ĐIỀU TRỊ TĂNG HUYẾT ÁP NƠI BN BỆNH THẬN MẠN/LỌC MÁU

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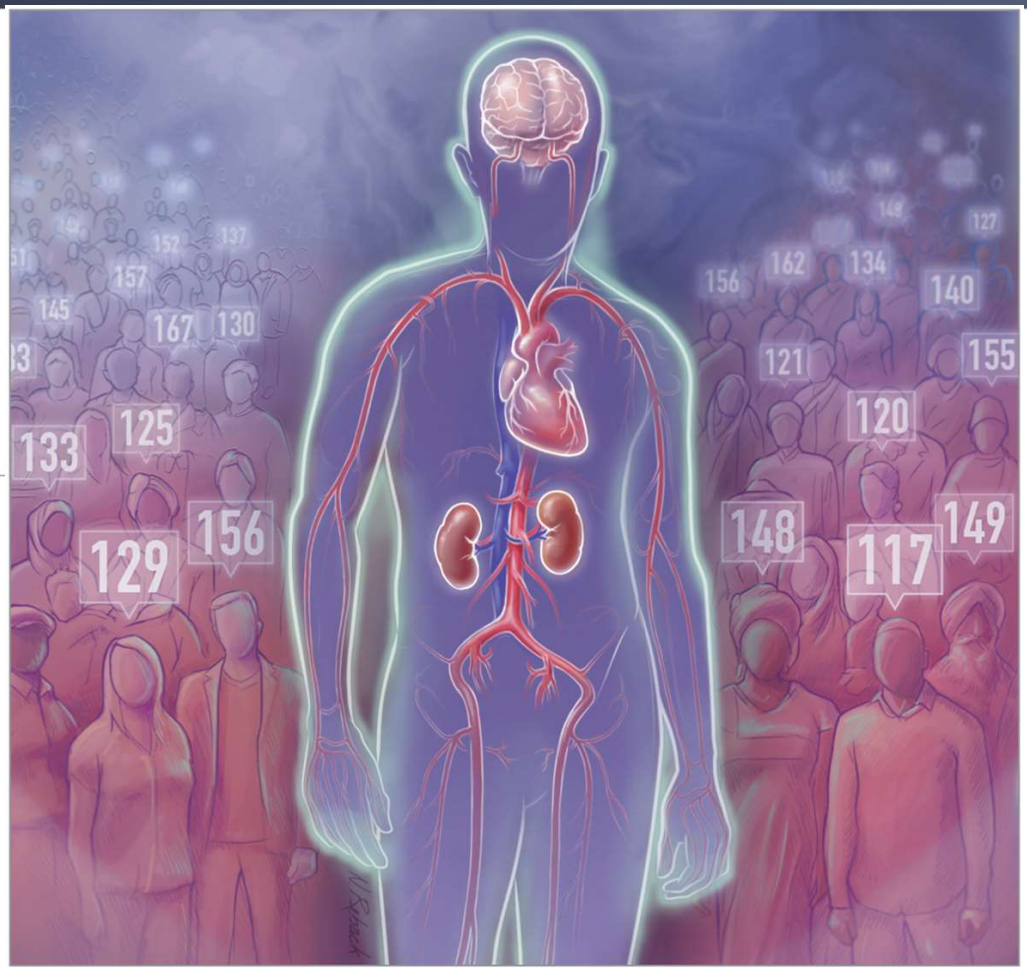
GS Thỉnh giảng ĐHYK Liege, Vương Quốc Bỉ

Hypertension Is a Major Risk Factor for CVD

Large cohort studies have demonstrated that high BP is an important risk factor for:



Munter P, et al. *JAMA*. 2020;324:1190-1200; Fuchs FD, Whelton PK. *Hypertension*. 2020;75:285-292.

Clinical Implications of Meta-Analysis Findings

Controversial line of thinking, but findings support that for people at risk of CVD, pharmacological BP-lowering treatment improves CV outcomes, irrespective of CVD status or baseline BP

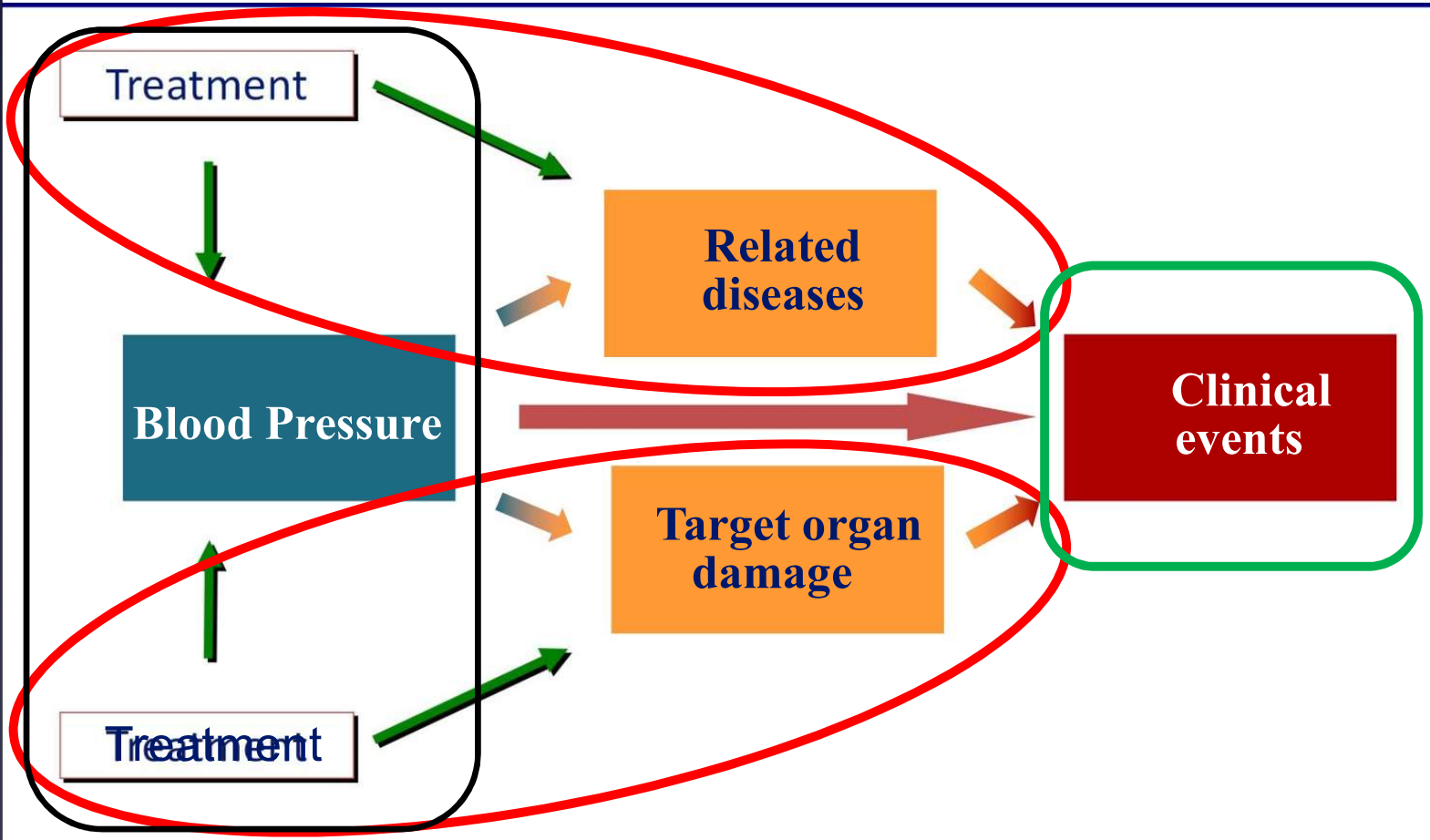
Findings suggest that physicians may need to assess risk and treat patients differently, and take a more prophylactic approach to prevent CVD

Potential advantage to implementing low-dose antihypertensive drug in patients with "normal" BP, but presenting with other CV risk factors

Bottom-line goal is to prevent CVD

Important to engage the patient in the decision-making process

Cardiovascular Prevention



Blood Pressure Control Needs to Be …

Lower

Faster

Better

Expert opinion.

ESC Guidelines 2024

Lower pressures → Lower CV event rates, → new **systolic BP target of 120 mm Hg to 129 mm Hg** for most patients receiving antihypertensive medications.

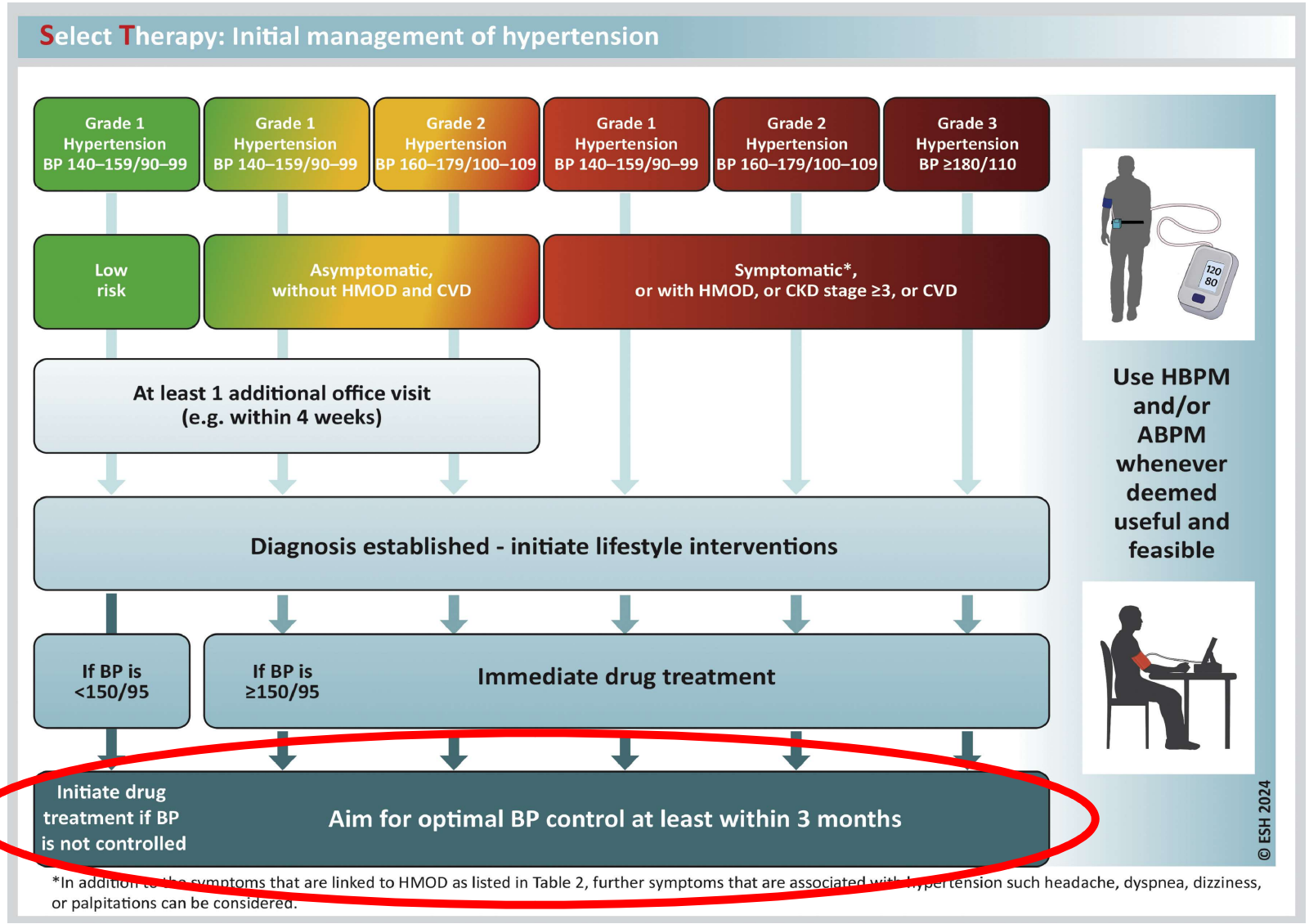
What to Know About the New Blood Pressure AHA Guidelines Oct, 2025

Great evidence: With heart health, brain health, kidney health…:

- "Lower BP is better."
- "Start BP treatment earlier & get to lower targets."

Abbasi J. What to Know About the New Blood Pressure Guidelines. *JAMA.* Published online October 31, 2025. doi:10.1001/jama.2025.17664

European Journal of Internal Medicine, Volume 126, , August 2024, Pages 1-15



KDIGO 2021 Clinical Practice Guideline for the Management of BP in CKD

3.2 Treatment with antihypertensive drugs, including RAS inhibitors (RASi)

Recommendation 3.2.1: We recommend starting renin-angiotensin-system inhibitors (RASi) (angiotensin-converting enzyme inhibitor [ACEi] or angiotensin II receptor blocker [ARB]) for people with high BP, CKD, and severely increased albuminuria (G1–G4, A3) without diabetes *(1B)*.

Recommendation 4.1: We recommend that a dihydropyridine calcium channel blocker (CCB) or an ARB be used as the first-line antihypertensive agent in adult kidney transplant recipients *(1C)*.

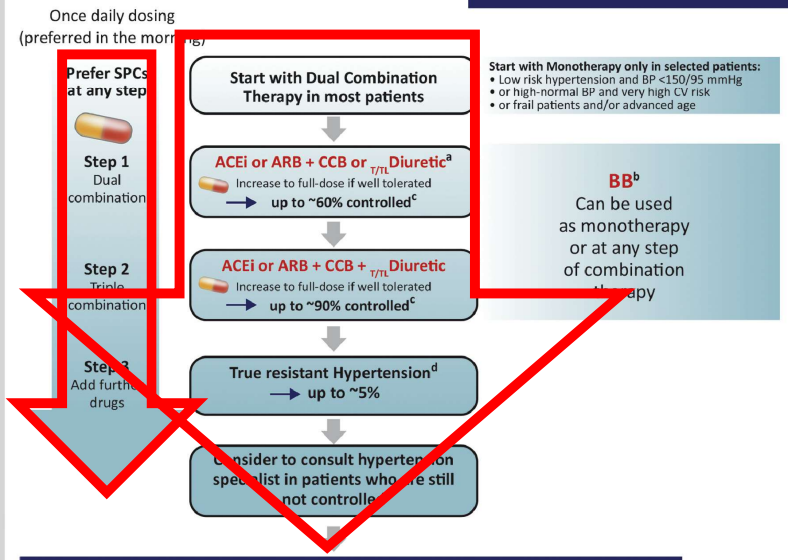
Practice Point 3.2.1: It may be reasonable to treat people with high BP, CKD, and no albuminuria, with or without diabetes, with RASi (ACEi or ARB).

Practice Point 3.2.2: RASi (ACEi or ARB) should be administered using the highest approved dose that is tolerated to achieve the benefits described because the proven benefits were achieved in trials using these doses.

Kidney International (2021) 99, S1–S87

Select Therapy: Pharmacological Treatment

General strategy in patients with hypertension



[a]Use of Diuretics:
- Consider transition to Loop Diuretic if eGFR is between 30 to 45 ml/min/1.73 m²
- If eGFR <30 ml/min/1.73m² use Loop Diuretic; consider combination with Chlorthalidone or other TL-Diuretic

[b]Use of BB: should be used as guideline directed medical therapy in respective indications or considered in several other conditions (Table 8)

[c]Controlled BP: if <140/90mmHg

[d]True resistant Hypertension: when SBP is ≥140 mmHg or DBP is ≥90 mmHg provided that:
- maximum recommended and tolerated doses of a three-drug combination comprising a RAS blocker (either an ACEi or an ARB), a CCB and a Thiazide/ Thiazide-like diuretic were used
- inadequate BP control has been confirmed by ABPM or by HBPM if ABPM is not feasible
- various causes of pseudo-resistant hypertension (especially poor medication adherence) and secondary hypertension have been excluded.

