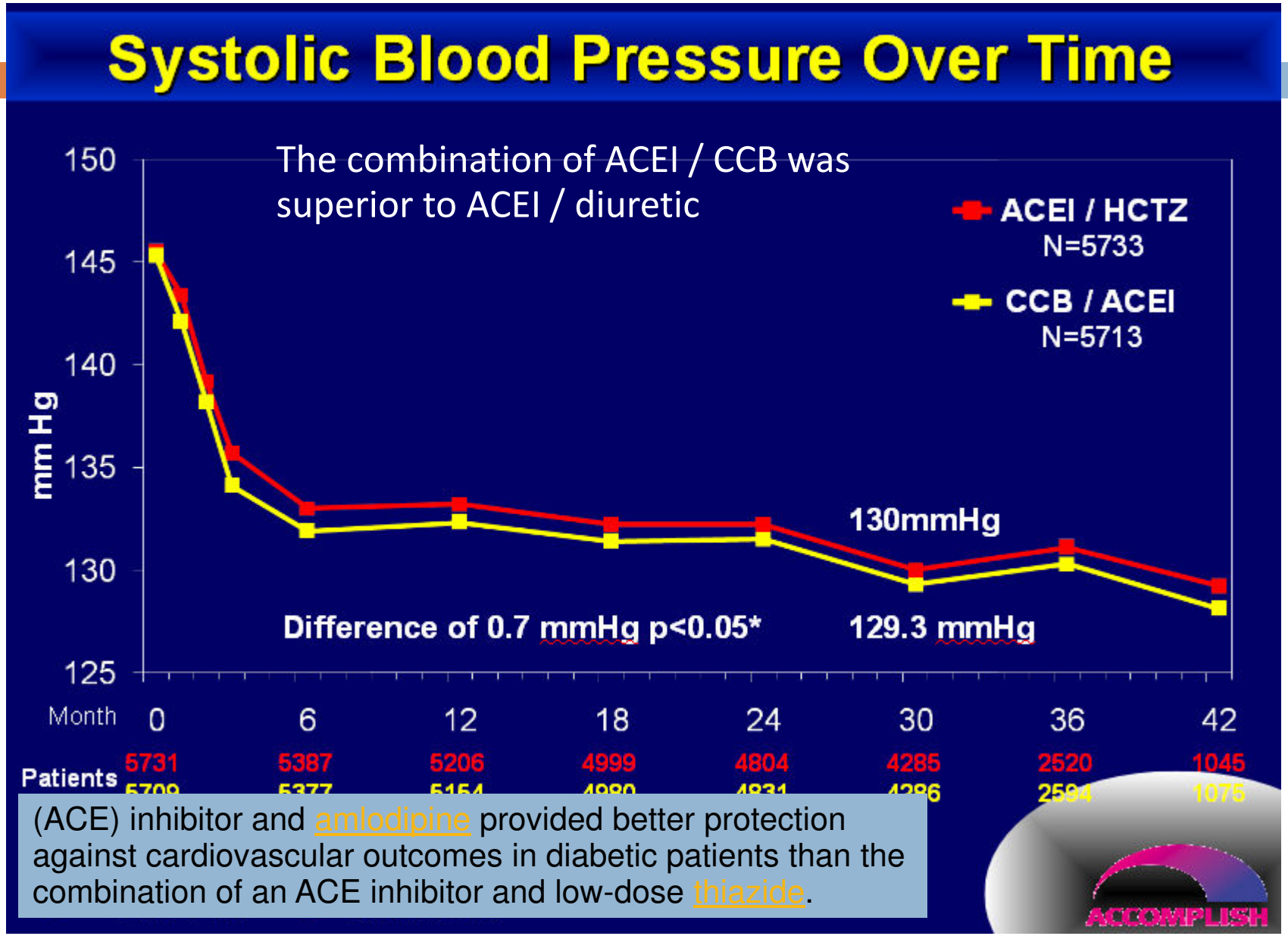
- The choice of antihypertensive agents in diabetic patients is based upon their ability to do the following:
  - Prevent mortality
  - Prevent adverse cardiovascular events, such as myocardial infarction, stroke, and heart failure
  - Prevent the progression of renal disease, if present

Diabetic Hypertension: Management

ACE inhibitors in the HOPE trial and ***ARBs*** in the ONTARGET trial have emphasised the importance of RAAS blockade to reduce the risk of complications of diabetes (Diabetic Nephropathy).

ESH and ESC Guidelines 2013

ACCOMPLISH Study



(ACE) inhibitor and amlodipine provided better protection against cardiovascular outcomes in diabetic patients than the combination of an ACE inhibitor and low-dose thiazide.

Summary: Antihypertensive in DM

- In patients with increased albuminuria, treat with an ACE inhibitor or an ARB.
- In patients without increased albuminuria, initial monotherapy can consist of an ACE inhibitor, ARB, thiazide diuretic, or calcium channel blocker.
  - Thiazide diuretics have the disadvantage of an adverse effect on glucose metabolism, choose an ACE inhibitor or ARB even in patients without albuminuria.
- In patients who require more than one drug to control their blood pressure, treat with a combination of an ACE inhibitor or ARB and a dihydropyridine calcium channel blocker.
- Combination therapy with an ACE inhibitor and ARB or direct renin inhibitor Should be avoided.

Hypertension Management in Diabetic Pregnant Mother

- **Methyldopa, calcium channel blockers** and **labetolol.**
- The use **of ACE inhibitors/ARBs is contraindicated.**
- Use of *diuretics during pregnancy can lead to reduction of plasma volume* resulting in decreased fetal growth / fetal damage.

ESH and ESC Guidelines 2013

Hypertension with Cerebrovascular Disease

Hypertension with Cerebrovascular Disease

- Antihypertensive therapy has been associated with *reductions in stroke incidence averaging 35% to 40%.*
- In acute intracerebral hemorrhage - **BP should be maintained below 180/105 mm Hg.**
- In acute cerebrovascular disease, blood pressure should be carefully monitor for the first 24 hours
- Combination of *perindopril and indapamide* reduced the risk of stroke by 43%
- A combination of *a ACEI and a diuretic* is preferable

Indian Guidelines on Hypertension JAPI 2013 ESH and ESC Guidelines 2013

ORIGINAL ARTICLE

The NEW ENGLAND JOURNAL of MEDICINE

Rapid Blood-Pressure Lowering in Patients with Acute Intracerebral Hemorrhage

Craig S. Anderson, M.D., Ph.D., Emma Heeley, Ph.D., Yining Huang, M.D., Jiguang Wang, M.D., Christian Stapf, M.D.,

N Engl J Med 2013; 368:2355-2365 | June 20, 2013 | DOI: 10.1056/NEJMoa1214609

- **METHODS**
  - Sample size: 2839 subjects
  - Subject selection:
    - Spontaneous intracerebral hemorrhage within the previous 6 hours
    - Elevated SBP to receive intensive treatment to lower their blood pressure (with a target systolic level of <140 mm Hg within 1 hour) or
    - Guideline-recommended treatment (with a target systolic level of <180 mm Hg)
  - The **primary outcome was death** or major disability

- **CONCLUSIONS**
  - In patients with intracerebral hemorrhage, **intensive lowering of blood pressure did not result in a significant reduction in the rate of the primary outcome of death** or severe disability

Hypertension in Elderly

Hypertension in Elderly

- HTN in the elderly patients represents a *management dilemma*
- BP reduction is the major determinant of reduction in CV risk
- Hypertension prevalence is *less in women* than in men *until 45 years of age* and **is much higher in women than men over 65 years of age*.**
- In the absence of a hypertensive emergency or urgency, blood pressure reduction should always be gradual.

