

Constitutional Hypotension

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GIMSI, Syncope 2023 Napoli, February 17-18, 2023

I have no conflict of interest in relation to this presentation.

Definition

Systolic Arterial Pressure (office blood pressure): < 110 mmHg in male
<100 mmHg in female
in the absence of other diseases.

Epidemiology

- 3 community surveys. (Pemberton J. Br Med J 1989;298:660)
1.6-2.7% of total male population
0.3%-3.6% of total female population
- German general practice population . (Donner-Banzhoff Family Practice 1994;11:368)
17% of all participants,
Proportion twice as high among women as in men
More common among younger subjects

Socioeconomic impact of low blood pressure

In the former west Germany, in 1978

- 9.5 millions of working days lost due to low blood pressure
- 1-8% of total population regularly took anti-hypotensive drugs
- Expenditure of about 380 millions DM

(Beske et al. Effizienzanalyse der medikamentösen Hypotonie Therapie.
Kiel: Institut für gesundheits-System-Forschung, 1983)

Table 2: Prevalence of reported symptoms in subjects with chronic constitutional hypotension (CHT) and in subjects with normal blood pressure (NBP).

	<u>CHT</u>	<u>NBP</u>	<i>p-value</i>
<u><i>Symptoms</i></u>			
<i>Pre-Syncope</i>	45%	24%	0.06
<i>Syncope</i>	45%	14%	0.05
<i>Palpitation</i>	50%	24%	0.07
<i>Chest discomfort</i>	30%	27%	ns
<i>Flushing</i>	58%	33%	ns
<i>Anxiety</i>	21%	24%	ns
<i>Cloudy thought</i>	58%	20%	0.02
<i>Migraine</i>	37%	24%	ns
<i>Intestinal symptoms</i>	30%	20%	ns
<i>Alcoholic intolerance</i>	20%	24%	ns

Table 3: Quality of life, assessed by SF-36 questionnaire in subjects with constitutional hypotension (CHT) and in subjects with normal blood pressure (NBP): Mean (Confidence Intervals 95%)

	<u>CHT</u>	<u>NBP</u>	
<u>SF-36 component</u>			<i>p-value</i>
<i>Physical Functioning</i>	93 (90-96)	94 (91-96)	<i>ns</i>
<i>Limitation d/t physical health</i>	80 (65-94)	92 (89-94)	<i>0.08</i>
<i>Limitation d/t emotional problem</i>	84 (70-96)	90 (84-93)	<i>ns</i>
<i>Energy / Fatigue</i>	54 (46-62)	82 (76-86)	<i>0.001</i>
<i>Emotional well-being</i>	68 (61-75)	87 (82-93)	<i>0.001</i>
<i>Social functioning</i>	62 (54-70)	70 (62-75)	<i>0.08</i>
<i>Pain</i>	77 (70-85)	72 (66-79)	<i>ns</i>
<i>General Health</i>	73 (66-79)	80 (84-96)	<i>0.12</i>

Does *Constitutional Hypotension* exist?

For Debate

(J Pemberton, BMJ 1989;298:660-662)

- In UK chief symptoms ascribed to chronic hypotension are commonly encountered in clinical practice but would probably be attributed to psychogenic factors and treated accordingly
- In Germany and other European Countries same symptoms are attributed to hypotension and patients are treated with anti-hypotensive agents
- American doctors admit that many patients are currently treated for chronic low blood pressure but are doubtful about its usefulness
- UpToDate (no chapter on Constitutional Hypotension)

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AIMs

- To assess symptoms, cardiovascular autonomic profile and baroreceptor sensitivity in 15 women with CHT compared with 12 NT
- To evaluate quality of life, by SF-36 questionnaire
- To assess plasma renin activity (PRA) and Aldosterone plasma levels
- To quantify left ventricular mass index by cardiac sonography at rest

Cardiovascular Autonomic Profile and Baroreceptor Sensitivity

Variables and Task

ECG

Beat by beat arterial pressure

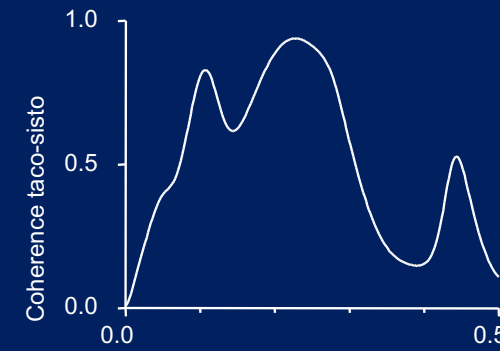
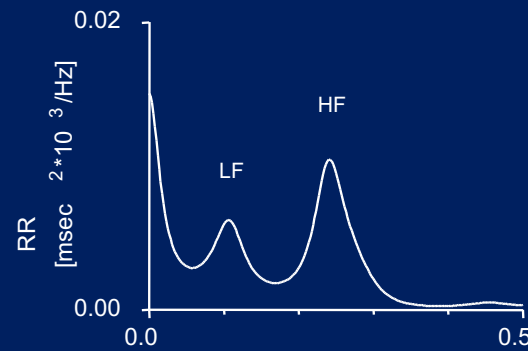
Respiratory activity

- Rest
- 75° head-up Tilt

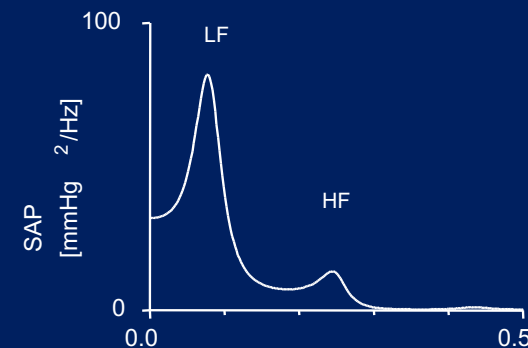
Spontaneous sequences techniques (Time domain analysis)

Spectrum and Cross-Spectrum Analyses of RR and SAP variability (Frequency domain analysis)

