

# TĂNG HUYẾT ÁP KHÁNG TRỊ

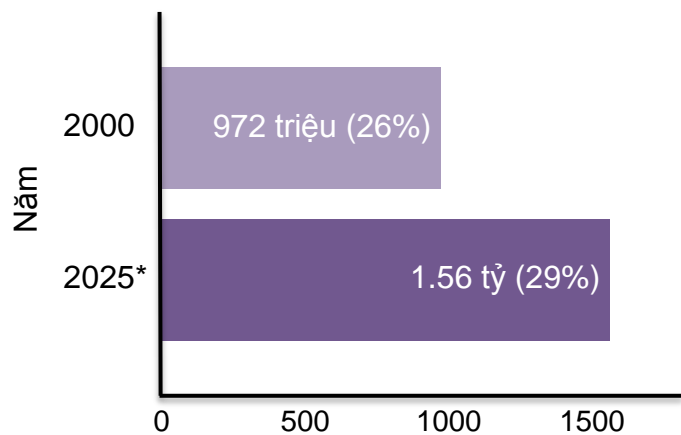
GS. TS. ĐỖ DOÃN LỢI

Viện trưởng Viện Tim mạch Việt Nam

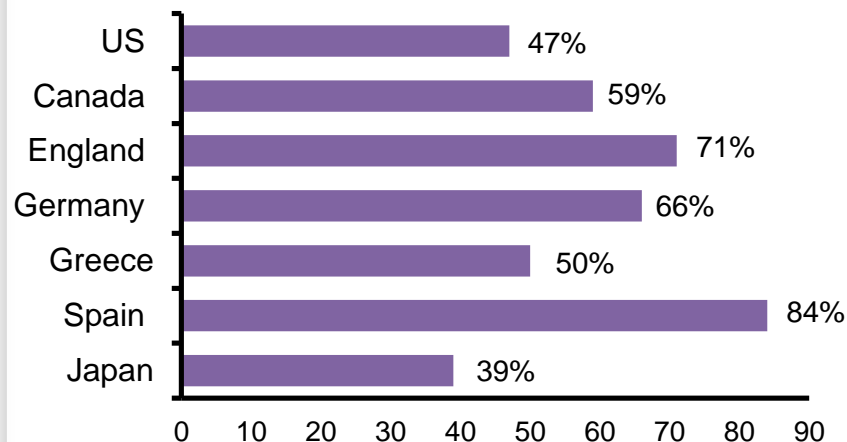
Phó Chủ tịch Hội Tim mạch Việt Nam

# THA và tần suất không đạt mục tiêu

## THA



## Tần suất điều trị không đạt mục tiêu



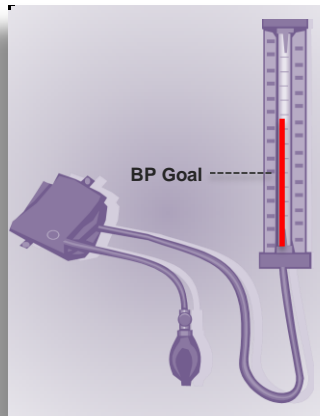
\*Projected. Most of the expected increase will be in economically developing regions.

† Based on a literature search of the MEDLINE database of studies from January 1980 through July 2003.

1. Kearney PM, et al. *Lancet*. 2005;365:217-223.
2. Kearney PM, et al. *J Hypertens*. 2004; 22:11-19.

# THA kháng trị

- HA không đạt mục tiêu mặc dù



- Dung nạp liều tối đa \* ...
- Của  $\geq 3$  thuốc hạ áp † ...
- Các nhóm khác nhau, có 1 lợi tiểu ...

- Đã xác định và xử lý các nguyên nhân gây THA



\*All medications should be titrated to the maximum in-label doses or until BP control is achieved, except in cases of intolerance, in which case treatments should be optimized to the maximum tolerated doses

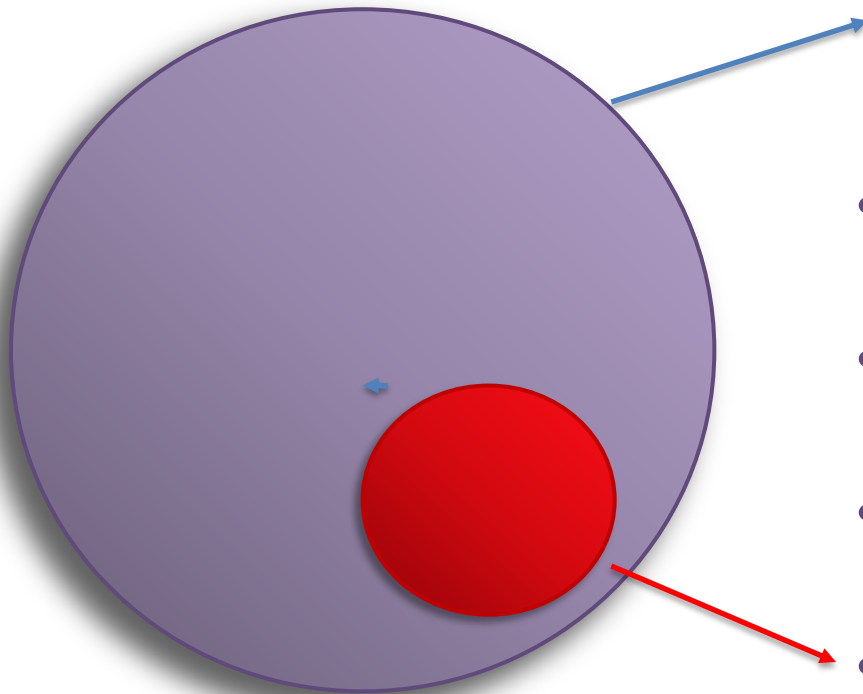
†Patients who require  $\geq 4$  antihypertensive agents to achieve BP control are also considered treatment resistant, according to some sources.<sup>1</sup>

1. Calhoun DA, et al. *Circulation*. 2008;117:e510-e526.

2. Mancia G, et al. *Eur Heart J*. 2007;28:1462-1536.

# HA không đạt mục tiêu $\neq$ THA kháng trị

HA không đạt mục tiêu = THA khó kiểm soát  
(*uncontrolled hypertension*)



- Điều trị chưa đúng
- Tuân thủ kém
- THA thứ phát nhưng không biết
- THA kháng trị thật sự

\*Patients who require  $\geq 4$  antihypertensive agents to achieve BP control are also considered treatment resistant, according to some sources.<sup>1</sup>

1. Calhoun DA, et al. *Circulation*. 2008;117:e510-e526.

2. Mancia G, et al. *Eur Heart J*. 2007;28:1462-1536.

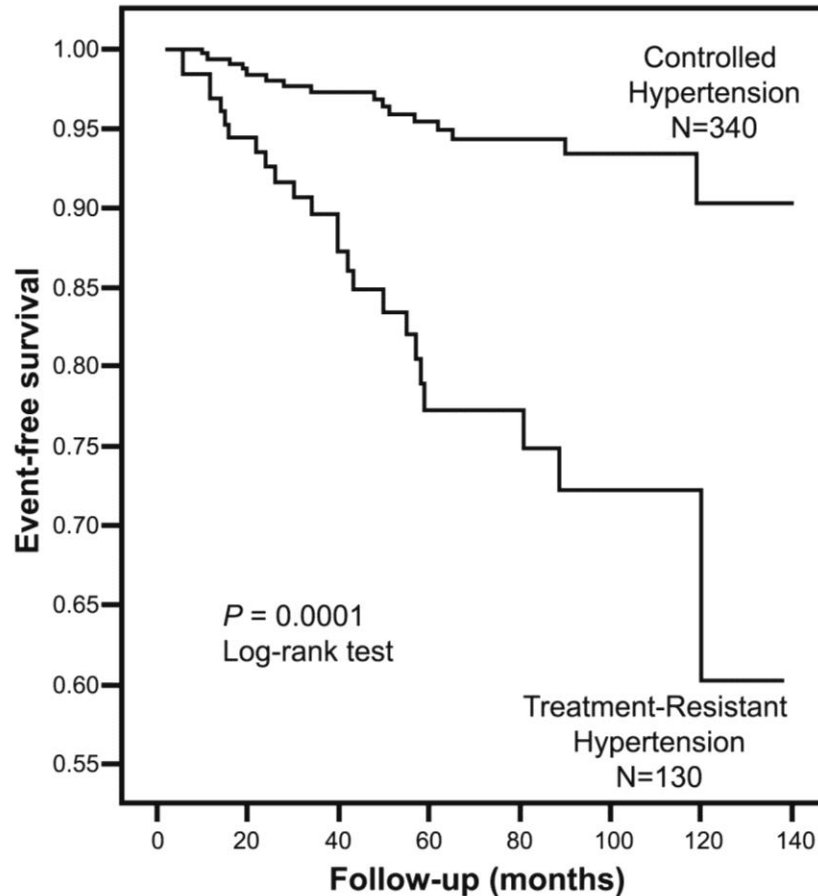
# THA kháng trị ngày càng tăng

- Khoảng 100 triệu người trên thế giới (15 - 20% số bn điều trị không đạt mục tiêu) <sup>1,2,3</sup>
- Mặc dù y học nhiều cố gắng: thuốc mới, chiến lược mới ... Nhưng số bn THA kh. trị tăng 62% trong 20 năm qua <sup>\*4,5</sup>

\*In the time periods 1988-1994 vs 2005-2008, the proportion of treated uncontrolled hypertensive patients reportedly taking  $\geq 3$  BP medications increased from 16% to 28%.