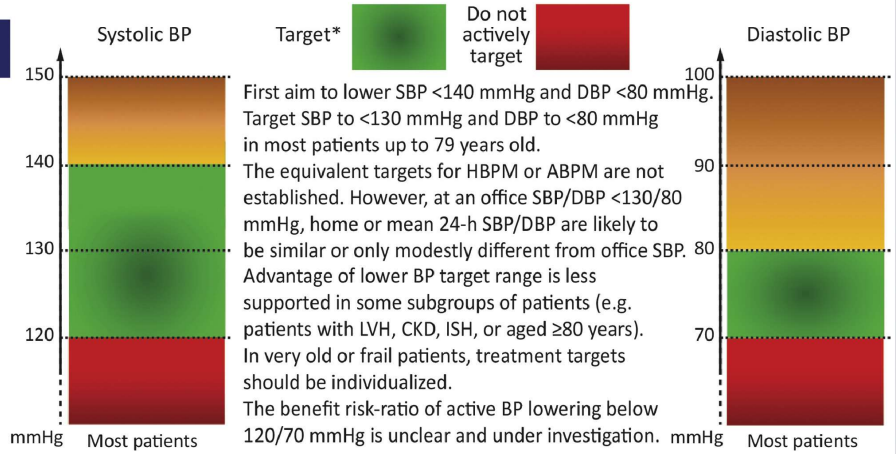
Consider additional therapies: drugs or renal denervation

In true resistant hypertension:
- Spironolactone (preferred) or other MRA; with caution if eGFR <45 ml/min/1.73 m² or serum potassium >4.5 mmol/l.
- BB or alpha1-blocker or centrally acting agent
- Direct vasodilator (not preferred)
- Renal denervation, if eGFR >40 ml/min/1.73 m²

In Heart Failure
- ARNI
- SGLT2i

In CKD
- SGLT2i
- NsMRA Finerenone (not in combination with other MRA)

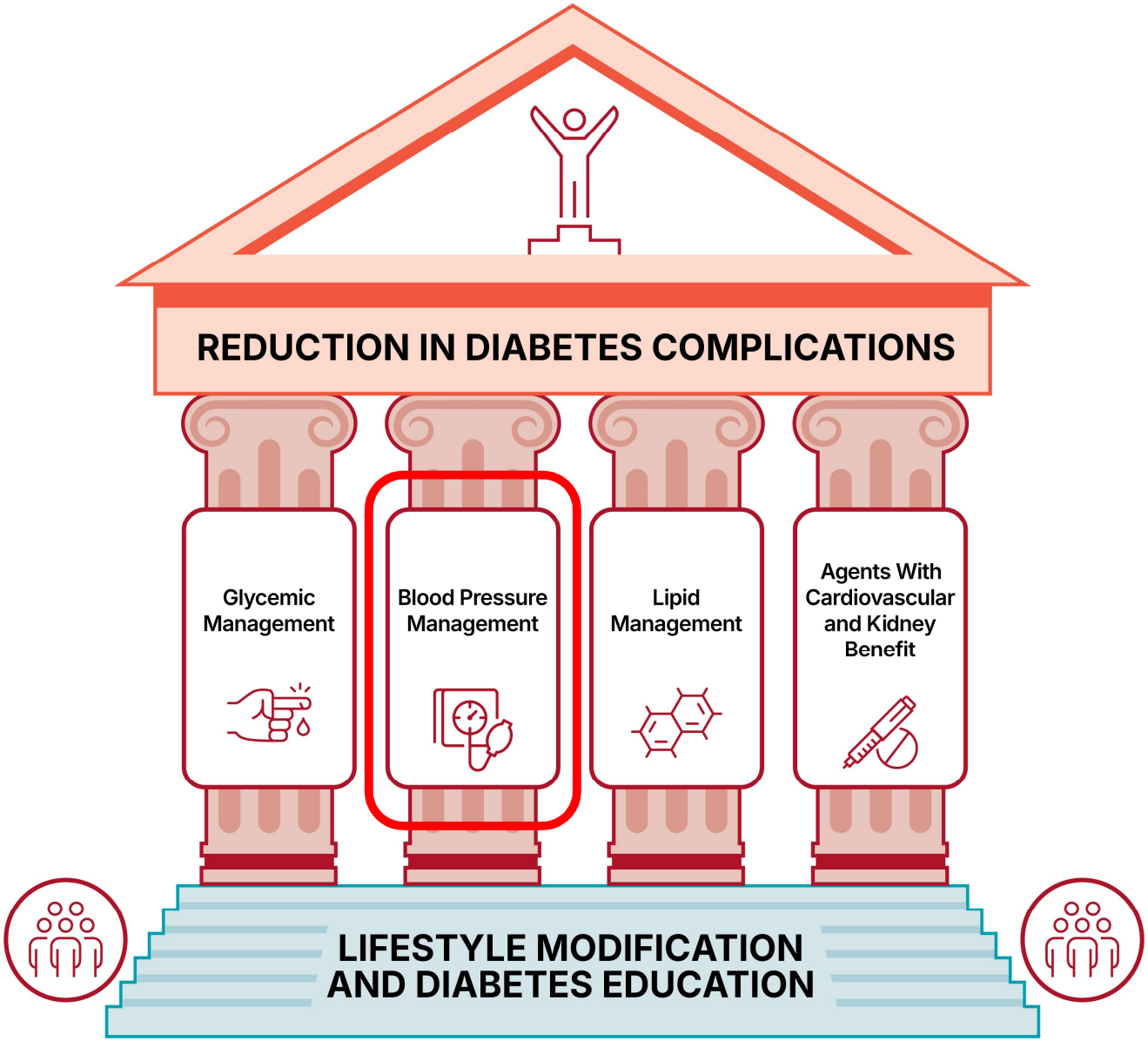
General office BP targets in patients with hypertension



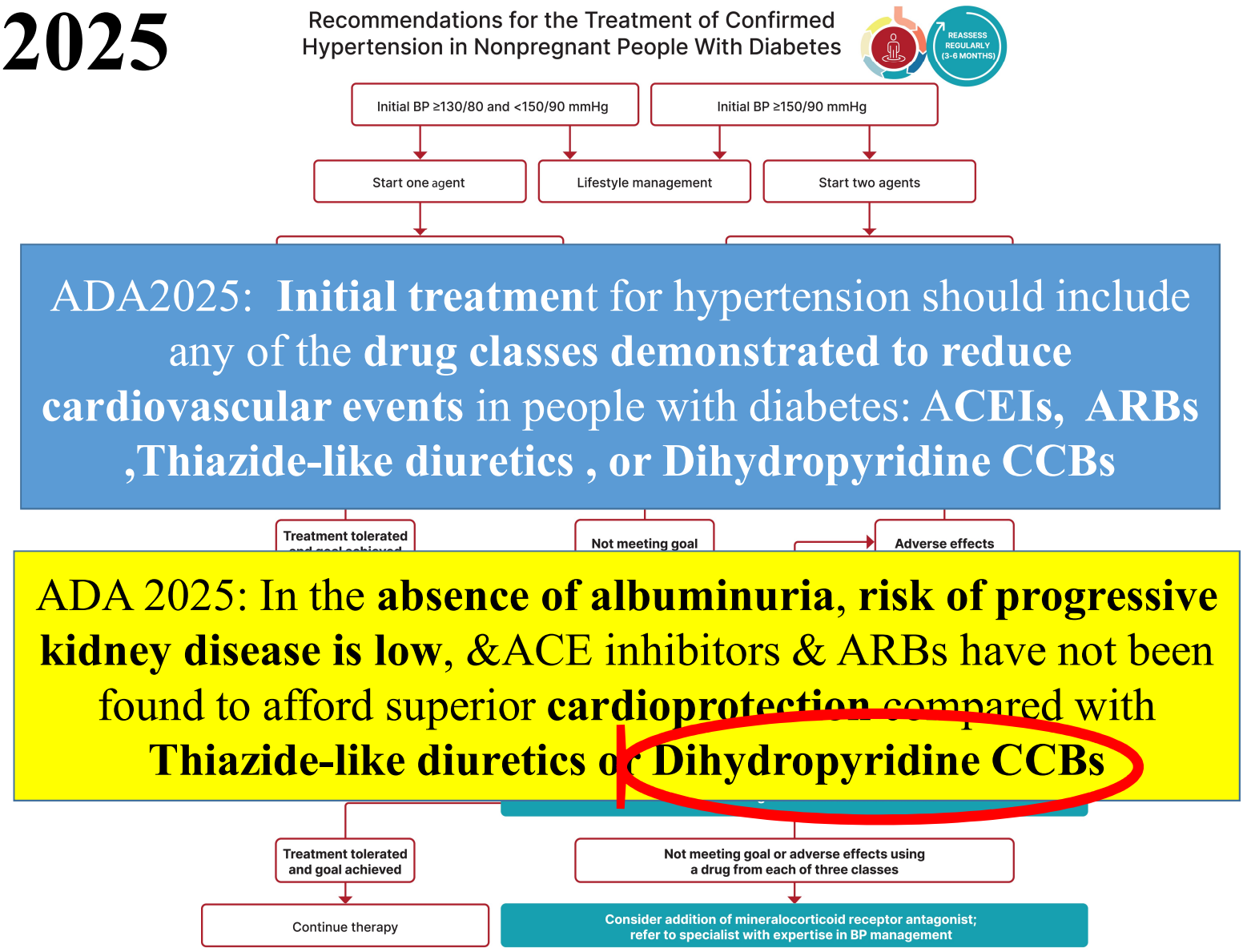
First aim to lower SBP <140 mmHg and DBP <80 mmHg.
Target SBP to <130 mmHg and DBP to <80 mmHg in most patients up to 79 years old.
The equivalent targets for HBPM or ABPM are not established. However, at an office SBP/DBP <130/80 mmHg, home or mean 24-h SBP/DBP are likely to be similar or only modestly different from office SBP.
Advantage of lower BP target range is less supported in some subgroups of patients (e.g. patients with LVH, CKD, ISH, or aged ≥80 years).
In very old or frail patients, treatment targets should be individualized.
The benefit risk-ratio of active BP lowering below 120/70 mmHg is unclear and under investigation.

*If well tolerated

ADA 2025


REDUCTION IN DIABETES COMPLICATIONS
Glycemic Management
Blood Pressure Management
Lipid Management
Agents With Cardiovascular and Kidney Benefit
LIFESTYLE MODIFICATION AND DIABETES EDUCATION

ADA 2025


Recommendations for the Treatment of Confirmed Hypertension in Nonpregnant People With Diabetes
REASSESS REGULARLY (3-6 MONTHS)
Initial BP ≥130/80 and <150/90 mmHg
Initial BP ≥150/90 mmHg
Start one agent
Lifestyle management
Start two agents
ADA2025: Initial treatment for hypertension should include any of the drug classes demonstrated to reduce cardiovascular events in people with diabetes: ACEIs, ARBs ,Thiazide-like diuretics , or Dihydropyridine CCBs
Treatment tolerated
Not meeting goal
Adverse effects
ADA 2025: In the absence of albuminuria, risk of progressive kidney disease is low, &ACE inhibitors & ARBs have not been found to afford superior cardioprotection compared with Thiazide-like diuretics or Dihydropyridine CCBs
Treatment tolerated and goal achieved
Not meeting goal or adverse effects using a drug from each of three classes
Continue therapy
Consider addition of mineralocorticoid receptor antagonist; refer to specialist with expertise in BP management