LF/HF

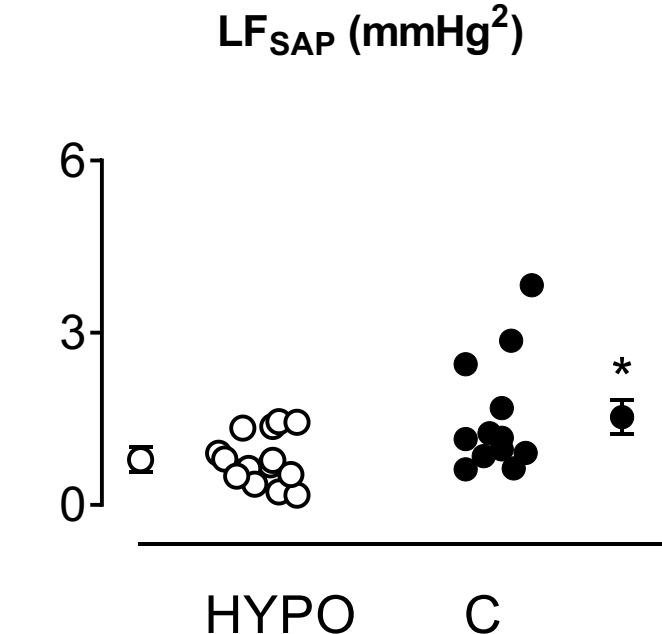
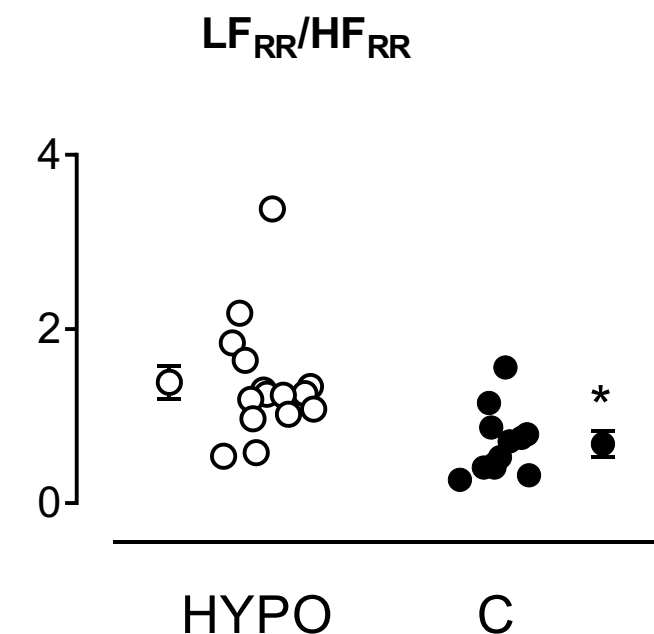
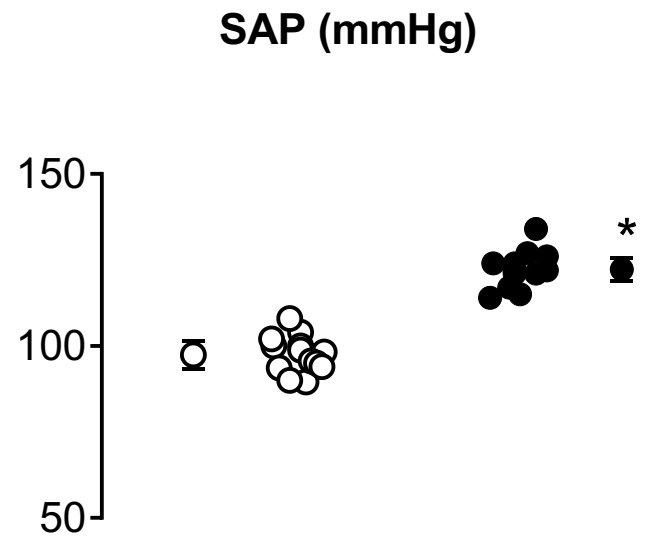
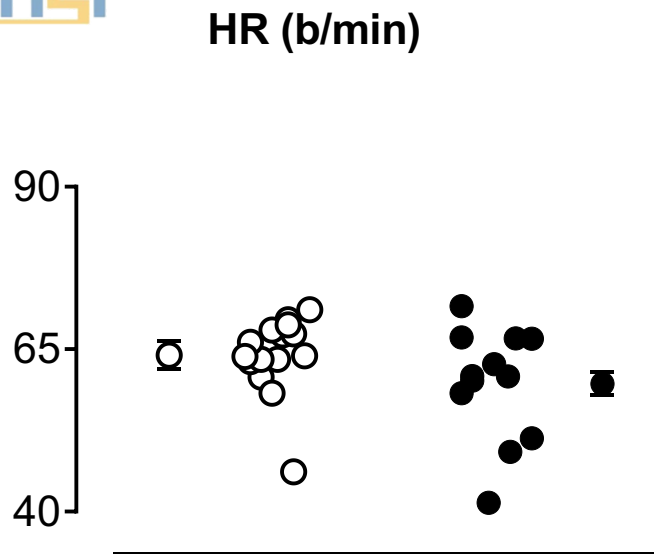


LF_{SAP}

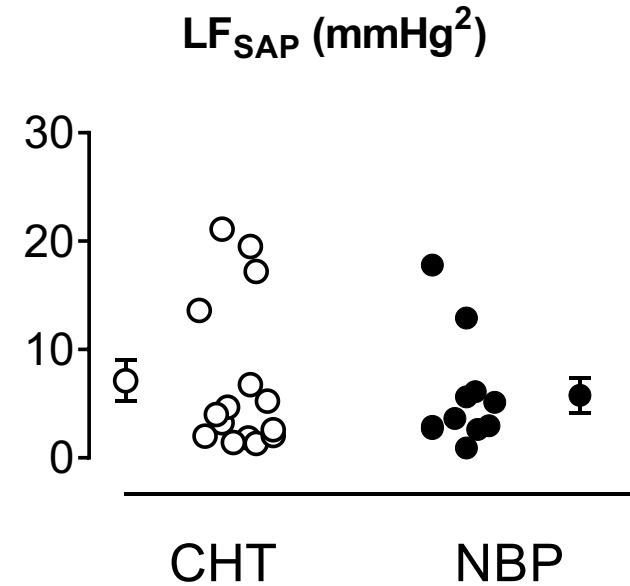
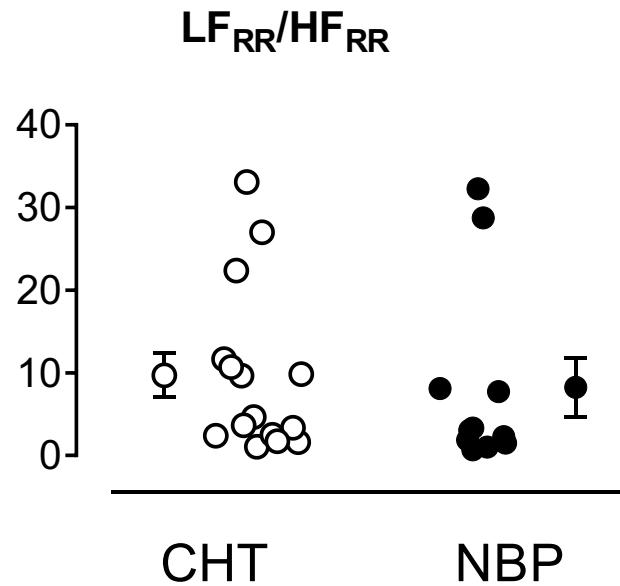
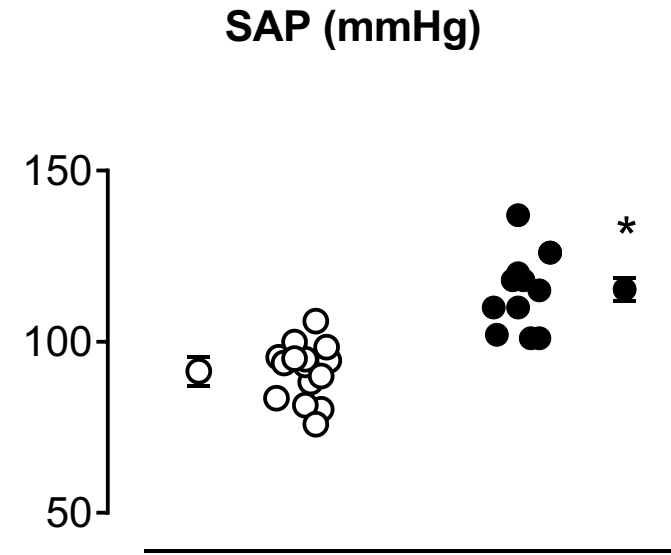
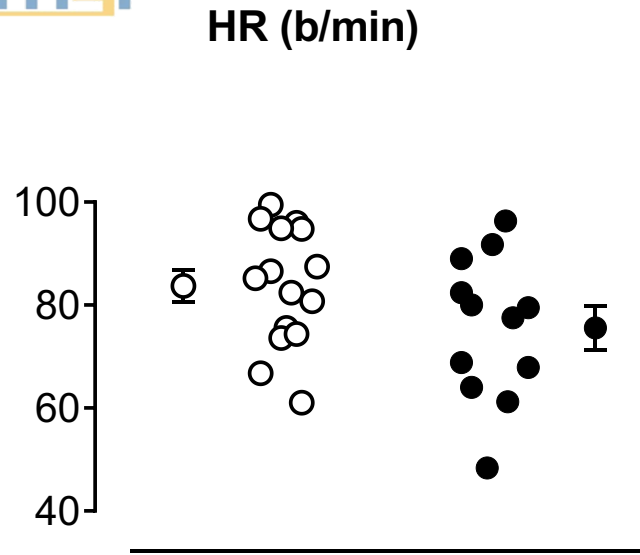