1. Persell, S. *Hypertension*. 2011;57:1076-1080.
2. Hypertension and cardiovascular disease. *World Heart Federation*. 2011. <http://www.world-heart-federation.org/cardiovascular-health/cardiovascular-disease-risk-factors/hypertension/>. Accessed March 2, 2012.
3. Lloyd-Jones D, et al. *Circulation*. 2010;121:e46-e215.
4. Calhoun DA, et al. *Circulation*. 2008;117:e510-e526.
5. Egan BM, et al. *Circulation*. 2011;124:1046-1058.

# Nguy cơ tim mạch tăng



*Biến cố tim mạch  
(sau 5 năm)*

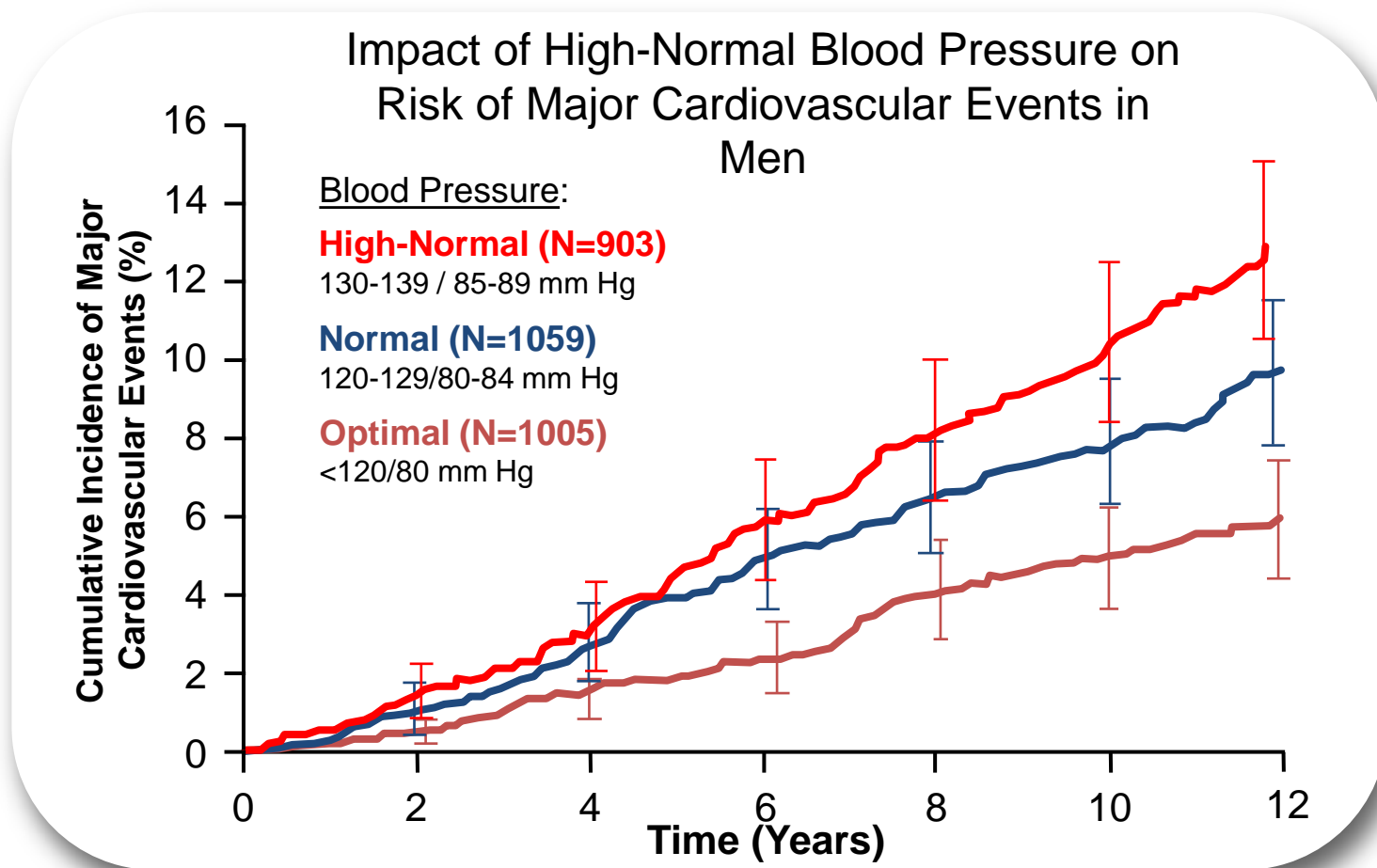
Bn đạt mục tiêu	5%
THA kháng trị	19%

Note: Study did not include outcomes in untreated hypertensives or in patients with uncontrolled hypertension on 1-2 antihypertensive medications.

CV=cardiovascular.

Adapted from Pierdomenico SD, et al. *Am J Hypertens.* 2005;18:1422-1428.

# Rationale for antihypertensive treatment: reduce CV risk



BP level has a strong, continuous, and significant positive association with CV disease outcomes.

Longitudinal data obtained from the Framingham Heart Study. Overall, those with high-normal BP had a 2-fold increase in relative risk for CV event compared with those with optimal BP levels (<120/80 mm Hg).

Used with permission from: Vasan RS, et al. *N Engl J Med.* 2001;345:1291-1297.

# Các bước tiếp cận

Khẳng định đo HA chính xác

Tối ưu hóa Phác đồ thuốc và Tuân thủ

Áp dụng đúng chế độ ăn, tập, nếp sống

Cân nhắc gửi tới BS. chuyên khoa

Đo ở cơ sở y tế:  
cách đo chuẩn chưa ?

Đo ở nhà, đo 24h:  
giảm hiệu ứng áo choàng  
trắng (20-30%) ?

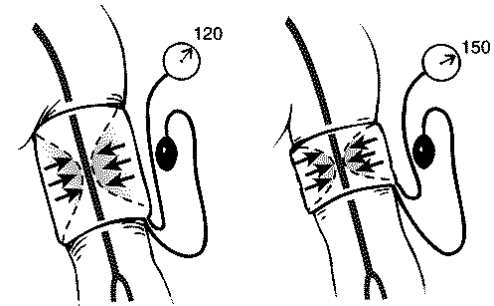




# Các nguyên nhân “giả kháng trị”

## • Cách đo HA

- Bn không nghỉ 5 phút trước đo, trời lạnh <sup>1,2</sup>
- Tay không để đúng mức tim <sup>1,2</sup>
- Băng quấn quá nhỏ <sup>1,2</sup>
- Sau uống rượu, hút thuốc, café, nhịn tiểu <sup>2</sup>



## • Các thuốc có thể làm tăng HA

- Chống viêm Nonsteroid (NSAIDs) và ức chế cyclooxygenase-2 (COX-2)
- Sympathomimetic: ephedra, phenylephrine, cocaine, amphetamines ...
- Thảo dược: cam thảo, ma hoàng
- Anabolic steroids
- Thuốc hạn chế thèm ăn
- Erythropoietin
- Thuốc tránh thai

1. Makris A, et al. *Int J Hypertens*.2011;598694.  
2. Pickering T, et al. *Hypertension*. 2005;45:142-161.

# Đối tượng nguy cơ cao



Người già



Nữ



Ăn mặn, mì chính



HA nền cao

Béo phì



Tiểu đường

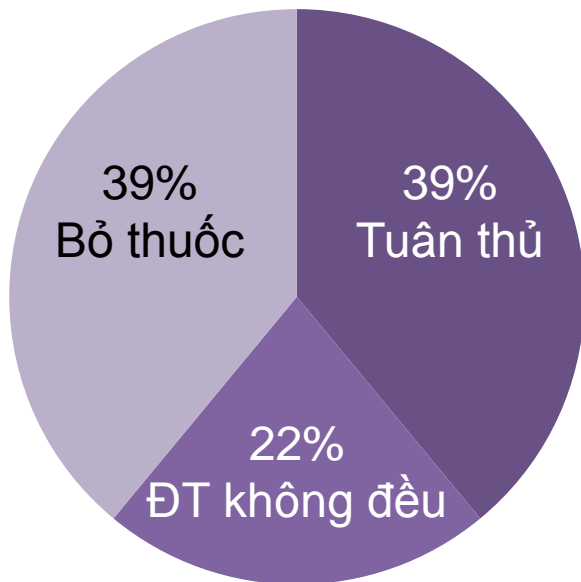


Bệnh thận mạn



\*Based on analyses of data from the Framingham Study and The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT).  
Calhoun DA, et al. *Circulation*. 2008;117:e510-e526.