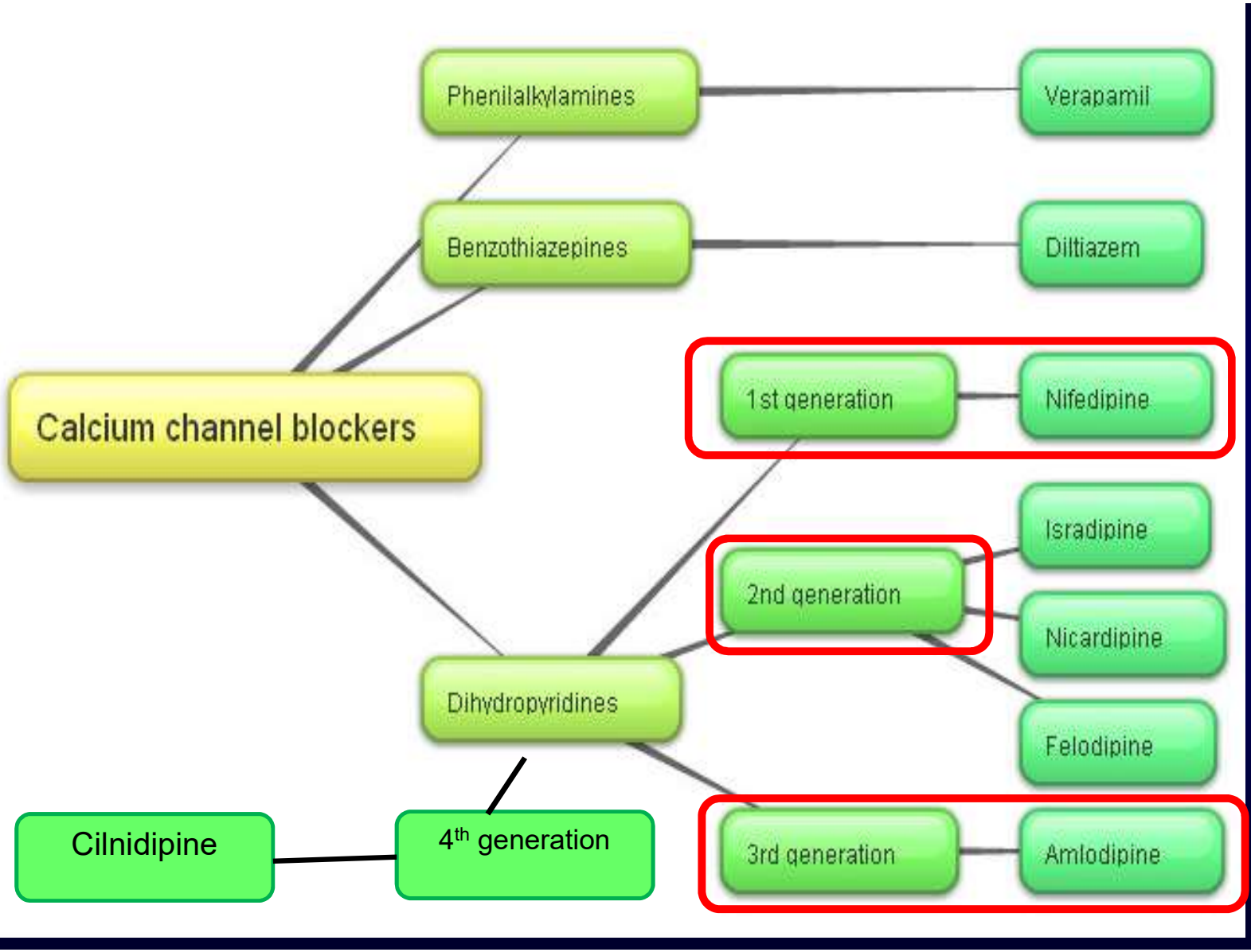
New Blood Pressure AHA Guidelines 2025

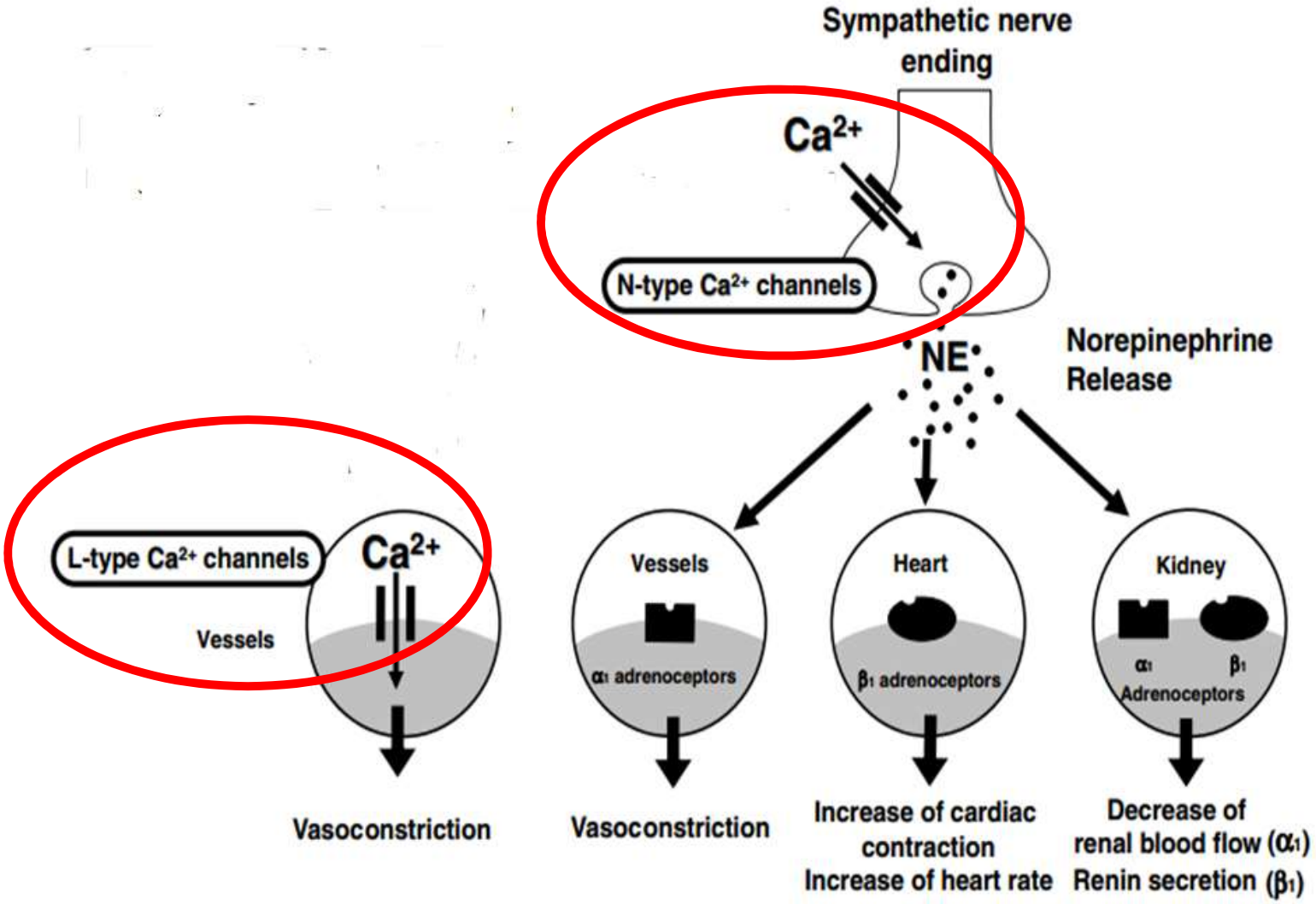
Primary Hypertension

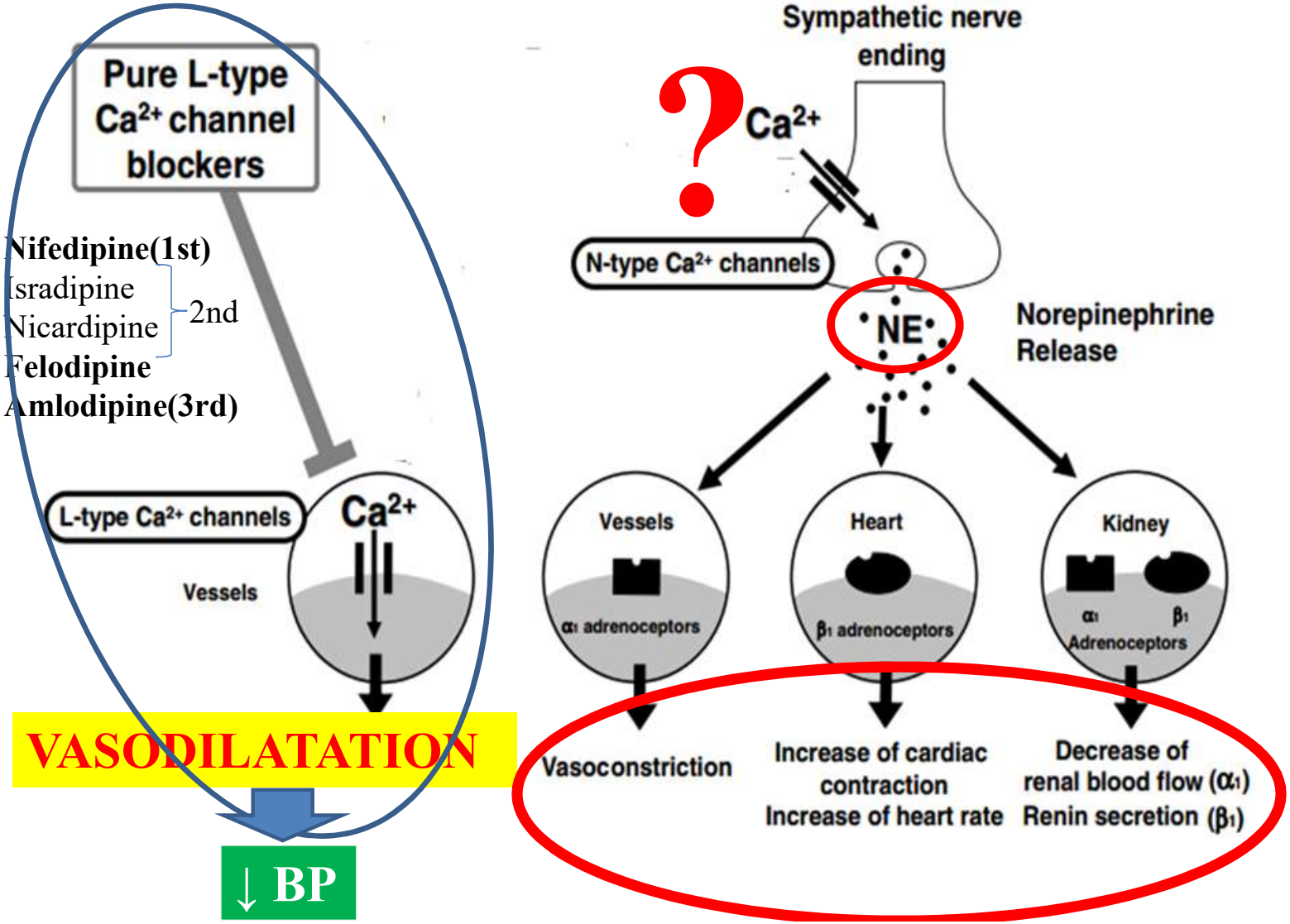
Recommendation for Initial Medication Selection for Treatment of Primary Hypertension
Referenced studies that support the recommendation are summarized in the Evidence Table.

COR	LOE	Recommendation
1	A	1. For adults initiating antihypertensive drug therapy, thiazide-type diuretics, long-acting dihydropyridine CCB, and ACEi or ARB are recommended as first-line therapy to prevent CVD.[1,2]

Abbasi J. What to Know About the New Blood Pressure Guidelines. *JAMA.* Published online October 31, 2025. doi:10.1001/jama.2025.17664


Calcium channel blockers
Phenilalkylamines
Verapamil
Benzothiazepines
Diltiazem
1st generation
Nifedipine
2nd generation
Isradipine
Nicardipine
Dihydropyridines
Felodipine
3rd generation
Amlodipine
4th generation
Cilnidipine


Sympathetic nerve ending
Ca2+
N-type Ca2+ channels
NE
Norepinephrine Release
L-type Ca2+ channels
Ca2+
Vessels
Vessels
α1 adrenoceptors
Heart
β1 adrenoceptors
Kidney
α1 β1
Adrenoceptors
Vasoconstriction
Vasoconstriction
Increase of cardiac contraction
Increase of heart rate
Decrease of renal blood flow (α1)
Renin secretion (β1)


Pure L-type Ca2+ channel blockers
Nifedipine(1st)
Isradipine
Nicardipine
2nd
Felodipine
Amlodipine(3rd)
L-type Ca2+ channels
Ca2+
Vessels
VASODILATATION
↓ BP
Sympathetic nerve ending
?
Ca2+
N-type Ca2+ channels
NE
Norepinephrine Release
Vessels
α1 adrenoceptors
Heart
β1 adrenoceptors
Kidney
α1 β1 Adrenoceptors
Vasoconstriction
Increase of cardiac contraction
Increase of heart rate
Decrease of renal blood flow (α1)
Renin secretion (β1)

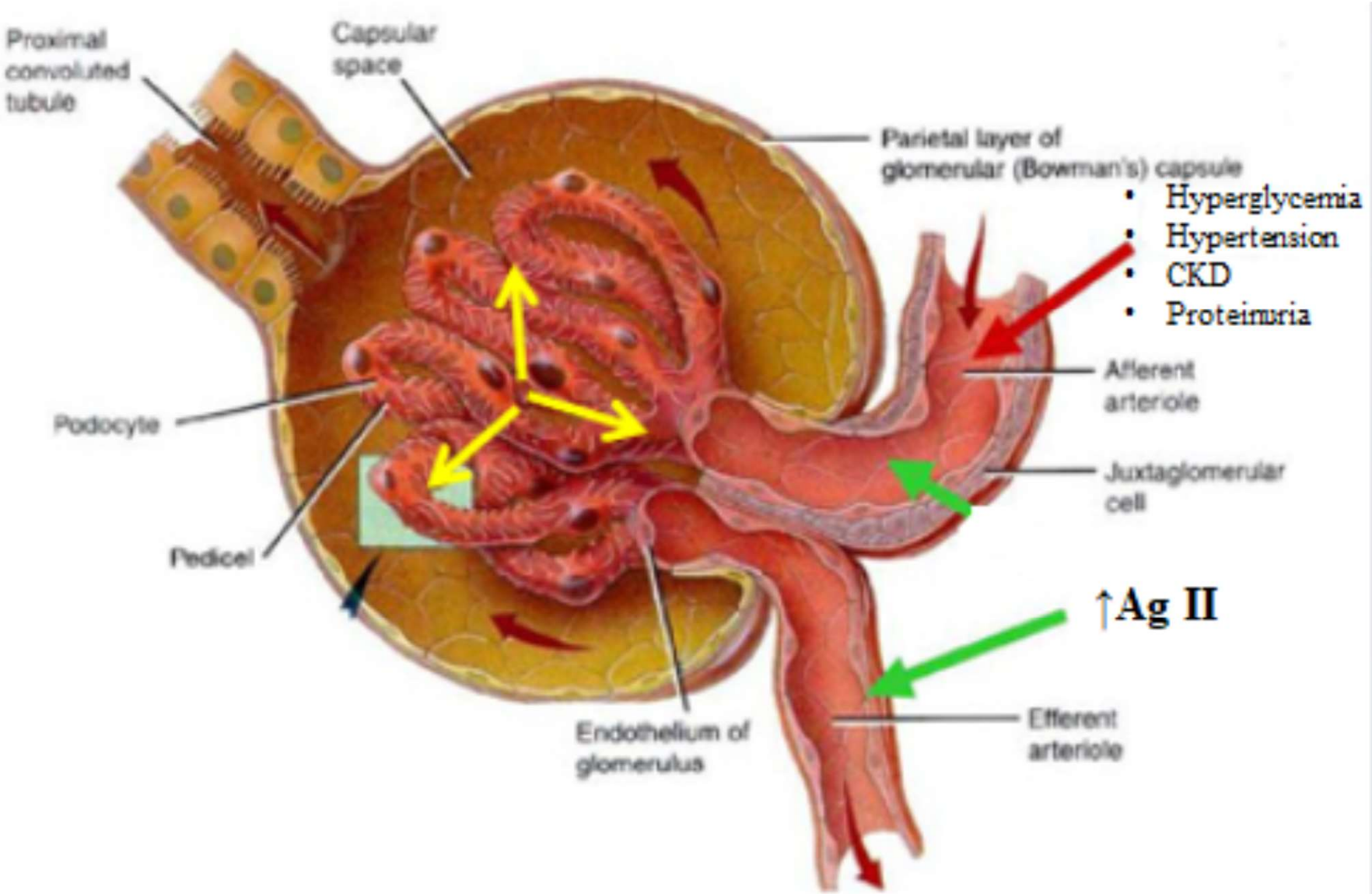
CHAPTER 145

Best Practices in Hypertension-2017

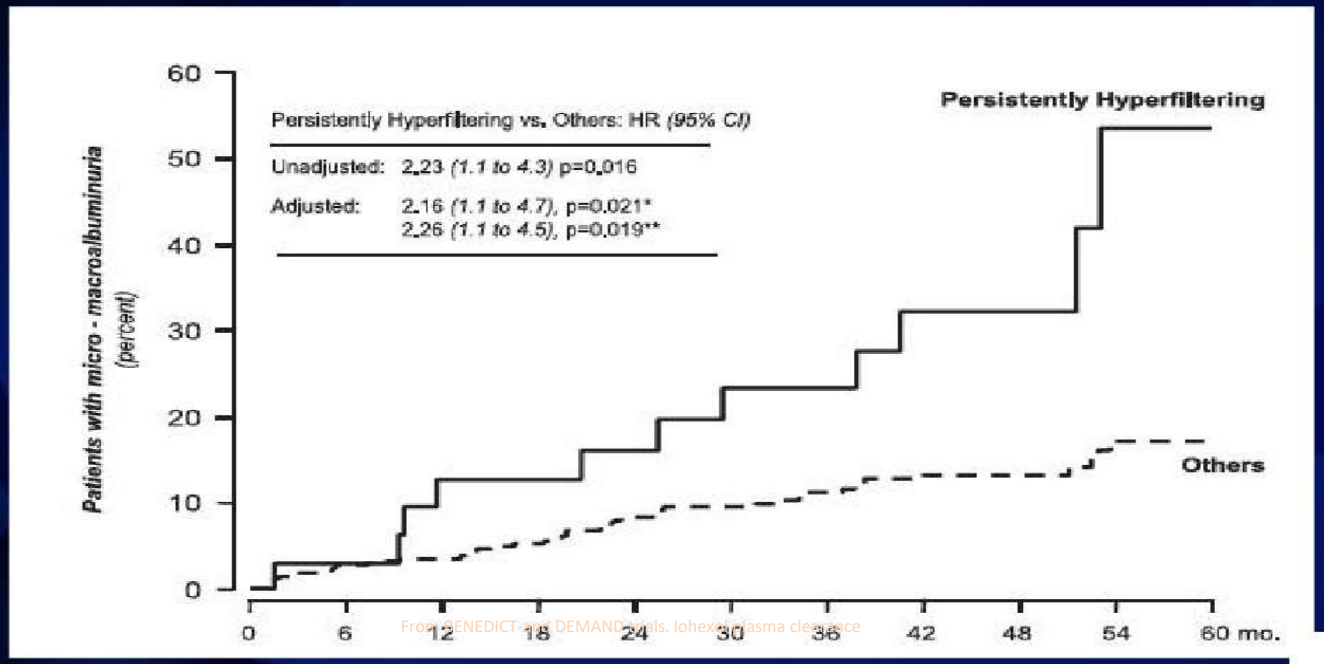
PC Manoria, Pankaj Manoria, Piyush Manoria, SK Parashar

