Are frail, very old subjects overtreated for their hypertension?

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15° Πανελλήνιο Συνέδριο Αρτηριακής Υπέρτασης
Θεσσαλονίκη 7 Μαρτίου 2015
Disclosures

- Honoraria
  - Boehringer
  - Fukuda
  - Novartis
  - Servier
  - Sanofi
Specificities of arterial hypertension in the very elderly

10° Πανελλήνιο Συνέδριο Αρτηριακής Υπέρτασης
Θεσσαλονίκη, Ιανουάριος 2010
No association between SBP and CV morbidity in very old frail populations

- No association between SBP/DBP and total/CV mortality in elderly (87 yo) hospitalized in long stay hospital

- No association between SBP and morbidity in a frail elderly nursing home population
Lower Systolic Blood Pressure Is Associated with Greater Mortality in People Aged 85 and Older

Lena Molander, Bsc, Hugo Lövheim, MD, PhD, Tove Norman, MD, Peter Nordström, MD, PhD, and Yngve Gustafson, MD, PhD

Figure 1. Survival curve based on multivariate Cox regression. P-values of comparison with the ≤120 mmHg group: 121–140 mmHg, P < .001; 141–160 mmHg, P < .001; > 160 mmHg, P = .03. *The curves for these two groups overlap.

Figure 2. Graph of multivariate Cox regression. Adjusted for sex, age, Mini-Mental State Examination score, activities of daily living according to Barthel score, atrial fibrillation, and diabetes mellitus. Risk associated with systolic blood pressure 140 mmHg (dotted line) was used as index ( = 100).
Hypertension after 80 Actif tt (indapamide ± perindopril) vs. placebo: The HYVET study

- All Stroke
- Stroke Death
- All cause mortality
- NCV/Unknown death
- CV Death
- Cardiac Death
- Heart Failure
- CV events

0.1 0.2 0.5 0 2

NEJM 2008;358
Specificities of arterial hypertension in the very old

Conclusions
(Thessaloniki January 2010)

• Treat all “robuste” hypertensives
• Target SBP<150 mmHg
• Individual approach for the disabled elderly: Quality of life is the first goal
• Gerontological evaluation for all elderly
• Start low (one drug for starting); Go slow
• Not more than 3 anti-Htn drugs
• Check for orthostatic hypotension
• Attention to the interactions (poly-medication, frailty)
2007: PARTAGE
Etude de la Pression ARTérielle des personnes AGées
vivant en EHPAD

French Minstry of Health Grant for Clinical Research
PHRC/DCV20070409250

Rôle of blood pressure and arterial stiffness
on morbidity, mortality and cognitive impairment
in very old people living in nursing homes

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Dijon

Pr Y. Rolland
Toulouse

Pr P Salvi
Cesena

Pr M Zamboni
Verona

- 1126 subjects
- 78% women
- Age: 87y at baseline
- 7.2 drugs/day
- 2-year follow up
PARTAGE Study: Publications 2010-2015


8. WATFA G et al. Do arterial hemodynamic parameters predict cognitive decline over a period of 2 years in individuals older than 80 years living in nursing homes? The PARTAGE study; *JAMDA* in press
SBP levels in treated hypertensive subjects (upper panel) and in subjects without history of hypertension (lower panel). The PARTAGE study

Benetos et al, *J. Hypertens* 2010
Flow chart with the data concerning deaths and major CV events during the follow up period.

- **Total population enrolled**: 1126 (100%)

  - **Major CV events**: 228 (20.2%)
    - **Initial lethal CV event**: 85 (7.5%)
    - **Initial non-lethal CV event**: 143 (12.7%)
    - **Subsequent lethal CV event**: 32 (2.8%)
    - **Alive at the end**: 96 (8.5%)
    - **Subsequent non-CV death**: 10 (0.9%)

  - **Lost to follow up**: 35 (3.1%)

  - **Non-CV Mortality**: 120 (10.7%)
    - **Alive at the end without Major CV events**: 743 (66.0%)

  - **Total CV deaths**: 117 (10.4%)

  - **Total non-CV deaths**: 130 (11.5%)

  - **Total non-CV deaths + Total CV deaths**: 247

  - **Lost to follow up**: 40

  - **Alive at the end of the follow up**: 839

  - **Total**: 1126

  - **Lost to follow up**: 5 (0.4%)
SBP and total mortality during the 2-year follow-up period

SBP tertiles

- L
- M
- H

Survival

TOTAL MORTALITY

Log-rank p=0.057

L: PAS = 85-130 mmHg

Benetos et al, J Am Coll Cardiol 2012
## Table 3: Risk Ratio (Cox Regression Analysis) for Total Mortality and Major CV Events According to Blood Pressure and Pulse Wave Velocity

<table>
<thead>
<tr>
<th></th>
<th>Risk Ratio</th>
<th>95% CI</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total mortality</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PWV, +1 m/s</td>
<td>1.00</td>
<td>0.97–1.03</td>
<td>0.792</td>
</tr>
<tr>
<td>SBP, +10 mm Hg</td>
<td>0.91</td>
<td>0.84–0.98</td>
<td>0.017</td>
</tr>
<tr>
<td>DBP, +10 mm Hg</td>
<td>0.84</td>
<td>0.72–0.99</td>
<td>0.037</td>
</tr>
<tr>
<td>MAP, +10 mm Hg</td>
<td>0.85</td>
<td>0.75–0.97</td>
<td>0.016</td>
</tr>
<tr>
<td>PP, +10 mm Hg</td>
<td>0.90</td>
<td>0.81–1.00</td>
<td>0.057</td>
</tr>
<tr>
<td><strong>Major CV events</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PWV, +1 m/s</td>
<td>1.00</td>
<td>0.98–1.03</td>
<td>0.797</td>
</tr>
<tr>
<td>SBP, +10 mm Hg</td>
<td>0.98</td>
<td>0.91–1.06</td>
<td>0.674</td>
</tr>
<tr>
<td>DBP, +10 mm Hg</td>
<td>0.97</td>
<td>0.84–1.13</td>
<td>0.716</td>
</tr>
<tr>
<td>MAP, +10 mm Hg</td>
<td>0.96</td>
<td>0.84–1.09</td>
<td>0.524</td>
</tr>
<tr>
<td>PP, +10 mm Hg</td>
<td>0.98</td>
<td>0.89–1.09</td>
<td>0.741</td>
</tr>
</tbody>
</table>