# Tuân thủ kém



Nghiên cứu 10 năm

- Dấu hiệu không tuân thủ
  - Không đi khám
  - Không có thay đổi triệu chứng
    - . HA không đổi
    - . Không thấy side effects thường gặp
- Kiểm tra việc tuân thủ
  - Bàn việc dùng thuốc với gia đình
  - Xác định ng. nhân không tuân thủ
  - Tư vấn cho bn và gia đình

## Blood pressure goals in hypertensive patients

Recommendations	
<b>SBP goal for “most”</b> <ul style="list-style-type: none"> <li>•Patients at low–moderate CV risk</li> <li>•Patients with diabetes</li> <li>•Consider with previous stroke or TIA</li> <li>•Consider with CHD</li> <li>•Consider with diabetic or non-diabetic CKD</li> </ul>	<b>&lt;140 mmHg</b>
<b>SBP goal for elderly</b> <ul style="list-style-type: none"> <li>•Ages &lt;80 years</li> <li>•Initial SBP <math>\geq</math>160 mmHg</li> </ul>	<b>140-150 mmHg</b>
<b>SBP goal for fit elderly</b> Aged <80 years	<b>&lt;140 mmHg</b>
<b>SBP goal for elderly &gt;80 years with SBP</b> <ul style="list-style-type: none"> <li>•<math>\geq</math>160 mmHg</li> </ul>	<b>140-150 mmHg</b>
<b>DBP goal for “most”</b>	<b>&lt;90 mmHg</b>
<b>DB goal for patients with diabetes</b>	<b>&lt;85 mmHg</b>

SBP, systolic blood pressure; CV, cardiovascular; TIA, transient ischaemic attack; CHD, coronary heart disease; CKD, chronic kidney disease; DBP, diastolic blood pressure.

# Hiệu quả của thay đổi nếp sống

<i>Biện pháp *</i>	<i>Khuyến cáo</i>	<i>Giảm HA tâm thu</i>
Giảm cân	BMI of 18,5 – 24,9 kg/m <sup>2</sup>	3 - 20
Chế độ ăn DASH	Nhiều rau quả, giảm mỡ và mỡ bão hòa, sữa ít béo	8 - 14
Ăn giảm mặn	< 100 mmol (2,4 g)/ngày)	2 - 8
Tăng hoạt động thể lực	Tập > 30 phút/ngày	4 - 9
Uống rượu bia hợp lý	Nam: ≤ 2 ly/ngày Nữ: ≤ 1 ly/ngày	2 - 4

\* Phối hợp ≥ 2 biện pháp có tăng hiệu quả: +/-

Chobanian AV, et al. *JAMA*. 2003;289:2560-2572.  
Blumenthal JA, et al. *Arch Intern Med*. 2000;160:1947-1958.  
Table courtesy of Hypertension Online. [www.hypertensiononline.org](http://www.hypertensiononline.org)



# Các giai đoạn thay đổi nếp sống

- Không đơn giản
- Thay đổi chế độ ăn, vận động: không dễ
- Không ổn định
- Bs. giải thích – Bn. quyết tâm