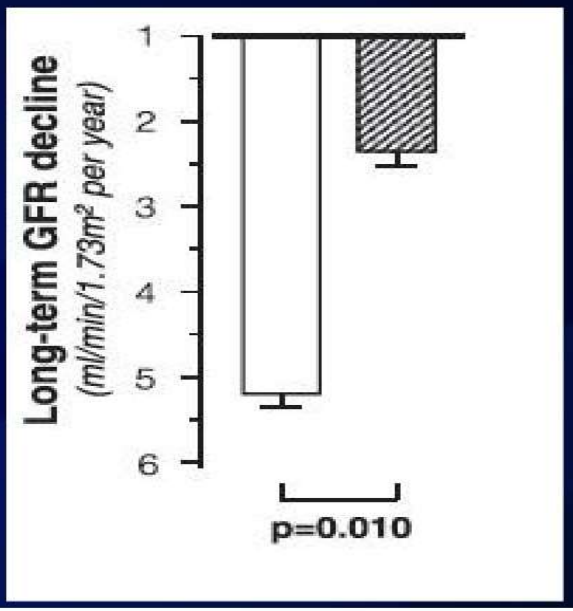
Different organs behave differently to decrease in BP:

- **Brain**→ dicta:" **lower is better**" lower the BP, less is the incidence of stroke(ACCORD BP & INVEST)
- **Heart**:$_{d}$BP< 70 - 80→↑ AMI incidence → J-shaped curved.
- **Kidney**: **intraglomerular pressure(IGP) matters > BP in renal arteries**:↑ IGP → proteinuria → adversely affect kidneys + CV syst → in renal hypertension, **drugs ↓ IGP like ACEI / ARBS / Cilnidipine preferred.**


Proximal convoluted tubule
Capsular space
Parietal layer of glomerular (Bowman's) capsule
• Hyperglycemia
• Hypertension
• CKD
• Proteinuria
Afferent arteriole
Podocyte
Juxtaglomerular cell
Pedicel
↑Ag II
Endothelium of glomerulus
Efferent arteriole

Hyperfiltration is associated with higher risk of CKD progression in the long term





Persistent hyperfiltration

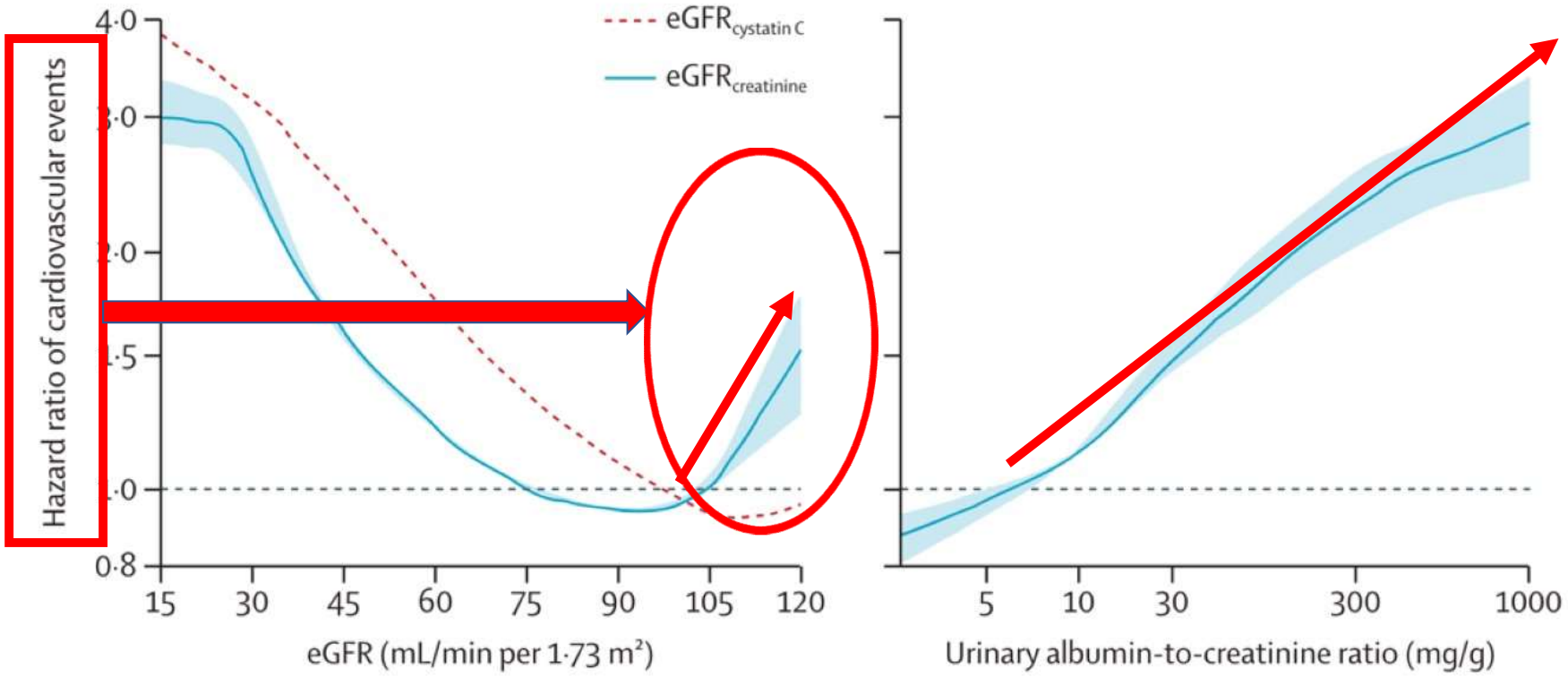
Ameliorated hyperfiltration

Ruggenenti P. Diab Care 2012;35:2061-2068

GFR reduction > 10% at month 6 were considered as patients with persistent hyperfiltration. Those with smaller reductions were categorized as “ameliorated hyperfiltration.”

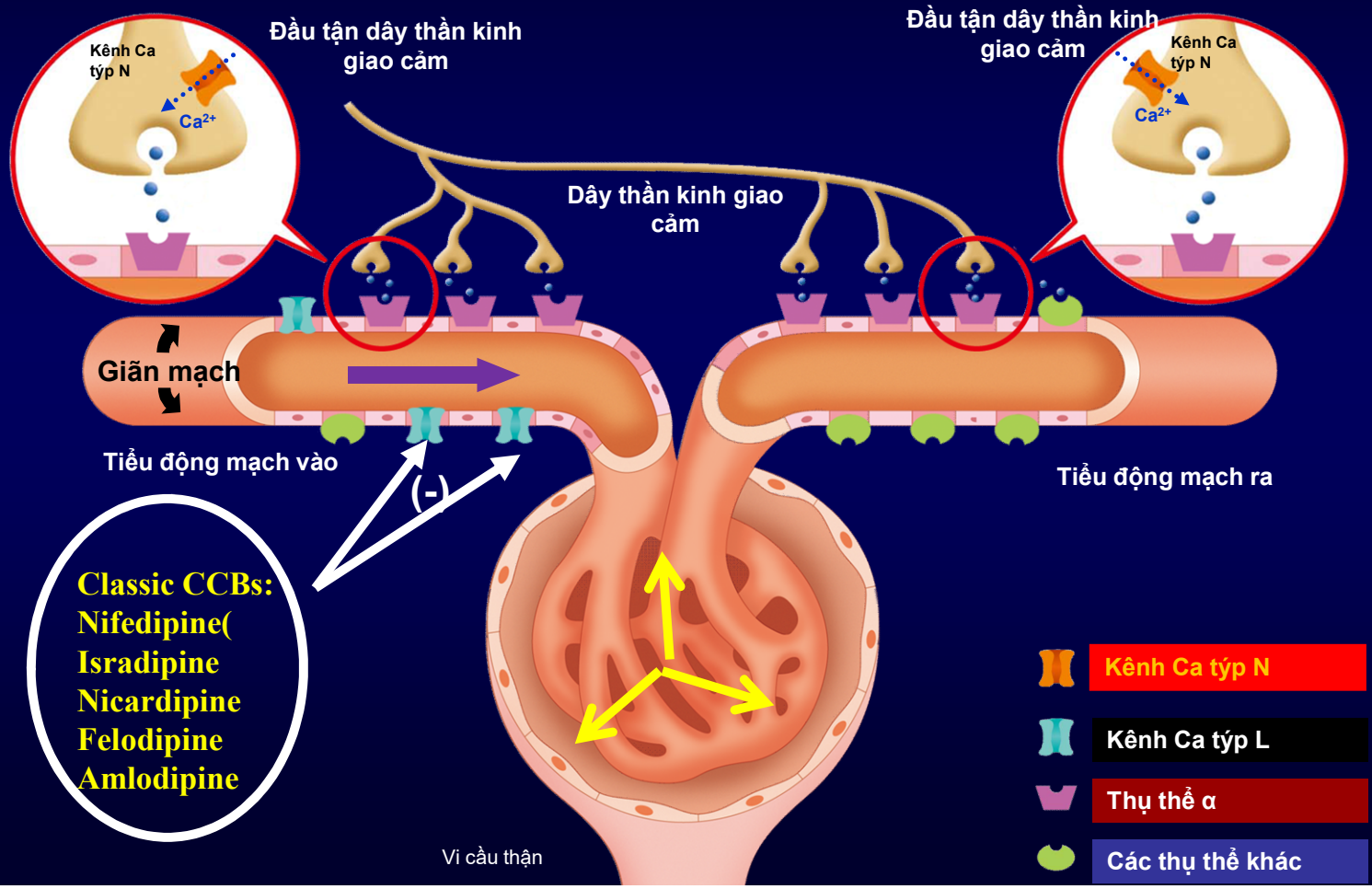
TĂNG ÁP LỰC CẦU THẬN CŨNG LÀM TĂNG NGUY CƠ TIM MẠCH

Risk of CV Events: Relationship With eGFR and UACR[1]



1. Kalantar-Zadeh K, et al. Lancet. 2021;398:786-802.

Thụ thể vi tuần hoàn thận



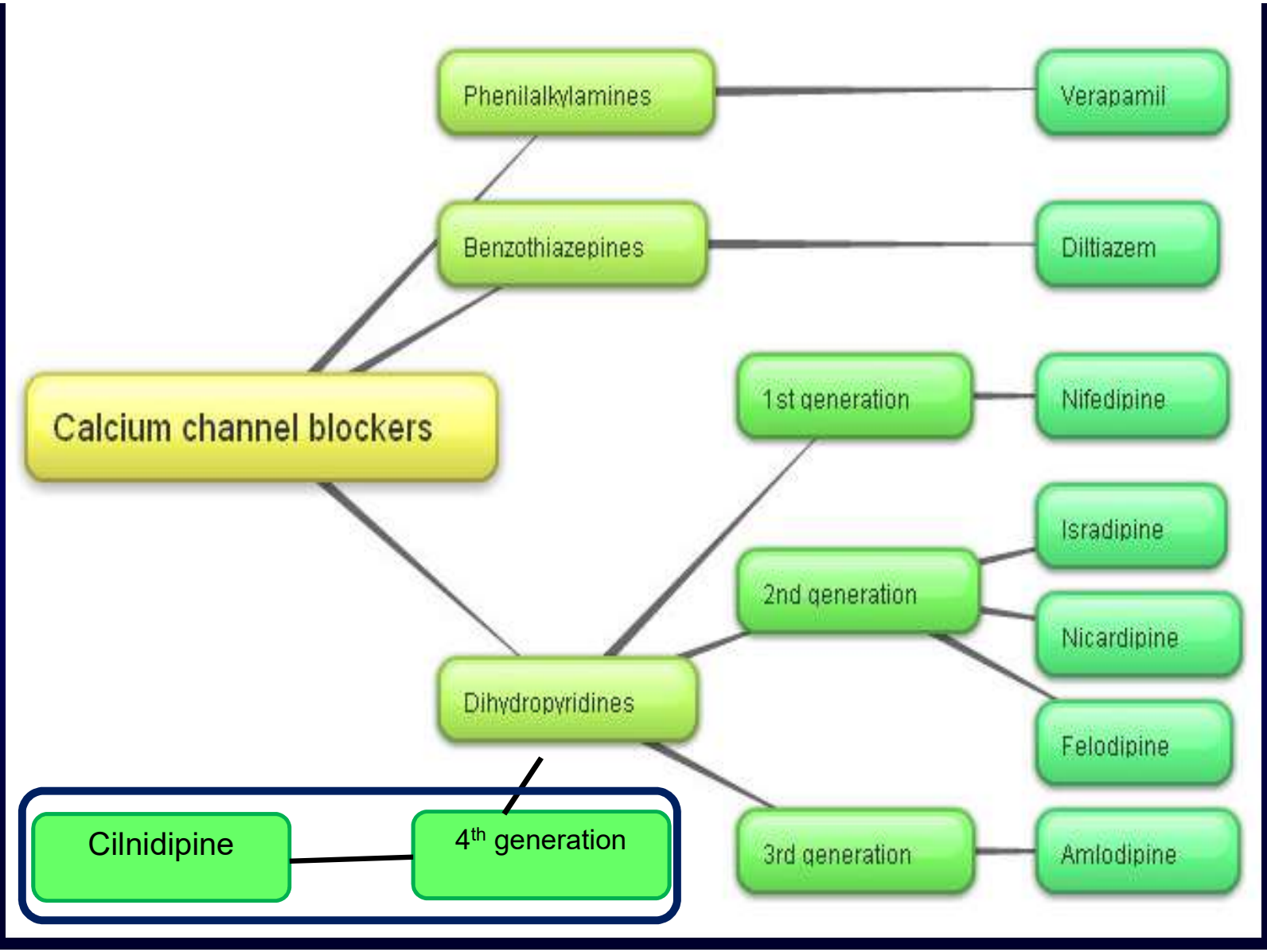
KDIGO 2013 Clinical Practice Guideline for the Management of BP in CKD

Nên tránh sử dụng dihydropyridine calcium channel blockers nơi BN BTM đã có Albumin niệu đặc biệt nếu không sử dụng đồng thời với ACE-I hoặc ARB

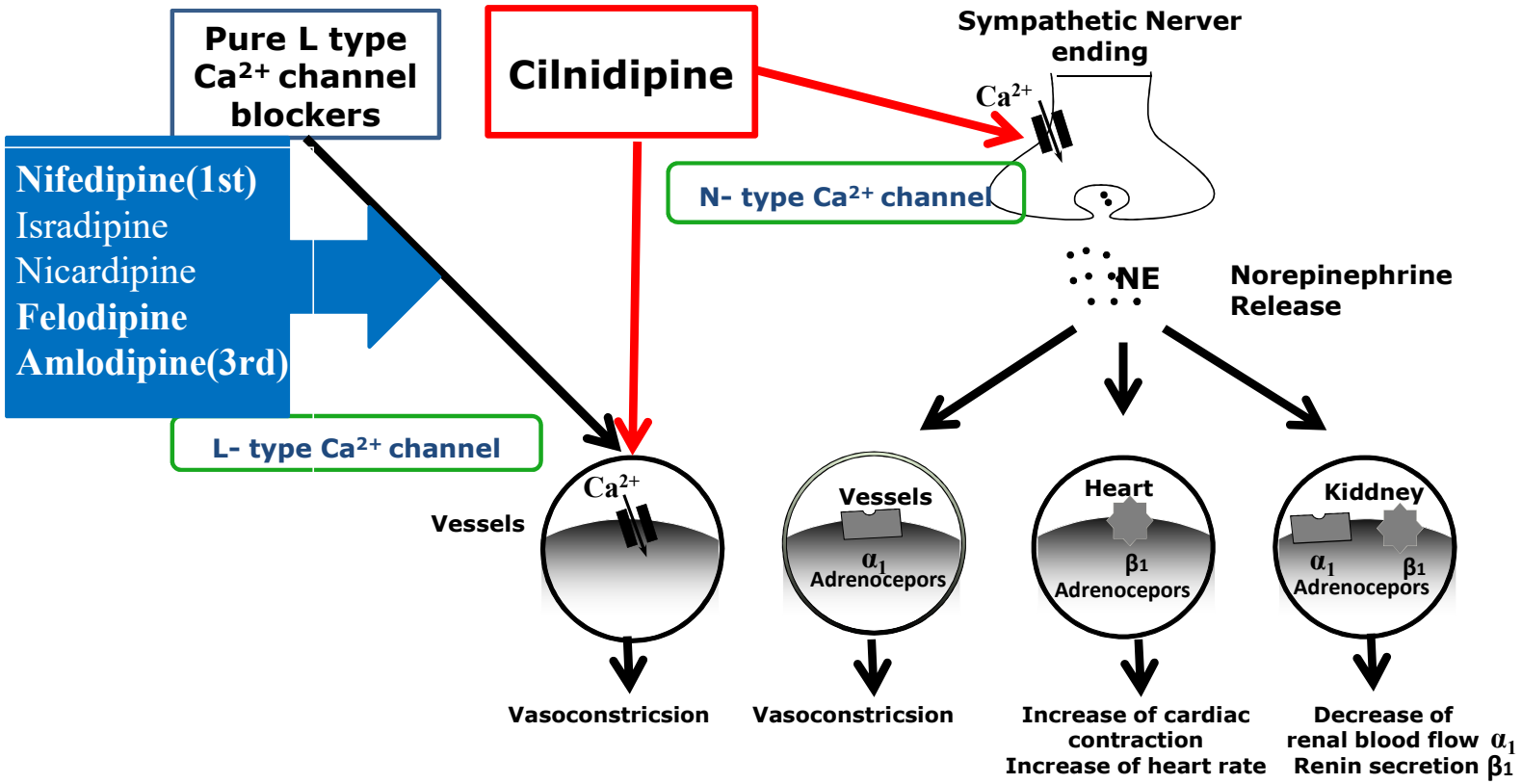
- Các thuốc CCBs khác nhau về tác dụng trên các tiểu động mạch cầu thận:
  - Kênh thụ thể L (chủ yếu trên tiểu động mạch đến). → → ↑ áp lực trong cầu thận →↑Albumin niệu
  - **Kênh thụ thể T/N** (có cả trên tiểu động mạch đến & đi) → ↓ áp lực trong cầu thận →**↓Albumin niệu**