Each variable presented in this table was included in a multivariate Cox model with the following covariates: age, sex, body mass index, activities of daily living, Charlson comorbidity index, and history of CV disease for total mortality; age, activities of daily living, Charlson comorbidity index, history of CV disease, and antihypertensive treatment for major CV events. For PWV, mean arterial pressure and heart rate were added in the multivariate models.

Cl = confidence interval; other abbreviations as in Tables 1 and 2.

Benetos et al, J Am Coll Cardiol 2012
What is the profile of the subjects with low BP having increased total mortality?
Original Investigation

Treatment With Multiple Blood Pressure Medications, Achieved Blood Pressure, and Mortality in Older Nursing Home Residents
The PARTAGE Study

Athanase Benetos, MD, PhD; Carlos Labat, BSc; Patrick Rossignol, MD, PhD; Renaud Fay, PharmD; Yves Rolland, MD, PhD; Filippo Valbusa, MD; Paolo Salvi, MD, PhD; Mauro Zamboni, MD, PhD; Patrick Manckoundia, MD, PhD; Olivier Hanon, MD, PhD; Sylvie Gautier, MD

Published online February 16, 2015.
Over-Mortality (X2) in patients with low SBP (<130 mmHg) under combination anti-hypertensive therapy
20% of the entire population

Benetos et al, JAMA Int Med 2015
Hazard ratios for all-cause mortality according to SBP levels, number of antihypertensive drugs and their interaction, both unadjusted (panel A) and after adjustment for several co-founders.

Low daytime SBP was independently associated with a greater progression of cognitive decline in older patients with dementia and MCI among those treated with AHDs.

Excessive SBP lowering may be harmful for older patients with cognitive impairment. Ambulatory blood pressure monitoring can be useful to help avoid high blood pressure overtreatment in this population.
Drug-induced low BP may be responsible for decreased perfusion of key organs (heart, brain, kidney…) in very old frail subjects

Should we modify our therapeutic strategy in these patients?
What do the guidelines propose in the presence of low BP under anti-Htn treatment?
### 2013 ESH/ESC Guidelines for the management of arterial hypertension

(Mancia et al J. Hypert 2013)

#### Antihypertensive treatment strategies in the elderly

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Level&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Ref. &lt;sup&gt;c&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>In elderly hypertensives with SBP ≥160 mmHg there is solid evidence to recommend reducing SBP to between 150 and 140 mmHg.</td>
<td>I</td>
<td>A</td>
<td>141, 265</td>
</tr>
<tr>
<td>In fit elderly patients &lt;80 years old antihypertensive treatment may be considered at SBP values ≥140 mmHg with a target SBP &lt;140 mmHg if treatment is well tolerated.</td>
<td>IIb</td>
<td>C</td>
<td>-</td>
</tr>
<tr>
<td>In individuals older than 80 years with an initial SBP ≥160 mmHg it is recommended to reduce SBP to between 150 and 140 mmHg, provided they are in good physical and mental conditions.</td>
<td>I</td>
<td>B</td>
<td>287</td>
</tr>
</tbody>
</table>
In frail elderly patients, it is recommended to leave decisions on antihypertensive therapy to the treating physician, and based on monitoring of the clinical effects of treatment.

Continuation of well-tolerated antihypertensive treatment should be considered when a treated individual becomes octogenarian.
THM (1): TREATING HYPERTENSIVE INDIVIDUALS OVER 80 YEARS OLD

ROBUST SUBJECTS

- Focus on SBP and PP, target SBP 130-150 mmHg
- Start with monotherapy; avoid using more than 3 antihypertensive drugs
- Always check for orthostatic hypotension
- Optimize treatment for global CVD protection
FRAIL SUBJECTS

- Reconciliation and revision of the prescription
- Evaluation (CGA) of the risk/benefit ratio (life expectancy, geriatric syndromes, polypharmacy, etc.)
- Start anti-HTn treatment with one drug; start low and go slowly, SBP goal 150 mmHg
- Identify/correct other factors/drugs decreasing BP
- If SBP<130 mmHg or orthostatic hypertension under treatment: Consider reducing antihypertensive treatment, especially in case of combination therapy
Conclusions

- SBP<130 under combination anti-HTn therapy is associated with a 2-fond increase in all-cause mortality
- This result persist even after several adjustments
- Interventional studies are warranted to assess the benefits/risks ratio of multi-drug antihypertensive treatment in the growing population of elderly frail patients.
Research Group and main collaborations

• Dpt of Geriatrics, CHU de Nancy
• and INSERM U1116, Univ. Lorraine

• Sylvie Gautier
• Anna Kearny-Schwartz
• Laure Joly
• Carlos Labat
• Paolo Salvi
• Mohamed Temmar
• Ghassan Watfa