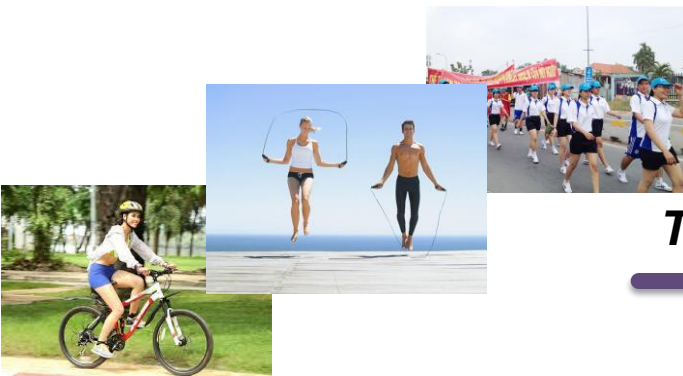
**Duy trì**

**Hành động**

**Chuẩn bị**

**Quyết định**

**Tiền quyết định**



1. Glanz K, Bishop DB. *Ann Rev Pub Health*. 2010;31:399-418.
2. Prochaska, JO. *Med Decis Making*. 2008;28:845-849.



# Cơ chế tác động các nhóm thuốc

Các thuốc tác động lên RAAS

=> giảm hoạt tính của hệ TK giao cảm<sup>1,2</sup>

## 1. ƯCMC

Giảm tạo angiotensin II

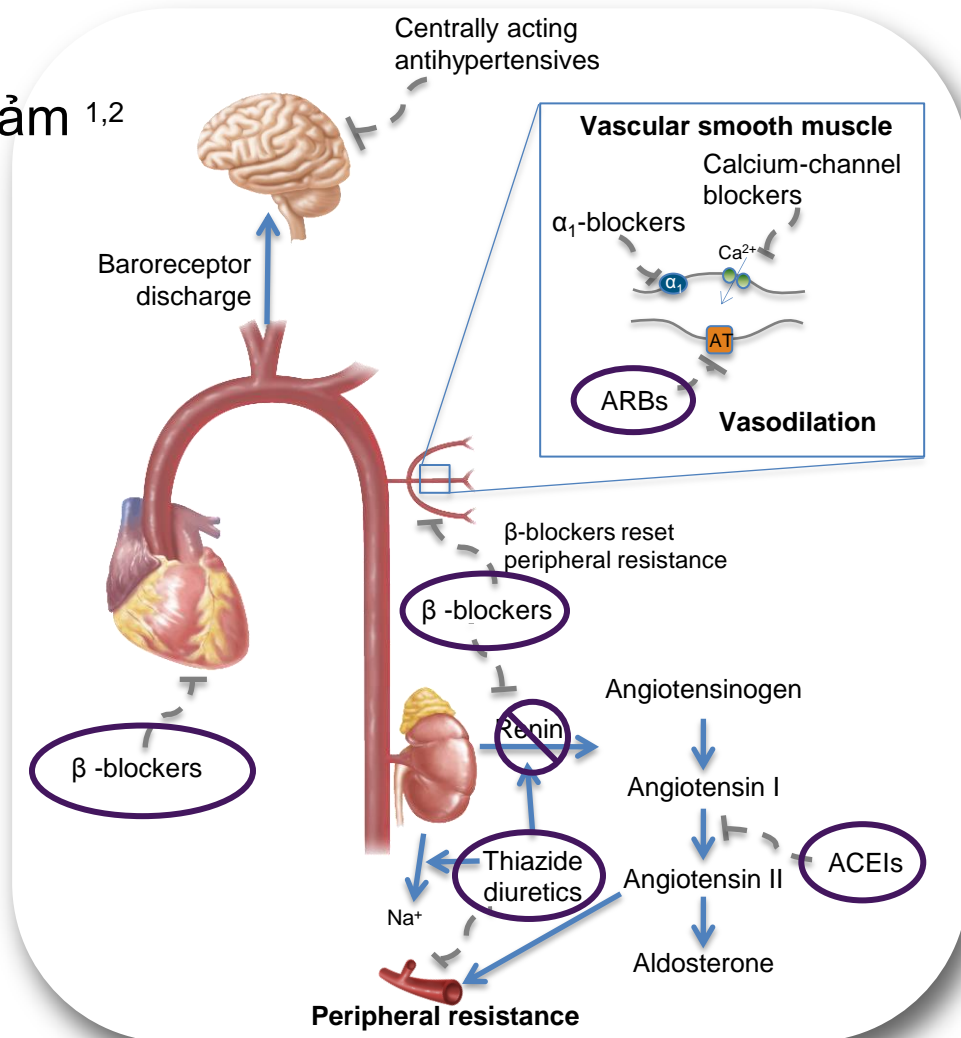
## 2. ƯCTT

Block các thụ thể angiotensin AT<sub>1</sub>

## 3. Chẹn β

## 4. Lợi tiểu

Thải muối và nước

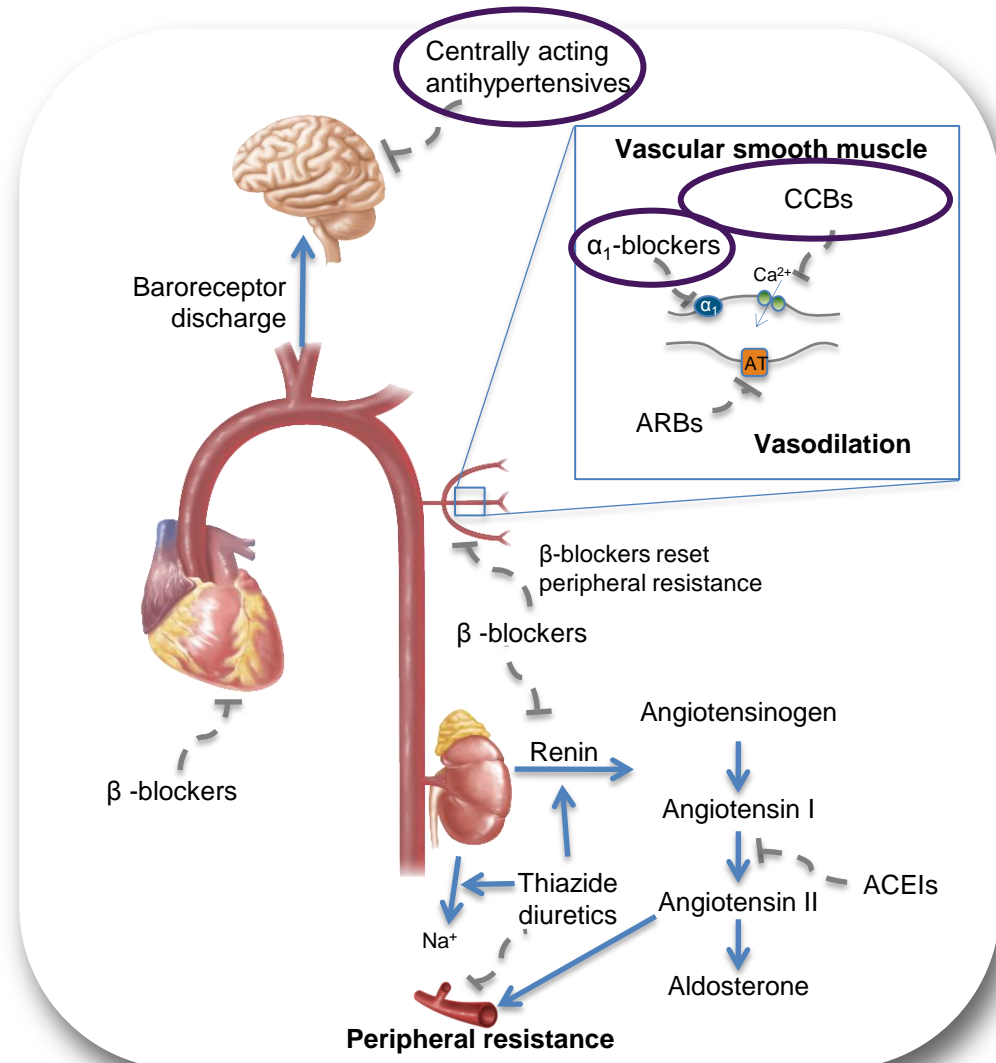


RAAS = renin-angiotensin-aldosterone system; ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin-receptor blocker; DRI = direct renin inhibitor.

1. Izzo JL, Black HR, Sica DA, eds. *Hypertension Primer*. 4th ed. 2008.
2. Schlaich MP, et al. *Hypertension*. 2009;54:1195-1201.

# Cơ chế tác động các nhóm thuốc

- **Chẹn kênh Canxi**  
Giãn ĐM và giảm sức cản ngoại biên
- **Chẹn  $\alpha$**   
Block tính co mạch của NE
- **Thuốc tác động TK TW**  
Tác động lên vùng dưới đồi

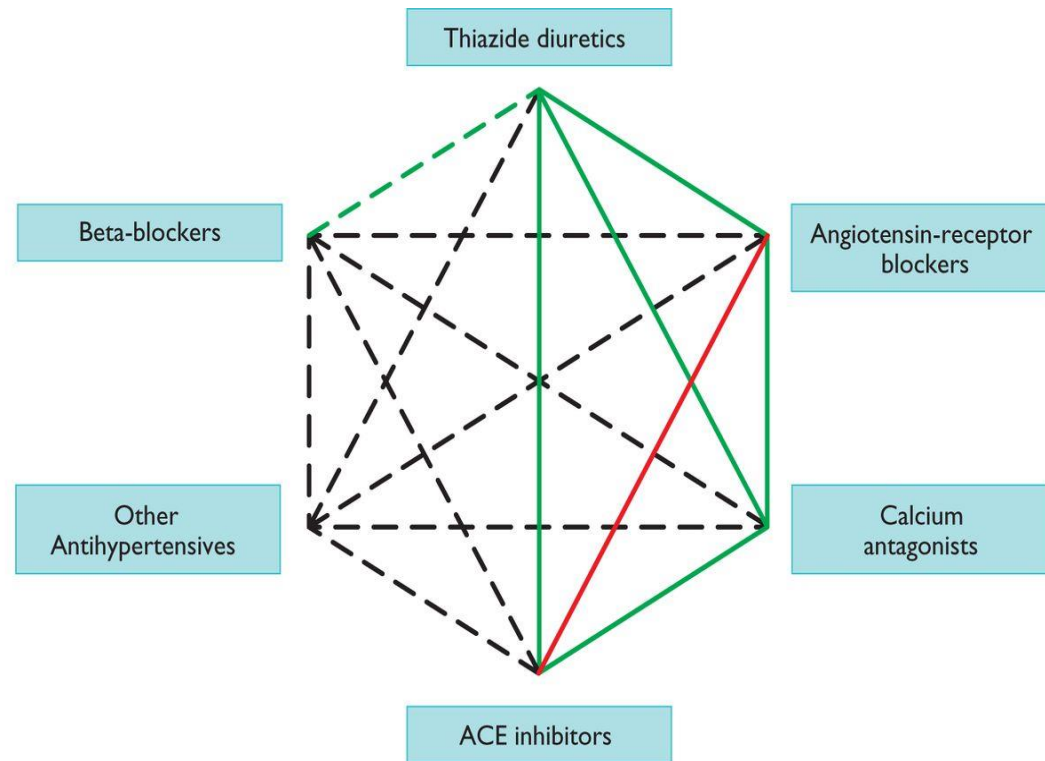


NE = norepinephrine.

Izzo JL, Black HR, Sica DA, eds. *Hypertension Primer*. 4th ed. 2008.



# Phối hợp thuốc hợp lý



- Trong 3 thuốc phối hợp nên có 1 thuốc lợi tiểu
- Liều: tối đa cho mỗi loại thuốc mà bệnh nhân dung nạp được <sup>1,2</sup> (maximum tolerated or in-label doses)
- Khuyến cáo: sau phối hợp không hiệu quả 3 thuốc, nên thêm spironolactone

ngotensin-converting enzyme.

# Các bước tiếp cận

Khẳng định đo HA chính xác

Tối ưu hóa Phác đồ thuốc và Tuân thủ

Áp dụng đúng chế độ ăn, tập, nếp sống

Cần nhắc gửi tới BS. chuyên khoa

THA thứ phát ?

Các nguyên nhân khác ?

# Tìm THA thứ phát và điều trị

## *Nguyên nhân*

## *Tần suất (%)*

Bệnh ĐM thận

3.0 - 4.0

Cường Aldosterone

1.5 - 15.0

Bệnh nhu mô thận

1.0 - 8.0

Cường/suy giáp

1.0 - 3.0

Hẹp eo ĐMC

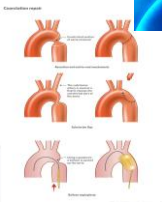
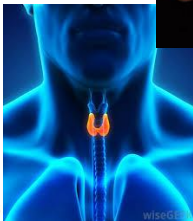
< 1.0

HC Cushing

< 0.5

Pheochromocytoma

< 0.5



Cushing's



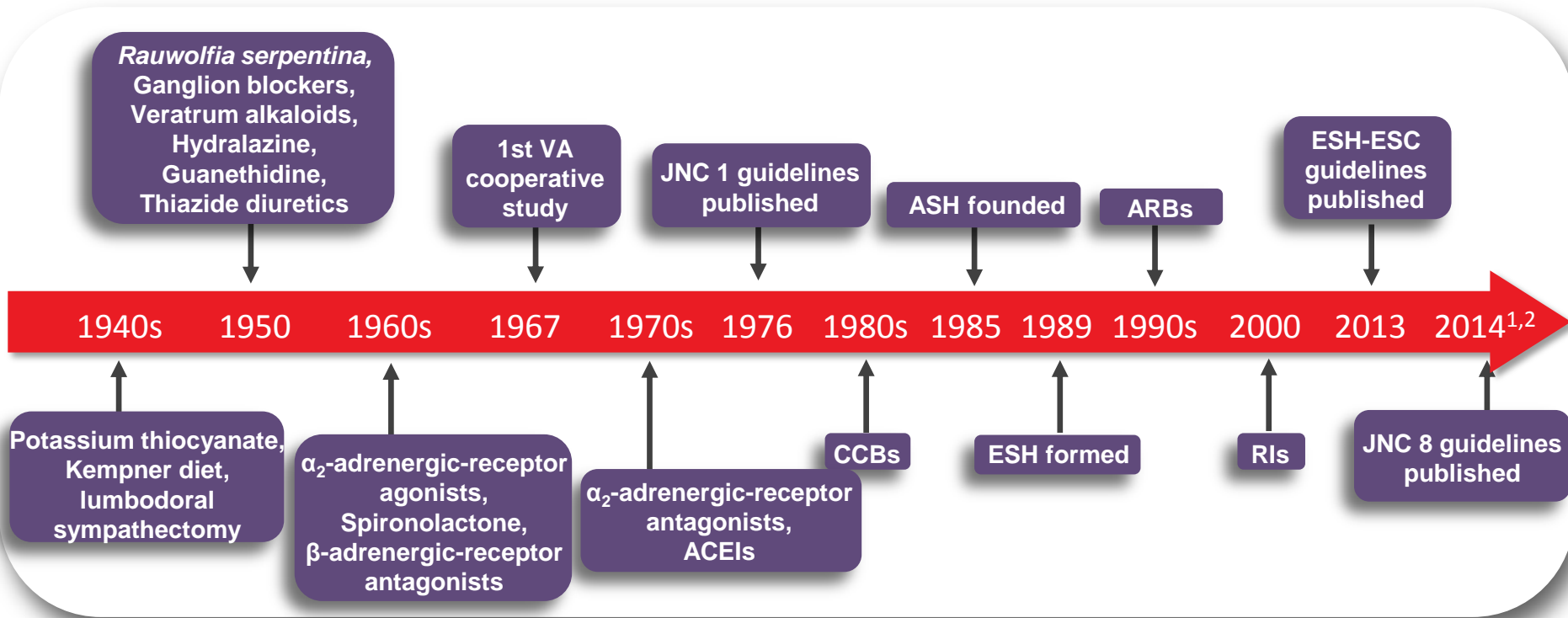
\*Many patients with renal artery stenosis or aldosteronism may achieve BP control without diagnosis of the underlying condition.

