Π.Γ.Ν.Α "ΛΑΪΚΟ"
ΚΑΡΔΙΟΛΟΓΙΚΗ ΚΛΙΝΙΚΗ

Στόχος Συστολικής Αρτηριακής Πίεσης στους Διαβητικούς

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Αντιπρόεδρος Ελληνικής Εταιρείας Υπέρτασης
The Two Terrorists

Diabetes Mellitus

Associated Hypertension
Association between DM and HTN:
epidemiological evidence from HDS
(a cross-sectional evaluation of UKPDS)

HTN prevalence (%)

Age distribution

Men
Women

Women; Total; 46.5

Women; Total; 34.7

Turner et al J Hypertens 1993;11:309
HOT-diabetes and UKPDS: more intense BP lowering, better CV outcomes

Diabetes Subgroup

![Graph showing the difference in mortality and patients with events between less tight control and tight control.](image)

- **Less tight control (mean BP 154/87 mmHg)**
- **Tight control (mean BP 144/82 mmHg)**

- **P<0.005**

- **Goal of therapy: target diastolic BP**
  - ≤ 90 mm Hg (n=501)
  - 85 mm Hg (n=501)
  - 80 mm Hg (n=499)

- **More tight lowering group: 143.7/81mmHg**


- **Tight BP control: 24% reduction of events (95% CI 8-38)**

- Years from randomization

- Patients with events (%)
Θεραπεία της ΑΥ στο Σακχαρώδη Διαβήτη
Η μείωση της ΑΠ μειώνει τις επιπλοκές στο διαβήτη

Η θεραπεία της υπέρτασης μειώνει τα ΚΑ επεισόδια στο διαβήτη: Μελέτη HOT

Σύνολο ασθενών (n=18,790)  Διαβήτης (n=1501)

<table>
<thead>
<tr>
<th>Διαστολική πίεση – στόχος (mmHg)</th>
<th>ΚΑ επεισόδια ανά 1000 ασθενειών-έτη</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 90</td>
<td>9.9</td>
</tr>
<tr>
<td>≤ 85</td>
<td>10.0</td>
</tr>
<tr>
<td>≤ 80</td>
<td>9.3</td>
</tr>
<tr>
<td>≤ 90</td>
<td>24.4</td>
</tr>
<tr>
<td>≤ 85</td>
<td>18.6</td>
</tr>
<tr>
<td>≤ 80</td>
<td>11.9</td>
</tr>
</tbody>
</table>

- 43% μείωση κινδύνου
  p<0.005

Επιτευχθείσα ΑΠ

144/85  141/83  140/81

Μελέτη ADVANCE

- 140/77 έναντι 135/75
- Περινδοπρίλη + ινδαπαμίδη

ADVANCE Collaborative Group. Lancet 2007
**Background**

There is no evidence from previous trials that lowering systolic blood pressure below 120 mm Hg prevents complications in type 2 diabetes. We investigated whether intensive treatment (systolic blood pressure target <119 mm Hg) reduces major cardiovascular events in patients at high risk for cardiovascular disease.

**Methods**

A total of 4733 participants with type 2 diabetes were randomly assigned to intensive treatment or to standard treatment with a systolic blood pressure target of <133 mm Hg. The results showed that intensive treatment reduced the risk of major cardiovascular events by 20% compared to standard treatment.
Η εντατικοποιημένη ρύθμιση της ΑΠ
dεν μείωσε τα καρδιαγγειακά επεισόδια

Κύριο καταληκτικό
-12%  
**p=0.2**  
0.73 -1.06

-13%  
**p=0.25**

Εγκεφαλικά επεισόδια
-37%  
**p=0.03**

Έμφραγμα μυοκαρδίου

Θάνατοι από καρδιαγγειακή νόσο
+6%  
**p=0.74**

No. at Risk  
<table>
<thead>
<tr>
<th>Intensive</th>
<th>Standard</th>
</tr>
</thead>
<tbody>
<tr>
<td>2362 2773 2182 2117 1770 1080 298 175 80</td>
<td>2371 2274 2196 2120 1793 1127 358 195 108</td>
</tr>
</tbody>
</table>