**World J Cardiol 2012 May 26; 4(5): 135-147*

Pathophysiology

- ***Arterial stiffness***
  - Elastic arteries show 2 major physical changes with age. They dilate and stiffen.
- ***Neurohormonal and autonomic dysregulation***
  - Renin-angiotensin- aldosterone system decline with age.
- ***The aging kidney***
  - Progressive development of glomerulosclerosis and interstitial fibrosis

BP Measurement and Goals

Guideline	BP goal (mmHg)
ACC/AHA , 2013	**<140/90**
JNC8, 2013	**< 150/90 (≥ 60 yrs)**
ASH/ISH, 2014	**<140/90**
ESC/ESH, 2013	**SBP: <140 (< 80 yrs), 140-150 (> 80 yrs)** **DBP: <90, <85 (Diabetics)**
CHEP	<140/90 (< 80 yrs) SBP: <150 (> 80 yrs)
NICE, 2011	<140/90 (< 80 yrs) <150/90 (> 80 yrs)

•J Hypertens. 2013; Circulation. 2013..; JAMA. 2014 ; J Clin Hypertension.2014; NICE clinical guideline

Precautions in BP Measurement

Measure BP in supine, sitting and standing positions-

- As older patients are more likely to have orthostatic hypotension

older patients may have falsely high readings due to excessive vascular stiffness.

Which agent is best?

- **Thiazide diuretics:** first line in large trials
- **ACE inhibitors:**
  - LIFE (Losartan Intervention for Endpoint Reduction) Losartan vs beta blocker:
    - Losartan decreased risk CV events
  - HOPE (Heart Outcomes Prevention Evaluation)
    - Patients with DM, over 55, CVD risk
    - Ramipril 10/day decreased morbidity/mortality at 5 years
    - Most pronounced effect seen in those over age 65

Which agent ?

- **Calcium channel blockers?**
  - **SHELL (SH in Elderly: Lacidipine Long Term Study)**
  - **CCB and thiazide equal**

Which agent ?

- **ALLHAT**
  - RCT 45,000 patients
  - Thiazide vs amlodipine, lisinopril, or doxazosin (doxazosin arm stopped due to increase risk CHF)
  - Overall NO difference
  - Trend for thiazide treated patients to have less risk of stroke and CHF

Which agent ?

- *Blood Pressure Lowering Treatment Trials Collaboration:* Meta-analysis of RCTs looking at different regimens for HTN
- BMJ 4/2008
- 31 trials, over 190,000 patients
- 1. *NO difference between age groups with benefit of treatment*; benefits seen in ALL age groups
- 2. ***NO differences between classes of drugs***

Summary: which agent ??

- Monotherapy with a low-dose *thiazide-type* diuretic, an *ACE inhibitor/ARBs,* or a long-acting *calcium channel blocker*.
- In systolic pressure more than 10/5 mmHg above goal-
  - Initial therapy with a *long-acting dihydropyridine calcium channel blocker.*
  - If additional therapy is required, a *long-acting ACE inhibitor/ARB* can be added

Hypertension in Pregnancy

Hypertension in Pregnancy

- Hypertension occurs in about 5% of all pregnancies.
- Hypertension in pregnancy is diagnosed by *recording phase IV of Korotkoff sounds* with the patient lying in a lateral position.
- ***DBP>85 mm Hg should be considered abnormal***

Indian Guidelines on Hypertension JAPI 2013

Hypertensive Pregnancy Disorders- Classification and Diagnostic criteria

- **Pre-eclampsia-**
  - BP≥140/90 mm Hg on at least 2 occasions, 6 hours apart, and proteinuria of 300 mg or greater in a 24-hour urine, after 20 weeks of gestation.
- **Preeclampsia superimposed on chronic HTN**
  - Increase in BP of 30 mm Hg systolic or 15 mm Hg diastolic together with the appearance of proteinuria or oedema.
- **Chronic HTN**
  - BP ≥ 140/90 mm Hg prior to pregnancy, or before the 20th week of gestation or that which persists beyond six weeks post-partum.
- **Gestational HTN**
  - Hypertension (≥ 140/90 mm Hg on at least 2 occasions, 6 hours apart), occurring for the first time after 20 weeks' gestation, in the absence of proteinuria.

Antihypertensive in Pregnancy

- **Calcium channel blockers** Nifedipine
- **Diuretic** Furosemide, thiazide diuretics
- **Vasodilators**
  - Arteriolar and venous Sodium nitroprusside
  - Alpha and beta blocker Labetolol,
  - Arteriolar Hydralazine
- **Drugs that decrease cardiac output**
  - Beta blockers Propranolol
- **Centrally acting agents**

  Alpha methyl dopa

ACE inhibitors, ARBs & sodium nitroprusside are contraindicated

Options for breastfeeding mothers

- Beta-adrenergic blockers and calcium channel blockers enter breast milk; however, most appear to be safe during lactation
- **Beta-blockers and alpha/beta-blockers** – Propranolol, metoprolol, and labetalol have the lowest transfer into milk.
- In contrast, atenolol and acebutolol are relatively extensively excreted into breast milk
- **Calcium channel blockers** – Diltiazem, nifedipine, nicardipine, and verapamil are associated with a relative infant dose of less than 2 percent.
- **ACE inhibitors** – These drugs are transferred into milk at very low levels. Captopril and enalapril have been reviewed by the AAP and are compatible for use in lactation.
- **Diuretics** may reduce milk volume, but compatible with breastfeeding.

Hypertension with Obesity and Metabolic syndrome

Diagnostic criteria for metabolic syndrome

Risk Factor	Defining Level
Abdominal obesity (Waist Circumference)	
Men	>90 cm
Women	>80 cm
Triglycerides	>150 mg/dl
HDL-Cholesterol	
Men	<40 mg/dL
Women	<50 mg/dL
Blood pressure	>130/>85 mm Hg
Fasting glucose	>110 mg/dL

Indian Guidelines on Hypertension JAPI 2013

Obesity and Metabolic syndrome

- Tight correlation between body weight and blood pressure, with 70% of hypertension in men and 60% in women being directly attributable to excess adiposity.
- Insulin resistance is very often associated with dyslipidaemia, obesity, hypertension and impaired glucose tolerance, a cluster termed the **"*metabolic syndrome or the insulin resistance syndrome*.**
- *Obstructive sleep apnea (OSA),* now considered a cause of secondary hypertension, is closely associated with obesity.