Calhoun DA, et al. *Circulation*. 2008;117:e510-e526.

Moser M, Setaro JF. *N Engl J Med*. 2006;355:385-392.

Kaplan NM, Victor R. *Kaplan's Clinical Hypertension*. 10th ed. Philadelphia, PA: Lippincott Williams & Wilkins, 2010.

# Liên tục đổi mới ....



CCB = calcium channel blocker.

ACEI = angiotensin-converting-enzyme inhibitor.

ARB = angiotensin receptor blocker.

RI = renin inhibitor.

1. Chobanian AV. *N Engl J Med*. 2009;361:878-887.

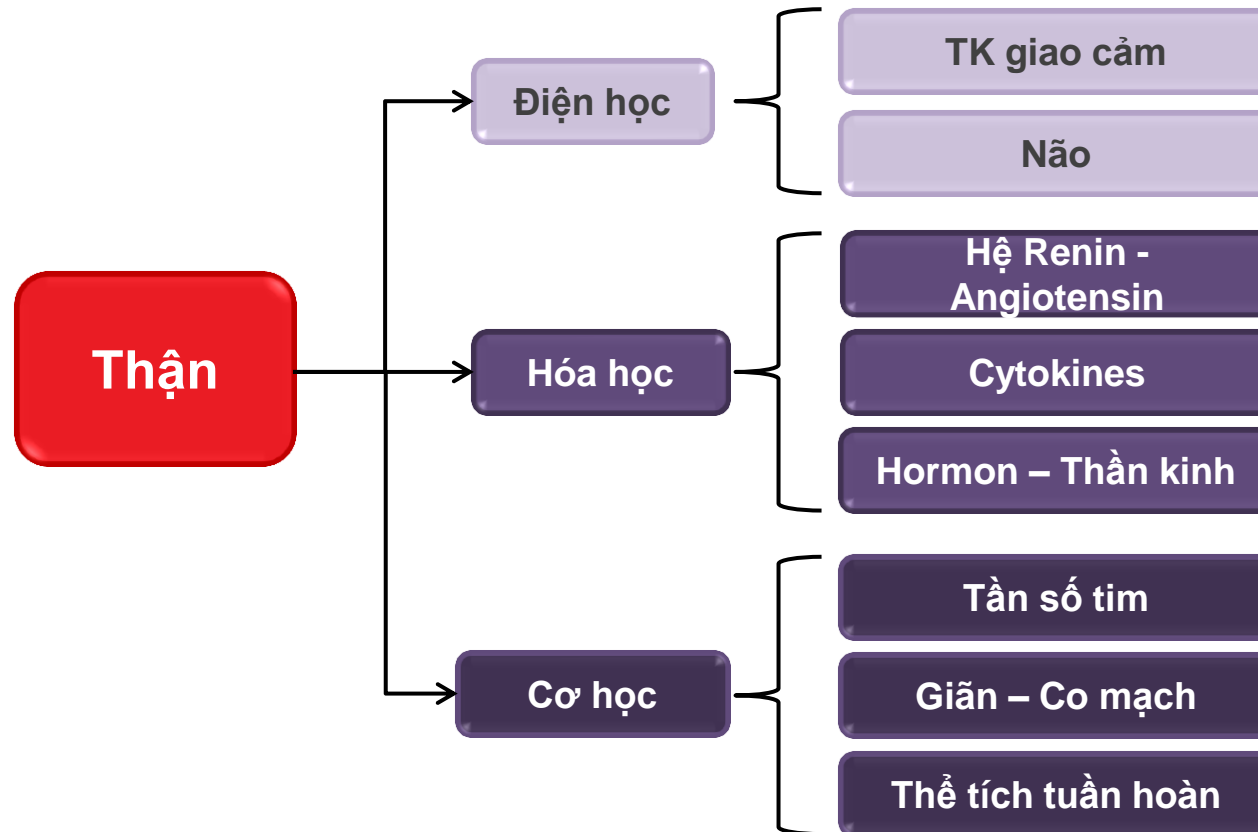
2. European Society of Hypertension History. ESH. <http://www.eshonline.org/About/ESHinBrief.aspx>. Accessed July 27, 2011.

3. Calhoun D, et al. *Circulation*. 2008;117:e510-e526.

4. Egan BM, et al. *Circulation*. 2011;124:1046-1058

# **Treatment-Resistant Hypertension: Pathophysiology**

# Thận - vai trò điều hòa các yếu tố kiểm soát HA



SNS = sympathetic nervous system.

RAAS = renin-angiotensin-aldosterone/system.

Campbell W. The Autonomic and Peripheral Nervous Systems. In: Campbell, WW, editor. *DeJong's The Neurologic Examination*. 6th ed.

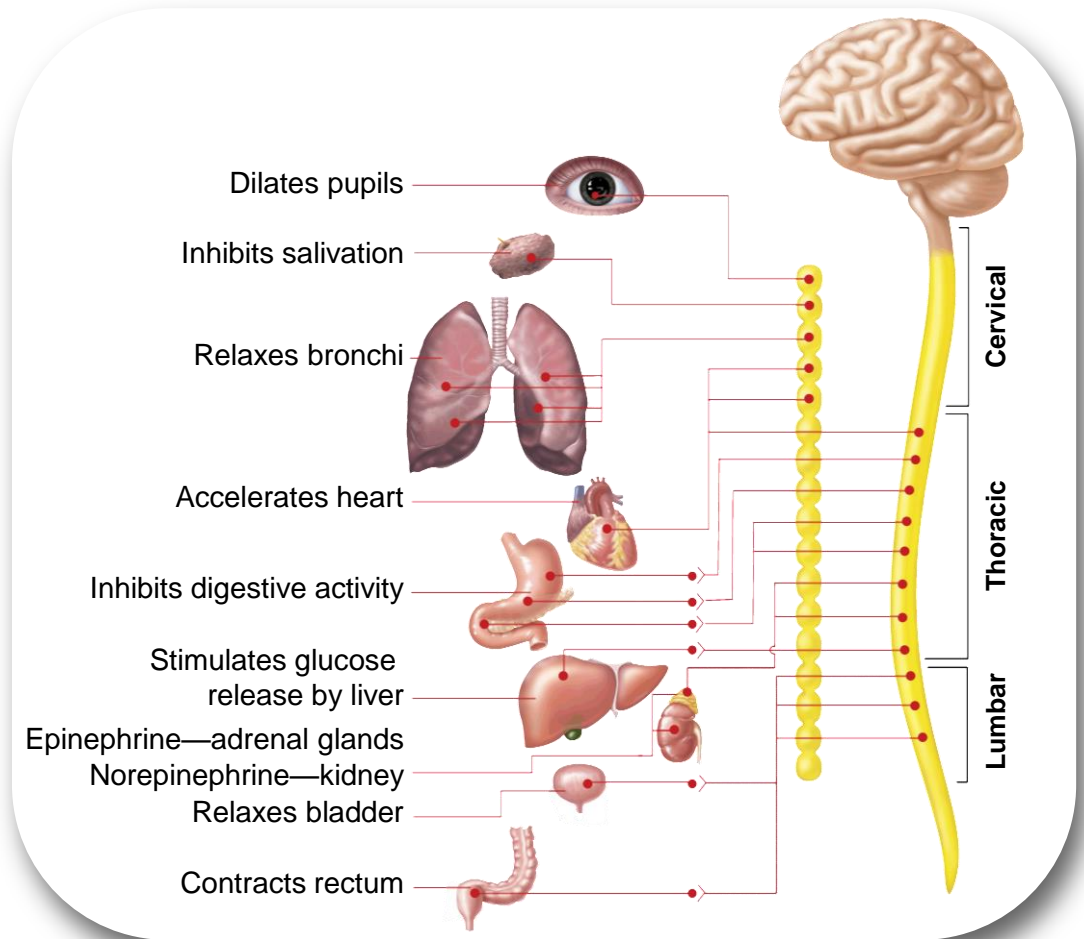
Philadelphia, PA: Lippincott Williams and Wilkins; 2005 p. 535-547. Cowley A. *Nat Rev Genetics*. 2006;7:829-840. Kaplan NM, Victor R.