No. at Risk  
<table>
<thead>
<tr>
<th>Intensive</th>
<th>Standard</th>
</tr>
</thead>
<tbody>
<tr>
<td>2362 2291 2223 2174 1841 1128 313 186 88</td>
<td>2371 2287 2235 2186 1879 1196 382 215 114</td>
</tr>
</tbody>
</table>

No. at Risk  
<table>
<thead>
<tr>
<th>Intensive</th>
<th>Standard</th>
</tr>
</thead>
<tbody>
<tr>
<td>2362 2704 2252 2201 1870 1143 317 188 91</td>
<td>2371 2313 2268 2218 1922 1220 393 221 118</td>
</tr>
</tbody>
</table>
2000s-2010s GLs for the treatment of HTN in patients with DM

Diabetes mellitus
- Start treatment: >130mmHg
- Lower BP to: <130 mmHg

Non-diabetes mellitus
- Start treatment: >140mmHg
- Lower BP to: <140mmHg

Based on HOT-DM and UKPDS-38

JNC 7, 2003
ESH/ESC 2003
ESC/ESH 2007
AHA/ADA 2007
ESH Reappraisal 2009
BP target in patients with diabetes mellitus
No clear evidence for < 130 mmHg SBP
Recent (after 2010) GLs for the treatment of HTN in patients with DM

It might be reasonable use RAS-b as first line drugs to treat HTN because of their protection on albuminuria levels and renal function.

ESC/ESH 2013 GLs
ESC/EASD 2013 GLs
ASH/ISH 2014 (Statement)
2013 Guidelines for the Management of Arterial Hypertension

European Society of Hypertension
European Society of Cardiology

Blood Pressure Goals In Hypertension

➢ **A SBP < 140 mmHg** recommended/considered, regardless the level of risk
  
  ➢ **Low/moderate risk (IB)**
  
  ➢ **Diabetes (IA)**

  ➢ **Diabetic/nondiabetic CKD (IIaB)**
  
  ➢ **Patients with CHD/previous stroke or TIA (IIaB)**

➢ **A DBP < 90 mmHg** recommended

  Diabetic Patients  **A DBP < 85 mmHg** recommended
HOT Diabetic Subgroup
Reduction in Cardiovascular Events

<table>
<thead>
<tr>
<th>Target diastolic BP (mmHg)</th>
<th>Achieved (\dagger) systolic BP (mmHg)</th>
<th>Achieved (\dagger) diastolic BP (mmHg)</th>
<th># of patients with diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>(\leq 90)</td>
<td>143.7</td>
<td>85.2</td>
<td>501</td>
</tr>
<tr>
<td>(\leq 85)</td>
<td>141.4</td>
<td>83.2</td>
<td>501</td>
</tr>
<tr>
<td>(\leq 80)</td>
<td>139.7</td>
<td>81.1</td>
<td>499</td>
</tr>
</tbody>
</table>

\(\dagger\) mean of all blood pressures for all study patients in BP subgroups from 6 months of follow-up to end of study

*Includes all myocardial infarction, all strokes, and all other cardiovascular deaths

Systolic Blood Pressure Intervention Trial (SPRINT)

An unmasked, open-label randomized controlled multicenter trial

SPRINT Important Goals

SPRINT will test whether a treatment strategy aimed at reducing systolic blood pressure to:

- **lower goal (SBP < 120 mm Hg)**
  
  compared with

- **currently recommended (SBP < 140 mm Hg)**

will reduce the occurrence of cardiovascular disease (CVD).

N = 9250 pts increased cardiovascular (CV) risk

Mean follow up period 3.26 years

**Primary hypothesis** : CVD composite event rate lower in intensive compared to standard treatment

Treatment target

The SPRINT trial

Intensive compared to standard treatment

- **Primary outcome**: -25% p < 0.001
- **All-cause mortality**: -27% p < 0.003
- **CV mortality**: -43% p < 0.005
- **Heart failure**: -38% p < 0.002