Obesity and Metabolic syndrome

- *Target BP < 140/90 mmHg*.
- ***Lifestyle changes-*** particularly weight loss and exercise.
- ACE inhibitors, low-dose diuretics, CCBs, ARBs and α-blockers (in dyslipidaemia or glucose intolerance)

* Newer vasodilating BB (carvedilol, nebivolol): affect insulin sensitivity LESS than metoprolol.

Nebivolol – not worsen glucose tolerance when added to HCTZ.

Hypertension Management in Chronic Kidney Disease

Indian CKD Guidelines 2013

Hypertension in Chronic Kidney Disease

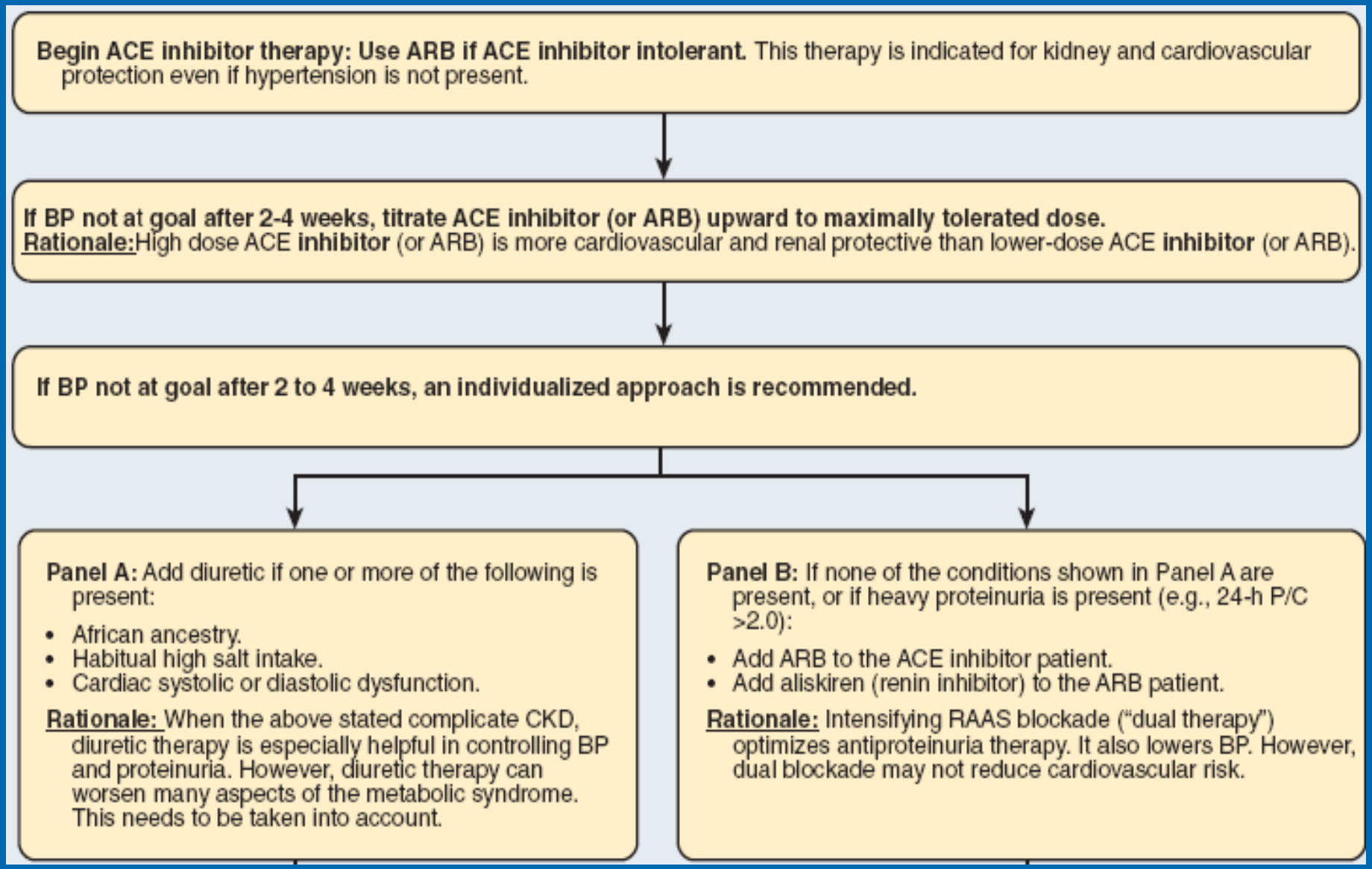
- Between *50% - 75%* of individuals with CKD stages 3 to 5 have hypertension (if it is defined as a blood pressure ≥140/80 mm Hg)
- Hypertension is a risk factor for progression of kidney disease and for CVD.
- Multidrug regimens are usually necessary to achieve blood pressure control.
- Most recommendations suggest targeting lower blood pressures ***(<130/80 mm Hg), especially in those with diabetes or proteinuria***.

BP Management In Diabetic Kidney Disease

- Maintain a **BP ≤140/90 mmHg** in ***diabetic hypertensive adults with CKD and urine albumin excretion <30 mg/24 hours***.
- Maintain a **BP <130/80 mmHg** in all hypertensive adults with ***diabetes with urine albumin excretion >30 mg/24 hours***.
- **ARBs or ACE-Is** in adults with diabetes and CKD not on dialysis with urine albumin excretion of 30 to 300 mg per 24 hours or >300mg per 24 hours.

Indian CKD Guidelines 2013

Algorithm : Initial Antihypertensive Therapy



Cont....
Algorithm : Initial Antihypertensive Therapy

If BP not at goal after 2 to 4 weeks of the Panel A or Panel B interventions:

- Panel A patients: add ARB to ACE inhibitor If already on ARB (i.e., ACE inhibitor intolerant), add aliskiren.
- Panel B patients: add diuretic.

↓

If BP not at goal after 2 to 4 weeks, reassess the following:

- Medication compliance (are prescribed medications collected from pharmacy?).
- Regular use of "over-the-counter drugs" that can raise BP (decongestants, vasoconstrictive nose spray or eye drops, NSAIDS) or alcohol (more than 2 drinks daily).
- Excessive salt intake (measure 24-hr urine Na or C if on $NaHCO_3$)
- Sleep apnea.
- New major life stressors.

If the above assessment is unrevealing, consider ambulatory blood pressure monitoring (ABPM). If ABPM confirms that patient's BP is not at goal, proceed to Algorithm 2 (Fig 76.7).