*Kaplan's Clinical Hypertension*. 10th ed. Philadelphia, PA: Lippincott Williams & Wilkins, 2010. Schlaich M, et al. *Hypertension*.

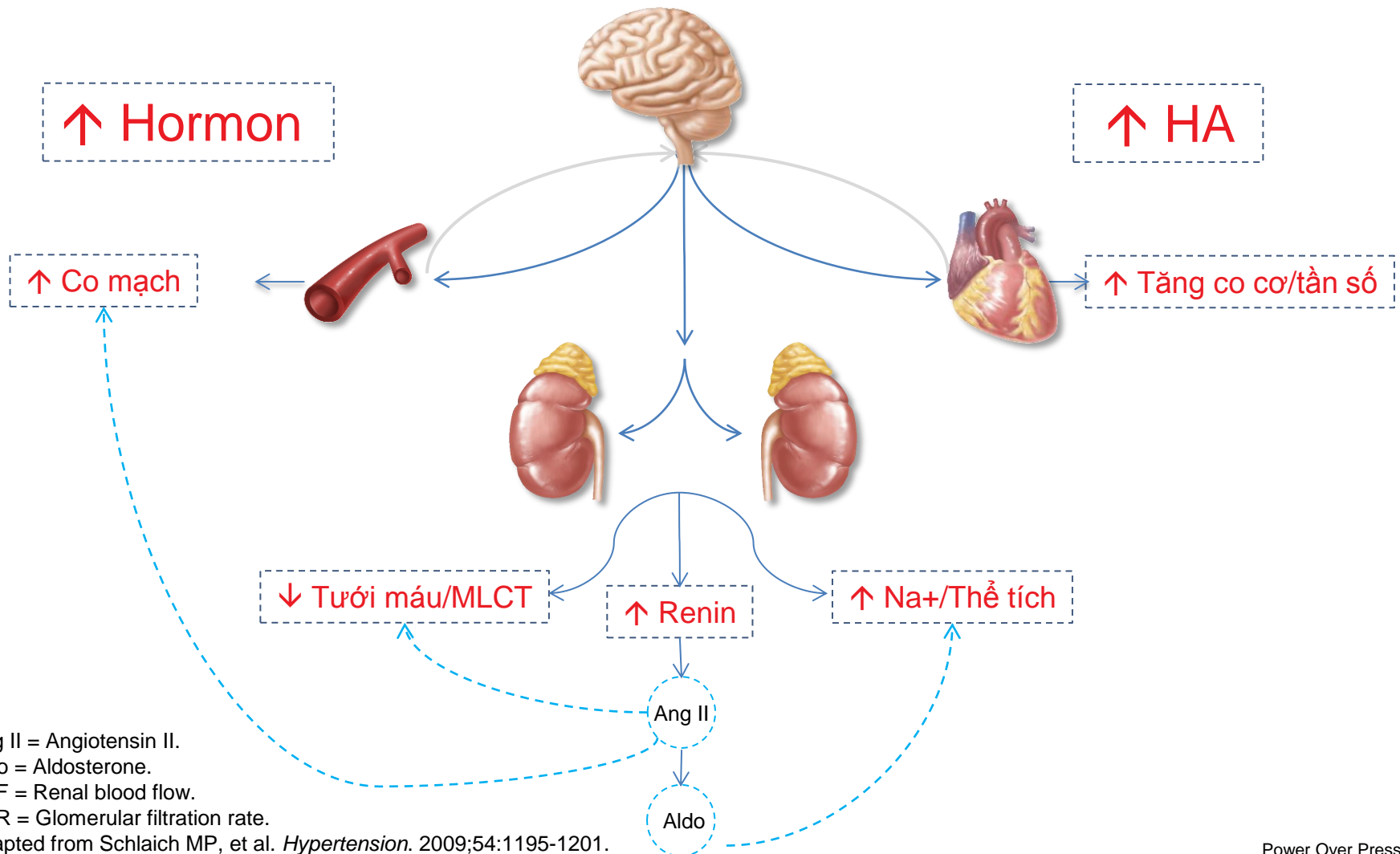
2009;54:1195-1201. Guyton AC. *Science*. 1991;252:1813-1816.

# TK giao cảm

- TK giao cảm kết nối não, tim, mạch máu, thận – các yếu tố điều hòa HA



# Thận - vai trò điều hòa các yếu tố kiểm soát HA



Ang II = Angiotensin II.

Aldo = Aldosterone.

RBF = Renal blood flow.

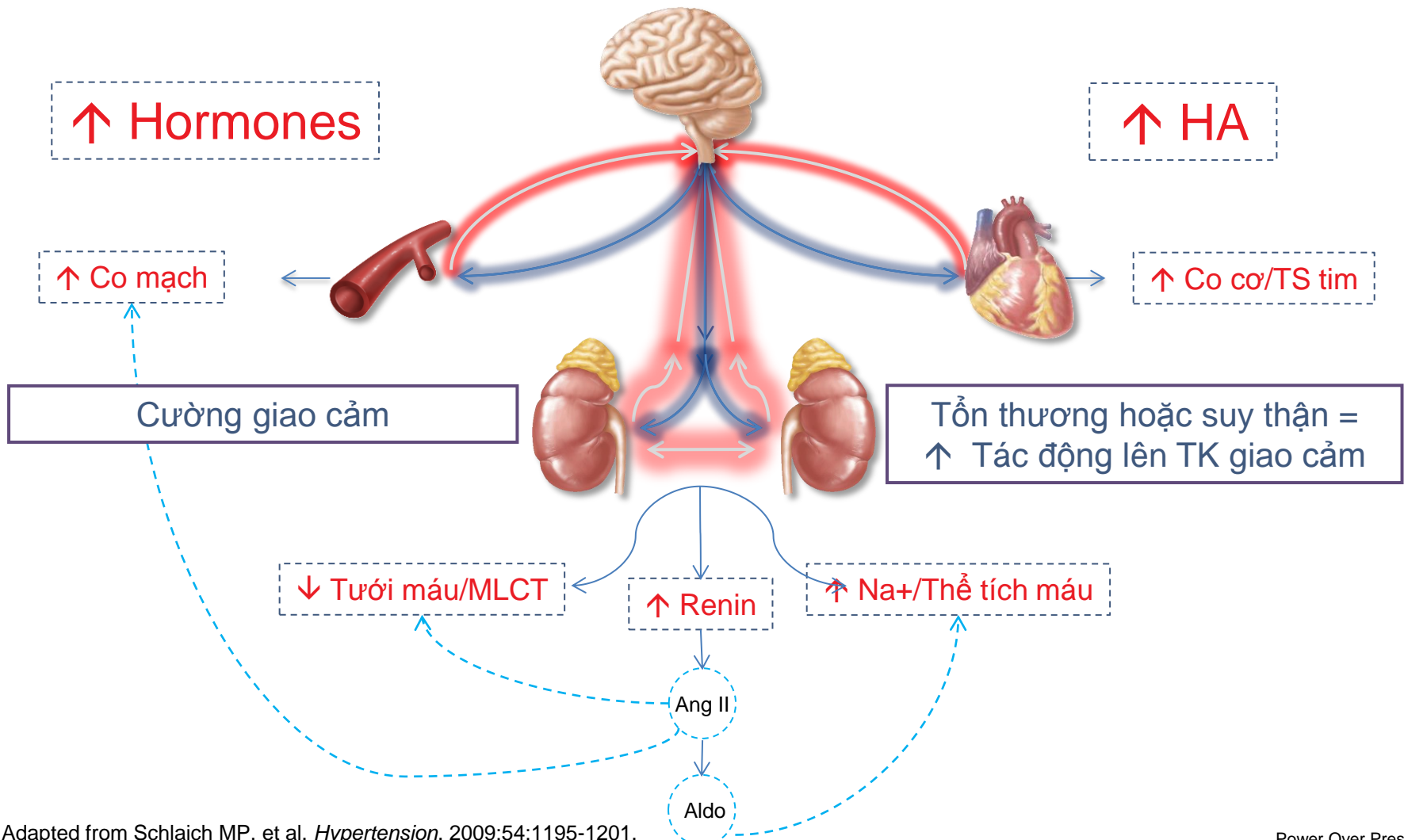
GFR = Glomerular filtration rate.

Adapted from Schlaich MP, et al. *Hypertension*. 2009;54:1195-1201.