$$\alpha_{LF} = \sqrt{\frac{(LF_{RR})}{(LF_{SAP})}}$$

Rest



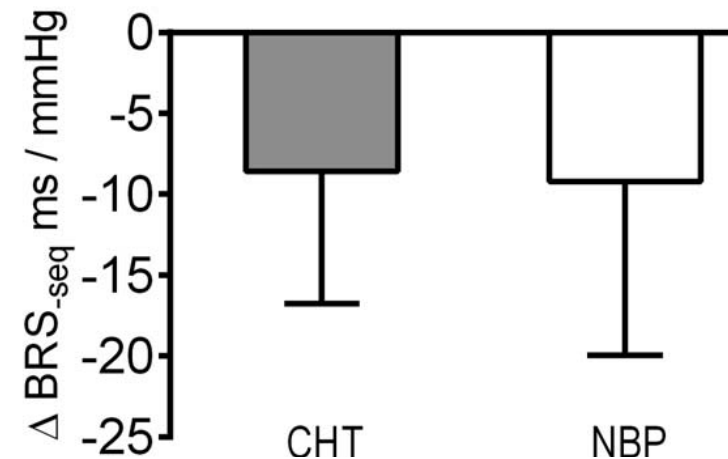
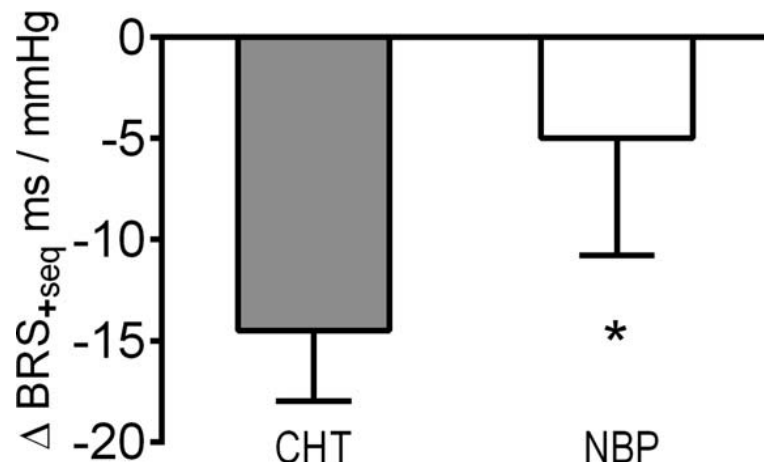
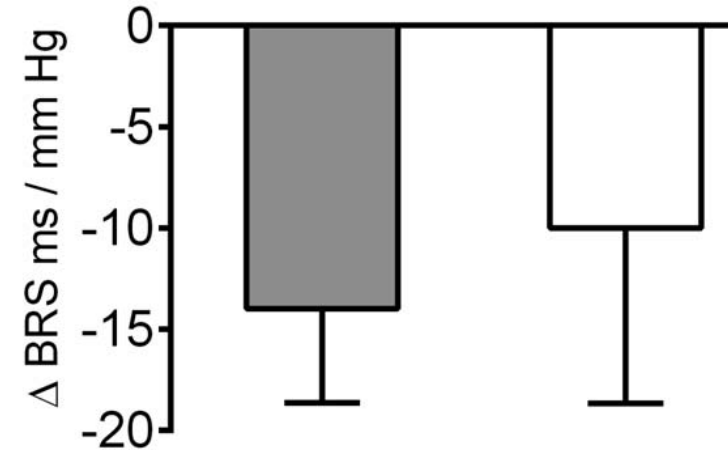
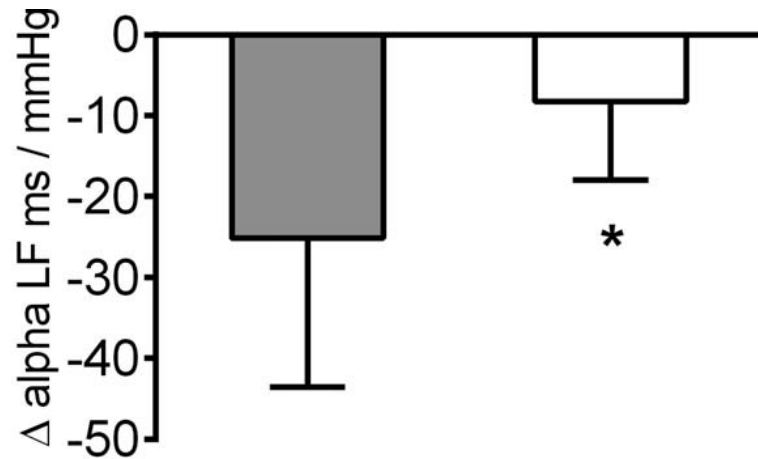
75° TILT