Các thuốc CCBs thế hệ sau (cilnidipine , manipine,) chẹn thụ thể T/N → Không làm ↑Alb niệu mà còn có thể làm ↓Albumin niệu

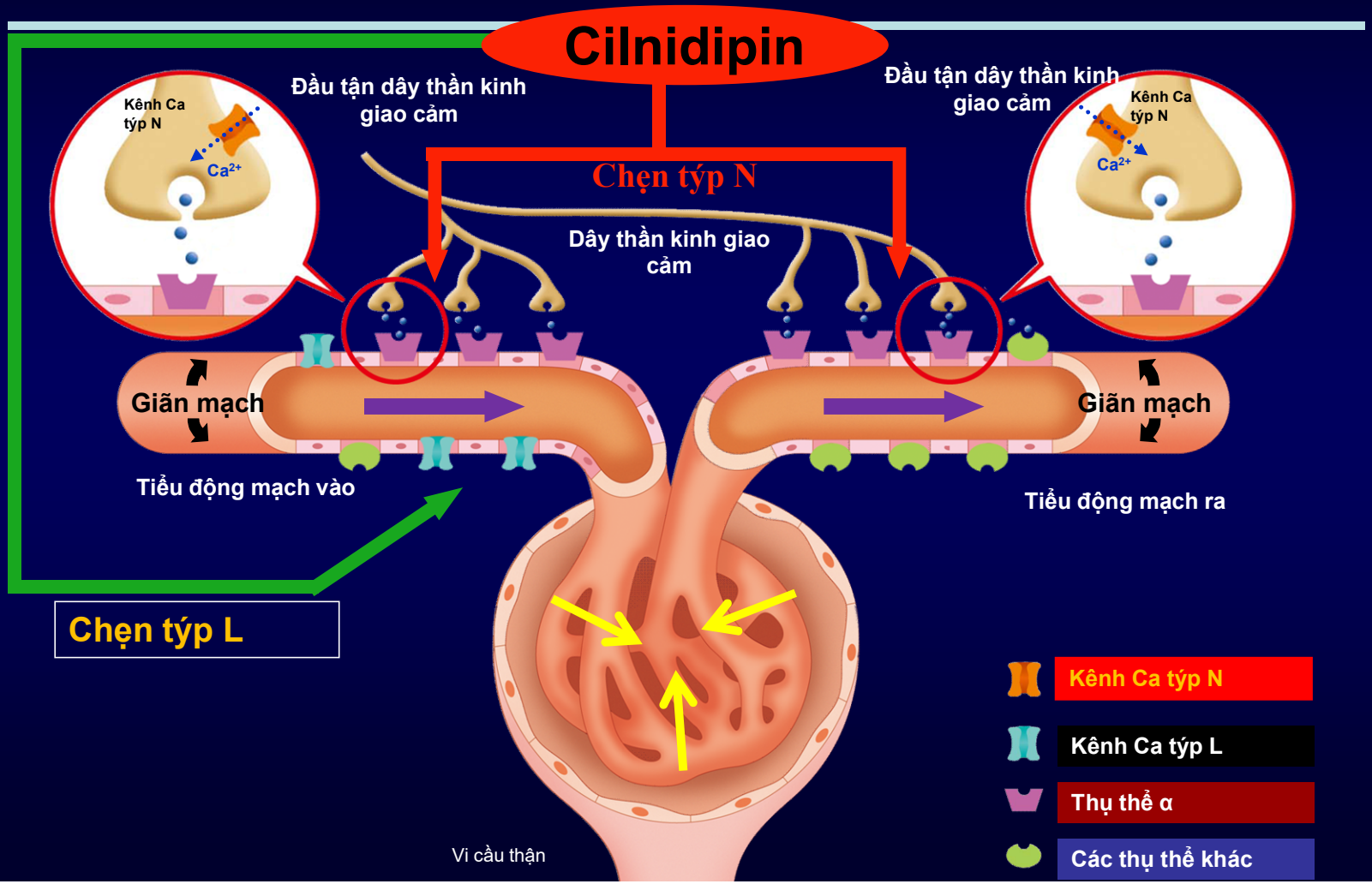
KDIGO(2012). Kidney Intern, suppl(2): 347-356


Calcium channel blockers
Phenilalkylamines
Verapamil
Benzothiazepines
Diltiazem
Dihydropyridines
1st generation
Nifedipine
2nd generation
Isradipine
Nicardipine
Felodipine
3rd generation
Amlodipine
4th generation
Cilnidipine

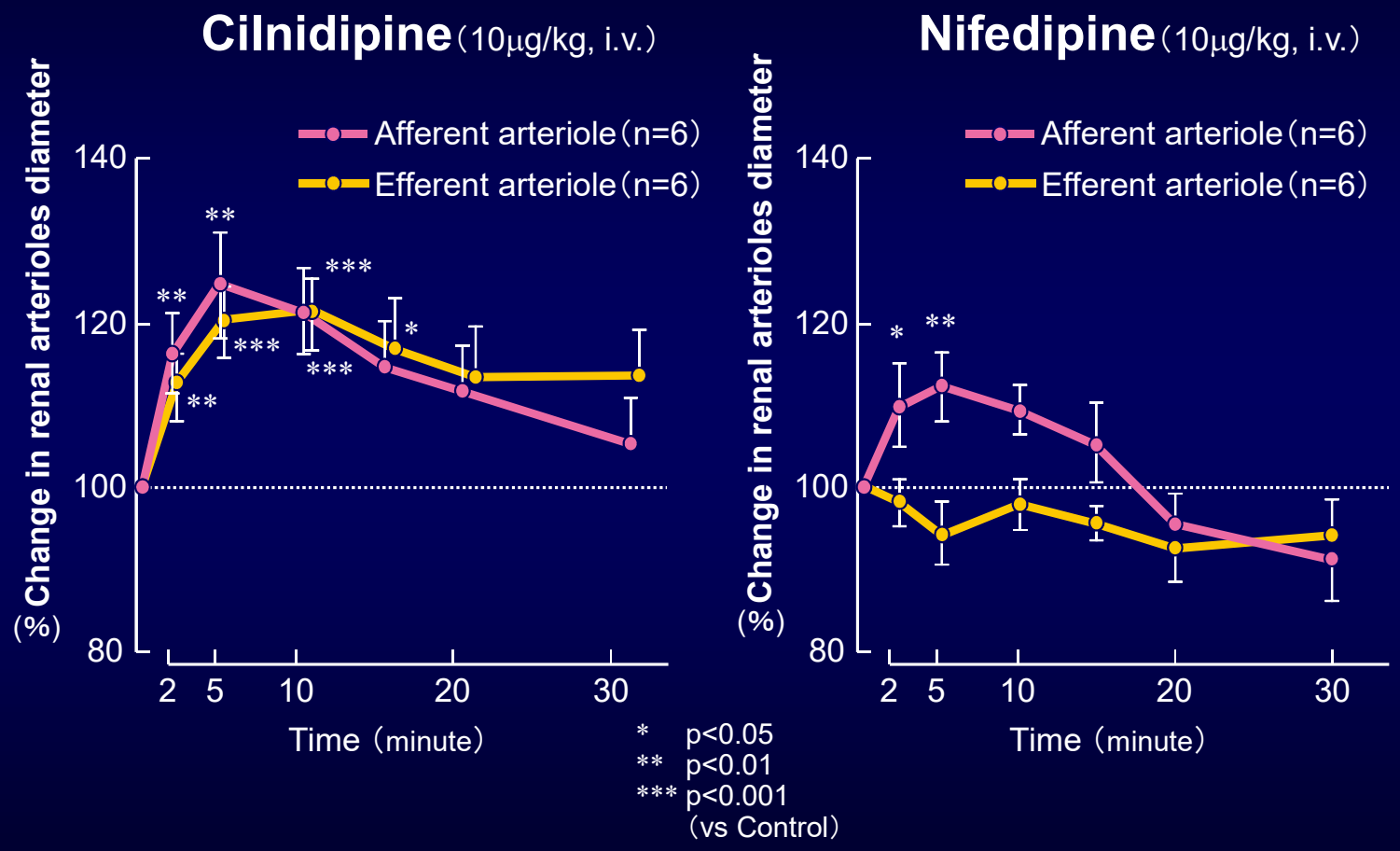
CCB thế hệ mới



Tóm tắt vi tuần hoàn thận



Renal vasodilator effect of Cilnidipine
~Effect to afferent and efferent arterioles~



S. Fujii et al. Pharmacology & Therapy 1999; 27: 163-8

Dihydropyridines CCBs and Renal Disease

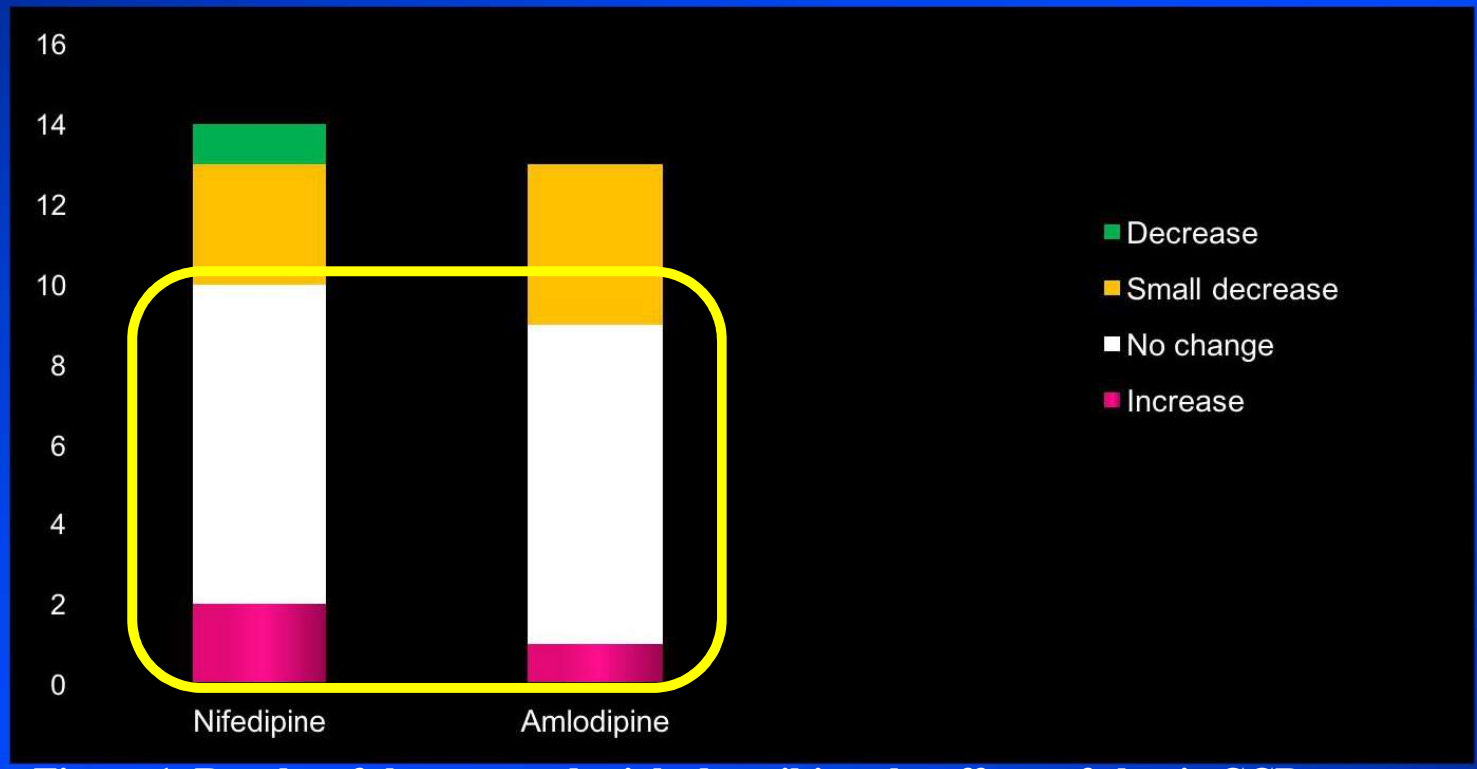


Figure 1 Results of the reported trials describing the effects of classic CCBs on albuminuria/proteinuria. Most of the trials cannot show a protective effect on proteinuria and/or albuminuria.

