Lifestyle Modification & Non-Drug Therapy

Sheila Kar, MD FACC
Attending Cardiologist & Past Clinical Chief
The Heart Institute
CASE: 49 year old man with drug-resistant HTN: Normal BMP, home SBP 135-155 and compliant with: amlodipine 10, irbesartan 300, indapamide 1.25, spironolactone 25, and carvedilol 25 BID

- Lifestyle modification?
  1. Stressful job (air traffic controller)
  2. Fast foody
  3. No regular exercise

- Device-based therapy?
  1. Invasive
  2. Non-invasive
Outline

- Lifestyle modification
- Novel non-drug interventions (devices)
Hypertensive mechanisms

- Neural
- Renal
- Hormonal
- Vascular

Factors:
- Genes
- Environmental Factors

Graph showing population distribution of systolic blood pressure with different conditions:
- Genetic susceptibility
- High sodium diet
- Obesity plus sodium
2013 AHA/ACC Guideline on Lifestyle Management to Reduce Cardiovascular Risk

Grade A Recommendations to Lower BP in Adults with HTN or Pre-HTN

DIET
1. Lower sodium intake
2. Adopt DASH-type diet & Mediterranean diet

EXERCISE
1. Engage in 3 or 4 40-minute sessions/week of moderately intense aerobic physical activity
Salt and Hypertension

Daily salt consumption:

- 1,000 mg Na = 2.5 g NaCl
- Prehistoric level: 0.5 g
- Current U.S. level: 10 g
- 80% from processed food

3.5 g NaCl

7.4 g NaCl

A sodium J-curve?

Association of Urinary Sodium and Potassium Excretion with Blood Pressure

Yes, based on a spot urine Na⁺

Original Article

Global Sodium Consumption and Death from Cardiovascular Causes

No, based on a single 24-hour urine Na⁺
Lower Levels of Sodium Intake and Reduced Cardiovascular Risk
Nancy R. Cook, Lawrence J. Appel and Paul K. Whelton

Trials of Hypertension Prevention

- 5-10 year follow-up (n=2,275)
- 3 to 7 24-hour urines

Goal: ≤ 2.5 grams Na⁺ per day (from 10g to 6g NaCl)
Consume no more than 2,400 mg of sodium/d
If the food industry would help reduce U.S. daily NaCl consumption from 10 to 7 g, systolic BP would fall by -5 mmHg in the general population and by -9 mmHg in the Black population.
This would translate into huge reductions in incident strokes and MIs, with the greatest benefit to NH Black men and women.
DASH
Dietary Approach to Stop Hypertension

IN BRIEF:
Your Guide To
Lowering Your Blood Pressure With DASH
<table>
<thead>
<tr>
<th>Food Group</th>
<th>Daily Serving</th>
<th>Examples and Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grains</td>
<td>7–8</td>
<td>Whole wheat bread, oatmeal, popcorn</td>
</tr>
<tr>
<td>Vegetables</td>
<td>4–5</td>
<td>Tomatoes, potatoes, carrots, beans, peas, squash, spinach</td>
</tr>
<tr>
<td>Fruits</td>
<td>4–5</td>
<td>Apricots, bananas, grapes, oranges, grapefruit, melons</td>
</tr>
<tr>
<td>Low-fat or fat-free dairy foods</td>
<td>2–3</td>
<td>Fat-free (skim)/low-fat (1%) milk, fat-free/low-fat yogurt, fat-free/low-fat cheese</td>
</tr>
<tr>
<td>Meats, poultry, fish</td>
<td>≤2</td>
<td>Select only lean meats, trim away fats; broil, roast, or boil; no frying, and remove skin from poultry</td>
</tr>
<tr>
<td>Nuts, seeds, dry beans</td>
<td>4–5/week</td>
<td>Almonds, peanuts, walnuts, sunflower seeds, soybeans, lentils</td>
</tr>
<tr>
<td>Fats and oils</td>
<td>2–3</td>
<td>Soft margarines, low-fat mayonnaise, vegetable oil (oil, corn, canola, or safflower)</td>
</tr>
<tr>
<td>Sweets</td>
<td>5/week</td>
<td>Maple syrup, sugar, jelly, jam, hard candy, sorbet</td>
</tr>
</tbody>
</table>

Summary of BP Reductions in DASH-I and DASH-II Na⁺ Diets: Hypertensive Patients and Overall

<table>
<thead>
<tr>
<th></th>
<th>SBP (mm Hg)</th>
<th>DBP (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DASH-I Overall</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Combination Diet vs Control</td>
<td>-5</td>
<td>-3</td>
</tr>
<tr>
<td>Diet</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dash-I Hypertensive Pts.</td>
<td>-10.7</td>
<td>-5.2</td>
</tr>
<tr>
<td>Comb. Diet vs Control Diet</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DASH-II Overall</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Comb. Low Na⁺ DASH Diet vs</td>
<td>-8.9*</td>
<td>-4.5*</td>
</tr>
<tr>
<td>Control high Na⁺ Diet</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DASH-II Hypertensive Pts.</td>
<td>-11.5*</td>
<td>-6.8*</td>
</tr>
<tr>
<td>Comb. Low Na⁺ DASH Diet vs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control high Na⁺ Diet</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*P<0.001.