BLOOD PRESSURE MANAGEMENT IN ELDERLY PERSONS WITH CKD

- Tailor BP treatment regimens by:
  - Carefully considering age, co-morbidities and other therapies, with gradual escalation of treatment.
  - **Close attention to adverse events -**
    - Electrolyte disorders,
    - Acute deterioration in kidney function,
    - Orthostatic hypotension and
    - Drug side effects.

Hypertension with Chronic Obstructive Pulmonary Disease

Hypertension with COPD

- Precipitating factors for Hypertension in COPD
  - Systemic steroids, β-agonists or nasal decongestants.
  - Stress
- Long acting calcium channel blockers such as amlodipine have been found to be relatively safe drugs.
- β -blockers and α-β blockers are not routinely recommended as they are known to exacerbate asthma.
- Inhaled corticosteroids and ipratropium bromide can be used safely in these patients.

Hypertension with Coronary Artery Disease

Hypertension with Coronary Artery Disease

- Hypertension is the major risk factor for CAD.
- Too rapid lowering of blood pressure, which can cause reflex tachycardia and sympathetic activation, should be avoided in patients with CAD.
- One may have to set the ***target of BP control even below 130-140/90 mm Hg.***
- All other risk factors should be treated appropriately.

ESH and ESC Guidelines 2013

Management: Hypertension with CAD

- **β-blockers and CCBs are the drugs of first choice**
- Treatment with **amlodipine** is associated with **fewer hospitalisations for unstable angina**
- **Verapamil and diltiazem** reduce risk of MI following non-Q-wave MI.
- **ACE inhibitors in combination with digoxin or low dose diuretics**, are effective in reducing morbidity and mortality in patients in heart failure.
- **Statins and aspirin** are recommended in patients with hypertension associated with CAD.

Hypertension with Congestive Cardiac Failure (CCF)

Hypertension with Congestive Cardiac Failure

- CCF is a common sequel of long standing hypertension
- **ACE inhibitors:** In patients with LVF due to hypertension.
- **Low dose diuretics** : In hypertension with heart failure, particularly when associated with fluid retention.
- Selective β-blockers **(metoprolol, bisoprolol)** and α-β blocker (**carvedilol)** started in low doses and then gradually increased.
- **Amlodipine :** In treating hypertensive patients with angina and LVF, when **added to ACE inhibitors, diuretics and digoxin**.

ESH and ESC Guidelines 2013

Hypertension with LVF:

- All antihypertensive drug can be used *except direct vasodilatation* e.g. HYDRALAZINE
- In one study treatment with *diuretics & an ACEi are better* than other drug.

Hypertension with BRADYCARDIA:

- Nifidipine & ACEi are preferable drugs.
- Better to **avoid β-BLOKERS, VERAPAMIL, DILTIAGEM**

Hypertension with GOUT

- All hypertensive drugs can be used
- But all Diuretics can increase serum uric acid level but rarely induced acute gout. So diuretics should be avoided if possible.
- Contraindications: NO DIURETICS

Hypertensive crises

Hypertensive crises

A) Emergency

i) Malignant HTN

ii) Accelerated HTN

B) Urgency

Goal of reducing BP 160/100 mm of Hg with in 24 hrs

Drugs of Choice:

ORAL	I/V
1. Clonidine	1. Nitroprusside
2. Labetalol	2. Nitroglycerin
3. Captopril	3. Labetalol
4. Prazosine	4. Hydralazine

Hypertension with Atrial Fibrillation

Hypertension with Atrial Fibrillation

- Hypertension is an important risk factor for atrial fibrillation.
- Atrial fibrillation increases the *risk of cardiovascular mortality by 2 to 5 fold* with a marked increase in the risk of embolic stroke.
- Stroke and bleeding episodes are more frequent when *SBP >140 mmHg.*

Management : AF with Hypertension

- Angiotensin receptor antagonist or ACE inhibitor reduce incidence of new atrial fibrillation.

- β-blockers: In atrial fibrillation and systolic heart failure patients.

Hypertension with Dyslipidaemia

Hypertension with Dyslipidaemia

- Lifestyle modifications: lower blood pressure and improve lipid levels.
- ACE inhibitors and calcium channel blockers: Lipid neutral drug
- **High dose** THIAZIDES, LOOPS DIURETICS & BETA BLOCKERS **may transiently increase total cholesterol, still has significant reduction CV morbidity & sudden death. So should be used without hesitation.**
- warrant lipid lowering therapy (statins)

Resistant Hypertension

Resistant Hypertension

- Resistant hypertension is defined as *the failure to reach goal BP* in patients who are adhering to *full doses of an appropriate 3-drug regimen of different classes that includes a diuretic.*
- About **12.2% of hypertensive** patients have Resistant Hypertension.
- *Ambulatory blood pressure monitoring* should be done in these patients in order to classify them as follows:
  - True resistant hypertensives (62.5%),
  - Pseudo or white-coat resistant hypertension (37.5%)

Resistant HT: Management

- More aggressive salt restriction and elimination of drugs interfering with action of anti-hypertensive agents should be looked at.
- One should look for secondary hypertension
- In case no secondary cause is found --- need multiple drugs in high dosages.
- Newer intervention-based treatment modalities (under evaluation)
  - Renal Sympathetic Denervation Therapy and
  - Carotid Baroreceptor Stimulation therapy

Newer Modalities For Managing Resistant Hypertension

Renal Sympathetic Nerve Ablation

- Defective diuresis and natriuresis by kidney is most important mechanism of sustained hypertension.

- There is evidence that an important cause of the defect in renal excretory function in hypertension is an increase in renal sympathetic nerve activity (RSNA) resulting from the direct action of angiotensin II on brain stem nuclei, increasing the basal level of RSNA and impairing its arterial baroreflex regulation .