Robles N et al. Hypertension Research 2017;40:21-28

Dihydropyridines CCBs and Renal Disease

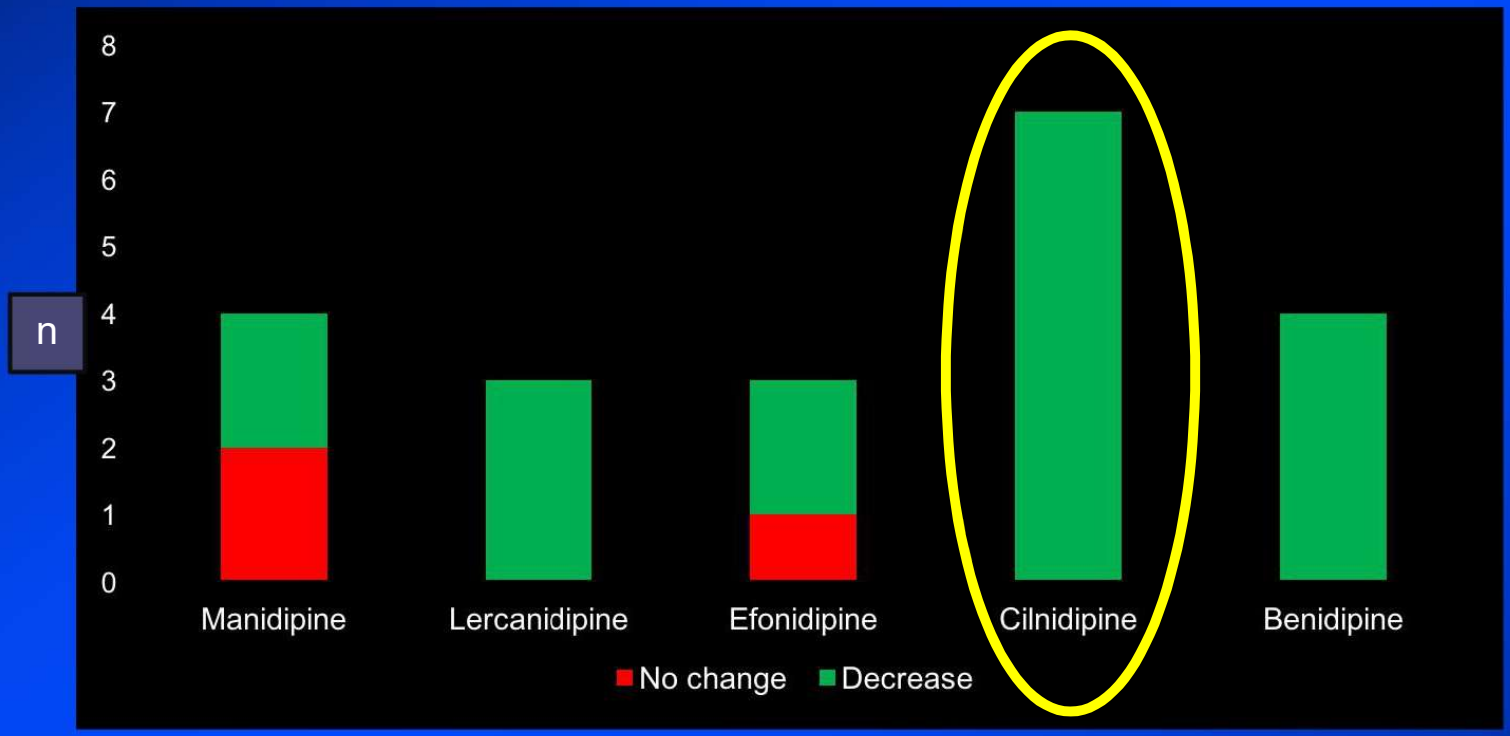
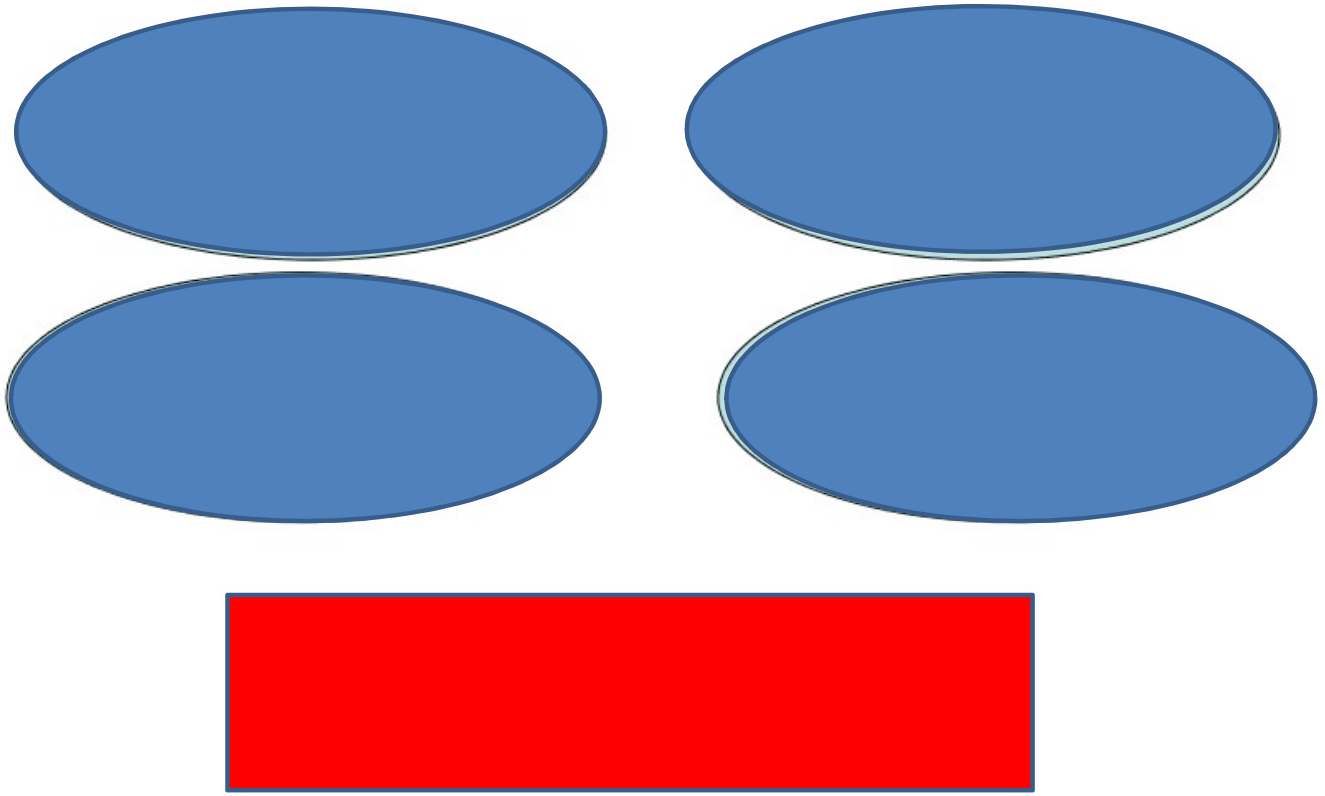


Figure 2 Results of the reports describing the effects of new CCBs on albuminuria/proteinuria. Most of the trials found a decrease in proteinuria/albuminuria after treatment.

Robles N et al. Hypertension Research 2017;40:21-28

Prognostic Value of Micro/Macroalbuminuria



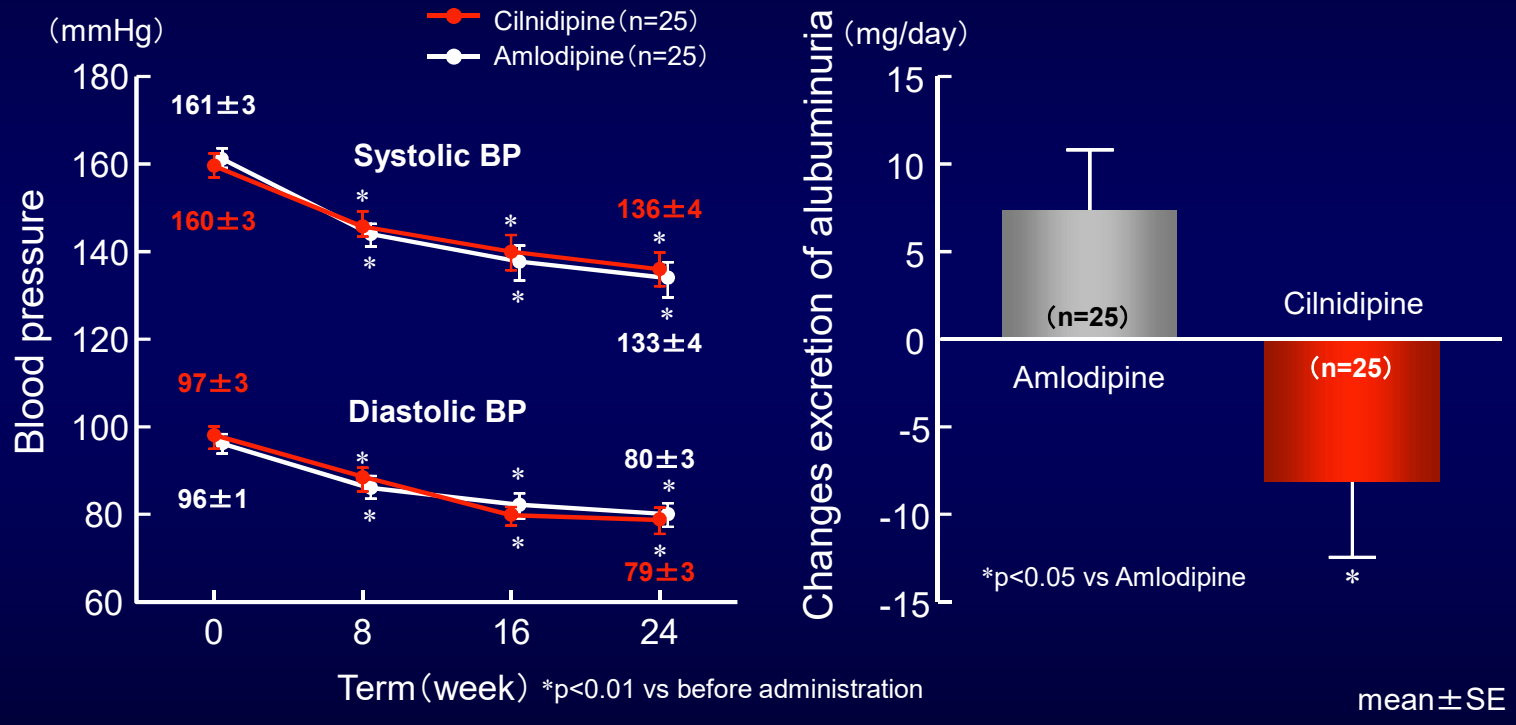
Novel Albuminuria Endpoints May Improve CKD Progression Trials

In the meta-analysis of RCTs, which included 29,979 participants and 41 treatment comparisons:

- Treatment effect on albuminuria significantly correlated with treatment effect on clinical endpoints over 6 months.
- **↓30% mean albuminuria with treatment→ ↓27% risk of a composite endpoint (ESRD, eGFR< 15 mL/min/1.73 m^2, or doubling of serum creatinine.**
- Stronger correlation in patients with high baseline albuminuria (urine ACR > 30 mg/g).

Heerspink HJL, Greene T, Tighiouart H, et al. Change in albuminuria as a surrogate endpoint for progression of kidney disease: a meta-analysis of treatment effects in randomised clinical trials. *Lancet Diabetes Endocrinol* 2019. DOI:10.1016/S2213-8587(18)30352-8. (Published online January 8, 2019)

Effect of Cilnidipine on urinary albumin excretion in patients with hypertension

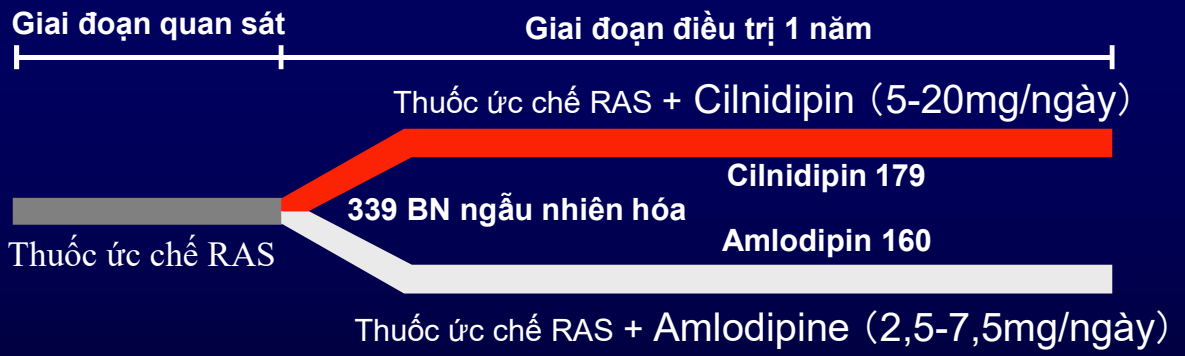


Morimoto S, et al. Journal of Hypertens 2007; 25: 2178-83

Nghiên cứu CARTER

Cilnidipine versus Amlodipine Randomized Trial for Evaluation in Renal Disease

- Thiết kế : Thử nghiệm ngẫu nhiên mở nhãn
- Đối tượng : 1. Tỉ số protein/creatinin nước tiểu: ≧300mg/g
  2. Creatinin huyết thanh: ≦3,0mg/dL
  3. HA: >130/85mmHg
  4. Đã điều trị với CTTA hoặc ƯCMC trong 2-3 tháng hoặc dài hơn
- Đề cương :



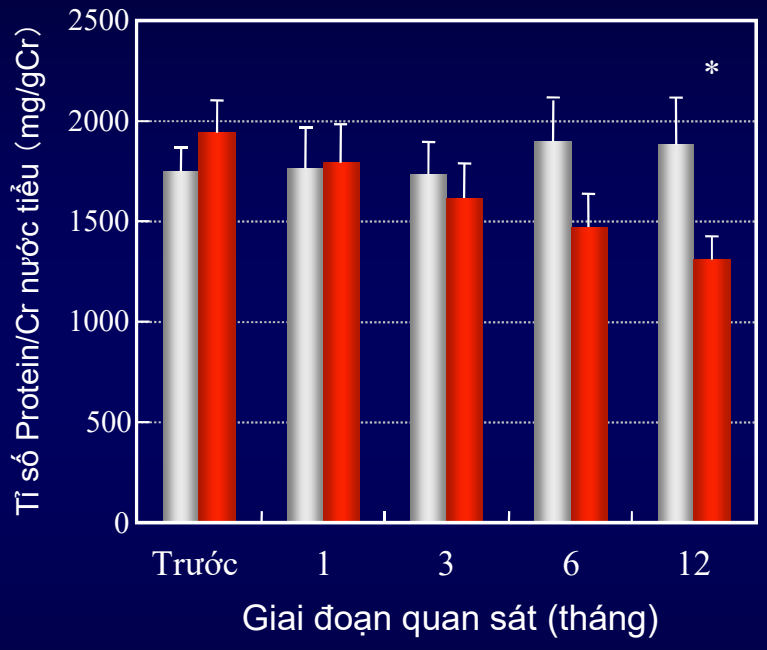
- HA đích : <130/85 mmHg

Nếu cilnidipin or amlodipin cộng với thuốc ức chế RAS không làm giảm đến HA đích, dùng thêm 1 thuốc thứ ba (khác với thuốc ức chế RAS hoặc chẹn kênh calci)

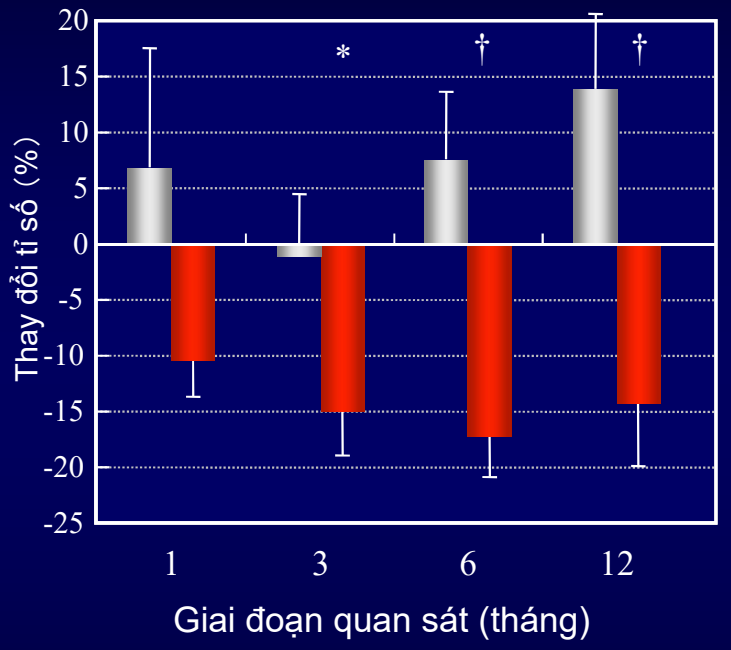
- Kết điểm : **Tỉ số protein/creatinin nước tiểu**