*NEJM*. 2001;344:3-10.
PREDIMED Trial

Mediterranean Diet Reduces 24-Hour Ambulatory Blood Pressure, Blood Glucose, and Lipids

One-Year Randomized, Clinical Trial

Mónica Doménech, Pilar Roman, José Lapetra, Francisco J. García de la Corte, Aleix Sala-Vila, Rafael de la Torre, Dolores Corella, Jordi Salas-Salvadó, Valentina Ruiz-Gutiérrez, Rosa-María Lamuela-Raventós, Estefania Toledo, Ramón Estruch, Antonio Coca, Emilio Ros

(Hypertension. 2014;64:69-76.)
Total n = 280
Mean age 67
85% with HTN, 1/3 men
Baseline office BP 145/80
EVOO, extra-virgin olive oil

(Hypertension. 2014;64:69-76.)
PREDIMED: Primary End Point (Acute MI, Stroke, or Death from CV Causes)


No. at risk:
- Control diet 2450 2268 2020 1583 1268 946
- Med diet, EVOO 2543 2486 2320 1987 1687 1310
- Med diet, nuts 2454 2343 2093 1657 1389 1031

Incidence of composite CV end point

- Med diet, EVOO: hazard ratio, 0.70 (95% CI, 0.53-0.91); *P*=0.009
- Med diet, nuts: hazard ratio, 0.70 (95% CI, 0.53-0.94); *P*=0.02
Dark Chocolate and Cocoa

• 15 subjects given 100 grams of dark chocolate with 500 mg polyphenols for 15 days
  – HOMA-IR reduced ($P<0.001$)
  – Reduced systolic BP by 6.4 mm Hg ($P<0.05$) but no significant change in diastolic BP
• Meta-analysis of 173 patients given cocoa reduced BP 4.7/2.8 mm Hg ($P=0.002$ to 0.006)
• Meta-analysis of 23 trials with 297 patients showed BP reduction of 3.2-4.5/2.0-3.2 mm Hg

References:
Am J Clin Nutr. 2005;8:611
Arch Intern Med. 2007;167:626
J of Clin Hypertension. 2007;9:647
JAMA. 2007;298:49
BMC. 2010;8:39
Am J Hypertension. 2010;23:97
Evidence Synthesis

Number 113

Behavioral Counseling to Promote a Healthy Lifestyle for Cardiovascular Disease Prevention in Persons With Cardiovascular Risk Factors: An Updated Systematic Evidence Review for the U.S. Preventive Services Task Force

Lin JS, O’Connor EA, Evans CV, Senger CA, Rowland MG, Groom HC.

Healthy Diet (HD) + High Intensity Physical Activity (PA)

- SLIM, 2011
- MDPS, 2012
- RIS, 1998
- E-LITE, 2013
- DPP, 2002
- PREDIAS, 2009
- EUROACT, 2008
- Live Well, Be Well, 2012
- FDPS, 2001
- Nilsson, 1992
- NC WiseWoman, 2008
- LIFEF, 2002
- Cochrane, 2012
- PREMIER, 2003
- DEER, 1998

Subtotal (I-squared = 29.4%, p = 0.136)

NOTE: Weights are from random effects analysis

$\Delta$ SBP, mmHg $\begin{cases} -5 & \text{Intervention better} \\ +5 & \text{Control better} \end{cases}$
Outline

● Lifestyle modification

● Novel non-drug interventions (devices)
Renal denervation (RDN)

- Afferent nerves
- Efferent nerves (renal SNA)

Renal vasculature
- ↓ Renal bloodflow

Juxtaglomerular granular cells
- ↑ Renin secretion rate

Renal tubular epithelial cells
- ↑ Renal tubular sodium reabsorption and urinary sodium excretion

↑ Renal sympathetic nerve activity
### Earlier vs. later RDN trials

<table>
<thead>
<tr>
<th>Trial Name</th>
<th>Sham-controlled trials</th>
<th>Non-sham-controlled trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>Desch et al. 29 (n=71)</td>
<td>SYMPPLICITY HTN-3 (REF 21) (n=535) 2014</td>
<td></td>
</tr>
<tr>
<td>SYMPPLICITY HTN Japan 66 (n=998) 2015</td>
<td>SYMPPLICITY Registry 65 (n=998) 2015</td>
<td></td>
</tr>
<tr>
<td>Global SYMPPLICITY Registry 65 (n=998) 2015</td>
<td>REDUCE-HTN 67 (n=146) 2015</td>
<td></td>
</tr>
<tr>
<td>RAPID 68 (n=50) 2015</td>
<td>Fadl Elmula et al. 69 (n=19) 2014</td>
<td></td>
</tr>
<tr>
<td>ENCOREd meta-analysis 70 (n=109) 2014</td>
<td>ABPM meta analysis 71 (n=346) 2014</td>
<td></td>
</tr>
<tr>
<td>Heidelberg Registry 72 (n=63) 2013</td>
<td>EnlightHTN-1 (REF 73) (n=46) 2013</td>
<td></td>
</tr>
<tr>
<td>Moderate CKD 74 (n=15) 2012</td>
<td>REDUCE 75 (n=15) 2012</td>
<td></td>
</tr>
<tr>
<td>SYMPPLICITY HTN-2 (REF 20) (n=102) 2010</td>
<td>SYMPPLICITY HTN-1 (REF 19) (n=153) 2009</td>
<td></td>
</tr>
</tbody>
</table>