Krum H et al. Lancet. 2009

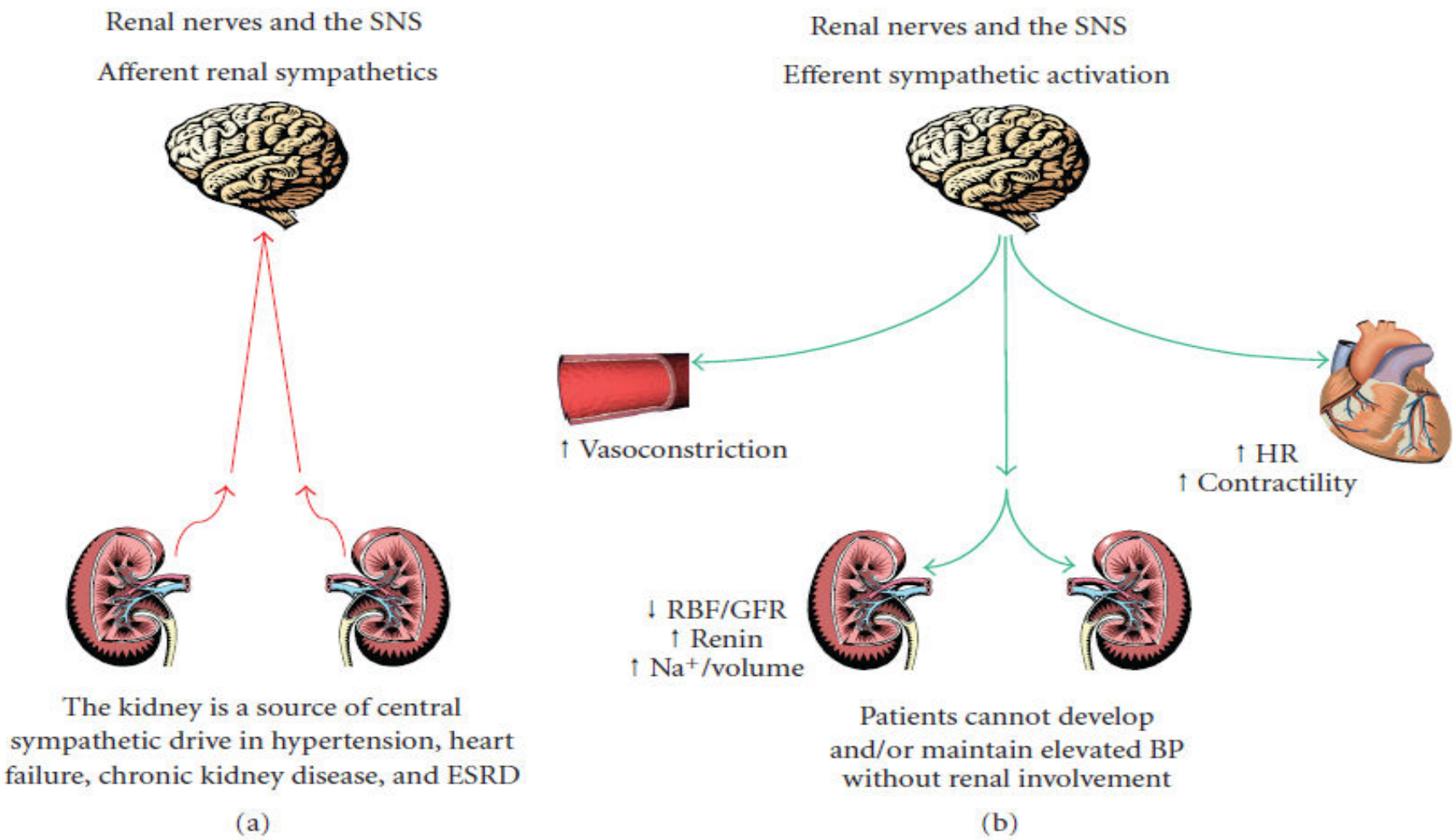
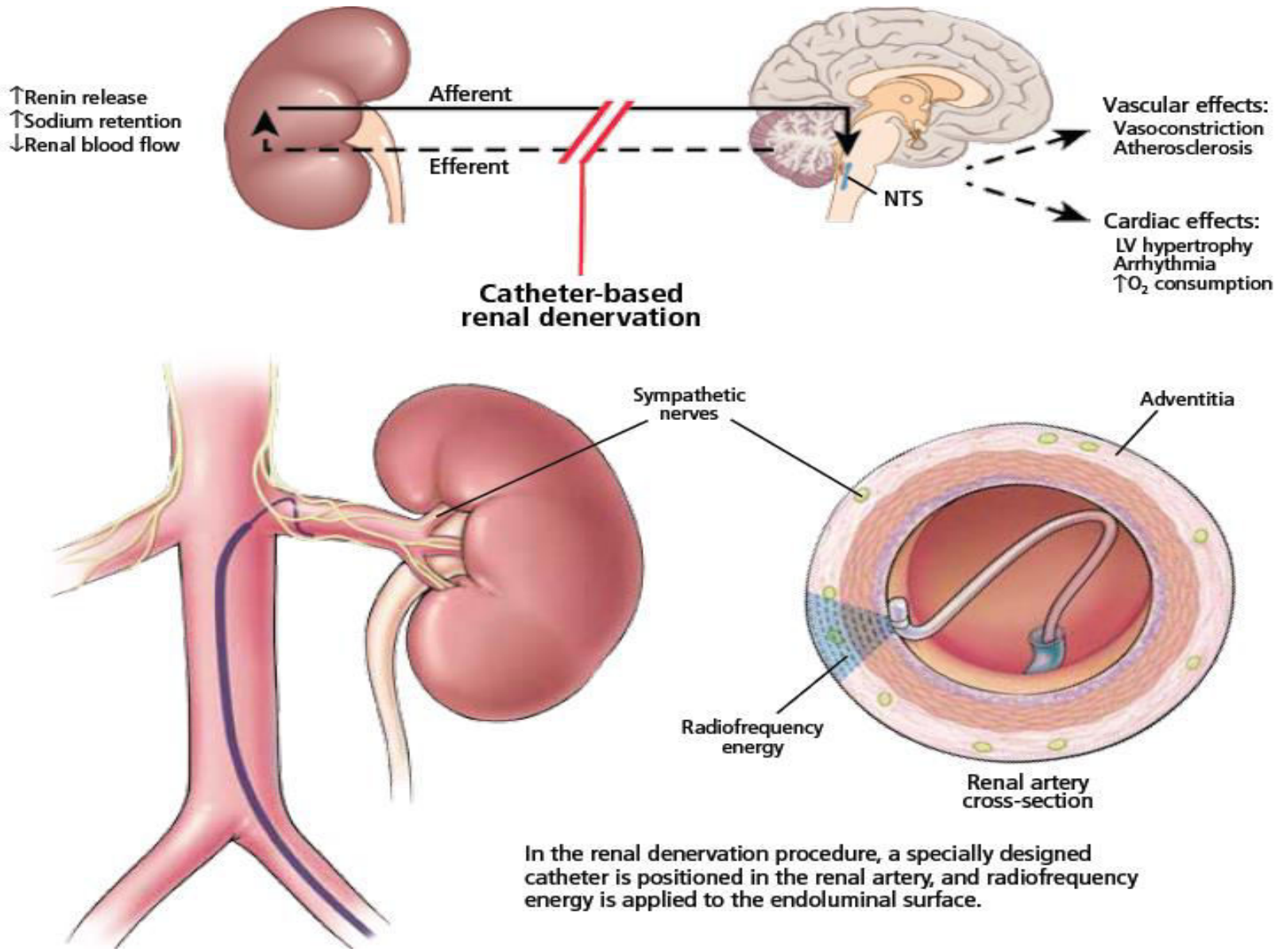


FIGURE 6: Afferent and efferent sympathetic innervations of the kidney.



In the renal denervation procedure, a specially designed catheter is positioned in the renal artery, and radiofrequency energy is applied to the endoluminal surface.