Which leads us to the question we started with: Is it time, after SPRINT, to introduce a new definition of hypertension? From the previous discussion, it would seem that since AOBP is not yet generally available, the definition of hypertension should remain BPs ≥140/90 mm Hg, and that the goal should remain to lower BP in most hypertensive patients to <140/90 mm Hg, and in those at higher cardiovascular risk, including chronic kidney disease patients, elderly individuals and those at a Framingham Risk Score of ≥15%, and perhaps as well diabetic subjects, goal BP should be <130/80 mm Hg.
Μείωση της ΑΠ < 130/80 mmHg

<table>
<thead>
<tr>
<th>Μετανάλυση</th>
<th>Αρ μελετών</th>
<th>Αρ ασθενών</th>
<th>Καρδ επεισόδια</th>
<th>Θνητότητα</th>
<th>ΑΕΕ μικροαγγ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emdin CA, et al.</td>
<td>40</td>
<td>100.345</td>
<td>-</td>
<td>-</td>
<td>↓</td>
</tr>
<tr>
<td>Xie X, et al.</td>
<td>19</td>
<td>44.989</td>
<td>↓</td>
<td>↓NS</td>
<td></td>
</tr>
<tr>
<td>Ettehad D, et al.</td>
<td>123</td>
<td>613.815</td>
<td>↓</td>
<td>↓</td>
<td>-</td>
</tr>
</tbody>
</table>

A new comprehensive meta-analysis

DM vs non-DM

- BP lowering trials
  - 57 RCTs (250,000 patients)
    - 17 RCTs in DM
    - 16 RCTs without DM
    - 24 RCTs (separated data for DM and non-DM)
  - 61,772 DM pts
  - 191,353 non-DM pts

- Head-to-head trials
  - 50 RCTs (225,000 patients)
    - 59,116 DM pts
    - 163,589 non-DM pts
    - Diuretics vs all others
      - 7 comparisons DM, n=23,721
      - 12 comparisons non-DM, n=55,684
    - Beta-blockers vs all others
      - 4 comparisons DM, n=13,490
      - 10 comparisons non-DM, n=57,248
    - CCBs vs all others
      - 21 comparisons DM, n=49,620
      - 18 comparisons non-DM, n=108,561
    - ACEi vs all others
      - 17 comparisons DM, n=26,113
      - 14 comparisons non-DM, n=54,661
    - ARBs vs all others
      - 6 comparisons DM, n=16,435
      - 7 comparisons non-DM, n=33768

Identity of meta

107 RCTs with separated data on DM and non-DM hypertensive patients almost 500,000 patients and 2,000,000 pts-years

Thomopoulos, Parati, Zanchetti. J Hypertens 2017;35
Τιμητική Θεραπεία Εκβάσεων σε Διαφορετικά Επίπεδα ΣΑΠ σε Ασθενείς με ΣΔ2

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Achieved SBP cut-off (mmHg)</th>
<th>N Trials</th>
<th>Standardized RR (95% CI)</th>
<th>Standardized RR (95% CI)</th>
<th>P trend</th>
<th>Mean Absolute Risk Reduction Per 1000 pts treated for 5 years</th>
<th>P trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke</td>
<td>≥140</td>
<td>11</td>
<td>0.52 (0.29-0.96)</td>
<td></td>
<td>0.13</td>
<td>-31 -19 -8</td>
<td>0.006</td>
</tr>
<tr>
<td></td>
<td>130-140</td>
<td>13</td>
<td>0.76 (0.60-0.98)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>&lt;130</td>
<td>4</td>
<td>0.74 (0.59-0.92)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CHD</td>
<td>≥140</td>
<td>10</td>
<td>0.41 (0.27-0.64)</td>
<td></td>
<td>0.007</td>
<td>-37 -22</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>130-140</td>
<td>12</td>
<td>0.72 (0.58-0.99)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>&lt;130</td>
<td>3</td>
<td>0.86 (0.72-1.02)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HF</td>
<td>≥140</td>
<td>6</td>
<td>0.45 (0.24-0.81)</td>
<td></td>
<td>0.010</td>
<td>-48 -11 -3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>130-140</td>
<td>9</td>
<td>0.77 (0.58-1.02)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>&lt;130</td>
<td>3</td>
<td>0.92 (0.75-1.14)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stroke+CHD</td>
<td>≥140</td>
<td>10</td>
<td>0.44 (0.32-0.63)</td>
<td></td>
<td>0.001</td>
<td>-73 -38 -11</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>130-140</td>
<td>15</td>
<td>0.72 (0.61-0.83)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>&lt;130</td>
<td>3</td>
<td>0.81 (0.70-0.94)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stroke+CHD+HF</td>
<td>≥140</td>
<td>8</td>
<td>0.49 (0.32-0.71)</td>
<td></td>
<td>0.003</td>
<td>-116 -51 -19</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>130-140</td>
<td>13</td>
<td>0.77 (0.65-0.91)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>&lt;130</td>
<td>3</td>
<td>0.86 (0.75-0.99)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CV Death</td>
<td>≥140</td>
<td>8</td>
<td>0.56 (0.26-1.21)</td>
<td></td>
<td>0.008</td>
<td>-37 -20 +4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>130-140</td>
<td>13</td>
<td>0.67 (0.41-1.07)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>&lt;130</td>
<td>4</td>
<td>1.28 (0.87-1.99)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All-cause Death</td>
<td>≥140</td>
<td>10</td>
<td>0.79 (0.53-1.21)</td>
<td></td>
<td>0.090</td>
<td>-35 -29 +1</td>
<td>0.018</td>
</tr>
<tr>
<td></td>
<td>130-140</td>
<td>15</td>
<td>0.71 (0.58-0.88)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>&lt;130</td>
<td>4</td>
<td>1.03 (0.86-1.23)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Thomopoulos, Parati, Zanchetti. J Hypertens 2017;35
Standards of Medical Care in Diabetes - 2017
What do the latest GLs say? ADA 2017