**Mean Δ office SBP at 6 mos. (mmHg)**

(R Gulati et al., Nature Reviews Cardiology 2016)
# 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.,

<table>
<thead>
<tr>
<th></th>
<th>RDN (n=353)</th>
<th>Sham (n=171)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline</strong></td>
<td>180</td>
<td>180</td>
<td>n.s.</td>
</tr>
<tr>
<td><strong>6 months</strong></td>
<td>166</td>
<td>168</td>
<td>n.s.</td>
</tr>
<tr>
<td><strong>Change</strong></td>
<td>-14</td>
<td>-12</td>
<td>n.s.</td>
</tr>
</tbody>
</table>
**On-Going RDN Trials**

- Higher RF energy, multipolar electrodes
- Deliver RF to more distal renal artery & branches
- Deliver RF to renal pelvis (ureteral catheter to destroy renal afferent nerves)
- Deliver neurotoxins rather than RF
- Deliver ultrasound by internal or external approaches

**More Extensive Denervation**

**Efficacy test? (difficult)**

**Target Specific Patient Subsets**

- Younger patients/milder HTN (SNS more important)
- Drug naïve (eliminate confounding by meds)

Carotid baroreflex activation therapy for resistant hypertension

Ronald G. Victor
Baroreflex Activation Therapy Lowers Blood Pressure in Patients With Resistant Hypertension

Results From the Double-Blind, Randomized, Placebo-Controlled Rheos Pivotal Trial

John D. Bisognano, MD, PhD,* George Bakris, MD,† Mitra K. Nadim, MD,‡ Luis Sanchez, MD,§ Abraham A. Kroon, MD, PhD,|| Jill Schafer, MS,¶ Peter W. de Leeuw, MD, PhD,|| Domenic A. Sica, MD#

322 patients with resistant HTN x 5 meds

- From a baseline of 169/101 mmHg, systolic BP was reduced by 25 mmHg in the experimental group vs. 17 mmHg in the sham group (p=ns).
- Cranial nerve injury in 9% (permanent in ½)
Miniaturized, unilateral **Barostim Neo**

Barostim Neo System in the Treatment of Resistant Hypertension

Trial registered…

[ClinicalTrials.gov](http://ClinicalTrials.gov) NCT01471834

Months from implant          Hoppe UC et al., *J Am Soc Hypertens.* 2012
RESPeRATE: the role of paced breathing in hypertension treatment

Relu Cernes, MD\textsuperscript{a,b} and Reuven Zimlichman, MD\textsuperscript{b,c,*}

1) Monitors breathing movements
2) Composes breathing-guiding tones
3) Synchronizes breathing movements with the guiding tones.

- Improves baroreflex sensitivity
- Reduces SNS activity
- Lowers home SBP 3-5 mmHg
- Class IIA, Evidence level B
- Cost $100-200
Enhanced Cardiac External Counterpulsation (EECP) for HTN?

May stimulate
- Collateral blood vessels
- Nitric oxide release
- Baroreflexes (↓SNS)
Enhanced external counterpulsation improves systolic blood pressure in patients with refractory angina

Alex R. Campbell, MD, a Daniel Satran, MD, a Andrey G. Zenovich, MSc, a Kayla M. Campbell, a Julia C. Espel, BS, a Theresa L. Arndt, RN, MA, a Anil K. Poulose, MD, a Charlene R. Boisjolie, RN, MA, a Kim Juusola, RN, b Bradley A. Bart, MD, b and Timothy D. Henry, MD a Minneapolis, MN

(Am Heart J 2008;156:1217-22.)

**Systolic BP**

108 patients, 80% men
Mean age 66
Open-label, no sham

**Diastolic BP**

$r = -0.637$
$P < .001$

$r = -0.647$
$P < .001$
CASE: 49 year old man with drug-resistant HTN: 
Normal BMP, and home SBP 135-155 and compliant with: amlodipine 10, irbesartan 300, indapamid 1.25, spironolactone 25, and carvedilol 25 BID

Non-drug and lifestyle recommendations:

1. Job stress ➢ RESPIReRATE
2. Fast foody ➢ DASH + EVOO/nuts + low salt
3. No exercise ➢ Hired a trainer

↓Amlodipine to 5 mg, carvedilol to 12.5 mg
Home systolic BP 125-145
Lifestyle Modification & Non-Drug Therapy

Sheila Kar, MD FACC
Cardiologist & Past Clinical Chief
The Heart Institute