Renal Nerve

- The effects of renal nerve stimulation on renin secretion are direct.
- A reduction in the pressor influences can be obtained by denervating the renal arteries through a **percutaneously inserted catheter capable of removing efferent sympathetic influences**

SYMPLICITY TRIAL-HTN2

Lancet. 2010

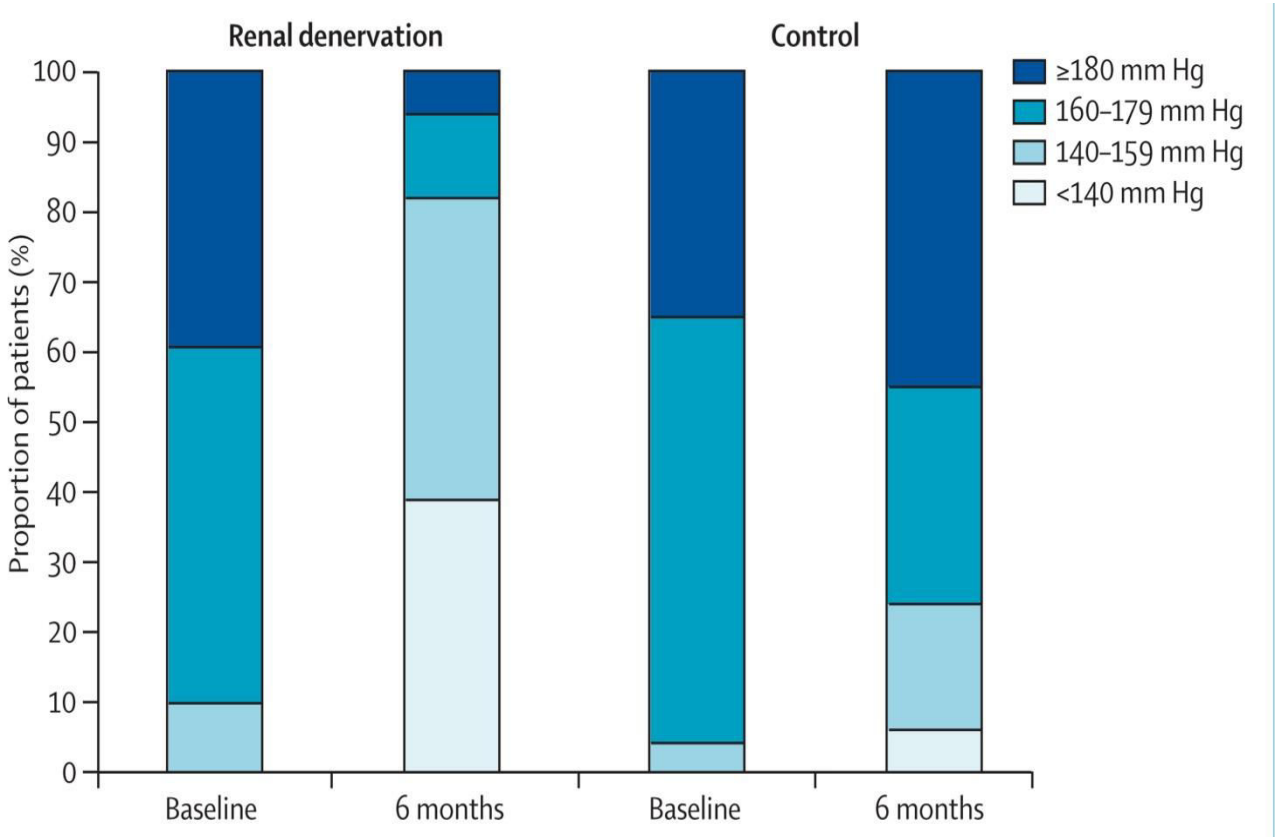
THE LANCET

Renal sympathetic denervation in patients with treatment-resistant hypertension (The Symplicity HTN-2 Trial): a randomised controlled trial

Symplicity HTN-2 Investigators*

- This trial assessed 106 patients with refractory hypertension.
- Patients were randomly assigned to renal sympathetic denervation (52) or control (54) groups.
- Renal denervation resulted in impressive reductions in mean office-based measurements of blood pressure (32/12mmHg at 6 months), whereas blood pressure remained almost unchanged in the control group.

SYMPLICITY TRIAL-HTN2



ORIGINAL ARTICLE

A Controlled Trial of Renal Denervation for Resistant Hypertension

Deepak L. Bhatt, M.D., M.P.H., David E. Kandzari, M.D., William W. O'Neill, M.D., Ralph D'Agostino, Ph.D., John M. Flack,

N Engl J Med 2014; 370:1393-1401 April 10, 2014

The NEW ENGLAND JOURNAL of MEDICINE

Method:

- Prospective, single-blind, randomized, sham-controlled trial.
- Patients with severe resistant hypertension were randomly assigned in a 2:1 ratio to undergo renal denervation or a sham procedure.

Result:

- n = 535 patients
- There were no significant differences in safety between the two groups.

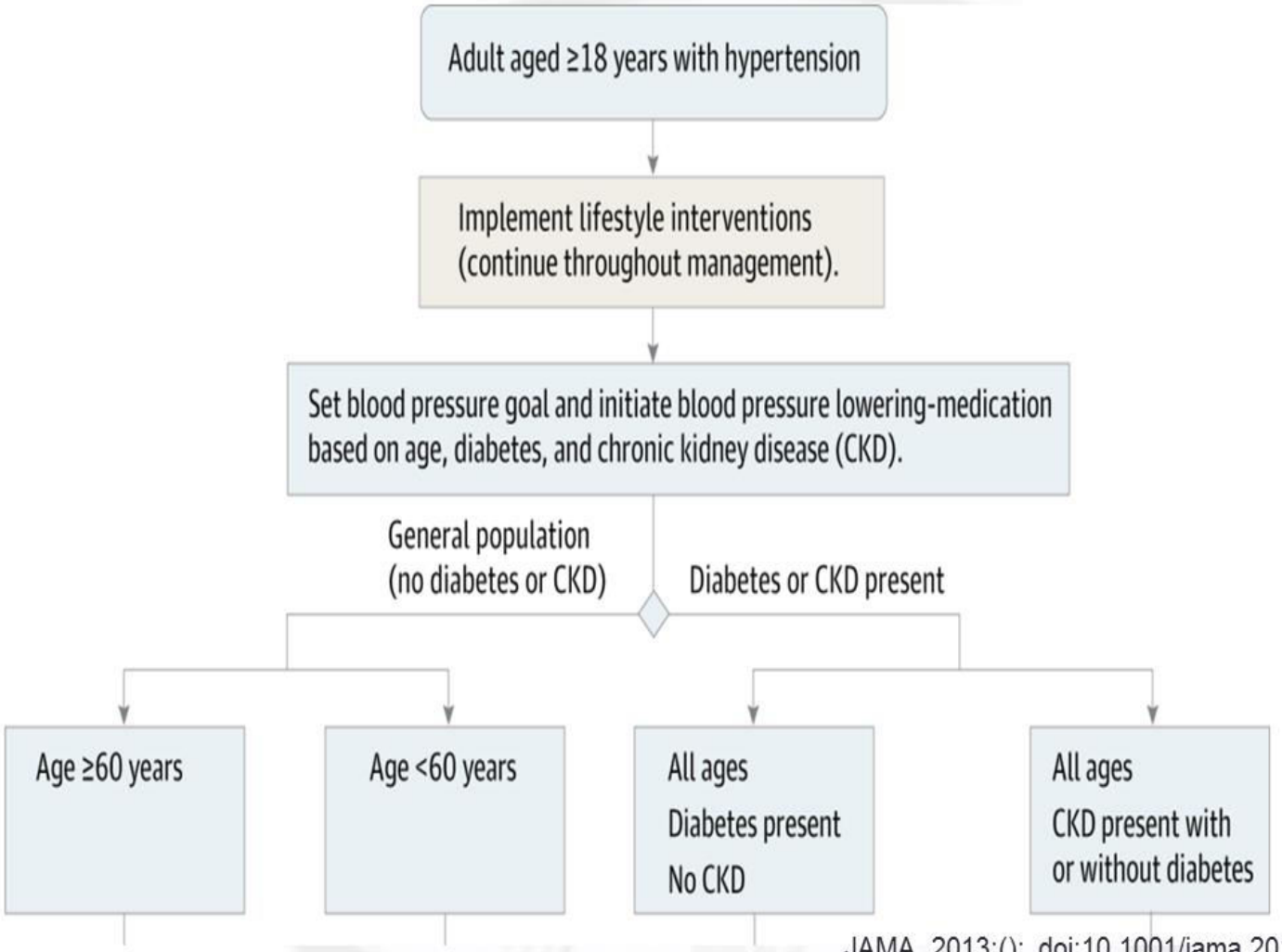
Conclusion:

- This blinded trial did not show a significant reduction of systolic blood pressure in patients with resistant hypertension 6 months after renal-artery denervation as compared with a sham control.

Hypertension Management Algorithm Guideline

JNC8 GUIDELINE ON HYPERTENSION

Management Algorithm Guideline

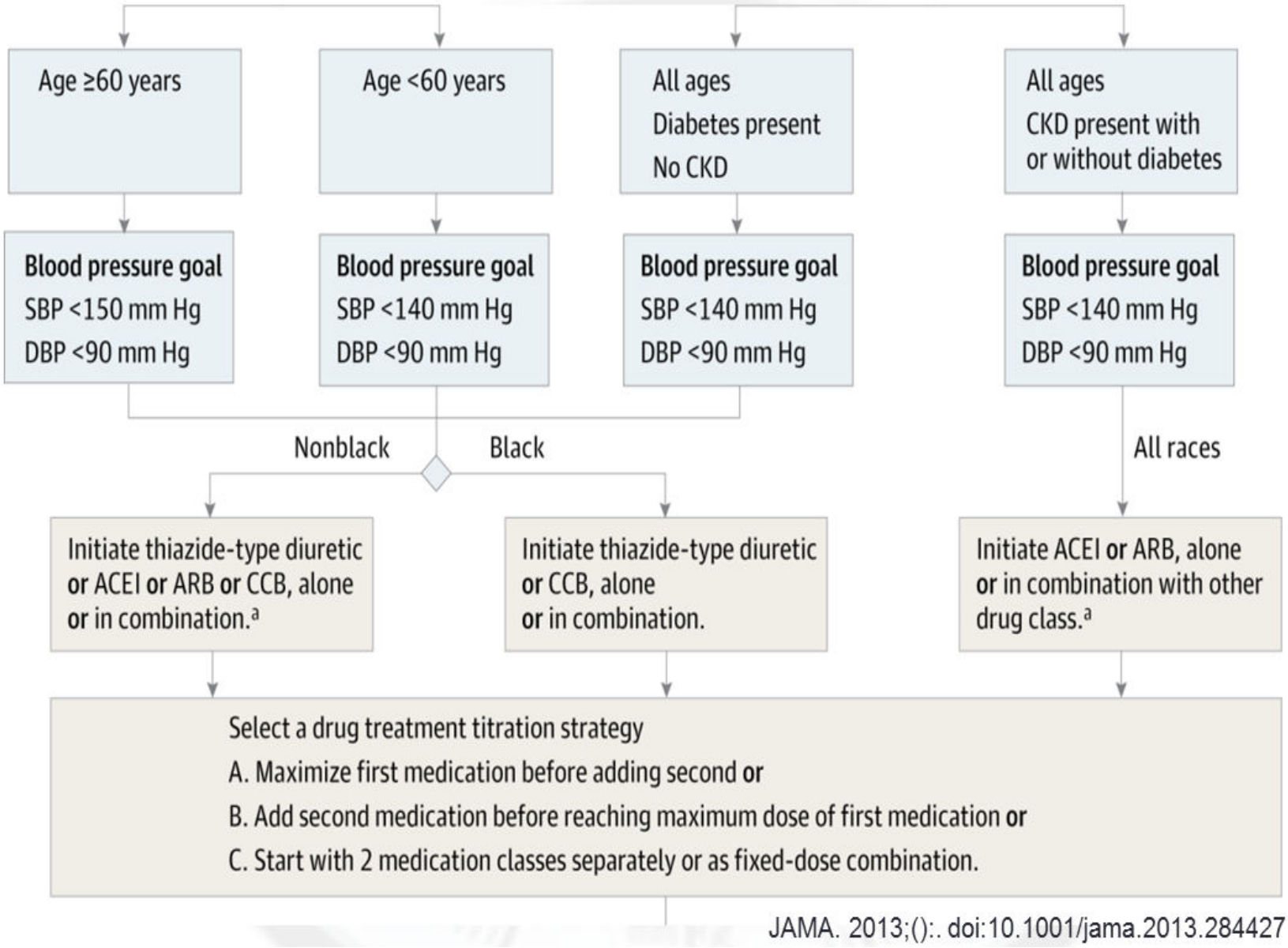


1

JAMA. 2013;():. doi:10.1001/jama.2013.284427

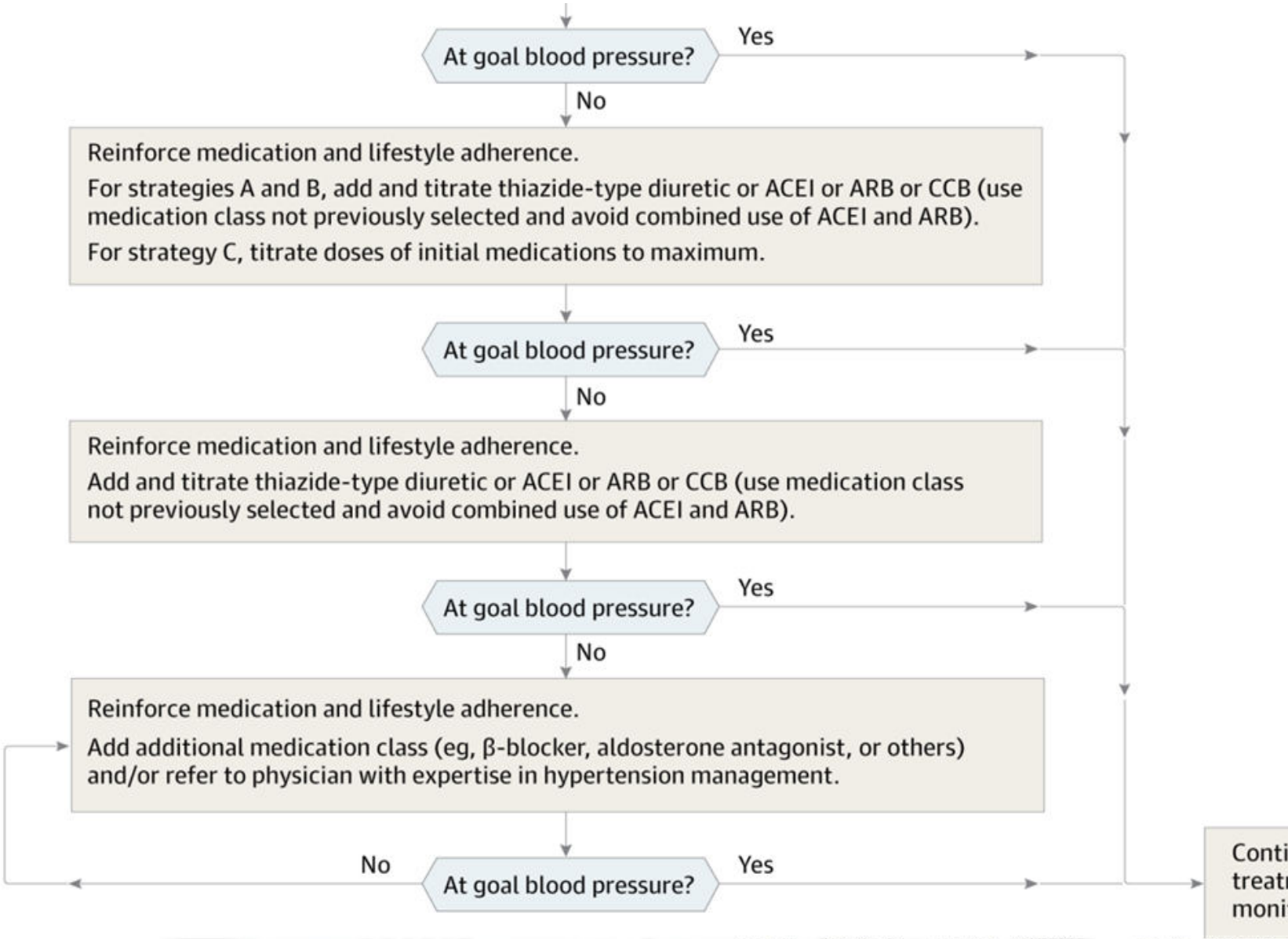
2014 Hypertension Guideline Management Algorithm SBP indicates systolic blood pressure; DBP, diastolic blood pressure; ACEI, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; and CCB, calcium channel blocker.[a]ACEIs and ARBs should not be used in combination.[b]If blood pressure fails to be maintained at goal, reenter the algorithm where appropriate based on the current individual therapeutic plan.

Management Algorithm Guideline



JAMA. 2013;():. doi:10.1001/jama.2013.284427

Management Algorithm Guideline



JAMA. 2013;():. doi:10.1001/jama.2013.284427

Summary:
Antihypertensive drugs

contra-indications to the use of antihypertensive drugs

Drug	Compelling	Possible
Diuretics (thiazides)	Gout	Metabolic syndrome Glucose intolerance Pregnancy Hypercalcaemia Hypokalaemia
Beta-blockers	Asthma A–V block (grade 2 or 3)	Metabolic syndrome Glucose intolerance Athletes and physically active patients Chronic obstructive pulmonary disease (except for vasodilator beta-blockers)
Calcium antagonists (dihydropyridines)		Tachyarrhythmia Heart failure
Calcium antagonists (verapamil, diltiazem)	A–V block (grade 2 or 3, trifascicular block) Severe LV dysfunction Heart failure	

contra-indications to the use of antihypertensive drugs

Drug	Compelling	Possible
ACE inhibitors	Pregnancy Angioneurotic oedema Hyperkalaemia Bilateral renal artery stenosis	Women with child bearing potential
Angiotensin receptor blockers	Pregnancy Hyperkalaemia Bilateral renal artery stenosis	Women with child bearing potential
Mineralocorticoid receptor antagonists	Acute or severe renal failure (eGFR <30 mL/min) Hyperkalaemia	