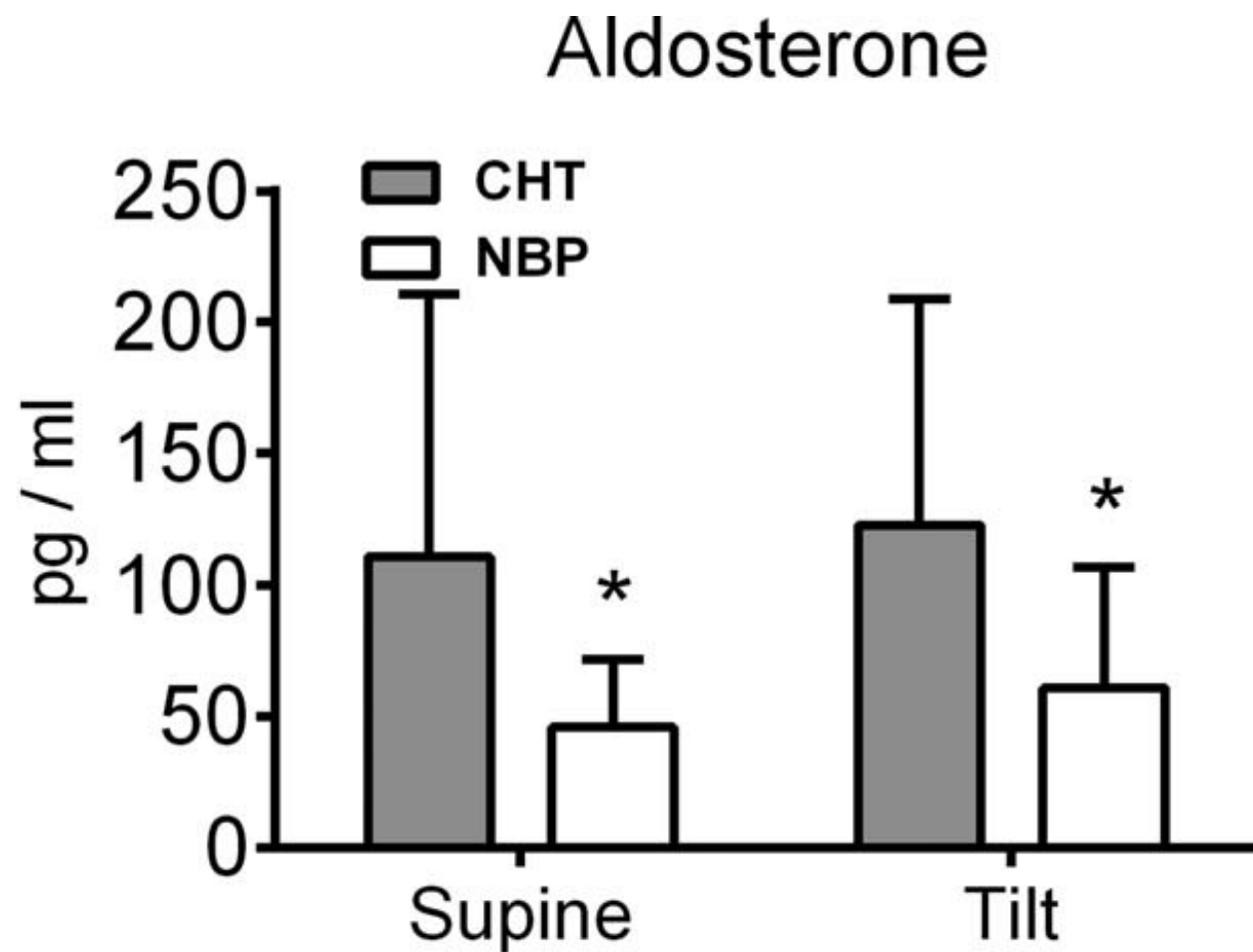
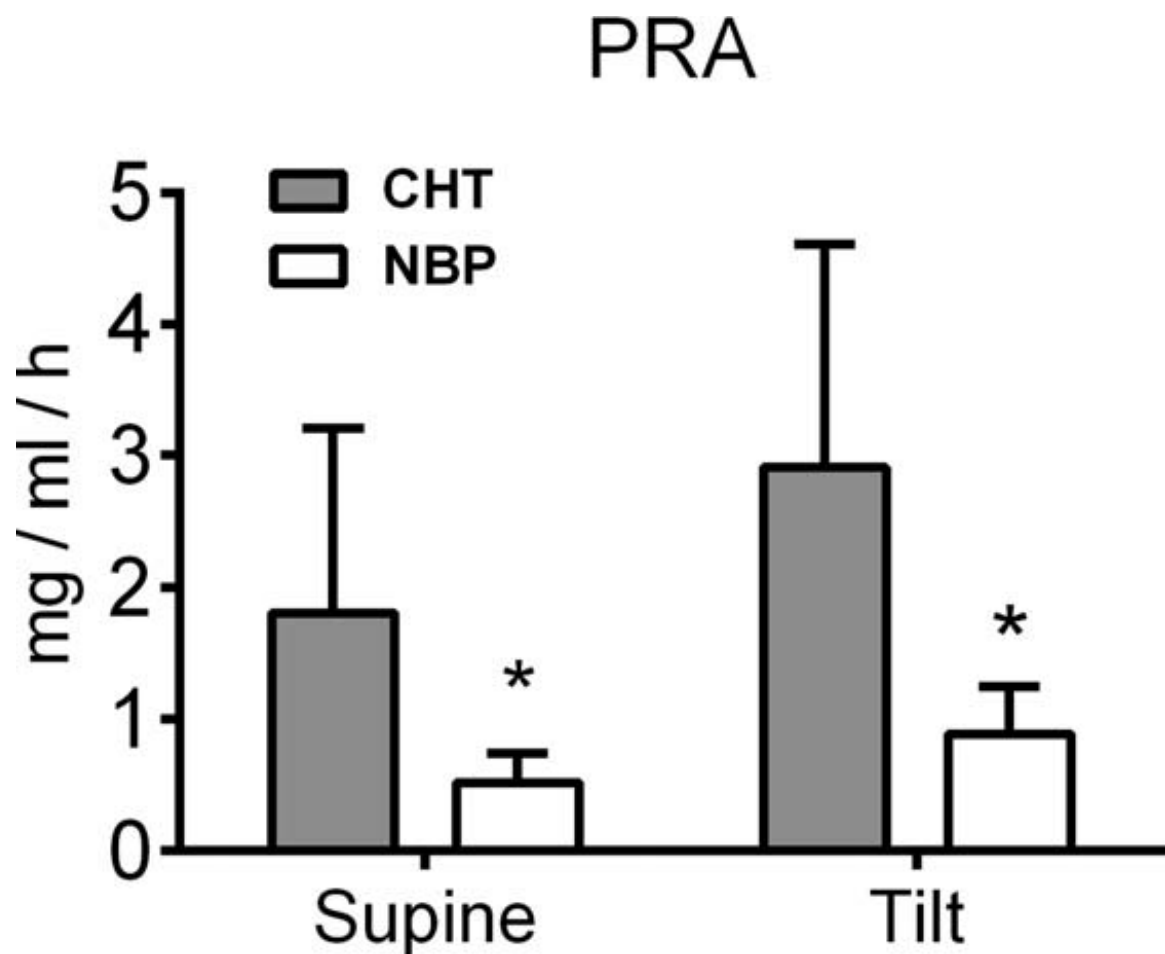