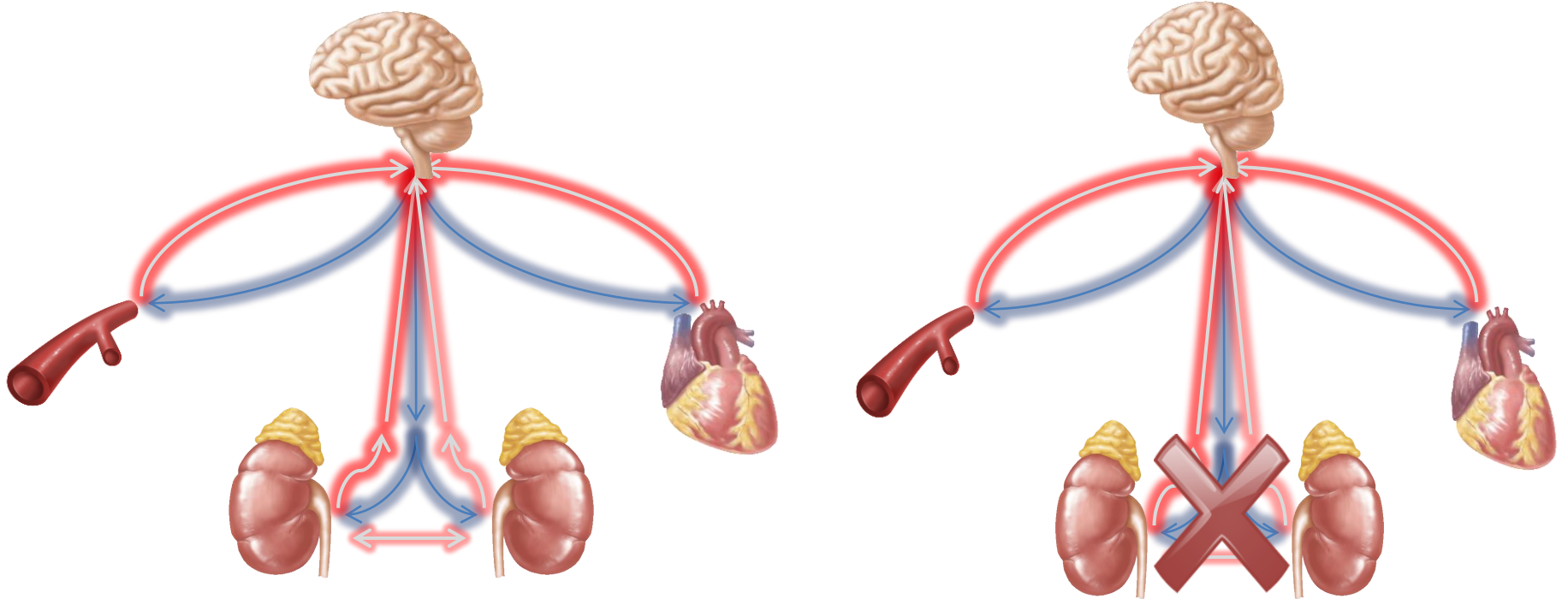
Hall JE, Guyton AC. *Textbook of Medical Physiology*. 12th ed. Philadelphia, PA: Saunders Elsevier, 2011.



# Thận - vai trò điều hòa các yếu tố kiểm soát HA



# Triệt TK giao cảm DM thận



# Renal denervation as a therapeutic approach

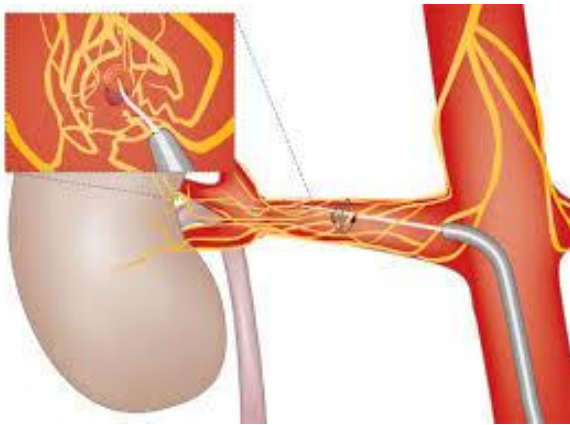
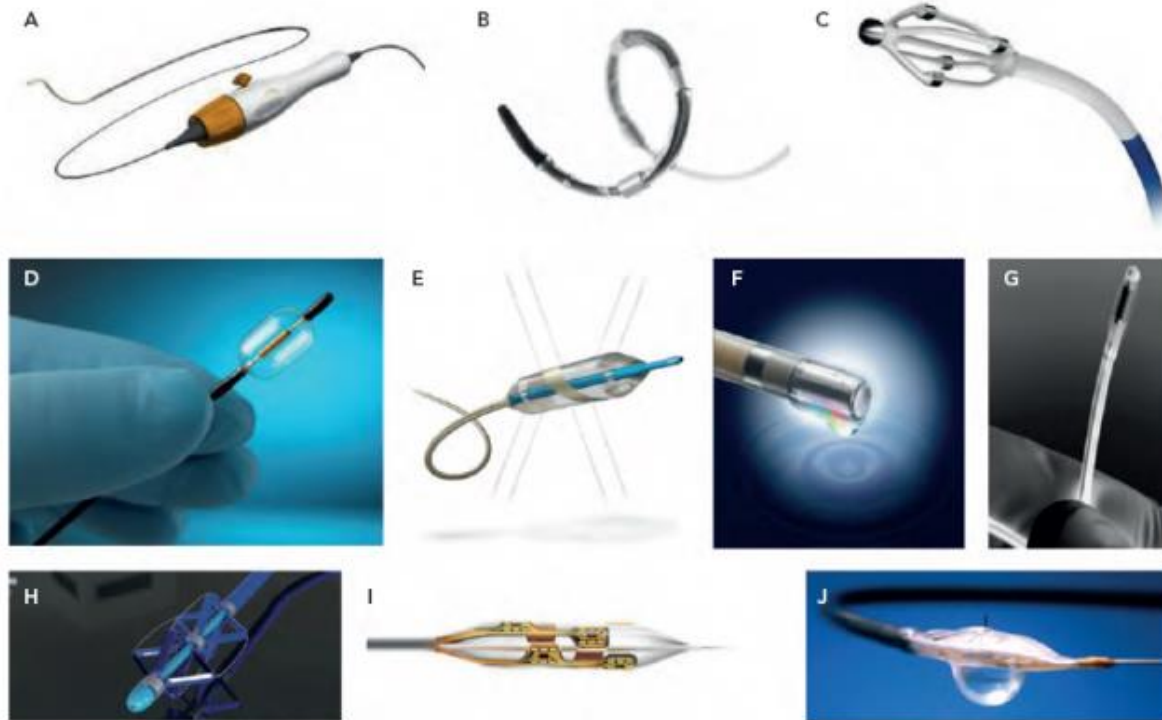


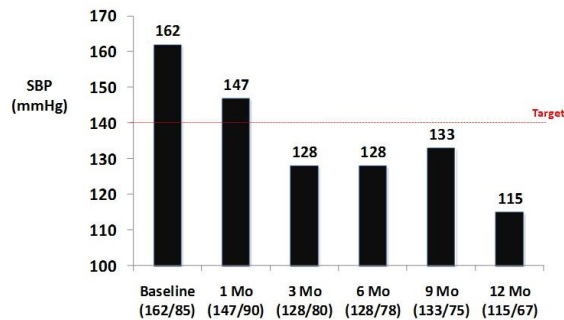
Figure 1: Current Renal Sympathetic Denervation Technologies



Medtronic Inc. first-generation Symplicity™ (a) and second-generation Symplicity Spiral™ (b) radio-frequency (RF) catheters; St Jude Medical multi-electrode, basket design EnLightn™ RF catheter (c); ReCor Medical Paradise™ circumferential irrigated balloon, ultrasound (US) catheter (d); Covidien One-Shot™ spiral RF catheter (e); Biosense ThermoCOOL™ irrigated multi-electrode RF catheter (f); CardioSonic TIVUS™ balloon US catheter (g); Verve Medical™ retro-ureteric multi-electrode basket RF catheter (h); Boston Scientific Vessix™ multi-electrode, balloon-mounted, bipolar RF catheter (i) and Mercator Bullfrog™ micro-needle catheter for perivascular guanethidine injection (j).