Drugs to be preferred in specific conditions

Condition	Drug
Asymptomatic organ damage	
LVH	ACE inhibitor, calcium antagonist, ARB
Asymptomatic atherosclerosis	Calcium antagonist, ACE inhibitor
Microalbuminuria	ACE inhibitor, ARB
Renal dysfunction	ACE inhibitor, ARB

Drugs to be preferred in specific conditions

Clinical CV event	
Previous stroke	Any agent effectively lowering BP
Previous myocardial infarction	BB, ACE inhibitor, ARB
Angina pectoris	BB, calcium antagonist
Heart failure	Diuretic, BB, ACE inhibitor, ARB, mineralocorticoid receptor antagonists
Aortic aneurysm	BB
Atrial fibrillation, prevention	Consider ARB, ACE inhibitor, BB or mineralocorticoid receptor antagonist
Atrial fibrillation, ventricular rate control	BB, non-dihydropyridine calcium antagonist
ESRD/proteinuria	ACE inhibitor, ARB
Peripheral artery disease	ACE inhibitor, calcium antagonist

Drugs to be preferred in specific conditions

Other	
ISH (elderly)	Diuretic, calcium antagonist
Metabolic syndrome	ACE inhibitor, ARB, calcium antagonist
Diabetes mellitus	ACE inhibitor, ARB
Pregnancy	Methyldopa, BB, calcium antagonist
Blacks	Diuretic, calcium antagonist

Take Home Message

- Addressing behavioural risk factors, e.g. unhealthy diet, harmful use of alcohol and physical inactivity, can prevent hypertension.
- Salt reduction initiatives can make a major contribution to prevention and control of high blood pressure.
- Monotherapy is not going to be effective. ACEI's/ARB's in combination with CCB's forms a good combination.
- Evaluation of antihypertensive scheme, emphasizing the use of diuretics and adequate combination and dosages of the two other drugs, which preferentially reduces cardiovascular risk and promotes prevention/regression of target organ damages.
- Prevention and control of hypertension is complex, and demands multi-stakeholder collaboration,including governments, civil society, academia and the food and beverage industry.
- Non pharmacological, interventional sympathetic denervation therapy has become recently available and is being evaluated.

Thank You