Fujita T, và cs. Kidney Int 2007; 72: 1543-9

Sự thay đổi tỉ số Protein/Cr nước tiểu trong giai đoạn điều trị



*: p<0,05 so với nhóm Cilnidipin



*: p<0,05, †: p<0,01 so với nhóm Cilnidipin

Amlodipin	160	147	142	137	130
Cilnidipin	179	168	168	160	146

Nhóm Amlodipin Nhóm Cilnidipin

Fujita T, và cs. Kidney Int 2007; 72: 1543-9

CCBs classification based on actions on ∑ nerves

Generation from the view of effect on Σ system	Sympathetic nerve activity	Generic name	Effect on NE release (vascular)	Plasma NE concentration (SHR)
Ⅰ	↑↑	Verapamil		
		Diltiazem		
		Nifedipine	No effect	Increase(+++)
		Nicardipine	No effect	Increase(+++)
Ⅱ	↑	Nilvadipine		
		Manidioine		Increase(++)
		Nitrendipine		
		Nisoldipine		
		Benidipine		Increase(++)
		Barnidipine		
		Efonidipine		
		Felodipine		
		Aranidipine		
Ⅲ	↗ ↘	Amlodipine	No effect	Increase(+)
		Azelnidipine		

↑↗ : Active ↘ : Suppress NE : Norepinephrine SHR : Spontaneously Hypertensive Rat

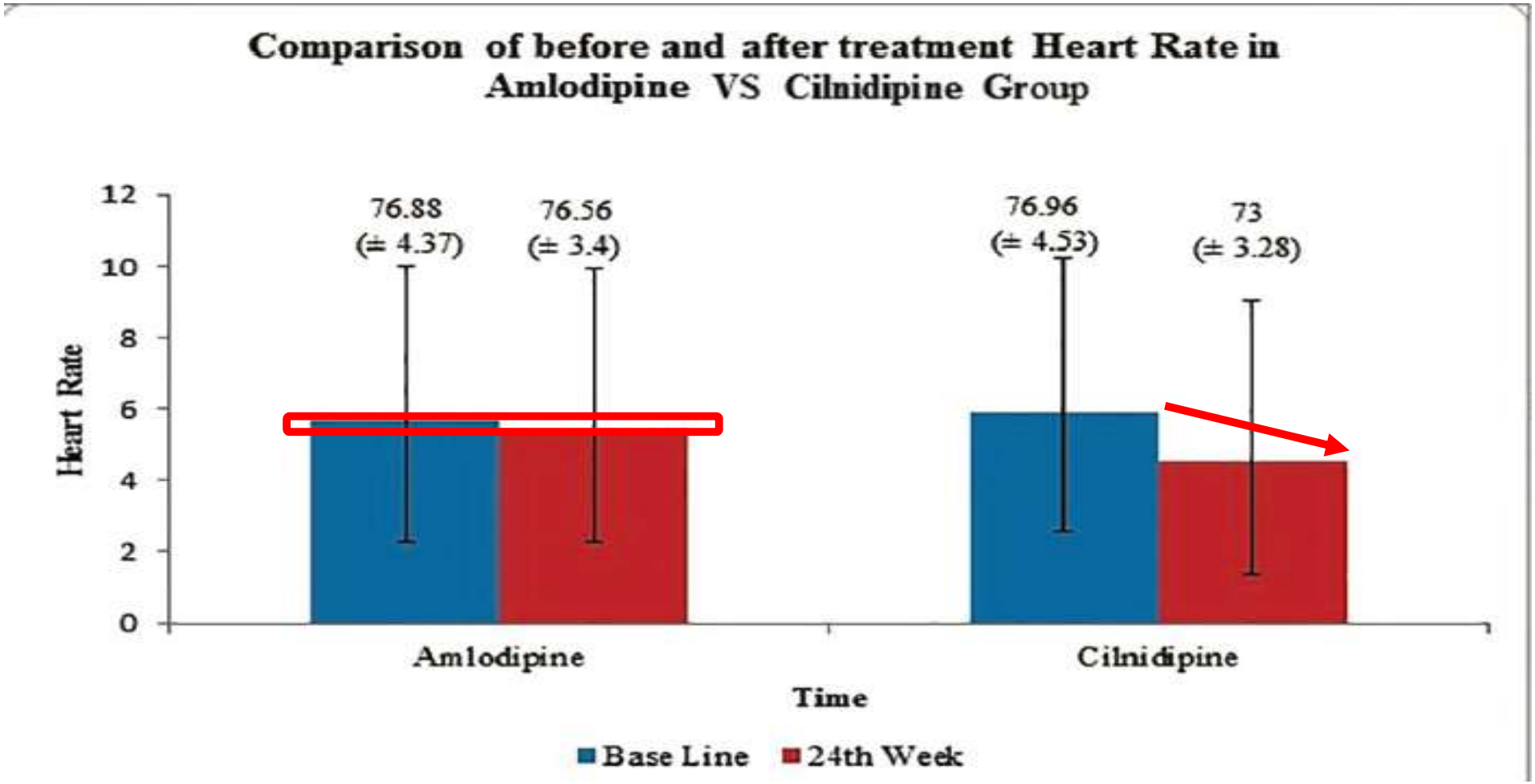
A. Takahara et al. Mebio 2005; 22: 89-100

Effects of Cilnidipine on Heart Rate and Uric Acid Metabolism in Patients With Essential Hypertension

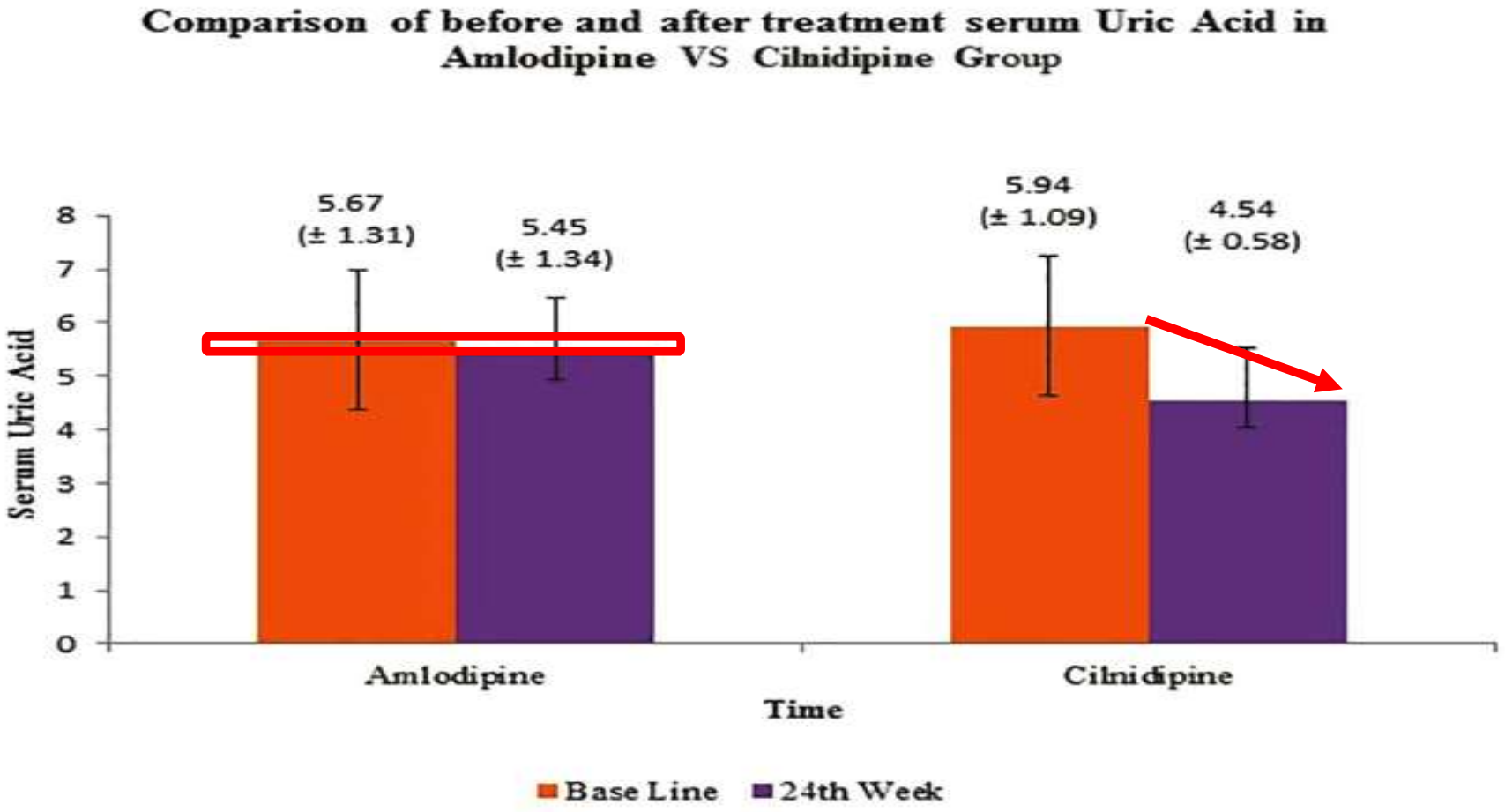
Table 1. General Characteristics of Patients of Amlodipine and Cilnidipine Groups

Parameters	Amlodipine	Cilnidipine
N	47	45
Male	25	23
Female	22	22
Age (years)	52.86 ± 5.81	53.14 ± 5.24
Body weight (kg)	67.56 ± 10.85	67.94 ± 9.59
Height (cm)	162.22 ± 6.79	162.78 ± 7.19
BMI	25.01 ± 5.1	25.51 ± 2.9

Effects of Cilnidipine on Heart Rate and Uric Acid Metabolism in Patients With Essential Hypertension



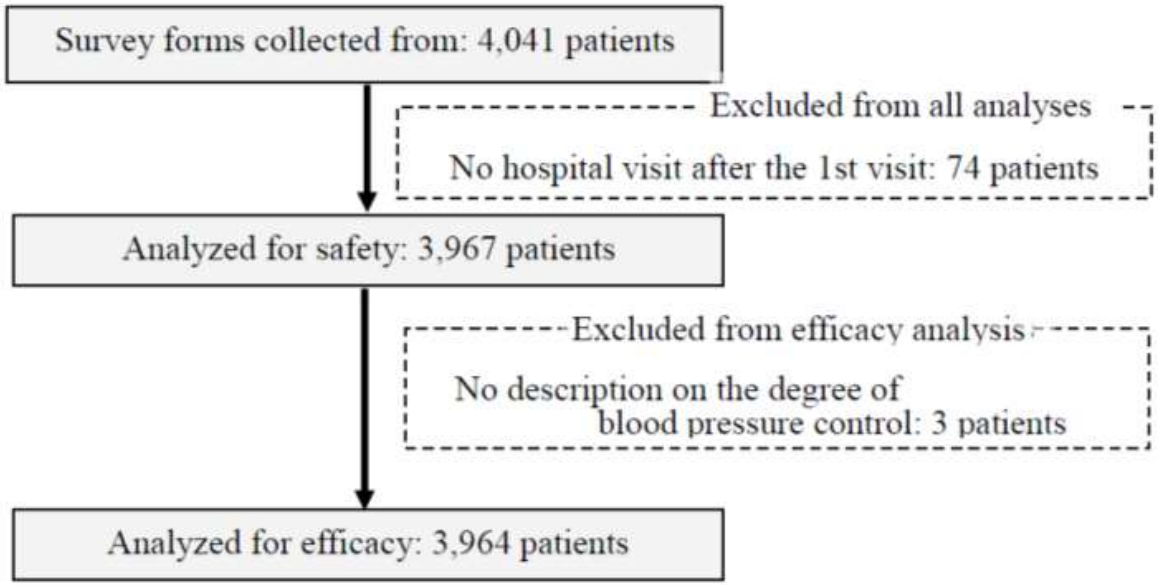
Effects of Cilnidipine on Heart Rate and Uric Acid Metabolism in Patients With Essential Hypertension



Medical Consultation & New Remedies No. 46 (5), 2009

Special drug use-results survey of cilnidipine (type L and type N calcium channel antagonist: Atelec® Tablets and Cinalong® Tablets) in hypertensive patients with diabetes

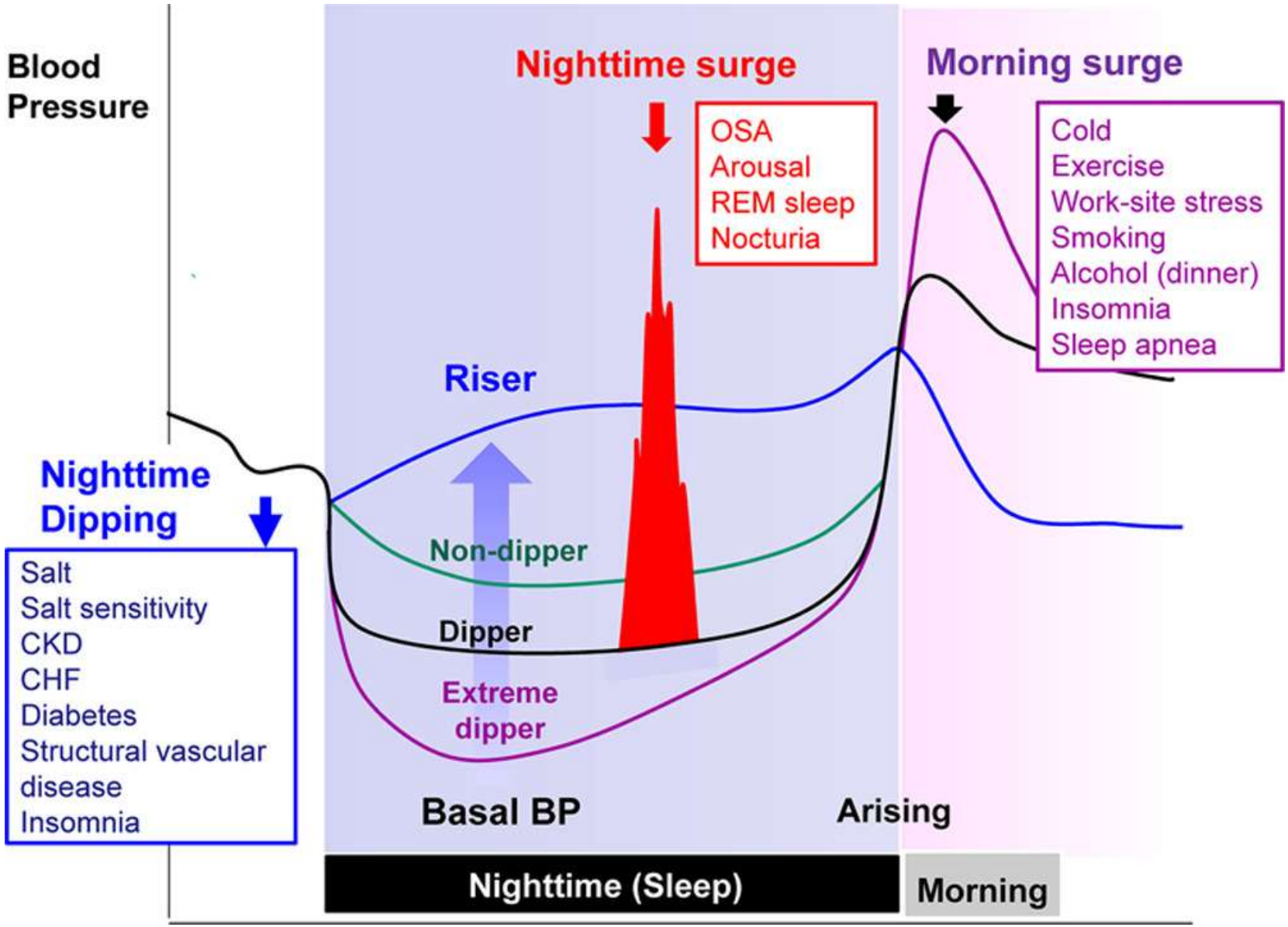
Number of patients: 4,041



3,964 patients were evaluated in this study who were complicated with hypertension and diabetes

Summary of Effects of Cilnidipine (*Atelec) in Hypertensive Patients with Diabetes*