- SBP/DBP < 140/90 mmHg (grade A)

- SBP/DBP < 130/80 mmHg, may be appropriate for certain individuals at high risk, if they can be achieved without undue treatment burden (grade C)

- In patients with albuminuria (grade A) or microalbuminuria (grade B) a RAS-b at the maximum tolerated dose should be instituted

- In patients without albuminuria all 4 classes of anti-HTN may be alternatively used for treatment initiation (grade A)
9.6. Diabetes Mellitus

Recommendations for Treatment of Hypertension in Patients With DM

References that support recommendations are summarized in Online Data Supplements 46 and 47 and Systematic Review Report.

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>SBP: B-R&lt;sup&gt;SR&lt;/sup&gt;</td>
<td>1. In adults with DM and hypertension, antihypertensive drug treatment should be initiated at a BP of 130/80 mm Hg or higher with a treatment goal of less than 130/80 mm Hg (1-8).</td>
</tr>
<tr>
<td></td>
<td>DBP: C-EO</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>A&lt;sup&gt;SR&lt;/sup&gt;</td>
<td>2. In adults with DM and hypertension, all first-line classes of antihypertensive agents (i.e., diuretics, ACE inhibitors, ARBs, and CCBs) are useful and effective (1, 9, 10).</td>
</tr>
<tr>
<td>IIb</td>
<td>B-NR</td>
<td>3. In adults with DM and hypertension, ACE inhibitors or ARBs may be considered in the presence of albuminuria (11, 12).</td>
</tr>
</tbody>
</table>

SR indicates systematic review.
Ορισμός υπέρτασης στον διαβήτη

AHA/ACC Guidelines 2017
ΑΠ ≥ 140/90 mmHg

Canadian Guidelines 2017
ΑΠ ≥ 130/80 mmHg

UKPDS

'Εμφραγμα

Μικροαγγειοπάθεια

2018 ESC-ESH Guidelines for the Management of Arterial Hypertension
Σε άτομα με διαβήτη και υπέρταση

- Έναρξη θεραπείας αν ΑΠ ≥ 140/90 mmHg

- ΑΠ στόχος
  - <140 προς 130 mmHg
  - < 130 mmHg αν είναι καλά ανεκτό
  - Όχι < 120 mmHg
  - ΔΑΠ <80 mmHg αλλά όχι < 70 mmHg

- Σε ηλικιωμένους ≥ 65 ετών
  - ΣΑΠ 130-139 mmHg
  - ΔΑΠ <80 mmHg αλλά όχι < 70 mmHg

Williams, Mancia et al., J Hypertension and Eur Heart J 2018