Baroreceptor sensitivity

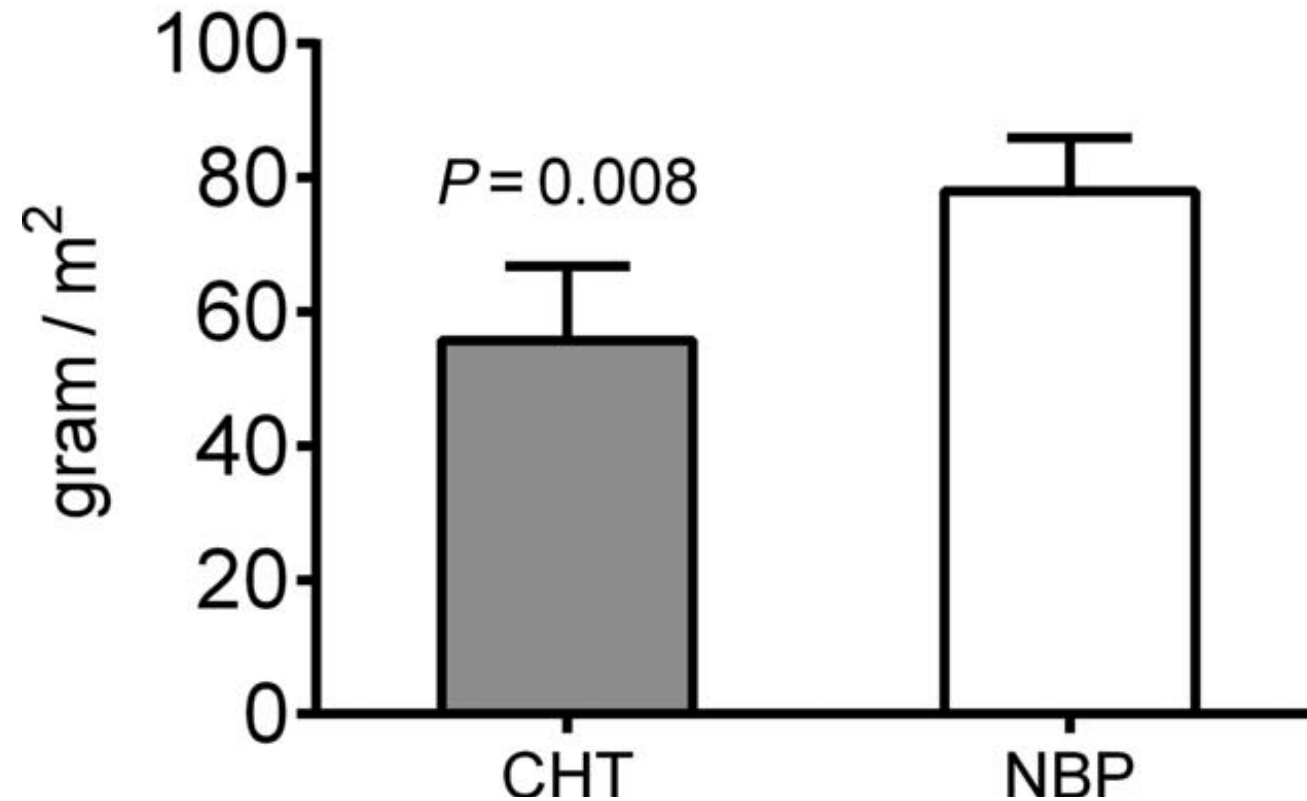
	Supine		Tilt	
	CHT	NBP	CHT	NBP
Alpha-LF, ms/mm Hg	39.1±4.7	20.1±2.5*	14.0±1.8	12.8±1.9
BRS, ms/mm Hg	29.2±0.7	25.2±1.6*	15.6±1.0	15.6±1.6
BRS_{+seq}, ms/mm Hg	27.2±0.5	16.5±1.6*	12.6±0.6	11.8±0.8
BRS_{-seq}, ms/mm Hg	24.0±1.2	26.7±1.9	15.6±1.0	17.4±2.2

Changes in baroreceptor sensitivity induced by Tilt





Left Ventricular Mass Index



Conclusions

- Peculiar cardiovascular autonomic control in CHT consistent with a marked *high cardiac sympathetic modulation low sympathetic vascular tone and increased baroreflex sensitivity*
- *Increased PRA and plasma Aldosterone* levels with reduced left ventricle mass index suggestive of a relative *hypovolemic state*

Therapy





Non - Pharmacologic Measures

- Physical countermeasures (leg-crossing, toe-raise, thigh contraction)
- Devices to Decrease Venous Pooling Waist-high compressor stockings (30 to 40 mmHg) or abdominal binders
- Physical exercise (aerobic and lower limb muscles isometrics)
- *Water per os and salt (NaCl)* to compensate for chronic hypovolemia

Pharmacological Therapy (?!?)

- Caffeine before eating and reduction of carbohydrate intake (at lunch)
- Midodrine (directly-acting α 1-agonist) improve orthostatic hypotension and orthostatic intolerance (JAMA 1997;277:1046); **2,5-10 mg 2-4 times /day**
- Fludrocortisone (has high Na^+ retention activity, expands plasma volume and increases α -adrenoreceptor sensitivity)
0,05-0,3 mg/day.
- Cortone acetato (mechanism similar to fludrocortisone); **6.25-25 mg/day**
- Droxidopa prodrug converted centrally and peripherally to norepinephrine , recently approved by the FDA **100-600 mg 3 times/day.**

Table 1: Demographics, hemodynamics, and sex-hormone profiles in subjects with constitutional hypotension (CHT) and in subjects with normal blood pressure (NBP).