- **↓ BP & HR in DM patients.**
- **↓ HbA1c in untreated DM patients.**
- **↓ Uric acid in hyperuricemia patients.**
- **↓ Total cholesterol & ↓ Triglyceride in patients not on hypolipidemic drugs.**


Blood Pressure
Nighttime surge
OSA
Arousal
REM sleep
Nocturia
Morning surge
Cold
Exercise
Work-site stress
Smoking
Alcohol (dinner)
Insomnia
Sleep apnea
Riser
Nighttime Dipping
Salt
Salt sensitivity
CKD
CHF
Diabetes
Structural vascular disease
Insomnia
Non-dipper
Dipper
Extreme dipper
Basal BP
Arising
Nighttime (Sleep)
Morning

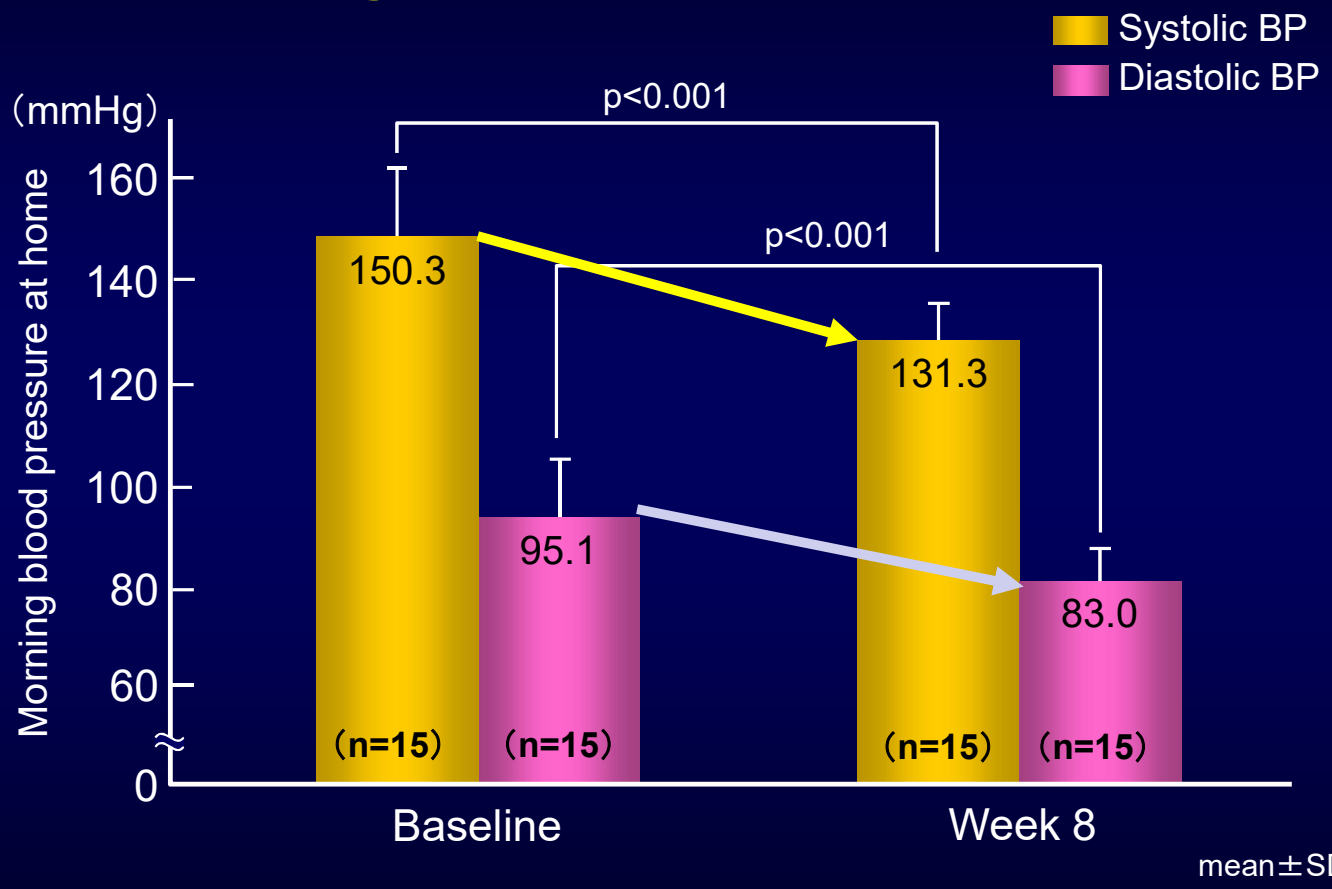
Dosing at Night to Cause BP 'Dipping'

- In HT, DM, CKD, → very difficult time dipping at night → ↑ BP load→ ↑ Stroke & MI risks

- **Dosing at night offers an advantage and increases the likelihood of converting people to dipping status from nondipping status.**

Carter BL,et al. J Clin Hypertens (Greenwich). 2014.- Roush GC, et al. J Clin Hypertens (Greenwich). 2014.- Rossen NB, et al. Hypertension. 2014.- Mallick SR, et al Curr Hypertens Rep. 2012.- Tofé Povedano S, et al. J Clin Hypertens (Greenwich). 2009.- Goswami P,et al. Curr Opin Nephrol Hypertens. 2009.

Effect of Cilnidipine (Atelec) on morning blood pressure at home



Yamagishi T. Hypertens Res 2006; 29: 339-44

CCBs and Edema

Table 1: Incidence of ankle edema with various calcium channel blockers

Nifedipine[3]	6	Lacidipine[6,7]	4-4.44
Nifedipine (extended release)[3]	10-30	Lercandipine[7,8]	1.2-9
Diltiazem[3]	6-10	Nicardipine[4]	3
Diltiazem (extended release)[3]	2-3	Nisoldipine[9]	6-19
Felodipine[3]	14	Manidipine[10,11]	4.9-6
Isradipine[4,5]	6	Mibefradil[12]	7
Amlodipine[1]	6-15		

Shetty et al(2013). *North American Journal of Medical Sciences*

CHAPTER

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Best Practices in Hypertension-2017

PC Manoria, Pankaj Manoria, Piyush Manoria, SK Parashar

reading of SPRINT 120 mm Hg will be higher by 10-15 mm Hg, if we record BP in the conventional manner in the clinic. Therefore lower goal of 120 mm Hg systolic of SPRINT cannot be applied in real practice as such. Among drugs used for hypertension, CTD is preferred over hydrochlorthiazide, Azilsartan a new sartan, has additional advantages and CCB Cilnidipine had additional advantage over amlodipine in that it provides renoprotection and has minimal chance of edema. Atenolol is out and currently vasodilatory betablockers are used for treatment of hypertension particularly when it is associated with coronary heart disease and heart failure. Angiotensin Receptor Neprilysin inhibitor is undergoing evaluation in hypertension with lot of

b.

ORIGINAL RESEARCH www.ijcmr.com

Assessment of Efficacy of Amlodipine with Cilnidipine in Hypertensive Patients: A Comparative Study

K. Anantha Babu[1]

90 hypertensive pts divided into 2 groups:

- G1 (45 pts): Amlodipin 5-10mg qd
- G2 (45 pts): Cilnidipine: 10-20 mg qd

P= NS

K. Anantha Babu1. International Journal of Contemporary Medical Research . Volume 4 | Issue 4 | April 2017 | ICV (2015): 77.83 | ISSN (Online): 2393-915X; (Print): 2454-7379

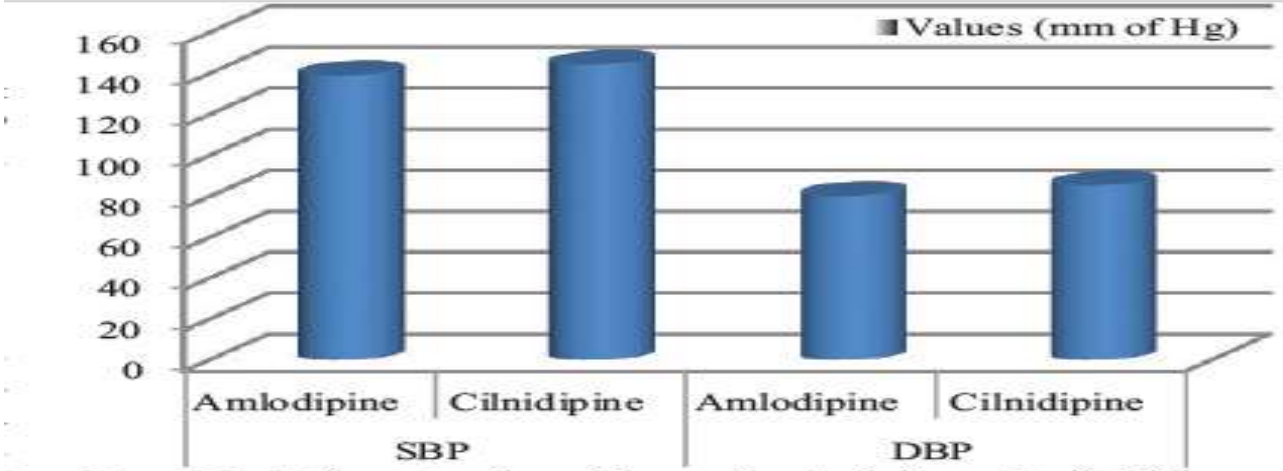
Parameter		Amlodipine	Cilnidipine
Number of patients		45	45
Mean age (years)		55.2	52.7
Gender	Males	18	18
	Females	27	27

Table-1: Demographic details of the patients

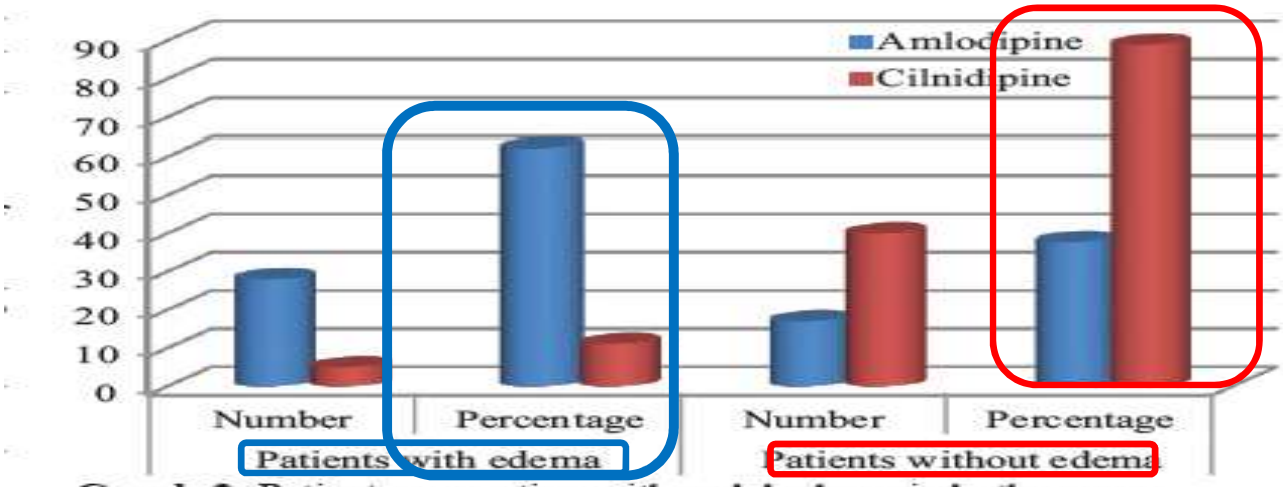
Blood pressure		Values (mm of Hg)	p-value
SBP	Amlodipine	139.1	0.58
	Cilnidipine	144.2	
DBP	Amlodipine	80.2	0.71
	Cilnidipine	85.3	

SBP: Systolic blood pressure, DBP: Diastolic blood pressure

Table-2: Comparative evaluation of antihypertensive efficacy of amlodipine with cilnidipine

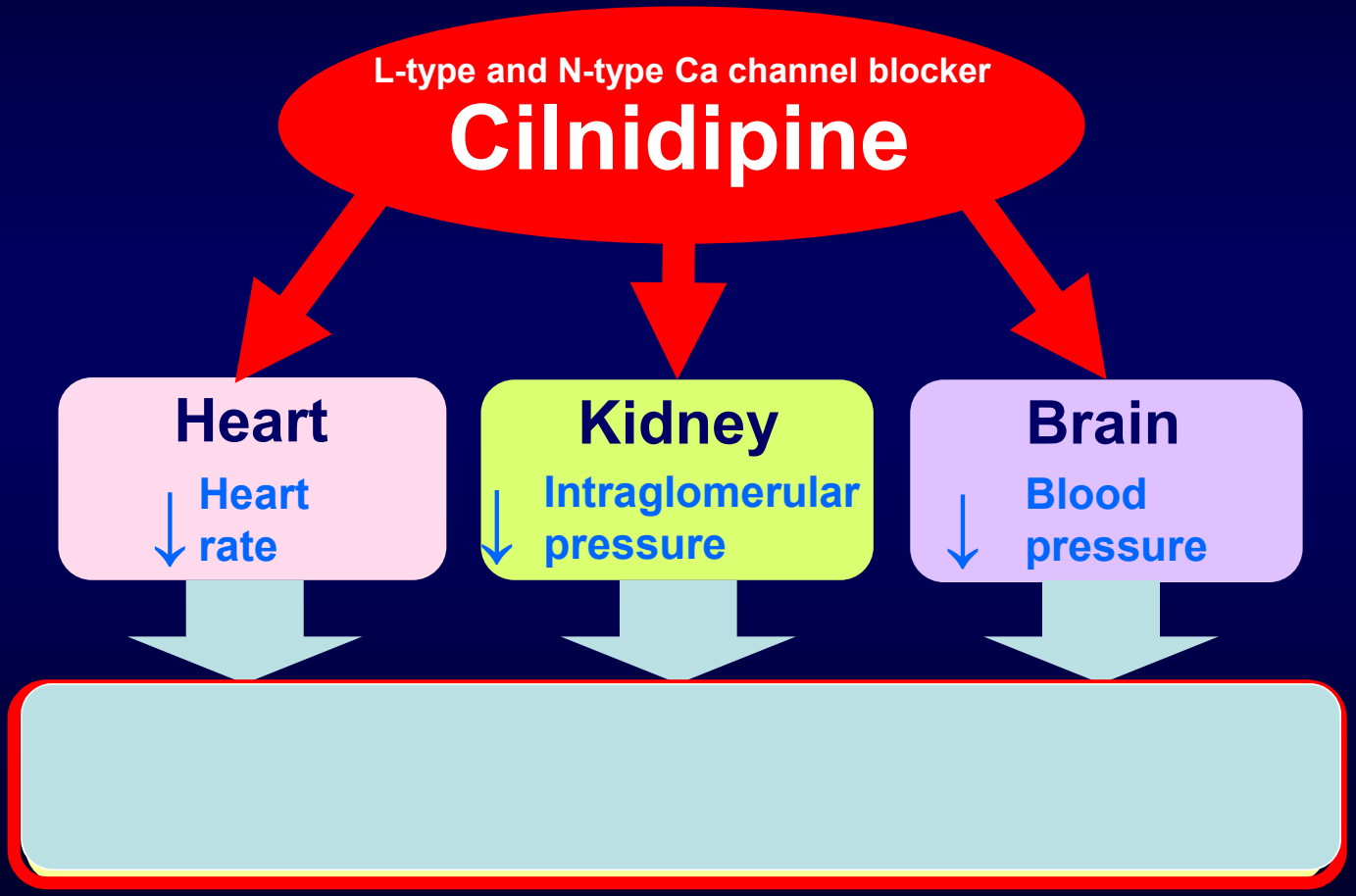


Graph-1: Antihypertensive efficacy of amlodipine with cilnidipine



Graph-2: Patients presenting with pedal edema in both groups

Summary of inhibitory action of Cilnidipine on development of CVD




Thank you for
your attention