euro  
**PCR**

## Clinical Results: BP Response



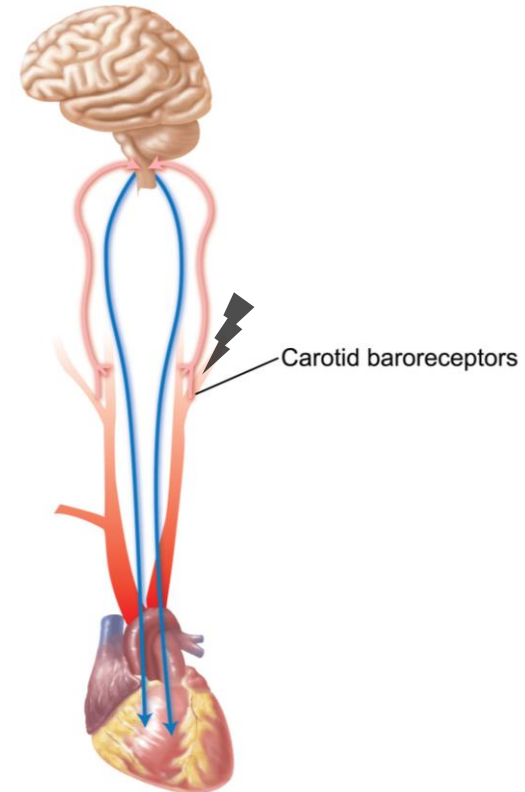
27.05.2010

No anti-HTN medication changes



# Kích thích TK phó giao cảm

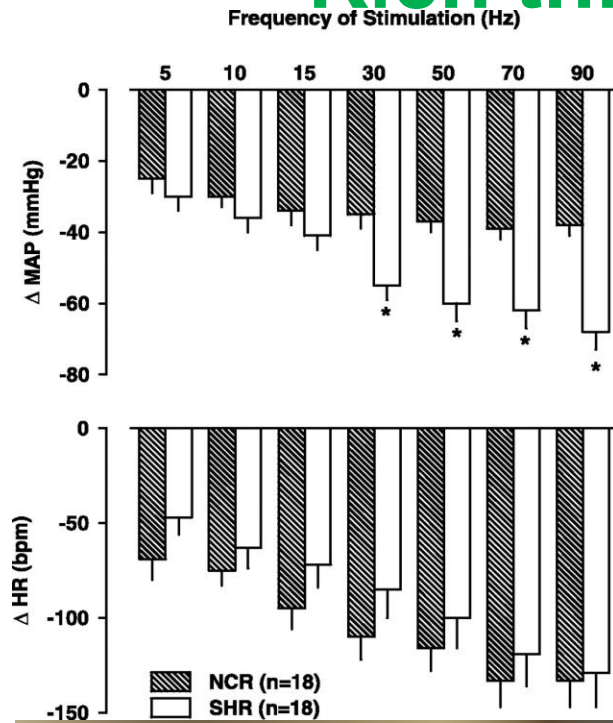
- System similar to a pacemaker  
=> electrical stimulation of the carotid baroreceptors



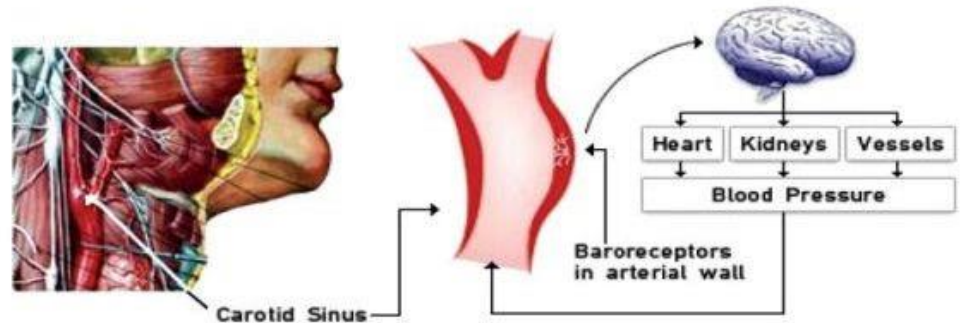
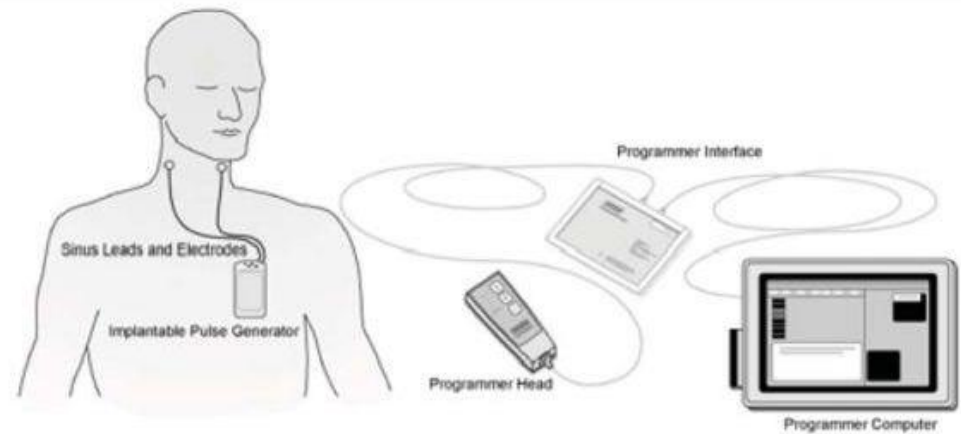
\*Device based approaches such as renal denervation and baroreceptor stimulation are not universally approved for use, and are under clinical investigation in some regions (such as the US and Japan).

1. Bisognano JD, et al. *J Am Coll Cardiol*. 2011;58:765-773.
2. Heusser K, et al. *Hypertension*. 2010;55:619-626.
3. Wustmann K, et al. *Hypertension*. 2009;54:530-536

# Kích thích TK phó giao cảm



Medscape



Source: Eur Heart J © 2011 Oxford

1. Bisognano JD, et al. *J Am Coll Cardiol.* 2011;58:765-773.
2. Heusser K, et al. *Hypertension.* 2010;55:619-626.
3. Wustmann K, et al. *Hypertension.* 2009;54:530-536

# Thế giới khoa học

UK<sup>1</sup>

The Joint UK Societies<sup>2</sup> for Renal Denervation for Resistant Hypertension



Steering Group: Mark Caulfield (Chair), John Collier, John Dewhurst, Aileen Gray, Michael Jones, Neil Powles, Ian Reid

On behalf of the British Hypertension Intervention Society, the British Society for Clinical Pharmacology Research, the British Association of Cardiovascular Nurses

This statement was developed with the aim of underpinning the procedures at Paris and the Revision of UK evidence guidelines of the Joint UK Societies wish to express their thanks

This statement is intended to be read alongside the Paris Declaration [www.esh-online.org/paris](http://www.esh-online.org/paris)

Issue 1: Live on web 27 January 2013

Prof Mark Caulfield, President, Director of UK Evidence Guidelines, Director of Research, The London North Cardiovascular Research, The London School of Hygiene and Tropical Medicine, London, UK. Tel: +44 (0)20 7547 6141 Fax: +44(0)20 7547 6142 <http://www.esh-online.org/paris>

Germany<sup>2</sup>

## Treatment Strategies for Resistant Arterial Hypertension

Mark Caulfield, John Collier, John Dewhurst, Aileen Gray, Michael Jones, Neil Powles, Ian Reid

### Summary

**OBJECTIVE:** Resistant hypertension is defined as persistently elevated blood pressure despite treatment with three or more antihypertensive drugs at optimal doses, including a diuretic, in a patient who is free of secondary causes, white coat hypertension, and other conditions that may affect blood pressure measurement.

**DEFINITION:** Resistant hypertension is defined as persistently elevated blood pressure despite treatment with three or more antihypertensive drugs at optimal doses, including a diuretic, in a patient who is free of secondary causes, white coat hypertension, and other conditions that may affect blood pressure measurement.

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Original Article

## ESH Position Paper: Renal denervation – an interventional therapy of resistant hypertension

Roland E. Schmieder<sup>1</sup>, George Kalousk<sup>2</sup>, Boris Braun<sup>3</sup>, Sven H. Kridener<sup>4</sup>, Stjepan Mavric<sup>5</sup>, Krzysztof Mielowski<sup>6</sup>, Giovanni Panini<sup>7</sup>, Lutz Rühlmann<sup>8</sup>, Philippe van de Borne<sup>9</sup>, and Costel I. Telea<sup>10</sup>

Objectives: The European Society of Hypertension (ESH) issued this position paper in order to summarize current evidence, assess needs and practical recommendations for the application of percutaneous catheter-based ablation of renal sympathetic denervation (RDN) as a novel interventional strategy for the treatment of resistant hypertension. The sympathetic nervous activation in the kidney and the sensory afferent signals to the central nervous system represent the targets of RDN. Clinical studies have demonstrated that catheter-based RDN decreases both blood pressure and arterial stiffness, whereas RDN leads to clinically meaningful systolic and diastolic blood pressure (BP) reduction in patients with resistant hypertension. This position statement intends to facilitate a better understanding of the effectiveness, safety, benefits and risks of RDN.

**Keywords:** European Society of Hypertension, interventional therapy, resistant hypertension

**Abbreviations:** BP, blood pressure; RDN, renal denervation

### THE GLOBAL BURDEN OF UNCONTROLLED HYPERTENSION

Arterial hypertension affects worldwide approximately 1.5 billion people and is the leading cause of cardiovascular morbidity and mortality. It is the leading cause of stroke, heart failure, and chronic kidney disease. The global burden of hypertension is increasing rapidly, with the number of people with hypertension expected to reach 2.5 billion by 2025 [1]. There is a clear relationship between blood pressure (BP) values and cardiovascular risk [2], and according to a worldwide analysis 75 million people are estimated to have uncontrolled hypertension, with 40% of people due to a lack of treatment [3]. Current approaches to address resistant hypertension are limited by a high proportion of patients. The overall burden of hypertension is increasing.

According to the European Society of Hypertension (ESH) Position Paper on Resistant Hypertension, the prevalence of resistant hypertension is 10–15% in the general population and 20–30% in patients with hypertension [4]. The prevalence of resistant hypertension is higher in patients with hypertension who are treated with three or more antihypertensive drugs at optimal doses, including a diuretic, in a patient who is free of secondary causes, white coat hypertension, and other conditions that may affect blood pressure measurement.

France<sup>4</sup>

Poland<sup>3</sup>

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