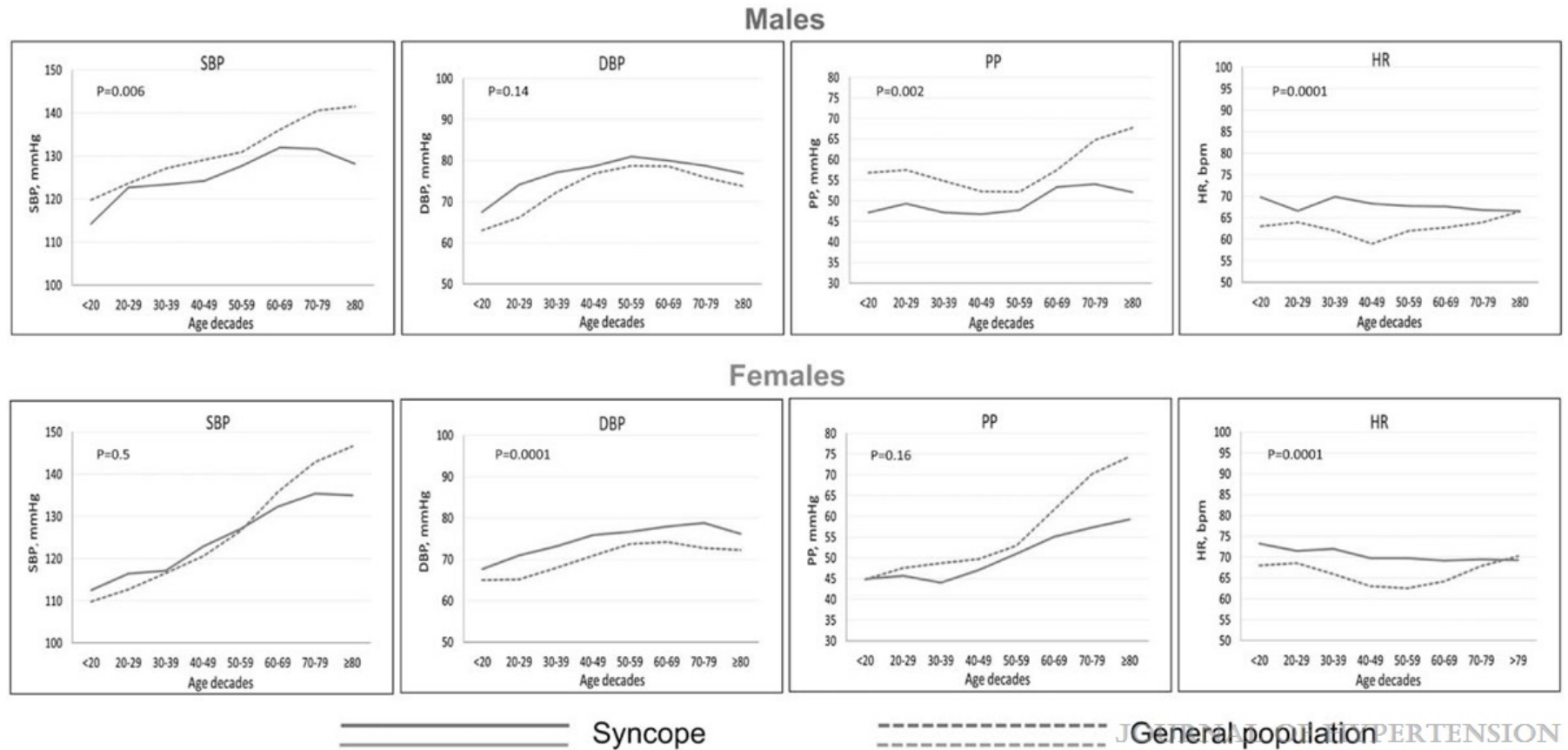
	<u>CHT</u>	<u>NBP</u>	<i>p-value</i>
Age, years	31±3	32±2	<i>ns</i>
Height, meters	1.67±1.5	1.63±2	<i>ns</i>
Body Mass Index, kg/m²	20.5±0.7	24±0.5	0.02
<u>Sex-hormones</u>			
Estrogen, pmol/L	230±45	295±35	<i>ns</i>
Progesterone, nmol/L	4.3±0.4	2.4±0.5	0.005
<u>Supine</u>			
 Systolic BP, mm Hg	97±1.5	126±3	<0.000
Diastolic BP, mm Hg	54±1.5	70±4	<0.000
 Heart Rate, bpm	65±1.5	63±3	<i>ns</i>
Respiratory Rate, cycles/min	14±1	17±1	0.01
<u>Tilt</u>			
 Systolic BP, mm Hg	96±1.8	124±2.5	<0.000
Diastolic BP, mm Hg	57±3	76±4	<0.000
 Heart Rate, mm Hg	86±3	77±5	0.10

G. Jacob et al J Hypertension 2018;36:2068

Low-blood pressure phenotype underpins the tendency to reflex syncope

Michele Brignolea , Giulia Rivasib , Richard Suttonc , Rose Anne Kennyd , Carlos A. Morilloe , Robert Sheldone , Satish R. Rajee , Andrea Ungarb , Raffaello Furlanf , Gert van Dijk g , Mohamed Hamdanh , Viktor Hamreforsij, Gunnar Engstromi , Chloe Parkk , Davide Sorannal , Antonella Zambonl,m , Gianfranco Paratiana,n , and Artur Fedorowskii,o

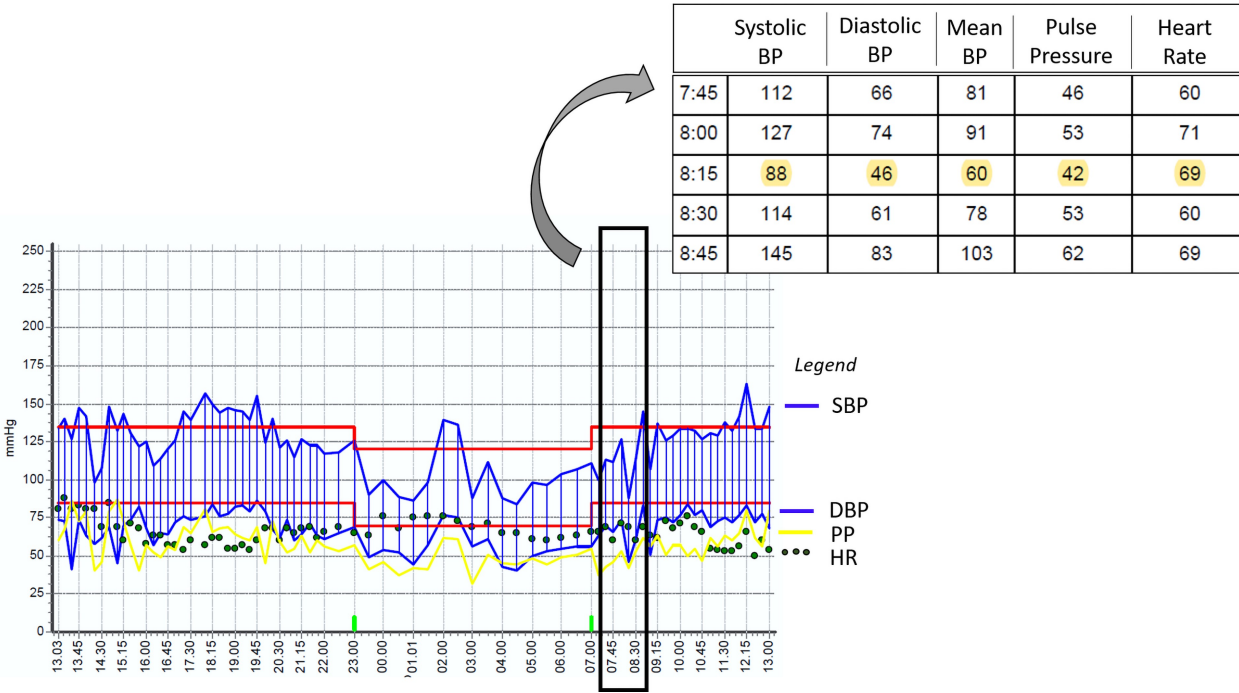
- Journal of Hypertension 39(7):1319-1325, July 2021. doi: 10.1097/HJH.0000000000002800



- Different hemodynamic profiles of SBP, DBP, pulse pressure (PP), and heart rate in beats per minute (bpm) in male and female individuals with reflex syncope and in the general population. Data are shown over the different decades, throughout the lifespan.

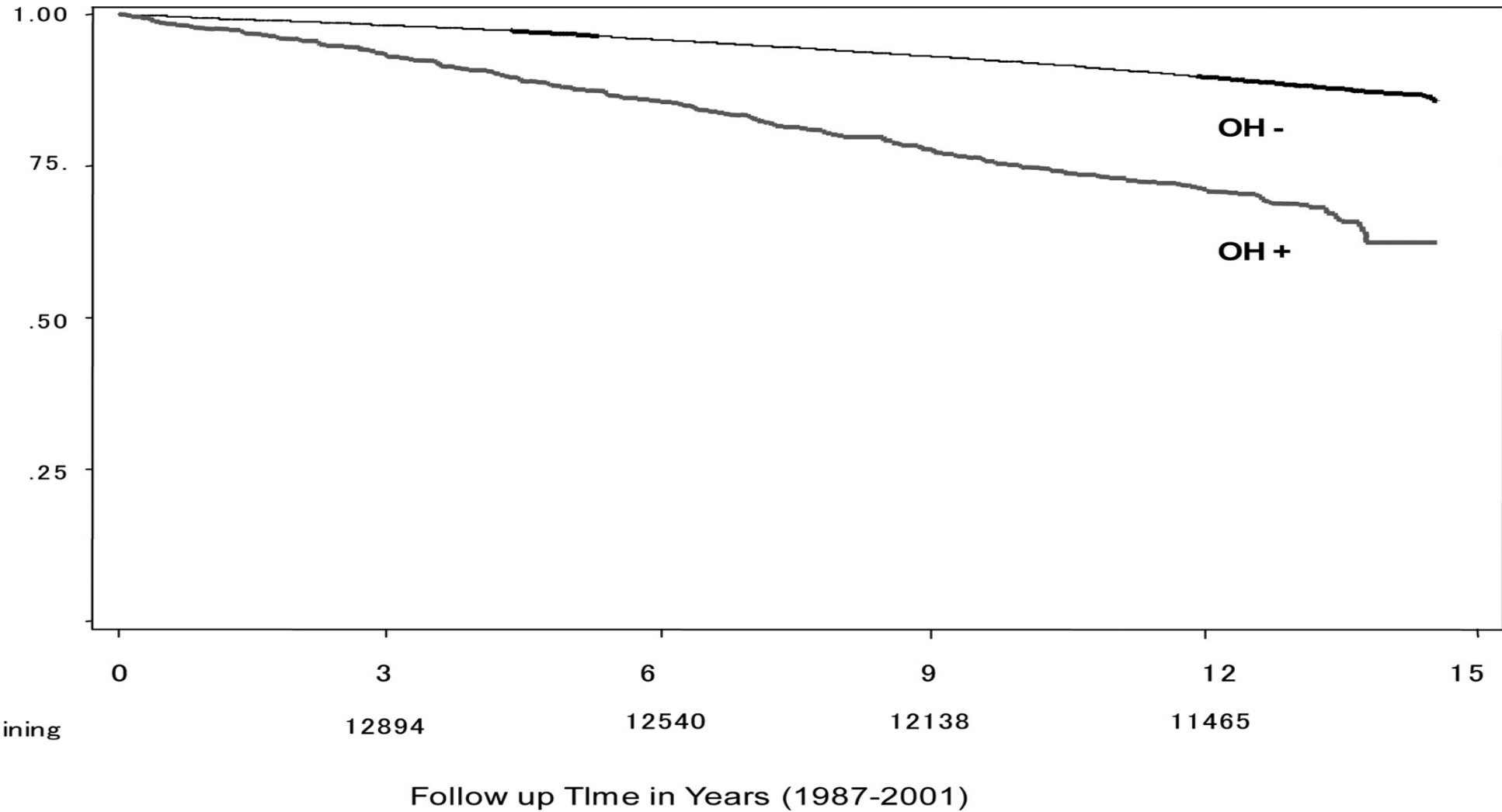
Association between hypotension during 24 h ambulatory blood pressure monitoring and reflex syncope: the SynABPM 1 study

Giulia Rivasi, Antonella Groppelli, Michele Brignole, Davide Soranna, Antonella Zambon, Grzegorz Bilo, Martino Pengo, Bashaar Sharad, Viktor Hamrefors, Martina Rafanelli, Giuseppe Dario Testa, Ciara Rice, Rose Anne Kenny, Richard Sutton, Andrea Ungar, Artur Fedorowski, Gianfranco Parati



SAP drops during ABPM are more frequent in patients with reflex syncope than in Controls.

Kaplan-Meier survival curves by OH status



Participants Remaining

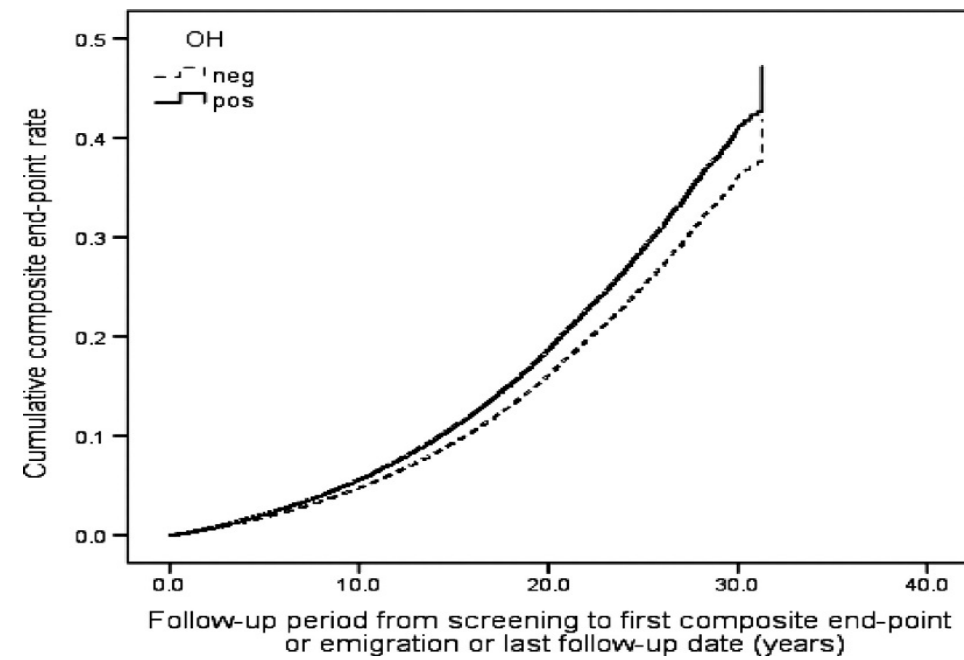
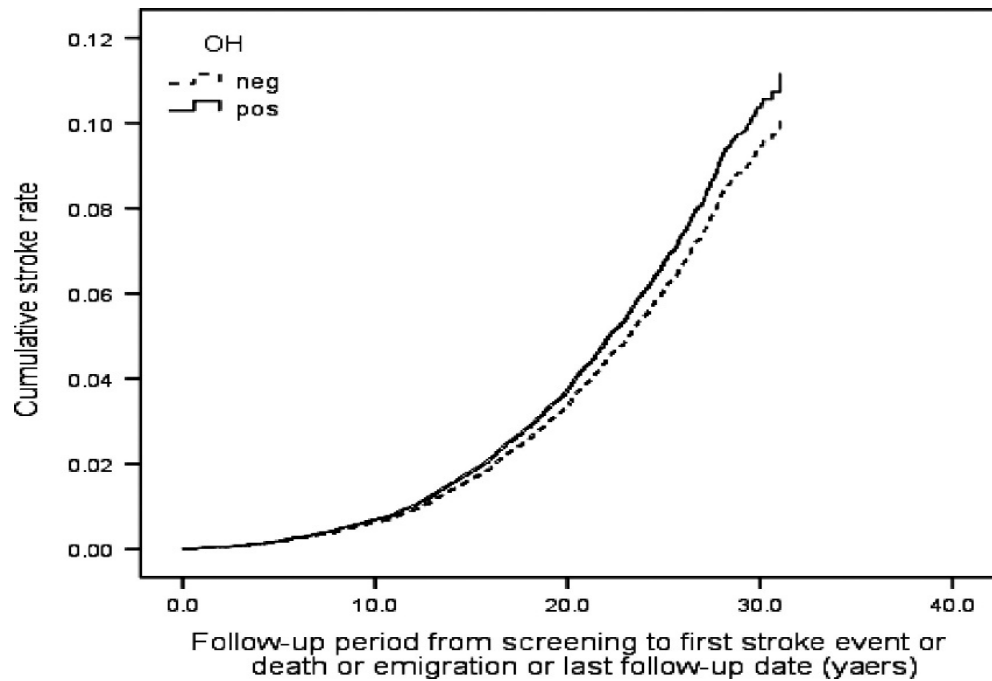
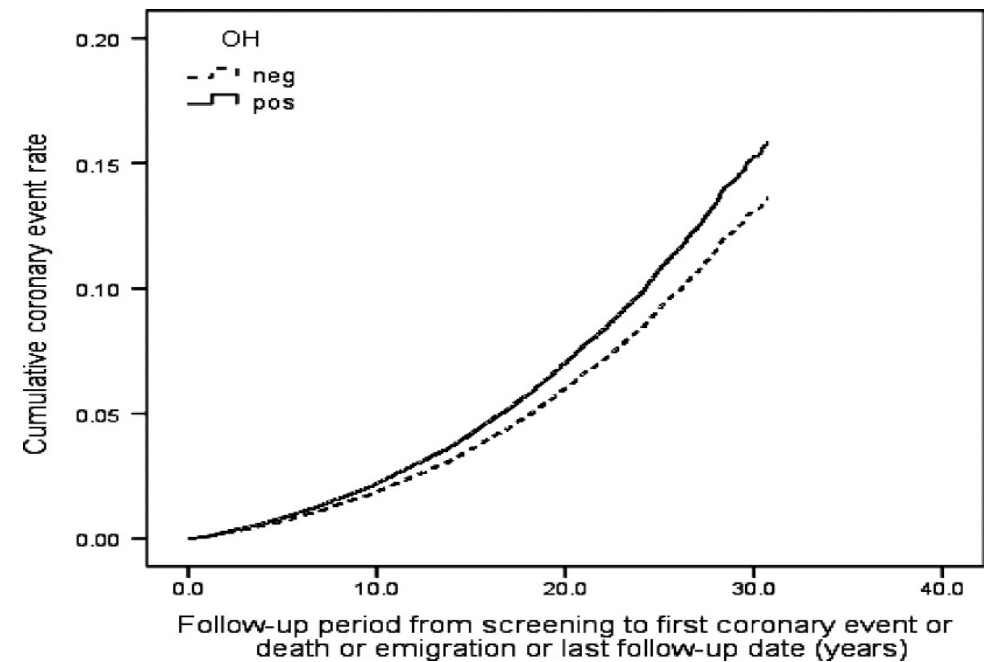
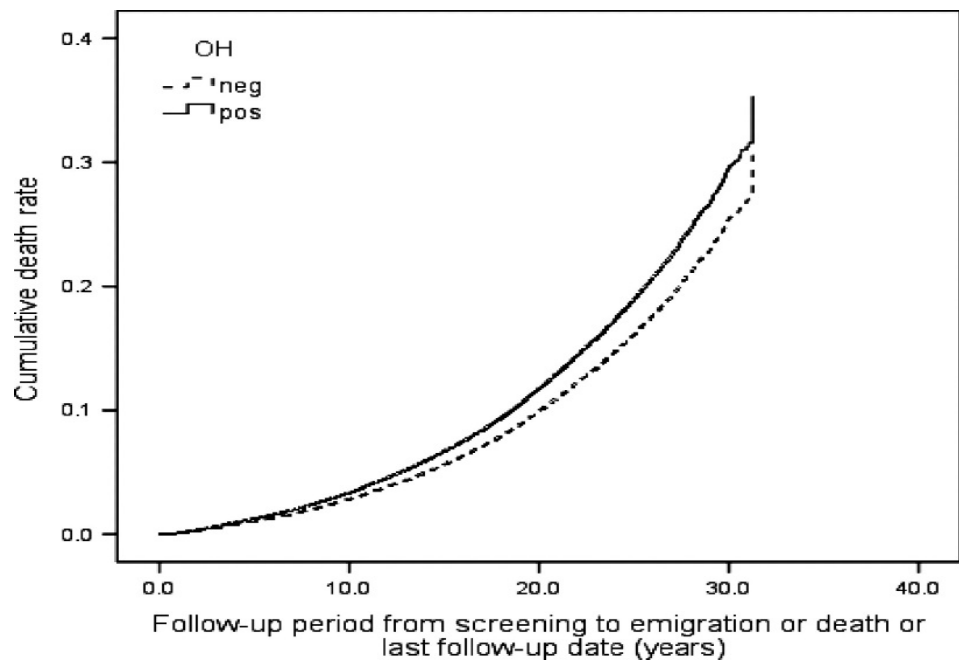
12894

12540

12138

11465

Follow up Time in Years (1987-2001)



Orthostatic Hypotension and Late-Life Depression

Longitudinal Association Between Orthostatic Hypotension at 30 Seconds Post-Standing and Late-Life Depression

Robert Briggs, Daniel Carey, Sean P. Kennelly, Rose Anne Kenny

seconds and initial OH did not predict depression. This study demonstrates that sOH-30 predicts incident depression in a population-representative sample of older people and may, therefore, represent a potentially modifiable risk factor for late-life depression. (*Hypertension*. 2018;71:946-954. DOI: 10.1161/HYPERTENSIONAHA.117.10542.) • [Online Data Supplement](#)

Novelty and Significance

What Is New?

- This is the first study to investigate the longitudinal relationship between orthostatic hypotension and depression in older people.
- It includes a large, well-described population-representative sample of older people with a diagnosis of orthostatic hypotension based on continuous beat-to-beat readings.

What Is Relevant?

- Orthostatic hypotension may be a modifiable risk factor for depression in later life.

- These findings are also relevant in the context of recent international research demonstrating better outcomes after more aggressive blood pressure control in older people.

Summary

Participants with symptomatic orthostatic hypotension had a 2-fold increased risk of depression during 4-year follow-up, independent of other risk factors including subthreshold depressive symptoms.